

Reducing Antibiotic Overuse in Pediatric Pneumonia

[Redacted]

Funding Path:

Academic Pediatric Association Young Investigator (APA YIA)

Primary Co-Mentor:

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Division Director:

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Department Chair:

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Participation Statement

If funded, I agree to participate in any conference calls and/or in-person grantee meetings.

[Redacted Signature]

Principal Investigator Signature

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I. Research Proposal

Background and Specific Aims: Community acquired pneumonia (CAP) is the fifth most common diagnosis among hospitalized children with >125,000 admissions annually.¹ Despite this large burden, no findings reliably distinguish bacterial CAP, which requires antibiotics, from viral CAP, which does not.^{2,3} Most pediatric CAP is likely viral. In the largest study of CAP etiology among hospitalized children, over 70% had viruses and only 15% had bacterial pathogens identified; yet 88% received antibiotics.⁴ This discrepancy suggests antibiotic overuse and highlights problems with current prescribing practices. Unnecessary antibiotics can lead to adverse events and side effects in children without benefits and contribute to antibiotic resistance.⁵ **Thus, there is a great need to reduce antibiotic overuse in pediatric CAP.**

To reduce unnecessary antibiotics, we need to identify children who do not benefit from treatment, suggesting that they are low risk for bacterial CAP and could safely be managed without antibiotics (Aim 1). A study of >300 children with suspected CAP in an Emergency Department (ED) found no difference in pneumonia-related return hospitalizations, provider changes in antibiotics, or quality-of-life measures between those who did and did not receive antibiotics, suggesting there are opportunities to safely reduce antibiotics in ambulatory settings.⁶ No similar safety studies have been performed in the inpatient setting. Given the unique opportunity for monitoring hospitalized children, this is an ideal cohort for antibiotic de-implementation. We propose a multicenter retrospective study of children hospitalized with CAP using linked data from the Pediatric Health Information System (PHIS) and chart review to address this gap.

Effectively reducing antibiotics also requires identifying factors that drive antibiotic use and can be targeted for future interventions (Aim 2). There is limited data on factors that influence antibiotic decisions for hospitalized children. Our pilot quantitative data from my mentors' single-site cohort of children hospitalized with CAP identified some factors associated with inpatient antibiotic use including receipt of antibiotics in the ED, chest radiograph (CXR) results, and need for oxygen (manuscript in progress). However, these findings demonstrate associations and are limited to patient factors. Given the limitations of using retrospective data to identify factors that influence provider decision-making, we propose a qualitative study to explore patient as well as provider and contextual factors to better define key drivers of antibiotic use.

Aim 1. Determine the association between inpatient antibiotic use and length of stay as well as secondary safety outcomes for children hospitalized with CAP. We will use propensity score matching to match patients who differ only by antibiotic status and assess outcomes with regression analysis.

Hypothesis 1: Among children with negative and equivocal CXRs, length of stay and secondary safety outcomes (death, revisits/readmissions, need for intensive care, and increased respiratory support) are similar between those who receive antibiotics and those who do not.

Aim 2. Examine factors that influence the decision to use antibiotics among children hospitalized with CAP. We will perform semi-structured interviews of pediatric hospitalists using specific case examples to examine factors that drive antibiotic decision-making.

Hypothesis 2: There are patient, provider, and contextual factors (e.g. receipt of antibiotics in the ED, positive CXRs, high illness severity at presentation, reduced provider experience, nighttime admissions, and perceived parental pressure) that influence the decision to prescribe antibiotics in the inpatient setting for children hospitalized with CAP.

Significance: Pediatric CAP is common, but significant knowledge gaps still exist. CAP is the second costliest reason for pediatric hospitalizations, costing \$1 billion per year in the U.S.^{1,7} It is a clinical diagnosis with no findings to reliably distinguish viral from bacterial CAP.^{2,3} While most pediatric CAP is likely viral, antibiotics are commonly used.^{4,8} The challenge of identifying which patients need antibiotics and which do not is an important unsolved problem.⁹

While antibiotics can be beneficial to some, the overuse of antibiotics when not needed place children at risk for adverse events with no benefits. They alter the microbiome which predisposes children to infection and are a major concern given rising resistance.^{5 10} Antibiotic-resistant bacteria cause >2.8 million infections, 35,000 deaths, and cost \$55 billion annually.¹¹ Reducing antibiotic overuse in CAP is a significant and timely goal that needs to be prioritized.

Hospitalized children are an ideal cohort for reducing antibiotic overuse given the unique ability to alter treatment based on changes in clinical status. However, no studies have evaluated outcomes based on receipt of antibiotics among children hospitalized with CAP. Our pilot PHIS data demonstrate great variability in antibiotic use - some hospitals used antibiotics in only 48% of children admitted with CAP, while others used them in 95% of patients (manuscript in progress). Similar outcomes suggest that many children likely do well without antibiotics and emphasizes the need to identify when antibiotics are *not* necessary to inform best practices.

Given that most CAP is likely viral, we hypothesize that there are identifiable subsets of children at “low risk” for bacterial CAP. Low risk is defined as children with similar outcomes, regardless of antibiotic use, suggesting they likely do not need treatment. We will leverage variability in care to compare outcomes between matched patients who differ only by antibiotic status. Length of stay is our primary outcome given that it represents time to clinical improvement and is clinically significant to families, clinicians, and hospitals.¹² We hypothesize that children with negative (no evidence of CAP) or equivocal CXRs (“atelectasis vs pneumonia”) are low risk. A study found negative CXRs had a 98% negative predictive value for bacterial CAP that required antibiotics, suggesting that those with negative CXRs rarely need antibiotics.¹³ However up to 40% of children treated for bacterial CAP have negative CXRs, suggesting that further research is needed.¹⁴ We will also explore factors such as age and illness severity to identify a low risk cohort in which we can safely defer antibiotics.⁷

We also need to identify factors that influence antibiotic decision-making. Little is known about what drives inpatient antibiotic use in CAP. Aim 2 will fill this critical knowledge gap and set up future studies targeting these barriers and facilitators of antibiotic de-implementation.

Impact and Future Directions: This study will help us understand opportunities for safely reducing antibiotics in the inpatient setting by defining low risk cohorts and identifying factors that drive antibiotic overuse using pre-specified case scenarios. Specific next steps include a K23 pilot RCT to examine prospectively, and in more detail, the safety of de-implementing antibiotics in low risk CAP patients. This will serve as supporting data for a future multi-center R01 study to examine the clinical efficacy, implementation and effectiveness of de-implementing antibiotics in these patients. My K23 will also prospectively evaluate factors that drive antibiotic use in real time (i.e. for specific patients that providers care for) across multiple institutions. This will allow for a deeper understanding of the breadth of patient, provider and system factors involved in antibiotic decision-making and barriers and facilitators to future de-implementation work. This proposed study is a critical first step in a series of studies needed to achieve the ultimate goal of reducing antibiotic overuse in children hospitalized with CAP.

Relevance to APA mission: This study directly addresses the mission of the APA, which is focused on nurturing the career development of pediatric researchers who are dedicated to ensuring optimal health and well-being for all children. This collaborative project aims to improve the health of children hospitalized with CAP by reducing antibiotic overuse. Our findings will provide a framework that can be used to improve the care of children hospitalized with CAP across the nation, non-hospitalized children with CAP, and children with other diagnoses that are frequently associated with antibiotic overuse. This award would also provide valuable career development opportunities that would be critical to my success as I strive to become an independently funded researcher dedicated to improving the care of children hospitalized with common infections.

Methods and Analysis Plan

AIM 1: Determine the association between inpatient antibiotic use and clinical outcomes

Data Sources: We propose a multicenter cross-sectional cohort study using complementary linked data from PHIS, a national database of children's hospitals, and chart review. Through PHIS we will identify the study cohort and obtain some patient-level data. Chart review is necessary to capture additional data not available in PHIS.

Setting: We will include 3 children's hospitals:

. Given variability in care across hospitals, a multicenter study is needed to yield generalizable results.¹⁵ These sites were chosen because they have sufficient patient volume, are geographically diverse, have variable antibiotic rates, and have investigators committed to assist (see letters of collaboration).

Population: We will identify children 2-18 years of age who present to the ED and are hospitalized from 2016-2019 with a diagnosis of CAP. CAP is defined using a validated PHIS algorithm based on primary or secondary discharge diagnoses of pneumonia or effusion/empyema.¹⁶ This algorithm was 91% specific and 90% sensitive for a provider-confirmed diagnosis of CAP based on chart review.¹⁶ To improve the specificity of this algorithm, we will only include patients with a confirmed diagnosis of CAP based on notes during chart review.¹⁶ We will exclude children <2 years given clinical overlap with bronchiolitis. To focus on community acquired pneumonia, patients must have a CXR on day 1-2, and we will exclude those at risk for healthcare-associated infections (prior hospitalization within 30 days, direct admissions, transfers from outside hospitals). To target antibiotics used for CAP, we will exclude children with common concurrent bacterial infections based on discharge diagnoses.^{17,18} To focus on the impact of antibiotics for children presenting with non-severe CAP, we will exclude those who go directly from the ED to intensive care unit (ICU). **Estimated N:** Based on pilot PHIS data we estimate 2,575 encounters and will exclude 18% for not having a confirmed diagnosis of CAP based on chart review (PHIS algorithm has 82% positive predictive value¹⁶), resulting in a sample size of 2,110.

Key Variables: The exposure is receipt of antibiotics in the *initial* inpatient setting, primary outcome is length of stay (LOS), as it is clinically significant to families, clinicians, and hospitals¹², and secondary safety outcomes are 30-day all-cause readmission or ED revisit, death, and care escalation (defined in **Table 1**). Because of the reciprocal relationship between antibiotic use (exposure) and care escalation (outcome), receipt of antibiotics needs to be defined before care escalation. Thus, we define our exposure based on receipt of antibiotics in the *first 24 hours* of the inpatient setting and care escalation *after* the first 24 hours. Covariates are listed in **Table 1**.

Table 1. Key Variables and Definitions		
Exposure	Outcome	Covariates
Receipt of antibiotics^a in the <i>initial</i> inpatient setting (receipt of ≥1 dose during the first 24 hours inpatient setting)	Primary: LOS; Secondary: 30-day all-cause readmission/ED revisit; Death; Care Escalation (ICU transfer, intubation of high-flow oxygen, positive pressure, mechanical ventilation, or chest tube <i>after</i> 24 hours inpatient setting)	CXR findings ^b ; Illness severity in the ED ^c ; Receipt of antibiotics in ED; Fever duration; Lung examination in the ED; Biographical variables including age, sex, and race; ED laboratory studies ^d

^a We will only include antibiotics commonly used for CAP: ampicillin, 2/3rd generation cephalosporins, vancomycin, macrolides & fluoroquinolones.¹⁹ Our primary focus is on whether or not these antibiotics were given, not antibiotic duration or specific type. Patient location at the time antibiotics were given will be determined based on antibiotic administration time relative to the ED-to-inpatient transfer time.

^b Two independent binary categorical CXRs into 3 groups using an established classification based on findings in the chart: positive (descriptors such as "consolidation", "infiltrate", "pneumonia"), negative ("normal", "no acute findings", "atelectasis", "peribronchovascular cuffing") or equivocal ("atelectasis vs infiltrate/pneumonia", "key atelectasis but cannot exclude/rule out pneumonia").²⁰ Discrepancies in categorization will be adjudicated by third party.

^c Defined based on the need for chest tube or respiratory support beyond low-flow oxygen in the ED, which is modified based on a published disease severity classification on pediatric CAP²¹

^d Use of complete blood count, C-reactive protein, blood culture, sputum culture, or viral testing in the ED. Depending on the percentage of patients with these tests performed, we may include test results as an additional covariate.

Statistics: Since those who receive antibiotics may differ from those who do not, and these differences may affect outcomes, we will use propensity score matching with inverse probability of

weighting for clustered data.^{22 23} The propensity score will be computed from a multivariable mixed effects logistic regression with covariates, and computed weights for each patient will be used in a linear mixed effects model for log-transformed LOS (due to skewness). Secondary outcomes will be analyzed with logistic mixed effects models. We will perform subgroup analyses by CXR findings, age, and ED illness severity. While we considered an instrumental variable approach based on clinicians' tendency to use antibiotics, based on pilot work, it is not feasible to readily and accurately assign antibiotics to specific providers with PHIS or chart review. **Power:** Our expected sample is 2,110 patients. From pilot data from a prospective study, we expect 64% receive antibiotics with mean and standard deviation (SD) of LOS in this group of 54 and 72 hours, respectively. Assuming a coefficient of variation (SD/mean) of 1.3, with 80% power ($\alpha=0.05$, two-sided) we can detect a ratio of means of 1.17 (9-hour difference in LOS). Thus, we are powered to detect a clinically meaningful difference, which based on team consensus and prior literature, is a difference of 12 hours.²⁴

AIM 2: Examine factors that influence antibiotic decision-making among children with CAP

Population: We will include up to 20 key informants who are front-line hospitalists at [REDACTED] who make decisions about antibiotic use for hospitalized children with CAP. This includes physicians and advanced practice providers, as well as providers who primarily work at our quaternary care hospital or affiliated community-based hospitals. Thus, all medical providers within the Section of Hospital Medicine ($n=98$) will be queried for interest in the study. Should there be more providers interested in the study than the sample size likely needed for thematic saturation ($n=20$) we will select the cohort so as to maximize heterogeneity among providers based on gender, age, years out of training, type of provider, and primary site of work. **Data sources:** Detailed interviewer notes and the transcripts of audiotaped interviews. **Design:** We will conduct semi-structured one-on-one interviews by a trained interviewer using established qualitative research methods.²⁵ Qualitative interview guides will be developed and pilot-tested prior to use. To feasibly conduct this study within the 1-year time frame, rather than conducting interviews on antibiotic decision-making in "real time" (i.e. for a specific patient they care for) we will use 5 clinical scenarios (e.g. healthy 3 year old admitted with respiratory distress and hypoxia requiring 0.5 liters of oxygen who was diagnosed with pneumonia based on focal findings on exam in the ED, had a CXR which was read as "atelectasis", and received a dose of ceftriaxone in the ED prior to hospitalization). Interviews will focus on factors that drive antibiotic use in their own practice, and provider-perceptions of factors that drive antibiotic use in the practice of other hospitalists (based on sign-outs during transitions of care). Interviews will use a combination of broad, open-ended questions as well as more specific probes that may drive antibiotic use (e.g. receipt of antibiotics in the ED, CXR findings, age, history of fever, laboratory results, severity of illness in the ED, time of day of admission, availability of final CXR result, years of experience of provider, and perceived parental pressure). The interviewer will take detailed notes during the session, and each interview will also be audiotaped. **Power:** We will target 20 interviews. If thematic saturation is reached earlier, then at least 15 interviews will be conducted. Additional interviews will be conducted if necessary to explore additional themes. This study is qualitative and thus formal power calculations are not appropriate. **Analytic Plan:** We will utilize a qualitative, iterative approach to analyzing data from individual interviews. The PI and another investigator will review interviewer notes and transcribed audiotapes with the oversight of a qualitative methods expert to develop working themes and hypotheses to be tested and revised in subsequent interviews. In addition, interview transcripts will be entered in to Atlas.ti qualitative data analysis software and data will be analyzed using the "editing" approach.²⁶ This particular analytic method encourages interpretation of the data using a team approach. Two investigators will independently read through the interview transcripts and highlight factors that appear to significantly impact antibiotic decision-making. The investigators will then meet to discuss interpretations of the data, and transcripts will be re-reviewed to

confirm or disconfirm initial and ongoing themes and codes. These themes will then be organized into an overall framework to describe key factors that drive antibiotic use.

Feasibility: External Site Effort (Aim 1): Each external site will be asked to complete ~550 chart reviews; to ensure feasibility, we will provide compensation for this review. Furthermore, this is feasible because the number of charts is an overestimation, as ~18% will be excluded without a confirmed CAP diagnosis. We have pilot tested the chart review to estimate the time required per chart (~15 minutes) and ensure that we have allocated sufficient time and funds. Interviewees (Aim 2): To ensure feasibility of recruiting providers for interviews we will perform interviews at our institution. Given that we have 98 hospitalists, identifying 20 is feasible. This work will be facilitated by the [REDACTED]

[REDACTED] which has the largest qualitative methods core in the country and with which I and my Mentor are already affiliated. Study completion: I have sufficient resources to complete this study in one year (Table 2). I will have 50% protected time for research. For Aim 1, I have

already identified two medical students who have begun chart review at our institution and faculty collaborators at two other institutions. For Aim 2, I will leverage the significant resources that already exist in the qualitative core of [REDACTED] to facilitate this study.

Aim	Research Activity	Pre	Q1	Q2	Q3	Q4
Aim 1	External site identification and IRB submission					
	Data Collection: PHIS data pull and multicenter chart review					
	Data analysis					
Aim 2	Pilot testing qualitative interview guides					
	Conduct provider interviews					
	Transcribe interviews and perform qualitative data analysis					
Aim 1+2	Dissemination: manuscripts (at least 1 per aim) and presentations					

Potential Limitations and Alternatives: Multicenter study (Aim 1): To mitigate potential challenges with a multicentered study, we will collaborate with a well-established national network of 109 children's hospitals, called [REDACTED] (see letter of collaboration). In addition to the already identified 2 external sites, we have also identified collaborators at other sites if unable to obtain sufficient numbers or a site has to drop out. Missingness (Aim 1): We do not expect missing exposures or outcomes because all are readily obtained in PHIS or chart review. There is potential for missing covariates which we will address using the missing indicator approach.²⁷ Confounding (Aim 1): Patients who receive antibiotics may present differently than those who do not receive antibiotics. To minimize this concern, we will match patients using propensity scores, allowing groups to be equivalent in all factors other than receipt of antibiotics. However, there still may be residual confounding, which we will minimize by collecting all necessary data to predict antibiotic use; if data is not readily available it will inform future prospective studies. Generalizability (Aim 2): There is potential for limited generalizability given that our findings may be context specific and limited to providers from a single institution. However, by including providers with diverse backgrounds and work experience, we increase the generalizability. Furthermore, this will provide important data for future work.

Key Personnel: The PI will be supported by a multidisciplinary mentorship team. [REDACTED] will serve as co-mentors (see biosketches and letters of support). [REDACTED] (Advisor; Associate Professor, [REDACTED]) is the [REDACTED]. [REDACTED] has a successful federally funded research career focused on CAP severity. [REDACTED] has met regularly with me over the last year, has collaborated extensively with [REDACTED], and will bring methods and content expertise in CAP and Emergency Medicine. [REDACTED] (Advisor; Professor, [REDACTED]) is an Infectious Diseases physician, [REDACTED], and international leader in antimicrobial stewardship. [REDACTED] has met with me regularly over the last 2 years and will bring content expertise in antibiotic stewardship and infectious diseases. Additional personnel include [REDACTED] (qualitative expert), [REDACTED] (biostatistician) and [REDACTED] (senior research analyst).

II. References

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III. Budget and Budget Justification

Item	Detail	In-kind	Amount requested from APA	Total	Justification
Research Coordinator at [REDACTED]	\$35/hr * 78 hours	0	\$0	\$2,730	<p>I will receive funds from the Section of Hospital Medicine to hire a research assistant to complete the remaining charts at [REDACTED] (see letter of support from [REDACTED]). Hourly rate verified with the [REDACTED] Financial Analyst.</p> <p>275 charts^a x 4 charts per hour^b = 68 hours + 5 additional hours for training^c = 78 hours</p> <p>^a Based on pilot PHIS data, there are 1,475 patient encounters that meet inclusion criteria at [REDACTED]. Two medical students have committed to volunteer their time to each complete at least 400 charts (see letters of collaboration). I will also complete 400 charts, leaving 275 charts remaining.</p> <p>^b Estimated 15 minutes per chart based on pilot testing with second year medical students who initially had limited experience working with our electronic medical record</p> <p>^c Estimated time per chart, additional five hours needed for training, and rates were discussed and agreed upon based on conversations between the PI and the [REDACTED] Financial Analyst and Clinical Research Supervisor who have extensive experience with this type of study</p>
Research Coordinators at External Site #1	\$35/hr * 142 hours	0	\$4,970	\$4,970	To ensure feasibility of Aim 1 of this study, we request financial support for a research coordinator at each external site (fee-for-service) to assist with chart review and data entry. Identified investigators at each site (see letters of collaboration) will assist with identifying, training and checking in regularly with these coordinators to ensure study completion. Hourly rates are based on rates at the [REDACTED] as exact rates at external sites will determined at time of study initiation. Additional funds are availa-
Research Coordinators at External Site #2	\$35/hr * 142 hours	0	\$4,970	\$4,970	

					<p>ble through the Section of Hospital Medicine (see letter of support by [REDACTED]) if this rate is an underestimation.</p> <p>550 charts per site^a x 4 charts per hour^b = 137 hours + 5 additional hours for training^c = 142 hours per site</p> <p>^a Estimated number of charts based on pilot PHIS data ^b Estimated 15 minutes per chart as explained above ^c As explained above</p>
Biostatistician	\$0	In-kind	\$0	\$0	Ph-D level biostatistical support for this project by [REDACTED] is provided in-kind (see letter of support by [REDACTED]). [REDACTED] will assist the PI and research analyst with developing and executing the analysis plan for Aim 1.
Research Analyst	\$0	In-kind	\$0	\$0	Support from [REDACTED], senior research analyst, for this project is provided in-kind (see letter of support by [REDACTED]). Angela will assist with the PHIS data pull, clean data pulled from PHIS and chart review, and perform the analysis for Aim 1 with the assistance of the PI and biostatistician.
Qualitative Core Expertise and Supplies	\$0	In-kind	\$0	\$0	PhD level qualitative expertise for this project will be provided by [REDACTED] in-kind. [REDACTED] will provide key oversight for Aim 2. Research assistant through the qualitative core at [REDACTED] with training in qualitative methods will perform interviews and assist with coding and analysis. Access to necessary supplies (recorders and Atlas software) will also be provided through the qualitative core (see letter of support by [REDACTED]).
Mentors and Advisors	\$0	In-kind	\$0	\$0	Mentors and advisors will provide in-kind support for this project and my overall career development.
PAS travel	\$0	In-kind	\$0	\$0	Provided by the Section of Hospital Medicine when in-person conferences resume.
TOTAL			\$9,940	\$12,670	

IV. BIOGRAPHICAL SKETCH – Applicant

NAME: [REDACTED]

eRA COMMONS USER NAME (credential, e.g., agency login): [REDACTED]

POSITION TITLE: Assistant Professor, Department of Pediatrics, Section of Hospital Medicine
EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]

A. Personal Statement

I am an Assistant Professor in Pediatric Hospital Medicine at [REDACTED] and currently a fellow in [REDACTED] Fellowship through [REDACTED]

[REDACTED] Throughout training and early in my career as a pediatric hospitalist, I have always been interested in high-value care, specifically related to diagnostic and antibiotic stewardship for common infections. *How can we optimize our use of diagnostics to inform antibiotic decisions that lead to improvements in this child's care?* In this proposal, we explore antibiotic use and outcomes among children hospitalized with community acquired pneumonia (CAP) and qualitatively evaluate factors that drive antibiotic use.

I have the longitudinal research experience, focused research training, academic passion, and mentorship necessary to successfully complete this study. I have been highly productive early in my career with 2 internal grants, 26 co-authored manuscripts, including 10 as the first author, and 11 platform presentations at national conferences. This efficiency demonstrates my ability to lead projects through to completion. From these experiences, I have gained skills in the use of administrative databases and chart review studies, designed and executed my own data analyses, and led and collaborated on multisite research projects. As Co-PI of two grant-funded projects, I have managerial experience leading large multidisciplinary teams, carrying out budgets, and adhering to timelines. As a result of my early career success and in recognition of my potential to be a successful clinical researcher, both the Department of Pediatrics and Section of Hospital Medicine have invested in my career by funding two key formal research training opportunities. During Hospital Medicine fellowship I completed a Master's in Clinical Science and acquired a solid foundation in biostatistics, epidemiology, and secondary data analysis. As a current [REDACTED] fellow, I have gained additional mentorship and focused training in health outcomes research. As an [REDACTED]-affiliated researcher I am also well supported by the expertise, resources and infrastructure at [REDACTED]. I have assembled a strong multidisciplinary mentorship team of mentors and advisors each of whom has a successful prior working relationship with me, and collectively have experience in multisite collaboration, quantitative and qualitative data analysis, clinical outcomes research, and content expertise in pneumonia and

antibiotic stewardship. My early career experiences and focused research training along with the guidance of my mentorship team will enable my successful completion of this proposal.

The APA Young Investigator Award is the ideal next step for my career in academic clinical research. It will provide me with the resources, experience, and external mentorship necessary to further develop my research skills and acquire key pilot data for a future career development award. My long-term goal is to become a national leader and independently funded investigator dedicated to improving outcomes for children hospitalized with common serious infections through dissemination and implementation of evidence-based stewardship interventions. In this proposal we aim to conduct a multicenter cross-sectional cohort study to identify “low risk” children hospitalized with CAP who currently receive but do not benefit from antibiotics and qualitatively explore factors associated with antibiotic use. My immediate next steps include a K23 application to the National Institute of Allergy and Infectious Diseases. In this K23 application, I will propose a pilot RCT to examine prospectively, and in more detail, the safety of de-implementing antibiotics in low risk CAP patients. I will also propose a multicenter prospective qualitative study in real time to allow for a deeper understanding of factors that drive antibiotic use in order to identify potential barriers and facilitators for future de-implementation work. This would set me up for a future multisite R01 study to examine the clinical efficacy, implementation, and effectiveness of de-implementing antibiotics in low risk children.

B. Positions and Honors

Positions and Employment

Other Experiences and Professional Memberships

Honors

[REDACTED]

C. Contributions to Science

1. Diagnostic and Antibiotic Stewardship

[REDACTED]

2. Multisite Research using Secondary Data Analysis

[REDACTED]

[REDACTED]

3. Clinical Outcomes Research in Respiratory Illnesses

[REDACTED]

4. Pediatric Liver Disease

[REDACTED]

[REDACTED]

See Complete List of Published Work in My Bibliography:

[REDACTED]

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

[REDACTED]

Completed Research Support

[REDACTED]

V. BIOGRAPHICAL SKETCH – Co-Mentor

NAME [REDACTED]	POSITION TITLE Professor of Pediatrics		
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	MM/YY	FIELD OF STUDY
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]

A. Personal Statement

I am a tenured Professor of Pediatrics at [REDACTED] and a senior faculty member of the [REDACTED] program. I also serve as the Research Director for the [REDACTED] Fellowship at [REDACTED], which provides extensive mentoring and education in health services research for junior faculty over a two-year period.

[REDACTED] is a junior faculty member in Pediatric Hospital Medicine and fellow in [REDACTED] program. Through both of these avenues I have served as [REDACTED] primary research mentor. I have met with [REDACTED] bi-weekly over the last two years and will continue to meet with [REDACTED] bi-weekly to complete this project and advance [REDACTED] research career. We already have a track record of successful publication together, and our ongoing work has recently resulted in two platform presentations at national conferences and manuscripts in progress. I am excited to serve as [REDACTED] primary mentor for this APA YIA proposal and subsequent career development awards.

I have extensive experience in mentoring junior faculty across a wide variety of disciplines (e.g. hospital medicine, neurology, oncology, endocrinology). Since joining the faculty at [REDACTED] in [REDACTED], I have mentored 8 junior faculty in their successful K awards. In addition, I have mentored each of the 18 faculty who have gone through [REDACTED] program. Given this prior experience and our past work together, I am well suited to be one of [REDACTED] primary mentor for this Young Investigator Award.

My research background is in immunization delivery, and I am recognized internationally for this work. I have >120 peer-reviewed publications and have received multimillion-dollar funding as a PI from PCORI, NIH, and CDC. Methodologically, I have expertise in using qualitative and quantitative methods to examine barriers to implementation of evidence-based interventions, health outcomes research, pragmatic trials, large database analysis, multisite studies, and the development and assessment of interventions to improve patient outcomes. This expertise aligns with [REDACTED] current proposal and [REDACTED] longitudinal research plan.

As a primary mentor for [REDACTED] proposal, I will bring my methodological, career and mentoring expertise, which are well aligned the research aims as outlined in this proposal as well as

B. Positions and Honors

[REDACTED]

Member, Academic Pediatric Association

1. [REDACTED]

[REDACTED]

2.

[REDACTED]

3.

[REDACTED]

a.

[REDACTED]

4.

[REDACTED]

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

[REDACTED]

[REDACTED]

Completed Research Support

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

VI. BIOGRAPHICAL SKETCH – Co-Mentor

NAME [REDACTED]		POSITION TITLE Associate Professor of Pediatrics	
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]

A. Personal Statement

I am currently a full-time Associate Professor in [REDACTED]. I also serve as the [REDACTED]. As one of [REDACTED] co-mentors, I have and will continue to meet with [REDACTED] bi-weekly to complete this project and advance [REDACTED] research career.

My interests and skillset align well with [REDACTED] current project aims and career goals. My long-term research goal is to improve outcomes for children with infections by developing methods to improve diagnostic accuracy, implementing these methods into clinical practice and improving the overall management of these children. The overall objective of this study is to identify patients hospitalized with pneumonia who likely do not benefit from antibiotics and qualitatively explore factors that drive antibiotic overuse. This work is critical because given that most of pediatric pneumonia is viral, and there is significant overuse of antibiotics which can negatively impact patient outcomes and contribute to growing antibiotic resistance.

I am uniquely positioned to serve as the co-mentor for [REDACTED] APA Young Investigator Award and will help [REDACTED] successfully complete the study as stated in this proposal. I will bring my methods expertise given my statistical and epidemiology background, content expertise as a successful researcher in pediatric pneumonia, and mentoring experience. Specifically, I have successfully mentored 20 trainees across multiple disciplines. Finally, [REDACTED] and I have a track record of successful publications together and have invested time in our mentor-mentee relationship through completion of a formal mentoring program. My record of academic research and mentoring success as well as my current successful collaboration with [REDACTED] will ensure the completion of the activities proposed in [REDACTED] application.

1. [REDACTED]

3. [REDACTED]

B. Positions and Honors
Positions and Employment

[REDACTED]

Other Experience and Professional Memberships

[REDACTED]
Member, Academic Pediatric Association
[REDACTED]

Honors

[REDACTED]

C. Contribution to Science

1. Pediatric Pneumonia Diagnosis and Management.

[REDACTED]

2. Biomarker Discovery.

[REDACTED]

[REDACTED]

3. **Implementation and Standardization of Care for Pediatric Pneumonia.**

[REDACTED]

4. **Methodological Expertise.**

[REDACTED]

a.

Complete List of Published Work in My Bibliography:

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

[REDACTED]

[REDACTED]

Completed Research Support

[REDACTED]

VII. Letter of Support: Co-Mentor ()

Dear Members of the APA Young Investigator Award Selection Committee,

I am pleased to write a letter of support as the co-mentor for application for the APA Young Investigator Award. is a junior faculty member in , and second-year fellow in Fellowship through . I am a tenured Professor of Pediatrics at . Fellowship. I have had the pleasure of serving as mentor over the last 2 years.

Candidate: has demonstrated passion, dedication, and clear talent for research. has been productive with each step: 2 manuscripts in college, 2 in a basic science laboratory, 8 from work in medical school, and 14 from residency, fellowship, and most recent year as junior faculty. While research topics have evolved as clinical interests have changed, has demonstrated incredible productivity that supersedes the vast majority of researchers at level. has also pursued training opportunities. In , completed a Masters in Clinical Science degree and in will complete the Fellowship. Both experiences provide a solid research foundation that will help launch a successful career. These experiences also demonstrate an incredible investment in future, highlighting recognized potential for continued success.

has focused interests in diagnostic and antibiotic stewardship, aiming to improve outcomes of children hospitalized with infections. has explored these concepts over the last 2 years in gastroenteritis. This work led to a first-author publication in the *Journal of Pediatrics*, presentations at national meetings, and a grant-funded quality improvement project. aims to apply what has learned in gastroenteritis towards antibiotic stewardship in pediatric pneumonia. As a hospitalist, commonly cares for children admitted with pneumonia, making it an excellent “test case” for to study. There is also a critical need for antibiotic stewardship given that most pneumonia is caused by viruses, but antibiotics are commonly prescribed. There are no guidelines to identify children who do not need antibiotics; thus, this is an important and clinically relevant topic that aligns well with the APA mission.

Research Aims: The aims of this project are to identify patients who currently receive, but do not benefit from antibiotics and qualitatively explore factors associated with inpatient antibiotic decision-making in pediatric CAP. I believe this proposal is an innovative way to study a challenging and important topic. Chart review, although time consuming, is necessary to acquire patient-level data that has not been previously obtained. The qualitative piece will nicely complement chart review and will allow to obtain rich data that would not otherwise be available.

Mentorship: While has established success early in career, needs continued mentorship to prepare for an NIH career development award. Specifically, this one-year award will provide with additional opportunities to collaborate with mentorship team, build on these existing relationships, and further expertise in this field. Furthermore, will directly benefit from an additional external mentor through this award. and I will serve as co-mentors. As the

VIII. Letter of Support: Co-Mentor ()

RE:

Dear Members of the APA Young Investigator Award Selection Committee,

It is my utmost pleasure to write a letter of support for [redacted] and [redacted] submission for the APA Young Investigator Award. I am an Associate Professor in [redacted]. I also serve as [redacted] Hospital Medicine and have been one of [redacted] primary mentors over the last 3 years. During this time, we have developed a rich relationship, collaborating on multiple projects through [redacted] fellowship and currently now as faculty. [redacted] combination of clinical understanding and research acumen make [redacted] an exceptional candidate for this award.

Candidate: [redacted] has an excellent track record with 26 peer-reviewed manuscripts, including articles in high impact journals such as the *Journal of Pediatrics*, *Journal of Hepatology*, *Nature Medicine*, and *Nature Immunology*. [redacted] has also obtained two internal grants. From my experience working with [redacted], I have no doubt [redacted] will experience continued success. [redacted] also has personal attributes that are essential for a research career. [redacted] is dependable, persistent, and efficient. I have been impressed by [redacted] ability to think about the overall impact of her scientific inquiries and the ability to execute [redacted] research efficiently and effectively. [redacted] has an intellectual inquisitiveness, enabling [redacted] to pursue novel studies. Finally, [redacted] has an eagerness to learn and an enthusiastic personality that makes [redacted] easy to mentor. I have mentored over 20 trainees, ranging from medical students and residents to doctoral students, fellows and junior faculty. My former mentees have been successful at securing academic positions with many receiving research funding. It is in this context that I can confidently say that [redacted] **is clearly one of the best and most talented young physician-scientists with whom I have worked.** My own research, combined with my mentorship experience, provides me with the expertise necessary to guide and monitor [redacted] progress toward accomplishing [redacted] proposed research agenda and becoming an independent investigator.

Research Proposal: [redacted] long-term goal is to improve outcomes for children hospitalized with common, serious infections through implementation of diagnostic and stewardship principles. For this proposal [redacted] will focus on improving the judicious use of antibiotics among children hospitalized with community acquired pneumonia (CAP) by identifying patients who receive but do not benefit from antibiotics, suggesting that they are low risk for bacterial CAP. [redacted] will use propensity score matching to compare outcomes between matched patients who differ only by antibiotic status. [redacted] will also start to explore ways to reduce overprescribing by understanding factors that influence antibiotic decision-making using qualitative methods. This will provide key data for a K23 award in which [redacted] will conduct a pilot RCT of antibiotic de-implementation in low risk patients to assess safety and further explore factors that drive antibiotic overuse through a multisite qualitative study. This will prepare [redacted] to launch an R01 to safely reduce unnecessary antibiotics and improve patient outcomes. [redacted] thoughtfully arrived

at this research plan after many months of self-reflection, brainstorming with [REDACTED] entire mentorship team, and discussions with prominent researchers both within and beyond our institution.

My Role as Co-Mentor: I am well equipped to serve as a co-mentor for [REDACTED] proposal. First, I have methods expertise in advanced study design, statistical analysis for health outcomes research, and multicenter studies. Second, I have key content expertise as my primary research interests aligns with that of [REDACTED]; I have developed a prolific extramurally funded research career focused on pediatric CAP diagnostics, treatment, and outcomes. The preliminary data presented in this proposal is derived from [REDACTED] and my prospective cohort of children with CAP. Third, I have significant prior experience successfully mentoring trainees ranging from medical students to junior faculty. Fourth, [REDACTED] and I already have an ongoing successful mentoring relationship. I have been meeting regularly with [REDACTED] for the last three years. I participated in her Master's Final Committee, we have published together, and we participated in a formalized mentoring program to further build our mentor-mentee relationship. In my role as co-mentor, I will supervise and assist all aspects of the proposed project along with [REDACTED] and bring expertise as explained above. Given the research network that I have created across institutions, I will connect [REDACTED] with other researchers, as I did with [REDACTED]. I commit to continuing to meet with [REDACTED] bi-weekly, meeting with the entire team at least twice yearly, and doing all that I can to ensure [REDACTED] success along the way.

Mentorship Team: [REDACTED] will also serve as co-mentor. Through our roles within the Section of Hospital Medicine, [REDACTED] and I have worked together to build research infrastructure and co-mentor others. As a result, we have built a strong working relationship which will position us well as co-mentors for [REDACTED] proposal. We also have complementary skills that will benefit [REDACTED] project and research career. In addition, [REDACTED] has assembled advisors in [REDACTED] mentorship team with research and clinical expertise that will support the goals of [REDACTED] proposal. These investigators are nationally recognized, well-funded, and truly invested in [REDACTED] success. [REDACTED] has already held meetings with [REDACTED] mentorship team to discuss [REDACTED] research career, which demonstrates [REDACTED] initiative and the group's ability to work together.

Conclusion: [REDACTED] has exhibited steadfast dedication to a research career, demonstrated incredible productivity, and assembled a qualified mentorship team to ensure [REDACTED] continued success. [REDACTED] has a logical long-term plan, is proposing a well-rounded project that will tackle difficult and impactful questions, and I have no doubt that [REDACTED] will become a leader who improves the management of children with CAP and other common infections. I am excited to serve as a mentor in [REDACTED] promising career. **[REDACTED] is an excellent candidate for this award** as [REDACTED] is the type of junior investigator who has already excelled and will seize the opportunities provided during this award to further [REDACTED] experience, training and develop key data needed to launch a successful career. **I offer my unconditional and highest support for [REDACTED] application.**

Sincerely,

[REDACTED]

IX. Letter of Collaboration: [REDACTED]

[REDACTED]

Dear Members of the Young Investigator Awards Program Leadership and Review Panel,

I am pleased to be writing you in support of [REDACTED] APA Young Investigator Award Proposal, "Reducing Antibiotic Overuse in Pediatric Pneumonia". I am the Chair of [REDACTED] Network, a multicenter pediatric hospital-based research network with over \$23 million in research funding over the past 8 years and a strong history of supporting research proposals in pediatric hospital medicine. The [REDACTED] Network partners with nearly 800 hospitalists from 109 pediatric centers across the United States and Canada, and the Executive Council consists of 16 renowned investigators and pediatric hospitalists from around the country. As such, we have the expertise, resources, and contacts to assist investigators with multi-center research.

The [REDACTED] mission is to improve healthcare delivery to hospitalized children through large, multi-institutional studies in areas that are relevant to clinicians and the decisions they face in everyday clinical practice. We are dedicated to continually defining best practices and how they should be implemented. This mission is highly aligned with the research aims of [REDACTED] proposal, which focus on gathering key pilot data for identifying antibiotic best practices and implementation strategies to address a widespread problem of antibiotic overuse among children with pneumonia. Our focus also fits with [REDACTED] career vision to improve the care of children hospitalized with common, serious infections.

Part of the goal of the [REDACTED] Network is to assist investigators with the creation, development, and implementation of key research initiatives that improve care for hospitalized children. This involves careful review of proposals, discussions with our Executive Council, and guided mentorship to ensure the project's success. We have read through [REDACTED] proposal and there is broad enthusiasm for the questions [REDACTED] has asked, their potential impact on patient care, and the great potential for sustained inquiry in this research. As clinicians we recognize the challenges of antibiotic decision-making in pediatric pneumonia and commonly witness the overuse of antibiotics, highlighting the importance of this research. Furthermore, we recognize [REDACTED] as an excellent and promising young investigator and the strong investigative team around [REDACTED] with expertise well aligned to the project. As such, we are excited to work closely with [REDACTED] and [REDACTED] team.

[REDACTED] study proposal is highly aligned with the APA and [REDACTED] Network's missions and will provide important knowledge around antibiotic use and outcomes for children hospitalized with pneumonia. This will launch a promising and exciting research trajectory including future prospective studies for targeted antibiotic de-implementation interventions. We look forward to collaborating with [REDACTED] during this APA Young Investigator Award period and beyond.

Sincerely,

[REDACTED]

[REDACTED]

[REDACTED]

X. Letters of Collaboration: External Institutions

[REDACTED]

[REDACTED]

Dear [REDACTED]

I am very pleased to support and collaborate with you on your project entitled “Reducing Antibiotic Overuse in Pediatric Pneumonia”. As you know, I am an Assistant Professor of Pediatrics at [REDACTED], and a Hospitalist at [REDACTED]. I am also an experienced clinical researcher, and both led and participated in multiple multi-center studies such as the one that you are proposing. Therefore, I have the necessary expertise to lead this project at our site. I will take a lead role coordinating the study at our institution. This will include identifying investigator(s) or research coordinators at our institution who are interested in and available to perform the chart review and administrative tasks necessary to complete this study and/or doing it myself. The funding allocated in the budget to support our time will ensure the feasibility of this project.

This proposal is a multi-center retrospective cohort study that aims to evaluate the association between antibiotics and outcomes and explore factors associated with antibiotic overuse among children hospitalized with pneumonia. This study will set up future de-implementation research aimed to reduce antibiotic overuse and improve outcomes for children with pneumonia. [REDACTED] has a track record of successful collaboration with multi-center studies. We have a robust volume of hospitalized pneumonia patients and are able to collect the data needed for this project. Further, antibiotic stewardship is a strong priority, and therefore we are committed to promoting judicious antibiotic use and improving outcomes for our patients hospitalized with pneumonia. Given our patient volumes and institutional focus on improvement of care for children hospitalized with pneumonia, we are able to provide the necessary data for this study.

In summary, I look forward to collaborating with you on this important project. The results of this study have the potential to significantly improve our management of children who are hospitalized with pneumonia, and I am thrilled to be a part of it.

Sincerely,
[REDACTED]
[REDACTED]



Dear [REDACTED],

I am very pleased to support and collaborate with you on your project entitled "Reducing Antibiotic Overuse in Pediatric Pneumonia".

This proposal is a multi-center, retrospective cohort study that aims to evaluate the association between antibiotics and outcomes and explore factors associated with antibiotic overuse among children hospitalized with pneumonia. This study will set up future de-implementation research aimed to reduce antibiotic overuse and improve outcomes for children with pneumonia. [REDACTED] has a track record of successful collaboration with multi-center studies, including multi-center studies specifically focused on diagnosis and management of children hospitalized with pneumonia. We have a robust volume of hospitalized pneumonia patients and are able to collect the data needed for this project. We are committed to promoting judicious antibiotic use and improving outcomes for our patients hospitalized with pneumonia. Therefore, we are able to successfully contribute to this project.

As an Assistant Professor of Pediatrics at [REDACTED] and a Pediatric Hospitalist at [REDACTED] who is committed to an academic research career, I will take a lead role coordinating the study at our institution. This will include identifying investigator(s) or research coordinators at our institution who are interested in and available to perform the chart review and administrative tasks necessary to complete this study and/or doing it myself. The funding allocated in the budget to support our time will ensure the feasibility of this project.

In summary, I look forward to collaborating on this important project that has the potential to significantly improve the care we provide to children hospitalized with pneumonia.

Sincerely,

[REDACTED]

[REDACTED]

[REDACTED]

XI. Letters of Collaboration: Students at [REDACTED]

To Members of the Young Investigator Awards Program Leadership and Review Panel,

I am a second-year medical student, and I have volunteered my time to assist with [REDACTED] pneumonia chart review study to obtain research experience during medical school. I have already received training by [REDACTED], and I have begun chart review and data collection in a REDCap database. I am committed to performing at least 400 charts to assist with this exciting project.

Sincerely,

[REDACTED]

[REDACTED]

To Whom it May Concern,

I am a second-year medical student, and I have volunteered my time to assist with [REDACTED] pneumonia chart review study to obtain research experience during medical school. I have already received training by [REDACTED], and I have begun chart review and data collection in a REDCap database. I am committed to performing at least 400 charts to assist with this exciting project.

Sincerely,

[REDACTED]

[REDACTED]