Using Electronically Derived AutoMated RePOrts of Appropriate Antibiotic use to Inform SteWardship IntERventions (EMPOWER)
Adult Inpatient Community Acquired Pneumonia
(EMPOWER-IN)

NCT06027593

Background:

Antibiotic resistance (AR) is increasing at an alarming rate, leading to substantial morbidity and mortality for patients with infections due to resistant bacteria. Antibiotic use, the main driver of antibiotic resistance, is common in clinical practice in both inpatient and outpatient settings. More than half of all adult and pediatric patients receive antibiotics during an inpatient stay [1, 2]. In the outpatient setting, the equivalent of 849 courses of antibiotics are prescribed for every 1,000 persons [3, 4]. However, up to 50% of these prescriptions are inappropriate [5-8].

Antibiotic stewardship (AS) has been shown to improve patient outcomes, decrease adverse events, and decrease antibiotic resistance [9]. Tracking antibiotic use is a fundamental component of AS. Although strategies to track antibiotic use in meaningful ways have been attempted, these metrics typically track aggregate antibiotic use and are at best surrogate markers of inappropriate antibiotic use. Further, minimal research has evaluated the relationship between aggregate antibiotic use measures and inappropriate antibiotic prescribing. Because aggregate antibiotic use metrics don't necessarily measure inappropriate antibiotic use, antibiotic stewardship programs (ASPs) must utilize time-intensive strategies reliant on manual electronic health record (EHR) review, such as medication use evaluations, in order to qualitatively assess the appropriateness of antibiotic use. Ultimately, these limitations make current metrics less meaningful to clinicians and actionable by ASPs.

The increasing availability of EHRs across healthcare settings provides a unique opportunity to extract more data elements than ever before from the level of individual patients to the level of healthcare facilities. Utilizing these data elements has the potential to create more actionable metrics using individual indicators or groups of indicators to better identify infectious disease diagnoses and measure inappropriate antibiotic use for these conditions. In order to utilize EHR data in this way, performance characteristics of candidate indicators need to be systematically evaluated and then integrated into software that allows ASPs to perform these analyses on an ongoing basis.

In a prior research project conducted at Children's Hospital of Philadelphia (CHOP) and Penn (SHEPheRD Contract #200-2016-91796, titled "Assessing Appropriate Antibiotic Use in Hospitals and Outpatient Settings Through Electronic Health Records"), our research group developed several electronic indicators measuring appropriate antibiotic use for community acquired pneumonia (CAP) that were extractable using electronic data sources[10-15]. These indicators measure two dimensions of antibiotic prescribing: 1) the choice of antibiotic agent and 2) the duration of antibiotic use[10-15].

The focus of the current protocol is to: 1) refine this electronic definition of CAP and the electronic indicators for appropriate antibiotic prescribing through a detailed chart review and validation process; 2) assess the impact of generating reports reflecting these indicators on the appropriateness of antibiotic use; and 3) to evaluate the acceptability and feasibility of delivering these reports to prescribers. If effective, these EHR-based approaches hold the promise to greatly enhance effectiveness and efficiency of AS initiatives.

As a secondary aim, we also seek to identify racial disparities in the appropriateness of antibiotic prescribing in patients hospitalized with CAP.

Project Goals:
The goals of this project are to:

Aim 1: Refine the electronic definition of CAP and the electronic indicators for appropriate antibiotic prescribing through a detailed chart review and validation process
Aim 2: Design and implement a scalable and sustainable AS feedback reported-based intervention for these populations informed by a rapid user-centered design process
Aim 3: Track the impact of the stewardship intervention and report to key stakeholders (e.g., prescribers)

Secondary aim: To identify racial disparities in the appropriateness of antibiotic prescribing in patients hospitalized with CAP

Study Design:
Aim 1:
We will first conduct a retrospective descriptive study to refine and validate the previously developed electronic definition of CAP and indicators for appropriate antibiotic choice and duration.

To do this, we will first refine an electronic definition of CAP, which may include ICD-10 codes, antibiotic orders, and orders for radiographic studies suggesting a diagnosis of CAP. We will validate this definition through chart review to ensure that the electronic definition of CAP correctly identifies patients being for CAP based on documentation in the EHR. We will also evaluate the impact of various inclusion and exclusion criteria within the cohort, such as ICU admission and presence of chronic comorbid conditions (e.g., lung cancer, cardiopulmonary disease) on the sensitivity and specificity of this electronic definition of CAP.

As a secondary component of this aim, we will also compare this electronic definition of CAP with provider-selected indication. Upon ordering antibiotics for inpatients, providers must select the indication for the antibiotic; one of the possible indications is CAP. We will perform chart review on a subset of patients ordered for azithromycin or doxycycline within the first 48 hours of admission, given that these are common antibiotics ordered for CAP. Chart review to assess for provider intention to treat for CAP will serve as the gold standard. We will then compare the performance of the electronic definition and provider-selected indication with the chart review-based findings, assessing sensitivity and specificity of these two methods.

We will also validate our indicators of antibiotic appropriateness, which include appropriate antibiotic choice and duration. To validate these indicators, we will compare sensitivity and specificity of the electronic definition of appropriate antibiotic choice and duration compared to a “gold standard” of manual chart review. We will iterate these definitions until acceptable performance characteristics for the electronic indicators are achieved. These measures of appropriateness are based on national guidelines for appropriate antibiotic prescribing.

Finally, we will also collect data on prescribers, including the attending of record and clinicians placing orders, to evaluate whether the indicators for appropriate antibiotic choice and duration can be attributed to individual prescribers. Study measures for this aim will be purely descriptive.

Aim 2:
We will then generate reports of appropriate antibiotic choice and duration using the indicators validated in Aim 1. Through a user-centered design process, we will optimize the structure and delivery of these feedback reports through conducting interviews with a small number of clinical provider stakeholders. We will also perform surveys of all clinicians during the intervention focused on feasibility and acceptability of the intervention.

Aim 3:
We will conduct a quasi-experimental study in the adult inpatient settings measuring the impact of implementing the feedback reports on appropriateness of antibiotic choice and duration for CAP using the validated indicators. The baseline, pre-intervention period will last approximately up to 24 months and the intervention period will last up to 24 months.

Secondary aim:
We will use the retrospective cohort from aim 1 to assess racial disparities in antibiotic prescribing for CAP. Briefly, we will use the two measures of antibiotic prescribing appropriateness to assess for differences in appropriate prescribing by race, adjusting for other variables.

Study sites:
Adult
The Hospital of the University of Pennsylvania (HUP) is a 774-bed academic quaternary acute care medical center. There are over 36,000 admissions, 1,500,000 outpatient visits, and 65,000 Emergency Department visits annually.

Penn Presbyterian Medical Center (PPMC) is a 324-bed urban community acute care hospital in West Philadelphia. There are 12,000 admissions, 130,000 outpatient visits, and 31,000 ED visits annually.

Chester County Hospital (CCH) is a 257-bed facility with 13,521 admissions, 425,107 outpatient visits, and 45,317 ED visits annually. The service area is primarily urban and suburban Chester County, Pennsylvania.

Study subjects:
There are two study populations for this study: patients and clinicians.

Patients with community acquired pneumonia
Inclusion:
1. Diagnosis of community acquired pneumonia based on ICD-10 diagnostic codes (see appendix 1)
2. Prescribed one or more antibiotic within the first 48 hours of hospitalization AND at least one dose administered between 24 and 48 hours OR discharged within 48 hours on antibiotics
3. Chest x-ray or chest CT within 48 hours of admission

Exclusion
1. Transfer from another healthcare facility
2. Died within the first 48 hours of admission

For the secondary component of Aim 1 in which we compare the electronic definition of CAP and provider selected indication with manual chart review, our eligible patient population will include all adult patients who received at least one dose of doxycycline or azithromycin within the first 48 hours of admission. Patients who die within the first 48 hours of admission will be excluded. A random sample will then be selected for chart review.

Our interaction with patients will be limited to review of existing EHR data. We will have no direct contact with patients. Appropriateness of antibiotic use will be reported on an encounter level; data will be aggregated prior to giving feedback to clinicians, though, clinicians may be provided with information on prescribing only for patients for whom they prescribed (or supervised the prescribing of) antibiotics.

Adult clinicians

The focus of the intervention is on delivering feedback reports to physicians caring for inpatients with CAP. Clinicians providing care to patients with CAP on the inpatient medical services, or in the ICU will be included. In addition, we will identify up to 30 clinician stakeholders for semi-structured interviews as part of the user centered design process to develop the feedback reports. Because feedback reports are a novel intervention in the inpatient environment, this stakeholder engagement and formative evaluation are critical elements of this protocol. In addition, all providers will receive a survey to evaluate their perceptions of the intervention post-intervention.

Intervention design and implementation:

The intervention will consist primarily of an automated prescribing feedback report delivered in aggregate to clinicians. The precise content of the report will be developed with stakeholder feedback, but we anticipate these reports will include such data as: 1) number of patients seen by the prescriber group with the target condition; 2) proportion of patients for which the choice of antibiotic was correct (based on electronic indicators); 3) proportion of patients for which duration of prescribing was correct; and 4) proportion of patients for which both indicators were correct. Clinicians may be provided with patient-level information on prescribing only for patients for whom they prescribed (or supervised the prescribing of) antibiotics.

We will work with our sponsor (the CDC) and key stakeholder champions to engage in a rapid user centered design process to create feedback reports that will fit the prescribing context[17]. In previous work we have found this contributes to greater levels of acceptance by clinicians[18,19]. First, we will optimize the form of the report (how information is displayed) and how the reports will be delivered to prescribers (e.g. individually via email, embedded in a dashboard, provided verbally and division quality improvement meetings). Second, we will determine appropriate implementation supports that will be needed to accompany the introduction of the feedback reports to each clinical setting. Potential implementation supports will include educational materials for prescribers, communication about the feedback reports to bolster prescriber understanding and trust, and champion-led meetings to ensure that prescribers are aware of the intervention. These activities will be designed with scalability in mind, and so they may be used across diverse settings without negatively impacting operations. Clinician champions will be engaged to inform this intervention as part of the study team, and providers will also be recruited as research subjects to participate in the design process.

We will implement the intervention at the completion of the rapid user centered design process. We will start by launching any educational materials or awareness-building activities as previously described before activating the feedback reports. Following the initial awareness-building activities, we would propose to circulate the antibiotic prescribing feedback reports using the format determined in consultation with stakeholders. In the post-intervention period,

we will assess feasibility and acceptability of the reports and implementation activities. To do this, we will conduct semi-structured interviews with our key stakeholder champions and administer a brief survey to prescribers. The survey will contain demographic questions, attitudinal questions about AS used in our previous research[20], the Feasibility of Intervention Measure (FIM) and the Acceptability of Intervention Measures (AIM). FIM and AIM have demonstrated strong psychometric properties to determine the extent to which stakeholders believe an intervention is feasible and acceptable[21]. Because inpatient providers may be on clinical service very sporadically, rather than administering the survey at one point in time, we will circulate the survey at multiple time points post-intervention to prescribers who have been on clinical service and have one or more encounters with a CAP patient.

Data collection:
Data elements obtained from the EHR include: patient demographics, address to calculate area deprivation index), preferred language, comorbidities (ICD-10 codes), admitting service, provider, antibiotic allergies, all medications for the previous 1 year, all diagnosis codes for the previous 1 year, laboratory testing, radiographic testing, discharge disposition, and ED visits/hospitalizations within 30 days after discharge. Antibiotic use measures specific to the condition (choice of agent and duration of therapy) will also be collected. This data will be extracted from the UPHS data warehouse (Clarity) that stores data from the electronic health record. These data will be used in feedback report generation as well as in outcome assessment.

Data will also be collected during the rapid user centered design process as well as during the intervention period in the form of surveys related to feasibility and acceptability of the intervention. Data collected will include interview and survey responses from individual providers. No direct identifiers will be collected.

Finally, we will measure provider engagement as is feasible, including attendance at educational sessions, interaction with data displays of feedback measures.

Outcomes:
For aim 1, we will assess sensitivity and specificity of the electronic definition of CAP and the antibiotic prescribing indicators.

In order to demonstrate the effect of the intervention (aims 2 and 3), we will track appropriateness of antibiotic use based on the key indicators in the automated reports for the selected targeted conditions prior to and following implementation of the stewardship interventions. The following indicators will be assessed:

1) Choice of antibiotic therapy: administration of a first-line agent within 48 hours of admission
2) Duration of therapy: all antibiotic durations ≤ 5 days are classified as appropriate

The primary outcome in this study is appropriate antibiotic use for CAP at the encounter level. If an encounter is associated with appropriate antibiotic use for both metrics, the encounter will be classified in the numerator as “appropriate” antibiotic use. The denominator will consist of all CAP encounters. As a secondary analysis, we will separately analyze appropriate antibiotic choice for CAP and appropriate antibiotic duration for CAP. Additional secondary outcomes include: hospital readmission within 30 days from the index visit, ED or primary care revisit within 30 days of the index visit with a new antibiotic prescription for a different antibiotic.

Finally, we will assess implementation metrics, including provider engagement with the feedback reports, as well as provider responses to interviews and surveys conducted as part of the assessment of feasibility and acceptability of the intervention.

Secondary aim: The same two outcomes of appropriateness (choice of antibiotic therapy and duration of therapy) will be used for this aim.

Analysis:
At the level of the encounter, patient-specific variables will be compared in the baseline and intervention periods using chi-squared or Wilcoxon rank-sum testing as appropriate. For the primary analysis, a multivariate logistic regression model will be performed at the encounter level, with the intervention (i.e., baseline period vs intervention period) as the primary binary exposure of interest. Calendar month will be included separately in the model, allowing for adjustment for seasonal variation in antibiotic prescribing. We will additionally analyze these data as a pre-post study with segmented regression analysis. This would allow us to assess the immediate change in the outcomes of interest (i.e., appropriate antibiotic use, reflecting antibiotic choice and antibiotic duration) as well as the slope of change occurring associated with the implementation of the intervention. In this analysis we would also control for potential confounders such as changes in the patient population, census, admissions, nurse staffing, etc.

Secondary aim: At the level of the encounter, differences in proportion of appropriate prescribing will be compared by race, using chi-squared testing. Then multivariate logistic regression will be performed at the encounter level, with race as the primary exposure of interest, incorporating other potential confounders in the model.

Sample size:
For the chart review/validation components of this study, we estimate needing up to 1500 charts for review.

The primary outcome of the interventional component of this study is appropriate antibiotic use for adults with CAP. In order to be classified as “appropriate,” both the antibiotic choice indicator and the duration indicator must be appropriate.

Based on preliminary data, we anticipate including up to up to 10,000 adults with CAP over the four-year study period (24 months pre-intervention and 24 months post-intervention). We estimate that approximately 50% of encounters will be associated with appropriate antibiotic prescribing. To detect an improvement to 60%, we require a sample size of 776 (total in the pre and post periods). Given the projected CAP case numbers, have adequate sample size to detect this difference.

Appendix 1. Diagnostic codes used to define Community Acquired Pneumonia (CAP)

ICD-10 Code	Code Description
J09.X1	INFLUENZA WITH PNEUMONIA
J10.00	INFLUENZA DUE TO OTHER IDENTIFIED INFLUENZA VIRUS WITH PNEUMONIA
J10.01	INFLUENZA DUE TO OTHER IDENTIFIED INFLUENZA VIRUS WITH THE SAME OTHER IDENTIFIED INFLUENZA VIRUS PNEUMONIA
J10.08	INFLUENZA DUE TO OTHER IDENTIFIED INFLUENZA VIRUS WITH OTHER SPECIFIED PNEUMONIA
J11.00	INFLUENZA DUE TO UNIDENTIFIED INFLUENZA VIRUS WITH UNSPECIFIED TYPE OF PNEUMONIA
J11.08	INFLUENZA DUE TO UNIDENTIFIED INFLUENZA VIRUS WITH SPECIFIED PNEUMONIA
J12.0	PNEUMONIA DUE TO ADENOVIRUS
J12.1	PNEUMONIA DUE TO RSV
J12.2	PNEUMONIA DUE TO PARAINFLUENZA VIRUS
J12.3	METAPNEUMOVIRUS PNEUMONIA
J12.8	OTHER VIRAL PNEUMONIA
J12.81	PNEUMONIA DUE TO SARS-ASSOCIATED CORONAVIRUS
J12.82	PNEUMONIA DUE TO CORONAVIRUS DISEASE 2019
J12.89	OTHER VIRAL PNEUMONIA
J12.9	VIRAL PNEUMONIA, UNSPECIFIED
J13	PNEUMONIA DUE TO STREPTOCOCCUS PNEUMONIAE
J14	PNEUMONIA DUE TO HEMOPHILUS INFLUENZAE
J15	PNEUMONIA DUE TO KLEBSIELLA PNEUMONIAE
J15.1	PNEUMONIA DUE TO PSEUDOMONAS
J15.2	PNEUMONIA DUE TO STAPHYLOCOCCUS, UNSPECIFIED
J15.21	PNEUMONIA DUE TO STAPHYLOCOCCUS AUREUS
J15.211	PNEUMONIA DUE TO METHICILLIN SUSCEPTIBLE STAPHYLOCOCCUS AUREUS
J15.212	PNEUMONIA DUE TO METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS
J15.29	PNEUMONIA DUE TO OTHER STAPHYLOCOCCUS
J15.3	PNEUMONIA DUE TO STREPTOCOCCUS, GROUP B
J15.4	PNEUMONIA DUE TO OTHER STREPTOCOCCI
J15.5	PNEUMONIA DUE TO ESCHERICHIA COLI
J15.6	PNEUMONIA DUE TO OTHER GRAM-NEGATIVE BACTERIA
J15.7	PNEUMONIA DUE TO MYCOPLASMA PNEUMONIAE
J15.8	PNEUMONIA DUE TO OTHER SPECIFIED BACTERIA
J15.9	UNSPECIFIED BACTERIAL PNEUMONIA
J16.0	CHLAMYDIAL PNEUMONIA
J16.8	PNEUMONIA DUE TO OTHER SPECIFIED INFECTIOUS ORGANISMS
J17	PNEUMONIA IN DISEASES CLASSIFIED ELSEWHERE
J18.0	BRONCHOPNEUMONIA, UNSPECIFIED ORGANISM
J18.1	LOBAR PNEUMONIA, UNSPECIFIED ORGANISM
J18.8	OTHER PNEUMONIA, UNSPECIFIED ORGANISM
J18.9	PNEUMONIA, UNSPECIFIED ORGANISM
A37.01	WHOOPING COUGH DUE TO BORDETELLA PERTUSSIS WITH PNEUMONIA

A37.11	WHOOPING COUGH DUE TO BORDETELLA PARAPERTUSSIS WITH PNEUMONIA
A37.81	WHOOPING COUGH DUE TO OTHER BORDETELLA SPECIES WITH PNEUMONIA
A37.91	WHOOPING COUGH, UNSPECIFIED SPECIES WITH PNEUMONIA
A48.1	LEGIONNAIRES' DISEASE
J22	UNSPECIFIED ACUTE LOWER RESPIRATORY INFECTION

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