

Cluster-Randomized Trial to Improve Antibiotic Use for Adults With Acute Respiratory Infections Treated in Emergency Departments

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Study objective: We evaluate the effectiveness of an educational program in hospital emergency departments (EDs) targeting reduction in antibiotic overuse for acute respiratory tract infections.

Methods: Sixteen hospitals participated in the cluster randomized trial, selecting a Veterans Administration (VA) and non-VA hospital within each of 8 metropolitan regions. Intervention sites received performance feedback, clinician education, and patient educational materials, including an interactive computer kiosk located in the waiting room. Medical records were reviewed at each site during the baseline year 1 and intervention year 2. The primary measure of effect was the percentage of visits for upper respiratory tract infections and acute bronchitis that were treated with antibiotics. Secondary outcomes, including return visits and visit satisfaction, were assessed by follow-up telephone interviews of patients. Alternating logistic regression models were used to adjust for baseline treatment rates, case mix differences, and provider characteristics.

Results: The adjusted antibiotic prescription level for upper respiratory tract infection/acute bronchitis visits was 47% for control sites and 52% for intervention sites in year 1. Antibiotic prescriptions at control sites increased by 0.5% between year 1 and year 2 (95% confidence interval –3% to 5%) and at intervention sites decreased by 10% (95% confidence interval –18% to –2%). There were no significant differences between control and intervention sites in the proportions of upper respiratory tract infection/bronchitis patients with return ED visits or in overall visit satisfaction.

Conclusion: Multidimensional educational interventions can reduce antibiotic overuse in the treatment of patients with upper respiratory tract infections and acute bronchitis in EDs. However, substantial antibiotic overuse persists despite this educational intervention. [Ann Emerg Med. 2007;xx:xxx.]

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Editor's Capsule Summary*What is already known on this topic*

Physicians often prescribe antibiotics for upper respiratory tract infection and bronchitis despite the lack of efficacy for these conditions.

What question this study addressed

Can unnecessary antibiotic use be decreased with a program of physician and patient education and performance feedback?

What this study adds to our knowledge

In this 16-hospital cluster-randomized trial of more than 5,500 emergency department patients during 2 years, antibiotic prescriptions for upper respiratory tract infections and bronchitis decreased by 10% in facilities with intervention, without increasing return visits or decreasing patient satisfaction. Many physicians continued to prescribe inappropriate antibiotics despite intervention.

How this might change clinical practice

Facilities should consider educational interventions to reduce unnecessary antibiotic use, but the cost-effectiveness of these interventions is unknown.

INTRODUCTION

In recent years, there has been a growing concern about the emergence of antibiotic resistance among bacterial pathogens.^{1,2} Because antibiotic resistance patterns are strongly correlated with antibiotic use patterns, multiple organizations have identified reductions in unnecessary outpatient antibiotic use as a critical component of efforts to combat antibiotic resistance.³ Targeting unnecessary antibiotic use is important because such use also confers unnecessary individual risk of adverse drug reactions, which are not uncommon with antibiotics.

At the center of campaigns to reduce unnecessary antibiotic use are efforts to understand and improve on management strategies for patients with acute respiratory tract infections.^{4,5} Acute respiratory tract infections, which include nonspecific upper respiratory tract infections, acute bronchitis, sinusitis, pharyngitis, otitis media, and pneumonia, account for the majority of outpatient antibiotic use,⁶ even though available evidence strongly demonstrates that the majority of acute respiratory tract infections, specifically upper respiratory tract infections and acute bronchitis, are not bacterial in origin and, therefore, are unlikely to benefit from antibiotic treatment.⁵ To date, most interventions to reduce unnecessary antibiotic use for acute respiratory tract infections have focused on primary care settings⁷⁻⁹ and have demonstrated that combined patient and clinician educational strategies can successfully reduce the use of antibiotics for acute respiratory tract infections. In addition, recent time trend analyses have demonstrated that broader

awareness of these issues has resulted in national downward trends in the use of antibiotics for acute respiratory tract infections in primary care settings.^{10,11}

Unfortunately, levels of antibiotic use for acute respiratory tract infections managed in the emergency department (ED) have not decreased to the same extent as that observed in primary care settings,¹² and overall levels of antibiotic prescribing remain high.¹³ The ED setting is distinct from the primary care setting in a number of ways, having a greater acuity of illness, the need for rapid triage and treatment, and limited previous and subsequent contact with patients. As a result, established methods for reducing antibiotic overuse for acute respiratory tract infections in primary care settings may not readily translate into ED settings.

The Improving Antibiotic Use in Acute Care Treatment (IMPAACT) project is examining the impact of interventions on antibiotic use for acute respiratory tract infections among a national sample of Veterans Administration (VA) and non-VA hospitals. The specific aim of the present study was to test the impact of a multidimensional patient and clinician educational program on reducing unnecessary antibiotic use for acute respiratory tract infections. Our primary endpoint was the proportion of antibiotics prescribed for patients with upper respiratory tract infections and acute bronchitis evaluated in the ED. Our secondary endpoints included antibiotic prescribing for antibiotic-responsive acute respiratory tract infection diagnoses (including community-acquired pneumonia, sinusitis, and acute exacerbations of chronic bronchitis), the frequency of return ED visits and hospital admissions within 2 weeks of the index visit, and overall visit satisfaction. We evaluated the program in VA and non-VA hospital EDs to test whether distinct health care structures modified the impact of the program.

MATERIALS AND METHODS**Study Design**

The IMPAACT randomized controlled trial involves EDs at 8 VA medical centers and 8 non-VA academic medical centers. The trial was conducted as part of a joint Agency for Healthcare Research and Quality and VA Health Services Research and Development Service Award to compare the translation of research into practice across VA and non-VA settings. Details of the hospital sampling strategy have been previously described.¹⁴ In brief, we surveyed all 135 major VA medical centers and all US non-VA hospitals with accredited emergency medicine residency programs or previous participation in a national ED research collaboration (Emergency Medicine Network, available online at <http://www.emnet-usa.org>) to identify hospitals that were willing to participate in the implementation and evaluation of an ED-based antibiotic quality improvement program. Eligible sites were further restricted to those metropolitan areas with at least 1 eligible VA site and 1 eligible non-VA site. To have 80% power to detect an absolute difference of 10% in the level of decrease in antibiotic prescribing during the 2-year period at intervention sites versus control sites for VA and non-

VA sites separately, we calculated that we would require 16 total sites (8 pairs of VA and non-VA hospitals) and 200 total acute respiratory tract infection visits sampled per site in each year.

Setting

We initially identified 28 eligible VA and non-VA sites in 13 major metropolitan areas. We stratified these metropolitan areas by US region (Northeast, South, Midwest, and West) to sample 2 metropolitan areas (each with a VA and non-VA hospital) within each region. One US region (Midwest) had only 2 eligible metropolitan areas, representing 2 eligible pairs of VA and non-VA hospitals; hence, all 4 hospitals were selected. For the other 3 US regions, we selected metropolitan areas after preliminary contact with potential site investigators at each hospital to identify the remaining 6 pairs of VA and non-VA hospitals. The 2 metropolitan areas within each region were randomly allocated to intervention or control status according to a simple coin flip, and all participating sites were informed of their allocation status. In the first year, one of the non-VA hospitals in a control area was unable to identify appropriate staff to participate in the study (despite an initial willingness to do so) and dropped out before data collection, leaving 15 eligible hospitals for this study. The patient and clinician characteristics of these hospitals, as well as antibiotic use patterns in year 1, have been described previously.¹³ Specifically, across all sites, 38% of patients diagnosed with upper respiratory tract infection and 72% of patients diagnosed with acute bronchitis received an antibiotic prescription, and the overall percentage of acute respiratory tract infection visits including an antibiotic prescription varied from 42% to 89% across the participating sites.¹³

Interventions

The multidimensional educational intervention emphasized principles of judicious antibiotic use for acute respiratory tract infections^{5,15,16} and was targeted at clinicians and patients. We based our intervention on the Predisposing, Reinforcing and Enabling Constructs in Educational Diagnosis and Evaluation (PRECEDE) model of behavior change.¹⁷ This model emphasizes the inclusion of predisposing strategies (ie, increasing provider knowledge about acute respiratory tract infection management), reinforcing strategies (ie, delivering feedback to providers on past patterns of antibiotic prescribing), and enabling strategies (patient education to reduce antibiotic demand). The clinician educational intervention included the following component. Clinical leaders were identified at each intervention site and participated in a 4-hour training session on the principles of judicious antibiotic use. They were provided with an informational slide set and reprints of relevant supporting journal articles from emergency medicine journals. The slide set emphasized the evidence against efficacy of antibiotic therapy for upper respiratory tract infection and acute bronchitis that were based on the Centers for Disease Control and Prevention's (CDC's) "Principles of Appropriate Antibiotic Use for Adults With Acute Respiratory Tract Infections"⁵

(available online at <http://medicine.ucsf.edu/impact/clinic.html>). The clinical leaders conducted a variety of one-on-one, small-group, and large-group educational sessions in the month preceding the onset of data collection for year 2 in their local ED, using these educational slide sets. The relative use of small-group versus large-group sessions varied by site. Sites were provided with aggregated site-specific data on their use of antibiotics for acute respiratory tract infections in the preintervention winter year (measured as described below). These results were benchmarked against the average for all other VA or non-VA sites (as appropriate), as well as against an evidence-based benchmark, according to literature review.¹⁸

The patient educational intervention included the following components. Waiting room posters and brochures incorporated messages that are part of the CDC's Get Smart antibiotics campaign (available online at http://www.cdc.gov/drugresistance/community/campaign_info.htm). In addition, a computerized educational module housed on a video kiosk in the waiting room provided information tailored to specific acute respiratory tract infection symptoms. The kiosk had touch screens that elicited information on a subject's chief complaint, language preference (English or Spanish), and clinician preference (white or black). The responses elicited condition-specific modules (cough, sinus, and throat symptoms) that included a video representation of a physician-patient encounter that provided information on the viral cause of most acute respiratory tract infections, signs of severe acute respiratory tract infections that might warrant antibiotic treatment, and the lack of efficacy of antibiotics for the majority of acute respiratory tract infections. Examination room posters summarized clinical trial evidence emphasizing the lack of clinical benefit for patients with acute bronchitis treated with antibiotics, as well as issues related to antibiotic resistance.⁸

Methods of Measurement

The methods used for measuring antibiotic prescription rates for acute respiratory tract infections at our study sites have been previously described.¹³ According to *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* billing codes (460 to 491 [acute respiratory tract infections], 786.2 [unspecified cough illness], and 034 [streptococcal pharyngitis]), we systematically sampled adult (age >18 years) visits with these acute respiratory tract infection discharge diagnoses between November 2003 and February 2004 (baseline period, year 1) and November 2004 and February 2005 (intervention period, year 2). We used a broad, nonspecific range of *ICD-9-CM* codes for initial sampling to ensure that acute respiratory tract infection visits would be similarly captured across sites despite differences in the use of *ICD-9-CM* coding strategies. However, for analytic purposes we relied on the discharge diagnosis listed by the clinician in the encounter note for each visit (see below). Thus, the *ICD-9-CM* discharge codes were used only to identify potentially eligible visits for abstraction.

The following clinical data were abstracted from medical records: patient demographics, smoking status, arrival time, discharge time, discharge status, vital signs, chief complaint, primary diagnosis, secondary diagnoses, comorbidities, medications, and diagnostic tests (eg, chest radiography). For each acute respiratory tract infection visit, the research assistant documented the identity and level of training of the ED provider according to the documented signature at the bottom of the encounter note. If there were multiple signatures, the research assistant assigned the visit to the highest-level provider and recorded whether a house officer or student was involved in the evaluation. Research assistants from each participating site attended a training session at one of the coordinating sites for orientation to the medical record abstraction tool. Subsequently, a research assistant at one of the coordinating sites reabstracted a sample of medical records from each site. The overall κ statistic for documentation of an antibiotic prescription was 0.77 (95% confidence interval [CI] 0.59 to 0.96); for primary diagnosis of acute bronchitis, 1.0 (95% CI 0.62 to 1.0); and for primary diagnosis of upper respiratory tract infection, 0.66 (95% CI 0.43 to 0.89).

At each site, in both year 1 and year 2, we also performed follow-up telephone interviews of up to 40 patients with a chief complaint of cough and an acute respiratory tract infection discharge diagnosis to assess the need for additional follow-up care. The sample size was chosen to provide adequate power to detect a 10% difference in the percentage of patients reporting dissatisfaction with the care provided at control versus intervention sites, adjusting for within-site clustering of satisfaction scores. These subjects were sampled separately from the medical record samples described above using a nonrandom convenience sampling method based on the availability of the research assistants at each site. We excluded subjects who were severely ill (requiring immediate medical attention for respiratory or cardiovascular support), those who lacked a telephone, and those who were cognitively impaired. Eligible subjects provided written informed consent for study participation and provided telephone contact information. Patients consented to review of their medical records for the current ED visit and a single follow-up telephone interview in 2 to 4 weeks from their ED visit. Patients who did not have an acute respiratory tract infection diagnosis in the encounter note for the current ED visit were dropped from subsequent analyses (N=22, 3% of total).

The telephone survey was administered from a centralized calling center located at the Philadelphia VA Medical Center. Subjects reported dates of return medical visits and any hospitalizations in the 2-week follow-up period. We did not verify any subject-reported hospitalizations or return medical visits. In addition, subjects rated overall satisfaction with the index visit on a 5-point Likert scale (1=very unsatisfied to 5=very satisfied).¹⁹

Primary Data Analysis

The primary outcome of this analysis was the proportion of visits for upper respiratory tract infection and acute bronchitis at which an antibiotic was prescribed. In addition, we calculated the proportion of visits for antibiotic-responsive acute respiratory tract infection diagnoses in which patients were prescribed antibiotics (specifically, community-acquired pneumonia, sinusitis, acute exacerbations of chronic bronchitis, otitis media, and pharyngitis, which we collectively refer to as antibiotic-responsive acute respiratory tract infections, recognizing that even within these categories there are bacterial and viral causes for the illnesses).¹³ We compared the distribution of discharge diagnoses at control and intervention sites for year 1 and year 2 to assess any effect of the intervention on diagnostic coding behaviors. According to follow-up interviews, we calculated the percentage of patients who reported return ED visits or hospitalizations. We also calculated the mean level of self-reported satisfaction with the visit for intervention and control sites in year 1 and year 2.

Descriptive statistics were performed to examine the distribution of provider, patient, and facility characteristics for upper respiratory tract infection or acute bronchitis visits across participating sites in year 1 and year 2. The impact of the intervention was calculated with alternating logistic regression equations to accommodate clustering of antibiotic prescribing patterns by practice site and provider and adjusted for potential confounding caused by patient and visit characteristics. Alternating logistic regression is a multilevel modeling technique using general estimating equations, allowing for simultaneous adjustment for multiple levels of clustering.²⁰ Confounders were entered into the adjusted models according to a screen of all patient, provider, and facility characteristics, testing for a significant association ($P<.20$), with the intervention status and period interaction term. The primary statistical test of interest was the interaction between intervention status and period (year 1 versus year 2). This interaction is a test of whether there was a statistically significant change in the proportion of visits with a documented antibiotic prescription between year 1 and year 2 at the intervention sites compared with the control sites, after adjusting for potential confounders and clustering by provider and site. Separate models were built for the upper respiratory tract infection or acute bronchitis visits and the antibiotic-responsive acute respiratory tract infection visits. Adjusted antibiotic prescription levels overall and for individual sites were estimated from the final alternating logistic regression models, and 95% CIs were calculated with the delta method.²¹ Adjusted values were calculated by setting the other covariates in the model equal to their mean values across the entire data set and using the ESTIMATE statement in SAS to obtain the adjusted percentage of visits during which patients were prescribed antibiotics (rather than odds ratios). The CIs were calculated according to the large sample variance-covariance matrix of the parameter estimates from the alternating logistic regression models, which

Table 1. Stability of ED discharge diagnoses across study sites and study years.

Discharge Diagnosis	Control Sites, %		Intervention Sites, %		P Value*
	Year 1 (N=1,317)	Year 2 (N=1,342)	Year 1 (N=1,496)	Year 2 (N=1,510)	
Nonspecific URI	33	31	34	35	.25
Acute bronchitis	23	24	22	21	.56
AECB	5	9	5	5	.36
Pneumonia	13	14	12	10	.25
Pharyngitis	14	10	12	17	.01
Other ARI diagnoses	12	12	15	12	.10

AECB, Acute exacerbation of chronic bronchitis; ARI, acute respiratory tract infection; URI, upper respiratory tract infection.
 *P value for interaction between intervention/control status and study year in terms of the proportion of visits with each diagnosis.

Table 2. Characteristics of ED visits for nonspecific upper respiratory tract infections and acute bronchitis at control and intervention sites in year 1 and year 2 winter seasons.

Characteristics	Control Sites (n=7 Sites)		Intervention Sites (n=8 Sites)		Interaction P Value*
	Year 1 (n=736 Patient Visits), No. (%)	Year 2 (n=736 Patient Visits), No. (%)	Year 1 (n=840 Patient Visits), No. (%)	Year 2 (n=848 Patient Visits), No. (%)	
Type of hospital					
VA	453 (62)	447 (61)	420 (50)	489 (58)	.02
Non-VA	283 (38)	289 (39)	420 (50)	359 (42)	
Patient characteristics					
Age, y					
18-44	284 (39)	281 (38)	384 (46)	323 (38)	.005
45-64	302 (41)	320 (43)	305 (36)	341 (40)	
>65	146 (20)	135 (18)	151 (18)	184 (22)	
Male sex	519 (71)	507 (69)	547 (65)	594 (70)	.03
Current smoker	222 (30)	216 (29)	201 (24)	240 (28)	.09
Previous ARI (within 6 weeks)	79 (11)	35 (5)	54 (6)	36 (4)	.42
Comorbidities					
Chronic lung disease†	71 (10)	58 (8)	63 (8)	68 (8)	.26
Diabetes	119 (16)	127 (17)	118 (14)	121 (14)	.76
Asthma	82 (11)	74 (10)	89 (11)	95 (11)	.44
Visit characteristics					
Chest radiography ordered	265 (36)	304 (41)	260 (31)	295 (35)	.73
Disposition					
Admitted	16 (2)	6 (1)	18 (2)	11 (1)	.43
Discharged	717 (97)	727 (98)	817 (97)	828 (98)	
Other	3 (1)	3 (1)	5 (1)	9 (1)	
Provider type					
Attending alone	261 (36)	308 (42)	700 (83)	618 (73)	<.001
Attending with house staff	361 (49)	391 (53)	75 (9)	75 (9)	
RN, PA, NP	106 (14)	37 (5)	62 (7)	155 (18)	
Not documented	8 (1)	0	3 (0.4)	0	

NP, Nurse practitioner; PA, physician assistant; RN, registered nurse.

*P value testing interaction term between site (control versus intervention) and time (year 1 vs year 2) in terms of the distribution of the characteristic.

†Includes chronic obstructive pulmonary disease and reactive airways disease.

generated standard errors that could be converted into CIs (± 1.96 multiplied by the standard errors). All statistical computations were performed with the SAS statistical software program (version 9; SAS Institute, Inc., Cary, NC).

This study was reviewed and approved by the institutional review board at each participating hospital before the start of data collection and implementation of the intervention. The study was also reviewed and approved by the institutional review board at the 2 coordinating centers for the study.

RESULTS

Characteristics of Study Sites

We examined a total of 2,659 visits for acute respiratory tract infection diagnoses at control sites and 3,006 visits for acute respiratory tract infection diagnoses at intervention sites across the year 1 and year 2 winter periods. Table 1 summarizes the final specific acute respiratory tract infection discharge diagnoses documented in the medical record, comparing intervention and

Table 3. Site-specific levels of antibiotic prescriptions for patients diagnosed with URI and acute bronchitis at control and intervention study sites.

Site	Visits Prescribed Antibiotic (95% CI), %			
	Year 1 Unadjusted	Year 2 Unadjusted	Year 1 Adjusted*	Year 2 Adjusted*
Control†				
Control 1	33.9 (25.2-42.7)	39.8 (30.4-49.3)	34.9 (27.8-42.8)	39.8 (30.9-49.4)
Control 2	44.4 (33.0-55.9)	52.8 (42.4-63.2)	46.2 (35.0-57.9)	53.5 (43.9-62.9)
Control 3	33.7 (24.3-43.0)	29.2 (20.1-38.3)	33.8 (25.2-43.6)	29.1 (20.7-39.3)
Control 4	36.4 (27.4-45.4)	24.1 (16.4-31.9)	35.6 (27.0-45.2)	25.7 (11.9-34.8)
Control 5	77.9 (69.9-85.9)	75.0 (66.5-83.5)	72.9 (61.1-82.1)	68.4 (57.9-77.4)
Control 6	27.6 (18.7-36.4)	28.7 (20.7-36.7)	26.6 (16.9-39.3)	30.1 (20.5-41.7)
Control 7	55.1 (46.1-64.1)	58.1 (48.7-67.5)	55.5 (43.6-66.8)	61.0 (48.7-72.0)
Intervention				
Intervention 1	38.8 (28.1-49.4)	32.9 (22.1-43.7)	36.6 (25.7-49.0)	31.4 (21.6-43.10)
Intervention 2	50.9 (41.4-60.5)	28.8 (18.8-38.7)	50.5 (38.8-62.1)	26.6 (18.7-36.5)
Intervention 3	77.9 (71.2-84.5)	62.8 (53.4-72.1)	71.7 (62.2-79.6)	54.6 (41.1-67.5)
Intervention 4	45.5 (33.4-57.5)	55.3 (45.3-65.4)	46.0 (28.1-64.9)	56.7 (37.4-74.1)
Intervention 5	75.4 (67.9-82.9)	60.9 (52.5-69.4)	78.5 (70.2-85.0)	62.7 (49.5-74.2)
Intervention 6	77.4 (69.7-85.0)	59.0 (50.1-67.9)	73.8 (59.8-84.2)	53.5 (34.7-71.5)
Intervention 7	53.7 (44.3-63.1)	48.3 (40.2-56.4)	50.4 (39.6-61.2)	53.0 (38.0-67.5)
Intervention 8	17.9 (9.7-26.1)	28.7 (19.9-37.5)	15.4 (9.3-24.5)	24.2 (17.3-32.9)

*Adjusted percentages are estimated from alternating logistic regression models, controlling for provider type, recorded temperature at visit, current patient smoking history, patient sex, and VA/non-VA sites.

†One of the original 8 control sites dropped out of the trial before data collection was initiated in year 1.

control sites during year 1 and year 2. Overall, nonspecific upper respiratory tract infection and acute bronchitis were the most common diagnoses across all study sites and the 2-year period, and this did not vary significantly between intervention and control sites. We did observe a significant increase in the diagnosis of pharyngitis at intervention sites compared to control sites between year 1 and year 2.

Characteristics of upper respiratory tract infection and acute bronchitis visits are shown in Table 2. The study sample from the control sites had disproportionately greater numbers of VA patients, which is due to dropout of 1 non-VA site in the control group. Overall, 2% of patients with diagnoses of upper respiratory tract infection and acute bronchitis at the study sites were hospitalized, and the hospitalization rate did not differ by study group or period (Table 2). However, a higher proportion of visits at control sites compared to intervention sites included evaluation with chest radiography in year 1 and year 2. In addition, a higher proportion of visits at control sites (51%) compared to intervention sites (10%) included documentation that a resident or student participated in the evaluation during baseline and intervention periods.

Main Results

Overall, at control sites, antibiotics were prescribed at 45% of visits for upper respiratory tract infection and acute bronchitis in year 1 and at 43% of visits in year 2. At intervention sites, antibiotics were prescribed at 59% of visits in year 1 and 49% of visits in year 2. Table 3 displays the changes in levels of antibiotic prescribing for upper respiratory tract infection and acute bronchitis for each control and intervention site. In addition, the table displays the adjusted levels of

antibiotic prescribing at each site in year 1 and year 2 after adjusting for significant confounders, including provider type, recorded temperature at visit, current patient smoking history, and patient sex. The site-level heterogeneity in the change in levels of antibiotic prescribing from year 1 to year 2 is further displayed in Figure 1A (control sites) and Figure 1B (intervention sites). In particular, among intervention sites, 4 sites demonstrated an approximately 10% to 20% decrease in antibiotic prescribing from year 1 to year 2, but 2 sites demonstrated an approximately 10% increase in antibiotic prescribing. Overall, the adjusted level of antibiotic prescribing was 47% in both year 1 and year 2 at control sites (adjusted difference 0.5%; 95% CI –3% to +5%) and decreased from 52% in year 1 to 42% in year 2 at intervention sites (adjusted difference –10%; 95% CI –18% to –2%) (Figure 2).

Though we designed the study a priori to examine the effect of the intervention on antibiotic prescribing for nonantibiotic-responsive acute respiratory tract infections (ie, the composite outcome of antibiotic treatment for upper respiratory tract infection and acute bronchitis), the decrease in antibiotic prescribing was much greater for upper respiratory tract infection visits compared with acute bronchitis visits. Specifically, for patients diagnosed with upper respiratory tract infection, the adjusted difference in antibiotic prescribing from year 1 to year 2 was a decrease of 0.3% at control sites and a decrease of 9.5% at intervention sites. For patients diagnosed with acute bronchitis, the adjusted difference in antibiotic prescribing from year 1 to year 2 was a decrease of 5.7% at control sites and 5.0% at intervention sites.

For antibiotic-responsive acute respiratory tract infection visits, at control sites the adjusted difference in the percentage of

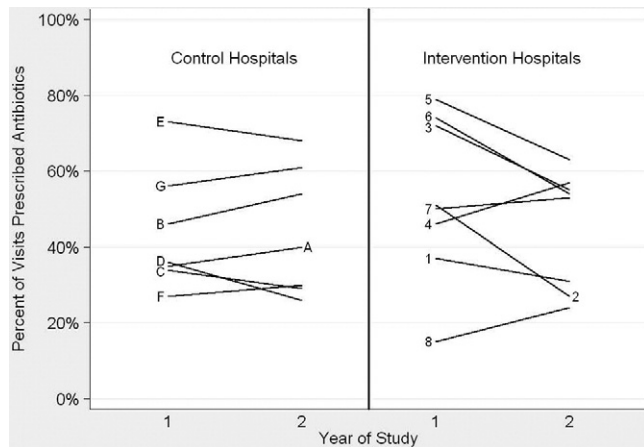


Figure 1. Adjusted levels of antibiotic prescribing for visits diagnosed as upper respiratory tract infection or acute bronchitis in Year 1 and Year 2. Levels of antibiotic prescribing are estimated from alternating logistic regression models adjusting for type of provider, recorded temperature at visit, current patient smoking history and patient gender. The control hospitals identified by letters (A–G) are matched to intervention hospitals identified by numbers (1–7), such that the paired order (eg, hospitals A and 1, hospitals B and 2) represent control and intervention hospitals in the same US region and same VA or non-VA status.

visits prescribed antibiotics from baseline to intervention winter seasons was -4% (95% CI -9% to 2%), and at intervention sites, the difference was -2% (95% CI -6% to 3%) (Figure 3). In all models, there was no statistically significant interaction effect between VA versus non-VA sites and the intervention effect.

For the assessment of secondary endpoints outcomes during the 2-week follow-up period, a total of 776 adults were enrolled across all sites during the 2 study periods. The proportion of adults who reported returning to an ED for follow-up care for their acute respiratory tract infection increased between year 1 and year 2. The increase was greater at control sites (5%) compared with intervention sites (1%), though the comparison was not statistically different after adjusting for visit, site, and provider characteristics ($P=.48$) (Table 4). Similarly, subsequent hospitalization rates for patients discharged from the ED were low across intervention and control sites and did not appear to change from year 1 to year 2 (Table 4). Finally, mean levels of patient satisfaction with care at the index ED visit increased from 2.7 to 2.9 at control sites and increased from 2.5 to 2.7 at intervention sites ($P=.71$ for comparison of the differences at control and intervention sites, adjusting for provider type, patient characteristics [age, sex, smoking status], and VA status).

LIMITATIONS

Hawthorne effects are always of concern in trials intended to modify physician or patient behaviors. As such, clinician coding

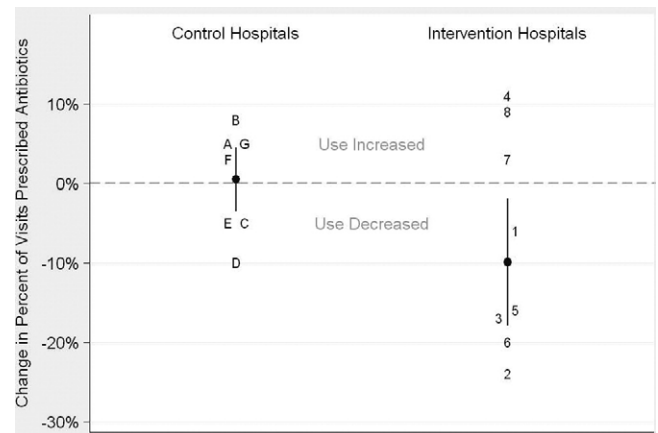


Figure 2. Adjusted difference in levels of antibiotic prescribing for visits diagnosed as upper respiratory tract infections and acute bronchitis (Year 2 minus Year 1). Levels of antibiotic prescribing for visits diagnosed as upper respiratory infection or acute bronchitis were calculated using alternating logistic regression, controlling for provider type, recorded temperature at visit, current patient smoking history, patient gender, and VA/non-VA sites. Individual hospital values are estimated from the regression (letters and numbers correspond to the same hospitals in Figure 1) as was the overall mean, approximately weighted for the number of visits per hospital (plotted as a dot). The line represents the overall 95% confidence interval, calculated using the delta method.

of diagnoses could be driven by treatment decisions such that physicians would be more likely to code for more antibiotic-responsive acute respiratory tract infections after deciding to prescribe an antibiotic. Indeed, we did observe a relative increase in the diagnosis of pharyngitis at intervention compared to control sites, which may have accounted for some of the observed decrease in antibiotic prescribing for upper respiratory tract infection and acute bronchitis, though the overall percentage of visits diagnosed as upper respiratory tract infection and acute bronchitis did not change.

A major strength of this trial was the cluster-randomized design because the patient and physician interventions were designed to operate on a hospital level, and therefore individual hospitals should be treated as individual units for randomization. However, the disadvantage of randomizing 16 sites is that it decreases the likelihood that randomization will result in balance of all relevant site, patient, and clinician characteristics. We used multivariable and multilevel regression to adjust for the effects of confounding and clustering of effects by site and provider. Despite these analytic strategies, residual imbalances in the sites could have contributed to some of our observed results. For example, the levels of antibiotic prescribing were higher at intervention sites compared with control sites during the baseline year, raising the possibility that some of the observed effect may have been due to regression to the mean. In

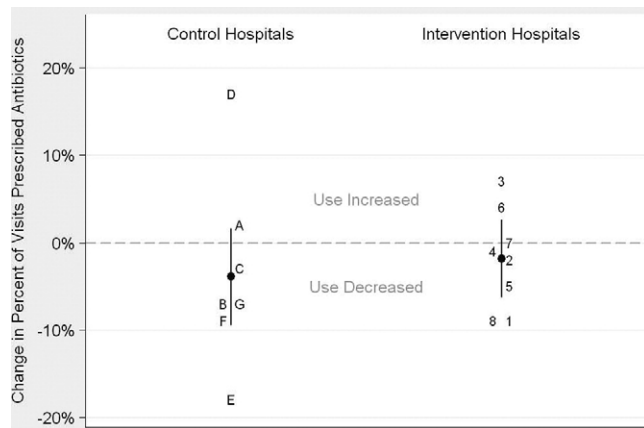


Figure 3. Adjusted difference in levels of antibiotic prescribing for all visits diagnosed as antibiotic responsive acute respiratory tract infections (Year 2 minus Year 1). Levels of antibiotic prescribing for visits diagnosed as any antibiotic responsive acute respiratory tract infection (ie, pneumonia, acute exacerbation of chronic bronchitis, sinusitis, otitis media, or pharyngitis) were calculated using alternating logistic regression, controlling for provider type, current patient smoking history, patient age and gender, patient history of chronic obstructive lung disease or diabetes mellitus, and VA/non-VA site. Individual hospital values are estimated from the regression (letters and numbers correspond to the same hospitals in Figure 1) as was the overall mean, appropriately weighted for the number of visits per hospital (plotted as a dot). The line represents the overall 95% confidence interval, calculated using the delta method.

addition, although we believe this largely reflects documentation differences as opposed to true differences in the structure of care delivery, house staff were documented to participate at a much higher proportion of visits at control sites compared to intervention sites, which may have influenced observed trends in antibiotic prescriptions. The assessment of secondary endpoints was based on a nonrandom sample of patients at each site, which could have biased the comparisons of control and intervention sites. Because we did not collect information on nonenrolled patients at each site, we were unable to estimate the potential magnitude of this sampling strategy. Finally, although we selected our participating sites according to a national survey of all academic EDs and VA medical centers, not all sites were willing to participate,¹⁴ potentially limiting the generalizability of the study results.

DISCUSSION

We found that a multidimensional educational intervention targeting patients and clinicians appears to reduce antibiotic prescribing for patients diagnosed with upper respiratory tract infection or acute bronchitis in the ED, 2 common conditions for which antibiotics are frequently overprescribed.¹⁸ The reduction in antibiotic prescribing for upper respiratory tract

infections or acute bronchitis was not associated with any apparent increase in the frequency of return visits or delayed hospitalizations, and overall patient satisfaction was not affected by the intervention. Finally, the effect size of the intervention was not statistically different at VA versus non-VA hospitals despite considerable differences in the patient populations and organization of the EDs.

The magnitude of the reduction in antibiotic prescribing for upper respiratory tract infections and acute bronchitis was modest (absolute difference 10%; relative decrease 19%) but comparable to that of other educational interventions targeting overuse of antibiotics for acute respiratory tract infections. In a recent systematic review of outpatient interventions to improve appropriate antibiotic use from the Agency for Healthcare Research and Quality, Ranji et al²² calculated a summary median effect size of -8.9% (interquartile range -12.4% to -6.7%); however, the majority of these trials were not conducted in EDs. Among primary care trials reporting results for upper respiratory tract infections or acute bronchitis, the absolute effect size ranged between -12% and -26% .^{7,8,23,24} Primary care practices have somewhat of an advantage in reducing antibiotic use because there is a greater sense of continuity of care and follow-up opportunities, providing a safety net for withholding antibiotics. Such follow-up care is less reliable in urgent and ED care settings, which are often providing primary care services for patients without adequate primary care. It is also possible that patients presenting to EDs with acute respiratory tract infections have more severe illness compared with patients presenting to physician offices. For example, one measure of this overall increased illness severity for patients presenting with acute respiratory tract infection complaints in ED settings, the proportion of acute respiratory tract infection visits diagnosed with community-acquired pneumonia, is considerably higher in our study sites (10% to 14%) compared with primary care sites (5%).²⁵ In a secondary analysis, we observed greater reduction in antibiotic prescribing for upper respiratory tract infection compared to acute bronchitis, perhaps reflecting that physicians continue to perceive acute bronchitis as a more antibiotic-responsive illness compared with upper respiratory tract infection,¹³ despite the lack of evidence supporting this conclusion.¹⁵

Another factor that may have limited the size of the intervention effect was the potential for variable uptake of the clinician educational components at intervention sites. The intervention sites demonstrated a relatively wide variation in the level of change in antibiotic prescribing from year 1 to year 2, ranging from some sites decreasing overall prescribing to some sites increasing overall prescribing. In contrast to primary care sites, clinicians at ED sites often work nonoverlapping shifts, and it was challenging to organize group meetings that could achieve close to 100% physician and nurse participation in the educational sessions. Ongoing work is evaluating the site-to-site variation in implementation of the intervention to better

Table 4. Comparison of the frequency of self-reported hospitalizations and return ED visits during the 2-week follow-up period in year 1 and year 2 for control and intervention sites.

Outcome	Control Sites			Intervention Sites			Interaction P Value*
	Reported Events per 100 Persons, No.			Reported Events per 100 Persons, No.			
	Year 1 n=181	Year 2 n=217	Difference	Year 1 n=111	Year 2 n=189	Difference	
Hospitalization	6.0	4.2	<1.8	6.3	4.8	<1.5	0.51
Return ED visit	5.5	10.1	+4.6	8.1	9.5	+1.4	0.48

*P value for interaction between site (control vs intervention) and time (year 1 vs year 2) in terms of proportion of subjects reporting subsequent hospitalization or return ED visit, adjusting for provider type, smoking status of patient, sex, age, and VA vs non-VA hospital type.

understand the heterogeneity in site response to the intervention.

This trial was specifically designed to test whether the educational intervention had a different effect size at VA versus non-VA hospitals. Patient and clinician populations differ between these types of hospitals. Moreover, the VA hospitals are part of a large integrated care network that includes more explicit linkage to primary care services, as well as on-site pharmacies. Furthermore, many VA ED sites function more like urgent care centers and do not accept high-acuity ambulance transports. Overall, we found no difference in the impact of the intervention at VA versus non-VA sites. It is possible that despite these obvious differences between VA and non-VA ED sites, these differences are less meaningful in explaining practice variation in the treatment of patients with lower-acuity illnesses, such as acute respiratory tract infections.

In Retrospect

Because we implemented a multidimensional program at all intervention sites, we do not know whether the intervention effect was primarily driven by a subset of the intervention components or required the presence of all educational components. Although the general conclusion of appropriate antibiotic use interventions in primary care practices is that interventions targeting multiple levels of patients, clinicians, and systems are more effective than unidimensional strategies, this may not necessarily be the case in acute care settings. Future studies will specifically investigate the cost-effectiveness of different components of the intervention.

In summary, we have shown that a multidimensional educational intervention targeting patients and clinicians in ED settings can reduce levels of antibiotic prescribing for patients diagnosed with upper respiratory tract infection and acute bronchitis. Although it is unknown what level of reduction in antibiotic prescribing will have a significant effect on influencing levels of antibiotic resistance among community-acquired bacterial pathogens, reducing prescription of antibiotic drugs that have no clear patient benefit without a concomitant increase in return visits is of considerable value in improving patient safety, reducing adverse drug events, and minimizing health care costs. Our results demonstrate that educational interventions can improve the quality of antibiotic use in ED

settings; however, further research is warranted to identify intervention or implementation strategies that have more robust effects.

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Author contributions: JPM, CAC, TM, CM, and RG were responsible for study conception and design. JPM, JM, SKL, AK, and RG were responsible for acquisition of data and administrative, technical, or material support. JPM, CAC, TM, CM, JM, and RG conducted analysis and interpretation of data. JPM, CAC, CM, JM, and RG were responsible for drafting of the article and statistical analysis. JPM, CAC, TM, and RG obtaining funding. All authors provided critical revision of the manuscript. JPM and RG were responsible for study supervision. JPM and RG takes responsibility for the paper as a whole.

Conflicts of interest: Dr. Metlay has served as a scientific consultant or received unrestricted educational funds from Aventis Pharmaceuticals and Roche Pharmaceuticals. Dr. Gonzales served as a consultant for Abbott Laboratories, Inc. to study C-reactive protein levels as a potential diagnostic test for outpatients with community-acquired pneumonia. Dr. Camargo has received financial support for participation in conferences, consulting, and medical research from the following industry sponsors with an interest in respiratory infections: Abbott, Aventis, Aventis Pasteur, GlaxoSmithKline, MedImmune, and Merck. None of the other authors have any conflicts of interest or financial disclosures.

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APPENDIX

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Editor's Capsule Summary *What is already known on this topic:* Physicians often prescribe antibiotics for upper respiratory tract infection and bronchitis despite the lack of efficacy for these conditions. *What question this study addressed:* Can unnecessary antibiotic use be decreased with a program of physician and patient education and performance feedback? *What this study adds to our knowledge:* In this 16-hospital cluster-randomized trial of more than 5,500 emergency department patients during

2 years, antibiotic prescriptions for upper respiratory tract infections and bronchitis decreased by 10% in facilities with intervention, without increasing return visits or decreasing patient satisfaction. Many physicians continued to prescribe inappropriate antibiotics despite intervention. *How this might change clinical practice:* Facilities should consider educational interventions to reduce unnecessary antibiotic use, but the cost-effectiveness of these interventions is unknown.