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A Cluster-Randomized Trial of Decision Support Strategies for Reducing Antibiotic Use for Acute Bronchitis

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Abstract

Background—National quality indicators show little change in the overuse of antibiotics for uncomplicated acute bronchitis. We compared the impact of two decision support strategies on antibiotic treatment of uncomplicated acute bronchitis.

Methods—We conducted a three-arm, cluster-randomized trial among 33 primary care practices belonging to an integrated health care system in central Pennsylvania. The printed intervention arm (n=11 practices) received decision support for acute cough illness through a print-based strategy, the computerized intervention group (n=11) received decision support through an electronic medical record-based strategy, and third group of practices (n=11) served as the control arm. Both intervention groups also received provider education and feedback on prescribing practices, and patient education brochures at check-in. Antibiotic prescription rates for uncomplicated acute bronchitis in the winter period (October 2009 – March 2010) following introduction of the intervention were compared with the previous three winter periods in an intent-to-treat analysis.

Results—Compared with the baseline period, the percentage of adolescents and adults prescribed antibiotics during the intervention period decreased at the printed (from 80.0% to

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Dr Gonzales serves as a Medical Advisor for Phreesia, Inc., a company that provides computerized patient check-in services. Dr Bloom serves on the Merck Speakers Bureau on the topic of "Patient Centered Medical Homes". None of the other authors report any potential conflicts of interest with this study, such as "work under consideration for publication", "relevant financial activities outside the submitted work", or any "other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing" what is written in the submitted work (based on all relationships that were present during the 3 years prior to submission).[20]

Dr Gonzales had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. The contributions of each author are as follows: Conception and design (RG; TA; CEM; FJB; JPM); Acquisition of data (TA; MS; MY; JM); Analysis and interpretation of data (RG; TA; CEM; JHM; FJB; TRG; JPM); Drafting of manuscript (RG; CEM; JHM; JPM); Critical revision of the manuscript for important intellectual content (RG; TA; CEM; JHM; FJB; TRG; MS; MY; JM; JPM); Statistical analysis (RG; CEM; JHM); Obtaining funding (RG; JPM); Administrative, technical, or material support (TA; FJB; TRG; MS; MY; JM; JPM); Supervision (TA; FJB; TRG).

68.3%) and computerized intervention sites (from 74.0% to 60.7%), but increased slightly at the control sites (from 72.5% to 74.3%). After controlling for patient and provider characteristics, and clustering of observations by provider and practice site, the differences for the intervention groups were statistically significant from control (control vs. printed *P*=0.003; control vs. computerized *P*=0.014) but no among themselves (printed vs. computerized *P*=0.67). Changes in total visits, proportion diagnosed as uncomplicated acute bronchitis and thirty-day return visit rates were similar between study groups.

Conclusions—Implementation of a decision support strategy for acute bronchitis can help reduce overuse of antibiotics in primary care settings. The impact of printed and computerized strategies for providing decision support was equivalent. The study was registered with Clinical Trials.Gov prior to enrolling patients (NCT00981994).

Overuse of antibiotics for acute respiratory tract infections (ARIs) is an important contributor to worsening trends in antibiotic-resistance patterns among community-acquired pathogens. In the U.S. among persons age 5 years and older, ARIs accounted for eight percent of all visits to ambulatory practices and emergency departments, and 58 percent of all antibiotics prescribed in these settings in 2006.[1] Particularly relevant to reducing total antibiotic use are the common cold, upper respiratory tract infections, not otherwise specified (URIs) and bronchitis, since the vast majority of these illnesses have a viral etiology and do not benefit from antibiotic treatment.[2,3] About 30 percent of office visits for the common cold, and non-specific URIs, and up to 80 percent of all visits for bronchitis, are treated with antibiotics in the U.S. each year. Although antibiotic prescribing for ARIs among children has declined, and is lower than among adults, antibiotic prescribing for acute bronchitis (when this diagnosis is used among children) has not changed.[1, 4–7]

Although national and local efforts appear to have helped reduce antibiotic use for some ARIs, reducing antibiotic treatment of acute bronchitis remains a challenge. Combining patient and physician education and feedback has been shown to help decrease antibiotic treatment of uncomplicated acute bronchitis in a variety of environments such as outpatient practices, urgent care clinics and emergency departments.[8–10] However, on a national level, not only is antibiotic prescribing for uncomplicated acute bronchitis not declining like it is for URIs and otitis media, but it actually appears to be worsening. The National Committee for Quality Assurance's (NCQA) Health Effectiveness Data and Information Set (HEDIS) includes a measure of the average percentage of adult visits for acute uncomplicated acute bronchitis with antibiotic treatment. Among participating health plans the measure was 71.3% in 2006, 74.6% in 2007, 75.4% in 2008 and 76.0% in 2009 (Source: NCQA—The State of Health Care Quality, 2010).

One feature that makes acute bronchitis evaluation and treatment unique from other ARIs is the potential for the clinician to miss the diagnosis of pneumonia—a common and potentially life-threatening condition in the differential diagnosis of acute cough illness. In the emergency department setting, we found a substantial decrease in antibiotic treatment of uncomplicated acute bronchitis (from 51% to 31%) when clinicians were provided with a simple clinical algorithm for estimating the probability of pneumonia among patients with acute cough illness.[11] Extending and adapting this approach to outpatient practices was the goal of the present study.

In the outpatient setting, we considered two different options for implementing the simple clinical algorithm at the point of care—traditional printed decision support (PDS) (often using an algorithmic approach) vs. a computerized decision support (CDS) strategy integrated into the work flow of an electronic health record (EHR). Although there is great enthusiasm for the potential for EHRs to support guideline implementation efforts, investigators and clinicians have also reported that CDS tools can be resource-intensive.[12, 13] This report describes the impact of PDS and CDS strategies, compared with a control group, for introducing a clinical algorithm for acute cough illness at the point of care into primary care practices with a mature EHR system.

METHODS

Setting

Geisinger Health System (GHS) is a non-profit physician-led, fully integrated health care delivery system in rural central and northeast Pennsylvania with a service area population base of 2.6 million people in 43 counties. The health system in 2010 consisted of 2 medical centers, an 829 physician multi-specialty group, and a 247,000 member health plan. The Community Practice Service Line (CPSL) of approximately 200 primary care providers located in 37 practices across the service area completed over 894,000 outpatient visits. GHS has been using a fully integrated EHR introduced in ambulatory care since 1996.

Study Design

We conducted a 3-arm cluster randomized trial of different implementation strategies to reduce antibiotic use for uncomplicated acute bronchitis—a PDS strategy arm, a CDS strategy arm, and a control arm. We excluded 4 practices because the annual number of visits with a primary diagnosis of bronchitis (ICD9=466 or 490) was < 100 in a sample of three recent years. One site served as a test site for the CDS development, and was automatically assigned as a control site. Among the remaining practices, 9 large practices (with 9,000 to 15,000 annual patient visits) were randomly assigned to each study arm, and among the remaining 23 smaller practices (with 2,000 to 9,000 annual visits) we randomly assigned 8 practices to PDS and CDS arms, and 7 practices to the control arm.

Intervention

Previous experience has shown that multidimensional implementation strategies are often more successful than strategies employing a single intervention tool.[14] The PDS and CDS arms both received intervention components guided by the PRECEDE-PROCEED model, which included tools addressing predisposing factors (provider education and practice guidelines), reinforcing factors (clinical champions; audit/feedback) and enabling factors (patient education and decision support).[15] Provider education was delivered by a clinical champion for each clinic who participated in a half-day training session (led by RG and JPM). Champions were provided with data on their specific clinic's performance on the acute bronchitis HEDIS measure, and a teaching slide set to use when reviewing this information with the providers in their respective clinics. Patient education was provided through the provision of CDC brochures developed by the Get Smart: Know When Antibiotics Work program ("Cold or Flu. Antibiotics Don't Work for You") (www.cdc.gov/getsmart).

At PDS sites, patient educational brochures were provided by triage nurses to patients with cough illness as part of routine care, and a poster displaying the clinical algorithm decision support was placed in all examination rooms.[16] (Figure 1) At CDS sites, when nurses entered "cough" as the chief complaint in the EHR, a "Best Practice Alert" for the nurse would appear, prompting the nurse to provide the educational brochure to the patient to read before being evaluated by the provider. At the CDS sites, the algorithm was programmed into the health system's EHR (EpicCare®) by the health system's information technology staff with input from doctors and nurses from a clinic site assigned to the control group, with the goals for the tool to enhance work efficiency, adapt to complex visits, and provide high-level documentation. The key features included a structured template for documenting relevant history and physical examination elements in patients with ARIs broadly. These elements provided the data necessary to categorize the patient's probability of pneumonia based on the acute cough clinical algorithm. Groups of electronic order sets (Smart Sets) were created that simplified relevant testing and treatment options for bronchitis, pneumonia, sinusitis, URI and influenza.

Subjects

Patients that were targeted by the intervention included all adolescents and adults (age ≥ 13 years) with an office visit for uncomplicated acute bronchitis during the baseline (2006–2007, 2007–2008, 2008–2009) and intervention (2009–2010) periods. We focused the intervention implementation during the periods of highest visit volumes for bronchitis; therefore, the analysis was restricted to visits occurring between October 1 through March 31 in each year. All clinicians caring for patients diagnosed with acute bronchitis were included in the analysis, including board-certified internal medicine and family practice physicians, nurse practitioners (NPs), physician assistants (PAs), and registered nurses (RNs). The clinicians at the control sites were not informed of the study's objectives. Waivers of informed consent from patients and providers were obtained from the health system's institutional review board.

Measurements

Incident adult office visits with the diagnosis of acute bronchitis (International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code 466.0) or bronchitis, not otherwise specified (ICD-9-CM code 490) during the specified periods were identified from the EHR. Although the HEDIS measure for acute bronchitis is based solely on ICD-9-CM code 466, we include both 466 and 490 because we previously found that significant coding shift toward the use of code 490 occurred within the study sites in efforts to improve performance on this measure.[17] Incident acute bronchitis visits were defined as not having an office visit for any ARI during the previous 30 days. We defined a return visit as a subsequent visit occurring within 30 days of an incident visit. To calculate antibiotic prescription rates for uncomplicated acute bronchitis—the primary outcome for this study—

we excluded visits by patients age less than 13 and greater than 64 years, or with secondary diagnoses of chronic heart and lung disease, HIV or malignancy, or with secondary diagnoses for ARIs for which antibiotic therapy might be indicated (sinusitis, pharyngitis, otitis media, pneumonia). (see Figure 2)

Information on electronic alert and Smart Set utilization is only captured at the record level, meaning that a count is registered each time an alert fires or Smart Set is opened. If a nurse or clinician closes the record in order to attend to another issue, then re-opens the record then the alert or Smart Set registers an additional count. Thus, alert and Smart Set counts will overestimate the utilization at the patient visit or provider levels. All office visit and prescription data were extracted from the EHR by individuals who were unaware of the allocation of randomization across the study sites. Other data collected for each visit from the medical record included patient age and gender, vital sign measures, smoking status and chest radiography ordering.

Statistical Analysis

Generalized estimating equations and alternating logistic regression (PROC GENMOD in SAS) were used to control for clustering of antibiotic prescribing patterns by both practice site and provider using patient visits as the unit of analysis. These models also adjusted for patient and provider characteristics (at the visit level) that demonstrated a statistically significant change (p-value < 0.05) within study arms between baseline and intervention periods, including provider type, provider specialty, smoking status and vital sign abnormalities. Statistical significance of a change in antibiotic prescribing between periods was defined as $p<0.05$ for the interaction term between intervention status and baseline vs. intervention period. Adjusted odds ratios with 95% confidence intervals (CI) for antibiotic treatment during the intervention period were calculated from parameter estimates. As a secondary analysis, we also examined changes in antibiotic prescription rates at the provider-level in order to assess the variation in provider prescribing behavior change. We restricted this analysis to clinicians with at least 10 patient visits in each study period in order to achieve more precise estimates of baseline and intervention prescription rates [n=31 (46% of PDS providers); n=26 (63% of CDS providers); and n=27 (59% of control providers)]. All statistical analyses were performed using the Statistical Application Program (release 9.2, SAS Institute, Inc, Cary, NC).

This study was approved by the Institutional Review Board at the participating clinical site and at the University of Pennsylvania and University of California, San Francisco. The study was registered with Clinical Trials.Gov prior to enrolling patients (NCT00981994).

RESULTS

A total of 9,808 incident visits for uncomplicated acute bronchitis took place during the baseline winter periods and 6,242 visits occurred during the intervention winter period. The number of visits and proportion of ARIs diagnosed as uncomplicated acute bronchitis remained stable across study sites between the baseline and intervention periods. The proportion of total ARIs diagnosed as uncomplicated acute bronchitis during baseline and intervention period, respectively, was: PDS (9.0% and 8.3%); CDS (7.8% and 8.0%); and control (10.3% and 9.5%). The comparison of patient and clinician characteristics associated with the final set of eligible study visits at PDS, CDS and control sites demonstrated modest differences between study arms during the baseline period (all except fever and tachypnea were statistically significant given the large sample size). (see Table 1) Comparing baseline and intervention years within study arms, there were statistically significant changes (p-value < 0.05) for several variables (proportion of visits with fever or tachypnea, smoking status, provider type, and provider specialty), which we subsequently included in the multivariable analysis of the intervention effects.

Compared with the baseline period, the percentage of adolescents and adults prescribed antibiotics for uncomplicated acute bronchitis during the intervention period decreased at the PDS (from 80.0% to 68.3%) and CDS sites (from 74.0% to 60.7%), but increased slightly at the control sites (from 72.5% to 74.3%). After controlling for patient temperature, respiratory rate, smoking status, provider type, provider specialty and clustering of observations by provider and practice site, the differences for the intervention groups were statistically significantly different from control (control vs. PDS P=0.003; control vs. CDS P=0.014), but not among themselves (PDS vs. CDS P=0.67). (Figure 3) The adjusted odds ratios for antibiotic treatment during the intervention period compared to baseline period were: PDS=0.57, (95% CI: 0.40, 0.82), CDS=0.64 (95% CI: 0.45, 0.91), and control=1.10 (95% CI: 0.85, 1.43).

We also measured changes in antibiotic prescription rates of individual providers in each group with sufficient volume of patient visits during baseline and intervention period (≥10 visits each period) to produce reliable estimates of prescription rates. This subset of providers accounted for 81.8% of total visits. The mean change in antibiotic prescription rates of these clinicians in the baseline and intervention periods was similar to the change based on the patient-level analysis above. (Figure 4) However, it is also observed that a significant proportion (about one-third) of providers reduced antibiotic prescription rates by over 20 percent at both types of intervention sites.

Return visit rates (an office visit ≤ 30 days from an incident visit for uncomplicated acute bronchitis) increased modestly at all study sites, and were not significantly different between study sites (Table 1). The proportion of patients diagnosed with uncomplicated acute bronchitis at the incident visit who were subsequently diagnosed as pneumonia at a return visit was very low, and ranged from 0.5% and 1.5%. Similarly, subsequent ED visits and hospital admissions were rare across all sites and time periods.

We counted 11,827 occasions where an electronic alert fired during the check-in process (ie, for chief complaint of “cough”). In 4,789 occasions, the patients were given an educational sheet about appropriate antibiotic use. To place these electronic alert firings into context, during this period the CDS clinics provided care to 12,082 adolescent and adult patients who were diagnosed as an acute respiratory tract infection (ARI), and 2,582 patients diagnosed as any type of bronchitis. For Smart Set use, the EHR system recorded 819 occasions in which the Smart Set was opened, representing 26 of 43 clinicians on staff at the CDS clinics during the intervention period.

COMMENTS

In this cluster randomized trial comparing the effectiveness of different implementation strategies for delivering clinical algorithm-based decision support for acute cough illness, we found that printed and computer-assisted approaches were equally effective at improving antibiotic treatment of uncomplicated acute bronchitis. There were no significant differences in the change in return visits between baseline and intervention periods between study arms, suggesting that application of the clinical algorithm and resulting decrease in antibiotic treatment were not associated with adverse clinical consequences. In aggregate, these findings support the wider dissemination and use of this clinical algorithm to help reduce overuse of antibiotics for acute bronchitis in primary care.

Our results demonstrate that conventional (non-computerized) methods of implementing decision support for specific treatment decisions may be as effective as approaches that utilize computerized decision support, although this single finding cannot be generalized to all decision support interventions. Review of the electronic utilization data shows that the CDS approach was not heavily utilized by the physicians at those sites and may have contributed to the fact that it did not lead to greater levels of improvement compared to the traditional print-based decision support. A study employing a CDS tool in a similar manner as our study (but targeting all ARIs instead of just cough illness) showed little use and no overall impact on antibiotic prescribing behavior,[18] whereas an ARI decision support tool delivered through personal digital assistant did report improvement.[19] The key finding from our study is that when coupled with other traditional patient and physician education materials, both PDS and CDS strategies can achieve improvement. The choice of specific strategy should be guided by local site resources and competing priorities, not by an inherent belief that one strategy is superior to another. While we do not believe that it is feasible for every algorithm to be subjected to this type of comparative evaluation of implementation strategies, future comparative effectiveness research should help create a framework for identifying the most effective platforms or modes for delivering this type of decision support.

Several limitations should be considered in the interpretation of our findings. This trial was conducted in an integrated health care delivery system with a comprehensive EHR in place for several years prior to our study. The study sites were small-to-medium size rural/semi-rural practices located outside of major metropolitan areas. One possible concern is that attention to the problem of antibiotic overprescribing for acute bronchitis could have led physicians to shift their use of diagnostic codes to more antibiotic appropriate codes. However, we have not detected such shifts during prior interventional trials.[8–10] It is possible that the impact of the intervention across a larger proportion of clinicians may take more time than one winter period. Longer follow-up may show a greater decline in antibiotic prescription rates, or separation in the relative effectiveness of the PDS and CDS strategies. Conversely, longer follow-up could also show a regression of the intervention effects. Because the decision support tools were embedded within a multidimensional intervention strategy that were evaluated prospectively, we cannot determine how much of the improvement in prescribing at PDS and CDS sites was due patient education, physician education, clinical champions or just knowing they were being monitored. However, combined patient and clinician educational interventions have been the standard approach to improving antibiotic use for acute bronchitis, and no studies have successfully improved prescribing patterns with single component interventions.

In conclusion, we find that an evidence-based algorithm to guide management of acute bronchitis can reduce overuse of antibiotics in primary care settings, but the mode of implementation does not appear to impact the magnitude of effect. Studies of computerized decision support tools that do not compare with more traditional implementation strategies may significantly overestimate the value of this type of decision support.

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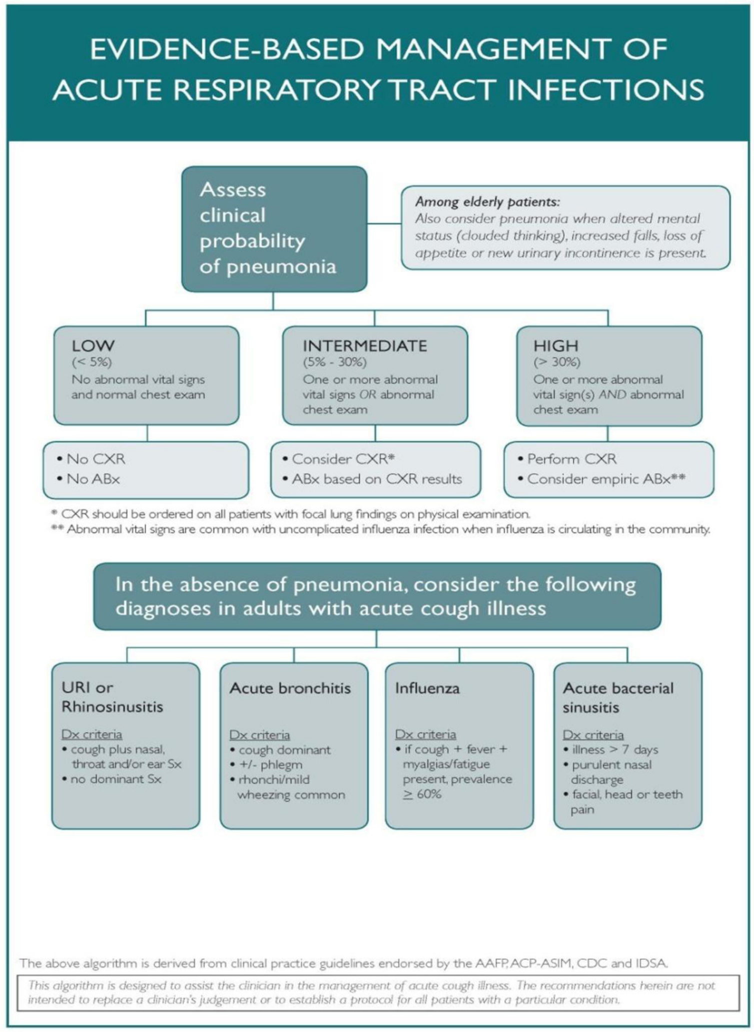

Figure 1. Printed decision support tool

This 11x17 inch poster was laminated and posted in each examination room of practices assigned to the Printed Decision Support intervention arm during the intervention period. The algorithm is based on an evidence-informed approach to assessing pneumonia in adults with acute cough illness.[14]

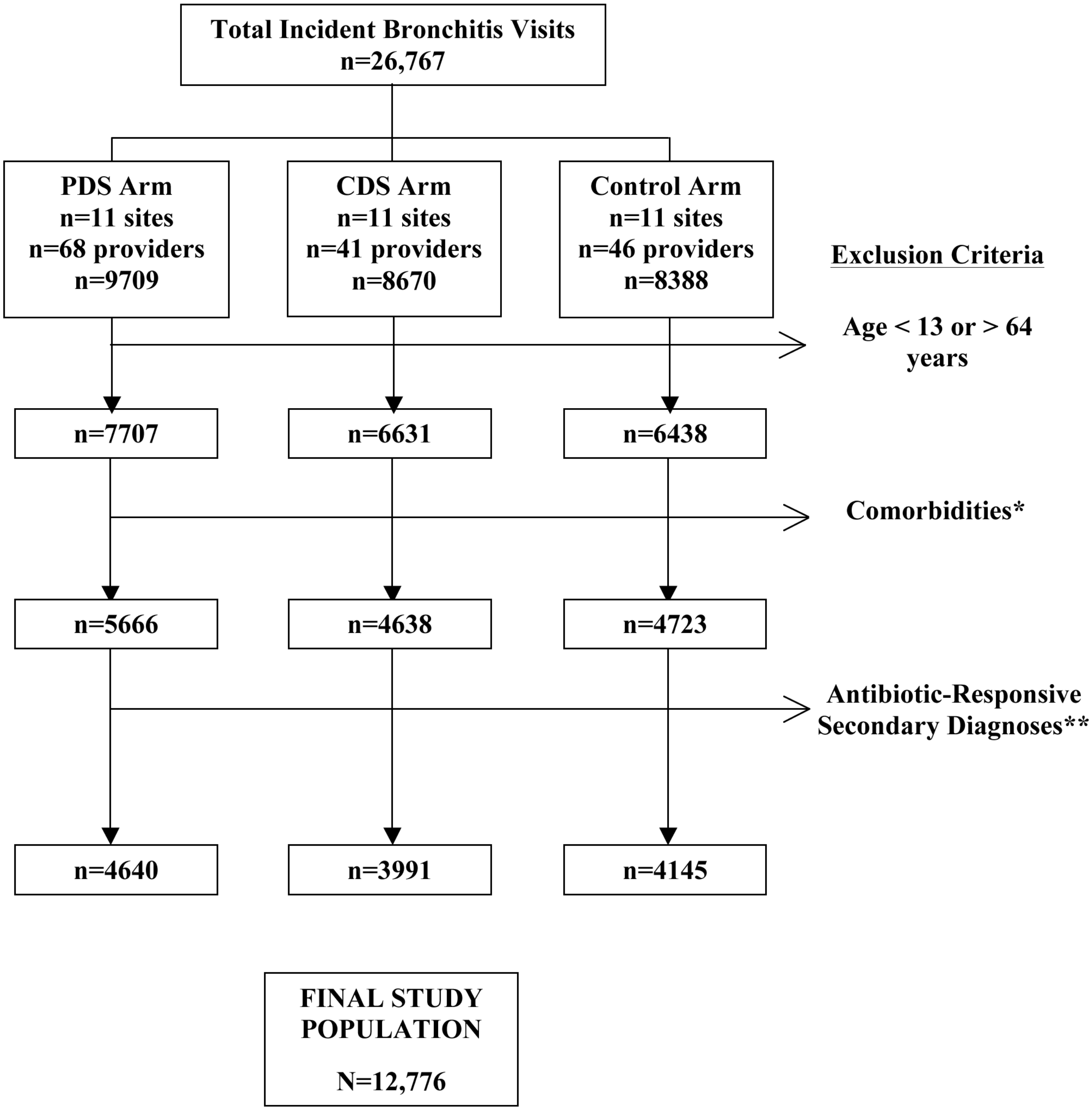

Figure 2. Determination of uncomplicated acute bronchitis visits in final study population

*Comorbidities include chronic lung disease, congestive heart failure, HIV, cystic fibrosis, and malignancy.

**Antibiotic-responsive secondary diagnoses include sinusitis, pharyngitis, otitis media, pneumonia.

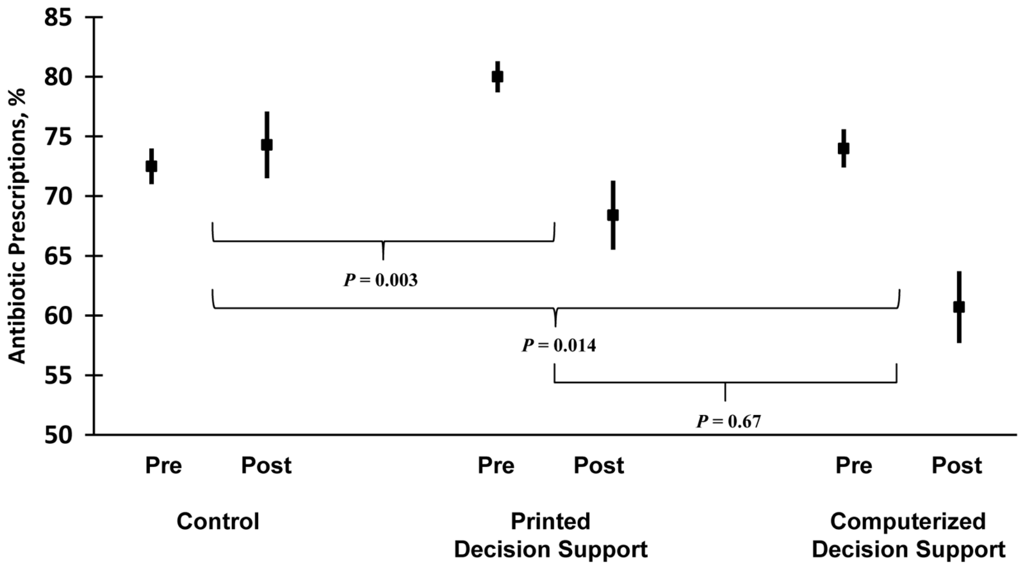

Figure 3. Impact of decision support strategies on antibiotic prescription rates for adolescents and adults diagnosed with uncomplicated acute bronchitis

Error bars for each estimate reflect 95% confidence intervals.

Statistical comparison between groups yielded the following p-values based on interaction terms from multivariable analysis: Δ Control vs. Δ Printed Decision Support = 0.003; Δ Control vs. Δ Computer Decision Support = 0.014; Δ Printed Decision Support vs. Δ Computer Decision Support = 0.67

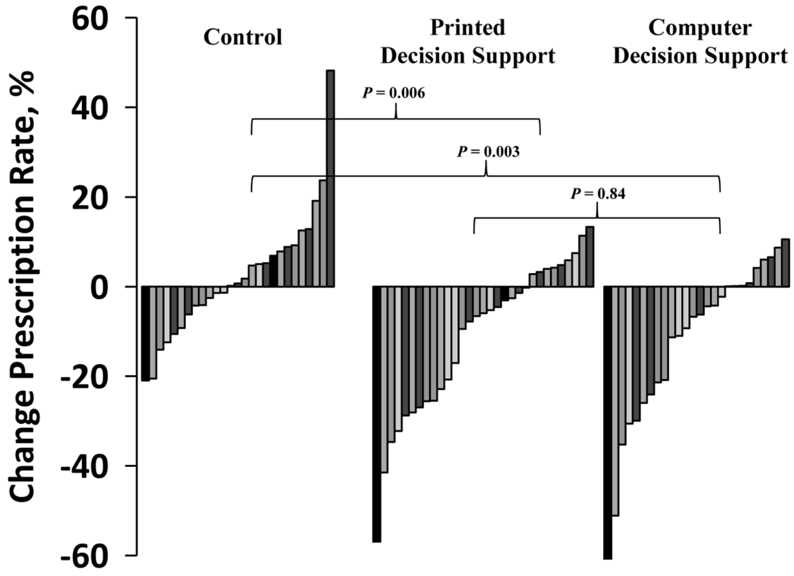

Figure 4. Distribution of changes in provider-level antibiotic prescription rates for adolescents and adults diagnosed with uncomplicated acute bronchitis following implementation of the decision support interventions

Each bar represents the absolute difference in antibiotic prescription rates between intervention and baseline years for an individual provider. Providers required to have at least 10 visits in baseline and intervention periods to be eligible for this analysis, representing 46% of PDS providers (n=31), 63% of CDS providers (n=26) and 59% of control providers (n=27). Statistical comparison between groups yielded the following p-values: Δ Control vs. Δ Printed Decision Support = 0.006; Δ Control vs. Δ Computer Decision Support = 0.003; Δ Printed Decision Support vs. Δ Computer Decision Support = 0.084

Table 1

Patient and provider characteristics related to incident uncomplicated acute bronchitis visits during baseline and study periods.

	Control Sites			Printed Decision Support Intervention Sites			Computer-assisted Decision Support Intervention Sites		
	Baseline Period* (n=3195)	**Study Period (n=950)**	***Between Period P-value***	**Baseline Period* (n=3639)**	**Study Period (n=1001)**	***Between Period P-value***	**Baseline Period* (n=2974)**	**Study Period (N=1017)**	***Between Period P-value***
Age groups**									
13–17 years	6.1%	6.7%		4.5%	4.2%		6.0%	5.5%	
18–34 years	27.5%	28.6%	0.76	28.5%	29.0%	0.91	29.6%	30.2%	0.70
35–49 years	35.6%	35.0%		36.0%	36.8%		36.3%	37.7%	
50–64 years	30.8%	29.7%		31.1%	30.1%		28.2%	26.7%	
Female**	56.3%	59.4%	0.09	59.6%	62.1%	0.14	58.8%	62.1%	0.07
Race/Ethnicity									
White	97.6%	96.6%		95.4%	95.9%		98.1%	97.6%	
Black	1.0%	0.8%	0.005	2.0%	1.5%	0.57	0.5%	0.5%	0.68
Hispanic	0.8%	2.1%		1.6%	1.3%		0.4%	0.4%	
Other/unknown	0.7%	0.4%		1.0%	1.3%		1.0%	1.5%	
Current Smoker**	32.3%	30.7%	0.36	29.9%	24.6%	0.001	30.1%	26.7%	0.04
Vital Sign Abnormalities#									
Temperature ≥ 100 F.	2.5%	2.3%	0.80	3.0%	1.7%	0.02	3.4%	2.0%	0.02
Respiratory Rate ≥ 24 breaths per minute	4.5%	5.4%	0.28	4.9%	6.7%	0.04	4.8%	2.8%	0.01
Heart Rate ≥ 100 beats per minute**	9.1%	8.8%	0.83	6.6%	7.4%	0.38	6.0%	6.0%	0.99
CXR performed**	4.9%	4.2%	0.41	3.6%	3.2%	0.57	5.4%	4.9%	0.57
Provider type**									
MD/DO	96.7%	96.2%	0.48	97.2%	97.5%	0.60	94.3%	90.2%	<0.001
Other	3.3%	3.8%		2.8%	2.5%		5.7%	9.8%	
Provider specialty**									

	Control Sites			Printed Decision Support Intervention Sites			Computer-assisted Decision Support Intervention Sites		
	Baseline Period* (n=3195)	**Study Period (n=950)**	***Between Period P-value***	**Baseline Period* (n=3639)**	**Study Period (n=1001)**	***Between Period P-value***	**Baseline Period* (n=2974)**	**Study Period (N=1017)**	***Between Period P-value***
Internal medicine	30.7%	28.0%	0.11	2.6%	0	<0.001	1.8%	5.5%	<0.001
Return visits§									
Office visits (any)	4.0%	7.6%	<0.001	4.6%	7.1%	0.002	4.5%	8.3%	<0.001
Office visits for bronchitis, pneumonia and COPD.***	0.3%	1.4%	<0.001	0.5%	0.9%	0.16	0.6%	0.5%	0.81
Emergency department visits (any)	0.2%	0.2%	1.0	0.8%	1.2%	0.19	0	0	--
Emergency department visits for bronchitis, Pneum/ COPD***	0.03%	0	1.0	0.03%	0	1.000	0	0	--
Hospitalizations (any)	0.7%	1.0%	0.35	0.7%	0.3%	0.16	0.5%	1.1%	0.07
Hospitalizations for bronchitis, pneumonia, COPD***	0.1%	0.1%	1.0	0.05%	0	1.000	0.1%	0	0.57

* Baseline Period reflects the 3 previous Winter Periods: October – March 2007, 2008 and 2009. The Study Period reflects October – March 2010.

** Between-group (study arm) p-values during baseline period < 0.05

*** Percents are percent of total visits, not of return visits

§ Return visit defined as a subsequent visit occurring within 30 days of an incident visit

Complete vital signs were not performed on all patient visits. Baseline and Study Period sample sizes were as follows: Temperature (Control: 3141; 942; PDS: 3606; 995; CDS: 2918; 1013); Respiratory Rate (Control: 2667; 865; PDS: 3247; 947; CDS: 2393; 953); Heart Rate (Control: 2954; 894; PDS: 3302; 973; CDS: 2664; 978)