The Core Elements of Outpatient Antibiotic Stewardship

Appendix

National Center for Emerging and Zoonotic Infectious Diseases
Division of Healthcare Quality Promotion

CS268900-A

Appendix A. Supplemental Evidence Supporting Outpatient Stewardship

Systematic Reviews

REFERENCE	INTERVENTIONS AND OUTCOMES	METHODS, PARTICIPANTS, AND SETTINGS	RESULTS	CONCLUSIONS
Arnold SR, et al. **Interventions to improve antibiotic prescribing practices in ambulatory care.** *Cochrane Database Syst Rev* 2005. 4:CD003539.	**Interventions** • Physician educational materials • Audit and feedback • Educational meetings • Educational outreach visits • Financial and healthcare system changes • Physician reminders • Patient-based interventions • Multi-faceted interventions **Outcomes** • Improve selection, dose and duration of antibiotics prescribed • Reduce incidence of pathogens with antimicrobial resistance	**Methods** • Systematic review **Participants** • Healthcare consumers or primary care providers **Setting** • Primary care clinics and ambulatory care clinics	• 39 studies • Only small changes observed for single interventions using printed educational materials or audit and feedback. • Active educational interventions are more effective than nonactive interventions. • Delayed prescriptions effectively reduced antibiotic use by patients without negatively affecting patient outcomes. • Multifaceted interventions were more successful in decreasing inappropriate antibiotic prescribing.	• Multifaceted interventions are most effective. • No single intervention is recommended for all settings.
Drekonja DM et al. **Antimicrobial stewardship in outpatient settings: a systematic review.** *Infect Control Hosp Epidemiol* 2015. Feb;36(2):142-52.	**Interventions** • Provider and or patient education • Provider feedback • Delayed prescribing • Communication skills training • Guidelines • Restriction Policies • Computerized clinical decision support • Financial incentives • Rapid diagnostics • Costs reporting **Outcomes** • Prescribing outcomes • Patient outcomes • Microbial outcomes • Costs	**Methods** • Systematic review **Participants** • Primarily healthcare consumers and primary care providers **Setting** • Primary care clinics and ambulatory care clinics	• 50 studies • Stewardship programs using communication skills training and laboratory testing can lower antibiotic use. • Several stewardship interventions can effectively improve antibiotic prescribing. • Patient outcomes were not often reported, but did not appear to worsen due to intervention.	• Outpatient antibiotic stewardship programs can improve antibiotic prescribing without negatively affecting patient outcomes. • Sustainability and scalability of specific interventions is less clear.

REFERENCE	INTERVENTIONS AND OUTCOMES	METHODS, PARTICIPANTS, AND SETTINGS	RESULTS	CONCLUSIONS
McDonagh M, et al. **Improving Antibiotic Prescribing for Uncomplicated Acute Respiratory Tract Infections.** *AHRQ Comparative Effectiveness Reviews* 2016. No. 163.	**Interventions** • Education • Communication • Clinical • System-level • Multifaceted interventions **Outcomes** • Improvement of appropriate antibiotic prescribing • Reduction in antibiotic resistance • Reduction in overall antibiotic prescribing for acute respiratory tract infections (RTIs) • Increases in adverse drug events • Increases in patient dissatisfaction	**Methods** • Systematic review **Participants** • Healthcare consumers (both adults and children) with acute RTIs • Primary care providers **Setting** • Primary care clinics and ambulatory care clinics	• 133 studies • Four interventions showed evidence of improving antibiotic prescribing with without worsening patient outcomes due to reductions in antibiotic prescribing: • Clinic-based parent education (21% reduction). • Public patient education campaigns combined with clinician education (7% prescribing reduction). • Procalcitonin for adults (12% to 72% prescribing reduction). • Electronic decision support systems (improved antibiotic selection and 5% to 9% reduction in prescribing). • Public parent education campaigns reduce overall prescribing without increasing followup visits.	• Several interventions safely reduced antibiotic prescribing or improved appropriate antibiotic prescribing without adversely affecting patient outcomes. • These include education for patients, parents, and clinicians, procalcitonin testing in adults, and electronic clinician decision support.
Ranji SR, et al. **Closing the quality gap: A critical analysis of quality improvement strategies.** (Vol. 4: Antibiotic Prescribing Behavior). Agency for Healthcare Research and Quality (US). 2006. Rockville, MD.	**Interventions** • Clinician education • Patient education • Delayed prescriptions • Audit and feedback • Clinician reminders • Financial or regulatory incentives **Outcomes** • Reductions in inappropriate antibiotic prescribing • Prescribing antibiotics for non-bacterial illnesses • Prescribing broad-spectrum antibiotics when narrow-spectrum agents are indicated	**Methods** • Systematic review **Participants** • Healthcare consumers (both adults and children) with acute respiratory infections • Primary care providers **Setting** • Primary care clinics and ambulatory care clinics	• 54 studies • Interventions demonstrated a median absolute effect of -8.9% reduction in prescribing antibiotic for non-bacterial illnesses. • Antibiotic resistance was measured in two studies, neither of which showed a reduction in resistance. • No individual intervention was most effective at reducing prescribing. • Active educational strategies target clinicians appeared more effective than passive strategies.	• Selected interventions appear effective at reducing both antibiotic overprescribing and inappropriate antibiotic selection. • No single intervention was clearly more effective than others. • Active clinician education interventions appear more effective than passive education.

REFERENCE	INTERVENTIONS AND OUTCOMES	METHODS, PARTICIPANTS, AND SETTINGS	RESULTS	CONCLUSIONS
Ranji SR, et al. **Interventions to reduce unnecessary antibiotic prescribing: A systematic review and quantitative analysis.** *Med Care* 2008. 46(8):847-62.	**Interventions** • Clinician education • Patient education • Audit and feedback • Clinician reminders **Outcomes** • Reduction in proportion of patients receiving antibiotics	**Methods** • Systematic review and quantitative analysis **Participants** • Healthcare consumers (both adults and children) with acute outpatient infections • Primary care providers **Setting** • Primary care clinics and ambulatory care clinics	• 43 studies • Most studies examined antibiotic prescribing for acute respiratory infections. • The quantitative analysis (n=30 studies) found a median reduction of 9.7% in the percent of patients receiving antibiotics • No single intervention was clearly superior. • Active clinician education strategies had a nonsignificant trend toward better efficacy compared to passive education strategies.	• Some interventions are effective at reducing antibiotic use in outpatient settings. • Active clinician education strategies appear to work better than passive education strategies. • Targeting antibiotic prescribing for all ARIs, versus single diagnoses, may lead to larger reductions in antibiotic use.
van der Velden AW, et al. **Effectiveness of physician-targeted interventions to improve antibiotic use for respiratory tract infections.** *Br J of Gen Pract* 2012. 62(605):e801-7.	**Interventions** • Educational materials (patients, clinicians, and the general public) • Educational meetings • Consensus procedure • Local opinion leaders • Near-patient testing • Audit and feedback • Financial incentives • Communications skills training **Outcomes** • Difference of differences for interventions with a before and after measurement with a control group • Differences for interventions with a before and after measurement without a control group • Difference in after measurement for interventions with a control group but without a before measurement	**Methods** • Systematic review **Participants** • Healthcare consumers (both adults and children) with acute outpatient infections • Primary care providers **Setting** • Primary care clinics in high income countries	• 58 studies • About 60% of studies contained interventions that led to significant improvements in antibiotic prescribing. • Interventions targeting decreases in overall antibiotic prescription were more often effective than interventions targeting improvements in antibiotic selection. • Antibiotic prescriptions were reduced on average by 11.6%. First-line antibiotic prescription increased on average by 9.6%. • Combination interventions targeting clinicians were more often effective compared to single interventions. • Interventions containing patient-directed materials demonstrated no added value. • Interventions with the largest effect sizes included communication skills training and point-of-care testing.	• Clinician education, including communication skills training, is important to optimize antibiotic use. • Combination interventions appear to be more effective than individual interventions.

Commitment

REFERENCE	INTERVENTIONS AND OUTCOMES	METHODS, PARTICIPANTS, AND SETTINGS	RESULTS	CONCLUSIONS
Meeker D, et al. **Nudging guideline-concordant antibiotic prescribing: A randomized clinical trial.** *JAMA Intern Med* 2014. 174(3):425-31.	**Interventions** • Poster containing a public commitment to use antibiotics judiciously with clinician picture and signature displayed in examination rooms at point of clinician-patient encounter **Outcomes** • Antibiotic prescribing rates for acute respiratory infections (ARIs) for which antibiotics are inappropriate	**Method** • Randomized clinical trial **Participants** • 15 primary care providers **Setting** • 5 primary care clinics in the United States	• 954 adults with ARI • Poster group had a 19.7 % decrease in inappropriate prescribing for acute respiratory infections compared to controls, p=0.02, controlled for baseline rates of antibiotic prescribing.	• Public commitments in a poster are a low-cost intervention that can result in reduced inappropriate prescribing.
Pollack LA, et al. **Antibiotic stewardship programs in U.S. acute care hospitals: findings from the 2014 National Healthcare Safety Network (NHSN) Annual Hospital Survey.** *Clinical Infectious Diseases* 2016. [Epub ahead of print].	**Interventions** • No intervention; observational study **Outcomes** • Level of variability in antibiotic stewardship programs (ASPs) by hospital characteristic and location	**Method** • Observational study **Participants** • Hospitals enrolled in the National Healthcare Safety Network **Setting** • 2014 National Healthcare Safety Network Annual Hospital Survey	• 4184 US hospitals • On self-report, 39% of hospitals have an ASP meeting all 7 CDC defined core elements of inpatient antibiotic stewardship. • 59% of hospitals with more than 200 beds (59%) had an ASP meeting all Core Elements • 25% of hospitals with less than 50 beds had an ASP meeting all Core Elements • States reporting a percentage of hospitals with all 7 core elements ranged from 7% to 58%. • Written support and salary support for ASP were significantly associated with having an ASP meeting all Core Elements.	• There is wide variability with ASP implementation. • Hospital leadership support appears crucial for comprehensive ASPs • ASPs can be established in hospitals of all sizes.

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DELAYED PRESCRIBING PRACTICES OR WATCHFUL WAITING				
REFERENCE	**INTERVENTIONS AND OUTCOMES**	**METHODS, PARTICIPANTS, AND SETTINGS**	**RESULTS**	**CONCLUSIONS**
Chao JH, et al. **Comparison of two approaches to observation therapy for acute otitis media in the emergency department.** *Pediatrics.* 2008. 121(5):e1352-6.	**Intervention** • Watchful waiting/observation therapy with no prescription or with a delayed antibiotic prescription **Outcomes** • Antibiotic use for AOM at 3 days (primary) and 7-10 days (secondary) • Parental visit satisfaction	**Methods** • Prospective randomized trial **Participants** • Children aged 2 to 12 years diagnosed with AOM and who met criteria for observation **Setting** • Pediatric emergency room of an urban public hospital in the United States (New York)	• 232 patients enrolled, 206 patients completed follow-up • At 3 days: 87% parents of children in the observation group with no antibiotic prescription reported no antibiotic use versus 62% parents of children in the of children in the observation group with a delayed antibiotic prescription. • At 7-10 days, 81% of the observation group with no antibiotic prescription reported no use of antibiotics compared to 53% in the group with a delayed antibiotic prescription. • No differences in satisfaction were observed between the groups.	• Observation therapy was well accepted by parents of children with AOM. • Observation without an antibiotic prescription led to lower antibiotic use for AOM than observation with a delayed antibiotic prescription without affecting visit satisfaction.

DELAYED PRESCRIBING PRACTICES OR WATCHFUL WAITING				
REFERENCE	**INTERVENTIONS AND OUTCOMES**	**METHODS, PARTICIPANTS, AND SETTINGS**	**RESULTS**	**CONCLUSIONS**
de la Poza A, et al. **Prescription strategies in acute uncomplicated respiratory infections: A randomized clinical trial.** *JAMA Intern Med* 2016. 176(1):21-9.	**Interventions** • 4 antibiotic prescriptions strategies for acute uncomplicated respiratory tract infections. • Delayed antibiotic prescription given to patients at the visit with instructions to wait to fill it unless not improving • Delayed antibiotic prescription awaiting patient at clinic, patient to return and collect prescriptions if not improving • Immediate antibiotic prescription issued at visit • No antibiotic prescription issued at visit **Outcomes** • Primary: symptom duration and severity • Secondary: antibiotic use, patient satisfaction, and belief about antibiotic effectiveness among patients complicated respiratory infections.	**Methods** • Open-label, randomized clinical trial **Participants** • Adults with acute, uncomplicated respiratory infections **Setting** • 23 primary care clinics in Spain	• 405 adult patients with acute, uncomplicated respiratory infections • Delayed prescription strategies led to lower antibiotic use: • 91% of patients used antibiotics in the immediate prescription group; • 33% of patients used antibiotics in the group with delayed prescription; • 23% of patients used antibiotics in the group who had to collect the delayed prescription; • 12% of patients used antibiotics in the no prescription group. • Delayed and no prescription strategies led to “slightly greater” symptom burden. • Similar satisfaction was observed among groups.	• Delayed prescription strategies for acute uncomplicated respiratory tract infections are effective in decreasing antibiotic use.

DELAYED PRESCRIBING PRACTICES OR WATCHFUL WAITING				
REFERENCE	**INTERVENTIONS AND OUTCOMES**	**METHODS, PARTICIPANTS, AND SETTINGS**	**RESULTS**	**CONCLUSIONS**
Francis NA, et al. **Delayed antibiotic prescribing and associated antibiotic consumption in adults with acute cough.** *Br J Gen Pract* 2012. 62(602):e639-46.	**Intervention** • No intervention; observational study **Outcomes** • Rates of delayed antibiotic prescribing in adults presenting with acute cough to primary care. • Duration of advised delay • Consumption of delayed antibiotic or another antibiotic at 28 days • Factors associated with antibiotic consumption	**Methods** • Prospective observational cohort study **Participants** • General practitioners • Adult patients with acute cough **Setting** • 14 primary care networks in 13 European countries	• 3368 patients with acute cough • About 6% (n=210) were prescribed delayed antibiotics (median recommended delay 3 days). • 44% (n=75/169) with consumption data used the delayed prescription antibiotic course by 28 days • 30% (n=50/169) started on the day the prescription was written. • 10% took another antibiotic by 28 days. • 45% took no antibiotic by 28 days. Upper respiratory tract/ viral infections diagnoses were associated with lower use of delayed prescription. • Patients who wanted antibiotics were more likely to consume the antibiotics.	• Delayed antibiotic prescribing was not used often for adults presenting to primary care. • Expanding delayed antibiotic prescribing and standardizing prescribing practices may improve antibiotic prescribing.
Little P, et al. **Information leaflet and antibiotic prescribing strategies for acute lower respiratory tract infection: a randomized controlled trial.** *JAMA* 2005. 22;293(24):3029-35.	**Interventions** • One of 3 prescribing strategies was used • Immediate antibiotics • No antibiotics • Delayed antibiotics available by request after 14 days • Information leaflet for acute lower respiratory tract infection **Outcomes** • Clinical signs and symptoms • Reported antibiotic use • Daily diary and satisfaction questionnaire	**Methods** • Randomized controlled trial • Factorial design involving 6 groups: leaflet or no leaflet and 1 of 3 prescribing strategies **Participants** • 37 English general practitioners • Patients aged ≥3 years with acute uncomplicated lower respiratory infections **Setting** • Primary care clinics in England	• 807 patients recruited • No implemented intervention altered cough duration or other clinical outcome. • Cough lasted on average 11.7 days. • The information leaflet did not have any impact on main outcome. • Fewer patients in the delayed and control groups, compared to immediate antibiotic group, used antibiotics, were “very satisfied” with visit, and believed in the antibiotic effectiveness.	• Not prescribing antibiotics, or offering a delayed antibiotic prescribing is associated with minimal differences in symptom burden and may reduce antibiotic use.

DELAYED PRESCRIBING PRACTICES OR WATCHFUL WAITING				
REFERENCE	**INTERVENTIONS AND OUTCOMES**	**METHODS, PARTICIPANTS, AND SETTINGS**	**RESULTS**	**CONCLUSIONS**
Little P, et al. **Delayed antibiotic prescribing strategies for respiratory tract infections in primary care: pragmatic, factorial, randomised controlled trial.** *Brit Med J* 2014. 348:g1606.	**Intervention** • Delayed antibiotic prescribing strategies • Re-contact for a prescription (i.e., patient calls for the prescription) • Post-dated prescription • Post-visit collection of a prescription • No antibiotic prescription **Outcome** • Primary: Symptom severity at days 2-4 • Secondary: antibiotic use by 14 days and patient belief about antibiotic effectiveness	**Methods** • Open, pragmatic, randomized controlled trial **Participants** • Patients aged ≥3 years with acute respiratory tract infections **Setting** • 25 primary care clinics in the United Kingdom	• 889 patients recruited • No significant differences in symptom severity were observed between those who received no prescription and those receiving delayed prescription via any strategy. • Symptom duration did not differ between groups, and no significant difference was observed for patient satisfaction. • Those receiving antibiotics did not appear to benefit from them based on symptom severity scores.	• Interventions involving delayed antibiotic prescriptions or no prescription strategies resulted in fewer than 40% of prescribed antibiotics being used among patients. • Interventions involving delayed prescriptions or no prescriptions were associated with less belief in antibiotic efficacy and similar symptom outcomes compared to immediate antibiotic prescriptions.
McCormick DP, et al. **Nonsevere acute otitis media: a clinical trial comparing outcomes of watchful waiting versus immediate antibiotic treatment**. *Pediatrics* 2005.115(6):1455-65.	**Intervention** • Watchful waiting (WW) versus immediate antibiotic prescription • Educational intervention **Outcome** • Patient satisfaction with care • Resolution of symptoms • Acute otitis media (AOM) failure/recurrence • Nasopharyngeal colonization with antibiotic-resistant Streptococcus pneumoniae	**Methods** • Single-blind, randomized controlled trial (investigators were blinded) **Participants** • Children aged 6 months to 12 years with nonsevere AOM **Setting** • Pediatric clinics in in the United States (Texas)	• 223 children recruited • Parent satisfaction with care did not differ between treatment groups. • Children treated with immediate antibiotics had faster symptom resolution. • In the WW group, 66% of children did not take antibiotics by day 30. • The WW group were reduced by 73% compared to the immediate antibiotic group. • Immediate antibiotic treatment group had more antibiotic adverse drug events than WW group. • Children in the immediate antibiotic group were more likely to have multi-drug resistant *S. pneumoniae* nasopharyngeal colonization at day 12.	• Immediate antibiotic treatment was associated with decreased treatment failures and improved symptom resolution compared to WW, but also higher adverse drug events and higher likelihood of carriage of multi-drug resistant *S. pneumoniae*. • Classification of AOM severity, parent education, symptom management, followup care, and access to effective antibiotics when needed are all important in implementing watchful waiting for children with AOM.

DELAYED PRESCRIBING PRACTICES OR WATCHFUL WAITING				
REFERENCE	**INTERVENTIONS AND OUTCOMES**	**METHODS, PARTICIPANTS, AND SETTINGS**	**RESULTS**	**CONCLUSIONS**
Siegel R, et al. **Treatment of otitis media with observation and a safety-net antibiotic prescription.** *Pediatrics* 2003. 112(3):527-31.	**Intervention** • Delayed antibiotic prescription ("safety-net prescription") **Outcomes** • Primary: parental willingness to treat AOM without antibiotics and with pain medicine alone • Secondary: filling of antibiotic prescription, parents' future plans to use antibiotics for AOM	**Methods** • Cohort study **Participants** • Children aged 1 to 12 years with nonsevere AOM **Setting** • 11 pediatric clinics in the United States	• 194 children enrolled, 175 with complete follow-up • At follow-up, 31% of parents had filled the antibiotic prescription. • 63% of parents reported willingness in future to use pain medicine only without antibiotics for AOM.	• Safety-net prescriptions can decrease antibiotic use for non-severe AOM, and some parents find it an acceptable treatment strategy.
Spiro DM, et al. **Wait-and-see prescription for the treatment of acute otitis media: a randomized controlled trial.** *JAMA.* 2006. 296(10):1235-41.	**Intervention** • "Wait and see" (i.e. delayed) antibiotic prescription versus standard prescription for children with acute otitis media (AOM) **Outcomes** Filling of the antibiotic prescription Clinical symptoms and symptoms resolution	Methods Randomized controlled trial Participants Children aged 6 months to 12 years with AOM Setting Emergency department in Northeastern United States	283 children More parents in the wait and see group did not fill the antibiotic prescription (62%) compared to the standard prescription group (13% did not fill antibiotic prescription, $p<0.001$). No differences between groups were observed for the frequency of fever, ear pain, or unscheduled medical visits. In the wait and see group, fever and ear pain were associated with filling the antibiotic prescription.	Wait and see antibiotic prescriptions reduced antibiotic use in children with AOM.

COMMUNICATION SKILLS TRAINING				
REFERENCE	**INTERVENTIONS AND OUTCOMES**	**METHODS, PARTICIPANTS, AND SETTINGS**	**RESULTS**	**CONCLUSIONS**
Little P, et al. **Effects of internet-based training on antibiotic prescribing rates for acute respiratory-tract infections: a multinational, cluster, randomised, factorial, controlled trial.** *Lancet.* 2013. 382(9899):1175-82.	**Intervention** • Internet based training on communication skills, C-reactive protein (CRP) testing, or both versus standard care **Outcome** • Changes in antibiotic prescribing for respiratory tract infections (RTIs)	**Methods** • Cluster randomized controlled trial **Participants** • Primary care providers **Settings** • 246 primary care clinics in 6 European countries	• 4264 patients • Training in CRP testing and communication skills independently led to reductions in antibiotic prescribing for RTIs, and combination of both trainings led to largest reduction.	• Internet training for CRP testing and communications skills led to reductions in antibiotic prescribing for RTIs.
Cals JW, et al. **Enhanced communication skills and C-reactive protein point-of-care testing for respiratory tract infection: 3.5-year follow-up of a cluster randomized trial.** *Annals of Family Medicine.* 2013. 11(2):157-64.	**Intervention** • Physician enhanced communication skills training • Point-of-care C-reactive protein (CRP) **Outcome** • Patient visits for respiratory tract infections (RTIs) • Percent of RTI episodes treated with antibiotics	**Methods** • Pragmatic, cluster-randomized controlled trial • 3.5 years of follow-up **Participants** • Patients with family physician visits for RTIs **Setting** • 20 family practices in the Netherlands	• 379 patients • No difference in number of patient visits for RTIs among groups. • RTI episodes treated by physicians who received communications training were less likely to receive antibiotics in follow-up period (26% with communications training v. 39% control, p=0.02). • No difference in antibiotic treatment during follow-up for RTI episodes in CRP group.	• Communications training led to sustained reductions in the percent of RTIs leading to antibiotic prescriptions, while CRP testing did not.

REQUIRE EXPLICIT WRITTEN JUSTIFICATION FOR NON-RECOMMENDED ANTIBIOTIC PRESCRIBING				
REFERENCE	**INTERVENTIONS AND OUTCOMES**	**METHODS, PARTICIPANTS, AND SETTINGS**	**RESULTS**	**CONCLUSIONS**
Meeker et al. **Effect of behavioral interventions on inappropriate antibiotic prescribing among primary care practices: A randomized clinical trial.** *JAMA* 2016. 315(6):562-70.	**Interventions:** **3 behavioral interventions** • Suggested alternatives to antibiotics placed within electronic health records for these diagnoses • Accountable justification required in medical record for non-recommended antibiotic prescribing • Peer comparison to top-performing peers **Outcomes** • Rate of antibiotic prescribing for acute respiratory tract infections for which antibiotics are not indicated	**Methods** • Cluster randomized clinical trial **Participants** • 248 primary care clinicians **Settings** • 47 primary care practices in the United States	• 31,712 visits for acute respiratory tract infections for which antibiotics are not indicated • 14,753 during baseline • 16,959 during intervention • Antibiotic prescribing decreased from: • Controls: 24.1% to 13.1% • Suggested alternatives: 22.1% to 6.1% ($P = .66$ for differences compared to control group) • Accountable justification: 23.2% to 5.2% ($P < .001$) • Peer comparison: 9.9% to 3.7 (**P** < .001). • Compared to the control group, no intervention showed significant diagnosis shifting.	• Accountable justification and peer comparison interventions reduced antibiotic prescribing for acute respiratory tract infections for which antibiotics are not indicated

CLINICAL DECISION SUPPORT				
REFERENCE	**INTERVENTIONS AND OUTCOMES**	**METHODS, PARTICIPANTS, AND SETTINGS**	**RESULTS**	**CONCLUSIONS**
McGinn TG, et al. **Efficacy of an evidence-based clinical decision support in primary care practices: A randomized clinical trial.** *JAMA Intern Med* 2013. 173(17):1584-11.	**Intervention** • Clinical decision support involving integration of Walsh rule for streptococcal sore throat and Heckerling rule for pneumonia **Outcomes** • Frequency of antibiotic prescriptions and streptococcal tests in experimental versus control group • Use of clinical prediction rule in EHR	**Methods** • Randomized clinical trial **Participants** • Attending physicians, fellows, residents and nurse practitioners • Patients with complaints consistent with pharyngitis or pneumonia **Setting** • Two large urban ambulatory care practices in the United States (New York)	• 168 primary care providers with 984 visits with clinical decision rule triggered • Clinicians in the intervention group used the clinical prediction rules in 58% of visits. • Intervention clinicians were less likely to prescribe antibiotics than control clinicians (RR = 0.75; 95% CI, 0.60-0.92). • Number needed to treat in order to prevent one antibiotic prescription was 10.8. • Intervention clinicians ordered rapid streptococcal tests for patients with pharyngitis less often than control clinicians (RR 0.75; 95% CI, 0.58-0.97).	• Clinical prediction rules integrated into EHRs can reduce inappropriate antibiotic prescribing.
Jenkins TC, et al. **Effects of clinical pathways for common outpatient infections on antibiotic prescribing.** *Am J Med.* 2013;126(4):327-35 e312.	**Intervention** • Clinical decision support targeting antibiotic prescribing for common conditions • Patient education materials **Outcomes** • Change in antibiotic prescribing over time for non-pneumonia acute respiratory infections (ARIs) • Change over time in broad-spectrum antibiotic prescriptions for ARIs	**Methods** • Quasi-experimental study **Participants** • Clinicians working in primary care clinics **Setting** • Primary care clinics in the United States (Colorado), including adult and pediatric clinics; urban, suburban and rural clinics; academic and private providers	• 8 primary care clinics • Antibiotic prescriptions for visits for non-pneumonia ARIs decreased from 42.7% to 37.9% (11.2% relative reduction) in the intervention group compared to 39.8% to 38.7% in the control group (2.8% relative reduction) during the intervention period. • Use of broad-spectrum antibiotics decreased from 26.4% to 22.6% in the intervention group (14.4% relative reduction) compared to a 20.0% to 19.4% reduction in the control group (3.0% relative reduction).	• Clinical decision support was associated with reduced antibiotic prescriptions for non-pneumonia ARIs and reduced use of broad-spectrum antibiotics during one year of implementation.

CLINICAL DECISION SUPPORT REFERENCE	INTERVENTIONS AND OUTCOMES	METHODS, PARTICIPANTS, AND SETTINGS	RESULTS	CONCLUSIONS
Gonzales R, et al. **A cluster randomized trial of decision support strategies for reducing antibiotic use in acute bronchitis.** *JAMA Intern Med* 2013. 173(4):267-73.	**Interventions** • Clinical decision support, through the electronic medical record, or printed tools targeting antibiotic prescribing for acute bronchitis • Clinician and patient education • Audit and feedback • Controls without interventions **Outcomes** • Reductions in antibiotic prescribing for acute uncomplicated bronchitis.	**Methods** • Cluster randomized controlled trial **Participants** • Primary care clinicians **Setting** • 33 primary care practices in the United States (Pennsylvania)	• 12,776 visits for acute bronchitis • Prescribing for acute bronchitis reduced by 11.7% in the print-based strategy and 13.7% in the EMR-based strategy. • Prescribing at control sites increased slightly.	• Clinical decision support strategies for acute bronchitis can help reduce overuse of antibiotics in primary care. • The observed effect in print-based versus computer-based interventions showed no significant differences.
Rattinger GB, et al. **A sustainable strategy to prevent misuse of antibiotics for acute respiratory infections.** *PLoS One* 2012. 7(12):e51147.	**Intervention** • Clinical decision support promoting adherence to clinical practice guidelines for acute respiratory infections (ARIs) **Outcomes** • Guideline concordance and proportion of inappropriate antibiotic prescribing • Reductions in fluoroquinolone and azithromycin use	**Methods** • Non-randomized retrospective controlled study **Participants** • Primary care providers for an outpatient veteran population **Setting** • Outpatient clinics in a veteran's healthcare system in the United States	• 3831 patients • Clinical decision support was associated with greater clinical practice guideline adherence (RR=2.57 95% CI, 1.87 to 3.54). • Inappropriate prescriptions for fluoroquinolones and azithromycin decreased from 22% to 3% (P<0.0001).	• A clinical decision support system decreased unwarranted use of fluoroquinolones and azithromycin for ARI and improved antibiotic use for ARI in an outpatient veterans' healthcare system.
Linder JA, et al. **Documentation-based clinical decision support to improve antibiotic prescribing for acute respiratory infections in primary care: A cluster randomised controlled trial.** *Inform Prim Care* 2009. 17(4):231-40.	**Intervention** • Electronic health record-based clinical decision support for acute respiratory infection (ARI) — "ARI Smart Form" versus standard care **Outcome** • Antibiotic prescribing for acute respiratory tract infections	**Methods** • Randomized controlled trial **Participants** • Primary care providers **Setting** • 27 primary care clinics in the United States (Massachusetts)	• 21,961 visits for ARIs • ARI Smart Form only used in 6% of eligible visits. • Antibiotic prescribing for intervention clinics was not different compared to controls: odds ratio (OR) 0.8; 95% CI 0.6-1.2. • When ARI Smart Form was used (per protocol analysis), ARI prescribing was modestly improved.	• A clinical decision support tool for ARIs, the ARI Smart Form, was rarely used by clinicians and thus did not improve antibiotic prescribing for ARIs.

CLINICAL DECISION SUPPORT

REFERENCE	INTERVENTIONS AND OUTCOMES	METHODS, PARTICIPANTS, AND SETTINGS	RESULTS	CONCLUSIONS
Forrest, C. B., et al. **Improving adherence to otitis media guidelines with clinical decision support and physician feedback.** *Pediatrics* 2013. 131(4): e1071-1081.	**Intervention** • Clinical decision support (CDS) in an electronic health record system • Audit and feedback to clinicians with peer comparison **Outcome** • Physician guideline adherence for management of acute otitis media (AOM) and otitis media with effusion (OME)	**Methods** • Factorial-design cluster randomized trial **Participants** • Primary care providers **Setting** • Primary care network in the United States (Pennsylvania, New Jersey, and Delaware)	• 24 practices with 139,305 visits for AOM and OME • Guidelines were adhered to in 15% and 5% of AOM and OME cases, respectively during the baseline period. • Improvements in guideline adherence was larger in visits with CDS and audit and feedback • Audit and feedback combined with CDS did not improve guideline adherence beyond levels observed for audit and feedback alone.	• Both CDS and audit and feedback effectively increased adherence to guidelines for treatment of AOM and OME • The effect of the individual interventions did not appear to be additive.

CALL CENTERS, NURSE HOTLINES, OR PHARMACIST CONSULTATIONS

REFERENCE	INTERVENTIONS AND OUTCOMES	METHODS, PARTICIPANTS, AND SETTINGS	RESULTS	CONCLUSIONS
Harper R, et al. **Optimizing the use of telephone nursing advice for upper respiratory infection symptoms.** *Am J Manag Care* 2015. 21(4): 264-270.	**Intervention** • Use of a nursing advice hotline to optimize self-care for upper respiratory infections **Outcomes** • Clinical outcomes associated with related cases • Sufficiency of advice as evidence by no return calls within 7 days leading to a "higher" level of care, such as an in-person appointment.	**Methods** • Retrospective observational study **Participants** • Adult patients 18 years and older who called into a self-care advice line for URI symptoms **Setting** • Large healthcare system in the United States (California)	• 279,625 calls • For 88% of initial advice calls, self-care advice over the phone alone was sufficient. • Most follow-up calls made by the patient were for additional advice or other information.	• URI symptoms can be effectively managed by nurses via a telephone advice line.

AUDIT AND FEEDBACK REFERENCE	INTERVENTIONS AND OUTCOMES	METHODS, PARTICIPANTS, AND SETTINGS	RESULTS	CONCLUSIONS
Gerber JS, et al. **Effect of an outpatient antimicrobial stewardship intervention on broad-spectrum antibiotic prescribing by primary care pediatricians: A randomized trial.** *JAMA* 2013. 309(22): 2345-52. Gerber JS, et al. **Durability of benefits of an outpatient antimicrobial stewardship intervention after discontinuation of audit and feedback.** *JAMA* 2014; 312(23): 2569-2570.	**Intervention** • Quarterly audit and feedback on antibiotic prescribing practices for sinusitis, pharyngitis, and pneumonia with peer comparisons • One hour of clinician education **Outcomes** • Broad-spectrum antibiotic prescribing rates for sinusitis, pharyngitis, and pneumonia • Antibiotic prescribing for viral infections	**Methods** • Cluster randomized controlled trial **Participants** • Pediatric primary care providers **Setting** • 18 pediatric primary care practices in the United States (New Jersey)	• Intervention group showed a reduction in broad-spectrum antibiotic prescribing compared to controls with6.7% difference in differences. • No change in group A *Streptococcus* pharyngitis prescribing or for viral infections, which were both relatively appropriate at baseline. • Broad-spectrum prescribing returned to baseline rates once audit-and feedback stopped.	• Audit and feedback with peer comparisons and with clinician education led to decreases in non-recommended broad-spectrum antibiotic prescribing. • Benefits were not sustained once the audit-and-feedback ended.
Meeker et al. **Effect of behavioral interventions on inappropriate antibiotic prescribing among primary care practices: A randomized clinical trial.** *JAMA* 2016;315(6):562-70.	**Interventions** **3 behavioral interventions** • Suggested alternatives to antibiotics placed within electronic health records for these diagnoses • Accountable justification required in medical record for non-recommended antibiotic prescribing • Peer comparison to top-performing peers **Outcomes** • Rate of antibiotic prescribing for acute respiratory tract infections for which antibiotics are not indicated	**Methods** • Cluster randomized clinical trial **Participants** • 248 primary care clinicians **Settings** • 47 primary care practices in the United States	• 31,712 visits for acute respiratory tract infections for which antibiotics are not indicated: • 14753 during baseline • 16959 during intervention period. • Antibiotic prescribing decreased from: • Controls: 24.1% to 13.1% • Suggested alternatives: 22.1% to 6.1% ($P = .66$ for differences compared to control group) • Accountable justification: 23.2% to 5.2% ($P < .001$) • Peer comparison: 9.9% to 3.7 ($P < .001$). • Compared to the control group, no intervention showed significant diagnosis shifting.	• Accountable justification and peer comparison interventions reduced antibiotic prescribing for acute respiratory tract infections for which antibiotics are not indicated

AUDIT AND FEEDBACK				
REFERENCE	**INTERVENTIONS AND OUTCOMES**	**METHODS, PARTICIPANTS, AND SETTINGS**	**RESULTS**	**CONCLUSIONS**
Butler CC, et al. **Effectiveness of multifaceted educational programme to reduce antibiotic dispensing in primary care: Practice based randomised controlled trial.** *BMJ* 2012. 344:d8173.	**Intervention** • Multifaceted clinician education, including communication skills, targeting antibiotic prescribing versus standard care • Audit and feedback of practice antibiotic dispensing data **Outcomes** • Primary: total number of antibiotics dispensed per 1000 patients by practice • Secondary: return visits and hospital admissions for respiratory tract infections, and cost	**Methods** • Randomized controlled trial **Participants** • General practitioners **Setting** • General practices in United Kingdom (Wales)	• 68 practices serving 480,000 patients • A 4.2% reduction in total antibiotic prescribing was observed in the intervention group compared to controls in one year (p=0.02). • No differences in hospital admissions or return visits for respiratory tract infections were observed between the intervention and control groups. • 5.5% non-significant decreased in antibiotic dispensing cost in intervention group compared to controls.	• A clinician educational intervention led to reductions in antibiotic dispensing with no changes in hospital admissions, return visits, or costs.
Finkelstein JA, et al. **Impact of a 16-community trial to promote judicious antibiotic use in Massachusetts.** *Pediatrics* 2008. 121(1):e15-23.	**Intervention** • Multi-faceted intervention with clinician education, parent education, and audit and feedback on antibiotic prescribing **Outcomes** • Overall oral antibiotic dispensing per person-year of observation for children 3 to <72 months of age	**Methods** • Community-level cluster-randomized controlled trial **Participants** • Clinicians, parents, and pediatric patients aged 6 years or younger **Setting** • Non-overlapping communities in the United States (Massachusetts)	• 16 communities with 223,135 person-years observed • Decreasing antibiotic prescribing was seen in all groups, including controls, during study period. • Intervention led to 4.2% decrease in overall antibiotic prescribing among children 24 to <48 months old and 6.7% among children 48 to < 72 months old compared to control communities. • No difference in antibiotic prescribing for intervention or control communities for children aged 3 to <24 months.	• A multifaceted, sustained, community level intervention modestly decreased antibiotic use.

AUDIT AND FEEDBACK REFERENCE	INTERVENTIONS AND OUTCOMES	METHODS, PARTICIPANTS, AND SETTINGS	RESULTS	CONCLUSIONS
Metlay JP, et al. **Cluster-randomized trial to improve antibiotic use for adults with acute respiratory infections treated in emergency departments.** *Ann Emerg Med* 2007. 50(3):221-30.	**Intervention** • Clinician and patient education • Audit and feedback on prescribing practices for upper respiratory infections (URIs) and acute bronchitis **Outcomes** • Primary: Proportion of patients URIs and acute bronchitis with antibiotic prescribed • Secondary: antibiotic prescribing for antibiotic-appropriate respiratory infections, return ED visits within 2 weeks, and hospital admission within 2 weeks	**Methods** • Cluster-randomized controlled trial **Participants** • Emergency department (ED) clinicians and patients **Setting** • Hospital EDs, including veterans and non-veterans hospitals in the United States	• 16 EDs with 5,665 visits by adults for acute respiratory infections • Intervention sites had a significant decrease in antibiotic prescribing for URIs and acute bronchitis (-10%; 95% CI -18 to -2%), compared to no change in control sites (0.5% 95% CI -3 to 5%). • No significant increases in emergency department return visits or patient satisfaction was observed among control or intervention sites.	• Multifaceted education interventions combined with audit and feedback can decrease antibiotic prescribing for ED patients with URIs and acute bronchitis.
Hallsworth M, et al. **Provision of social norm feedback to high prescribers of antibiotics in general practice: a pragmatic national randomised controlled trial.** *The Lancet* 2016. 387:1743-52	**Interventions** • Audit and feedback as a letter from England's Chief Medical Officer sent to the high-prescribing practices defined as the top 20% for their National Health Service (NHS) Local Area Team versus no communication • Patient education materials versus no materials **Outcomes** • Rate of antibiotics dispensed per 1000 weighted population, controlling for past prescribing	**Methods** • Pragmatic factorial randomized controlled trial • Analysis by intention-to-treat **Participants** • General practitioners (GP) **Setting** • GP practices NHS clinics across England	• 1581 practices • Letters sent to 3227 GPs • Intervention group had 126.98 antibiotics dispensed per 1000 population versus and 131.25 antibiotics dispensed per 1000 population in the control group (difference of 3.3%, $p<0.001$). • Estimated 73,406 fewer antibiotics dispensed in intervention group. • No difference in antibiotic prescribing for patient educational materials.	• Audit and feedback from an important figure (e.g. England's Chief Medical Officer) reduced antibiotic prescribing at the national level.

Education

EVIDENCE SUPPORTING EDUCATIONAL EFFORTS TARGETING PARENTS AND PATIENTS TO IMPROVE ANTIBIOTIC USE				
REFERENCE	**INTERVENTIONS AND OUTCOMES**	**METHODS, PARTICIPANTS, AND SETTINGS**	**RESULTS**	**CONCLUSIONS**
Mangione-Smith R, et al. **Communication Practices and Antibiotic Use for Acute Respiratory Tract Infections in Children.** *Ann Fam Med* 2015. 13(3): 221-227.	**Intervention** • No intervention; observational study. **Outcome:** • Communication techniques used by providers that were associated with prescribing antibiotics for acute respiratory tract infections (ARTIs) and with parent visit satisfaction	**Methods** • Cross-sectional study with parent and provider post-visit surveys **Participants** • Pediatric providers • Parents of children (6 months to 10 years old) presenting with complaints consistent with ARTIs **Setting** • 10 pediatric practices in the United States (Washington)	• 28 pediatric providers • 1,284 parents • Communication techniques using recommendations for treating symptoms were associated with lower risk of antibiotic prescribing for ARTIs. • Communication techniques that combined explanations of why antibiotics are not needed with recommendations for treating symptoms were associated with lower risk of antibiotic prescribing and higher parental visit satisfaction.	• Communication strategies combining explanations of why antibiotics are not needed with recommendations for treating symptoms may help providers decrease inappropriate antibiotic prescribing while helping maintain parental visit satisfaction.
Mangione-Smith R, et al. **Parent expectations for antibiotics, physician-parent communication, and satisfaction.** *Arch Pediatr Adolesc Med* 2001;155(7): 800-806.	**Intervention** • No intervention; observational study. **Outcome** • Physician perception of parental pressure for antibiotics • Physician-perceived pressure to prescribe antibiotics • Parental visit-specific satisfaction	**Methods** • Qualitative study involving pre- and post-visit survey **Participants** • Physicians and eligible parents who attended acute care visits for their child **Setting** • 2 private practice pediatric clinics in the United States (California)	• 10 physicians and 295 parents • Half of parents expected antibiotics prior to the visit, but only 1% of visits verbally requested them. • Physicians perceived parental expectation for antibiotics 34% of the time without a direct request by parents for antibiotics. • Offering a contingency plan of possibly receiving future antibiotics if their child did not improve was associated with higher satisfaction among parents who expected but did not receive antibiotics.	• A contingency plan should be considered for parents expecting antibiotics for their children who do not need antibiotics.

EVIDENCE SUPPORTING EDUCATIONAL EFFORTS TARGETING PARENTS AND PATIENTS TO IMPROVE ANTIBIOTIC USE

REFERENCE	INTERVENTIONS AND OUTCOMES	METHODS, PARTICIPANTS, AND SETTINGS	RESULTS	CONCLUSIONS
Roberts, RM, et al. **Can Improving Knowledge of Antibiotic-Associated Adverse Drug Events Reduce Parent and Patient Demand for Antibiotics?** *Health Serv Res and Man Epi* 2015. 1-5.	**Intervention** • No intervention; observational study. **Outcomes** • Patient and parent knowledge and attitudes about antibiotics and adverse drug events (ADEs) from antibiotics	**Methods** • Computer assisted telephone focus groups Participants • Adult patients and mothers of young children **Setting** • United States	• Familiarity with side effects of antibiotics were common. • Few mothers were familiar with severe antibiotic-associated ADEs. • Most mothers felt strongly that information about severe ADEs should be shared with parents at the time an antibiotic is prescribed. • Adult patients did not believe that antibiotic-associated ADEs was a significant issue.	• Parents of pediatric patients are interested in information about antibiotic-associated ADEs. • Adult patients may be less receptive about receiving information about antibiotic-associated ADEs.

EVIDENCE SUPPORTING EDUCATIONAL EFFORTS TARGETING CLINICIANS TO IMPROVE ANTIBIOTIC USE

REFERENCE	INTERVENTIONS AND OUTCOMES	METHODS, PARTICIPANTS, AND SETTINGS	RESULTS	CONCLUSIONS
Butler CC, et al. **Effectiveness of multifaceted educational programme to reduce antibiotic dispensing in primary care: Practice based randomised controlled trial.** *BMJ* 2012;344:d8173.	**Intervention** • Multifaceted clinician education, including communication skills, targeting antibiotic prescribing versus standard care • Audit and feedback of practice antibiotic dispensing data **Outcomes** • Primary: total number of antibiotics dispensed per 1000 patients by practice • Secondary: Return visits and hospital admissions for respiratory tract infections, and cost	**Methods** • Randomized controlled trial **Participants** • General practitioners **Setting** • General practices in the United Kingdom (Wales)	• 68 practices serving 480,000 patients • A 4.2% reduction in total antibiotic prescribing was observed in the intervention group compared to controls in one year (p=0.02). • No differences in hospital admissions or return visits for respiratory tract infections were observed between the intervention and control groups. • 5.5% non-significant decreased in antibiotic dispensing cost in intervention group compared to controls	• A clinician educational intervention led to reductions in antibiotic dispensing with no changes in hospital admissions, return visits, or costs.

EVIDENCE SUPPORTING EDUCATIONAL EFFORTS TARGETING CLINICIANS TO IMPROVE ANTIBIOTIC USE				
REFERENCE	**INTERVENTIONS AND OUTCOMES**	**METHODS, PARTICIPANTS, AND SETTINGS**	**RESULTS**	**CONCLUSIONS**
Harris RH, et al. **Optimizing antibiotic prescribing for acute respiratory tract infections in an urban urgent care clinic.** *J Gen Internal Med* 2003.18(5):326-34.	**Intervention** • Clinician education targeting antibiotic prescribing for acute respiratory tract infections (ARTIs) • Posters directed at providers placed in exam rooms • Patient education through an interactive computerized education (ICE) module. • Patients who chose not to participate in the ICE were considered to have been exposed to the "limited" intervention **Outcomes** • Proportion of patients with ARTIs who received antibiotics	**Methods** • Prospective, nonrandomized controlled trial **Participants** • Adults with ARTIs **Setting** • Urban urgent care clinic serving the major public hospital in the United States (Colorado)	• 554 adults with ARTIs • Antibiotic prescribing for patients diagnosed with acute bronchitis decreased from 58% to 30% in those exposed to the limited intervention, and to 24% among those exposed to full intervention ($p<0.001$ compared to baseline). • Antibiotic prescribing for nonspecific upper respiratory tract infections decreased from 14% to 3% in those exposed to the limited intervention, and to 1% among those exposed to the full intervention ($p<0.001$ compared to baseline).	• A combination of patient and provider educational materials can reduce antibiotic prescribing for adults with ARTIs.
Juzych NS, et al. **Improvements in antimicrobial prescribing for treatment of upper respiratory tract infections through provider education.** *J Gen Internal Med* 2005. 20(10):901-5.	**Intervention** • Clinician education using interactive and case-based learning targeting antibiotic prescribing for upper respiratory tract infections (URIs) **Outcomes** • Improvements in antibiotic prescribing for URIs	**Methods** • Prospective nonrandomized controlled trial **Participants** • Primary care physicians **Setting** • Four primary care clinics within a staff model health maintenance organization in the United States (Michigan)	• 30 primary care physicians • Antibiotic prescribing in the intervention group decreased 24.6% for both pediatric and adult medicine clinicians. • In the control group, no significant decline in antibiotic prescribing was observed.	• An educational program involving interaction and case-based learning improved antibiotic prescribing for URIs by primary care providers.

ACADEMIC DETAILING				
REFERENCE	**INTERVENTIONS AND OUTCOMES**	**METHODS, PARTICIPANTS, AND SETTINGS**	**RESULTS**	**CONCLUSIONS**
Gjelstad, S., et al. **Improving antibiotic prescribing in acute respiratory tract infections: cluster randomised trial from Norwegian general practice** (prescription peer academic detailing (Rx-PAD) study). *BMJ* 2013. 347: f4403.	**Intervention** • Academic detailing on antibiotic prescribing for respiratory tract infections • Clinician education • Audit and feedback **Outcomes** • Improvements in antibiotic prescribing for respiratory tract infections • Improvements in broad-spectrum antibiotic prescribing	**Methods** • Cluster randomized controlled trial **Participants** • General practitioners **Setting** • General practice clinics in Norway	• 382 general practitioners • Reductions in antibiotic prescribing were observed in the intervention group compared to the control groups (odds ratio 0.72, 95% confidence interval 0.61 to 0.84). • Prescribing of non-penicillin V drugs also decreased in the intervention arm (0.64, 0.49 to 0.82).	• Education interventions improved antibiotic prescribing among general practitioners in Norway.