Supplementary Evidence Supporting Outpatient Stewardship Systematic Reviews

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| 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. |
| 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:  o Clinic-based parent education (21% reduction).  o Public patient education campaigns combined with clinician education (7% prescribing reduction).  o Procalcitonin for adults (12% to 72% prescribing reduction).  o Electronic decision support systems (improved antibiotic selection and 5% to 9% reduction in prescribing).  o Public parent education campaigns reduce overall prescribing without increasing follow-up 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. |
| 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 with 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 with 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

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| 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 with 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 department 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 with 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. |
| 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.  o Delayed antibiotic prescription given to patients at the visit with instructions to wait to fill it unless not improving  o Delayed antibiotic prescription awaiting patient at clinic, patient to return and collect prescriptions if not improving  o Immediate antibiotic prescription issued at visit  o 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:  o 91% of patients used antibiotics in the immediate prescription group;  o 33% of patients used antibiotics in the group with delayed prescription;  o 23% of patients used antibiotics in the group who had to collect the delayed prescription;  o 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. |
| 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 with 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. |
| Little P, et al. Delayed antibiotic prescribing strategies for respiratory tract infections in primary care: pragmatic, factorial, randomized controlled trial.  *Brit Med J* 2014. 348:g1606. | **Intervention**  • Delayed antibiotic prescribing strategies  o Re-contact for a prescription (i.e., patient calls for the prescription)  o Post-dated prescription  o 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 with 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 with 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 with 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, follow-up care, and access to effective antibiotics when needed are all important in implementing watchful waiting for children with AOM. |
| 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 with 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, randomized, 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. |

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| 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  o 14,753 during baseline  o 16,959 during intervention  • Antibiotic prescribing decreased from:  o Controls: 24.1% to 13.1%  o Suggested alternatives: 22.1% to 6.1% (p = 0.66 for differences compared with control group)  o Accountable justification: 23.2% to 5.2% (p<0.001)  o Peer comparison: 9.9% to 3.7 (p<0.001).  • Compared with 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 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 with 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 with 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. |
| 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 randomized 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 with 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. |
| 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. |

Tracking and Reporting

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| 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 with 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:  o 14753 during baseline  o 16959 during intervention period.  • Antibiotic prescribing decreased from:  o Controls: 24.1% to 13.1%  o Suggested alternatives: 22.1% to 6.1% (p = 0.66 for differences compared with control group)  o Accountable justification: 23.2% to 5.2% (p<0.001)  o Peer comparison: 9.9% to 3.7 (p<0.001).  • Compared with 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 |
| Butler CC, et al. Effectiveness of multifaceted educational program to reduce antibiotic dispensing in primary care: Practice based randomized 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 with 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 with 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 with control communities.  • No difference in antibiotic prescribing for intervention or control communities for children aged 3 to <24 months. | • A large community intervention modestly decreased antibiotic use. |
| 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 with 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 randomized 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

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| Evidence Supporting Educational Efforts Targeting Parents and Patients to Improve Antibiotic Use | | | | |
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| **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.  **Outcomes**  • 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 before 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 can be considered for parents expecting antibiotics for their children who do not need antibiotics. |
| 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 program to reduce antibiotic dispensing in primary care: Practice based randomized 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 with 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 with controls | • A clinician educational intervention led to reductions in antibiotic dispensing with no changes in hospital admissions, return visits, or costs. |
| 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 with 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 with 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)  **Outcome**  • 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 randomized 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 with 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. |