

ORIGINAL RESEARCH

Ambulatory Antibiotic Stewardship through a Human Factors Engineering Approach: A Systematic Review

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Introduction: In the United States, most antibiotics are prescribed in ambulatory settings. Human factors engineering, which explores interactions between people and the place where they work, has successfully improved quality of care. However, human factors engineering models have not been explored to frame what is known about ambulatory antibiotic stewardship (AS) interventions and barriers and facilitators to their implementation.

Methods: We conducted a systematic review and searched OVID MEDLINE, Embase, Scopus, Web of Science, and CINAHL to identify controlled interventions and qualitative studies of ambulatory AS and determine whether and how they incorporated principles from a human factors engineering model, the Systems Engineering Initiative for Patient Safety 2.0 model. This model describes how a work system (ambulatory clinic) contributes to a process (antibiotic prescribing) that leads to outcomes. The work system consists of 5 components, tools and technology, organization, person, tasks, and environment, within an external environment.

Results: Of 1,288 abstracts initially identified, 42 quantitative studies and 17 qualitative studies met inclusion criteria. Effective interventions focused on tools and technology (eg, clinical decision support and point-of-care testing), the person (eg, clinician education), organization (eg, audit and feedback and academic detailing), tasks (eg, delayed antibiotic prescribing), the environment (eg, commitment posters), and the external environment (media campaigns). Studies have not focused on clinic-wide approaches to AS.

Conclusions: A human factors engineering approach suggests that investigating the role of the clinic's processes or physical layout or external pressures' role in antibiotic prescribing may be a promising way to improve ambulatory AS. (J Am Board Fam Med 2018;31:417–430.)

Keywords: Antibiotics, Antimicrobial Stewardship, Clinical Decision Support Systems, Patient Safety, Point-of-Care Testing, Quality Improvement

Antibiotic resistance is increasing worldwide, largely driven by excessive antibiotic use.^{1–3} In the United States, antibiotic resistance contributes to 23,000 deaths annually and \$20 billion in excess health care costs.⁴ Antibiotic stewardship (AS) min-

imizes the development of resistance as well as the risk of harm from antibiotic-associated adverse events by ensuring that only patients who need antibiotics get them and that each patient who needs antibiotics receives the right anti-

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otic at the right time at the right dose for the right duration.⁵

Although implementation of hospital-based AS teams have been recommended for a decade⁶, the majority of human antibiotic expenditures (62%) and use occurs in the ambulatory setting.⁷ At least 30% of these prescriptions are inappropriate.⁸ Reducing inappropriate ambulatory antibiotic prescribing is essential to decreasing antibiotic resistance.^{9,10}

Human factors engineering is the “scientific discipline concerned with understanding interactions among humans and other elements of a system.”^{11,12} According to a health care-specific human factors engineering model, the Systems Engineering Initiative in Patient Safety (SEIPS 2.0) model,¹³ the characteristics of a workplace (eg, an ambulatory clinic) interact in a work system (comprised of person(s), tools and technologies, the organization, tasks, and the physical environment, within a larger external environment); this work system impacts processes such as antibiotic prescribing, which influence outcomes.¹³

Although human factors engineering approaches have been occasionally used in ambulatory clinics to improve patient safety and quality of care^{14–18}, human factors engineering approaches and models have not been applied to understanding ambulatory AS. We performed a systematic review because human factors engineering approaches describing the clinic’s work system could explain influences on antibiotic prescribing and lead to more effective AS interventions. For example, human factors engineering could explain how clinic characteristics such as the ease with which clinicians adapt the electronic health record (EHR) could enhance the intervention’s success. We used the SEIPS 2.0 model¹³ to frame what is known about effective ambulatory AS interventions and identify barriers and facilitators to successful implementation of ambulatory AS interventions.

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Methods

Literature Search and Inclusion Criteria

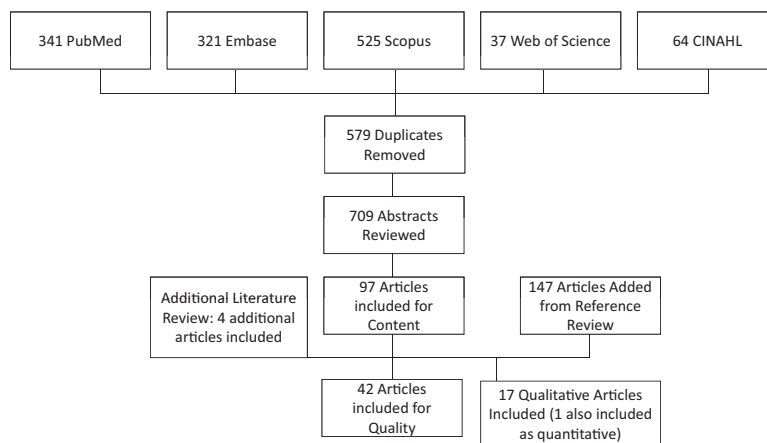
We included quantitative studies to learn whether ambulatory AS interventions were efficacious and qualitative studies to describe barriers and facilitators to AS. We defined ambulatory settings as outpatient practices or offices in which patients came and left on their own (excluding dentistry and emergency medicine practices). We searched the OVID MEDLINE, Embase, Scopus, Web of Science, and CINAHL databases through November 7, 2016, by using a predetermined set of search terms (Appendix A). We identified additional titles from the Cochrane database as well as from the citations in identified articles. Citation titles and abstracts were screened independently by 2 reviewers (SCK and PDT), and full texts were retrieved for all potentially relevant studies. Duplicate studies were removed.

Studies were limited to English-language human studies of antibiotic-prescribing interventions or qualitative studies seeking to understand antibiotic prescribing practices. Quantitative and qualitative studies were assessed by 2 reviewers (SCK and PDT) to determine if they evaluated AS interventions conducted in ambulatory clinics. We considered AS interventions as any intervention that sought to improve the appropriate use of antibiotics in an ambulatory clinic. We included studies that measured the application of an intervention targeting antibiotic prescriptions, described the factors that influence antibiotic prescribing, or explained the process of implementing approaches to improve antibiotic prescribing. For quantitative studies, we a priori only included studies with rigorous designs: randomized controlled trials (RCTs) or quasi-experimental studies using stepped wedge or interrupted time series approaches. Qualitative studies were included if they described the context in which antibiotic prescribing decisions were made or the context, barriers, or facilitators of AS interventions. Any disagreements about study inclusion were discussed until consensus was achieved.

SEIPS 2.0 Model and Data Extraction

Data for studies meeting inclusion criteria were abstracted using components of the SEIPS 2.0 work system model.^{13,19} The SEIPS 2.0 work system includes 5 components within a wider external environment: (1) person(s), (2) tools and technolo-

Figure 1. Flow chart demonstrating inclusion of articles in the review. Rigorously designed quantitative studies of ambulatory antibiotic stewardship interventions (randomized controlled trials and quasi-experimental studies with stepped wedge and interrupted time series approaches), as well as qualitative studies describing barriers and facilitators to ambulatory antibiotic stewardship were included. Databases were searched through November 7, 2016, with additional titles added based on knowledge of the literature and relevance to the work.



gies, (3) organization, (4) tasks, and (5) physical environment. The work system centers around the person(s), including health care professionals, the patient and family, their individual characteristics (eg, age and education), and connections between individuals (eg, a patient-clinician relationship).¹³ Tools and technologies include objects that people use to do work, such as information technologies, educational materials, medical devices, testing equipment, and physical tools. Organization refers to the structures that organize clinic time, space, resources, and activities, including staff member roles. Tasks are specific actions (eg, placing an electronic order) and have qualities such as difficulty, complexity, ambiguity, variety, and sequence. The physical environment includes the clinic's physical space. The work system lies within a larger external regulatory and cultural environment, including societal, economic, and policy forces that impact a clinic.¹³

We used these work system components to organize aspects of the interventions and the context of AS and to understand which processes and outcomes were addressed by AS interventions. Our aim in using this approach was to identify how aspects of the clinic work system could affect AS intervention successes. We evaluated identified sources and recorded study design and aspects of the studies that could be interpreted in the context of the SEIPS 2.0 model. We also described how measures and outcomes of the studies could be

interpreted in the context of the SEIPS 2.0 work system.

Results

Search Results

The search identified 1,288 abstracts (Figure 1). Four additional studies meeting inclusion criteria identified through knowledge of the literature were added based on their relevance to the work. Ultimately, 42 quantitative and 17 qualitative articles met the eligibility criteria, with 1 study considered both quantitative and qualitative.¹⁹ Fourteen of the quantitative studies were RCTs^{20–33}, 1 was a randomized crossover trial³⁴, 2 were pragmatic RCTs^{35,36}, 14 were cluster randomized trials^{37–48}, 2 were pragmatic cluster randomized trials^{49,50}, and 9 were quasi-experimental, interrupted time series studies.^{19,51–58}

Of the qualitative studies, 3 were follow-up studies to prior quantitative work^{19,59,60} (1 of which had been described in the quantitative review).^{19,38} Eight studies used semistructured interviews^{61–68} and 1 used focus groups.⁶⁹ One combined interviews and focus groups⁷⁰ and 2 involved surveys.^{71,72} A single study focused on written physician self-reflection, prompting them to review the medical charts of patients.⁶⁹ Finally, 1 study used a “think-aloud” approach where physicians commented on their inner thought processes.⁷³

AS Interventions and the SEIPS 2.0 Work System

Table 1, Appendix B, and Figure 2 describe how aspects of included studies fit into components of the clinic work system.¹³ Appendix C describes the processes and outcomes used in each included study.

Tools and Technology

Tools and technologies include objects and technologies that people use to do work. AS interventions incorporating tools and technologies included clinical decision support systems (CDSS), interventions based in EHRs, educational tools (eg, newsletters, booklets, and videotapes), AS messaging tools (eg, magnets and lapel pins), and point-of-care (POC) testing.

CDSS tools and other EHR-based interventions were frequent and often effective. Highlighting several CDSS tools, a CDSS incorporated into an EHR encounter template decreased acute respiratory infection (ARI) antibiotic prescriptions from 43% to 38% (versus 40% to 39% in control groups).⁴¹ An RCT of a computerized patient flow manager with evidence-based prompts decreased antibiotic prescriptions for acute otitis media by 34%.^{32,74}

EHR-based tools have incorporated behavioral interventions. In a $2 \times 2 \times 2$ randomized factorial study comparing accountable justification (providing a written explanation for prescribing nonindicated antibiotics) and suggested alternatives (pop-up messages with education and nonantibiotic alternatives), the suggested alternatives arm was associated with decreased antibiotic prescriptions for ARIs.²⁰ In a larger cluster randomized trial, suggested alternatives did not decrease antibiotic prescription, but accountable justification decreased inappropriate antibiotic prescribing (23% to 5%).⁴³

However, the context in which electronic tools were deployed impacted their implementation. Factors associated with unsuccessful incorporation of CDSS tools and EHR technologies into clinics included nonintuitive tools, need for additional software,⁵¹ computers not being available in examination rooms, and slow internet connectivity.¹⁹ CDSS tools needed to be used to have an effect; in a cluster randomized trial, EHR-integrated CDSS did not impact antibiotic prescribing, but the CDSS tool was used in only 6% of intervention clinic visits.⁷⁵

The effect of educational tools was mixed. Educational booklets (eg, on self-care for respiratory infections, potential harms of antibiotics, and other topics) were developed with the goals of assisting patients with understanding harms associated with unnecessary antibiotic use and supporting clinicians with antibiotic prescribing.^{59,66} As a broader intervention including physician feedback, mailing brochures to parents of children successfully decreased community-wide antibiotic use by 4.6% among those aged 2 to 4 years and by 6.7% among those aged 4 to 5 years.⁴² However, in another study involving mailed patient and clinician education, antibiotic use did not decrease.⁵⁵ In addition, in a trial of patient educational materials including a letter from the medical director along with pamphlets compared materials mailed to patients and to office practices, pamphlets mailed to offices only, and usual care on antibiotic prescription for acute bronchitis.⁵⁶ Only the full intervention sites showed a decline in antibiotic prescriptions for acute bronchitis visits, from 74% to 48%.⁵⁶

Evidence was similarly mixed regarding the impact of multifaceted educational tool bundles. In a cluster randomized trial in 16 Massachusetts communities, clinicians were given tools with AS messages (ie, stickers, lapel pins, and otoscope insufflators), bimonthly newsletters regarding AS, and prescription pads with written recommendations for symptomatic treatment of viral ARIs.^{46,53} Parents of young children were also mailed brochures and advertisements were placed in child care centers and pharmacies.⁴⁶ Although there was no difference in ARI antibiotic prescribing in children <2 years, a 5% decrease in children 2 to 3 years and a 7% decrease in children 4 to 5 years was observed.⁴⁶ In an additional cluster randomized trial, a multifaceted intervention (educational information at pharmacies and clinics, patient mailings, clinic posters, refrigerator magnets, flip charts, patient-initiated chart documentation tools, and CDSS tools) resulted in a decrease in antibiotic prescriptions among children <6 years.³⁷ Another multifaceted intervention (CDSS, clinician education, audit and feedback, and patient education brochures) also led to decreases in the percentage of adolescents and adults prescribed antibiotics for ARIs at CDSS sites (decreased 12%) versus control sites (increased 1%), with no impact on 30-day return visits.⁴⁰

Table 1. Aspects of Ambulatory Antimicrobial Stewardship Interventions as Applied to Components of the Ambulatory Work System, SEIPS 2.0^{13*}

Tools / Technology Components	Person(s) / Components	Organizational Components	Task Components	Physical Environment Components	External Environment Components
<ul style="list-style-type: none"> • EHR-based CDSS^{20,38,41 to 42,50,54,67,70,72} • Hyperlink to patient education^{20,54,66} 	<ul style="list-style-type: none"> • Commitment to use and agreement with CDSS²⁰ • Technically savvy staff²⁰ 	<ul style="list-style-type: none"> • CDSS alters practice workflow²⁰ • Role of person initiating task is different in different clinics (ie, triage nurse, medical assistant, and clinician)^{20,69} 	<ul style="list-style-type: none"> • Improves efficiency²⁰ • Ordering an antibiotic in EHR²¹ 	<ul style="list-style-type: none"> • Computer location^{20,33} • Brochures and posters in exam rooms and waiting rooms^{2,3,4,13,38,46,53,60,66} 	<ul style="list-style-type: none"> • External clinician guidelines^{20,26,30,37,39-41,54-55,65-67,76} • New guidelines written⁵⁷
<ul style="list-style-type: none"> • Hyperlink to and accessibility of guidelines^{39,40,54,66} • EHR-based audit and feedback²⁰ 	<ul style="list-style-type: none"> • Comfort with prior ARI templates²⁰ • Providers signed letter/poster soliciting support^{27,31,56,58,59} 	<ul style="list-style-type: none"> • Computerized patient flow manager designed by clinics³³ • Patients see physicians with different practices^{66,72,73} 	<ul style="list-style-type: none"> • Protocols support decision making⁷³ • Amoxicillin as placebo if physician did not think they need antibiotics⁷⁶ 	<ul style="list-style-type: none"> • Regional clinician newsletter^{61,72} • Insurance policies regarding cost-sharing^{25,66} 	<ul style="list-style-type: none"> • Meetings with community leaders³⁸
<ul style="list-style-type: none"> • EHR-based antibiotic prescribing agreement⁴⁹ 	<ul style="list-style-type: none"> • Prescribing feedback^{2,23,37,3-41,44,46,51,54,57,60,62-63,67} 	<ul style="list-style-type: none"> • Previsit triage and education by nurses may prevent visits⁷² 	<ul style="list-style-type: none"> • Limited time during patient visits, antibiotics to save time^{66,72,73,77} 	<ul style="list-style-type: none"> • Mass media campaign^{38,56,61,72,74} 	<ul style="list-style-type: none"> • Meetings with community leaders³⁸
<ul style="list-style-type: none"> • Template for ARI clinic visits⁴¹ 	<ul style="list-style-type: none"> • Intensive intervention for highest prescribers³⁸ 	<ul style="list-style-type: none"> • Large health systems enable system-level alerts⁶⁶ • Need for hospital lab^{35,69} 	<ul style="list-style-type: none"> • Competing demands⁷² • Restricted susceptibility testing⁷⁰ 	<ul style="list-style-type: none"> • Education at pharmacies, health fairs, child care centers, and offices^{38,47,48,75} 	<ul style="list-style-type: none"> • Mass media campaign^{38,56,61,72,74} • Education at pharmacies, health fairs, child care centers, and offices^{38,47,48,75}
<ul style="list-style-type: none"> • EHR-based accountable justifications and suggested alternatives (pop-up of alternatives and educational material)^{21,44} • Limited printing capabilities²⁰ • Tool adaptability^{20,62,77} 	<ul style="list-style-type: none"> • Clinician instruction on problem solving and communication^{30,49,52,53,59} • Older prescribers: prescriptions influenced by habit⁷⁰ • Newer prescribers: nervous about making mistakes⁷³ 	<ul style="list-style-type: none"> • Peer comparison^{21,23,44,46,51,60,62-63} • Other clinicians see accountable justification^{21,44} • Group follow-up meetings with individual feedback^{2,43,2-94} 	<ul style="list-style-type: none"> • Diagnostic uncertainty^{72,76} • Checklist completed by clinician and patient⁶² • Communicating with patients^{59,64,65,77} 	<ul style="list-style-type: none"> • CDC campaigns for judicious antibiotic use^{33,54} • Disclosed prescribing status monthly to patients, health authorities, and health workers⁴⁵ • Health ministry-required tasks⁷⁰ 	<ul style="list-style-type: none"> • CDC campaigns for judicious antibiotic use^{33,54} • Disclosed prescribing status monthly to patients, health authorities, and health workers⁴⁵ • Health ministry-required tasks⁷⁰
<ul style="list-style-type: none"> • Mailed intervention^{2,23,38,43,47,48,55,58 to 60,75} • Printed patient education^{2,3,5,6,41-43,47,59-60,65,70,71,73,75} • Letters/posters/videos about avoiding inappropriate antibiotic prescribing with clinician photos or signatures^{27,31,56,58,59} • Refrigerator magnets^{38,59,60} 	<ul style="list-style-type: none"> • Depend on patient to decide to take antibiotics⁶⁶ • Engaged patients: focus groups with elderly volunteers⁶⁰ • Patient/family pressure and expectations^{62,64,72,74} • Patient physical traits^{20,64,65,67,70,77} 	<ul style="list-style-type: none"> • On-site group educational time^{2,4,38-41,43,57,66,67} • Academic detailing^{67,75,52-54,58,67} • Large training sessions^{55,59} • Local clinicians led initiative at local hospital medical staff meetings³⁸ 	<ul style="list-style-type: none"> • Setting expectations^{36,64,66} • Educating patients^{39,64,66,70,73} • Use physical exam to communicate^{64,77} • Flexible interventions increase feasibility⁶⁷ 	<ul style="list-style-type: none"> • Performance-based incentives^{66,70,72} • Patient can get antibiotics elsewhere^{66,68} • Other countries or healthcare settings thought to be responsible for resistance⁶⁸ • Willing to postpone treatment if told others would do the same⁷¹ 	<ul style="list-style-type: none"> • Performance-based incentives^{66,70,72} • Patient can get antibiotics elsewhere^{66,68} • Other countries or healthcare settings thought to be responsible for resistance⁶⁸ • Willing to postpone treatment if told others would do the same⁷¹

Continued

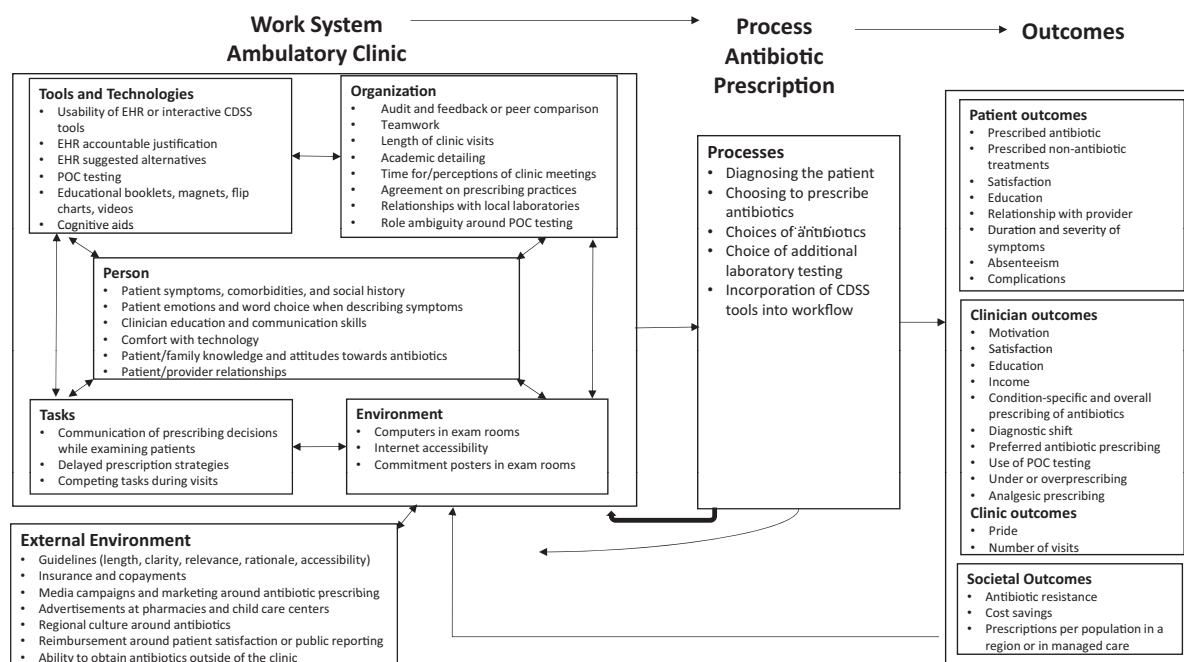
Table 1. Continued

Tools / Technology Components	Person(s) Components	Organizational Components	Task Components	Physical Environment Components	External Environment Components
<ul style="list-style-type: none"> ● Flip chart or reference card for ARI self-management^{35,60} ● Stickers, lapel pins, and otoscope insufflators^{47,75} ● All received printed versions of poster and electronic version of guideline⁴⁶ ● Discussion guide at well-child visits^{20,47,75} ● Prescription pads for treatment of viral infections^{47,58,71,75} ● Delayed prescription: prescribe antibiotics to take only if symptoms worsen^{16,71} ● Website for feedback required physicians to log in with individual access code³⁷ ● Dashboard⁵¹ ● Want local resistance data⁶⁸ ● Limit antibiotic availability in outpatient settings⁶⁰ ● CRP POC testing^{24,35,52,53,62,65,69,77} ● Procalcitonin testing²⁶ ● POC streptococcal testing⁶⁵ ● Multiplex PCR for respiratory viruses³² 	<ul style="list-style-type: none"> ● Patient symptoms^{20,62,64,65,73} ● Patient background and knowledge⁷⁴ ● Avoiding confrontation⁶⁴ ● Negotiating with patients⁶⁴ ● Hedging⁶⁴ ● Patient reward for copays and taking off work⁶⁶ ● Most PCPs did not see antibiotic resistance as a problem in their practice⁶⁸ ● Worried about patient illness from not prescribing antibiotics^{67,70} 	<ul style="list-style-type: none"> ● Clinicians compensated for each visit⁸ ● Practice-specific antibiotic prescribing rates^{39,40,43,49,59,70} ● Clinic champions⁴¹⁻⁴³ ● Kick-off dinners^{47,75} ● Peer review of colleague transcripts with simulated patients^{2,5,33} ● Clinics set goals⁵⁹ ● Clinic pride⁶⁴ ● Relationships with patients^{64,71} ● GPs assume practice already follows guidelines⁶⁷ ● Antibiotic resistance seen as issue for secondary care rather than primary care⁶⁸ ● No accountability for prescribing² ● Peer support helpful with demanding patients⁷³ ● Fewer visits, decreased income⁷⁷ ● Dermatologic consultation²⁷ ● Institutional guidelines²⁹ ● Prior approval of ID physician⁷⁰ 	<ul style="list-style-type: none"> ● Interventions should engage GPs⁶⁷ ● CRP testing has associated tasks (eg, quality assurance)⁶⁹ 	<ul style="list-style-type: none"> ● Social capital⁷¹ ● Loss of income from POC testing and reimbursement⁶⁹ ● Legal protections⁷³ ● School or day care requires antibiotics⁷⁴ ● Adaptability of intervention to regional culture⁷⁷ 	

SEIPS, Systems Engineering In Patient Safety; PCP, primary care provider; CDSS, clinical decision support system; POC, point of care; ARI, acute respiratory infection; EHR, electronic health record; CDC, Centers for Disease Control and Prevention; GP, general practitioner; CRP, C-reactive protein; ID, infectious diseases; PCR, polymerase chain reaction.

*Studies described include rigorously designed quantitative and qualitative studies describing antibiotic stewardship interventions and the context around antibiotic prescribing decisions, included through November 7, 2016.

Figure 2. Adaptation of the Systems Engineering Initiative for Patient Safety (SEIPS) 2.0 model of the health care work system to approaches taken in the literature to improve antibiotic stewardship in the ambulatory setting.



Abbreviations: EHR: electronic health record; CDSS: clinical decision support system; POC: point of care.

Interventions involving tools for patient and family education were not always successful. An intervention including mailed information and guideline distribution did not decrease antibiotic use among elderly patients with ARIs.⁵⁷ Meanwhile, providing patients with an educational pamphlet and videotape of their pediatricians did not decrease the number of viral ARI visits, antibiotic prescriptions for acute otitis media or sinusitis, or total antibiotic prescriptions.²⁷ Patient characteristics such as older age and the need to open the pamphlet or view the videotapes may have made these interventions less effective.

Other studies focused on POC testing as a tool. C-reactive protein (CRP) POC testing may perform better than clinical symptoms and signs in predicting the diagnosis of pneumonia⁵², but decreases clinician confidence in reducing antibiotic prescribing and decreases patient satisfaction.⁵⁹ In a study of POC CRP testing availability, antibiotic prescription improved⁴⁹, but on follow-up 2 to 3 years later, POC CRP testing was only performed in 4% of eligible patient visits.⁵⁰ POC tests have also been criticized for their short shelf life, need for quality control testing, and difficulties linking the test result to the EHR.⁷⁶ These factors may

have made the tools more difficult to incorporate into practice and limited their effectiveness.

Person

The person component of the SEIPS 2.0 work system describes individual characteristics and relationships between individuals. However, characteristics and perspectives of other clinic staff members such as medical assistants, nurses, and front desk staff were not described.

Patients and Families

Patient factors such as symptoms and comorbidities influence whether a clinician would prescribe antibiotics.^{19,61,66} Patient and family factors such as education, knowledge of antibiotics, or trust in their physician decreased requests for antibiotics.^{35,67,71}

Clinicians

Clinician training, particularly focusing on communication training, problem-solving strategies, and peer review, was also studied. In an RCT, French general practitioners were randomized to a day-long seminar focusing on problem-solving strategies after all attended a 2-day seminar on

evidence-based ARI management.²⁹ The intervention group sustained a decrease in the proportion of antibiotics prescribed over 30 months.²⁹ General practitioners who attended a training session or received in-office instruction along with clinician-specific feedback increased adherence to community-acquired pneumonia guidelines.⁴⁵ A workshop including peer reviews of transcripts of interactions with standardized patients reduced antibiotic prescriptions from 54% to 27%,⁴⁹ sustained for 2 to 3 years.⁵⁰

Clinician and Patient Relationships

Relationships between individuals are an important part of the ambulatory work system.¹³ Some physicians think that patients want antibiotics⁶¹ and prescribe antibiotics to meet perceived patient expectations.⁶⁸ Physicians may also believe that patients want something (ie, an antibiotic prescription) in exchange for taking off work and paying copays.⁶³

Organization

The organization refers to the structures and roles that organize a clinic. Characteristics of the clinic, roles of clinic members, and the larger organizations in which clinics operate were explored through investigating roles of clinic team members, comparing clinicians to peers, and learning how clinic structures allow clinician education or improve communication.

Few studies involved changing roles of nonclinician staff members to impact AS. Only 1 study included a nonclinician staff member in an educational intervention and the role of this person was not specified.⁵¹ In a qualitative study, clinicians suggested using nurses to perform previsit triage and education.⁷² In POC testing interventions, participants found that it was unclear which staff members to train in POC testing, as various organizational roles performed the test in different clinics.^{76,77}

Audit and feedback interventions, where clinicians are compared with others, have had success.^{20,48} In a Canadian RCT where clinicians were mailed educational information or prescribing feedback, the feedback group was more likely to use first-line antibiotic prescriptions.²¹ In a cluster randomized trial, comparing clinicians with top performers (those who seldom prescribe antibiotics inappropriately) decreased inappropriate prescrip-

tions from 20% to 4%.⁴³ In an RCT, antibiotic use decreased among providers who received a letter from England's chief medical officer saying they were prescribing more antibiotics than 80% of local practices.²² An RCT found that the combination of clinician education and audit and feedback decreased antibiotic prescribing overall and broad-spectrum prescribing in particular.³⁸

However, audit and feedback may not be universally successful. In the above RCT,³⁸ after the termination of audit and feedback, prescribing of broad-spectrum antibiotics returned to a level above baseline.³⁹ In a follow-up qualitative study, some clinicians expressed skepticism and discounted the reports.⁶⁰ Furthermore, in a recent RCT of high-prescribing physicians across Switzerland, receiving letters and an online log-in code with information about antibiotic prescribing did not impact antibiotic prescribing over 2 years.³⁶ Only 11% of physicians in the intervention group viewed their prescribing data.³⁶ Similarly, a cluster randomized trial of an audit and feedback dashboard led to no difference in antibiotic prescribing for ARI visits⁷⁸, but only 28% of intervention-group physicians used the dashboard. These clinicians had a lower ARI antibiotic prescribing rate (42% versus 50%).⁷⁸

Organizational structures could pose barriers to AS. Clinic visits were often too brief to discuss guidelines with patients.^{63,70} If patients saw multiple clinicians in a practice with different prescribing practices, patients may have expected to receive antibiotics.^{63,70} Many clinics did not have protected time for group education.⁶³ However, in practices where physicians discussed AS guidelines, outcomes improved.^{52,46}

If clinics had protected time for group education, academic detailing, where an expert visits a practice to discuss AS,^{51,64} was successful.⁵⁵ In a study comparing (1) office-based patient education, (2) office- and home-based patient and clinician education (practice profiling, setting clinic goals, and academic detailing), and (3) usual care, full intervention sites had a substantial decline in antibiotic prescriptions for acute bronchitis (74% to 48%), whereas the control and limited intervention sites did not.⁵⁶

Tasks

Tasks describe specific actions and their characteristics. Clinicians pick particular words when de-

scribing physical examination findings to patients or perform a thorough physical examination to explain to patients why they were not prescribing antibiotics.^{61,66,73}

In delayed prescription strategies, the clinician gives the patient a prescription and leaves it up to the patient whether to fill it after a specified time or with worsened symptoms. Patients with acute uncomplicated ARIs were randomized: (1) deciding to fill the prescription after 2 days, (2) returning to the clinic after 2 days for a prescription, (3) no prescription, or (4) immediate prescription.³⁵ Patient satisfaction was similar in all groups, and antibiotic use and belief in antibiotic effectiveness was lower in all groups compared with the immediate prescription group.³⁵

Physical Environment

The physical environment refers to the clinic's layout. Most physical environment-based interventions used posters.^{24,38,46,59,60} By themselves, posters about avoiding antibiotics for "chest colds" did not decrease antibiotic prescription for acute bronchitis.⁵⁶ However, visible signed commitments about avoiding unnecessary antibiotics decreased unnecessary antibiotic prescribing by up to 20%.³¹ Studies did not discuss optimizing the placement of these posters.^{37,45,46,53,56,57}

External Environment

The larger external environment includes guidelines and societal, economic, and policy forces that impact a clinic. External guidelines were not always used because they were sometimes difficult to locate^{63,64,69}, too long⁶⁴, or not seen as relevant.⁶⁴ Some physicians did not trust guidelines, wondering whether they were intended to save money instead of improving care.⁶⁴

Media campaigns reinforced what clinicians conveyed.⁶⁶ A Colorado-wide campaign of billboards, bus signs, radio advertisements, and newspaper op-eds decreased population-wide antibiotic dispenses.^{53,57} Advertisements in child care centers and pharmacies also reduced antibiotic use.⁴⁶ In another community-level study, interventions including news releases, community meetings, and presentations at health fairs decreased antibiotic prescriptions.³⁷ In an Italian study, region-wide campaign materials (posters, brochures, and local media advertisements) and a

doctor and pharmacist newsletter decreased antibiotic prescribing by 4%.⁵⁸

Discussion

Human factors engineering approaches have only recently been used in ambulatory clinics to describe defects in testing,¹⁴ apply new EHR technologies^{15,18}, and improve clinic workflows.^{16,17} Our review is the first to incorporate a human factors engineering approach to understanding ambulatory AS.

In the SEIPS 2.0 work system, tools and technologies refer to objects and technologies. Tools and technologies used in ambulatory AS interventions have included CDSS and EHR-based interventions, educational materials, and POC testing. CDSS and EHR-based and educational materials improved AS but only if they were used. POC tools such as CRP testing impacted AS, but many clinicians stopped using the POC tests over time. Human factors engineering would suggest that to make these tools more effective, researchers should make them easier to use.

The person component of the work system includes individual characteristics and relationships between individuals. In particular, clinician communication training had a sustained positive impact on AS, and interventions aimed at educating patients and families also showed a positive impact on AS. However, although clinicians have mentioned the potential impact of other members of the health care team, characteristics of other health care team members have not been studied. Human factors engineering would suggest that the role of other members of the health care team in AS interventions should be studied and these team members should be engaged.

Few studies focused on the organization component of the work system model or the structures and roles that organize a clinic. Audit and feedback and academic detailing had a positive impact on AS. However, we know little about the role of nonclinicians in AS. Engagement of the entire ambulatory team has the potential to send a consistent message about appropriate antibiotic prescribing.⁶⁸ Human factors engineering would suggest research exploring the roles of clinic staff and clinic flow in an intervention's effectiveness.

Similarly, few interventions focused on the work system component of tasks or specific actions and

their characteristics, although delayed prescription strategies were promising. Few interventions focused on the impact of the physical environment of the clinic on antibiotic prescription. However, clinic posters with signed commitments advocating AS positively impacted AS. Human factors engineering would suggest an investigation into the role of the location of clinic posters and other elements of the physical environment, as well as qualities of tasks related to antibiotic prescription, on AS interventions.

Finally, the work system occurs within the external regulatory and cultural environment. Several interventions incorporated the external environment, showing that media-based interventions could improve AS at a community level and showing that external guidelines needed to be accessible to clinicians and trusted by clinicians. The role of the external environment in the form of external pressures on AS interventions such as patient satisfaction-based reimbursement has not been fully examined and should be a focus of future research.

Our review has several limitations. We only included well-controlled quantitative studies and may have missed other domains if they were targeted only in uncontrolled studies. We did not assess for publication bias. Finally, our findings are more applicable to ARIs, the focus of most studies, as we were unable to identify many high-quality studies that implemented AS for other conditions (eg, urinary tract infections and cellulitis).

Evidence-based AS interventions impact different portions of the ambulatory work system, and using a human factors engineering approach may facilitate the intervention's success. However, interventions did not typically engage all clinic staff in the implementation, a model that has led to successes in patient safety and quality improvement.^{79–84} Few interventions have accounted for physical environment or task characteristics in implementing interventions. Future work in ambulatory AS should address the entire work system in which the intervention is implemented. Such work system interventions, if rigorously evaluated, may have greater potential than isolated interventions to improve the effectiveness of ambulatory AS.

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Appendix A: Search Terms

PubMed 341 Results, 11/7/2016

(“Anti-Infective Agents”[Mesh] OR “Anti Infective Agents” OR “Anti Infective Agent” OR “Antiinfective Agents” OR “Antiinfective Agent” OR “Anti-infective agents” OR “anti-infective agent” OR “Microbicides” OR “antimicrobial agents” OR “antimicrobial agent” OR “antimicrobials” OR “Anti-Microbial Agents” OR “antimicrobial agent” OR “Anti Microbial Agents” OR “anti microbial agent” OR “antibiotics” OR “antibiotic” OR “antibiotics” OR “antibiotic” OR “Anti Bacterial Agents” OR “Anti Bacterial Agent” OR “Antibacterial Agents” OR “Antibacterial Agent” OR “Bacteriocidal Agents” OR “Bacteriocides” OR “Anti-Mycobacterial Agents” OR “Anti Mycobacterial Agents” OR “Antimycobacterial Agents”) AND (“stewardship” OR “stewards” OR “antimicrobial management” OR “antimicrobial prescribing behavior” OR “antibiotic stewardship” OR “antimicrobial stewardship” OR “appropriate use” OR “Drug Utilization”[Mesh] OR “ASP”) AND (“Ambulatory Care”[Mesh] OR “ambulatory care” OR “ambulatory health services” OR “outpatient care”

OR “outpatient health services” OR “outpatient health service” OR “urgent care” OR “urgent cares”).

Embase 321 Results, 11/7/2016

(“antiinfective agent”/exp OR “anti infective agent*” OR “antiinfective agent*” OR “anti-infective agent*” OR “microbicide*” OR “antimicrobial*” OR “antimicrobial agent*” OR “anti microbial agent*” OR “antibiotic*” OR “antibiotic*” OR “anti bacterial agent*” OR “antibacterial agent*” OR “bacteriocidal agent*” OR “bacteriocide*” OR “antimycobacterial agent*” OR “anti mycobacterial agent*”) AND (“drug utilization”/exp OR “drug utilization” OR “drug utilization” OR “stewardship” OR “stewards” OR “antimicrobial management” OR “antimicrobial prescribing behavior” OR “antibiotic stewardship” OR “antimicrobial stewardship” OR “appropriate use” OR “asp”) AND (“ambulatory care”/exp OR “ambulatory care” OR “ambulatory health service*” OR “outpatient care*” OR “outpatient health service*” OR “urgent care*” OR “dispensary care” OR “extramural care”).

Scopus 525 Results, 11/7/2016

(TITLE-ABS-KEY (“antiinfective agent*” OR “anti infective agent*” OR “anti-infective agent*” OR “microbicide*” OR “antimicrobial*” OR “antimicrobial agent*” OR “anti microbial agent*” OR “antibiotic*” OR “antibiotic*” OR “anti bacterial agent*” OR “antibacterial agent*” OR “bacteriocidal agent*” OR “bacteriocide*” OR “antimycobacterial agent*” OR “anti mycobacterial agent*”) AND (TITLE-ABS-KEY (“stewardship” OR “stewards” OR “antimicrobial management” OR “antimicrobial prescribing behavior” OR “antibiotic stewardship” OR “antimicrobial stewardship” OR “appropriate use” OR “Drug Utilization” OR “drug utilization” OR “ASP”)) AND (TITLE-ABS-KEY (“ambulatory care*” OR “ambulatory health service*” OR “outpatient care*” OR “outpatient health service*” OR “urgent care*” OR “dispensary care” OR “extramural care”)).

Web of Science 37 Results, 11/7/2016

TS = (“antiinfective agent*” OR “anti infective agent*” OR “anti-infective agent*” OR “microbicide*” OR “antimicrobial*” OR “antimicrobial agent*” OR “anti microbial agent*” OR “antibiotic*” OR “antibiotic*” OR “anti bacterial agent*” OR “antibacterial agent*” OR “bacteriocidal agent*” OR “bacteriocide*” OR “antimycobacterial agent*” OR “anti mycobacterial agent*”) AND TS = (“stewardship” OR “stewards” OR “antimicrobial management” OR “antimicrobial prescribing behavior” OR “antibiotic stewardship” OR “antimicrobial stewardship” OR “appropriate use” OR “Drug Utilization” OR “drug utilization” OR “ASP”) AND TS = (“ambulatory care*” OR “ambulatory health service*” OR “outpatient care*” OR “outpatient health service*” OR “urgent care*” OR “dispensary care” OR “extramural care”).

CINAHL 64 Results, 11/7/2016

((MH “Antiinfective Agents+”) OR “antiinfective agent*” OR “anti infective agent*” OR “anti-infective agent*” OR “microbicide*” OR “antimicrobial*” OR “antimicrobial agent*” OR “anti microbial agent*” OR “antibiotic*” OR “antibiotic*” OR “anti bacterial agent*” OR “antibacterial agent*” OR “bacteriocidal agent*” OR “bacteriocide*” OR “antimycobacterial agent*” OR “anti mycobacterial agent*”) AND ((MH “Drug Utilization”) OR “stewardship” OR “stewards” OR “antimicrobial management” OR “antimicrobial prescribing behavior” OR “antibiotic stewardship” OR “antimicrobial stewardship” OR “appropriate use” OR “drug utilization” OR “ASP”) AND ((MH “Ambulatory Care”) OR “ambulatory health service*” OR “outpatient care*” OR “outpatient health service*” OR “urgent care*” OR “dispensary care” OR “extramural care”).

An asterisk indicates that a word stem was used as a search term (for example, antibiotic signified that either “antibiotic” or “antibiotics” was searched for).

Appendix B: Aspects of Ambulatory Antimicrobial Stewardship Interventions as Applied to Components of the Ambulatory Work System (SEIPS 2.0).^{13*}

SEIPS 2.0 Element							
Reference	Study Type	Tools / Technology Components	Person(s) Components	Organizational Components	Task Components	Physical Environment Components	External Environment Components
Litvin et al ²⁰	Qualitative analysis of quasi-experimental study	<ul style="list-style-type: none"> ● CDSS through EHR note template ● Hyperlink to patient education ● EHR audit and feedback ● Limited printing capabilities ● Not tailored to multiple complaints ● Facilitates discussion ● Tool adaptability ● Network issues 	<ul style="list-style-type: none"> ● Patient symptoms ● Patient age ● Commitment to use CDSS ● Agreement with CDSS ● Technically savvy staff ● Comfort with prior ARI templates 	<ul style="list-style-type: none"> ● CDSS alters practice workflow ● Role of person initiating CDSS is different in different clinics (ie, triage nurse, medical assistant, and clinician) 	<ul style="list-style-type: none"> ● Improves efficiency 	<ul style="list-style-type: none"> ● Computer location 	<ul style="list-style-type: none"> ● External clinician guidelines
Persell et al ²¹	2 × 2 × 2 RCT of patients with ARIs comparing (1) accountable justification, (2) suggested alternatives, and (3) peer comparison with educational module	<ul style="list-style-type: none"> ● EHR used for accountable justifications and suggested alternatives (pop-up of alternatives and educational material) 		<ul style="list-style-type: none"> ● Monthly peer comparison emails ● Other clinicians see accountable justification 	<ul style="list-style-type: none"> ● Ordering an antibiotic in EHR 		
Hux et al ²²	RCT of PCPs in Ontario randomized to mailed intervention combining prescribing feedback with educational bulletins	<ul style="list-style-type: none"> ● Mailed intervention 	<ul style="list-style-type: none"> ● Prescribing feedback 				
Hallsworth et al ²³	Randomized 2 × 2 factorial trial of GPs who prescribed antibiotics in the upper 20th percentile randomized to (1) patient educational leaflet and feedback and (2) patient-focused intervention	<ul style="list-style-type: none"> ● Patient education leaflet ● Patient-focused information 	<ul style="list-style-type: none"> ● Feedback intervention given letter saying they prescribed ≥80% of local practices 				

Continued

Appendix B: Continued

SEIPS 2.0 Element

Reference	Study Type	Tools / Technology Components	Person(s) Components	Organizational Components	Task Components	Physical Environment Components	External Environment Components
Strykowski et al ²⁴	Spanish RCT of GPs: acute exacerbation of COPD or chronic bronchitis, comparing (1) multifaceted intervention and CRP POC, (2) multifaceted intervention alone, and (3) usual care	<ul style="list-style-type: none"> CRP POC testing 		<ul style="list-style-type: none"> Both groups had follow-up meetings with individual feedback Both groups had training on ARIs 		<ul style="list-style-type: none"> Brochures and posters in waiting rooms 	
Foxman et al ²⁵	RCT of nonelderly patients in 6 areas in United States assigned to insurance plans varying by level of cost sharing						<ul style="list-style-type: none"> Insurance policies regarding cost sharing
Long et al ²⁶	Shanghai RCT of patients with suspected CAP, randomized to procalcitonin or guidelines alone	<ul style="list-style-type: none"> Procalcitonin testing 					<ul style="list-style-type: none"> Guidelines for CAP treatment
Arakaki et al ²⁷	Nonblinded RCT of adults diagnosed with cellulitis by PCP, randomized to outpatient dermatologic consultation			<ul style="list-style-type: none"> Dermatologic consultation 			
Taylor et al ²⁸	RCT of educational intervention aimed at parents of children <2 years of age	<ul style="list-style-type: none"> Pamphlet, videotape with local pediatrician promoting judicious antibiotic use More chest X-rays in the control group 					
Torres et al ²⁹	Observer-blinded RCT parallel-group study of clinical prediction rule of which children have bacterial pneumonia						
Le Corvoisier et al ³⁰	RCT of GPs: interactive seminar presenting evidence-based guidelines for ARIs		<ul style="list-style-type: none"> Subgroups: 2-day evidence-based medicine course only or with 1-day problem-solving course 	<ul style="list-style-type: none"> Alternative: management based on institutional guidelines 			<ul style="list-style-type: none"> Specific French guidelines

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Appendix B: Continued

SEIPS 2.0 Element							
Reference	Study Type	Tools / Technology Components	Person(s) Components	Organizational Components	Task Components	Physical Environment Components	External Environment Components
Meeker et al ¹	RCT in 5 adult primary care clinics to posted commitment letter or usual care in ARI	<ul style="list-style-type: none"> Letters/posters about avoiding inappropriate antibiotic prescribing photos and signatures Multiple PCR for respiratory viruses 				<ul style="list-style-type: none"> Poster-sized commitment letters in exam rooms 	
Brittain-Long et al ²	Swedish randomized open label study to receive a rapid (next day) or delayed (8 to 12 days) result of PCR throat swab						
Christakis et al ³	RCT of primary care pediatricians for POC evidence delivery on otitis media	<ul style="list-style-type: none"> Computerized patient flow manager and online prescription manager 	<ul style="list-style-type: none"> NPs, physicians, and housestaff 	<ul style="list-style-type: none"> Computerized patient flow manager designed by clinics Needed hospital lab 		<ul style="list-style-type: none"> Computer workstations 	
Dahler-Eriksen et al ^{3,5}	Danish randomized crossover trial of CRP measured within 3 minutes or with results in 1 to 2 days	<ul style="list-style-type: none"> Intervention group: measure CRP within 3 minutes and got results 1 to 2 days later 					
De la Poza Abad et al ^{3,6}	Pragmatic open label RCT among 23 Spanish primary care centers and ARI to (1) delayed patient-led prescription, (2) delayed prescription collection strategy requiring patients to collect prescription from PCP, (3) immediate prescription, or (4) no antibiotics	<ul style="list-style-type: none"> All patients given information about antibiotics Delayed prescription: prescribe antibiotics to take only if symptoms worsen 	<ul style="list-style-type: none"> Patients told it was normal to feel worse at first, depend on patient to decide to take antibiotics 		<ul style="list-style-type: none"> Patients told it was normal to feel worse at first 		
Hemkens et al ^{3,7}	Swiss pragmatic randomized trial of PCPs with highest antibiotic prescribing randomized to quarterly prescription feedback over 2 years or usual care	<ul style="list-style-type: none"> Website required for log in with individual access code 	<ul style="list-style-type: none"> Personalized feedback by mail and online 				<ul style="list-style-type: none"> 1 time provision of evidence-based guidelines for ARI and UTIs

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Appendix B: Continued

SEIPS 2.0 Element							
Reference	Study Type	Tools / Technology Components	Person(s) Components	Organizational Components	Task Components	Physical Environment Components	External Environment Components
Samore et al ³⁸	Cluster RCT in rural communities in Utah and Idaho comparing community intervention with CDSS on paper and CDSS with handheld computer	<ul style="list-style-type: none"> • Mailings to parents • Refrigerator magnets • Spiral bound flip chart for ARI self-management • 3 CDSS tools made for ARIs • Patient-initiated documentation tool • CDSS generated diagnostic and therapeutic recommendations 		<ul style="list-style-type: none"> • Local clinicians led initiative at local hospital medical staff meetings • Continuing medical education • Clinicians compensated for each visit and could keep handheld computers 		<ul style="list-style-type: none"> • Exam room posters and brochures 	<ul style="list-style-type: none"> • Meetings with community leaders • News releases on self-management of ARIs • Self-care materials distributed at health fairs • Education at pharmacies and offices
Gerber et al ³⁹ and Gerber et al ⁴⁰	Cluster randomized trial of pediatric practices focusing on ARIs, ³⁹ and follow-up for 18 months after intervention ⁴⁰	<ul style="list-style-type: none"> • ARI guidelines available as links in EHR 	<ul style="list-style-type: none"> • Quarterly personalized feedback and audit 	<ul style="list-style-type: none"> • 1 hour on-site clinician education • Practice-specific antibiotic prescribing rates 			<ul style="list-style-type: none"> • Used prescribing guidelines
Gonzales et al ⁴¹	3-arm cluster randomized trial, with 11 practices in each group: (1) printed CDSS, (2) computerized CDSS, and (3) control.	<ul style="list-style-type: none"> • Arm 1: printed CDSS for acute cough • Arm 2: EHR CDSS • Arm 3: no decision support • Arm 1 and 2: printed patient education material • Arm 1 and 2: template for ARI clinic visits 	<ul style="list-style-type: none"> • Provider education and feedback in both intervention groups 	<ul style="list-style-type: none"> • Half-day training session 	<ul style="list-style-type: none"> • Provider education • Practice guidelines • Clinical champions • Audit and feedback 		
Jenkins et al ⁴²	Cluster randomized study of 8 primary care clinics randomized to CDSS pathway and patient education or usual care	<ul style="list-style-type: none"> • 1 page CDSS pathway incorporated into EHR encounter template • Patient education 	<ul style="list-style-type: none"> • Peer champion provider at each clinic 				

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Appendix B: Continued

SEIPS 2.0 Element

Reference	Study Type	Tools / Technology Components	Person(s) Components	Organizational Components	Task Components	Physical Environment Components	External Environment Components
Finkelstein et al ¹³	Cluster randomized trial: 12 pediatric practices in 2 MCOs in eastern Massachusetts and Washington State	<ul style="list-style-type: none"> Parents mailed CDC brochure on antibiotic use 		<ul style="list-style-type: none"> Physician peer leaders reviewed prescribing guidelines in practice meetings Given feedback on practice prescribing 		<ul style="list-style-type: none"> Education displayed in waiting rooms 	<ul style="list-style-type: none"> CDC campaigns for judicious antibiotic use
Meeker ⁴⁴	Cluster randomized study of 47 primary care practices randomized to receive 0, 1, 2, or 3 behavioral interventions: (1) suggested alternatives, (2) accountable justification, and (3) peer comparison	<ul style="list-style-type: none"> Suggested alternatives: electronic order sets suggesting nonantibiotic treatments Accountable justification: prompts to enter justifications for prescribing antibiotics for nonindicated diagnoses All groups received online ARI diagnosis and treatment education 	<ul style="list-style-type: none"> Peer comparison: emails comparing antibiotic prescribing rates with those of top performers 	<ul style="list-style-type: none"> Accountable justification: written justification would be seen in EHR as a note 			
Yang et al ⁴⁵	Matched-pair cluster randomized trial in China						<ul style="list-style-type: none"> Disclosed prescribing status monthly to patients, health authorities, and health workers
Schnoor et al ⁴⁶	Cluster randomized trial of 8 German clinical centers and 4 computer-based interventions	<ul style="list-style-type: none"> All received printed versions of poster and electronic version of guideline 	<ul style="list-style-type: none"> Every other month, GPs given peer comparison 			<ul style="list-style-type: none"> All received poster 	

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Appendix B: Continued

SEIPS 2.0 Element

Reference	Study Type	Tools / Technology Components	Person(s) Components	Organizational Components	Task Components	Physical Environment Components	External Environment Components
Finkelstein et al ⁴⁶ and Ackerman et al ⁴⁷	Controlled, community-level cluster randomized trials in 16 Massachusetts communities: physician behavior change strategy ⁴⁷ with follow-up ^{7,5}	<ul style="list-style-type: none"> ● Discussion guide at well-child visits ● Prescription pads for treatment of viral infections ● Stickers, lapel pins, and otoscope insufflators ● Bimonthly educational briefs ● Patient brochure ● Educational newsletters 	<ul style="list-style-type: none"> ● Introductory letter to pediatricians and family practitioners 	<ul style="list-style-type: none"> ● Educational coordinator visited practices ● Kick-off dinners 			<ul style="list-style-type: none"> ● Advertisements at child care centers and pharmacies
Huang et al ⁴⁸	Cluster randomized trial of 3-year community-wide intervention for parents of children in 16 communities ¹¹	<ul style="list-style-type: none"> ● Educational newsletters 					<ul style="list-style-type: none"> ● Educational materials in pediatrician offices, pharmacies, and child care settings
Vervloet et al ⁴⁹	Matched randomized study of meeting with PCPs and pharmacists, 4 groups with intervention, and 4 matched controls	<ul style="list-style-type: none"> ● PCP communication skills training ● Antibiotic prescribing agreements in EHR 		<ul style="list-style-type: none"> ● Feedback session about group's prescribing ● More variation between physicians than within practices 			
Linder et al ⁵⁰	Cluster randomized trial of 27 primary care practices to receive an EHR-integrated ARI CDSS	<ul style="list-style-type: none"> ● CDSS tool integrated into EHR 	<ul style="list-style-type: none"> ● Audit and feedback 				
Linder et al ⁵¹	Cluster RCT of 27 primary care practices, by using an ARI quality dashboard	<ul style="list-style-type: none"> ● ARI quality dashboard 					
Cals et al ⁵² and Cals et al ⁵³	Pragmatic cluster randomized trial of Dutch PCPs of the impact of POC CRP testing and communication skills on antibiotic use in LRTIs, ⁵² with follow-up of 3.5 years ⁵³	<ul style="list-style-type: none"> ● POC CRP testing 	<ul style="list-style-type: none"> ● Communication training for physicians 	<ul style="list-style-type: none"> ● Peer review of colleague transcripts with simulated patients 			

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Appendix B: Continued

SEIPS 2.0 Element							
Reference	Study Type	Tools / Technology Components	Person(s) Components	Organizational Components	Task Components	Physical Environment Components	External Environment Components
Maimous et al ⁵⁴	Quasi-experimental design with 3-month baseline data collection period and 15-month follow-up in 9 intervention and 61 control practices	<ul style="list-style-type: none"> EHR CDSS tool is populated when ARI diagnosis entered CDSS installed on each practice's EHR progress note template Hyperlinks to patient and provider education Guidelines mailed to GPs and available on website 	<ul style="list-style-type: none"> Performance review Audit and feedback 	<ul style="list-style-type: none"> Quarterly meetings with audit and feedback Academic detailing Monthly phone calls with staff 			<ul style="list-style-type: none"> NIH and CDC guidelines to improve antibiotic prescribing for ARI's CDC Get Smart program Regional guidelines Mass media campaign including outdoor and radio advertisements, billboards, bus tails, bus stop posters, interior bus signs, health fairs, and opinion pieces New guidelines written
Slekovec et al ⁵⁵	Quasi-experimental study of French GPs on quinolone prescription for UTIs			<ul style="list-style-type: none"> 200 GPs attended training sessions 			
Gonzales et al ⁵⁶	Quasi-experimental community-level study of mass media campaign in Colorado with comparison communities		<ul style="list-style-type: none"> Providers signed postcard soliciting support 				
Hurlimann et al ⁵⁷	Swiss quasi-experimental study of sustained feedback of antibiotic prescription for ARI's and UTIs		<ul style="list-style-type: none"> Sustained individual feedback 				
Vinnard et al ⁵⁸	Quasi-experimental study with concurrent control groups of academic detailing and educational mailings	<ul style="list-style-type: none"> Educational mailings to providers and patients Prescription pads for symptomatic treatments Providers signed letters to patients 	<ul style="list-style-type: none"> Intensive intervention for highest prescribers 	<ul style="list-style-type: none"> Academic detailing of providers (visits from pharmacist and antimicrobial stewardship expert) 			

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Appendix B: Continued

SEIPS 2.0 Element

Reference	Study Type	Tools / Technology Components	Person(s) Components	Organizational Components	Task Components	Physical Environment Components	External Environment Components
Gonzales et al ⁵⁹	Nonrandomized controlled trial, with (1) full intervention, (2) limited intervention, or (3) usual care	<ul style="list-style-type: none"> ● Full intervention: household and office-based patient education materials ● Limited intervention: office-based educational materials ● Full intervention: educational refrigerator magnets ● Full intervention: patients mailed pamphlet and letter from medical director 	<ul style="list-style-type: none"> ● Focus groups with elderly volunteers for feedback 	<ul style="list-style-type: none"> ● Full intervention: clinician education ● Full intervention: clinic-specific antibiotic prescription rate for acute bronchitis ● Full intervention: 30 minutes of staff meeting ● Full intervention: setting clinic goals 	<ul style="list-style-type: none"> ● Full intervention: education on acute bronchitis management ● Full intervention: clinicians taught how to refuse antibiotic prescriptions 	<ul style="list-style-type: none"> ● Both intervention groups: educational posters in exam rooms 	
Gonzales et al ⁶⁰	Nonrandomized controlled trial of elderly patients with ARI: 4 intervention practices and 51 control practices in Denver	<ul style="list-style-type: none"> ● Mailed campaign to patients ● Office-based materials ● Introductory letter from Department of Public Health ● Patient reference card on ARI ● Patient refrigerator magnet ● Patient brochures on antibiotic resistance 	<ul style="list-style-type: none"> ● Focus groups with elderly volunteers for feedback 	<ul style="list-style-type: none"> ● Individual prescribing profiles 	<ul style="list-style-type: none"> ● Colorado-wide initiative to provide PCPs with performance feedback 	<ul style="list-style-type: none"> ● Office-based materials: CDC posters, patient reference cards, and exam room posters 	
Formoso et al ⁶¹	Community-level, controlled, nonrandomized trial in northern Italy of educational campaign						<ul style="list-style-type: none"> ● Region-wide posters, brochures, and local media advertisements ● Region-wide physician and pharmacist newsletter

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Appendix B: Continued

SEIPS 2.0 Element

Reference	Study Type	Tools / Technology Components	Person(s) Components	Organizational Components	Task Components	Physical Environment Components	External Environment Components
Yardley et al ⁶²	Process analysis of RCT of GPs in study of LRTI antibiotic prescribing, including web-based training in use of CRP	<ul style="list-style-type: none"> ● Training software modifiable ● Patient booklet with checklist ● CRP intervention helpful 	<ul style="list-style-type: none"> ● Symptoms important to patients 	<ul style="list-style-type: none"> ● Skepticism of audit and feedback reports ● One respondent admitted to gaming behavior 	<ul style="list-style-type: none"> ● Completing patient booklet checklist 		
Szymczak et al ⁶³	Semistructured interviews with pediatricians, following an intervention ³⁹		<ul style="list-style-type: none"> ● Parental pressure as a barrier to stewardship 	<ul style="list-style-type: none"> ● Clinicians ask patients about antibiotic expectations ● Pride ● Rapport 			
Mustafa et al ^{64,65}	Semistructured interviews of family doctors on ARIs		<ul style="list-style-type: none"> ● Avoiding confrontation ● Negotiating with patients ● Hedging ● Physical traits ● Exaggerated symptoms ● Patient expectations 		<ul style="list-style-type: none"> ● Use physical exam findings to minimize signs ● Careful word choice ● Thorough exam ● Education ● Setting expectations ● All bacteria must be treated 		<ul style="list-style-type: none"> ● Clinical presentation outweighs guidelines for management of Streptococcal pharyngitis
Grondal et al ⁶⁵	Semistructured interviews of GPs regarding pharyngitis	<ul style="list-style-type: none"> ● GPs believed rapid Streptococcus test to be unreliable, as it only detects one bacterium ● CRP used to diagnose bacterial pharyngitis as way to screen for all bacterial infections 	<ul style="list-style-type: none"> ● Clinical presentation outweighs test results ● Streptococcal pharyngitis should be diagnosed based on appearance 				

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Appendix B: Continued

SEIPS 2.0 Element

Reference	Study Type	Tools / Technology Components	Person(s) Components	Organizational Components	Task Components	Physical Environment Components	External Environment Components
Munoz-Plaza et al ⁶⁶	In-depth interviews of 6 PCPs and 3 urgent care providers about acute sinusitis	<ul style="list-style-type: none"> Need to find guideline when needed Visual cards and graphs to show patients when they will improve EHR with web-based patient education 	<ul style="list-style-type: none"> Help patients understand symptoms Patients want reward for copays and taking off work 	<ul style="list-style-type: none"> Patients see physicians with different practices No protected group education time Large health systems enable system-level alerts Limited time during patient visits 		<ul style="list-style-type: none"> Large educational posters in exam rooms 	<ul style="list-style-type: none"> External pressures for patient satisfaction Patient can get antibiotics elsewhere Information overload with updated guidelines Copays for visits
Tonkin-Crine et al ⁶⁷	Semistructured interviews of experts involved in GP ARI guideline development across 5 countries	<ul style="list-style-type: none"> Complementary patient education Computer reminders to reinforce guidelines 	<ul style="list-style-type: none"> Address GP concerns and explain the need for guidelines GPs worry about patients becoming ill without prescription Prescribing feedback helpful 	<ul style="list-style-type: none"> Academic detailing GPs assume practice already follows guidelines GPs may not engage with mandatory meetings 	<ul style="list-style-type: none"> Flexible interventions increase feasibility Interventions should engage GPs 		<ul style="list-style-type: none"> Develop guidelines based on research, not to save money Guidelines should be consistent Guidelines difficult to locate and lengthy Local versions of national guidelines Governmental funding and national campaigns

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Appendix B: Continued

SEIPS 2.0 Element

Reference	Study Type	Tools / Technology Components	Person(s) Components	Organizational Components	Task Components	Physical Environment Components	External Environment Components
Wood et al ⁶⁸	Qualitative interviews with PCPs in 9 European countries	<ul style="list-style-type: none"> Request access to local resistance data 	<ul style="list-style-type: none"> Most PCPs did not see antibiotic resistance as a problem in their practice 	<ul style="list-style-type: none"> Antibiotic resistance seen as issue for secondary care rather than primary care 			<ul style="list-style-type: none"> Other countries thought to be responsible for resistance Self-prescribing of antibiotics Prescribing by dentists and hospital physicians leads to resistance
Mauffrey et al ⁷⁰	Qualitative study of French PCPs about preferences for interventions	<ul style="list-style-type: none"> Dedicated prescription for antibiotics considered excessive Limit antibiotic availability in outpatient settings Computerized prescription aids Educational resources for patients in office 	<ul style="list-style-type: none"> Physician training Patient characteristics Avoiding prescribing antibiotics is dangerous Older prescribers: prescriptions influenced by habit 	<ul style="list-style-type: none"> Practice evaluation is difficult due to competing demands Prior approval of ID physician would make practice harder 	<ul style="list-style-type: none"> Restricted susceptibility testing Explain and repeat key messages Role of PCPs in educating patients Too many other health ministry-required tasks 		<ul style="list-style-type: none"> Performance-based incentives Public campaigns reinforce what they tell patients Physician awareness campaigns
Ronnerstrand et al ⁷¹	Qualitative semistructured interviews: patients asked to imagine seeing a physician for ARI, and how long they would delay filling prescription	<ul style="list-style-type: none"> Given prescription to fill later 	<ul style="list-style-type: none"> More trust means patients would delay prescription 				<ul style="list-style-type: none"> Willing to postpone treatment if told others would do the same Social capital
Dempsey et al ⁷²	Semistructured interviews of 13 PCPs	<ul style="list-style-type: none"> Prefer of GDSS Prefer over-the-counter prescription pad Prefer patient educational materials 	<ul style="list-style-type: none"> Meet patient expectations 	<ul style="list-style-type: none"> No accountability for prescribing Other clinicians' misconceptions about acute bronchitis Previsit triage and education by nurses may prevent visits 	<ul style="list-style-type: none"> Prescribe antibiotics to save time and money Diagnostic uncertainty 		<ul style="list-style-type: none"> Reporting of quality measures may help

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Appendix B: Continued

SEIPS 2.0 Element							
Reference	Study Type	Tools / Technology Components	Person(s) Components	Organizational Components	Task Components	Physical Environment Components	External Environment Components
Huddy et al ⁶⁹	Qualitative focus group study of barriers and facilitators to use of CRP for diagnosing CAP among European GPs	<ul style="list-style-type: none"> Want not just POC CRP but other lab testing in the same system Need to test equipment and stay aware of shelf life of cartridges 	<ul style="list-style-type: none"> CRP as aid to communication 	<ul style="list-style-type: none"> Centralized labs Different people perform test in different clinics (GP, nurse, and in-house lab) 	<ul style="list-style-type: none"> Quality control tasks Responsibility of GP 	<ul style="list-style-type: none"> Protocols support decision making Visits are time consuming and complex Provide self-management education Educate patients to prevent return visits 	<ul style="list-style-type: none"> Although CRP is cost-effective, individual practices may be liable for the cost of the test Loss of income to central labs Legal protection of NPs versus GPs
Rowbotham et al ⁷³	Semistructured interviews and focus groups of UK NPs about experience with ARI	<ul style="list-style-type: none"> Used drawings or information leaflets to teach patients 	<ul style="list-style-type: none"> New NPs worried about making mistakes Patients exaggerated symptoms 	<ul style="list-style-type: none"> Peer support helpful with demanding patients Previous experiences with getting antibiotics from other providers 	<ul style="list-style-type: none"> Alternatives to antibiotics 	<ul style="list-style-type: none"> Media information about antibiotics School or day care requires antibiotics External guidelines 	
Kuzujanakis et al ⁷⁴	Parenteral surveys		<ul style="list-style-type: none"> Parents demand antibiotics Privately insured and with more or older children had more knowledge Children less likely to receive antibiotics 				
Murphy et al ⁷⁵	Qualitative interview of GPs reviewing own charts of ARI encounters				<ul style="list-style-type: none"> Amoxicillin as placebo if physician did not think they need Uncertainty in prescribing antibiotic 		

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Appendix B: Continued

SEIPS 2.0 Element							
Reference	Study Type	Tools / Technology Components	Person(s) Components	Organizational Components	Task Components	Physical Environment Components	External Environment Components
Anthierens et al ⁷⁷	Qualitative study using think-aloud approach with European GPs about using online tool for CRP ordering	<ul style="list-style-type: none"> ● Online intervention ● CRP used as evidence for patients on condition's seriousness ● Tailoring for individual countries and languages 	<ul style="list-style-type: none"> ● Considering needs of patients ● Level of attention and time taken needs to be brief 	<ul style="list-style-type: none"> ● Managing patient demands, fewer visits, decreased income 	<ul style="list-style-type: none"> ● GPs use communication skills ● Clarity of intervention ● Physical exam used to communicate to patients 		<ul style="list-style-type: none"> ● Countries differ in how involved patients expect to be in the decision ● Study in one country may not help in other countries

PCP, primary care provider; CDSS, clinical decision support system; RCT, randomized controlled trial; POC, point of care; ARI, acute respiratory infection; EHR, electronic health record; NIH, National Institutes of Health; CDC, Centers for Disease Control and Prevention; GP, general practitioner; LRTI, lower respiratory tract infection; CRP, C-reactive protein; ID, infectious diseases; MCO, managed care organization; CAP, community-acquired pneumonia; COPD, chronic obstructive pulmonary disease; NP, nurse practitioner; UTI, urinary tract infection; PCR, polymerase chain reaction; GAS, Group A Streptococcus; CAP, community-acquired pneumonia; UTI, urinary tract infection.

*Studies described include rigorously designed quantitative and qualitative studies describing antibiotic stewardship interventions and the context around antibiotic prescribing decisions, included through November 7, 2016.

Appendix C. Summary of the Impact of Ambulatory Antimicrobial Stewardship Interventions*

Reference	Process Outcome	Patient Outcome	Provider Outcome	Clinic Outcome	System Outcome
Litvin et al ²⁰		<ul style="list-style-type: none"> Choice of prescribing antibiotics 			
Persell et al ²¹	<ul style="list-style-type: none"> Prescribing antibiotics 		<ul style="list-style-type: none"> Prescribed antibiotics in 24.7% of inappropriate ARI diagnoses prior to and only 5.2% after the study Suggested alternative antibiotic prescribing intervention decreased Suggested alternatives and peer comparisons decreased Antibiotic prescribing for all ARI diagnoses combined Most providers were satisfied with intervention More first line antibiotics used Antibiotic prescription/1,000 people decreased 	<ul style="list-style-type: none"> Median prescription cost rose in control group 	
Hux et al ²²					
Hallsworth et al ²³					
Strykowski et al ²⁴					
Foxman et al ²⁵					<ul style="list-style-type: none"> GPs in full intervention reduced antibiotic overprescribing (OR, 0.35; 95% CI, 0.18 to 0.68) Underprescribing was not significantly increased (OR, 0.25; 95%CI, 0.06 to 1.0; $P = .075$) 85% more antibiotics prescribed among those without copays than among those with copays
Long et al ²⁶		<ul style="list-style-type: none"> Median duration of antibiotic: 5 days in intervention versus 7 days in control group Prescription of antibiotics 84.4% in intervention versus 67.5% in control group 			
Arakaki et al ²⁷	<ul style="list-style-type: none"> Diagnosis of cellulitis made in 2/20 in intervention group and 3/9 in control group 	<ul style="list-style-type: none"> Antibiotic use in 2/20 patients in intervention versus all in control group All improved 1 week later 			

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Appendix C. Continued

Reference	Process Outcome	Patient Outcome	Provider Outcome	Clinic Outcome	System Outcome
Taylor et al ²⁸		<ul style="list-style-type: none"> Number of ARI visits did not change Number of diagnoses and antibiotic prescriptions for otitis media and sinusitis did not change Antibiotic prescriptions per patient did not change Five patients in each group had unfavorable outcomes 			
Torres et al ²⁹				<ul style="list-style-type: none"> Antibiotic use decreased in clinical prediction group (48.6% versus 86.6%, $P < .001$) 	
Le Corvoisier et al ³⁰			<ul style="list-style-type: none"> Proportion of prescriptions containing an antibiotic decreased in intervention (15.2% to 12.3%; $P < .001$) but not control (15.3% to 16.4%; between group difference 3.93%) Maintained improvement for 30 months after intervention terminated More symptomatic treatment prescribed in treatment than control (7.8% versus 3.9%) No diagnostic coding shift 		
Meeker et al ³¹		<ul style="list-style-type: none"> Antibiotic prescribing for nonindicated ARIs decreased in intervention (42.8% to 33.7%) but not control (43.5% to 52.7%) Posted commitment letter decreased antibiotic prescribing for nonindicated diagnoses by 19.7% No change in appropriate antibiotic prescriptions Rapid test result group prescribed fewer antibiotics per hour of visit (4.5% versus 12.3%) No difference in symptoms at follow-up No significant adverse events 			
Brittain-Long et al ³²					

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Appendix C. Continued

Reference	Process Outcome	Patient Outcome	Provider Outcome	Clinic Outcome	System Outcome
Christakis et al ³³			<ul style="list-style-type: none"> ● Proportion of prescriptions for otitis media <10 days decreased 34% in intervention group ● Less likely to prescribe antibiotics in intervention 		
Dahler-Eriksen et al ³⁵		<ul style="list-style-type: none"> ● Antibiotics started earlier in patients with lower CRP concentrations ● No reduction in antibiotics 		<ul style="list-style-type: none"> ● Use of ESRs decreased by 8% in intervention ● Blood samples sent to hospital lab decreased by 6% ● Proportion of study patients needing a follow-up telephone call reduced from 63% to 53% 	
De la Poza Abad et al ³⁶		<ul style="list-style-type: none"> ● Symptom duration increased only for the no-prescription group ● No difference in symptom severity ● Antibiotic use less in no-prescription and delayed strategies ● Patient satisfaction similar across all groups ● Patient belief in antibiotic effectiveness decreased in no-prescription and delayed strategies 			
Hemkens et al ³⁷	<ul style="list-style-type: none"> ● Only 11% of physicians in the intervention group logged onto the online audit and feedback tool 		<ul style="list-style-type: none"> ● Overall antibiotic prescription in defined daily doses/100 clinic visits did not decrease in the first or second year (0.81%, $P = .64$; -1.73%, $P = .32$; respectively) ● Antibiotic prescribing decreased 8.61% among 6 to 18-year-old children in first year only ($P = .01$) ● Antibiotic prescribing declined 4.59% among adults aged 19 to 65 in second year only ($P > .10$) 		

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Appendix C. Continued

Reference	Process Outcome	Patient Outcome	Provider Outcome	Clinic Outcome	System Outcome
Samore et al ³⁸					<ul style="list-style-type: none"> ● Macrolides decreased in CDSS but not in community intervention alone ● Greater decrease in antibiotic prescribing in CDSS than in community intervention alone
Gerber et al ³⁹			<ul style="list-style-type: none"> ● Combination of 2 practices decreased overall and broad-spectrum antibiotic prescribing 		
Gerber et al ⁴⁰				<ul style="list-style-type: none"> ● Antibiotic prescribing increased after intervention ended (intervention, 16.7% to 27.9%; controls, 25.4% to 30.2%; $P = .02$) 	
Gonzales et al ⁴¹				<ul style="list-style-type: none"> ● Educational intervention did not further decrease ARI antibiotic prescription 	
Jenkins et al ⁴²				<ul style="list-style-type: none"> ● Antibiotic prescriptions decreased 42.7% to 37.9% versus 39.8% to 38.7% 	
Finkelstein et al ⁴³				<ul style="list-style-type: none"> ● Decreased broad-spectrum antibiotic use ● Ages 3 months to 3 years: intervention decreased 18.6% versus 5.1% in controls (16% adjusted effect) ● Age 3 to 5 years: intervention decreased 15% versus 9.8% in controls (12% adjusted effect) 	
Meeker ⁴⁴			<ul style="list-style-type: none"> ● Control practices: antibiotic prescription decreased from 24.1% to 13.1% ● Suggested alternatives: prescriptions decreased from 22.1% to 6.1% (insignificant) ● Accountable justification: prescriptions decreased from 33.2% to 5.2% ● Peer comparison: prescriptions decreased from 19.9% to 3.7% ● No interactions seen 		

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Appendix C. Continued

Reference	Process Outcome	Patient Outcome	Provider Outcome	Clinic Outcome	System Outcome
Yang et al ⁴⁵			<ul style="list-style-type: none"> ● Reporting at individual and institutional level 		<ul style="list-style-type: none"> ● Public reporting resulted in 9% decline in antibiotics
Schnoor et al ⁴⁶		<ul style="list-style-type: none"> ● Decrease in CAP-related mortality higher in intervention (2.9% versus 0.5%) ● No change in patient adherence to duration of treatment 	<ul style="list-style-type: none"> ● Increased proportion of visits adhering to antibiotic guidelines (5.6%) 		
Finkelstein et al ⁴⁷					<ul style="list-style-type: none"> ● Downward trend in prescribing even without intervention ● Change in antibiotics dispensed per person-year: no decrease in those <2 years, but 4.6% decrease in 2 to 3 years and 6.7% decrease in 4 to 5 years ● More parents in intervention communities correctly answered survey questions
Huang et al ⁴⁸					
Vervloet et al ⁴⁹		<ul style="list-style-type: none"> ● Number of ARI antibiotic prescriptions decreased overall, but intervention group improved more 			
Linder et al ⁵⁰	<ul style="list-style-type: none"> ● 69% of ARI visits in the CDS group used the CDS 		<ul style="list-style-type: none"> ● Antibiotic prescribing rate for ARIs 39% in intervention versus 43% in control clinics (OR, 0.8; 95% CI, 0.6 to 1.2) ● For antibiotic-appropriate ARIs, no difference antibiotic prescribing in intervention and control clinics (54% versus 59%) ● For nonantibiotic appropriate diagnoses, no difference in intervention and control clinics (32% versus 34%) ● When CDSS used, associated with a lower antibiotic prescribing rate for acute bronchitis (OR, 0.5; 95% CI, 0.3 to 0.8) 		

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Appendix C. Continued

Reference	Process Outcome	Patient Outcome	Provider Outcome	Clinic Outcome	System Outcome
Linder et al ⁵¹	<ul style="list-style-type: none"> Only 28% of intervention clinicians logged into the quality dashboard 		<ul style="list-style-type: none"> No difference in antibiotic prescribing for ARI visits overall (47% versus 47%, $P = .87$), antibiotic-appropriate ARI visits (65% versus 64%, $P = .68$), or nonantibiotic-appropriate ARI visits (38% versus 40%, $P = .70$) Those who used the dashboard had a lower ARI prescribing rate (42% versus 50%, $P = .02$) 		
Cals et al ⁵²		<ul style="list-style-type: none"> Antibiotic prescribing at index visit: 31% in CRP and 53% without CRP; 27% in education and 54% in no training Antibiotic prescribing during 28-day follow-up: no difference Total antibiotic prescribing: 45% versus 58% with and without CRP and 38% versus 63% in communication skills training Long-term follow-up over next 2 to 3 years: no difference number of LRTI visits 			
Cals et al ⁵³				<ul style="list-style-type: none"> CRP not used over time: only in 3.7% of visits 2 to 3 years later Communication training led to a long-term decrease of 10.4% in visits resulting in antibiotic prescription 	
Mainous et al ⁵⁴	<ul style="list-style-type: none"> Use of CDSS tool Help with diagnosis Decide about antibiotics How often CDSS template used 	<ul style="list-style-type: none"> Decreased overall prescribing of broad-spectrum antibiotics in adults and children (16.6% in adults and 11.1% in children) (16.7% to 0.9%, respectively) and antibiotics overall among adults 	<ul style="list-style-type: none"> How often CDSS template used Inappropriate prescribing Diagnostic shift 		

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Appendix C. Continued

Reference	Process Outcome	Patient Outcome	Provider Outcome	Clinic Outcome	System Outcome
Slekovec et al ⁵⁵					<ul style="list-style-type: none"> Quinolone prescriptions decreased by 9%, but nitrofurantoin and fosfomycin increased by 36.8% and 28.5% respectively Cost savings 3.8% decrease in antibiotic prescriptions/1000 persons 8.8% decrease in antibiotic dispenses/1000 managed care members
Gonzales et al ⁵⁶	<ul style="list-style-type: none"> No adverse impact on emergency department visits or ARI complications 			<ul style="list-style-type: none"> Fewer pediatric clinic visits 	
Hurlimann et al ⁵⁷				<ul style="list-style-type: none"> Increased percentage of prescriptions of penicillins for ARIs treated with antibiotics (49% to 57%) Did not decrease the percentage of COPD exacerbations treated with fluoroquinolones Did not decrease the proportion of sinusitis and other upper ARIs treated with antibiotics 	
Vinnard et al ⁵⁸			<ul style="list-style-type: none"> Nonindicated antibiotic prescriptions decreased from 43% to 33% in academic detailing group 		
Gonzales et al ⁵⁹		<ul style="list-style-type: none"> Full intervention decreased antibiotic prescription for acute bronchitis (74% to 48%) but not control (78% to 76%) or limited intervention (82% to 77%) Antibiotic prescribed to 64% of respondents at intervention and control clinics Patient satisfaction did not differ: 99% very good or excellent satisfaction in intervention clinic, 63% in control clinic 			
Gonzales et al ⁶⁰				<ul style="list-style-type: none"> Diagnoses of acute bronchitis did not change 	

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Appendix C. Continued

Reference	Process Outcome	Patient Outcome	Provider Outcome	Clinic Outcome	System Outcome
Formoso et al ⁶¹					<ul style="list-style-type: none"> Defined daily doses of antibiotics/1,000 person-days decreased 4.3% in intervention area Broad-spectrum antibiotics decreased more Intervention did not affect knowledge and attitudes about antibiotic resistance CRP testing means less antibiotics
Yardley et al ⁶²	<ul style="list-style-type: none"> Communication patient and clinician Decision to provide antibiotic 	<ul style="list-style-type: none"> Belief in harm or need for antibiotics Attitudes towards antibiotics CRP: patient feels less enabled and less satisfied 	<ul style="list-style-type: none"> Importance of reducing antibiotic use Perceptions of damage to patient/clinician relationship Those who did CRP testing showed trend of lost confidence in ability to reduce antibiotic prescribing Belief in audit and feedback reports Avoid confrontation Patient/provider relationship Dissatisfaction Be a good physician 		
Szymczak et al ⁶³	<ul style="list-style-type: none"> Gaming of audit and feedback 				
Mustafa et al ⁶⁴	<ul style="list-style-type: none"> Learn patient expectations Decide on antibiotic 	<ul style="list-style-type: none"> Patient/provider relationship Education Set expectations with next ARI Antibiotics prescribed 		<ul style="list-style-type: none"> Pride in practice 	<ul style="list-style-type: none"> Antibiotic resistance
Gronald et al ⁶⁵	<ul style="list-style-type: none"> Choice to do rapid Streptococcus test Choice to do CRP 				
Munoz-Plaza et al ⁶⁶					
Tonkin-Crine et al ⁶⁷	<ul style="list-style-type: none"> Use of guidelines among GPs 		<ul style="list-style-type: none"> Unwarranted prescribing practices for sinusitis Poor patient satisfaction score Engage GPs in interventions 		<ul style="list-style-type: none"> GPs perceive antibiotic resistance as due to secondary care, pharmacists, dentists, and even other countries
Wood et al ⁶⁸					
Mauffrey et al ⁷⁰				<ul style="list-style-type: none"> Interventions should not impact clinic flow 	
Ronnerstrand et al ⁷¹					<ul style="list-style-type: none"> Patient trust in others

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Appendix C. Continued

Reference	Process Outcome	Patient Outcome	Provider Outcome	Clinic Outcome	System Outcome
Dempsey et al ⁷²					
Huddy et al ⁶⁹	<ul style="list-style-type: none"> Quality checks of POC CRP testing 	<ul style="list-style-type: none"> Perception of patient requests Patients like the test 	<ul style="list-style-type: none"> Increase job satisfaction 	<ul style="list-style-type: none"> Too many visits 	
Rowbotham et al ⁷³			<ul style="list-style-type: none"> Clinician confidence 		
Kuzuhanakis et al ⁷⁴		<ul style="list-style-type: none"> Prescribed antibiotic Education on antibiotics 			
Ackerman et al ⁷⁵	<ul style="list-style-type: none"> Preferred an exam room poster with diagnostic algorithm 	<ul style="list-style-type: none"> Patient expectations seen as impacting prescribing 	<ul style="list-style-type: none"> Compared with prior surveys, clinicians demonstrated greater awareness of antibiotic resistance and impact of their prescribing decisions Reminder of danger of antibiotic resistance 		
Murphy et al ⁷⁶					
Anthierens et al ⁷⁷	<ul style="list-style-type: none"> Communication with patients 	<ul style="list-style-type: none"> Patient satisfaction 	<ul style="list-style-type: none"> Education about antibiotic resistance 	<ul style="list-style-type: none"> Fewer visits, decreased income 	

ARI, acute respiratory infection; CDSS, clinical decision support system; OR, odds ratio; CI, confidence interval; CAP, community-acquired pneumonia; CRP, C-reactive protein; LRTI, lower respiratory tract infection; COPD, chronic obstructive pulmonary disease; ESR, erythrocyte sedimentation rate; POC, point of care; GP, general practitioner.

*As studied in rigorously designed quantitative and qualitative studies describing the context around antibiotic prescribing decisions and antibiotic stewardship interventions, through November 7, 2016 on outcomes, including process outcomes and outcomes to the patient, provider, clinic, and health system.