Infection Control & Hospital Epidemiology (2020), **41**, 833–840
doi:10.1017/ice.2020.94

SHEA
The Society for Healthcare Epidemiology of America

Review

Antimicrobial stewardship in the outpatient setting: A review and proposed framework

Jasmine R. Marcelin MD, FACP[1], Philip Chung PharmD, MS, BCIDP[2] and Trevor C. Van Schooneveld MD, FACP[1]

[1]Division of Infectious Diseases, University of Nebraska Medical Center, Omaha, Nebraska and [2]Department of Pharmacy, Nebraska Medicine, Omaha, Nebraska

Abstract

Antimicrobial misuse is still a significant problem, and most inappropriate use occurs in the outpatient setting. In this article, we provide a review of available literature on outpatient antimicrobial stewardship in primary care settings, and we propose a novel implementation framework.

(Received 18 November 2019; accepted 21 March 2020; electronically published 28 April 2020)

Antimicrobial-resistant infections affect nearly 3 million Americans annually, causing some 35,000 deaths each year.[1] Antimicrobial resistance is the inevitable result of antibiotic use, and it is exacerbated by overuse and inappropriate use of antibiotics. Some 50% of antibiotics prescribed in the outpatient setting for acute respiratory infections (ARIs) are superfluous,[2] and the Department of Veterans' Affairs estimate that >75% of outpatient antibiotic prescriptions are inappropriately prescribed.[3] Skin and soft-tissue infections (SSTIs) are frequently overtreated. One study showed that 85% of inpatient and 48% of outpatient nonpurulent cellulitis cases received unneeded antimethicillin-resistant *Staphylococcus aureus* (MRSA) therapy.[4] This unnecessary antibiotic use has financial implications: 59% of antibiotic expenditures (or $33.2 billion) occur in the outpatient setting, and $28.7 billion of prescriptions are dispensed in community pharmacies.[5]

Despite much published data on antimicrobial stewardship in the acute-care setting, the right formula for outpatient antimicrobial stewardship is not well defined. Prior studies have focused on improving prescriber practices, raising patient and public awareness, or leveraging diagnostic stewardship to reduce inappropriate antibiotic prescribing.[6,7] Although these approaches have had varying degrees of success, uncertainty remains about how to reduce inappropriate prescribing. The first executive order of the National Action Plan for Combating Antibiotic Resistant Bacteria was to reduce inappropriate outpatient antibiotic prescribing by 50% by the year 2020.[8] Unfortunately, there has been little progress toward this goal; prescribing trends have remained largely unchanged over the last several years.[9]

In this review, we summarize current literature regarding outpatient antimicrobial stewardship, and we provide a concept map for developing antimicrobial stewardship strategies in the outpatient setting. We focus on primary care practices; discussion of antimicrobial stewardship in other outpatient settings is outside the scope of this review. However, consideration of antimicrobial stewardship in dental offices, retail stores, the urgent care setting, and telemedicine practices is also important.

Author for correspondence: Jasmine R Marcelin, E-mail: jasmine.marcelin@unmc.edu
Cite this article: Marcelin JR, Chung P, and Van Schooneveld TC. (2020). Antimicrobial stewardship in the outpatient setting: A review and proposed framework. *Infection Control & Hospital Epidemiology*, 41: 833–840, https://doi.org/10.1017/ice.2020.94

© 2020 by The Society for Healthcare Epidemiology of America. All rights reserved.

Reasons for antibiotic misuse

Patient expectations

Patient expectations (or clinician perception of their expectations) may impact antibiotic prescribing.[10] In a recent study, only 19% of patients with ARI symptoms contacted their doctors, but more than half of these patients expected antibiotics.[11] Unfortunately, clinicians generally do not have a good sense of when these expectations are present. In a study of 287 outpatient visits for ARIs, parents and clinicians completed questionnaires that assessed expectations for antibiotics. Physicians initiated a discussion about antibiotics in 74% of encounters. Parents did so only 8% of the time, with mostly indirect mentions rather than requests for antibiotics. Nevertheless, physicians thought that parents expected antibiotics in these encounters, so they prescribed antibiotics 48% of the time (compared to 10% of the time if they perceived no expectations; $P < .001$).[12] Interestingly, parents who expected antibiotics but did not receive them had much higher satisfaction scores if the physician provided a contingency plan (eg, what to do if symptoms do not improve and promise of re-evaluation). In short, patients rarely ask for or expect antibiotics, but physicians think they do and are likely to prescribe them. Therefore adjusting communication strategies regarding antibiotics may have significant impact on antibiotic prescribing and patient satisfaction.

Risks of illness versus risk of antibiotic treatment

Clinician prescribing practices may depend more on the effect they believe antibiotics will have on their patients' health than on their awareness of appropriate antibiotic indications. One study demonstrated that if emergency department clinicians believed the risk of antibiotic adverse effects were negligible, and there was even a slight possibility that antibiotics would make their patients feel better (i.e., "Why not take a risk?"), they were more likely to prescribe non–guideline-concordant antibiotics (odds ratio [OR], 1.28; 95% confidence interval [CI], 1.06–1.54).[13] In contrast, clinicians who

believed that antibiotics produce a small risk of harm to the patient (i.e., "antibiotics may be harmful") were less likely to prescribe inappropriately (OR, 0.81; 95% CI, 0.67–0.98).[13] These findings demonstrate why antimicrobial stewardship strategies should emphasize the potential harms of antibiotics to patients, especially where there is no benefit (eg, bronchitis or viral upper respiratory infection) or the benefit is slight (eg, sinusitis). Furthermore, despite fewer concerns about antimicrobial resistance, patients and parents of patients still have valid concerns about adverse drug effects and may actually prefer to avoid unnecessary antibiotic use.[14] Therefore, notwithstanding perceptions of their expectations, primary care clinicians should partner with patients and parents in shared decision making about appropriate antibiotic use as part of their antimicrobial stewardship efforts.

Health disparities in prescribing practices

Adults older than 65 years are more likely to be prescribed antibiotics than any other group of adults,[15] and the highest prescribing rate for adults occurs in those older than 75 years.[16] These patients are more likely to receive fluoroquinolone antibiotics, despite mounting evidence of their adverse effects.[17] The southeastern and south-central United States are traditionally the most affected by healthcare disparities, and several studies have demonstrated higher antibiotic prescribing rates in these regions.[15,16,18] Earlier studies also showed more inappropriate antibiotic prescribing for patients in lower poverty quartiles, those with lower rates of college education, those who are uninsured, and those who smoke cigarettes.[19,20] These findings suggest that local strategies that consider the local race and ethnicity, socioeconomic status, and insurance status may be more helpful in addressing inappropriate prescribing than blanket national programs.

Developing an outpatient antimicrobial stewardship program with currently available resources

The Society for Healthcare Epidemiologists of America (SHEA) and Infectious Diseases Society of America (IDSA) collaborated to create guidelines for implementing an antimicrobial stewardship program (ASP). Many of their general recommendations are applicable to outpatient antimicrobial stewardship.[21] In 2016, the Centers for Disease Control and Prevention (CDC) released its "Core Elements of Outpatient Antibiotic Stewardship," in which they outlined a framework for ASPs in the outpatient setting.[22] In this document, the CDC recommends that healthcare organizations do the following:

1. Commit to a program to improve appropriate antibiotic use
2. Create and implement at least 1 policy or practice to achieve this goal
3. Track and report antibiotic prescribing rates to clinicians
4. Provide education to clinicians prescribing and patients receiving antibiotics

More recently, the Joint Commission announced, "Effective January 1, 2020, new antimicrobial stewardship requirements will be applicable to Joint Commission-accredited ambulatory health care organizations."[23] In their reports, the CDC and Joint Commission ask healthcare organizations to think about how to reduce inappropriate outpatient antibiotic prescribing, how to put a plan into action, and how to be accountable for that plan.



Fig. 1. C-DIFF (Collaboration/Communication, Data, Interventions, Feedback, and Follow-up): a proposed framework for an outpatient antimicrobial stewardship program.

Review of outpatient antimicrobial stewardship within a proposed framework

The first steps toward antimicrobial stewardship in an organization are (1) to identify a leader or leaders for the program and (2) to allocate sufficient administrative support for the ASP. The most successful work in quality improvement is often performed by teams rather than individuals. Infectious diseases (ID) physicians[24,25] and ID pharmacists[26-28] are highly trained and have the antibiotic expertise required for co-leadership roles in these efforts. Outpatient facilities without specific ID clinicians may consider regional consultation or teleconsultation services to access this expertise. Experts should engage with clinic leadership because local engagement in improvement efforts is essential to success. Leaders should also collaborate with clinicians from other outpatient specialties, nurses, microbiologists, clinic managers, and administrative personnel. This collaboration should lead to brainstorming on specific problems and designing appropriate interventions, followed by evaluation, re-evaluation, and further collaboration. Figure 1 shows a proposed framework for outpatient antimicrobial stewardship efforts entitled C-DIFF (Collaboration/Communication, Data, Interventions, Feedback, and Follow-up), which is reviewed in the following sections.

Collaboration/Communication

Role of pharmacists in outpatient antimicrobial stewardship

Given that >90% of Americans live within 5 miles of a pharmacy,[29] pharmacists may be the most accessible healthcare professionals in the community. Numerous opportunities exist for pharmacists to improve antibiotic prescribing. The Society of Infectious Diseases Pharmacists recently outlined a number of potential pharmacist-led outpatient antimicrobial stewardship initiatives including antibiotic prescription reviews, patient counseling, and prescriber education, as well as more innovative initiatives such as point-of-care testing and initiation of treatment based on a physician–pharmacist collaborative practice agreement.[28] A randomized pilot study demonstrated increases in guideline-concordant antibiotic prescribing and use of less costly antibiotic therapy by general practitioners after a 15-minute academic detailing visit by a clinical pharmacist that included antibiotic prescribing best practices, the

https://doi.org/10.1017/ice.2020.94 Published online by Cambridge University Press

distribution of laminated treatment recommendation charts, and encouraging prescribers to resist patient pressure.[30] Similarly, a meta-analysis found that involvement of pharmacists in antibiotic stewardship interventions led to a significant reduction in antibiotic prescribing (OR, 0.86; 95% CI, 0.78–0.95) and improvement in the rate of antibiotic prescribing adherence (OR, 1.96; 95% CI, 1.56–2.45) by general practitioners.[31] Pharmacist roles in these interventions included facilitating clinician huddles, creating workshops with clinicians, development and delivery of educational materials, and audit and feedback.[31]

Pharmacists have also been engaged in developing treatment guidance for outpatient clinicians. A multidisciplinary team that included a pharmacist designed a clinical decision support tool to guide management of uncomplicated urinary tract infections.[32] This collaboration led to significant reductions in the use of fluoroquinolone (27%) and trimethoprim/sulfamethoxazole (20%), and increases in nitrofurantoin use for cystitis (31%) and guideline-directed duration of therapy (32%).[32] A multistate evaluation of a collaborative practice agreement between physicians and free-standing pharmacies found that pharmacists were able to accurately triage and manage patients presenting with influenza-like illness.[33] In this study, 35% of patients had no primary care physician and 39% visited outside of normal clinic hours; these findings demonstrate the potential value of care using this model.

Role of nurses in outpatient antimicrobial stewardship

Because they function in multiple roles in outpatient settings and communicate with both patients and clinicians, numerous possibilities exist for nurses to affect antimicrobial use. For instance, nurse managers and nurse educators supported implementation of ASPs in 6 outpatient dialysis facilities, resulting in significant decreases in monthly antimicrobial doses while the rate of hospital admissions remained unchanged.[34] In another study, a urine culture follow-up program was implemented in a pediatric urgent care network in which a nurse reviewed urine culture results, forwarded negative results from patients who received empiric antibiotics to clinicians for review, and notified patients or caregivers of plans to discontinue therapy.[35] This program resulted in an increase in antibiotic discontinuation from 4% to 84%, resulting in >3,000 antibiotic days avoided.[35]

Other potential areas of nurse involvement in outpatient antimicrobial stewardship include taking accurate antimicrobial allergy histories, instructing patients on how to provide appropriate specimens for culture, and providing patient education about antibiotics.[36]

Data

Once the collaborative team is established, the next step is to evaluate what data are available to be analyzed and acted upon. Prescriber attribution may be relatively easy to assign in a nonacademic setting in which the individual who signs the antibiotic prescription is generally the treating clinician, but in clinics with a training model, trainees may order antibiotics that may be attributed to themselves or to their supervisors. Obtaining data on antibiotic prescribing practices in the outpatient setting may be difficult because care episodes are shorter, prescriptions are dispensed outside the clinic, and some prescribing may be delayed and asynchronous to a visit. Although indication data may not be available because it is not required in most practices, it can often be attributed using visit coding data. *International Classification of Disease* (ICD) codes for indications are typically extractable from the electronic medical record; however, these codes do not always reflect the actual clinical diagnosis.[37] Despite this lack of fidelity, a clinician's volume-adjusted prescribing rate has been shown to correlate with their rate of inappropriate prescribing.[37]

Identifying high-priority conditions

The CDC recommends that programs identify high-priority conditions to focus on, and the new Joint Commission standards require that at least 1 annual goal must be identified. This section describes suggestions for high-priority conditions that could be targeted.

Acute respiratory infections

Antibiotic prescribing in the outpatient setting generally follows seasonal patterns, and more antibiotics are prescribed in the fall and winter seasons during the respiratory viral season.[9] During the 2013–2014 and 2014–2015 influenza seasons, 41% of all patients presenting to outpatient clinics with ARI were prescribed antibiotics.[38] Based on the documented diagnoses, 41% of all antibiotics were not indicated.[38] Within that same cohort, of 440 patients who were prescribed antibiotics for pharyngitis, 38% had negative group A streptococcal testing, and 38% were prescribed antibiotics for acute sinusitis that were not indicated.[38] Numerous opportunities exist to both prevent unneeded antibiotic prescribing and to improve the use of guideline-compliant antibiotics.

Urinary tract infections

Urinary tract infections (UTIs) are another common indication for outpatient prescribing. Durkin et al[39] used a commercial insurance database to retrospectively evaluate outpatient management of UTIs in nonpregnant young women before and after the release of an IDSA clinical practice guideline. A slight decrease in inappropriate antibiotic utilization was observed in the postguideline period. The guideline recommended avoidance of fluoroquinolones as first-line therapy, but their use decreased only minimally in the postintervention period (44.04% vs 41.71%; $P < .001$), and they continued to be prescribed inappropriately (49.78% vs 47.85%; $P < .001$), with >75% prescribed for inappropriate durations.[39]

Skin and soft-tissue infections

Skin and soft-tissue infections (SSTIs) are another clinical syndrome in which antibiotics are often utilized. In a study of outpatient pediatric practices, 77% of antibiotics prescribed for SSTIs were for a duration of >7 days, and 10% of antibiotics prescribed were not first-line agents.[40] Furthermore, compared with emergency medicine and family medicine clinicians, pediatricians in that study were more likely to prescribe first-line antibiotics for longer than necessary.[40]

Interventions to reduce inappropriate antibiotic prescribing

Outpatient clinics present a challenge to antimicrobial stewardship efforts because they may be spread out across large geographic areas. Additionally, pharmacy dispensing occurs in different locations than prescribing, and the patients and clinicians are less

https://doi.org/10.1017/ice.2020.94 Published online by Cambridge University Press

readily available. Interventions to reduce inappropriate antibiotic prescribing in the outpatient setting are often multifaceted, making assessment of individual components of interventions difficult.[41]

Behavioral interventions

Evidence shows that social and behavioral interventions can influence prescribing practices. For example, individuals are more likely to follow through with specific actions if they have publicly declared those intentions. Publicly displayed posters with physician signatures committing to responsible antibiotic prescribing led to a 19.7% reduction in prescribing rates.[42] One medical group created a patient wellness bag containing tissues, cough drops, hand sanitizer, and patient education materials that was distributed to patients with symptoms of bronchitis. This decreased inappropriate antibiotic prescribing from 84% to 8% in primary care clinics and from 67% to 54% in the emergency room.[43] Interventions in SSTI might include clinician education of guideline-concordant prescribing coupled with clinical decision support to limit the type and duration of antibiotics prescribed. Similar interventions have shown significant improvement in prescribing.[44]

Other efforts include "accountable justification" in the electronic medical record (EMR), whereby the prescriber was prompted to justify antibiotic prescription out of guidelines; "suggested alternatives" where an EMR flag based on ARI diagnosis coding displayed treatment alternatives based on diagnosis coding; or "peer comparison" where clinicians who were not in the top decile of appropriate prescribers received an email telling them they were "not a top performer," along with their rates compared to top performers.[45] A study comparing these 3 approaches found that mean antibiotic prescribing rates decreased by 5% (95% CI, 7.8%–0.1%; $P = .66$) for suggested alternatives, decreased by 7% (95% CI, 9.1%–2.9%; $P < .001$) for accountable justification, and decreased by 5.2% (95% CI, 6.9%–1.6%; $P < .001$) for peer comparison.[45] Furthermore, after discontinuing the behavioral interventions, only the prescribers in the peer comparison group demonstrated lasting decreases in inappropriate antibiotic prescribing.[46] All 3 behavioral interventions required minimal change in prescriber workflow with no diagnosis shifting or documented harm. Another study focused on antibiotic prescribing in pediatric practices and, utilizing education and peer comparison, these researchers demonstrated significant improvements in appropriate antibiotic prescribing for URI, acute bacterial sinusitis, and acute otitis media. However, in this study, the authors suggested that some diagnosis shifting may have occurred.[47]

Financial incentives

Pay-for-performance initiatives are sometimes used to drive better outcomes from best practices.[48] In the United Kingdom, the National Health Services (NHS) Quality Premium program provided a 10% quality premium reward to clinical commissioning groups (comprising local general practitioners, and responsible for commissioning healthcare for the community), thereby incentivizing "improved antibiotic prescribing (ie, fewer total prescriptions, fewer broad-spectrum antibiotics, and better prescription data validation) in primary and secondary care."[49] Balinskaite et al[50] evaluated antibiotic prescribing before and after this incentive program and found that financial incentives were associated with decreased overall and broad-spectrum antibiotic prescribing rates, with no adverse effects to patients or community.[51]

Laboratory testing-guided stewardship

C-reactive protein (CRP) has been associated with the prediction of bacterial pneumonia, and Cals et al[52,53] trained physicians in the use of CRP to predict pneumonia in respiratory illnesses, resulting in a 20% reduction of antibiotic prescribing rates. A multinational European trial randomized practices to receive training in the use of point-of-care CRP testing in respiratory illnesses, or enhanced communication training, or both.[54] The combination of CRP training and enhanced communication training resulted in the highest reduction in antibiotic use compared with either alone. Procalcitonin may be used to guide prescribing for acute respiratory syndromes. One study randomized a group of physician practices to procalcitonin-guided antibiotic prescribing and usual care; the group with procalcitonin-guided treatment had a 72% reduction in antibiotic prescribing compared to the usual care group.[55] However, this approach required procalcitonin measurements during the visit and within 24 hours after the visit and close follow-up, which may not be practical in practice settings in the United States where the no-show rate is very high.

Laboratory testing-guided stewardship is also another area where pharmacists can have an impact. Previously mentioned pharmacist collaborations involved clinical decision support and triaging that resulted in improved stewardship outcomes for UTI[32] and influenza-like illness.[33] Pharmacist prospective review of cultures (predominantly urine) whenever outpatient oral antibiotics were prescribed in a New York Veterans' Affairs system found that ~20% of prescription encounters with cultures resulted in pharmacist intervention and that 74% of interventions required a change in the antibiotic regimen.[56] Pharmacist interventions led to reduced rates of 30-day treatment failure (5.4% vs 28.3%; $P < .0001$) or 30-day hospital admission (0.7% vs 10.9%; $P = .0005$), when their interventions were accepted.[56]

Feedback

Clinician feedback on prescribing is essential for assessment and adjustment of prescribing practices. The audit and feedback method is used frequently in the hospital but has not been widely adopted in the outpatient setting. However, a study of pediatric practices showed that when coupled with intensive clinician education on guideline-concordant antibiotic prescribing, an audit-and-feedback intervention reduced guideline-discordant prescribing for bacterial pneumonia by 10% compared with controls.[57] However, in the practices studied, the EMR was set up so that antibiotic prescribing required an indication, and just this process detail alone could have reduced rates of inappropriate antibiotic prescribing.

Peer comparison, described earlier in this review, is another method of feedback that can influence prescribing. The UK clinicians who overprescribed antibiotics received a letter from England's chief medical officer explaining that they prescribe more antibiotics than 80% of their peer practitioners. This intervention was associated with a small but significant reduction in antibiotic prescribing suggesting that both the message and method of feedback may influence its effectiveness.[58]

Follow-up and reassessment

Similar to any other quality improvement initiative, effective ASPs should have built-in accommodations for follow-up and reassessment. Intensive interventions can result in a significant decrease in inappropriate antibiotic prescribing, but these may not persist over time. For instance, an intervention in which intensive clinical

https://doi.org/10.1017/ice.2020.94 Published online by Cambridge University Press

Table 1. Selected Key Resources Compiled to Help Guide the Creation and Successful Implementation of an Outpatient Antimicrobial Stewardship Program

Author(s)	Title/Content	Summary
Michael Klepser et al[60]	A call to action for outpatient antibiotic stewardship https://www.sciencedirect.com/science/article/pii/S1544319117301450?via%3Dihub	Describes how to build an AS team, discusses metrics and tracking outpatient antibiotic use
Quality improvement organizations; contracted by Centers for Medicare & Medicaid Services (CMS)[62]	A field guide to antibiotic stewardship in outpatient settings https://qioprogram.org/sites/default/files/editors/141/C310_Field_Guide_20180730_FNL.pdf	Describes resources, strategies, and examples that support the CDC outpatient AS recommendations
The Joint Commission[23]	Antimicrobial stewardship in ambulatory health care https://www.jointcommission.org/assets/1/18/R3_23_Antimicrobial_Stewardship_AMB_6_14_19_FINAL2.pdf	Describes the rationales and references for The Joint Commission outpatient AS recommendations
Tamar Barlam et al[21]	Implementing an antibiotic stewardship program: guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America https://www.idsociety.org/globalassets/idsa/practice-guidelines/implementing-an-antibiotic-stewardship-program-guidelines-by-the-infectious-diseases-society-of-america-and-the-society-for-healthcare-epidemiology-of-america.pdf	Describes implementation of an AS program generally, but focuses on inpatient AS; some aspects can be applied to outpatient setting
Larissa May et al[63]	MITIGATE (A Multifaceted Intervention to Improve Prescribing for Acute Respiratory Infection for Adults and Children in Emergency Department and Urgent Care Settings) tool kit http://shea-online.org/images/priority-topics/MITIGATE_TOOLKIT_final.pdf	Describes implementation of an intervention in Emergency Departments and Urgent Care settings, not covered elsewhere in this article
Centers for Disease Control & Prevention (CDC)[64]	Core elements of outpatient antimicrobial stewardship https://www.cdc.gov/antibiotic-use/core-elements/outpatient.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fantibiotic-use%2Fcommunity%2Fimproving-prescribing%2Foutpatient-stewardship.html	Description of core AS recommendations, checklist for clinicians and facilities, and supporting evidence resource
Health Services Advisory Group (HSAG)[65]	Health Services Advisory Group collaboration with Centers for Medicare & Medicaid Services quality improvement organizations: https://www.hsag.com/en/medicare-providers/antibiotic-stewardship/	Resources for clinicians and patients/families to understand AS
Agency for Healthcare Research and Quality (AHRQ)[66]	AHRQ safety program for improving antibiotic use https://safetyprogram4antibioticstewardship.org/page/AHRQ-Safety-Program-for-Improving-Antibiotic-Use	National program to collaborate with other organizations on outpatient AS
Nebraska Antimicrobial Stewardship Assessment and Promotion Program (ASAP)[67]	Nebraska ASAP ambulatory stewardship https://asap.nebraskamed.com/ambulatory-care/	Freely available web modules on outpatient AS
Health Quality Innovators (HQI)[68]	Antimicrobial stewardship toolkit: implementing the core elements of outpatient antibiotic stewardship into your facility http://www.hqi.solutions/wp-content/uploads/2017/11/Antibiotic-Stewardship-Toolkit_04172019-1_508.pdf	List of resources for implementation of each of the CDC core element of outpatient AS
Logan, Andrea Y. et al[69]	Establishing an antimicrobial stewardship collaborative across a large, diverse health care system. The Joint Commission Journal on Quality and Patient Safety 2019;45:591–599. https://doi.org/10.1016/j.jcjq.2019.03.002	Describes creation of an outpatient AS network in collaboration with >150 primary care practices
Comagine Health[70]	Tools and resources https://healthinsight.org/tools-and-resources/category/167-outpatient-antibiotic-stewardship	Multiple resources and tip sheets for treatment recommendations, guidelines and patient information

Note. AS, antimicrobial stewardship; CDC, Centers for Disease Control and Prevention.

education was combined with audit and feedback successful decreased antibiotic use but 18 months after discontinuation of audit and feedback, the rates of broad-spectrum antibiotic prescribing had increased to 11.2% above the preintervention baseline.[59] Therefore, success requires active implementation of control measures to ensure ongoing improvement. This reassessment can lead to new collaboration and communication to address deficiencies and further improve antimicrobial prescribing.

Key resources and future needs

A multidisciplinary approach to outpatient antimicrobial stewardship is often most successful.[60] Various resources highlighted in Table 1 discuss how to build an antimicrobial stewardship team, track outpatient antibiotic use, implement CDC best practices, and utilize them in various outpatient settings.

The C-DIFF framework described here was developed to provide a systematic approach to addressing outpatient antimicrobial stewardship goals. Areas for which more data are needed include the following:

1. Patient engagement: Numerous patient resources are available to assist clinician discussions, but new approaches are needed to engage the community and develop partnerships in antimicrobial stewardship. Furthermore, focusing on improving health literacy and clearer communication

https://doi.org/10.1017/ice.2020.94 Published online by Cambridge University Press

strategies between clinicians and patients will be beneficial in strengthening those partnerships.[61]
2. Clinician engagement: Similarly, numerous tools exist for clinician education on appropriate antibiotic use but a better understanding of why clinicians prescribe inappropriately is needed, followed by strategies to address these behaviors.
3. Data collection: Amassing data in the outpatient setting remains challenging and could be improved with a national database of antibiotic prescribing with required indication.
4. Impacts of outpatient stewardship: After implementation of outpatient antimicrobial stewardship initiatives it would be useful to measure impacts on antimicrobial resistance. However, local and state public health departments may not have the resources do this. Additionally, the fact that most outpatient visits do not result in routine clinical culture makes this challenging. Effects of stewardship efforts on long-term patient outcomes, healthcare utilization, and patient satisfaction have been poorly explored.
5. Engagement with clinicians in non–primary care settings: Dental offices, urgent care settings, and telehealth settings can track antibiotic use and implement plans to reduce inappropriate prescribing.
6. Providing more data: Information about adverse events associated with antibiotic overprescribing can highlight the risk of prescribing these medications.

In conclusion, antimicrobial overuse and inappropriate use remains a significant problem. Antimicrobial stewardship is needed in the outpatient setting to achieve reduced antibiotic prescribing and to limit antibiotic resistance. Novel approaches are required so that we never return to the pre-Fleming, pre-penicillin era, when infections were a major cause of death.

Acknowledgments. The authors thank Catherine Hiller for her assistance with manuscript preparation.

Financial support. No financial support was provided relevant to this article.

Conflicts of interest. All authors report no conflicts of interest relevant to this article.

References

1. Antibiotic resistance threats in the United States, 2019. Centers for Disease Control and Prevention website. https://www.cdc.gov/drugresistance/biggest-threats.html. Accessed November 18, 2019.
2. Fleming-Dutra KE, Hersh AL, Shapiro DJ, *et al.* Prevalence of inappropriate antibiotic prescriptions among us ambulatory care visits, 2010–2011. *JAMA* 2016;315:1864–1873.
3. Shively NR, Buehrle DJ, Clancy CJ, Decker BK. Prevalence of inappropriate antibiotic prescribing in primary care clinics within a Veterans' Affairs health care system. *Antimicrob Agents Chemother* 2018;62(8): pii: e00337-18.
4. Jenkins TC, Sabel AL, Sarcone EE, Price CS, Mehler PS, Burman WJ. Skin and soft-tissue infections requiring hospitalization at an academic medical center: opportunities for antimicrobial stewardship. *Clin Infect Dis* 2010;51:895–903.
5. Suda KJ, Hicks LA, Roberts RM, Hunkler RJ, Matusiak LM, Schumock GT. Antibiotic expenditures by medication, class, and healthcare setting in the United States, 2010–2015. *Clin Infect Dis* 2018;66:185–190.
6. Drekonja DM, Filice GA, Greer N, *et al.* Antimicrobial stewardship in outpatient settings: a systematic review. *Infect Control Hosp Epidemiol* 2015;36:142–152.
7. Zetts RM, Stoesz A, Smith BA, Hyun DY. Outpatient antibiotic use and the need for increased antibiotic stewardship efforts. *Pediatrics* 2018;141(6): pii: e20174124.
8. National action plan for combating antibiotic-resistant bacteria. The White House website. http://www.whitehouse.gov/sites/default/files/docs/national_action_plan_for_combating_antibotic-resistant_bacteria.pdf. Accessed May 19, 2018.
9. Durkin MJ, Jafarzadeh SR, Hsueh K, *et al.* Outpatient antibiotic prescription trends in the United States: a national cohort study. *Infect Control Hosp Epidemiol* 2018;39:584–589.
10. Kohut MR, Keller SC, Linder JA, *et al.* The inconvincible patient: how clinicians perceive demand for antibiotics in the outpatient setting. *Fam Pract* 2020;37:276–282.
11. McNulty CAM, Nichols T, French DP, Joshi P, Butler CC. Expectations for consultations and antibiotics for respiratory tract infection in primary care: the RTI clinical iceberg. *Brit J Gen Pract* 2013;63:e429–e436.
12. Mangione-Smith R, McGlynn EA, Elliott MN, McDonald L, Franz CE, Kravitz RL. Parent expectations for antibiotics, physician-parent communication, and satisfaction. *Arch Pediatr Adolesc Med* 2001;155:800–806.
13. Klein EY, Martinez EM, May L, Saheed M, Reyna V, Broniatowski DA. Categorical risk perception drives variability in antibiotic prescribing in the emergency department: a mixed methods observational study. *J Gen Intern Med* 2017;32:1083–1089.
14. Szymczak JE, Klieger SB, Miller M, Fiks AG, Gerber JS. What parents think about the risks and benefits of antibiotics for their child's acute respiratory tract infection. *J Pediatric Infect Dis Soc* 2018;7:303–309.
15. Hicks LA, Bartoces MG, Roberts RM, *et al.* US outpatient antibiotic prescribing variation according to geography, patient population, and provider specialty in 2011. *Clin Infect Dis 2015*;60:1308–1316.
16. Kabbani S, Palms D, Bartoces M, Stone N, Hicks LA. Outpatient antibiotic prescribing for older adults in the United States: 2011 to 2014. *J Am Geriatr Soc* 2018;66:1998–2002.
17. FDA updates warnings for fluoroquinolone antibiotics on risks of mental health and low blood sugar adverse reactions. US Food and Drug Administration website. https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm612995.htm. Accessed November 5, 2018.
18. Hersh AL, Shapiro DJ, Pavia AT, Fleming-Dutra KE, Hicks LA. Geographic variability in diagnosis and antibiotic prescribing for acute respiratory tract infections. *Infect Dis Ther* 2018;7:171–174.
19. Barlam TF, Soria-Saucedo R, Cabral HJ, Kazis LE. Unnecessary antibiotics for acute respiratory tract infections: association with care setting and patient demographics. *Open Forum Infect Dis* 2016;3(1):ofw045.
20. Barlam TF, Morgan JR, Wetzler LM, Christiansen CL, Drainoni M-L. Antibiotics for respiratory tract infections: a comparison of prescribing in an outpatient setting. *Infect Control Hosp Epidemiol* 2015;36:153–159.
21. Barlam TF, Cosgrove SE, Abbo LM, *et al.* Implementing an antibiotic stewardship program: guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis* 2016;62(10):e51–e77.
22. Sanchez GV FK, Roberts RM, Hicks LA. Core elements of outpatient antibiotic stewardship. *MMWR Recomm Rep* 2016;65(No. RR-6):1–12.
23. Antimicrobial stewardship in ambulatory health care. The Joint Commission website. https://www.jointcommission.org/assets/1/18/R3_23_Antimicrobial_Stewardship_AMB_6_14_19_FINAL2.pdf. Accessed August 7, 2019.
24. Ostrowsky B, Banerjee R, Bonomo RA, *et al.* Infectious diseases physicians: leading the way in antimicrobial stewardship. *Clin Infect Dis* 2018;66:995–1003.
25. Day SR, Smith D, Harris K, Cox HL, Mathers AJ. An infectious diseases physician-led antimicrobial stewardship program at a small community hospital associated with improved susceptibility patterns and cost-savings after the first year. *Open Forum Infect Dis* 2015;2(2):ofv064–ofv.
26. Essack S, Bell J, Shephard A. Community pharmacists—leaders for antibiotic stewardship in respiratory tract infection. *J Clin Pharm Ther* 2018;43:302–307.
27. Dodds Ashley E, Davis SL, Heil EL, LaPlante KL, Chahine EB, Bosso JA. Best care for patients achieved through multidisciplinary stewardship. *Clin Infect Dis* 2018;67:1637.
28. Blanchette L, Gauthier T, Heil E, *et al.* The essential role of pharmacists in antibiotic stewardship in outpatient care: an official position statement of

the Society of Infectious Diseases Pharmacists. *J Am Pharm Assoc (2003)* 2018;58:481–484.
29. Klepser ME, Adams AJ, Klepser DG. Antimicrobial stewardship in outpatient settings: leveraging innovative physician-pharmacist collaborations to reduce antibiotic resistance. *Health Secur* 2015;13:166–173.
30. Ilett KF, Johnson S, Greenhill G, *et al.* Modification of general practitioner prescribing of antibiotics by use of a therapeutics adviser (academic detailer). *Br J Clin Pharmacol* 2000;49:168–173.
31. Saha SK, Hawes L, Mazza D. Effectiveness of interventions involving pharmacists on antibiotic prescribing by general practitioners: a systematic review and meta-analysis. *J Antimicrob Chemother* 2019;74:1173–1181.
32. Eudaley ST, Mihm AE, Higdon R, Jeter J, Chamberlin SM. Development and implementation of a clinical decision support tool for treatment of uncomplicated urinary tract infections in a family medicine resident clinic. *J Am Pharm Assoc* 2019;59:579–585.
33. Klepser ME, Klepser DG, Dering-Anderson AM, Morse JA, Smith JK, Klepser SA. Effectiveness of a pharmacist-physician collaborative program to manage influenza-like illness. *J Am Pharm Assoc* 2016;56: 14–21.
34. D'Agata EMC, Lindberg CC, Lindberg CM, *et al.* The positive effects of an antimicrobial stewardship program targeting outpatient hemodialysis facilities. *Infect Control Hosp Epidemiol* 2018;39:1400–1405.
35. Saha D, Patel J, Buckingham D, Thornton D, Barber T, Watson JR. Urine culture follow-up and antimicrobial stewardship in a pediatric urgent care network. *Pediatrics* 2017;139(4):e20162103.
36. American Nurses Association and Centers for Disease Control & Prevention. Redefining the antibiotic stewardship team: recommendations from the American Nurses Association/Centers for Disease Control and Prevention Workgroup on the Role of Registered Nurses in Hospital Antibiotic Stewardship Practices. Centers for Disease Control and Prevention website. https://www.cdc.gov/antibiotic-use/healthcare/pdfs/ANA-CDC-whitepaper.pdf. Accessed June 14, 2019.
37. Livorsi DJ, Linn CM, Alexander B, Heintz BH, Tubbs TA, Perencevich EN. The value of electronically extracted data for auditing outpatient antimicrobial prescribing. *Infect Control Hosp Epidemiol* 2018;39:64–70.
38. Havers FP, Hicks LA, Chung JR, *et al.* Outpatient antibiotic prescribing for acute respiratory infections during influenza seasons. *JAMA Network Open* 2018;1(2):e180243.
39. Durkin MJ, Keller M, Butler AM, *et al.* An assessment of inappropriate antibiotic use and guideline adherence for uncomplicated urinary tract infections. *Open Forum Infect Dis* 2018;5(9):ofy198–ofy.
40. Jaggi P, Wang L, Gleeson S, Moore-Clingenpeel M, Watson JR. Outpatient antimicrobial stewardship targets for treatment of skin and soft-tissue infections. *Infect Control Hosp Epidemiol* 2018;39:936–940.
41. Drekonja DM, Filice GA, Greer N, *et al.* Antimicrobial stewardship in outpatient settings: a systematic review. *Infect Control Hosp Epidemiol* 2015;36:142–152.
42. Meeker D, Knight TK, Friedberg MW, *et al.* Nudging guideline-concordant antibiotic prescribing: a randomized clinical trial. *JAMA Intern Med* 2014;174:425–431.
43. Choosing Wisely initiative of American Board of Internal Medicine. Bagging Antibiotics in Maine. Choosling Wiselt website. http://www.choosingwisely.org/resources/updates-from-the-field/bagging-antibiotics-in-maine/. Accessed November 14, 2018.
44. Jenkins TC, Knepper BC, Sabel AL, *et al.* Decreased antibiotic utilization after implementation of a guideline for inpatient cellulitis and cutaneous abscess. *Arch Intern Med* 2011;171:1072–1079.
45. Meeker D, Linder JA, Fox CR, *et al.* Effect of behavioral interventions on inappropriate antibiotic prescribing among primary care practices: a randomized clinical trial. *JAMA* 2016;315:562–570.
46. Linder JA, Meeker D, Fox CR, *et al.* Effects of behavioral interventions on inappropriate antibiotic prescribing in primary care 12 months after stopping interventions. *JAMA* 2017;318:1391–1392.
47. Clegg HW, Bean RA, Ezzo SJ, Hoth AN, Sheedy DJ, Anderson WE. Impact of education and peer comparison on antibiotic prescribing for pediatric respiratory tract infections. *Pediatr Qual Safety* 2019;4(4):e195.
48. CMS value-based programs. Centers for Medicare and Medicaid Services website. https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/Value-Based-Programs/Value-Based-Programs.html. Accessed November 9, 2018.
49. Quality premium 2015/16. England National Health Services website. https://www.england.nhs.uk/wp-content/uploads/2013/12/qual-prem-guid.pdf. Accessed November 12, 2018.
50. Balinskaite V, Johnson AP, Holmes A, Aylin P. The impact of a national antimicrobial stewardship programme on antibiotic prescribing in primary care: an interrupted time series analysis. *Clin Infect Dis* 2018:ciy902-ciy.
51. Balinskaite V, Bou-Antoun S, Johnson AP, Holmes A, Aylin P. An assessment of potential unintended consequences following a national antimicrobial stewardship program in England: an interrupted time series analysis. *Clin Infect Dis* 2018;69:233–242.
52. Cals JWL, Butler CC, Hopstaken RM, Hood K, Dinant G-J. Effect of point of care testing for C reactive protein and training in communication skills on antibiotic use in lower respiratory tract infections: cluster randomised trial. *BMJ* 2009;338:b1374.
53. Cals JWL, Schot MJC, de Jong SAM, Dinant G-J, Hopstaken RM. Point-of-care C-reactive protein testing and antibiotic prescribing for respiratory tract infections: a randomized controlled trial. *Ann Fam Med* 2010;8: 124–133.
54. Little P, Stuart B, Francis N, *et al.* Effects of internet-based training on antibiotic prescribing rates for acute respiratory-tract infections: a multinational, cluster, randomised, factorial, controlled trial. *Lancet* 2013;382: 1175–1182.
55. Briel M, Schuetz P, Mueller B, *et al.* Procalcitonin-guided antibiotic use vs a standard approach for acute respiratory tract infections in primary care. *Arch Intern Med* 2008;168:2000–2007.
56. Wattengel BA, Sellick JA, Mergenhagen KA. Outpatient antimicrobial stewardship: Optimizing patient care via pharmacist led microbiology review. *Am J Infect Control* 2020;48:189–193.
57. Gerber JS, Prasad PA, Fiks AG, *et al.* Effect of an outpatient antimicrobial stewardship intervention on broad-spectrum antibiotic prescribing by primary care pediatricians: a randomized trial. *JAMA* 2013;309: 2345–2352.
58. Hallsworth M, Chadborn T, Sallis A, *et al.* Provision of social norm feedback to high prescribers of antibiotics in general practice: a pragmatic national randomised controlled trial. *Lancet* 2016;387:1743–1752.
59. Gerber JS, Prasad PA, Fiks AG, *et al.* Durability of benefits of an outpatient antimicrobial stewardship intervention after discontinuation of audit and feedback. *JAMA* 2014;312:2569–70.
60. Klepser ME, Dobson EL, Pogue JM, *et al.* A call to action for outpatient antibiotic stewardship. *J Am Pharm Assoc* 2017;57:457–463.
61. Hermsen ED, MacGeorge EL, Andresen M-L, Myers LM, Lillis CJ, Rosof BM. Decreasing the peril of antimicrobial resistance through enhanced health literacy in outpatient settings: an underrecognized approach to advance antimicrobial stewardship. *Adv Ther* 2020;37:918–932.
62. A field guide to antibiotic stewardship in outpatient settings (July 2018). Quality Innovation Network National Coordinating Center (QIN NCC) website. https://qioprogram.org/sites/default/files/editors/141/C310_Field_Guide_20180730_FNL.pdf. Accessed November 18, 2019.
63. Larissa May, Kabir Yadav, Samuel D. Gaona, *et al.* mitigate antimicrobial stewardship toolkit. SHEA website. http://shea-online.org/images/priority-topics/MITIGATE_TOOLKIT_final.pdf. Accessed November 18, 2019.
64. Core elements of outpatient antimicrobial stewardship. Centers for Disease Control and Prevention website. https://www.cdc.gov/antibiotic-use/core-elements/outpatient.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fantibiotic-use%2Fcommunity%2Fimproving-prescribing%2Foutpatient-stewardship.html. Accessed November 18, 2019.

https://doi.org/10.1017/ice.2020.94 Published online by Cambridge University Press

65. Outpatient antibiotic stewardship. Health Services Advisory Group (HSAG) website. https://www.hsag.com/en/medicare-providers/antibiotic-stewardship/. Accessed November 18, 2019.
66. Agency for Healthcare Research and Quality (AHRQ). AHRQ Safety Program for Improving Antibiotic Use. Agency for Healthcare Research and Quality (AHRQ) website. https://safetyprogram4antibioticstewardship.org/page/AHRQ-Safety-Program-for-Improving-Antibiotic-Use. Accessed November 18, 2019.
67. Nebraska Antimicrobial Stewardship Assessment and Promotion Program (ASAP). Nebraska ASAP Ambulatory Stewardship. Nebraska Medicine website. https://asap.nebraskamed.com/ambulatory-care/. Accessed November 18, 2019.
68. Antimicrobial stewardship toolkit: implementing the core elements of outpatient antibiotic stewardship into your facility. Health Quality Innovators (HQI) website. http://www.hqi.solutions/wp-content/uploads/2017/11/Antibiotic-Stewardship-Toolkit_04172019-1_508.pdf. Accessed November 18, 2019.
69. Logan AY, Williamson JE, Reinke EK, Jarrett SW, Boger MS, Davidson LE. Establishing an antimicrobial stewardship collaborative across a large, diverse health care system. *Joint Comm J Qual Patient Safety* 2019;45:591–599.
70. Comagine Health. Tools and resources: outpatient antibiotic stewardship. Health Insight website. https://healthinsight.org/tools-and-resources/category/167-outpatient-antibiotic-stewardship. Accessed November 18, 2019.

https://doi.org/10.1017/ice.2020.94 Published online by Cambridge University Press