

**Clinical impact of pharmacist-led antibiotic stewardship programs in outpatient settings in the United States: A scoping review**

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**Purpose.** To provide an overview of the impact of pharmacist interventions on antibiotic prescribing and the resultant clinical outcomes in an outpatient antibiotic stewardship program (ASP) in the United States.

**Methods.** Reports on studies of pharmacist-led ASP interventions implemented in US outpatient settings published from January 2000 to November 2020 and indexed in PubMed or Google Scholar were included. Additionally, studies documented at the ClinicalTrials.gov website were evaluated. Study selection was based on predetermined inclusion criteria; only randomized controlled trials, observational studies, nonrandomized controlled trials, and case-control studies conducted in outpatient settings in the United States were included. The primary outcome was the observed differences in antibiotic prescribing or clinical benefits between pharmacist-led ASP interventions and usual care.

**Results.** Of the 196 studies retrieved for full-text review, a cumulative total of 15 studies were included for final evaluation. Upon analysis, we observed that there was no consistent methodology in the implementation of ASPs and, in most cases, the outcome of interest varied. Nonetheless, there was a trend toward improvement in antibiotic prescribing with pharmacist interventions in ASPs compared with that under usual care ( $P < 0.05$ ). However, the results of these studies are not easily generalizable.

**Conclusion.** Our findings suggest a need for a consistent approach for the practical application of outpatient pharmacist-led ASPs. Managed care organizations could play a significant role in ensuring the successful implementation of pharmacist-led ASPs in outpatient settings.

**Keywords:** antibiotic prescribing, antibiotic resistance, antibiotic stewardship program, antimicrobial stewardship program, outpatient settings, pharmacist interventions

In the United States, over 260 million antibiotics were prescribed in outpatient settings in 2011,<sup>1</sup> 76% of which were inappropriately prescribed.<sup>2-6</sup> As antibiotic use is a primary contributor to antibiotic resistance,<sup>7</sup> exposure to improper antibiotic use increases the risk of adverse effects and antibiotic resistance.

Inappropriate antibiotic prescribing has societal and economic implications. It is also associated with a high risk of developing antibiotic-resistant *Clostridioides difficile* infections and a high incidence of community-acquired *C. difficile* infections.<sup>8,9</sup> According to a 2019 US Centers for Disease Control and Prevention (CDC) report, over 2.8 million infections and 35,000 deaths each year are associated with antibiotic resistance.<sup>7</sup> In 2017, 223,900 illnesses and 12,800 deaths are related to *C. difficile* infections.<sup>7</sup> Additionally, direct healthcare costs related to antibiotic resistance in the United States range from \$20 to \$35 billion per year. It is expected that with an increasing number of outpatient centers in the United States,<sup>10</sup> antibiotic resistance will continue to place high epidemiological and economic burdens on the US healthcare system and society.

In 2015, CDC set a plan to decrease the risk and incidence of infections caused by antibiotic-resistant organisms<sup>11-13</sup> and to reduce the inappropriate use of antibiotics by 50% in the year 2020 (the White House National Action Plan for Combating Antibiotic-Resistant Bacteria [CARB]).<sup>14</sup> The 2017 interim CARB report showed improved use of antibiotics with antibiotic stewardship programs (ASPs).<sup>15</sup> Consequently, the ensuing 2020 CARB report placed a renewed emphasis on the prevention of antibiotic resistance and laid out 5-year evidence-based strategic actions to identify the source and change of the antibiotic resistance course.<sup>16</sup>

Despite efforts to reduce unnecessary antibiotic prescribing by the implementation of ASPs, most published data on ASP implementation in the United States are specific to inpatient settings.<sup>17-</sup>

<sup>19</sup> The results from these inpatient studies have demonstrated that the implementation of ASPs is

associated with improved patient outcomes and decreased rates of inappropriate antibiotic prescribing.<sup>17-19</sup>

From an outpatient perspective, a systematic review and meta-analysis of studies evaluating the effect of collaboration between pharmacists and general practice physicians in antibiotic prescribing revealed an overall improvement in antibiotic prescribing practices by general practitioners and a reduction in the number of inappropriately prescribed antibiotics.<sup>20</sup> Although the studies included were conducted outside the United States, it is evident that pharmacists are presented with a unique opportunity to improve outcomes and expand clinical services through the implementation of an ASP.<sup>21,22</sup>

Despite positive outcomes of pharmacist-led ASPs in inpatient settings and primary care clinics located outside the United States, few studies have been conducted in outpatient settings in the United States. Most outpatient studies conducted in the United States were conducted in emergency room settings, and little is known of their impact on clinical outcomes. With the mandate from the Joint Commission to implement ASPs in all outpatient settings,<sup>23</sup> there is an imminent call to mandate ASPs in outpatient settings as a required quality measure. Therefore, there is a critical need to understand the potential role of pharmacist-led antibiotic stewardship in an outpatient setting to prevent antibiotic overuse.

The aim of the scoping review described here was to provide an overview of the impact of pharmacist interventions on antibiotic prescribing and the resultant benefits in an outpatient ASP in the United States. The goal was to identify gaps in the literature by characterizing pharmacist interventions in ASPs according to key research findings and provide policy recommendations for their effective implementation.

## Methods

The scoping review followed the PRISMA extension for scoping reviews) guidelines to provide a critical overview of the clinical outcomes of all studies associated with pharmacist-led ASPs and adapted the scoping review framework developed by Arksey and O'Malley<sup>24</sup> along with recent advancements by Levac et al.<sup>25</sup>

**Identifying research questions.** The 2 main research questions were as follows: (1) Which pharmacist interventions are currently implemented in reducing inappropriate antibiotic prescribing in outpatient settings in the United States?; and (2) What are the clinical benefits associated with pharmacist-led ASPs?

**Identifying relevant studies.** A literature search of articles published from January 2000 to November 2020 and indexed in the US National Library of Medicine's PubMed database, ProQuest MEDLINE (ProQuest, Ann Arbor, MI), and Google Scholar was conducted using the following broad keyword phrases: "pharmacist and antibiotic stewardship program," "pharmacist and antibiotic stewardship program and outpatient setting," "pharmacist and antibiotic stewardship program and ambulatory care," "pharmacist and antimicrobial stewardship program," and "antibiotic stewardship." Clinical trials registered at Clinicaltrials.gov were reviewed for randomized controlled studies. The search in Clinicaltrials.gov was conducted without restriction on publication year, and the keyword phrase used was "antimicrobial stewardship program." These broad keyword phrases were chosen to enable the identification of all relevant studies.

**Study selection process.** Bibliographic records obtained from the literature search were examined for duplicate identification and removal. Two reviewers (A.N.) and (J.L.) were involved in judging the eligibility of resultant articles following title/abstract and full-text screenings. Only articles published in the English language were selected for clinical review. Disagreements between reviewers regarding the inclusion of a particular study were resolved by discussion.

*Inclusion and exclusion.* Studies identified were selected based on the following inclusion and exclusion criteria:

- Study design—Reports and studies that were included in the scoping review comprised randomized controlled trials, nonrandomized controlled trials, observational cohort studies, and case-control studies. Editorials and descriptive or case reports were excluded.
- Population—Only studies involving adult patients (at least 18 years of age) with infections resulting from antibiotic usage were included. Only studies conducted in outpatient settings in the United States were included; those in inpatient or acute care settings were excluded.
- Interventions—Studies evaluating pharmacist interventions on antibiotic prescribing in an ASP were included. Interventions involving antiviral or antifungal agents were excluded.
- Comparator—Only studies comparing the impact of pharmacist-led ASPs on either the usual care (standard practice) or other healthcare professional interventions were included.
- Outcome—The primary outcome was the benefits of the pharmacist-led ASP (or ASP involving pharmacists) on antibiotic prescribing compared with those under usual care. Examples of outcomes evaluated are as follows: antibiotic prescribing pattern, healthcare utilization, antibiotic use, and time to review culture results.

**Data extraction and synthesis.** Data from the selected papers were extracted and synthesized using a predefined extraction form (Table 1). As suggested by Arksey and O'Malley, the quality and strength of evidence of each study included in the scoping review were not assessed.<sup>24</sup>

## Results

Our initial database search using the selected keyword phrases generated 15,045 studies (Figure 1). Following the initial search, we screened for duplicates while screening for unrelated topics based on a review of the titles and abstracts only. After removing duplicates and studies unrelated to our topic (determined through review of titles and abstracts), 196 studies were retrieved for full-text review. In line with our inclusion and exclusion criteria, 15 studies were identified through full-text review.<sup>26-40</sup> The various reasons for exclusion are presented in Figure 1. Ten studies were conducted in specific outpatient settings: emergency department (ED),  $n = 8$ ; urgent care (UC),  $n = 1$ ; and primary care,  $n = 3$ . Additionally, 1 study evaluated the cumulative outcomes of UC and ED, and several studies independently evaluated cumulative outcomes from the combined outpatient services of their respective healthcare systems (ie, UC, primary care, and ED combined).

Because of the heterogeneity of the study designs and settings, our results are categorized based on the clinical setting in which an ASP was implemented. Furthermore, the studies included in this review are summarized in Table 1.

**ED setting.** *Selected study report.* James et al (2019)<sup>26</sup> conducted a retrospective study on adult patients admitted with urinary tract infections (UTIs). Pharmacist intervention included the provision of education to improve antibiotic prescribing by physicians to patients with UTIs and the development of treatment algorithms for patients with abnormal urinalysis results. The primary outcome was the proportion of patients who received antibiotics for UTIs in the absence of signs and symptoms associated with UTIs before and after the intervention. The results for the primary outcome revealed a significant reduction in the frequency of antibiotic use after versus before intervention: 31 (23.1%) versus 84 (31.3%),  $P = 0.004$ . In contrast, the frequency of ED visits was similar between the preintervention and postintervention groups. One major limitation is that this study was not adequately powered to show significant differences in the frequency of ED visits post index ED visit.

Jorgensen et al (2018)<sup>27</sup> conducted a retrospective study to evaluate the impact of the development and implementation of a UTI treatment algorithm by an ASP team and the provision of education to enhance awareness of the algorithm and improve antibiotic prescribing by physicians. The outcome of interest was 30-day ED visits before and after the intervention. The implementation of the UTI treatment algorithm was associated with fewer 30-day return visits than occurred in the preintervention period (adjusted odds ratio [OR], 0.547; 95% confidence interval [CI], 0.312-0.960; Table 1).

Davis et al (2016)<sup>28</sup> conducted a retrospective (pre-post analysis) chart review, post ASP implementation, to measure the number of clinical interventions in which inappropriate antibiotics were changed to appropriate antibiotics following a review of positive cultures by pharmacists, compared with the number in the preintervention period. The outcome of interest was the number of clinical interventions made before versus after the intervention. Their analysis showed that the proportion of clinical interventions was higher among patients in the intervention group (80%) than among patients in the usual care group (50%). One major limitation of the study is that it was not designed to show if an increase in the number of interventions made by the pharmacists would translate to a significant improvement in clinical outcomes.

Baker et al (2012)<sup>29</sup> conducted a retrospective case-control study to compare the “time to culture follow-up and patient notification” between patients seen by pharmacists (the intervention group) and those treated with usual care (no pharmacist intervention). In the intervention group, the pharmacist provided education on the appropriate empiric antimicrobial selection and followed up with patients in cases in which a change in therapy was needed. The outcome of interest was the impact of the pharmacist intervention on the “time to positive culture follow-up.” The results showed that the time to positive culture review and time to patient or physician notification were shorter in the intervention group than in the usual care group.<sup>29</sup> Additionally, with the implementation of a pharmacist-driven ASP, the median time to positive culture review or primary care provider notification was reduced by 1 day. However, there was no significant difference in the



numbers of inappropriate prescribing occurrences before and after the implementation of the pharmacist-driven ASP. One possible explanation is that the study was not sufficiently powered to assess any differences in the number of antibiotic-prescribing occurrences between the intervention and usual care groups.

Additionally, Dumkow et al (2014)<sup>30</sup> conducted a quasi-experimental study evaluating the effect of involving pharmacists in a multidisciplinary ASP team in a “culture follow-up (CFU) program” on the frequency of ED visits compared with usual care (no pharmacist intervention). Before the intervention (usual care), the culture review was mostly physician driven, without any pharmacist involvement. In contrast, during the CFU intervention, pharmacists were involved during a review of culture results and antimicrobial prescribing. The outcomes of interest were ED visits and hospital readmission 72 hours post index ED visit. In the unadjusted analysis, there was no significant difference in ED visits within 72 hours, 30-day readmissions, or combined ED visits and 30-day readmissions. However, 2 major confounding factors were the frequency of urination and dysuria. After adjusting for the presence of dysuria and urinary frequency, CFU was associated with a decreased likelihood of ED visits and readmission compared with usual care (adjusted OR, 0.477; 95% CI, 0.234-0.973;  $P = 0.042$ ). Interestingly, in a subset of uninsured patients, the occurrence of ED visits after intervention was reduced from 15.3% in the usual care group to 2.4% in the CFU group ( $P = 0.044$ ).

Finally, Shealy et al (2020)<sup>31</sup> conducted a retrospective pre-post study evaluating the benefits of pharmacist-driven culture review with rapid diagnostic test (RDT) use among patients with sexually transmitted diseases. Pharmacist intervention included review of positive urine, blood, and stool cultures or a positive RDT for *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Trichomonas vaginalis*. The main outcome was “time from ED discharge to result review anytime from ED discharge to completion of outpatient follow-up” before and after implementation of the program. The preliminary report revealed a mean reduction in the time to result review of 27.3

hours after the implementation period ( $P < 0.001$ ). However, as this approach in the ED setting is novel, a more robust study is needed to address its clinical relevance.

Unlike previous studies, which were retrospective, the studies by Zhang et al (2016)<sup>32</sup> and Stoll et al (2020)<sup>33</sup> were the only prospective studies in this category. Zhang et al evaluated the impact of pharmacist antibiotic-prescribing interventions following a review of urine culture results of nonpregnant and asymptomatic adult patients. The outcome of interest was the duration of antibiotic use before and after the intervention. In their analysis, pharmacist interventions following a review of urine culture results were associated with a reduction in the duration of antibiotic use compared with the duration in the preintervention period (Table 1). Notably, 2 significant factors influenced antibiotic use: the presence of leukocyte esterase (OR, 4.5; 95% CI, 1.2-17.2;  $P = 0.03$ ) and nitrites (OR, 10.8; 95% CI, 1.7-68.1;  $P = 0.01$ ) in the urine.

Similarly, Stoll et al (2020)<sup>33</sup> conducted a pre-post analysis to evaluate the prescribing practices of ED practitioners who provided treatment to patients with community-acquired pneumonia (CAP), skin and soft tissue infections (SSTIs), and UTI before and after the implementation of an algorithm concordant with Infectious Diseases Society of America (IDSA) guidelines. The main outcome was the proportion of prescriptions concordant with the IDSA guidelines. The results of the primary outcome analysis revealed that the percentage of prescriptions concordant with the IDSA guidelines in the postintervention group (61.5%) was higher than that in the preintervention group (11.7%) ( $P < 0.00001$ ). In a secondary analysis, the investigators reported a reduction in 30-day ED or UC visits among the postintervention group versus the preintervention group (15.3% vs 21.5%,  $P = .035$ ).

In summary, despite the heterogeneity of study designs in evaluations of the implementation of an ASP in the ED, the reviewed studies suggest that an ASP may be associated with reduced ED visits and an improved antibiotic-prescribing pattern.

**Mixed ED and UC settings.** *Selected study report.* Dumkow et al (2018)<sup>34</sup> conducted a quasi-experimental retrospective study of patients with pharyngitis in both ED and UC settings. The

primary goal was to compare the proportion of patients who received appropriate antibiotics before and after the implementation of an ASP. The proportion of patients who received appropriate antibiotics was higher post ASP implementation than before ASP implementation (81.5% vs 6%,  $P < 0.001$ ). The frequency of antibiotic prescribing decreased from 97% to 71.3% ( $P < 0.001$ ). Furthermore, no statistically significant difference in 72-hour revisit rates was observed ( $P = 0.121$ ). One major limitation of the study was the lack of a control group of patients of similar clinical characteristics.

**UC setting. Selected study report.** Fay et al (2019)<sup>35</sup> also conducted a retrospective pre-post, quasi-experimental study and evaluated the impact of a collaborative agreement that involved pharmacists' reviews of UC patients with positive cultures following implementation of an established antimicrobial stewardship protocol for antibiotic selection. They evaluated all patients irrespective of infectious disease state. The primary outcome of the study was the total percentage of antibiotics prescribed concordantly with the protocol. They also evaluated the frequency of ED visits and hospital readmission 72 hours post index UC visit. The percentage of prescribed guideline-concordant antibiotics was higher in the intervention period than in the preintervention period (53.3% vs 41.3%,  $P = 0.037$ ). Similarly, the frequency of guideline-concordant antibiotic selection was higher during the intervention period (68%) than during the preintervention period (51%;  $P = 0.01$ ). However, there was no significant difference in the frequency of guideline-concordant antibiotic prescribing between the pre- and postintervention periods. There were no statistical differences in the frequencies of UC, ED, and hospital visits between the pre- and postintervention periods. The obvious limitation of this study was that patients were not stratified based on the severity of illness, which may have affected the likelihood of detecting any difference in healthcare utilization.

**Primary care setting. Selected study report.** Eudaley et al (2019)<sup>36</sup> conducted a retrospective chart review to evaluate the influence of a multidisciplinary team consisting of pharmacists, physicians, quality coordinators, and a coding and billing specialist on antimicrobial prescribing for uncomplicated UTI before and after the implementation of a clinical decision support (CDS) tool for

the guideline-directed management of UTI. This study was conducted in 2 phases. In phase 1, the clinical collaborators developed the CDS tool by employing local susceptibility patterns and formulating a clinic-specific antibiogram. In the second phase, the CDS tool was integrated into the clinic's electronic health record (EHRs) to guide diagnosis, documentation, and antibiotic prescribing. The primary outcome of the study was the rate of empiric antibiotic prescribing before and after the implementation of the CDS tool. Based on their observation, the collaborative approach with the implementation of the CDS tool was associated with a 27% decrease in the use of fluoroquinolones (OR, 0.25; 95% CI, 0.13-0.5;  $P < 0.001$ ) and a 20% decrease in the use of trimethoprim/sulfamethoxazole (OR, 0.21; 95% CI, 0.45-0.955;  $P = 0.003$ ) compared with usage rates in the preintervention period. Additionally, the use of nitrofurantoin for cystitis increased by 31% (OR, 3.83; 95% CI, 1.32-11.1;  $P = 0.01$ ), and adherence to guideline-directed duration of therapy increased by 32% (OR, 4.34; 95% CI, 1.48-12.73;  $P = 0.005$ ). This study did not directly address whether pharmacist intervention had a direct impact on the measured outcomes. However, it showed the potential role of pharmacists in the implementation of the CDS tool, which translated to improved antibiotic prescribing among patients with UTI.

Craddock et al (2020)<sup>37</sup> conducted a retrospective, quasi-experimental study evaluating the impact of educational interventions on the antibiotic prescribing pattern for viral acute upper respiratory tract infections. Interventions made under the ASP included the development of institution guidelines, roundtable discussions, and creation of "poster-size antibiotic commitment letters." The primary outcome was the proportion of antibiotics prescribed for viral acute upper respiratory tract infections before and after the intervention. Based on their results, the percentage of antibiotics inappropriately prescribed was lower after the intervention (13.1%) than before the intervention (17.2%;  $P = 0.02$ ). One major limitation of this study was the presence of misclassification bias, which is typical of a retrospective chart review.

McCormick et al (2020)<sup>38</sup> conducted a retrospective, pre-post analysis evaluating the impact of a pharmacist-led ASP on the antibiotic prescribing pattern for uncomplicated cystitis

pyelonephritis. Interventions made under the ASP included the development of clinic-specific guidelines, EHR built-in notes for easy access to the treatment summary, education materials, and audits of inappropriate prescribing. The primary outcome was the composite proportion of antibiotic prescription in accordance with the guideline-approved first-line therapy before and after the intervention periods. Based on their results, the researchers found that the proportion of appropriate antibiotic prescription was higher after the intervention (71.6%) than before the intervention (37%;  $P < 0.001$ ). Of particular note, the majority of patients seen (93.8%) had cystitis.

In all studies evaluated, the provision of guideline-directed education as part of an ASP initiative was associated with improved outcomes with regard to the antibiotic prescribing pattern.

**Health-system outpatient services.** *Selected study report.* Wattengel et al (2020)<sup>39</sup> conducted a 1-year prospective chart review of adult patients to evaluate the effect of a pharmacist-led culture review service. In this study, an infectious diseases pharmacist reviewed all cultures ordered and the appropriateness of antibiotics empirically prescribed before culture ordering. They evaluated the percentage of the infectious diseases pharmacist's interventions accepted versus the infectious disease pharmacist's interventions rejected. The outcomes evaluated were as follows: "30-day all-cause mortality, 30-day representation rates, 30-day admission rates, and 30-day treatment failure rates." The 30-day treatment failure and 30-day admission rates were significantly lower when the infectious diseases pharmacist's interventions were accepted than when they were rejected (5.4% vs 28.3% [ $P < 0.0001$ ] and 0.7% vs 10.9% [ $P = 0.0005$ ], respectively). However, there was no significant difference in 30-day all-cause mortality. A major limitation of the study was the small number of interventions evaluated (148 interventions accepted versus 48 interventions rejected), which might have led to type I error. Of particular note, the majority of the prescriptions reviewed (138 out of 194) were indicated for UTI. Thus, the observed differences were mostly driven by the interventions made for UTI patients.

Finally, Lin et al (2020)<sup>40</sup> conducted a retrospective chart review to evaluate the effect of an ASP on the prescribing pattern of fluoroquinolones for UTI. As part of the ASP initiatives, recurrent

education on the use of fluoroquinolones was routinely provided to the providers. Additional interventions, such as the inclusion of fluoroquinolone warning labels as part of the institution's electronic medical record system and suppression of ciprofloxacin susceptibilities if isolated organisms were susceptible to cephalosporins, were implemented. The primary outcome of the study was "the total number of outpatient fluoroquinolone prescriptions normalized per 1000 patient visits with the percentage of inappropriate indications." Based on their results, they found that the total number of fluoroquinolones used decreased by 13% ( $P < 0.01$ ). Two years after the intervention, the number of fluoroquinolones used decreased by 39% ( $P < 0.01$ ). Despite the reduction in fluoroquinolone usage, the study did not address if this led to an increase in the usage of other antibiotics.

Wattengel et al<sup>39</sup> and Lin et al<sup>40</sup> demonstrated improved outcomes with the implementation of an ASP. However, it is not clear if the observed impacts translated to an improvements in the frequency of ED visits or hospital readmissions post index visit.

## Discussion

The purpose of this review is to provide an overview of the potential benefit of a pharmacist-led ASP in outpatient settings. Although the methodological quality of each study was low, the observed quality of evidence was not different from what has been observed in other studies relating to ASPs.<sup>41</sup>

Notwithstanding methodological differences, much can be learned from these different studies that can help shape future studies on pharmacist-led ASPs in outpatient settings. First, the inclusion of the pharmacist in outpatient settings was associated with an increased number of interventions made, which led to appropriate antibiotic prescribing. A similar finding was observed in a systematic review and meta-analysis of studies conducted in non-US primary care centers, as reported by Saha et al (2019).<sup>20</sup>

Second, pharmacist review of cultures led to an improved quality of antibiotic prescribing. We deduce that such an intervention may improve healthcare costs associated with disease burden or antibiotic resistance. However, it is unclear if appropriate antibiotic prescribing led to a reduction in the frequency of preventable ED visits and rehospitalizations associated with infectious disease. The available data on the impact of a pharmacist-led ASP on ED visits and readmissions were inconclusive. The differences in the infectious diseases targeted by the various reported pharmacist-led ASP teams may explain the observed inconsistency in results. For example, in the studies of both Dumkow et al<sup>30</sup> and Jorgensen et al,<sup>27</sup> wherein a reduction in the frequency of ED visits and readmissions was observed; the predominant infectious disease targeted in a pharmacist-led ASP was UTI. On the contrary, Fay et al,<sup>35</sup> who reported a lack of a significant difference in rates of ED and admission visits, evaluated both urine and wound cultures. Evaluating the effect of the ASP on the frequency of hospital readmission and ED and UC visits presents an area of focus for future studies, especially in primary care and UC settings. In addition to our observations, to the best of our knowledge, no outcome-driven study has focused on outpatients undergoing dialysis, for whom 30% of prescribed antibiotics are unnecessary.<sup>42</sup> This observation presents another area of practice-based research focus.

Furthermore, as antibiotic resistance is associated with increased mortality<sup>7</sup> and information on the impact of a pharmacist-led ASP on mortality is lacking, it would be interesting to explore the effect of a pharmacist-led ASP on mortality. Clinical studies examining the effects of implementation of an outpatient ASP on inpatient outcomes, such as hospital length of stay and hospital readmissions associated with infectious diseases, will be pertinent. Finally, an analysis of costs and benefits of implementation of an ASP in outpatient settings should be conducted.

Our scoping review had some limitations. First, there was a potential for publication bias. Finally, based on our review of different studies, there has not been a consistent approach in implementing an ASP for outpatients, which might have led to differences in outcomes.

The implementation of a pharmacist-led ASP has public health and policy implications. Acknowledging the importance of an ASP, both IDSA and the Pediatric Infectious Diseases Society of America have mandated that an ASP be interwoven throughout healthcare, with similar regulatory requirements as those of the Centers for Medicare and Medicaid Services imposed.<sup>43</sup> As inpatient implementation of an ASP is not mutually exclusive to the outpatient implementation of an ASP, without the appropriate implementation of an ASP in the outpatient setting, the control of antibiotic resistance in the community will be difficult, consequently leading to increasing inpatient use of broad-spectrum antibiotics.

Currently, ASP implementation is required by the Joint Commission for all ambulatory care clinics, excluding ambulatory surgery centers.<sup>23</sup> Therefore, managed care organizations (MCOs) can play a significant role in ensuring the successful implementation of pharmacist-led ASPs in outpatient settings by providing incentives. These incentives, in the form of monetary reimbursement, can help alleviate the 2 widely recognized barriers to the effective implementation of an ASP, which are cost and the need for rapid decision making with limited diagnostic information. Actions by MCOs can be enhanced by the regulatory oversight of the National Committee for Quality Assurance, which is responsible for evaluating the quality and service provided by MCOs, and by incorporating the development of an ASP as one of the required quality measures for outpatient settings.

We recognize that the limited availability of resources such as manpower can be a major barrier in implementing a pharmacist-led ASP in an outpatient setting. To minimize the effect of this barrier, we recommend that an ASP should not be a standalone or a silo program, but instead should be integrated as part of pharmacist services. In other words, an ASP can be integrated with pharmacist-led transition of care and comprehensive medication therapy management services. An approach proposed by Okere (2018)<sup>44</sup> could be adapted to any outpatient setting when rectifying or reconciling all drugs (including antibiotics) prior to patient discharge.



As noted in this article, multidimensional approaches were deployed in the implementation of ASPs in outpatient settings. The development of IDSA-concordant guidelines and education were found to be the most effective and potentially cost-effective approaches. Nonetheless, other novel approaches such as RDT use or penicillin skin testing can be integrated as part of the process. However, additional pharmacist training may be required.

The successful implementation of an ASP in outpatient settings requires commitment from policymakers, healthcare administrators, and clinicians. According to CDC, improving antibiotic prescribing involves the effective implementation of strategies to “modify prescribing practices to align them with evidence-based recommendations for diagnosis and management.”<sup>45</sup> Therefore, for the successful implementation of pharmacist-led ASPs resulting in improved patient outcomes, clinics (including other outpatient settings) should consider reviewing and incorporating the core elements of an ASP, such as “commitment, action, tracking and reporting, education, and expertise.”<sup>46</sup>

## **Conclusion**

An effort to reduce inappropriate antibiotic prescribing requires a team approach that allows the inclusion of pharmacists. Our findings revealed a need for a consistent approach for the effective implementation of outpatient pharmacist-led ASPs. Interventions made by a pharmacist in an ASP were associated with a small improvement in the quality of antibiotic prescribing. It is our opinion that MCOs can play a significant role in ensuring the successful implementation of pharmacist-led ASPs in outpatient settings. A change in policy, requiring the provision of monetary incentives and inclusion of an ASP (with regulatory oversight) as a required outpatient quality measure, will ensure its successful implementation in an outpatient setting.

## **Disclosures**

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Accepted Manuscript



Figure 1. Flowchart of article selection for scoping review. ASP indicates antimicrobial stewardship program.

### Key Points

- Outpatient settings are a major contributor to inappropriate antibiotic prescribing and antibiotic resistance in the community.
- Implementation of pharmacist-led antibiotic stewardship programs can improve outpatient antibiotic prescribing.
- Integrating provider education, developing algorithms concordant with Infectious Diseases Society of America guidelines, and auditing providers' prescribing patterns as an integral part of pharmacist-led antibiotic stewardship programs can be a cost-effective approach to improve antibiotic prescribing in outpatient settings.

**Table 1.** Summary of Studies Included in Scoping Review

Setting and Authors	Design	Eligible Participants	Pharmacist Intervention(s)	Type of Pharmacist	Infection, Organism, or Specimen	Outcome(s) of Interest	Results
Emergency department							
James et al <sup>26</sup>	Retrospective, single-center pre-post cohort analysis	268 patients	Pharmacist provision of education on management of asymptomatic bacteriuria and abnormal urinalysis (pre-post analysis)	Pharmacist	Asymptomatic bacteriuria	Percentage of patients who received antibiotics for UTI in absence of UTI signs/symptoms in pre- and postintervention periods	31.3% (84 patients) in preintervention period vs 23.1% (31 patients) in postintervention period ( $P = 0.004$ )
Jorgensen et al <sup>27</sup>	Retrospective, single-center pre-post analysis	752 patients	Development of antimicrobial treatment algorithm for patients with UTI and audit feedback to ED physicians	ED pharmacist and ID pharmacist	UTI	30-day ED visit post discharge with empiric nitrofurantoin use in pre- and post-intervention periods	Adjusted OR for revisit in postintervention period, 0.547 (95% CI, 0.312-0.96)
Davis et al <sup>28</sup>	Retrospective, electronic chart review (pre-post analysis)	472 patients	Review of urinalysis and positive culture results with follow-up	ED pharmacist	All positive cultures	Number of clinical interventions made in pre- and postintervention periods	50% (nursing staff intervened on 21 of 42 positive cultures) in preintervention period vs 80% (pharmacist intervened on 24 of 30 positive cultures) in postintervention period ( $P = 0.01$ )

Baker et al <sup>29</sup>	Retrospective case-control (pre-post) analysis	212 patients	Education on appropriate empiric therapy, review of cultures, and patient follow-up for change in therapy	ED pharmacist	All positive cultures	Time to positive culture review in pre- and postintervention periods	Median of 3 days in preintervention period vs 2 days in postintervention period ( $P = 0.0001$ )
Dumkow et al <sup>30</sup>	Retrospective quasi-experimental study	320 patients	Pharmacist review of positive cultures and follow-up	Pharmacy resident supervised by ED pharmacist	All positive blood and urine cultures	Composite rate of revisit to ED within 72 hours of ED discharge or admission to hospital within 30 days of ED discharge	Results NS for composite outcome
Shealy et al <sup>31</sup>	Retrospective pre-post analysis	127 patients	Review of culture and positive RDT results	Pharmacy resident supervised by ED pharmacist	All positive culture and RDT results	Time from ED discharge to result review and time from ED discharge to completion of outpatient follow-up	Mean of 75.2 hours in preintervention period vs 47.9 hours in postintervention period ( $P < 0.001$ )
Zhang et al <sup>32</sup>	Prospective cohort study	136 patients	Culture review and antibiotic recommendation	ED pharmacist	Urine cultures	Duration of antibiotic use before and after implementation of intervention	Mean of 426 days in preintervention period vs 122 days in postintervention period ( $P = 0.03$ )
Stoll et al <sup>33</sup>	Prospective interventional (pre-post) analysis	678 patients	Development of antibiotic-prescribing algorithms for CAP, SSTI, and UTI	ED pharmacist	CAP, SSTI, and UTI	Proportion of prescriptions concordant with IDSA guidelines	11.7% in preintervention period vs 61.5% in postintervention period ( $P = 0.035$ )

Mixed ED and urgent care

	Dumkow et al <sup>34</sup>	Retrospective quasi-experimental study	280 patients	Review of positive group A <i>Streptococcus</i> culture and RDT results, with follow-up	Residency-trained ID pharmacist	Group A <i>Streptococcus</i>	Revisit to ED within 72 hours after discharge, appropriateness of antibiotics prescribed with urgent care follow-up	No significant difference in ED or urgent care revisits; appropriateness of antibiotic prescription higher after pharmacist follow-up ( $P < 0.001$ )
Urgent care	Fay et al <sup>35</sup>	Retrospective quasi-experimental study	300 patients	Pharmacist-led review of urgent care cultures and education to urgent care provider staff	ED and ID pharmacist	All positive cultures and serologies	Total guideline-concordant antibiotic prescription and selection (pre-post analysis); urgent care or ED revisit within 72 hours, and hospital admission within 30 days	Total guideline-concordant antibiotic prescription was higher in postintervention group vs preintervention group (53.3% vs 41.3%, $P = 0.037$ ); no statistical difference in urgent care or ED visits between groups
Primary care	Eudaley et al <sup>36</sup>	Retrospective chart review-based analysis	28 patients	Use of clinical decision tool developed and implemented by pharmacy in collaboration with additional departments for guideline-directed diagnosis and prescribing	Clinical pharmacist	UTI	Rate of empiric antibiotic prescribing for UTI	20% decrease in sulfamethoxazole/trimethoprim use (OR, 0.21; 95% CI, 0.45-0.955; $P = 0.003$ ); 27% decrease in fluoroquinolone use (OR, 0.25; 95% CI, 0.13-0.5; $P < 0.001$ )

Craddock et al <sup>37</sup>	Retrospective quasi-experimental study	2,817 patient encounters	Provision of education through dissemination of institutional guidelines and poster-sized algorithm for management of acute upper respiratory tract infections	Ambulatory care pharmacist and PGY2 ambulatory care pharmacy resident	Acute upper respiratory tract infections	Proportion of antibiotics prescribed for viral acute upper respiratory tract infections before and after intervention periods	17.2% in preintervention period vs 13.1% in postintervention period ( $P = 0.02$ )
McCormick et al <sup>38</sup>	Retrospective pre-post analysis	162 patients	Provision of clinician education, built-in EHR note template, and clinic treatment summary concordant with IDSA guidelines	Clinical pharmacist	UTI	Composite proportion of prescribed antibiotics in accordance with guideline-approved first-line therapy before and after intervention periods	37% in preintervention period vs 71.6% in postintervention period ( $P < 0.001$ )
Health-system outpatient services (all outpatient visits combined)							
Wattengel et al <sup>39</sup>	Prospective chart review-based analysis	965 encounters <sup>a</sup>	Pharmacist review of all cultures ordered	ID pharmacist	All cultures	Comparative outcomes with acceptance vs nonacceptance of pharmacist interventions	Rate of 30-day treatment failure, 5.4% with acceptance vs 28.3% with nonacceptance ( $P < .0001$ ); rate of 30-day admission, 0.7% with acceptance vs 10.9% with nonacceptance ( $P = .0005$ )
Lin et al <sup>40</sup>	Retrospective chart review-based analysis	1,033 outpatient fluoroquinolone	Included provision of routine education on use of fluoroquinolones for urinary tract	ID pharmacist	UTI and SSTI	Total number of outpatient fluoroquinolone prescriptions per 1,000	During 1-year intervention period, total prescriptions per 1,000 patient visits decreased by 13%; during 2-year postintervention period, total

prescriptions<sup>a</sup> infections, inclusion of fluoroquinolones warning labels as part of institution's electronic medical record system, suppression of ciprofloxacin if isolated organisms susceptible to cephalosporins

patient visits

prescriptions per 1,000 patient visits decreased by 39% ( $P < 0.01$ )

Abbreviations: CAP, community-acquired pneumonia; CI, confidence interval; ED, emergency department; EHR, electronic health record; ID, infectious diseases; IDSA, Infectious Disease Society of America; NS = not significant; OR, odds ratio; PGY2, postgraduate year 2; RDT, rapid diagnostic test; SSTI, skin and soft tissue infection; UTI, urinary tract infection.

<sup>a</sup>Number does not equate to number of eligible patients recruited or enrolled.

