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Sarah B. Green
Department of Pharmacy, Emory University Hospital

Kayla R. Stover
Department of Pharmacy Practice, University of Mississippi School of Pharmacy

Katie Barber
Department of Pharmacy Practice, University of Mississippi School of Pharmacy

Jeannette L. Bouchard
Department of Pharmacy, WakeMed Health and Hospitals

Matthew L. Brown
Department of Pharmacy, University of Alabama at Birmingham Hospital

See next page for additional authors

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Author(s)

Sarah B. Green, Kayla R. Stover, Katie Barber, Jeannette L. Bouchard, Matthew L. Brown, Connor R. Deri, Bailey J. Francis, Timothy P. Gauthier, Jillian E. Hayes, Ashley H. Marx, Edoabasi U. McGee, Krutika Mediwala, Rachel J. Musgrove, Douglas Slain, Stefanie A. Stramel, Christopher M. Bland, and P Brandon Bookstaver

Open Forum Infectious Diseases

REVIEW ARTICLE

A Baker's Dozen of Top Antimicrobial Stewardship Intervention Publications in 2020

Sarah B. Green,[1] Kayla R. Stover,[2] Katie Barber,[2] Jeannette L. Bouchard,[3] Matthew L. Brown,[4] Connor R. Deri,[5] Bailey J. Francis,[6] Timothy P. Gauthier,[7] Jillian E. Hayes,[8] Ashley H. Marx,[9] Edoabasi U. McGee,[10] Krutika Mediwala,[11] Rachel J. Musgrove,[12] Douglas Slain,[13] Stefanie A. Stramel,[14] Christopher M. Bland,[15] and P. Brandon Bookstaver[16]

[1]Department of Pharmacy, Emory University Hospital, Atlanta, Georgia, USA, [2]Department of Pharmacy Practice, University of Mississippi School of Pharmacy, Jackson, Mississippi, USA, [3]Department of Pharmacy, WakeMed Health and Hospitals, Raleigh, North Carolina, USA, [4]Department of Pharmacy, University of Alabama at Birmingham Hospital, Birmingham, Alabama, USA, [5]Department of Pharmacy, Duke University Hospital, Durham, North Carolina, USA, [6]Department of Pharmacy, Novant Health Forsyth Medical Center, Winston-Salem, North Carolina, USA, [7]Baptist Health South Florida, Clinical Pharmacy Enterprise, Miami, Florida, USA, [8]Department of Pharmacy AdventHealth Orlando, Orlando, Florida, USA, [9]Department of Pharmacy, University of North Carolina Medical Center, Chapel Hill, North Carolina, USA, [10]Department of Pharmacy Practice, Philadelphia College of Osteopathic Medicine–Georgia Campus, School of Pharmacy, Suwanee, Georgia, USA, [11]Pharmacy Services, Medical University of South Carolina Health, Charleston, South Carolina, USA, [12]Department of Pharmacy, St Joseph's/Candler Health System, Savannah, Georgia, USA, [13]Department of Clinical Pharmacy and Section of Infectious Diseases, West Virginia University, Morgantown, West Virginia, USA, [14]Department of Pharmacy, Memorial Hermann Memorial City Medical Center, Houston, Texas, USA, [15]Clinical and Administrative Pharmacy, University of Georgia College of Pharmacy, Savannah, Georgia, USA, and [16]Department of Pharmacy, University of South Carolina College of Pharmacy, Columbia, South Carolina, USA

The number of articles related to antimicrobial stewardship published each year has increased significantly over the last decade. Keeping up with the literature, particularly the most innovative, well-designed, or applicable to one's own practice area, can be challenging. The Southeastern Research Group Endeavor (SERGE-45) network reviewed antimicrobial stewardship–related, peer-reviewed literature from 2020 that detailed actionable interventions. The top 13 publications were summarized following identification using a modified Delphi technique. This article highlights the selected interventions and may serve as a key resource for teaching and training, and to identify novel or optimized stewardship opportunities within one's institution.

Keywords. antibiotics; antimicrobial stewardship; infectious diseases; metrics; resistance.

More than a decade since the release of national guidelines for establishing antimicrobial stewardship programs (ASPs), there continues to be an emphasis on evidence-based approaches to optimizing stewardship in the literature. The lack of strong evidence supporting antimicrobial stewardship (AS) guideline recommendations is well documented, and many stewards report not measuring the impact of common tools such as rapid diagnostics that support many ASPs [1]. From 2010 to 2020, there has been a nearly 3000% increase in PubMed-indexed papers with a mention of AS (Figure 1) [2]. Efforts to bolster research within ASPs also continues to garner attention as experts in the field and leading infectious diseases (ID) organizations have published recommendations or provided programming to enhance scholarly efforts [3–7].

A recent white paper released from a Society of Healthcare Epidemiology of America working group identified 4 key research gaps in the AS literature. The most important but resource-intensive of these is the need for advanced study designs and optimal analytical methods to answer questions regarding optimal stewardship delivery and measurement of impact [4]. Over the past year, funded studies to support ID therapeutic research and the use of advanced study designs, including randomized controlled trials, have become more common [8, 9]. Perhaps as a tangible result, leading ID journals have published several high-impact articles focused on AS interventions. The Southeastern Research Group Endeavor (SERGE-45) network is one of several supporting mentored, collaborative research in ID and AS and has methodically selected the top AS articles for the previous 4 years [10–14]. Detailed in this article are the top AS intervention publications from 2020 as determined by the SERGE-45 network [8, 9, 15–25].

METHODS

Using a modified Delphi technique (detailed previously), members of the SERGE-45 network identified AS publications from 2020 considered to be significant using the following inclusion criteria: (1) published in 2020, including electronic, "early-release" publications, and (2) included an actionable intervention [26]. An actionable intervention was defined as an AS strategy that was implemented in practice and resulted in measurable outcomes. Clinical practice guidelines, official statements, review articles, and articles without an actionable intervention were excluded.

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Correspondence: Sarah B. Green, PharmD, Emory University Hospital, Department of Pharmacy, 1364 Clifton Rd NE, Atlanta, GA 30322, USA (sarah.b.green@emoryhealthcare.org).

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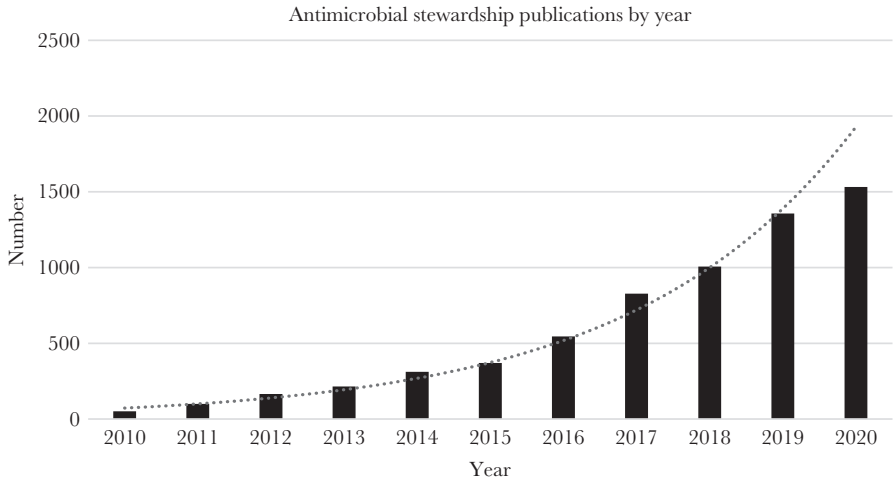

Figure 1. Number of publications indexed in PubMed by the term "antimicrobial stewardship" each year from 2010 to 2020.

A PubMed search using "antimicrobial stewardship" for 2020 revealed 1501 potential publications. Abstracts were screened to ensure that all relevant articles were considered. Seventy publications were submitted by the network for evaluation and those meeting criteria not previously identified were also included for consideration. A total of 121 article citations and abstracts were distributed to the SERGE-45 network for ranking via REDCap survey of the top 13 articles based on contribution and/or application to ASPs [27]. Follow-up email reminders were sent to encourage participation in the voting process. Of note, no conflict of interest disclosure was required of participating voters.

Of the 84 network members at the time of survey, 30 rank lists (36% participation) were submitted. Article ranks from the group were averaged and the top-scoring articles were reviewed by S. B. G., B. J. F., P. B. B., and C. M. B. via teleconference. This group discussed rankings and settled disputes on article rankings based on inclusion criteria and diversity of topics included, and a final consensus on the top 13 articles was established. Included articles are presented in the discussion in a random order and should not be considered to be ranked according to placement. Figure 2 is a flowsheet of the article selection process, and Table 1 provides a summary of the selected articles.

RESULTS

Peer Comparison–Based Stewardship Intervention in the Emergency Department

The focus of AS activities has expanded to include outpatient primary care offices and emergency departments (EDs). Traditional inpatient stewardship strategies such as prospective audit and feedback (PAF) are not always feasible in the ED's fast-paced environment. Using an adapted framework based on a successful ASP in their Veterans Affairs (VA) primary care clinics [28], Buehrle and colleagues implemented an ED ASP [15]. A prospective observational study was conducted to evaluate the impact of peer comparison on antibiotic prescribing by ED physicians at patient discharge.

An ID physician presented a 30-minute educational module on antibiotic overuse, diagnosis, and treatment of commonly seen infections in the ED. Following the presentation, ED physicians received monthly emails with de-identified bar graphs comparing their antibiotic prescribing to that of their peers. Upon initiation of the peer comparison emails, prescriptions decreased at a monthly rate of 10.4 per 1000 ED visits. The rate of antibiotics prescribed without an indication also decreased. This study illustrates the effectiveness of de-identified peer feedback in a new setting with unique challenges to traditional stewardship intervention implementation. There were no *Clostridioides difficile* infection (CDI) tests ordered during the 90 days after prescriptions were reviewed; readmissions and other adverse events were not reported. Limitations to this study include its retrospective nature and lack of control group. Development of the educational module and scheduling ED staff to attend may represent challenges to implementing this type of intervention in addition to time needed to create de-identified feedback on a monthly basis.

Multidisciplinary Penicillin Allergy Delabeling

Many hospitals have initiated programs to evaluate medication allergies given the abundance of data reflecting the benefits of accurate allergy assessments [29–31]. In particular, rates of true allergic reactions to penicillins have been shown to be far less than previously reported [32]. Chua and colleagues conducted a multicenter, prospective study to evaluate rate of penicillin allergy delabeling following review by trained nursing, pharmacy, or medical staff using a validated assessment tool [16]. Based on risk stratification, patients were directly delabeled, offered oral penicillin challenge, or referred for outpatient allergy assessment.

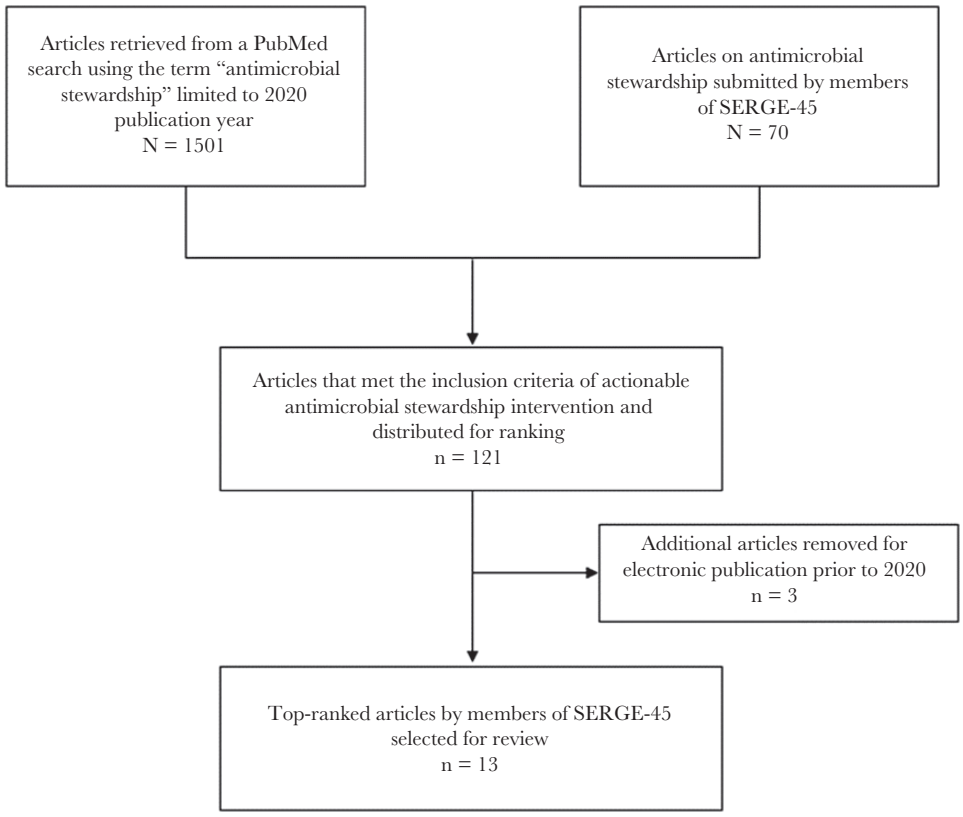

Figure 2. Flowchart of the database search and article selection process. Abbreviation: SERGE-45, Southeastern Research Group Endeavor.

A total of 1225 patients with 1264 reported penicillin allergies were included in the analysis. Of these, 558 (45.6%) patients were determined to be low risk. Approximately 30% of patients were delabeled (355/1225) following the allergy assessment, the majority in the low-risk group. Estimated costs of delabeling for the 355 patients were $6825 in the inpatient setting compared to $60 447 for the same group if referred for outpatient assessment: $21 125 for direct delabeling and $39 322 for oral challenge. Limitations included lack of diversity of patient acuity and inability to generalize across healthcare centers. This study demonstrated efficacy and potential cost savings of a multidisciplinary, inpatient penicillin allergy delabeling protocol without negative impact on readmission, length of stay (LOS), or mortality.

Clinical Impact of Rapid Identification and Susceptibility Testing for Gram-Negative Bacteremia

Gram-negative bloodstream infections (BSIs) represent a serious infection process associated with high mortality rates [33]. With increasing antimicrobial resistance rates, the need for prompt, appropriate therapy is imperative [34]. Banerjee and colleagues conducted a prospective, multicenter, randomized controlled trial assessing the clinical impact of the Accelerate Pheno system compared to standard of care (SOC) for patients with gram-negative bacteremia (GNB) [9]. Both groups received PAF from the ASP, using scenario-based standardized recommendations.

In total, 497 patients were included with *Escherichia coli*, the most frequently identified organism in blood cultures. The primary outcome, time to first antibiotic change from randomization, was faster in the intervention group compared to the SOC group with a median difference of 6.3 hours ($P = .02$). Similarly, time to gram-negative antibiotic change was faster by nearly 25 hours ($P < .001$). Third-generation cephalosporin– and carbapenem-resistant Enterobacterales occurred in roughly 20% and 3% of cases, respectively. Antibiotic escalations occurred 43.3 hours faster in the intervention group compared to the SOC group ($P = .01$). Thirty-day mortality occurred in 25 (11%) patients in the intervention group and 18 (8%) patients in the SOC group ($P = .27$). Of note, 10% of the organisms identified were not on the Accelerate Pheno panel, thus representing a limitation for infections caused by rare organisms. This study provides prospective data in gram-negative BSI supporting rapid diagnostics in conjunction with ASP intervention for faster time to appropriate therapy.

Ambulatory Care Pharmacist-Led Interventions Effect on Antimicrobial Prescribing

Approximately 30%–50% of outpatient antibiotic prescriptions are either unnecessary or inappropriate [35]. Education

alone may be an insufficient AS strategy in this setting [36]. Westerhof and colleagues evaluated the impact of a multifaceted, outpatient ASP led by 2 ambulatory care pharmacists (AMCPs) on prescribing practices for upper respiratory infections (URIs), urinary tract infections (UTIs), and skin and soft tissue infections at a family medicine resident clinic [17]. The

Table 1. Summary of Top 13 Antimicrobial Stewardship Intervention Publications, 2020

Study Citation	Study Design	Intervention Summary	Primary and Key Secondary Outcomes
Buehrle et al, 2021 [15]	Prospective, observational cohort study to evaluate antibiotic prescribing by ED physicians for discharged patients and the impact of a peer-comparison stewardship intervention	Following an educational module given by an ID physician, ED physicians were emailed antibiotic de-identified prescribing information comparing their antibiotic prescribing to that of their peers	Primary outcomes: - Rate of antibiotic prescriptions for patients discharged from the ED - Overall monthly decrease of 10.4 prescriptions per 1000 ED visits (95% CI, –21.7 to 1.0; $P = .07$) - Relative decrease of 9.9 prescriptions per 1000 ED visits from established baseline through intervention period (95% CI, –20.9 to –1.0; $P = .07$). - Random review found rate of unnecessary antibiotic prescriptions to be 55.6% preintervention and 38.7% postintervention
Chua et al, 2020 [16]	Prospective, multicenter study evaluating impact of a detailed allergy assessment on penicillin allergy delabeling	Detailed allergy assessment by trained nursing, pharmacy, or medical staff in patients prospectively identified from 21 Jan 2019 through 31 Aug 2019. Assessments included evaluation and risk stratification using the validated antibiotic allergy assessment tool. Based on risk stratification, patients were directly delabeled, offered direct oral penicillin challenge, or referred for outpatient allergy assessment	Primary outcome: - 355/1225 (29%) had penicillin allergy delabeling - 161/355 patients (45%) had direct delabeling (150 low-risk allergy, 11 high-risk) - 194/355 patients (55%) had delabeling following oral penicillin challenge - 344/558 (62%) of low-risk allergies were delabeled Secondary outcomes: - Increased use of penicillins, reduced cephalosporins, and reduced restricted antibiotics (lincosamides, fluoroquinolones, vancomycin, carbapenems, 3rd- or 4th-generation cephalosporins) in delabeled patients posttesting - No difference in readmission rates, LOS, or mortality between delabeled and non-delabeled groups
Banerjee et al, 2020 [9]	Prospective, multicenter study evaluating clinical impact of rapid identification for GNB	GNB patients randomized Oct 2017–Oct 2018 to 2 groups: SOC culture and antimicrobial susceptibility testing vs rapid organism identification and phenotypic susceptibility testing with Accelerate Pheno system	Primary outcome: - Median time (hours) to first antibiotic change after randomization was decreased by 6.3 hours in Rapid vs SOC groups (8.6, IQR 2.6–27.6 vs 14.9, IQR 3.3–41.1; $P = .02$) Secondary outcomes: - Median time (hours) to first gram-negative antibiotic change was decreased by 24.8 hours in Rapid vs SOC groups (17.3, IQR 4.9–72 vs 42.1, IQR 10.1–72; $P < .001$). - No difference in 30-d mortality, LOS, readmission, ICU LOS, HO-CDI, or acquisition of MDRO
Westerhof et al, 2020 [17]	Retrospective, quasi-experimental study in a single family medicine resident clinic including adult and pediatric patients	3-pronged intervention: 1. Resident educational sessions 2. Local health system treatment guideline pocket cards 3. Biweekly AMCP audit and feedback	Primary outcome: - Total guideline-concordant antibiotic prescribing at baseline was 38.9% (URI, 53.3%; SSTI, 16.7%; UTI, 46.7%) and improved across all 3 infection types to 57.9% (URI, 61.2%; SSTI, 57.6%; UTI, 53.5%; $P = .001$). Secondary outcomes: - Significant improvements were seen in guideline-concordant antibiotic selection (68.9% vs 80.2%; $P = .018$), dose (76.7% vs 86.2%; $P = .023$), and duration of therapy (73.3% vs 86.2%; $P = .02$).
Watson et al, 2020 [18]	Multicenter, quasi-experimental, before-and-after intervention study of an electronic order set for urine studies	An electronic order set required providers to choose an indication for urine studies. CDS directed providers to order the appropriate urine study according to the indication.	Primary outcomes: - Number of UCs performed per 10 000 PD decreased by 40.4% (1175.8 vs 701.4; $P < .01$) - Antibiotic DOT/1000 PD for UTIs decreased by 15.2% (102.5 vs 86.9; $P < .01$) - CAUTI SIR decreased from 1.0 to 0.8 ($P = .21$) - Cost per 1000 PD decreased by US$2112 ($P < .01$), representing an annual total estimated cost savings of US$535 181
Nace et al, 2020 [19]	Multifaceted quality improvement intervention evaluation	1-hour introductory webinar, pocket-sized educational cards, tools for system change, and educational clinical vignettes addressing the diagnosis and treatment of suspected uncomplicated cystitis. Monthly web-based coaching calls were held for staff of intervention nursing homes. All facilities received quarterly feedback reports regarding the management of uncomplicated cystitis.	Primary outcome: - Lower incidence of AU for unlikely cystitis (AIRR, 0.73 [95% CI, .59–.91]; $P = .004$) Secondary outcomes: - Lower overall AU for any UTI (AIRR, 0.83 [95% CI, .70–.99]; $P = .04$) - Reduced adjusted rate of CDI (AIRR, 0.35 [95% CI, .19–.64]; $P < .001$) - No difference in incidence of UCs performed, all-cause hospitalization, or death

Table 1. Continued

Study Citation	Study Design	Intervention Summary	Primary and Key Secondary Outcomes
Coussement et al, 2021 [20]	Multicenter, randomized, open-label superiority trial in kidney transplant recipients who had ASB and were ≥2 months posttransplantation	Antibiotics or no therapy for kidney transplant recipients ≥2 months posttransplantation with ASB	Primary outcome: - No difference in the incidence of symptomatic UTI: 27% vs 31%; HR 0.83 (95% CI, .50–1.40) Secondary outcomes: - Death: 4% vs 3%; *P* = NS - Graft loss: 2% vs 3%; *P* = NS - Biopsy-proven graft rejection: 3% vs 2%; *P* = NS - Pyelonephritis: 17% vs 16%; *P* = NS - Number of participants in whom second episode of bacteriuria was caused by a more resistant bacteria than was their baseline episode of ASB: 18% vs 4%; *P* = .003
Elligsen et al, 2020 [8]	Quasi-experimental study evaluating impact of individualized predictive models on antibiotic prescribing in patients with monomicrobial GNB	Application of a retrospectively derived and validated logistic regression model was used to predict probability of susceptibility and guide subsequent, pharmacist-initiated antimicrobial recommendations for a predefined cascade of antimicrobials, from narrow to broad: ceftriaxone, ciprofloxacin, ceftazidime, piperacillin-tazobactam, and meropenem/ertapenem	Primary outcomes: - Antibiotic de-escalation: Intervention group was more likely to have their therapy de-escalated: 29% vs 21%; aOR, 1.77 (95% CI, 1.09–2.88) - Adequacy of therapy: No difference in the proportion of patients who were on adequate therapy at time of culture finalization: 96% vs 97% (*P* = .774) Secondary outcomes: - Proportion of patients on narrowest adequate therapy at time of culture finalization: 55% vs 44%; aOR, 2.04 (95% CI, 1.27–3.27) - Time to adequate therapy: 5 h vs 4 h (*P* = .95) - Mortality: 13% vs 13% (*P* = .99) - LOS: 9.7 vs 8.4 days (*P* = .50) - CDI: 4% vs 3% (*P* = .86) - Overall recommendation acceptance rate: 78%
Moghnieh et al, 2020 [21]	Single-center, retrospective interrupted time series analysis assessing formulary restriction vs handshake stewardship on antibiotic consumption, expenditures, nosocomial bacteremia, and patient outcomes	A "handshake"-based antimicrobial stewardship program using PAF plus education and local guideline dissemination was compared to a program consisting of an antimicrobial restriction policy for select agents only	No primary endpoint was identified. - Broad-spectrum antibiotic consumption: mean use density of imipenem and meropenem decreased by 13.7% (*P* = .017) with decreased rate of prescriptions (–24.83 defined daily dose per 1000 PD per month; *P* = .02) - Antibiotic expenditures: 24.6% cost reduction (*P* = .0001) - Incidence of nosocomial bacteremia caused by carbapenem-resistant GNB: 34.8% decrease (*P* = .13) - Patient outcomes: no change was detected for all-cause mortality, LOS, or 7-day readmissions
Claeys et al, 2021 [22]	Retrospective, quasi-experimental, nonrandomized, intervention study comparing rates of urine cultures before and after policy intervention for conditional urine reflex orders	Conditional urine reflex policies were implemented to allow for testing based only on specific criteria met on UA in adults admitted to acute-care beds. Three sites served as intervention sites and 3 as control. Two sites allowed culturing when WBC >10 cells/HPF (restrictive criteria) and 1 site allowed culturing when urine was positive for leukocyte esterase, nitrites, or had WBC >10 cells/HPF (permissive criteria)	Primary outcome: - Rate of UCs performed per 1000 PDs: 21% decrease in culture at intervention site relative to control sites (*P* ≤ .01) - Control - Preintervention: 40.3 cultures/1000 PDs vs postintervention: 44.2 cultures/1000 PDs (*P* = .67) - Preintervention: 35.8 cultures/1000 PDs vs postintervention: 33.7 cultures/1000 PDs (*P* = .29) Secondary outcome - Rate of GNB per 1000 PDs postintervention: 0.8 cases/1000 PDs at intervention site vs 0.6 cases/1000 PDs at control site (*P* = .13)
Ridgway et al, 2020 [23]	Multicenter, randomized controlled trial with crossover design investigating the impact of WISCA on patient outcomes	Intervention consisted of ASP physician performing PAF on patients who were identified via the WISCA tool within 24 h of antibiotic start via page or phone call to primary provider and via written documentation in the EMR vs control of ASP physician–recorded antibiotic recommendations in the study base unless regimen caused concern for harm	Primary outcome: - Mean hospital LOS (4.54 d vs 4.50 d; *P* = .6899) Secondary outcomes: - 30-d readmission (344 vs 374; *P* = .8180) - 30-d mortality (178 vs 194; *P* = .8730) - Antibiotic charges ($546.75 vs $548.72; *P* = .8931) - CDI within 180 d (151 vs 165; *P* = .8717) - New-onset MDRO within 180 d (55 vs 52; *P* = .5950)

Table 1. Continued

Study Citation	Study Design	Intervention Summary	Primary and Key Secondary Outcomes
Howard-Anderson et al, 2020 [24]	Quasi-experimental analysis of HO-CDI testing 2 y before and after implementation of an EMR intervention leading to default CDI test cancellation	EMR intervention was an alert that prompted prescribers to consider CDI test cancellation as the default when patients were admitted >3 d and had documented laxative or stool softener administration within the prior 24 h	Primary outcome: - Median (IQR) monthly rates of total monthly HO-CDI orders per 1000 PD: 10.9 (10.5–11.6) vs 7.0 (6.4–7.6); $P < .001$ - Rate ratio for level change in total HO-CDI testing, 0.79 (95% CI, .73–.86) - Median (IQR) monthly rates of inappropriate monthly HO-CDI orders per 1000 PD: 0.8 (0.8–1.0) vs 0.4 (0.3–0.6); $P < .001$ - Rate ratio for level change in rate of inappropriate HO-CDI testing, 0.8 (.61–1.05) - Proportion of inappropriate tests decreased 8% to 6% ($P < .001$) Secondary outcome: - Change in rate of HO-CDI LabID events per 1000 PD before and after: rate ratio level change, 0.74 (95% CI, .60–.91). Note: rate decreased only in 1 of 4 hospitals
Sapozhnikov et al, 2021 [25]	Single-center, retrospective descriptive study at a health system including a 604-bed academic medical center and 2 community hospitals	The ASP team reviewed requests for additional AST with the multidisciplinary team during microbiology rounds. The ASP approach to AST requests focused on decreased treatment of culture contaminants, recommendations for narrow-spectrum, less toxic, and less costly treatment alternatives if appropriate. If approved by the AST team, the requested tests were released for viewing or performed if not already completed.	Primary outcome: - Of the susceptibility request (n = 67), 59.7% were from physicians and 34.3% were from ID providers. Of the requests from ID providers 65.2% ($P = .039$) were approved. - ASP pharmacist completed chart reviews for 92.5% of patients and contacted the requester or primary team 74.6% of the time - Interventions included approval of susceptibility in 47.8% of requests, education of providers in 43.4%, ASP referral in 7%, and ID consult referral in 1% - Potential benefits were prevention of unnecessary susceptibility testing (47.8%), opportunities for providing physician education (40.3%), discouraged treatment of contaminant (19.4%), optimized susceptibility request (16.4%), avoided need for parenteral therapy (10.4%), and additional workup performed (7.5%).

Abbreviations: AIRR, adjusted incidence rate ratio; AMCP, ambulatory care pharmacist; aOR, adjusted odds ratio; ASB, asymptomatic bacteriuria; ASP, antimicrobial stewardship program; AST, antimicrobial susceptibility testing; AU, antimicrobial use; CAUTI, catheter-associated urinary tract infection; CDI, *Clostridioides difficile* infection; CDS, clinical decision support; CI, confidence interval; DOT, days of therapy; ED, emergency department; EMR, electronic medical record; GNB, gram-negative bacteremia; HO-CDI, hospital-onset *Clostridioides difficile* infection; HPF, high-power field; HR, hazard ratio; ICU; intensive care unit; ID, infectious diseases; IQR, interquartile range; LOS, length of stay; MDRO, multidrug-resistant organism; NS, not significant; PAF, prospective audit and feedback; PD, patient-days; SIR, standardized infection ratio; SSTI, skin and soft tissue infection; SOC, standard of care; UA, urinalysis; UC, urine culture; URI, upper respiratory infection; UTI, urinary tract infection; WBC, white blood cell; WISCA, weighted incidence syndromic combination antibiogram.

study evaluated the effect of a 3-pronged ASP intervention on the rate of prescribing concordance with local guidelines. Based on their previous pilot study, biweekly AMCP feedback provided positive reinforcement of prudent prescribing with constructive and supportive comments highlighting better options when available [37].

Overall, 525 antibiotic prescriptions were audited. Guideline concordance at baseline was 38.9% and improved across all 3 infection types to 57.9%. Improvements were most notable in antibiotic selection, proper dose, and duration of therapy with no significant differences by indication. This novel study provides evidence that non-ID-trained AMCPs can be effective in ambulatory ASPs. The major limitation of the style of intervention is that it is not in "real time" and does not allow the AMCPs to intervene on the patient case, but rather allows the AMCP to teach and encourage change in prescribing habits for the future.

Impact of Clinical Decision Support for Urine Studies

Integration of clinical decision support (CDS) into the electronic medical record (EMR) is recommended to help ASPs meet targeted goals [36]. CDS may also be leveraged for diagnostic stewardship, which can improve the accuracy of infectious diagnoses and better inform decisions regarding antimicrobial therapy [38]. Watson and colleagues evaluated the impact of CDS embedded in an electronic order set intended to guide appropriate selection of urine studies [18]. The order set required providers to choose an indication for the urine study from 3 options: (1) suspected UTI, (2) noninfectious indications, or (3) screening purposes or neutropenic patients with urinary symptoms. Specific types of urine studies could then be ordered according to the indication. For suspected UTI, a hard stop also required the provider to document the signs or symptoms by selecting from a list of criteria established by the Infectious Diseases Society of America (IDSA) [39]. Urine cultures (UCs) could not be ordered for noninfectious indications.

Following implementation of the order set, there was a significant reduction in the number of UCs performed, antibiotic days of therapy for UTIs, and costs. A non–statistically significant reduction in the catheter-associated UTI standardized infection ratio was also observed. Implementation of CDS for urine studies requires adequate support from information technology resources and relies on accurate selection of the indication by the ordering clinician. Overall, this study highlights computerized CDS as an effective tool to improve outcomes

that align with the goals of both AS and infection prevention programs.

A Multifaceted ASP for the Treatment of Uncomplicated Cystitis in Nursing Home Residents

UTIs are commonly diagnosed in nursing home residents. Age and inadequate communication in this population often lead to misdiagnosis and inappropriate antimicrobial use (AU). Nace and colleagues conducted a multifaceted quality improvement intervention to target uncomplicated and unlikely cystitis [19]. Unlikely cystitis was defined as asymptomatic bacteriuria, contaminated urinary specimens, or noninfectious conditions that can be confused with cystitis (eg, nonspecific symptoms in the absence of urinary-specific symptoms). The intervention nursing homes received an introductory webinar, pocket-sized educational cards, established guidelines, and educational clinical vignettes. They also received monthly web-based coaching calls and quarterly feedback reports for the management of uncomplicated cystitis.

At baseline, intervention facilities had higher rates of UTIs, unlikely cystitis treated with antimicrobials, and all-cause death at baseline; however, none were statistically significant. Postintervention, significant reductions were observed in AU for unlikely cystitis, overall AU for any UTI, and adjusted CDI rates with no differences in all-cause hospitalization or death. Limitations included lack of randomization by baseline antibiotic use and facility blinding, personnel staffing differences, and dedicated resources for education that may not be readily present at most institutions. However, this study provides additional support for education with feedback strategies in nursing home settings.

Treatment of Asymptomatic Bacteriuria in Kidney Transplant Recipients

Asymptomatic bacteriuria (ASB) is a common observation after kidney transplantation, occurring in roughly half of recipients [40]. Due to limited evidence in guiding management, the tendency to screen and treat ASB varies by institution and treating clinician. A recent European survey demonstrated that >70% of physicians always screen for ASB, and ASB is often treated among surveyed physicians [41].

Coussement and colleagues sought to evaluate the impact of ASB treatment on the incidence of symptomatic UTI during the 1-year transplant follow-up period [20]. There was no difference in the cumulative incidence of symptomatic UTI between the antibiotic and no-therapy groups. Additionally, withholding antibiotic therapy for ASB resulted in similar incidences of death, graft loss, biopsy-proven graft rejection, pyelonephritis, and BSI due to UTI compared to the antibiotic group. Not surprisingly, the antibiotic group (1) developed bacteriuria caused by a more resistant bacteria compared to the index bacteriuria episode at a higher rate and (2) had a lower rate of ASB at 12 months post–study inclusion, both of which were statistically significant.

Overall, a screen-and-treat strategy for ASB in kidney transplant recipients ≥1–2 months after transplantation increases AU, promotes antimicrobial resistance, and most importantly, does not seem to improve clinical outcomes. This study adds important evidence and further supports the 2019 IDSA guideline recommendation against the treatment of ASB in kidney transplant recipients >1 month posttransplantation; however, results of this study may not be generalizable to ASB in kidney transplant recipients during the immediate posttransplantation period.

Improving Decision Making in Empiric Antibiotic Selection for GNB

Selection of empiric antimicrobials requires balancing receipt of active therapy with avoidance of unnecessarily broad-spectrum agents [42, 43]. Tools to determine patient-specific risk for antimicrobial resistance or inadequate therapy may assist clinicians in decision making [44–46]. Elligsen and colleagues conducted a quasi-experimental evaluation of predictive, multivariable models to guide AU in the treatment of GNB [8]. The intervention group received pharmacist-initiated recommendations for patients with GNB when speciation was available with susceptibility results pending. Patients were identified via a local stewardship database thrice daily during working hours. The pharmacist used validated logistic regression models to recommend the lowest level of a predefined cascade of antimicrobials while maintaining a 90% probability of susceptibility for patients with quick Sequential Organ Failure Assessment score of 3 and 80% for those with scores <3 [47, 48].

Patients in the intervention group were more likely to undergo de-escalation, primarily driven by GNB caused by *E coli* and *Klebsiella* species. While time to adequate therapy was similar between groups, patients receiving the intervention were more likely to be on narrowest adequate therapy at time of culture finalization. There was no difference in mortality nor length of stay between groups. Overall suggestion acceptance was 78%. This study demonstrates that individualized predictive models for resistance can facilitate early de-escalation of antimicrobials while maintaining adequate activity in patients with GNB; however, replication of this study may be limited by resource requirements and necessity for a high level of prescriber engagement.

Effect of Handshake Stewardship Versus Formulary Restriction

"Handshake" stewardship has been described as the use of prospective antibiotic prescription audits with rounding-based feedback to prescribers, ideally in person, coupled with an absence of antimicrobial restriction [49]. It is a unique ASP strategy that accounts for the importance of human interaction and relationship building in impacting antimicrobial prescribing practices. While "handshake" stewardship appears a promising option for ASPs, there are limited publications on the topic and it can be resource-intensive. Moghnieh and colleagues

analyzed AU, cost, nosocomial bacteremia, and patient outcomes in a comparison of a formulary restriction policy versus a "handshake" stewardship approach [21]. Practices during the period of restriction were based upon specialist approvals and driven by targeting broad-spectrum or expensive agents. Practice during the "handshake" period included feedback during daily rounds as well as education and dissemination of local guidelines and treatment pathways of common infectious syndromes.

The "handshake" stewardship approach was associated with significant decreases in broad-spectrum AU and nosocomial, carbapenem-resistant GNB. No change was detected for all-cause mortality, LOS, or 7-day readmission. For facilities that have the resources to support it, a "handshake" stewardship approach may have positive effects on broad-spectrum antibiotic consumption and expenditures without impacting patient outcomes.

Evaluation of a Practice-Based Research Network Diagnostic Stewardship Intervention

Indiscriminate ordering of UCs may lead to inappropriate ASB treatment [50, 51]. Diagnostic stewardship may be utilized in conjunction with AS to prevent unnecessary urine culturing and subsequent AU [52]. Claeys and colleagues evaluated the effectiveness of conditional urine reflex policies across hospitals within the VA-CDC Practice-Based Research Network [22]. Six VA sites, each with different conditional reflex policies, were included.

There were 224573 UCs performed during the study period. Trends in UC ordering did not differ between the pre- and postintervention periods for either the control group or the intervention group. Restrictive reflex criteria saw the largest reduction in UC orders (21.1 cultures/1000 patient-days vs 13.1 cultures/1000 patient-days, $P < .01$). Nine hundred cases of BSI were documented with no significant difference in the rate of gram-negative BSIs at the intervention sites. The implementation of conditional reflex policies during differing years and the variable populations between sites could have influenced the pre- and postintervention periods, leading to the lack of significance. Despite trends not differing within intervention sites, this study highlights a reduction in cultures between intervention and control without increasing the risk of bacteremia. With the incorporation of separate control sites, this study provides a unique design that emphasizes the importance of the role of research networks in conducting meaningful multicenter comparative studies.

Weighted Incidence Syndromic Combination Antibiogram Tool

Due to antimicrobial overuse and increased resistance, it is recommended that computerized decision tools be incorporated into ASP practices [53–56]. The weighted incidence syndromic combination antibiogram (WISCA) was previously developed to assess the likelihood for appropriate coverage based on individual real-time data [23, 57]. WISCA previously showed an increased likelihood of coverage [58], reduction in time to effective coverage, and identification of narrower choices than previously prescribed [59, 60]. This trial investigated WISCA impact during active ASP surveillance on LOS, mortality, readmission, adverse events, and costs. Inpatient microbiological data were collected over a 3-year period. The ASP physician reviewed WISCA-identified regimens that primarily included UTI and abdominal biliary infection (ABI), with 18 and 22 combinations, respectively. However, it was prespecified that all 6 clinical syndromes were part of the inclusion criteria, whereas previously only UTI and ABI were of focus. It is unclear if the subgroup syndromic analysis adjusted for multiple tests. Logistic regression models assessed regimen coverage for isolated organisms. The ASP physician contacted the primary provider within 24 hours of antibiotic start for intervention of identified patients. Control group patients had recommendations recorded in the study database only, unless a concern for harm was identified.

The enrolled 6849 patients received antibiotics for ABI (32.33%), UTI (24.88%), community-acquired pneumonia (CAP) (7.11%), and cellulitis (5.93%). Overall, WISCA was not associated with improved primary and most secondary outcomes. However, intervention for CAP diagnosis was associated with significantly decreased odds of 30-day mortality (adjusted odds ratio, 0.582 [95% confidence interval, .396–.854]; $P = .0204$), and cellulitis diagnosis was associated with significantly shorter LOS. Of note, the previous WISCA study discussed that certain infections may not be amenable with utilization of the WISCA tool due to syndromes, such as pneumonia, not allowing for a robust sample size. Thus, this finding may be a chance result achieved by increased testing. However, this study reinforces continued investigation into computerized methods to support ASP practices.

Impact of an EMR Nudge on Reduced Testing for Hospital-Onset CDI

In 2020, ASPs continued to publish results of efforts to reduce inappropriate testing for CDI. Howard-Anderson et al described an EMR intervention that prompted a warning screen for prescribers to cancel CDI tests when test orders were placed for patients admitted >3 days who had received laxatives or stool softeners in the prior 24 hours [24]. Prescribers were able to continue with the order if they selected a button to proceed.

This "nudge" approach was associated with decreases in both monthly total hospital-onset CDI (HO-CDI) testing and inappropriate testing rates. In segmented regression analysis designed to control for unmeasured variables, the rate ratio for monthly total HO-CDI orders per 1000 patient-days reflected a 21% decrease in testing for HO-CDI. The proportion of inappropriate HO-CDI tests, defined as tests ordered when a laxative or stool softener was administered within the previous 24 hours,

also decreased significantly. The rate of inappropriate testing continued to decrease each month during the postintervention period, but implementation was not associated with an immediate level change. ASPs may consider this strategy to address testing in the HO-CDI population when other explanations for diarrhea exist.

Impact of an ASP Pharmacist During Microbiology Rounds

Successful ASPs typically use a multipronged approach to achieve its goals. One approach that has been previously described is the impact of adding an ASP pharmacist to microbiology plate rounds in the inpatient setting [60]. The impact of this effort in both the inpatient and outpatient settings has not been studied. Sapozhnikov and colleagues evaluated the impact of participation of an ASP pharmacist in review of antimicrobial susceptibility testing request from both inpatient and ambulatory adults at a large academic health system [25]. The institution utilized selective and cascade reporting to guide antimicrobial prescribing. The enhanced ASP team had various responsibilities, including participation in telephonic rounds with the microbiology laboratory, to provide further interpretation of microbiologic results.

Over a 6-month period, the team reviewed 67 susceptibility requests. The ASP pharmacist completed chart reviews for 92.5% of patients and contacted the requester or primary team 74.6% of the time. The interventions included approval of susceptibility in 47.8% of requests. While education of providers occurred in 43.4%, ASP referral occurred in 7% and ID consult referral in 1% of the requests. Benefits of ASP pharmacist involvement included prevention of unnecessary susceptibility testing, opportunity for education, decreased treatment of contaminants, optimized susceptibility request, evaluation of potential oral options, and additional workup recommendations. This was a single-center retrospective observational study at a large academic health system, with a robust ASP team, that shows the positive impact of an ASP pharmacist on microbiology rounds. However, a limitation of this study is the difficulty in duplicating at an underresourced institution with a limited ASP team.

DISCUSSION

ASPs continue to mature within traditional inpatient settings and expand into a number of outpatient settings, both for general and specialized populations. Stewardship responsibilities are often layered upon various existing responsibilities, making identification of best stewardship interventions paramount to maximize benefit with limited resources. Two important themes were identified within the 13 articles chosen for 2020: First, a number of articles demonstrated the importance of microbiology personnel within AS practices. Microbiology input historically has been minimal or absent within day-to-day stewardship activities at many sites despite clear recommendations from national stewardship guidelines [61]. From coordination of blood culture notification and management to unique opportunities within microbiology rounds, full integration of microbiology in ASP practice and patient care is important to ensure beneficial outcomes [9, 25].

Second, many successful ASP interventions incorporate diagnostic stewardship. This year's baker's dozen included diagnostic interventions using electronic decision support to decrease ordering of UCs and CDI testing, and rapid diagnostic technology for treating the sickest patient populations [9, 18, 24]. ASPs can examine all steps in the diagnostic process for opportunities to improve patients' management.

The trend toward higher-quality data supporting specific ASP interventions is encouraging. ASPs can use these data to evaluate and refine daily activities. As programs expand in scope and into new settings, literature documenting actionable and reproducible interventions will help advise future metrics and agendas.

Notes

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