3-1-2024

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REVIEW ARTICLE

A Baker's Dozen of Top Antimicrobial Stewardship Intervention Publications in 2022

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Keeping abreast of the antimicrobial stewardship–related articles published each year is challenging. The Southeastern Research Group Endeavor identified antimicrobial stewardship–related, peer-reviewed literature that detailed an actionable intervention during 2022. The top 13 publications were selected using a modified Delphi technique. These manuscripts were reviewed to highlight actionable interventions used by antimicrobial stewardship programs to capture potentially effective strategies for local implementation.

Keywords. antibiotics; antimicrobial stewardship; emergency department; long-term care facility; outpatient.

The term antimicrobial stewardship (AS) is no longer limited to the interior of inpatient acute care facilities or to United States institutions but rather has expanded across the continuum of care and throughout the globe. For many infectious diseases (ID) clinicians and antimicrobial stewards, 2022 marked an emergence from the unique burden of managing pandemic responsibilities [1]. Although scholarly output in AS did not show the continued growth as in previous years (Figure 1), significant contributions from non–US-based institutions were common, representing approximately 30% of stewardship intervention publications identified.

Importantly in 2022, the Infectious Diseases Society of America continued its efforts to provide front-line clinicians with published guidance on managing difficult-to-treat drug-resistant infections [2]. Additionally, an increase in statewide stewardship efforts was observed with novel ways to connect to and synergize with institutions in a shared geographic region [3–5]. National pharmacist organizations, such as the American Society of Health-System Pharmacists and the Society of Infectious Diseases Pharmacists, also continued to highlight AS as a priority. These groups recently provided recommendations to guide and support ID and AS pharmacists as leaders in stewardship efforts, and they also aim to empower all pharmacists to incorporate AS practices into their daily workflows [6].

Not unexpectedly, the volume of published stewardship interventions in the outpatient setting remains significantly less than acute care counterparts (approximately one-third). However, one may argue the value of these published interventions is disproportionately higher as institutions explore novel methods of expansion into ambulatory stewardship. The use of outpatient parenteral antibiotic therapy remains at an all-time high—more than 2 million home infusion users in 2020—and

Received 09 November 2023; editorial decision 22 December 2023; accepted 02 January 2024; published online 4 January 2024

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https://doi.org/10.1093/ofid/ofad687

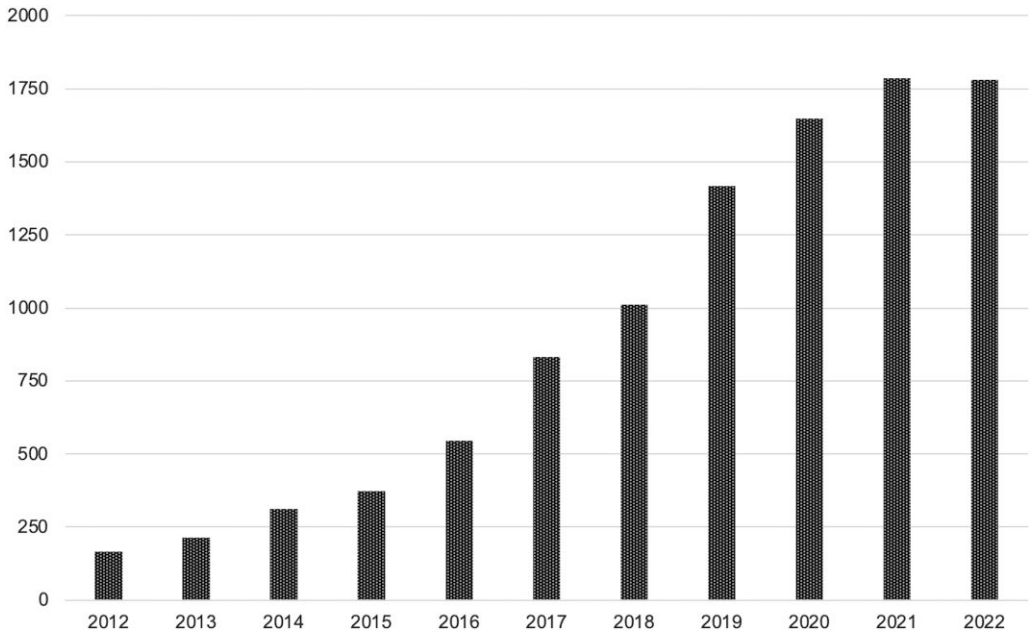

Figure 1. Number of antimicrobial stewardship publications indexed in PubMed, 2012–2022.

evidence grows supporting the use of complex outpatient (oral) antibiotic therapy for infections requiring protracted courses [7]. These modalities share some commonalities in management but also have unique patient-specific needs and coordination efforts dictating the need for identifying more efficient and effective interventions [8, 9]. A 2022 publication highlighted the work being done in outpatient parenteral antibiotic therapy, demonstrating examples of effective AS interventions and the increased number of publications in this arena [10].

The Southeastern Group Endeavor (SERGE-45) research network, an interprofessional group of highly trained ID clinicians in the Southeastern United States, has systematically reviewed and compiled publications involving AS interventions annually since 2016 [11–17]. In 2021, the volume of stewardship intervention publications provided the opportunity for sister publications uniquely focusing on acute care and ambulatory care environments, respectively [16, 17]. This year, the team returned to a combined publication and the top 13 stewardship intervention publications across the continuum of care determined by an interprofessional panel of antimicrobial stewardship experts as having the highest impact on AS are detailed here and briefly reviewed in Table 1.

METHODS

Using a previously detailed modified Delphi technique, members of the SERGE-45 network identified AS publications from 2022 considered to be significant using the following inclusion criteria: (1) published in 2022, including electronic publication ahead of print; and (2) included an actionable intervention [31]. 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.

A PubMed search using "antimicrobial stewardship" for 2022 revealed 1770 potential publications. Abstracts were screened to ensure that all relevant articles were considered, electronic publications before 2022 were removed, and publications were stratified between hospitalized and nonhospitalized populations. In addition, 123 publications were submitted by the network (71 hospitalized and 52 nonhospitalized), and those meeting criteria and not previously identified by the literature search were also included for consideration. A total of 179 articles (137 hospitalized and 42 nonhospitalized) were distributed to the entire SERGE-45 network for ranking via electronic survey of the top 13 articles based on contribution and/or application to antimicrobial stewardship programs (ASPs). Of the 103 network members at the time of the survey, 31 rank lists (30% participation) were submitted for the hospitalized articles and 29 rank lists (28% participation) were submitted for the nonhospitalized articles. The network rankings were reviewed by lead authors R. K. B., M. L. B., P.B.B., and C. M. B. via teleconference, and the top 7 hospitalized and top 6 nonhospitalized articles were identified to compose the top 13 articles, which are described here. Figure 2 outlines the manuscript selection process, and Table 1 provides a summary of the selected manuscripts. Manuscripts are presented grouped by theme.

Table 1. Summary of Top 13 Antimicrobial Stewardship Intervention Publications, 2022

Study Citation	Study Design	Intervention Summary	Primary and Key Secondary Outcomes
Evaluation of an opt-out protocol for antibiotic de-escalation in patients with suspected sepsis: A multicenter, randomized, controlled trial Moehring RW, et al. [18]	Multicenter, prospective, randomized, partially blinded, controlled trial evaluating an opt-out protocol for antibiotic de-escalation in low-risk adults with suspected sepsis	A 5-step AS protocol was implemented in 10 hospitals: (1) eligibility screen; (2) safety check; (3) randomization; (4) opt-out procedure to stop antibiotics; and if front-line clinicians opted out, (5) guided de-escalation discussion between AS personnel and clinicians. The safety check required detailed manual chart review, and the opt-out procedure included standardized language to guide the verbal discussion with prescribers.	Primary: • 78.6% of patients received antibiotics in the intervention arm vs 84.4% in the control arm, resulting in an OR of 0.68 (95% CI, .47–.98) • Mean DOT among those with antibiotics continued was 10.4 in the intervention arm vs 9.9 in the control arm, resulting in a ratio of mean DOT of 1.06 (95% CI, .88–1.26) • 36.0% of patients received extended-spectrum antibiotics in the intervention arm vs 43.5% in the control arm, resulting in an OR of 0.73 (95% CI, .55–.98) Secondary: • Readmission rates were 15.9% in the intervention arm vs 14.8% in the control arm • Relapse of suspected sepsis occurred in 7.8% of patients in both arms • CDI occurred in 1.0% of patients in the intervention arm vs 1.8% in the control arm • ICU admission occurred in 6.8% of patients in the intervention arm vs 8.6% in the control arm • Death occurred in 2.6% of patients in the intervention arm vs 4.2% in the control arm • Median postrandomization LOS was 2 d in both arms • Reinitiation of inpatient antibiotics after >48 h of no antibiotics was 4.2% in both arms • The DOOR-RADAR probability for the intervention arm vs control arm was 0.52 (95% CI, .48–.56)
A comparison of active versus passive methods of responding to rapid diagnostic blood culture results Chandler E, et al. [19]	Retrospective, observational study evaluating the impact of active versus passive response methods to rapid diagnostic gram-positive blood culture results in adult ICUs and adult oncology units at a tertiary-care academic medical center	Three notification methodologies for communicating positive blood culture results were compared: 1. The control group was the standard method of reporting PCR results where a laboratory technician called the nurse who then reported the critical result to the medical provider. 2. The passive group included the standard method and real-time EHR in-basket notifications for clinical pharmacists to address during work hours. 3. The active group was an around-the-clock, on-call service where trained pharmacy residents received the initial result and communicated the result and AS recommendations to the medical provider.	Primary: • Time from blood culture collection to first dose of optimal antibiotic therapy was shorter in the active group compared with passive and control group (23.4 h vs 42.2 h vs 45.9 h, $P = .028$) Secondary: • Median time to de-escalation was 12 h shorter in the active group compared with passive and control groups (34.4 h vs 46.5 h, vs 46.6 h, $P = .23$). • Time to microbiologically active therapy and DOT were similar • LOS from time of positive culture and inpatient mortality were not statistically significant
A fully integrated ID and AS telehealth service improves SAB bundle adherence and outcomes in 16 small community hospitals Veillette JJ, et al. [20]	Multicenter, retrospective, quasi-experimental study evaluating the impact of IDt and tAS surveillance on SAB management and outcomes at 16 small community hospitals	A formal IDt program, including IDt physician consultation and tAS pharmacist support, was established. IDt services were available through phone advice only, chart review with documentation (eConsult), or telemedicine consultation. Surveillance via tAS identified SAB patients and provided recommendations for SAB management and IDt consultation.	Primary: • Adherence to the entire SAB bundle and SAB components 1–3 were significantly higher in the IDt group than control group among patients admitted to an SCH (components 1–3: 73% vs 24%, $P < .001$) and among patients receiving definitive management at an SCH (components 1–3: 79% vs 23%, $P < .001$). Secondary: • No significant difference in in-hospital mortality, 30-day mortality, 30-day

Table 1. Continued

Study Citation	Study Design	Intervention Summary	Primary and Key Secondary Outcomes
			all-cause readmission, or 90-day SAB recurrence. Among patients receiving definitive management at an SCH, 30-day SAB-related readmission was lower in the IDt group compared with control (9% vs 17%, $P = .045$).
Analysis of an antibiotic stewardship program for ASB in the VA Health Care System Grigoryan L, et al. [21]	Interrupted time series quality improvement study at multiple sites within the VA Health Care System evaluating the effectiveness of an AS on reducing unnecessary urine cultures and antibiotic use in patients with ASB	Case-based teaching occurred on how to apply an evidence-based algorithm to distinguish UTI and ASB. Implementation at 4 intervention sites and 4 comparison sites occurred through external facilitation by a centralized coordinating center and internal facilitation by a site champion at each intervention site. Sites included both acute care and LTCF.	Primary: • Significant reduction in number of urine cultures ordered by 3.24 urine cultures per 1000 bed-days ($P = .003$) Secondary: • Significant relative percentage decrease of antibiotic DOT per 1000 bed-days (46.1 to 37.0) was 21.7% ($P = .007$) • Significant relative percentage decrease of length of antibiotic therapy per 1000 bed-days in days (36.7 to 29.6) was 21.0% ($P = .001$)
The effects of avoiding extended antimicrobial drain prophylaxis on *Clostridioides difficile* and postprocedural infection rates: A 5-year retrospective Marino AC, et al. [22]	Retrospective, pre-/postintervention study evaluating the impact of a change in postprocedural drain prophylaxis for neurosurgical patients on the incidence of CDI and postprocedural infection rates	Antimicrobial prophylaxis was limited to 24 h after the procedure or 1 dose preprocedure for EVD placement. Outcomes were compared with patients who received antimicrobial prophylaxis for the entire duration of drain placement.	Primary: • Incidence of hospital-onset CDI per 1000 patient days: 1.1% vs 0.31%, $P = .0020$ Secondary: • Incidence of postprocedural infections: 1.2% vs 1.4%, $P = .39$
Pharmacist-driven transitions of care practice model for prescribing oral antimicrobials at hospital discharge Mercuro NJ, et al. [23]	Quality improvement, nonrandomized, stepped-wedge design in adults admitted to general medical and/or surgical wards at a health system in Southeast Michigan	Pharmacist recommendations were completed at discharge and discussed on rounds or via telephone. Recommendations were based on health system guidelines for appropriate antimicrobial selection, dose, and duration. Orders for discharge were entered by the pharmacists to be consigned by the provider.	Primary: • Optimal antimicrobial prescription at discharge preintervention 36% (144/400) vs postintervention 81.5% (326/400), $P < .001$ Secondary: • Total antimicrobial duration decrease postintervention (−1.1 d; 95% CI, −1.7 to −.6) • Optimal prescribing increase was consistent in academic and community (37.4%, 95% CI, 27.5–46.7 and 43.2%, 95% CI, 32.4–52.8, respectively) • Time-adjusted GEE OR (95% CI) for: ◦ Clinical resolution: 0.91 (0.63–1.30) ◦ 30-day readmission: 0.77 (0.60–0.98) ◦ 30-day mortality: 0.80 (0.09–7.18)
Impact of clinical pharmacist discharge prescription review on the appropriateness of antibiotic therapy: A retrospective comparison Spigelmyer A, et al. [24]	Single-center, retrospective evaluation of the impact of non-ID pharmacist review of discharge antibiotic prescriptions	Non–ID-trained clinical pharmacists provided discharge medication review for antibiotics prescribed for pneumonia, UTI, CDI, ABSSSI, or gram-negative BSI. Antibiotic appropriateness was compared with prescriptions for antibiotics that did not undergo routine review by a rounding pharmacist before hospital discharge.	Primary: • Antibiotic appropriateness in pharmacist-reviewed group vs standard of care, 125/150 (83.3%) vs 81/150 (54.0%) respectively, $P < .00001$ Secondary: • Incorrect duration of therapy in pharmacist-reviewed group vs standard of care, 19 (12.7%) vs 49 (32.7%) respectively, $P = .0004$ • Antibiotics deemed unnecessary in pharmacist-reviewed group (0) vs standard of care (10), $P = .0017$ • Appropriateness of discharge antibiotic for UTI in pharmacist-reviewed group (82%) vs standard of care (46%), $P = .0019$

Table 1. Continued

Study Citation	Study Design	Intervention Summary	Primary and Key Secondary Outcomes
			• Appropriateness of discharge antibiotic for pneumonia in pharmacist-reviewed group (89%) vs standard of care (58%), $P = .0001$ • All other secondary outcomes were not statistically significant
Implementation of an ASP in LTCFs across the US Katz MJ, et al. [25]	Multicenter, quality improvement study with a pre-post design in 439 LTCFs	15 webinars conducted over 12 months accompanied by additional tools (activities, posters, pocket cards)	Primary: • Reduction in antibiotic starts per 1000 resident days from 7.9 to 7.5 Secondary: • Reduction in days of antibiotic therapy per 1000 resident days from 64.1 to 61.1 • Reduction in number of urine cultures per 1000 resident days from 3.0 to 2.6 • CDI laboratory-identified events per 100 000 resident days remained stable
AS to reduce inappropriate antibiotic prescribing in integrated academic health-system urgent care clinics Patel D, et al. [26]	Multifaceted, quality-improvement project to improve antibiotic prescribing in urgent care practices.	Clinician comparative feedback, clinician education, and patient education was provided on appropriate treatment of viral respiratory illnesses recommending against antibiotic use.	Primary: • Stewardship measured antibiotic prescribing rates from FY 2019 to FY 2021 all decreased 1. URI in children 12% to 4% 2. Pharyngitis in children 23% to 9% 3. Pharyngitis in adults 30% to 12% 4. Acute bronchitis, URI, or flu in adults 44% to 16% Secondary: • Diagnosis shifting decreased from 63% to 35% • All antibiotic prescribing decreased from 30% to 10%
A multimodal intervention to decrease inappropriate outpatient antibiotic prescribing for URIs in a large integrated healthcare system Davidson LE, et al. [27]	Interrupted time series analysis of antibiotics prescribed in 162 primary care practices	Education combined with a web-based provider prescribing dashboard for URI assessed in an after period of May 2018–March 2020 compared with a before period of April 2016–October 2017	Primary: • Significant reductions in inappropriate prescribing were found in the difference before and after the intervention for family medicine (−20.4%), internal medicine (−19.5%), pediatric medicine (−17.2%), and urgent care (−16.6%)
Improving antibiotic use for sinusitis and URIs: A virtual-visit antibiotic stewardship initiative Wasylyshyn AI, et al. [28]	Interrupted time series evaluating antibiotics prescribed during 5151 e-visits for URIs	The intervention focused on sinusitis/URIs, and included: 1. Modification of an e-visit URI questionnaire to identify appropriate patients, encourage guideline-concordant antibiotic use for sinusitis, and reduce inappropriate prescribing 2. Development of evidence-based sinusitis guidelines 3. Physician-provided audit and feedback related to antibiotic choice and duration	Primary: • Antibiotic prescriptions: 43.2% pre-intervention vs 28.9% post-intervention ($P < .001$) • Guideline-concordant antibiotic selection: 37.9% (amoxicillin-clavulanate) and 13.8% (doxycycline) pre-intervention vs 66.1% and 22.7%, respectively, post-intervention ($P < .001$) • Median antibiotic duration: 10 d preintervention vs 5 d postintervention ($P < .001$)
Impact of education and data feedback on antibiotic prescribing for UTIs in the ED: An interrupted time-series analysis Nys CL, et al. [29]	Quasi-experimental, multicenter, prospective AS intervention- with appropriate UTI diagnosis and management in 3 EDs	3 phases including a baseline and 2 intervention phases for appropriate diagnosis and antibiotic prescribing of adult patients discharged from the ED with a prescription for UTI 1. Baseline 2. Phase 1 = introduction of urine-specific antibiogram and UTI guideline, education, and department-specific feedback on UTI diagnosis and antibiotic prescribing 3. Phase 2 = re-education and provider-specific feedback	Primary: • Initial 15% increase in guideline-concordant antibiotic prescribing in phase 1 compared with baseline (IRR, 1.15; 95% CI, 1.03–1.29) Secondary: • Significant 3% increase in guideline-concordant prescriptions with every 2-week interval during phase 2 (IRR, 1.03, 95% CI, 1.01–1.04) • No change in UTI diagnosis • No change in rate of UTI diagnosis

Table 1. Continued

Study Citation	Study Design	Intervention Summary	Primary and Key Secondary Outcomes
Impact of advanced practice pharmacists on a culture response program in the ED Cornell WK, et al. [30]	Quasi-experimental pre- vs. postimplementation evaluation of a pharmacist-driven culture response program in a 91-bed adult and pediatric ED	ED culture follow-up program interventions were evaluated before and after transition of the program from nurse-driven to clinical pharmacist practitioner-driven	Primary: • Median time from initial culture review to intervention: 5.27 h preimplementation vs 2.95 h postimplementation ($P < .001$) Secondary: • Proportion of positive cultures intervened on: 27.3% preimplementation vs 40.4% postimplementation ($P < .001$) • Median time from actionable culture result to initial review: 4.84 h preimplementation vs 1.67 h postimplementation ($P < .001$)

Abbreviations: ABSSSI, acute bacterial skin and skin structure infection; AS, antimicrobial stewardship; ASB, asymptomatic bacteriuria; BSI, bloodstream infection; CDI, *Clostridioides difficile* infection; CI, confidence interval; DOOR-RADAR, desirability-of-outcome ranking response adjusted for duration of antibiotic risk; DOT, days of therapy; ED, emergency department; EHR, electronic health record; EVD, external ventricular drain; FY, fiscal year; GEE, generalized estimating equation; ICU, intensive care unit; ID, infectious diseases; IDt, infectious diseases telehealth; IRR, incidence rate ratio; LOS, length of stay; LTCF, long-term care facility; OR, odds ratio; PCR, polymerase chain reaction; SAB, *Staphylococcus aureus* bacteremia; SCH, small community hospital; tAS, tele-antimicrobial stewardship; UTI, urinary tract infection; VA, Veterans Affairs.

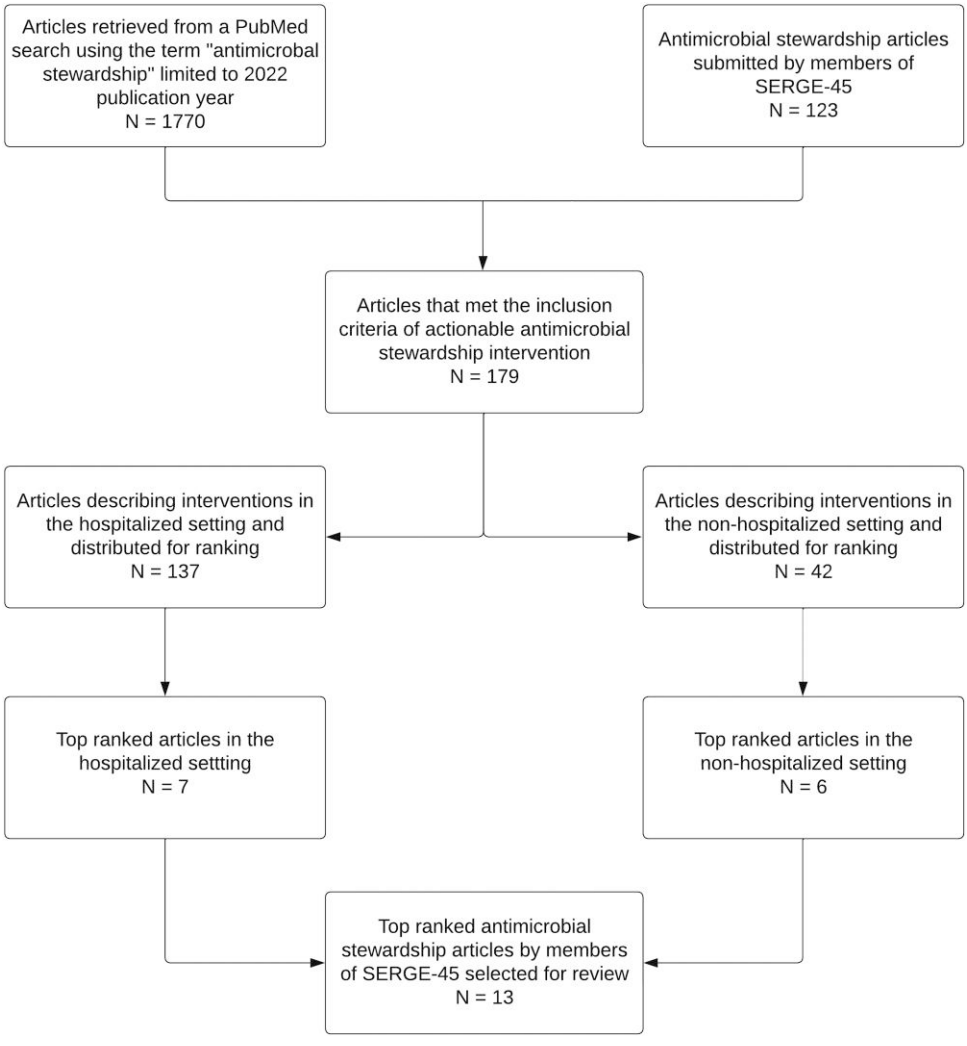

Figure 2. Flowchart of the database search and article selection process.

RESULTS

Evaluation of an Opt-Out Protocol for Antibiotic De-escalation in Patients With Suspected Sepsis

The Surviving Sepsis guidelines recommend prompt administration of antibiotics to adults with suspected sepsis and daily assessment for an opportunity to de-escalate therapy [32]. Moehring and colleagues conducted a multicenter, prospective, randomized, partially blinded, controlled trial to evaluate the impact of an opt-out protocol for antibiotic de-escalation versus standard of care in low-risk adults with suspected sepsis outside the intensive care unit (ICU) [18]. Detailed chart review was performed to conduct a 23-item safety check to identify patients eligible for the opt-out protocol. Clinicians caring for intervention patients were contacted to discuss antibiotic discontinuation using standardized language guided by the protocol.

The primary outcome was postenrollment antibiotic days of therapy (DOT), defined as the number of days antibiotics were used during hospitalization plus the intended days prescribed at discharge. A total of 9606 patients were assessed for eligibility, but only 767 were randomized because 8673 patients did not pass the safety check. The odds of antibiotic continuation was 32% lower in the intervention arm; however, DOT among patients who continued antibiotics were similar. In addition, the odds of receiving extended-spectrum antibiotics was 27% lower in the intervention arm. Common reasons for continuing antibiotics were treatment of localized infection and belief that stopping antibiotics was unsafe. Thirty-day safety outcomes revealed minor differences with fewer events occurring in the intervention arm. This trial demonstrated that an antibiotic opt-out protocol targeting carefully selected low-risk adults with suspected sepsis resulted in more antibiotic discontinuations compared with standard of care, but similar DOT when antibiotics were continued and no evidence of harm. Limitations include the extensive eligibility criteria for safety checks, efficiency in identifying real-time opportunities for stewardship, and variability in antibiotic stops by hospital, suggesting effects of site-specific implementation or personnel.

A Comparison of Active Versus Passive Methods of Responding to Rapid Diagnostic Blood Culture Results

Faster time to organism identification and detection of genetic elements that confer resistance through the use of rapid diagnostic tests (RDTs) leads to improved time to optimal therapy [33]. The combination of RDTs and active AS interventions has demonstrated more robust benefits; however, AS availability and resources vary across healthcare settings [34]. Chandler and colleagues conducted a retrospective, observational study of 209 intensive care or oncology adult patients with gram-positive blood cultures comparing standard laboratory methods of communicating RDT results with either the addition of passive in-basket notification in the electronic health record (EHR) to the clinical pharmacist on service or active, around-the-clock response of AS trained pharmacy residents [19].

Coagulase-negative staphylococci and *Staphylococcus aureus* were the most common pathogens identified by the institution's multiplex polymerase chain reaction (PCR) platform. Time to optimal therapy was significantly reduced in the active arm. Although not statistically significant, time to de-escalation and antibiotic duration for contaminant isolates was reduced in the active arm. Length of stay was significantly longer in the active arm; however, more patients with hematologic malignancies were represented. Time between in-basket notification and the clinical pharmacist addressing the notification was not assessed in the passive arm.

This study provides support that active communication of RDT results is more effective than passive notification in decreasing time to optimal antimicrobial therapy, time to de-escalation, and decreased treatment of contaminate pathogens. Stewards should consider the method of communicating laboratory results when designing RDT interventions. Application of the study results may be difficult in resource limited settings or settings where around-the-clock on-call pharmacy services are not routinely available.

A Fully Integrated ID and AS Telehealth Service Improves *Staphylococcus aureus* Bacteremia Bundle Adherence and Outcomes

In-person ID consultation improves outcomes for patients with *S. aureus* bacteremia (SAB) [35–42]. However, little is known about the clinical benefit of ID telehealth (IDt) on SAB and the impact of various telehealth modalities (eg, electronic consults vs telemedicine consults). Veillette and colleagues conducted a multicenter, retrospective, quasi-experimental study to describe the impact of a physician-driven IDt consultation service with integrated tele-antimicrobial stewardship (tAS) surveillance, conducted by ID-trained pharmacists, on SAB management across 16 small community hospitals (SCHs) [20]. Outcomes between IDt and control groups were assessed in SCH admission and SCH management populations.

SAB bundle adherence to every component (ie, echocardiogram, negative repeat blood cultures obtained, optimal intravenous antibiotics within 72 hours, source control within 72 hours, optimal intravenous antibiotic prescribed at discharge, and optimal duration prescribed at discharge), and the first 3 components were significantly higher in the IDt group than the control group for both the SCH admission and SCH management populations. There was no difference between IDt and control groups with respect to in-hospital mortality, 30-day mortality, 30-day all-cause readmission, or 90-day SAB recurrence. The 30-day SAB-related readmission was significantly lower (9% vs 17%, $P = .045$) and median length of stay was significantly longer in the IDt group compared with control for the SCH management population. No differences in outcomes were found based on IDt consult

type (ie, electronic consults vs telemedicine consults). This study demonstrates the importance of IDt consultation paired with tAS to improve SAB management in resource-limited settings.

Analysis of an Antibiotic Stewardship Program for Asymptomatic Bacteriuria in the Veterans Affairs Health Care System

A common target of both quality improvement programs and ASPs is inappropriate treatment of asymptomatic bacteriuria (ASB) [43]. A report from the Veterans Administration Antimicrobial Stewardship Task Force found 72% of 1210 ASB cases received antibiotics; additionally, a recent meta-analysis found treatment of ASB to be 45% [44, 45]. To improve on ASB management, Grigoryan and colleagues evaluated the effectiveness of a stewardship intervention on reducing unnecessary urine cultures and antibiotic use in patients with ASB [21]. The intervention included a validated evidence-based algorithm and case-based education to prescribers on how to apply the algorithm to distinguish urinary tract infection (UTI) from ASB. Implementation included a central coordinating center that provided external facilitation; internal facilitation was by designated site champions.

Each site went through 2 phases of data collection: baseline and intervention. Main outcomes and measures included urine culture orders, DOT, and length of antibiotic therapy associated with urine cultures, standardized by 1000 bed-days. Comparing intervention sites with control sites, there was a significant reduction in the number of urine cultures ordered by 3.24 cultures per 1000 bed-days. This led to relative percentage decreases of DOT of 21.7% (46.1 to 37.0 per 1000 bed-days) and length of antibiotic therapy of 21.0% (36.7 to 29.6 per 1000 bed-days). This quality improvement study illustrates use of AS to improve diagnostic processes and management of ASB across a healthcare system.

The Effects of Avoiding Extended Antimicrobial Drain Prophylaxis On *Clostridioides difficile* and Postprocedural Infection Rates

Postprocedural infections cause significant morbidity and mortality along with excess cost to the healthcare system [46, 47]. Healthcare systems have developed guidelines for preventing such infections through appropriate administration of periprocedural antimicrobials. Previous studies in neurosurgical populations have shown that antimicrobial prophylaxis beyond completion of the procedure does not reduce risk of postprocedural infection [48, 49]. With antimicrobial resistance and adverse effects such as *C. difficile* infection (CDI) directly caused by overuse of antimicrobials, the need to reassess optimal duration of antimicrobial prophylaxis is prudent. Marino and colleagues conducted a retrospective study to assess the impact of an institutional change to postprocedural drain prophylaxis (PPDP) for neurosurgical patients [22]. Historical practice at the institution allowed PPDP until drains, including external ventricular drains (EVDs), were removed. In May 2017, PPDP was limited to 24 hours after surgery or 1 dose preprocedure for EVD placement.

A total of 7204 patients were included, with 3770 in the preintervention cohort and 3434 in the postintervention cohort. The primary outcome of CDI occurred in 27 patients in the preintervention cohort and 7 patients in the postintervention cohort. The incidence per 1000 patient days decreased from 1.1% to 0.31% ($P = .0020$). Surgical site infections did not differ between the 2 cohorts (1.2% vs 1.4%, $P = .39$). Limitations of the study include patients were only evaluated for CDI while admitted to the neurosurgical service, and the diagnostic approach for CDI was not described. Changes in drain practices occurred during the study period; however, subgroup analysis of specific procedure types did not reveal any differences. This study provides evidence that limiting PPDP in neurosurgical patients decreases the incidence of CDI without increasing rates of surgical site infections.

Pharmacist-driven Transitions of Care Practice Model for Prescribing Oral Antimicrobials at Hospital Discharge

The transition from an acute care facility to outpatient has been identified as an area of opportunity for AS intervention [50]. Given data suggesting antibiotics at discharge make up approximately half of antibiotic days related to hospitalizations, there is a growing need to target antibiotic prescribing at discharge [51]. Mercuro and colleagues conducted a nonrandomized stepped-wedge designed quality improvement study in adults discharged from the hospital with antimicrobial prescriptions for uncomplicated infections [23]. Five hospitals in a large health system participated, ranging from large academic (877-bed) to smaller community (191-bed) institutions. Pharmacists involved in the intervention were alerted to target patients via EHR notification, direct communication from nursing and case management, or discussion during collaborative multidisciplinary rounds. Recommendations were communicated during rounds or via telephone, and discharge orders were entered or modified by the pharmacist and cosigned by the prescriber. The primary endpoint was frequency of discharge with an optimized antimicrobial regimen. Other endpoints included hospital length of stay, antimicrobial duration, and safety endpoints (eg, antimicrobial-related adverse effects and 30-day mortality).

Of a total of 1440 patients were screened, 800 were included (400 preintervention and 400 intervention). The most common exclusion was complicated or severe infection. There were no major differences between groups at baseline, and the median length of stay was 3 days. Optimal prescription at discharge was higher in the intervention period (36% vs 81.5%; $P < .001$), and effects were sustained regardless of hospital setting. The intervention period was also associated with a decrease in total antimicrobial duration, which was driven by prescriptions for respiratory tract infections. There were no differences in clinical resolution, readmission, or mortality.

There were also fewer antimicrobial-related adverse effects postintervention. The authors concluded that review of antimicrobials at discharge leads to improvement in discharge prescribing. In settings where transitions of care via pharmacy are already established, this prescription review model may be beneficial in furthering stewardship efforts.

Impact of Clinical Pharmacist Discharge Prescription Review on the Appropriateness of Antibiotic Therapy

As mentioned previously, combating inappropriate prescribing of antibiotics on hospital discharge has been identified as an important target for inpatient ASP and transitions of care programs. Although there is no optimal or universally accepted approach to improve appropriateness of discharge prescriptions, Spigelmyer and colleagues aimed to assess the impact of hospital-based clinical pharmacist discharge prescription review on the appropriateness of antibiotic prescriptions [24]. Non–ID-trained pharmacists covering the internal medicine service intervened by providing discharge prescription review on antibiotics for the treatment of pneumonia, UTI, CDI, acute bacterial skin and skin structure infections, or gram-negative bacteremia. The inpatient hospital services without a dedicated rounding pharmacist served as the standard of care or control group.

A total of 300 patients met inclusion criteria, with 150 in each cohort. Antibiotic appropriateness was significantly higher in the dedicated rounding pharmacist-reviewed group versus the control group (83.3% vs 54.0%, respectively; $P < .00001$). The most common type of inappropriate prescription error was duration of therapy (12.7% vs 32.7%, rounding pharmacist vs control group, respectively), with a trend toward longer durations than recommended by guidelines. Discharge prescriptions were deemed unnecessary for 10 patients in the control group versus none in the rounding pharmacist-reviewed group ($P = .0017$). Limitations of the study include its retrospective design and inclusion criteria based on antibiotic prescription at discharge. Overall, this study describes leveraging non-ID pharmacists to successfully improve the appropriateness of antibiotics prescribed at the point of hospital discharge. Stewards should look for opportunities to engage other front-line staff to extend the reach of ASP interventions.

Implementation of an Antibiotic Stewardship Program in Long-term Care Facilities Across the United States

The Agency for Healthcare Research and Quality Safety Program for Improving Antibiotic Use was an initiative designed to enhance antibiotic stewardship programs in long-term care facilities (LTCF), focusing on both cultural aspects, such as patient safety, and technical knowledge of antibiotic prescribing. Conducted from December 2018 to November 2019, the program aimed to improve antibiotic use and processes in participating LTCF sites. The study involved 523 LTCF, with 83.9% completing the 1-year program. The program's website received substantial traffic, with nearly 1900 unique users accessing materials and more than 4000 downloads recorded.

Each LTCF site designated a champion to facilitate changes and an antibiotic stewardship team to lead improvements. The intervention used the Four Moments of Antibiotic Decision Making framework, tailored for LTCF settings, and included webinars, presentations, posters, and pocket cards. The Four Moments consist of (1) make the diagnosis, (2) cultures and empiric therapy, (3) duration of therapy, and (4) stop, narrow, change to oral. Monthly antibiotic data for both intravenous and oral antibiotics were collected for analysis. Results indicated a reduction in antibiotic starts from 7.9 to 7.5 per 1000 resident-days, as well as decreased days of antibiotic therapy from 64.1 to 61.0 per 1000 resident-days. Facilities with high webinar engagement experienced the most significant reductions in antibiotic use.

The study demonstrated increased engagement in antibiotic stewardship activities, including staff training, prescribing recommendations, review with feedback, and antibiotic use tracking. Although there was a decrease in the number of urine cultures, the number of *C. difficile* laboratory-identified events remained relatively stable. The findings highlight the positive impact of the Agency for Healthcare Research and Quality Safety Program on antibiotic use and processes in LTCF, particularly for those with active engagement [25].

Antibiotic Stewardship to Reduce Inappropriate Antibiotic Prescribing in Integrated Academic Health-system Urgent Care Clinics

Up to 50% of ambulatory antibiotics may be unnecessary, and ambulatory antibiotics account for greater than 60% of antibiotic costs. Urgent care practices have higher antibiotic prescribing rates than other ambulatory sites of care [52, 53]. Patient satisfaction is of particular concern at urgent care practices, which compete with themselves and other sites of care based on convenience and patient experience [54]. Northwestern Medicine is an integrated academic healthcare system in the Chicago area that includes 23 urgent care clinics. The Northwestern Medicine Ambulatory Antimicrobial Stewardship Committee was implemented in 2018 with provider champions in multiple areas, including urgent care. The Ambulatory Antimicrobial Stewardship Committee implemented stewardship activities in 2020 that included measure development, comparative feedback, and clinician and patient education.

Antibiotic prescribing rates decreased in all targeted areas including upper respiratory tract infections (URI) in children, pharyngitis in adults and children, and acute bronchitis, URIs, and flu for adults. Decreases in diagnosis shifting (ie, an increase in the number of related antibiotic-appropriate diagnoses) and all antibiotic prescribing were observed during the intervention period. Patient satisfaction rates increased by

6% during the intervention period and were not associated with antibiotic prescribing rates. Some limitations of the study include lack of randomization and comparator group, study conducted during COVID-19 pandemic, and lack of uniform implementation across all practice sites. AS interventions paired with education can lead to reduced prescribing rates for URIs without affecting patient satisfaction. Ambulatory stewardship targeting urgent care practices has potential to improve antibiotic prescribing rates in targeted disease states [26].

A Multimodal Intervention to Decrease Inappropriate Outpatient Antibiotic Prescribing for Upper Respiratory Tract Infections

URIs are an important outpatient diagnosis associated with antibiotic prescribing, of which up to 50% has been found to be inappropriate [55]. Although advances have been made to better identify opportunities for stewarding antibiotic decision making related to URI, a gap remains for sustainable large-scale implementation of such work. Advancement of knowledge in this area comes from work performed by Davidson and colleagues who executed a interrupted time series analysis of a multicomponent outpatient stewardship program aimed at reducing inappropriate antibiotic prescribing for URI [27].

This study took place at 162 outpatient practices within a single healthcare system, including adult and pediatric encounters for URI at family medicine, internal medicine, urgent care, and pediatric locations. The multicomponent strategy engaging an interdisciplinary team was implemented over a 4-month period between the pre- and postdata analysis periods. It included education to patients, education to prescribers, and production of an interactive prescriber dashboard accessible to prescribers and administrators. The provider dashboard produced visualized year-to-year and rolling 12-month data comparisons viewable by indication, antibiotic class, and more.

In comparing the 20 months of preintervention data to 24 months of postintervention data, 286 580 of 704 248 (40.7%) URI encounters were prescribed antibiotics versus 277 177 of 832 200 (33.3%) URI encounters, respectively. The relative reductions were −20.4% for family medicine, −19.5% for internal medicine, −17.2% for pediatric medicine, and −15.6% for urgent care. An important limitation of this study was that fill rates were not assessed, but rather data were analyzed at the encounter level.

Improving Antibiotic Use for Sinusitis and Upper Respiratory Tract Infections: A Virtual-visit Antibiotic Stewardship Initiative

Acute respiratory infections are responsible for the highest number of antibiotic prescriptions in adults, and up to half of those may be inappropriate [56, 57]. Wasylyshyn and colleagues conducted a pre-post intervention interrupted time series to evaluate the effect of a multifaceted stewardship intervention on e-visit prescribing [28]. The intervention consisted of improved follow-up questions for patients reporting sinusitis or upper respiratory symptoms, a sinusitis order set, and physician-led audit and feedback for prescribers (Table 1).

A total of 4534 patients (972 preintervention, 3562 postintervention) were included. Of note, the postintervention period (6/1/2019–9/30/2020) occurred during the initial outbreak of COVID-19 and includes significantly more patients than the preintervention period (1/1/2018–12/31/2018). Less sinusitis (50.3% vs 45.9%) but more flu (46.9% vs 54.1%) was seen postintervention. Antibiotic prescriptions for sinusitis (69.9% vs 56.4%, $P < .001$) and flu (15.6% vs 5.5%, $P < .001$) decreased significantly postintervention. Follow-up visits to a primary physician or emergency department (ED) within 14 days of e-visit significantly decreased from 4.5% of all visits to 2.9% ($P = .02$).

This study demonstrated that a multifaceted stewardship intervention improved use of guideline-concordant antibiotics and reduced inappropriate antibiotic prescribing in e-visits for sinusitis or URI. Study limitations include inability to assess accuracy of diagnoses, prescriber turnover, and confounding by the COVID-19 pandemic.

Impact of Education and Data Feedback on Antibiotic Prescribing for Urinary Tract Infections in the Emergency Department

Nys and colleagues performed a quasi-experimental, prospective, multicenter study in an academic and 2 community hospital EDs evaluating the impact of education and data feedback on guideline-concordant antibiotic prescribing for UTIs [29]. Adult patients discharged from the ED with an antibiotic prescription for a UTI were included in the study and evaluated in a baseline and 2 intervention phases. Phase 1 involved introduction of a urine-specific antibiogram and UTI guideline, education, and department-specific feedback on UTI diagnosis and antibiotic prescribing. Phase 2 included re-education, more department-specific feedback, and provider-specific feedback.

A regression analysis showed a 15% overall improvement in guideline-concordant antibiotic prescribing from baseline to phase 1 with an incidence rate ratio of 1.15 (95% confidence interval [CI], 1.03–1.29). Though there was no significant improvement from phase 1 to phase 2 or phase 0 to phase 2, the analysis showed a 3% improvement in guideline-concordant antibiotic prescribing in every 2-week interval in phase 2 (95% CI, 1.01–1.04), suggesting that antibiotic prescribing continued to improve week over week with re-education and provider-specific feedback after an initial improvement with standard stewardship interventions.

This study showcases the sustained and continued impact the use of large datasets can have to inform prescribers of their comparative prescribing patterns and improve rates of guideline adherence. Additionally, it displays flexibility in showing improvement in prescribing appropriateness in both the academic and community settings as well as application of stewardship initiatives in the ED setting. Finally, this study

underlines the importance of continual provider-specific feedback on prescribing patterns.

Impact of Advanced Practice Pharmacists on a Culture Response Program in the Emergency Department

Infectious diagnoses account for millions of ED visits every year with many patients discharged while cultures are still pending [30, 58]. With the incorporation of pharmacists into the ED workflow, culture review and follow-up programs represent an opportunity for meaningful AS interventions outside the hospital setting.

Cornell and colleagues performed a quasi-experimental, pre- and postimplementation evaluation of an advanced practice pharmacist-driven culture response program for 4 infections commonly treated in the ED [30]. Before the transition, the culture response team consisted of a nurse and physician. In the postimplementation period, a pharmacist performed the review and followed up independently with a physician available as needed for consultation.

This study's primary outcome was time from initial culture review to intervention defined as the first time the culture was viewed following the posting of an actionable result. Data were collected on 200 interventions in each timeframe. There was a statistically significant difference in the primary outcome at 5.27 hours in the nurse-driven program versus 2.95 hours in the pharmacist-driven program ($P < .001$). Several secondary outcomes also reached statistical significance including an increase in positive cultures with interventions, decreased median time from actionable result to initial review, and reduced overall culture response process time. Intervention types were also different between the 2 periods, but all antibiotic choices were appropriate according to study criteria. Incorporating advanced practice pharmacists into the ED culture response program and empowering them to practice independently streamlined workflow while also increasing meaningful and timely interventions.

DISCUSSION

The chosen articles for the 2022 Baker's Dozen edition consist of a number of very practical interventions for ASPs that should help stewardship providers and extenders achieve program goals and ultimately improve patient care. However, during the screening of 2022 articles, it was clear that a significant number of articles described interventions that have been published several times previously and therefore would not be very helpful for clinicians looking to expand stewardship services in innovative ways. In particular, the high proportion of international stewardship publications described interventions that have previously demonstrated success in the United States, which likely explains why these articles were not ranked higher by SERGE-45 network members. The study design of many articles was also less rigorous or described in less detail than desired. Therefore, it is imperative that, as AS services and programs mature both in the inpatient and nonhospitalized settings across the globe, that well-designed research is performed to best ensure quality intervention strategies [59]. Applying principles of implementation science to AS research can help promote common knowledge, collaboration, and broader application of intervention frameworks or methodologies [60–62].

Several themes arose among the evaluated manuscripts related to hospitalized patients. First, the management of bacteremia was represented in several articles included. A number of beneficial interventions focused on the process within the management of bloodstream infections rather than the treatment itself, such as shorter time to optimal therapy when active notification of results was used rather than passive communication. A telehealth ID consultative service also demonstrated a decreased 30-day readmission for SAB among nearly 20 community hospitals, providing practical expertise for a challenging disease state.

Transitions in care, specifically at the time of hospital discharge, was also an important theme within this year's articles. The need for stewardship services across the continuum of care is well known as a high number of days of antimicrobial therapy occur once the patient has left the hospital [63]. These services targeting optimized discharge antibiotic prescribing at hospitals of various patient populations demonstrated improved antibiotic appropriateness, decreased duration of therapy, as well as overall less adverse effects.

In addition to continuous quality and process improvement initiatives, regulations and demands continue to increase for stewards. Hospitals participating in the Centers for Medicare and Medicaid Services Promoting Interoperability Program will be required to report both antimicrobial use and antimicrobial resistance data to the National Healthcare Safety Network beginning in 2024 [64]. This is yet another time- and resource-intensive initiative, particularly for institutions that have not participated in the NHSN antimicrobial use and antimicrobial resistance options previously.

To help meet these increasing demands and support the sustainability of ongoing efforts from ASPs, additional dedicated inpatient stewardship personnel may be needed. Stewards will also need to identify creative ways to improve efficiency and leverage additional resources to extend their reach. This includes training other non-ID pharmacists and healthcare providers as stewardship extenders to incorporate AS practices into their routine patient care activities. In addition, the importance of precision therapeutics will be prudent leveraging emerging data and availability of services (eg, therapeutic drug monitoring of agents such as beta-lactams or linezolid).

As AS practice continues to expand into nonhospital settings, data are needed for busy outpatient providers to choose interventions that will provide the most benefit. Educational

interventions continued to be the primary implemented strategy evaluated. Positive interventions were demonstrated that decreased antibiotic prescribing in URIs as well as UTIs, which are both common clinical conundrums. These strategies were successful in a number of different outpatient settings, including LTCF, ED, urgent care, and even virtual through e-prescribing. These findings are encouraging as stewardship programs multiply and mature.

Future stewardship intervention research from nonacademic settings, including rural clinics, is needed to demonstrate comparative benefits to academic settings. The sustainability of these beneficial interventions would be the next step to evaluate, considering the long-term effects on stewardship outcomes are largely unknown. Integration of long-acting agents, such as lipoglycopeptides and rezafungin, should be evaluated, because these agents could be given in these settings to avoid admission or shorten hospitalization. With increased focus, attention, and workload on stewardship within the nonhospital setting, there is a growing need for full-time-equivalent positions devoted to stewardship in these settings as outlined by the Centers for Disease Control and Prevention rather than increasing workload on existing clinicians, which may lead to suboptimal outcomes. Proper training of pharmacists and physicians within stewardship, who most likely would lead these efforts, is critical to ensure long-term success. Leveraging the EHR in unique ways and incorporating artificial intelligence into workflows will be of interest to stewards looking to maximize their impact in 2023 and beyond [65]. As stewards begin to tackle these new and exciting endeavors, robust evaluation of interventions and dissemination of findings will be critical to the advancement of the ever-evolving field of antimicrobial stewardship.

Notes

Author contributions. C. M. B., P. B. B., M. L. B., and R. K. B. all supported idea and content development. All authors provided written content and edits for the manuscript.

Financial support. This work received no financial support.

Potential conflicts of interest. All authors: No reported conflicts. The views and opinions expressed in this paper represent those of the authors and do not necessarily reflect the position or policy of any previous, current, or potential future employer.

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