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Author(s): Lucas Schulz, PharmD, BCPS; Kurt Osterby; Barry Fox, MD

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ORIGINAL ARTICLE

The Use of Best Practice Alerts with the Development of an Antimicrobial Stewardship Navigator to Promote Antibiotic De-escalation in the Electronic Medical Record

Lucas Schulz, PharmD, BCPS;¹ Kurt Osterby;² Barry Fox, MD³

OBJECTIVE. Develop a clinical decision support tool comprised of an electronic medical record alert and antimicrobial stewardship navigator to facilitate antimicrobial stewardship.

DESIGN. We analyzed alerts targeting antimicrobial de-escalation to assess the effectiveness of the navigator as a stewardship tool. The alert provides antimicrobial recommendations, then directs providers to the navigator, which includes order management, relevant patient information, evidence-based clinical information, and bidirectional communication capability.

SETTING. Academic, tertiary care medical center with an electronic medical record.

INTERVENTION. Alerts containing stewardship recommendations and immediate access to the navigator were created.

RESULTS. Antibiotic use and response data were collected 1 day before stewardship recommendation via the best practice alert (BPA) tool and 1 day after the BPA tool response. A total of 1,285 stewardship BPAs were created. Two hundred and forty-four (18.9%) of the BPAs were created and acted upon within 72 hours for the purpose of de-escalation: 169 (69%) were accepted, 30 (12%) were accepted with modification, and 45 (18%) were rejected. Statistically significant decreases in total antibiotic use as well as in use of broad-spectrum (anti-methicillin-resistant *Staphylococcus aureus* and anti-pseudomonal) agents occurred when accepted recommendations were compared with rejected recommendations.

CONCLUSIONS. We describe the successful development of a clinical decision support tool to perform prospective audit and feedback comprised of an alert and navigator system featuring evidence-based recommendations and clinical and educational information. We demonstrate that this tool improves antibiotic use through our example of de-escalation.

CLINICAL TRIALS IDENTIFIER. This project was registered at ClinicalTrials.gov (NCT01573195).

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Antimicrobial stewardship programs (ASPs) use a variety of methods to improve patient care and outcomes through judicious use of antimicrobial agents, including education and direct interaction and feedback to the prescriber. The Infectious Diseases Society of America (IDSA) and the Society of Healthcare Epidemiology of America (SHEA) identified 2 core strategies and 8 supplemental strategies that comprise a comprehensive stewardship program.¹ One of these core strategies is prospective audit and feedback, which is often labor intensive, necessitating up to 0.5 full-time equivalent physicians and 0.5 to 1 full-time equivalent pharmacist for most programs.² Considerable time is spent paging, calling, texting, and educating prescribers about ASP recommendations.

Clinical decision support (CDS) tools provide prescribers with selected, relevant data at the time of decision making

and prescribing and can significantly improve the care of patients and the efficiency of ASP. Decision support for antimicrobial prescribing is not a new phenomenon³ and demonstrated improved clinical and financial outcomes 20 years ago.⁴ Some CDS services and electronic medical records have also demonstrated ASP efficacy and reduced antibiotic-associated errors since the initial publications.⁵ The increasing prevalence of electronic health and medical records (EMRs) will encourage additional development of CDS tools.

We developed an integrated CDS tool to make ASP recommendations in our EMR (Epic; Verona, WI). Our best practice alert (BPA) tool creates a BPA in the EMR and directs providers to a single location to review the ASP's evidence-based recommendation; evaluate laboratory, radiology, and microbiology data; act on anti-infective orders; and respond

Affiliations: 1. Department of Pharmacy, University of Wisconsin Hospital and Clinics, Madison, Wisconsin; 2. Center for Clinical Knowledge Management, University of Wisconsin Hospital and Clinics, Madison, Wisconsin; 3. Department of Infectious Diseases, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin.

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FIGURE 1. Example of the top half of the antimicrobial stewardship best practice navigator screen. This includes the antimicrobial stewardship team recommendation, written as a progress note, and a response option for the primary team. If the primary team declines the recommendation, a second row appears and allows for bi-directional communication with the stewardship team.

to the ASP recommendation. Recommendations and subsequent BPAs are based on strategies outlined in the IDSA/SHEA guidelines.¹ In this article, we describe the pilot application of the BPA tool, demonstrate integration of an evidence-based recommendation with BPA in the EMR, and present data supporting this technique as an effective means to encourage antimicrobial de-escalation.

METHODS

The University of Wisconsin Hospital and Clinics (UWHC) is a 586-bed tertiary academic medical center with active transplant and critical care programs and an affiliated pediatric hospital. Since 2008, the institution has implemented various phases of Epic EMR, including computerized physician order entry; clinical documentation; and pharmacy, oncology, and anesthesia modules. Our hospital is currently using Epic, version Spring 2010.

The ASP is composed of an infectious disease physician and an infectious disease-trained pharmacist. Ancillary mem-

bers of the team include clinical pharmacists, microbiology staff, information technologists, respiratory therapists, and nursing staff.

Patient antimicrobial regimens are reviewed on weekdays by the ASP pharmacist using third-party vendor software (SafetySurveillor; Premier) to identify targeted interventions. Generally, we do not use lists from the EMR for targeting stewardship initiatives, because ASP tools in the EMR are still in their embryonic stage. Third-party alerts include but are not limited to initiation of broad-spectrum or restricted antibiotics, use of vancomycin at 72 hours without a positive culture result, and antibiotics eligible for parenteral to enteral interchange and other targeted antimicrobials used for defined periods of time.

Before creation of our BPA tool, Epic provided limited CDS. The ASP was the first group at UWHC to comprehensively implement a CDS in near real-time format that allowed for prescriber feedback. The ASP pharmacist reviews patients identified in the third-party report and uses the EMR to

evaluate clinical progress. When an intervention is identified, it is reviewed with the ASP physician and a recommendation is created using the BPA tool. The BPA tool (Figs. 1 and 2) includes the ASP recommendation, dedicated infectious disease clinical information derived from the EMR, antimicrobial orders, and optional educational links. The ASP recommendation is written as a progress note and is available for all providers to view. The dedicated infectious disease clinical information includes temperature curve, white blood cell result trends, and anti-pyretic and antimicrobial medication administration data information. To reduce the complexity of the patient medication profile, the BPA tool presents only antimicrobial orders and excludes all nonantimicrobial orders. Finally, educational links are provided to both external and internal guidelines and selected evidence-based resources. There are currently 8 broad intervention themes, as follows: (1) de-escalation, (2) duration of therapy, (3) duplicate coverage, (4) susceptibility mismatch, (5) microbiology cultures needed, (6) dosing adjustments, (7) route interchange, and (8) drug interaction notification.

Bi-directional communication is possible via the BPA tool. If the prescriber either rejects or accepts with modifications the ASP recommendations, a dialogue box allows for feedback. Previously, ASP recommendations were communicated in joint patient care rounds, if they occurred, or via paging, text, or telephone conversation with the primary provider. The BPA tool maintains the prospective feedback and educational aspect fundamental to a successful ASP while providing a mechanism for providers to respond.

To assess the effectiveness of our novel BPA tool, we investigated a single intervention theme, antimicrobial de-escalation. De-escalation was defined as either reduction in the total number of antibiotics administered or reduction in the spectrum of antibiotics administered. Antibiotics were analyzed according to spectrum range; broad-spectrum antibiotics defined by the investigators included aminoglycosides, anti-pseudomonal β -lactams, fluoroquinolones, carbapenems, and gram-positive agents with activity against methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* species, or both. Narrow-spectrum antibiotics were defined as all antibiotics not considered to be broad spectrum. All included antibiotics and their categories are listed in Table 1. Agents were also divided during the analysis by route of administration, either enteral or parenteral, using the prescribed route of administration. Intravenous to oral conversions were not considered to be de-escalation. Antifungal and antiviral agents were excluded from analysis. Patients were excluded if they were discharged from the hospital within 24 hours after a response in the BPA tool was recorded.

Prescribers could accept, accept with modification, or reject the recommendation using the BPA tool. Acceptance was defined as a change consistent with the ASP recommendation. Accept with modification was defined as a change to a de-escalated antibiotic regimen but not the complete recom-

mended regimen. Reject was defined as either a nonresponse without change in antibiotic regimen or active feedback to the AMS team refuting the recommendation without alteration of the antibiotic regimen. In circumstances in which the prescribing team did not formally respond in the BPA tool but changes to antibiotics were made by the primary team, the ASP pharmacist determined the appropriate response category on the basis of EMR progress note review. If no therapeutic changes were made and the BPA tool response system did not indicate a rejected recommendation within 72 hours, prescribers were directly contacted. In these rare instances, the patient was excluded from the analysis, because the subsequent prescribing action was likely attributable to active ASP team intervention rather than to the BPA tool.

Activation of the BPA tool was regarded as day 0. Baseline antibiotic use was determined using the EMR on the calendar day before BPA activation (day -1). Antibiotic use after recommendation (via the BPA tool) was determined using the EMR on the calendar day after the BPA response (recommendation response day [RRD] +1). If the recommendation was rapidly accepted and antibiotic changes made on day 0, antibiotic use was measured on RRD +1. BPA responses were measured within 72 hours after being issued.

The difference between number of antibiotics before and after BPA tool responses were compared using a 1-way analysis of variance. Pairwise means comparisons were made using the Tukey honestly significant difference test (JMP Statistics). Analysis of means for proportions was used to generate likelihood ratios for certain individual antibiotics that included vancomycin, piperacillin-tazobactam, and ciprofloxacin. A *P* value of less than .05 was considered to be statistically significant.

Institutional review board exemption was initially granted, because this project fell under the University of Wisconsin quality assurance activities. Subsequently, because there was partial funding from the pharmaceutical industry, it was approved as a minimal risk protocol. A Health Insurance Portability and Accountability Act waiver and a waiver of informed consent were granted.

RESULTS

The ASP began entering recommendations using the BPA tool in March 2011. Data collection continued for 548 days (18 months) through August 2012. A total of 1,285 BPAs were written during 393 ASP service-days, and 249 (19.4%) were written for de-escalation in patients who remained hospitalized for at least 72 hours. Sixty-one percent (153 of 249) of the BPAs were written for surgical patients. Forty-seven percent (118 of 249) of the BPAs were written for patients in an intensive care unit. Recommendations were most commonly written 48–72 hours after empirical broad-spectrum antibiotic therapy was initiated for suspected bloodstream infection and healthcare-associated pneumonia, especially in cases in

Select Pt Data

Select Font Size

Vital signs min/max (last 24 hours)
None

Intake/Output
None

Current Anti-infectives

Start	Stop	Status	Route	Frequency	Ordered
09/03/13 1530		-- Sent	IV	EVERY 12 HOURS	09/03/13 1516
ciprofloxacin (CIPRO) 400 mg in dextrose 5% 200 mL bag Question Answer Comment: Indication Infection-Suspected Site (select all that apply) Lower RTI Cultures Ordered (Y/N) Yes Type of Therapy New Therapy Coverage (select all that apply) Enteric GNR					
09/03/13 1530		-- Sent	IV	EVERY 8 HOURS	09/03/13 1516
piperacillin-tazobactam (ZOSYN) 3.375 g vial + minibag - (PROLONGED PIPERACILLIN/TAZOBACTAM INFUSION) Question Answer Comment: Indication Infection-Suspected Site (select all that apply) Lower RTI Cultures Ordered (Y/N) No Type of Therapy New Therapy Coverage (select all that apply) Enteric GNR					
09/03/13 1530		-- Sent	IV	EVERY 8 HOURS	09/03/13 1516
vancomycin (VANCOGIN) 1 g in dextrose 5% 200 mL bag Question Answer Comment: Indication Infection-Suspected Site (select all that apply) Lower RTI Cultures Ordered (Y/N) No Type of Therapy New Therapy					

Select Labs (Last 36 hours)
** None **

Microbiology Results
None

Radiology Results (Last 48 hours)
** None **

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FIGURE 2. Example of the bottom half of the antimicrobial stewardship best practice navigator screen. Selected patient data can be presented, including vital signs, infectious disease-specific laboratory results, and microbiology results. Also included are current anti-infective agents extracted from the medication record.

which there was a reduction in double gram-negative coverage and lack of identification of MRSA.

Of the 249 de-escalation recommendations using the BPA tool, 244 had responses within 72 hours: 169 (69%) were accepted, 30 (12%) were accepted with modifications, and 45 (18%) were rejected. Five patients were excluded because the BPA tool response system did not indicate reject and the therapeutic regimen remained unchanged at least 73 hours after BPA recommendation. Two common reasons for rejection included new information from outside the hospital microbiology laboratory or deterioration in patient condition. The difference between the number of accepted and modified BPAs was not statistically different in all cases. Comparison

of antibiotic use based on accepted, modified, and rejected BPA responses is presented in Table 2. When the BPA tool was accepted, the absolute number of antibiotics, the use of broad-spectrum (including anti-MRSA and anti-pseudomonal agents) antibiotics, and the use of parenteral antibiotics significantly decreased. Acceptance of the BPA tool did not affect the use of narrow-spectrum antibiotics compared with rejection of the BPA.

Analysis of individual antibiotics demonstrated that the likelihood of vancomycin, piperacillin-tazobactam, and ciprofloxacin use on the day of BPA recommendation was the same for all groups (likelihood ratio >.05). When the BPA tool was accepted, the use of these antibiotics significantly

TABLE 1. Breakdown of Antibiotics and Categorization by Spectrum

Drug	Activity spectrum designation			
	Broad	Narrow	Anti-MRSA	Anti-pseudomonal
Amikacin	X	X
Amoxicillin	...	X
Amoxicillin-clavulanate	...	X
Ampicillin	...	X
Ampicillin-sulbactam	...	X
Azithromycin	...	X
Aztreonam	X	X
Cefazolin	...	X
Cefepime	X	X
Cefoxitin	...	X
Cefpodoxime	...	X
Ceftazidime	X	X
Ceftriaxone	...	X
Cefuroxime	...	X
Ciprofloxacin	X	X
Clindamycin	...	X	X	...
Daptomycin	X	...	X	...
Dicloxacillin	...	X
Doxycycline	...	X
Ertapenem	X
Fosfomycin	...	X	X	...
Gentamicin	X	X
Imipenem-cilastatin	X	X
Levofloxacin	X	X
Linezolid	X	...	X	...
Meropenem	X	X
Metronidazole	...	X
Moxifloxacin	X
Nitrofurantoin	...	X
Oxacillin	...	X
Penicillin	...	X
Piperacillin-tazobactam	X	X
Tetracycline	...	X
Tigecycline	X	...	X	...
Tobramycin	X	X
Vancomycin	X	...	X	...

NOTE. MRSA, methicillin-resistant *Staphylococcus aureus*.

decreased ($P < .05$ for all, data not shown) compared with rejection of the BPA.

DISCUSSION

We created a convenient, real-time, interactive CDS tool using our EMR software to improve antibiotic use by facilitating prospective audit and feedback. Prospective audit by the ASP occurs using third-party software in conjunction with the EMR. With our CDS tool, once an ASP recommendation is created and BPA activated, the navigator provides the primary medical team with the recommendation, clinical information, electronic order modification options, and educational links to an internal ASP work space dedicated to internal and external evidence-based medicine references and documents

supporting antimicrobial de-escalation in a single location. Return feedback from the medical team to the ASP team also occurs via the navigator.

Historically, antimicrobial streamlining and de-escalation, a supplemental IDSA/SHE strategy, has been shown to be difficult to implement in clinical practice,^{6,7} especially in the intensive care unit.⁸⁻¹⁰ Diffusion of de-escalation practice into clinical activities has been slow, with published percentages between 10% in uncontrolled studies and 69% in controlled de-escalation studies.^{11,12} In contrast, de-escalation recommendations made through our BPA tool were accepted 81% of the time, resulting in decreased use of broad-spectrum agents including vancomycin, piperacillin-tazobactam, and ciprofloxacin as well as increased use of narrow-spectrum

TABLE 2. Antibiotic Use by Best Practice Alert (BPA) Response

Antibiotic	Day -1				RRD +1				Means comparison
	BPA response			ANOVA	BPA response			ANOVA	
	A	M	R		A	M	R		
Overall	2.38	2.33	2.27	0.7117	1.26	1.40	2.09	<.0001	A<R; M<R; A=M
Broad spectrum	2.041	2.133	1.978	0.7413	0.734	1.200	1.644	<.0001 ^a	A<R; A=M; M<R
Narrow spectrum	0.343	0.200	0.289	0.3497	0.527	0.200	0.444	.0264 ^a	A=R; A>M; R=M
IV administration	1.56	1.57	1.60	0.9375	0.54	0.93	1.31	<.0001 ^a	A<R; A<M; M<R
Oral administration	0.82	0.77	0.67	0.3707	0.72	0.47	0.78	.1184	
Anti-MRSA	0.645	0.600	0.756	0.3296	0.172	0.300	0.556	<.0001 ^a	A<R; M<R; A=M
Anti-pseudomonal	1.391	1.533	1.267	0.1871	0.538	0.867	1.067	<.0001 ^a	A<R; A<M; M=R

NOTE. Data are the raw number of antibiotics, unless otherwise indicated. The statistical comparison is a 1-way analysis of variance (ANOVA) and a pairwise means comparison with Tukey's honestly significant difference test. A, accepted ($n = 169$); IV, intravenous; M, accepted with modifications ($n = 30$); MRSA, methicillin-resistant *Staphylococcus aureus*; R, rejected ($n = 45$); RRD, recommendation response day.

^a Statistical significance of the ANOVA F test.

antibiotics. Our high acceptance rate over an extended period of time speaks to the utility of our recommendations and use of the BPA tool.

Before use of our BPA tool, the ASP would make de-escalation interventions by contacting the primary team by pager, text, or telephone call. Although the BPA system, which allows for response to recommendation via the BPA navigator, is slightly less personal, this is outweighed by the benefits of increased efficiency, because the former methods were distracting to the flow of patient care rounds and surgical procedures. As programmed currently, when the ASP identifies an intervention (we are unable to reliably automate this process at this time) and activates the BPA tool, it creates a yellow box in the patient chart that may either be acted upon or ignored. The passive nature of the BPA tool reduces interruptions to consultants and nonprescribers and allows the targeted audience (primary prescribing team) to act on ASP recommendations as time allows. The 2-way communication option allows for the respondent to provide an explanation of why they are modifying or rejecting the recommendation. This feedback is useful because the ASP is rarely at the patient bedside. Providers who routinely rejected or ignored the BPA were personally contacted for mutual discussion and potentially direct education.

Alerts in the EMR commonly experience a diminishing return, a condition known as "alert fatigue." However, using our BPA tool, residents at our institution reported satisfaction with BPAs and the resulting recommendations and anticipated their placement in the medical progress notes. We believe that this is attributable to well-devised recommendations targeted at improving patient care and not simply at attaining fiscal goals. Linking the BPA with a specially designed ASP navigator also allowed the prescribers to have the information needed to answer the recommendation without jumping back and forth to a different section of the EMR and provided hyperlinks to evidence-based infectious disease medicine education. Our rate of acceptance was consistent across the

entire investigated time period. Because of the rapidly increasing adoption of EMR technology, the potential for the assimilation of ASP-associated CDS tools into the EMR appears to be unprecedented.

Theoretically, integrating CDS tools into the EMR is an important step toward improving the quality of care. However, a recent study of ambulatory care assessed the role of CDS and EMR and found no consistent association with improved quality.¹³ The Rand report predicted significant cost savings on the basis of EMR implementation,¹⁴ which has yet to come to fruition. However, a recent response to the Rand report still supports potential savings but notes that "providers must do their part by reengineering care processes to take full advantage of efficiencies offered by health [information technology]."^{15(p63)} We believe that creation of the BPA tool is a step in the right direction, toward redesigning our workflow and processes using EMR technology to improve the use of antibiotics. We are working with our EMR vendor to incorporate the tools of the ASP directly into future versions of the EMR.¹⁶

This report describes a CDS tool as a mechanism to effect ASP goals, specifically antimicrobial de-escalation. De-escalation is a high-priority target for ASPs, because the overuse of broad-spectrum antimicrobials drives resistance and is associated with adverse drug events or "collateral damage."¹⁷ We did not study these outcomes in association with our BPA tool. However, our results demonstrate decreased anti-MRSA and anti-pseudomonal agent use as well as a reduction in overall antibiotic consumption among patients with an ASP intervention using the BPA tool, which is a positive surrogate marker for the above goals.

We recognize the absence of a universally accepted definition of narrow and broad spectrum and believe that our definition is consistent with providing safe, effective, and fiscally responsible antibiotic therapy. We did not examine length of stay, mortality, or fiscal outcomes, although these outcomes would be of interest in future studies. Other out-

comes of interest include prescriber satisfaction and educational value. We did not query prescribers on their satisfaction with the BPA tool.

In summary, we created a minimally intrusive CDS tool using a BPA and EMR navigator to encourage and facilitate good antimicrobial stewardship. The BPA tool integrates an evidence-based recommendation and directs providers to a navigator where orders management, clinical information, bidirectional feedback mechanisms, and educational materials are available. This tool successfully reduced antibiotic exposure to patients, reduced prescribing of broad-spectrum antibiotics, and increased parenteral to enteral conversion. Prescriber satisfaction and associated clinical outcomes as well as a broad analysis of all BPA alerts remain to be investigated. After initial information technology investment time, the BPA tool is an effective mechanism for promoting sensible use of antimicrobials.

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Address correspondence to Lucas Schultz, PharmD, BCPS, Critical Care and Infectious Diseases Clinical Pharmacist, University of Wisconsin Hospital and Clinics, 600 Highland Avenue, F6/133–1530, Madison, WI 53792 (lschulz2@uwhealth.org).

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