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Transitions of care: An untapped opportunity for antimicrobial stewardship

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Abstract

Over half of antimicrobials ordered at hospital discharge are not optimized, many of which having longer than necessary durations or inappropriate for the indication. Unnecessary antimicrobial exposures increase the risks of adverse events, antibiotic resistance, and *Clostridioides difficile* infections. However, discharge prescribing often escapes the purview of inpatient antimicrobial stewardship programs and few interventions have been implemented to optimize antibiotic use during transitions of care (TOC). Herein, the aim was to highlight critical steps and challenges in the implementation of a TOC antimicrobial stewardship program designed to improve prescribing at hospital discharge. In a five-hospital health system, a pharmacist-led intervention was implemented during TOC, with the objective of improving oral antibiotic selection and duration. Among a multidisciplinary team of physicians, case managers, and nurses, the pharmacists engaged in three strategies: (a) early identification of patients to be discharged on oral antibiotics; (b) collaborative planning and communication regarding guideline-recommended antibiotic selection and duration; and (c) facilitation of discharge antibiotic prescription with appropriate stop date. Barriers to completing the intervention on each patient in this experience included: timely identification of eligible patients prior to discharge, stewardship periods of reduced staffing during evenings and weekends, and onboarding of new staff and trainees to the process. Other major challenges that stewardship and pharmacy departments will face include adoption of best-practice guidelines for discharge, obtaining support from local physician champions, extending the intervention to various service lines and departments with limited resources, and engaging stakeholders to support the program and intervention. This experience demonstrated that pharmacist-led antimicrobial stewardship at discharge can be successful in both academic and community settings.

KEYWORDS
antibiotics, antimicrobial stewardship, discharge, pharmacist, transitions of care

Nicholas J. Mercuro and Susan L. Davis are joint senior authors.

1 | BACKGROUND

Antibiotics offer tremendous benefit to patients with infectious diseases (IDs) and are among the most commonly prescribed medicines; however, up to 50% of prescriptions are classified as "inappropriate."[1,2] It is now a national priority to reduce unnecessary antibiotic exposure to reduce adverse events and antibiotic resistance.[1-5] The 2015 *National Action Plan for Combating Antibiotic-resistant Bacteria* was developed to address the urgent and serious drug-resistant threats with implementation of healthcare policies and collaborative antibiotic stewardship programs (ASP).[2] A major goal of *the National Action Plan* was to reduce inappropriate antibiotic use by 50% and 20% in outpatient and inpatient settings, respectively, by 2020; this had since been updated with a goal to lower overall outpatient antimicrobial dispensing with a focus on identifying prescribing patterns and unnecessary antibiotics.[6] While hospital-based ASP interventions successfully improve inpatient prescribing practices, these actions may not translate into a reduction of inappropriate prescribing at discharge, highlighting the need to target transitions of care (TOC).[7]

Antimicrobials prescribed at discharge typically feature excessive treatment durations and unneeded broad spectrum of activity.[8-11] Almost half of hospitalized patients discharged with a diagnosis of urinary tract infection (UTI) or pneumonia are subject to antibiotic overuse.[11] Each additional antimicrobial day increases the risk of medication-related harms such as *Clostridioides difficile* infection (CDI) and drug resistance, thus orders during TOC should be evaluated and entered judiciously.[12-14] Prolonged drug exposures can be mitigated through application of evidence that shorter durations of therapy are safer and effective for various common infections. TOC represents an opportune moment to reconcile antimicrobial selection, dosage, and duration prior to discharge.[15] As an adjunct to standard of care, pharmacist-driven interventions at TOC have reduced hospital readmissions.[16] Pharmacists and antimicrobial stewards are well-positioned stakeholders in ASP to facilitate optimized antimicrobial therapy delivery and improve quality of prescribing at discharge.[5,17]

Current experiences in the application of ASP at TOC for oral antimicrobials are limited. Significant attention and expertise are directed toward outpatient parenteral antimicrobial therapy with consult teams due to severity of infection and potential complications. However, far more patients are discharged with oral antimicrobials, many of which belonging to antimicrobial classes associated with severe adverse events and subsequent emergency department visits. In recognition of the urgent need to improve antibiotic use across all healthcare settings, the Centers for Disease Control and Prevention recommends implementation of ASP in acute, postacute, and ambulatory settings.[4,18] This study describes the basis of ASP during TOC and the implementation of a multidisciplinary ASP intervention, and opportunity for pharmacist-involvement, for patients discharged from general medical units on oral antimicrobials for common infections.

2 | ANTIBIOTIC PRESCRIBING AT DISCHARGE: SETTING AND POPULATIONS

The culmination of data reporting antibiotic prescribing during TOC are largely in the hospital or emergency department settings.[19,20] Post-discharge antibiotic therapy is often discordant with recommendations for national and/or institutional guidelines and several authors have highlighted opportunities to optimize therapy in these settings.[8,9,11] Using the Veterans Affairs database, Feller et al[21] reported that 20% of patients discharged are prescribed an oral antimicrobial, and 40% of the therapy is administered in the postacute setting. Chavada et al found that inappropriate prescribing was driven by excess durations of therapy with 71% of patients receiving an antibiotic course in excess of guideline-recommended length of treatment at discharge; however those who had active ASP interventions were more likely to receive an appropriate course.[17] In a multicenter cohort study, Vaughn et al[11] identified dramatic variability between hospitals and appropriateness of antibiotic prescribing for pneumonia and UTI. Respectively, 57% and 39% of patients with pneumonia or UTI-experienced antibiotic overuse. Subjects who did not experience antibiotic use were more likely to be in an academic center and in hospitals with higher bed capacity.[11] In more resource-limited settings, piloting a targeted disease states or population (eg, high risk for readmissions, mortality, or adverse events) could increase the likelihood of success in an intervention (Table 1).[22] Examples of case-based interventions for optimization of antibiotics during TOC and potential barriers are highlighted in Tables 2 and 3.

Antibiotic consumption metrics used for reporting with hospitalized patients in the United States do not include the discharge prescription. While capturing this "total course" metric would be complex and difficult to standardize, the discharge prescription/duration alone represents about half (or more) of the total antibiotic duration/therapy.[8,23] In 2020, antimicrobial stewardship in the ambulatory setting was mandated by the Joint Commission on Accreditation of Healthcare Organizations. The timeframe of prescribing antibiotics at discharge can address stewardship in the hospital, postacute care, and ambulatory practice. To gain momentum and support in stewarding this period (TOC) of antibiotic prescribing, demonstrating feasible and beneficial ASP interventions is crucial.[23]

2.1 | Health system experience

The ASP TOC intervention was implemented across a five-hospital health system, to target adults admitted to general and specialty medical wards who will be discharged on oral antimicrobial therapy.[24] One hospital was an academic center with a fully decentralized clinical pharmacy practice model, two IDs pharmacy residents and one pharmacy fellow. The pharmacy trainees operated under supervision of an IDs preceptor. The four community hospitals had mixed models of decentralized and centralized pharmacy staffing (Table S1). Each hospital had dedicated ASP full-time equivalents for pharmacists and/or physicians. The established multidisciplinary ASP in the health system used formulary preauthorization, prospective audit, and feedback methods for stewardship activities. Before the intervention, decisions for antibiotic

TABLE 1 Common questions surrounding a transitions of care intervention

FAQ	
Where should I start?	An institution or health system wide rollout for all patients discharged on antimicrobials would be a large undertaking and significant investment of resources. Consider first assessing where the highest-yield interventions and populations are in the institution to have a targeted and informed approach. The CDC refers to resources such as a Gap Analysis Tool (https://www.henryford.com/-/media/files/henry-ford/hcp/antimicrobial-stewardship-transitions-of-care/amstoc-gapanalysis.pdf?la=en&hash=16E8888D0FB17BFBE9E70A0B0C1485FF) and education for healthcare professionals related to antimicrobials at discharge.[22] Discussing and reviewing these checklists with colleagues and collaborators will ensure preparation for an ASP TOC intervention.
What are some populations of interest to start the intervention on a smaller scale?	Piloting an intervention with supportive providers and/or on wards with reliable communication and patient identification strategies will increase the likelihood of success of the intervention. Some initial approaches could include limited populations: • Disease state based with clear evidence for short-course durations (eg, CAP, UTI) • High-risk readmission and polypharmacy (geriatric, high comorbidity scores) • High risk for antibiotic mismatch (eg, pending microbiologic data, multidrug resistance) • Antibiotics with higher toxicity risks (eg, fluoroquinolones, sulfonamides)
What are common antibiotic prescribing errors at discharge?	One of the most common oversights is lack of consideration of the inpatient duration into the total antibiotic duration for the discharge prescription. This, in addition to other "counting errors" such as copying/pasting antibiotic day number, can lead to excessive durations. Other opportunities also include continued prescribing for noninfectious indications (such as ASB), incorrect dosages, and inappropriate drug (eg, fluoroquinolone for uncomplicated cystitis without allergies).
What types of pharmacists were engaged in this intervention on a day-to-day basis?	• Decentralized unit-based pharmacists involved in the routine care and order verification are in a prime position to intervene during TOC. • Outpatient and central pharmacists can improve patient identification and medication access. • Pharmacist extenders, including pharmacy residents, students, and other trainees. • Infectious diseases and antimicrobial stewardship pharmacists. • TOC pharmacists managing chronic disease states and medication reconciliation.
How can I convince administration and C-suite to leverage resources to take on discharge prescribing?	Investment in new resources and/or expansion of existing resources is a difficult decision which requires extensive consideration of financial impact, clinical impact, return on investment, possible loss of services from other areas. However, ASP TOC interventions have shown to significantly improve patient safety by reducing antibiotic durations, excessively broad selection of therapy, and serious adverse effects. The ASP TOC process can also facilitate conversations about oral therapies and accurate documentation, which can impact length of stay if the intervention occurs early in care. Other authors have also identified signals in reduction of readmissions, which could be leveraged particularly in high-risk populations.
Are there automated/EHR interventions that can improve prescribing patterns at discharge?	• Removal of automated durations. • References to guidelines or nudging in the order-entry process. • Review of order sets for inappropriate antibiotics and/or durations. • Streamlining of reports for anticipated discharge to facilitate patient identification.

Abbreviations: ASB, asymptomatic bacteriuria; ASP TOC, antimicrobial stewardship transitions of care program; CAP, community-acquired pneumonia; CDC, Centers for Disease Control and Prevention; EHR, electronic health record; FAQ, frequently asked questions; TOC, transitions of care; UTI, urinary tract infection.

selection and duration at discharge were limited to passive interventions with guidelines and education. Diagnoses of interest targeted common infections with supporting evidence for criteria-dependent short durations of therapy, in alignment with health system guidelines (Table S2): UTI, pneumonia, upper respiratory tract infections, acute exacerbations of chronic obstructive pulmonary disease, skin/skin structure infections, and infection of intra-abdominal sites after adequate source control.[25] Those with solid organ or hematopoietic stem cell transplants, and complicated infections (eg, prostatitis, empyema, osteomyelitis), were excluded from receiving the intervention given limited application of evidence-based short-course therapies in these populations.

3 | INTERVENTIONS AND PHARMACIST ROLE IN STEWARDSHIP AT TOC

Pharmacists practicing in antimicrobial stewardship, emergency department, general medicine, and outpatient settings have played

TABLE 2 Vignettes for transitions of care cases

Case	Description of case	Action	Result
UTI in an 81-year-old-female	An 81-year-old-female with history of dementia and CKD presented with altered mental status, dysuria, and was started on ceftriaxone. On hospital day 2 during rounds, the medical resident is discussing the case and plan for discharge given her clinical improvement. Based on pyuria and urine culture results ciprofloxacin 500 mg PO twice daily for 5 days was discussed.	Given this patient's diagnosis (cystitis), age, and comorbid conditions, a fluoroquinolone is not an ideal choice. Based on guidelines and institutional recommendations, the pharmacist recommends one more of cefpodoxime a total duration of 3 days. She improved with ceftriaxone, which reaches high and sustained urinary concentrations. The team and staff physician agree, and the inpatient order is placed with a stop date and the plan is documented in the progress note. The pharmacist places the antibiotic discharge order with dose and duration for cosign and leaves documentation in the EHR with the correlating regimen.	After rounds, the medical resident places all other discharge orders. They cosign the antibiotic order that was already placed by the pharmacist. The patient is discharged with one more day of renally adjusted cefpodoxime 200 mg PO BID. Early conversations about discharge antibiotics were able to help avoid a fluoroquinolone for an elderly patient with an uncomplicated infection. On a large scale, such interventions can prevent rare, but serious adverse events.
Nonpurulent skin/soft tissue infection in a 63-year-old male	A 63-year-old male with history of CKD and CHF was admitted with heart failure exacerbation and erythema of right lower limb. The decentralized pharmacist sees that the patient is now stable and on day 3 of vancomycin; a planned discharge date for today is marked in the EHR monitoring column. They review discharge information and find a pending order for SMT 2 DS BID for 7 days.	The decentralized pharmacist calls the team and discusses the choice of SMT with the medical resident, given the patient's CKD and concomitant lisinopril and spironolactone. The cellulitis has improved and the suspected pathogens are streptococci; he has not failed prior therapies nor has antibiotic allergies. The team agrees to a total 5-day course with an oral beta-lactam. The pharmacist updates the discharge regimen. They place a note in the EHR with the agreed upon regimen and end date. The plan in the discharge summary is appropriately updated.	The provider signs the discharge order, and the patient is discharged with cephalexin 500 mg PO TID for two more days to complete 5 days of therapy for nonpurulent SSTI. A longer duration of 2 DS BID SMT in this specific case may have resulted in serious renal injury or electrolyte disturbances.
CAP in a 57-year-old female	A 57-year-old female with history of type 2 diabetes and hypertension is admitted with fevers, cough, shortness of breath, diagnosed with CAP. Ceftriaxone and doxycycline were started. On day 2 of hospitalization, she is afebrile, off supplemental oxygen, and cultures remain negative. In discussions at collaborative rounds, the resident plans to complete the course with cefuroxime and doxycycline. The correct antibiotics are ordered, but for another 5 days.	The pharmacist brings up the order that was placed for discharge—there was miscommunication between the overnight resident placing the discharge orders, and the intention was to account for the inpatient days as well, for a total of 5 days. The pharmacist updates the discharge order and includes an additional comment to discharge pharmacy with the correct antibiotic end date-making sure to include a single evening dose of doxycycline before starting the cefuroxime the next day (ceftriaxone had already been administered in the morning).	The provider signs the order, and patient is discharged and educated on taking cefuroxime 500 mg PO BID and doxycycline 100 mg PO BID for a total of 3 days after discharge. Lack of accounting for inpatient antibiotic duration is a common error in discharge prescribing. Careful review and clear instructions for stop dates and progress notes can help mitigate the additional risks that each additional antibiotic day may carry.

Abbreviations: CAP, community-acquired pneumonia; CHF, congestive heart failure; CKD, chronic kidney disease; EHR, electronic health record; SMT, sulfamethoxazole-trimethoprim; SSTI, skin/soft tissue infection; UTI, urinary tract infection.

TABLE 3 Examples of barriers to ASP during TOC in hospital pharmacy models

Barriers to TOC	Description	Examples of approaches to barriers
Staffing—Extra time and resources are needed to quickly and accurately identify patients approaching discharge, assess the clinical case, contact/communicate with the prescriber/prescribing team, enter or change order, and document the plan	• Competing needs such as: order verification, patient education, dispensing, management of public health/outbreak-related responsibilities • Certain pharmacy practice models, areas of practice, or units include a higher patient to pharmacist ratio and/or higher acuity of patients • Staff shortages, call-ins or staffing shortages, redistribution of patient/unit responsibilities	• Departmental buy-in to have allotted resources for TOC in clinical pharmacy services. If possible collect preliminary data at the site to show the need for improvements in safety and medication errors • Gain advocacy from prescriber groups with proposal of additional benefits to improve quality of care during TOC • Start in a focused/smaller population with high likelihood of benefit and success • Collaboration with informative technology services can help triage and identify patients approaching discharge, optimize order sets, and remove any inappropriate automated durations • Partner with the outpatient pharmacies, if on site, to increase bandwidth in identification of patients • Implement guidelines with objective criteria for therapies to streamline evidence-based information for discharge prescribing
Weekends and "off-hours"—Monitoring prescribing in periods of unavailability (evening discharges, discharges during limited staffing periods)	• Limited clinical pharmacy services are available on the weekends and off-hours (eg, outside of 0700-1600), which can contribute to missed opportunities in optimizing antibiotics during TOC • ASP workflows may not extend beyond weekday shifts or include TOC interventions	• Initiate interventions and communications prior to discharge dates • Ensure that documentation from the primary team and pharmacist related to antibiotic discharge plan are documented ahead of time, if discharge over weekend or evening is anticipated • Use protocolized interpharmacy handoff mechanisms (eg, i-Vents in Epic hospitals) to communicate future plans • Delegate TOC responsibilities for oral antibiotics to the covering PharmD/physician if there are mechanisms in place to support ASP on weekends
Communication—Reduced information sharing, difficult to reach prescribers	• Communication between pharmacist and prescriber can vary based on the practice model, resources, and hospital type • The time of day and/or service (eg, admitting residents or surgical teams in the operating rooms) • Paging systems that rely on-call back may delay communications regarding antibiotic discharge plans	• Participate in TOC activities during collaborative rounding periods to involve all parties (nursing, case management, physicians, nurse practitioners, physician assistants, etc.), if possible • Have a protocol in place for designated contacts for each patient assignment in the prescribing and discharge process • Promote early implementation and documentation of discharge plans and orders • Use secure messaging platforms to confirm antibiotic plans when paging, rounding, or phone is not possible • Develop institutional policies and collaborative practice where discharge orders can be entered (or modified) per protocol for future cosign for patients who meet strict criteria
Acceptance and participation—Obtaining and sustaining buy-in and support from individuals and the health system	• Prescribing inertia may occur, especially after antibiotic plans and orders have already been discussed and entered • Burnout and competing priorities can limit the sustainability of an intervention	• Allow perprotocol modification/entry of discharge antibiotic by pharmacist, for future cosign • Promote multidisciplinary guidelines throughout institution to increase comfort of participating in TOC interventions for all clinicians • Delegate team or unit-based physician champions; consider obtaining signed letters of support and routine collaborative meetings related to guidelines, workflows, and challenges • Communicate that lack of ability to intervene should not delay discharge; if it better suits the institution, the additional support from pharmacy should be ancillary rather than required • Require training programs specific to the institution for participating pharmacists • Allow mechanisms for ASP/ID/Medicine leadership involvement in controversial or difficult cases • Share positive feedback and success stories with all healthcare teams

Abbreviations: ASP, antimicrobial stewardship program; ID, infectious diseases; TOC, transitions of care.

TABLE 4 Examples of antimicrobial stewardship TOC interventions

	Population	Stakeholders	Patient identification	Discharge assessment and communication	Action and/or Documentation
Yogo et al[26]	• Academic center, adults on general medicine/surgical wards with CAP, UTI, or skin/soft tissue infection	• Stewardship Program • Pharmacy • P&T Committee • Clinical guidelines committee • Hospital Chief Clinical Officer	• Manual chart review at time of discharge antibiotic entry by both staff and ASP pharmacist	• Hospital guidelines and pocket cards for discharge therapies adopted and reviewed by pharmacist	• Direct feedback to primary team at time of discharge antimicrobial, when needed • Recommendation acceptance documented in standard reporting form
Su et al[27]	• Community teaching center, adults discharged on oral or intravenous anti-infectives from family medicine service	• Stewardship Program • Pharmacy • Infectious Diseases • Family Medicine	• -ASP pharmacist contacts primary team for list of patients with an anticipated discharge	• ASP pharmacist performed interventions related to safety, efficacy, or simplification in accordance with institutional guidelines • Verbal communications	• Direct feedback provided to primary team prior to discharge
Zampino et al[28]	• Academic center, adults on general medicine/surgical wards	• Stewardship Program • Pharmacy	• Manual chart review by one ASP pharmacist, triggered by entry of discharge antibiotic	• ASP worksheet including recommendations and appropriateness of discharge antimicrobial	• Direct feedback provided to primary team
Leja et al[20]	• Academic center, adults at high risk for mortality	• Pharmacy • Stewardship Program	• TOC pharmacists used electronic scoring tool to find those at high risk for mortality	• ASP guidelines used for preferred antibiotic choices, doses, durations	• Direct feedback provided to primary team, if needed • Discussion with patient for medication education prior to discharge when able • Recommendations documented in internal database for quality improvement
Giesler et al[29]	• Academic medical center, adults on hospitalist service	• Stewardship Program • Pharmacy • Internal Medicine • Hospitalists	• Collaborative pharmacy rounds with "time-out" prior to discharge • Automated page to covering pharmacist when a discharge antibiotic order was signed	• Institutional guidelines and pocket cards for discharge therapies adopted and reviewed by pharmacists • Antibiotic timeout checklist which included: assessment of infection, opportunity for oral therapy, and documentation plan • In-person or phone communications	• Direct feedback provided to primary team prior to, or at discharge • Checklist review for documentation of dose, indication, and total planned duration in discharge summary

(Continues)

TABLE 4 (Continued)

	Population	Stakeholders	Patient identification	Discharge assessment and communication	Action and/or Documentation
Parsels et al[30]	• Academic medical center, patients with any oral antimicrobial prescriptions sent to the hospital outpatient pharmacy	• Stewardship Program • Pharmacy	• Manual chart review by one adult and one pediatric ASP pharmacist, triggered by entry of discharge antibiotic	• Discharge prescriptions reviewed for drug-related problems (dose, duration, interactions) • Prescribers contacted via HIPAA compliant EHR messaging	• Direct feedback provided to primary team • Standardized templates used to log interventions and drug-related problems for quality improvement purposes
Jones et al[19]	• Academic medical center, adults discharged on an oral antimicrobial with unresulted culture data	• Stewardship Program • Infectious Diseases • Microbiology • Pharmacy	• Electronic reporting tool for patients on antimicrobials in EHR • Electronic reporting tool for patients discharged with unresulted culture data reviewed by ASP pharmacist	• Criteria for inappropriate therapy based on final microbiologic result • Prescribers contacted by page and/or phone	• ASP pharmacist discussed recommendations with on-call ID physician • If deemed necessary, prescriber contacted by ASP/ID to make change in care
Henry Ford Health System Experience[24,31]	• One academic and four community centers, adults prescribed oral antibiotics for respiratory, urinary, intra-abdominal, and skin-soft tissue infections	• Stewardship Program • Pharmacy • Internal Medicine • Infectious Diseases • Family Medicine • Hospitalist • Nephrology • Cardiology • Pulmonology • Nursing • Case management	• Anticipated discharges discussed at collaborative • EHR column flag and progress note review for anticipated discharge • Communication from case management reports for anticipated discharge • Communication from the outpatient pharmacy at time of discharge order	• Institutional guidelines reviewed by pharmacists and primary team • In-person, verbal, or remote/ paging communication depending on hospital model and staffing	• Direct feedback provided to primary team • Discharge order entered for cosign if none present • Discharge order edited as needed if already entered • Discharge antibiotic plan documented in medical chart note

Abbreviations: ASP, antimicrobial stewardship program; CAP, community-acquired pneumonia; EHR, electronic health record; HIPPA, The Health Insurance Portability and Accountability Act; ID, infectious disease; P&T, pharmacy and therapeutics; TOC, transitions of care.

essential roles in ASP during TOC (Table 4).[19,20,24,26-31] Workflows and checklists for pharmacists were integrated into multiple ASP TOC care models. A common approach for antimicrobial review is providing audit and feedback in real-time once a prescription has been entered or signed. A limitation of this strategy is that a prescriber may be less likely to adjust or modify an order that has already been processed or filled. Working closely with the outpatient pharmacy, case management, and the primary team will also improve the accuracy of an anticipated discharge. Discussed in greater detail below, pharmacists can be involved with early patient identification—this approach is more resource intensive but may capture more patients. Often, the intervention type and acceptance rate are documented by the pharmacist as a quality improvement metric. Development of local guidelines along careful oversight of order sets can promote best practices in discharge antimicrobials—particularly, in disease states with an evidence base for short-course therapy.[26] Communicating recommendations to the prescriber, when needed, facilitates optimal antimicrobial courses.[30] Direct entry of prescription by pharmacist into electronic discharge medication queues for cosign is another strategy which takes on more active role, and also offsets workload from primary teams.[24] Some hospitals with existing structures for TOC pharmacists were able to provide additional patient education about their antibiotic course and administration instructions.[20]

3.1 | Health system experience: Patient identification and pharmacist role

Pharmacists across the health system were responsible for identifying patients with active antimicrobial therapy for infections that may be eligible for oral therapy for discharge. Using Epic as the electronic health record (EHR), pharmacists assessed patients' clinical stability,

infection type, and potential discharge barriers (Figure S1). The pharmacist communicated with the provider via phone, page, or in-person depending on the pharmacy practice model and unit at the respective hospital. Once the discharge antibiotic selection, dose, and duration were agreed upon, the pharmacist entered the discharge order in the EHR per protocol, with an additional note on the appropriate end date, to be signed by the provider. The pharmacist could also send an electronic discharge medication cost inquiry to the discharge pharmacy queue to review medication coverage and copayments prior to placing the discharge order.[32] A note was then placed in the EHR by the pharmacist as a plan of care document, describing the discharge antimicrobial regimen and end date.

3.1.1 | Academic medical center experience

In the academic hospital, decentralized pharmacists practicing on the general medical units participated in daily collaborative rounds where readiness for discharge and potential discharge barriers were discussed with physicians, nurses, case managers, and other healthcare providers at the front line of patient care. Each pharmacist typically cared for an estimated 40 patients. The academic units comprised the initial intervention rollout (Phase 1) and half of second rollout (Phase 2) (Figure S2). Hospital team structures and responsibilities to patients were location-based, in alignment with the service. Pharmacy responsibilities included a focus on TOC, specifically on optimizing medication management and patient education at discharge. Collaborative rounds created opportunities for early patient identification for discharge, interventions with the team, discussion of TOC, and confirmation of medication access. Education for rotating residents and students was routine on internal medicine wards. Certain floors had pharmacy residents and students who would participate on teaching rounds and in discussions on antimicrobial discharge regimens. As pharmacy extenders, they assisted the team and unit-based pharmacists with discharge planning and the ASP TOC intervention. In addition, antimicrobial stewardship staffing occurred between 8 AM and 5 PM during the week. Weekend coverage for stewardship was staffed by trainees in IDs pharmacotherapy, one fellow and two residents. They managed the ASP TOC interventions on the weekends due to reduced clinical pharmacy services by the unit-based pharmacists.

Electronic patient reports containing columns with antimicrobial information and anticipated discharge dates were also added to patient care lists in the EHR in the attempt to identify candidates early in the admission. Pharmacists opened an electronic handoff communication (i-vent) in the EHR as a handoff mechanism for flagging TOC opportunities for patients that may be soon discharged. Once patients were identified as "possible discharge," antibiotic therapy and duration was discussed during collaborative rounds. End dates were encouraged to be added to the inpatient antibiotic orders and an electronic tool in the EHR was used to communicate discharge medication cost and accessibility. The antimicrobial orders for discharge were placed in the EHR with appropriate selection, dose, and end dates concordant with institutional practice guidelines, and then signed by a licensed prescriber. The final antimicrobial regimen was documented in a short note in the EHR by the pharmacist, and patients were educated on antimicrobial safety and administration by a licensed nurse or pharmacist prior to discharge.

3.1.2 | Community hospital experience

TOC interventions for oral antimicrobials at discharge in the community hospitals were completed by an ASP pharmacist or delegated general medicine pharmacists who underwent appropriate training. Each general medicine pharmacists at the community hospitals typically cover 50 to 60 patients. The target population of patients resided in both location-based prescriber models (ie, prescribers practicing on a single floor/unit) (two hospitals) and team-based models (prescribing teams managing hospitalized patients regardless of unit/floor location). In the location-based models, areas of high-volume discharge antimicrobials were targeted, such as general and surgical medical units. For team-based models (nonlocation-based), hospitalist and academic teams were selected, and identified in ASP workflow through an electronic report/column in the EHR. In community hospitals that did not have a consistent model for pharmacist rounding, other mechanisms such as notification from case management or the outpatient pharmacy were used to assist in patient identification. The IDs physician played a crucial role, as many patients meeting criteria for the TOC intervention in community hospitals also had active ID consults.

Interprofessional communication was primarily pager-based. After discussion with the provider and finalization of the antibiotic plan, an optimized order was placed in the discharge queue to be signed by a licensed prescriber. Like the academic model, in cases where the discharge prescription had already been ordered, the ASP pharmacist communicates with the outpatient pharmacy to adjust the order, if appropriate, after confirming with the provider. The final antibiotic therapy, indication, dose, and duration were documented in a short note in the EHR by the pharmacist.

4 | IMPLEMENTATION AND LEADERSHIP IN A TOC MODEL

The case for improving patient safety with interventions at TOC continues to grow. Impactful interventions that are feasible, practical, and nonresource intensive are of highest value to both ASPs and health system administrators. Antimicrobial stewardship interventions during TOC are associated with reduced antibiotic-related adverse effects and readmissions; however, treatment-related effects on such outcomes are generally multifactorial and confounded, and these results have only been demonstrated in nonrandomized study settings to date.[20,31] Conducting medication-use evaluations to identify opportunities specific to the health system can increase the likelihood of success and uptake of a pilot study/intervention. Process endpoints such as duration of therapy and antimicrobial selection continue to serve as

quality improvement metrics in ASP and surrogates for safety measures.

Broad engagement with all stakeholders is crucial for the success of any intervention that can impact thousands of patients annually. Peer comparison and letters of commitment are behavioral intervention strategies that have improved antimicrobial prescribing in clinics.[33,34] Historically, key collaborators in ASP TOC interventions include, but are not limited to: pharmacists, Pharmacy and Therapeutics (P&T) Committees, IDs, internal medicine, hospitalist groups, family medicine, nursing, case management, and so forth (Table 4).

4.1 | Health system experience

Metrics on health system antibiotic discharge prescribing were presented to the system ASP, which prompted the need for review of antibiotics prescribed during TOC. Specifically, the frequency of incorrect prescribing of fluoroquinolones and local trends in antibiotic-related adverse events were highlighted as opportunities for quality improvement.[35] The TOC protocol was approved and rolled-out sequentially in academic and community hospitals every 3 months following extensive training of all healthcare providers involved. The selection and order of intervention implementation for each hospital and unit was generally based on "readiness," which required available resources, education, broadcasting, and staffing. Educational materials and workflow guidance were available electronically and on pocket cards for pharmacists (Figure S1) as well. Pharmacists were required to attend an ASP TOC training seminar to exercise the protocol in the health system. Nursing units, resident conferences, and specialty groups were introduced to the protocol and lead physicians were appointed on different wards. Letters of support were drafted and signed by stakeholders in the Departments of Pharmacy, Internal Medicine, Antimicrobial Stewardship, Infectious Diseases, Pulmonology, Nephrology, Cardiology, Hospitalist, and Family Medicine.

5 | MEASURING SUCCESSES AND CHALLENGES IN A TOC MODEL

Monitoring the successes and challenges following implementation provides transparency related to the quality, sustainability, and barriers to the progress of the intervention. Both clinical and quality metrics are important to collect and disseminate among stakeholders. Su et al[27] and colleagues implemented a pharmacist review of antimicrobials at TOC from a family medicine service and identified a prevalence of 42% in medication errors among 45 discharged patients, in which 13 errors were avoided. The study was noncomparative and was unable to evaluate impact on clinical outcomes, and the investigators described the intervention as difficult to sustain and resource intensive. Yogo et al[26] used institutional guidelines, tools, and intervention to improve quality of prescribing at TOC for patients receiving oral antibiotics for respiratory, skin, and UTIs. Pharmacists reviewed 39.5% of eligible patients with antimicrobials sent to the outpatient discharge pharmacy and notified providers in 10.8% of cases for guideline-discordant regimens. While the total number of fluoroquinolone prescriptions and duration of discharge prescription was reduced, there was no significant difference in inappropriate prescribing, total duration of therapy, or adverse drug events; however only 7.2% of antibiotics prescribed at discharged had dose, selection, or duration optimized from the intervention.[26] Zampino et al expanded ASP services for discharge antibiotic from medical/surgical wards by having an ASP pharmacist provide audit and feedback at the time of discharge. Even when the discharge prescriptions have already been entered and ordered, this program was able to improve appropriateness of therapy from 47.5% to 85.2%.[28] On a statewide scale, Vaughn et al directed 41 centers in Michigan in an intervention for reporting and benchmarking antibiotic prescribing for community-acquired pneumonia. Over the study period, duration of antibiotic and frequency of adverse events decreased.[36] The clinical impact on safety and patient-centered outcomes will prove to be critical in future efforts in advocacy for ASP TOC support, with authors reporting improvements in quality or prescribing, adverse events, and even possibly readmissions.[28,31,36]

In a mixed-method approach, Giesler et al reviewed process outcomes to describe impact of a pilot TOC intervention on antimicrobial use at discharge following "timeouts" on a hospitalist floor. The authors also assessed the feasibility, acceptability, adherence, and awareness surrounding the intervention. Most pharmacists and hospitalists described the intervention feasible and helpful, and found that it improved patient care (79%).[29] Each patient intervention was an additional 5 min to the pharmacists' workflow, however, could be up to 20 min if the discharge prescription had already been signed and sent to the pharmacy prior to communication with a team.[29] Parsels et al also found a high frequency of intervention acceptance (76%) using a model involving patient identification from the hospital outpatient pharmacy, to the ASP pharmacist, who made further recommendations to the primary team when needed. When the interventions were accepted, the antibiotic duration decreased by 4 days on average; interventions generally required less than 15 min.[30] These are key datapoints in implementation science to quantify intervention uptake, sustainability, and monitoring of intervention success.

5.1 | Health system experience

Multiple mechanisms of monitoring were in place to sustain quality improvement of the intervention and provide continued feedback to end-users. A poster was displayed in the hospital pharmacy to report the number of patients impacted by the intervention, the percentage of interventions completed on eligible patients (protocol adherence) and photographs of key stakeholders. The poster was updated each month and information was disseminated to the pharmacists. To monitor the quality of intervention uptake and protocol adherence, 25 eligible patients were randomly screened each month when the intervention was in place. Adherence to protocol

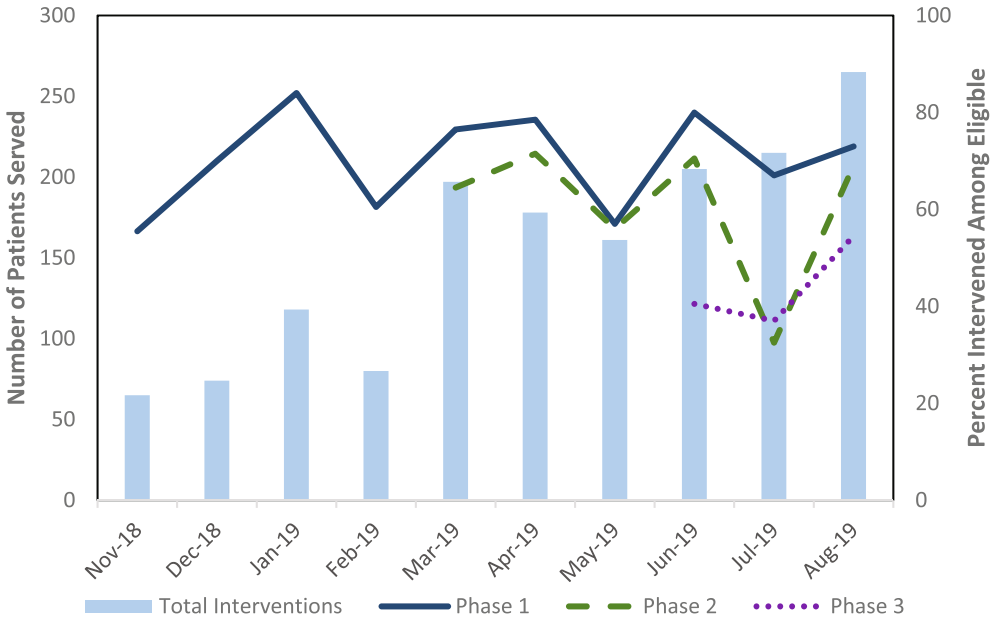

FIGURE 1 Interventions completed and percent of interventions completed on eligible subjects by month and study period

was defined as documentation in the EHR by pharmacist of an oral antimicrobial discharge plan (antimicrobial dose, duration, and selection based on institutional guidelines with authorizing prescriber). Root-cause analyses of nonadherent and nonguideline concordant cases were also intermittently reviewed to target areas or groups in need for quality improvement. Challenges and guideline-discordant cases were encouraged to be shared with the physician and pharmacist principal investigators to undergo peer review. Every quarter, an "open-house" was held where stakeholders were invited to attend a presentation on TOC intervention progress with lunch and questions.

The ASP TOC intervention was implemented across five hospitals on 18 distinct units and provider teams (Figure S2). Over this period, we were able to optimize the discharge antibiotics of over 1500 patients (Figure 1). The overall protocol adherence during this time was 63%, sustained over a 9-month period.[31] Adherence in the first phase (academic center) was 70%, 61% in the second (academic and community centers), and 44% in the third (community centers) (Figure 1). All cases were reviewed for possible qualities associated with nonadherence including: discharges on weekends (18%), postcall (after 5 PM) prescribing (17%), and admissions <24 h (8%). Despite this, the intervention was completed in 70% and 46% of subjects among eligible in the academic and community hospital models, respectively. By service line, protocol adherence was as follows: Family Medicine, 71%; Internal Medicine, 64%; Pulmonology, 76%; Hospitalist, 73%; Infectious Diseases, 79%; Cardiology, 59%; Nephrology, 68%. Following the implementation of the intervention, the frequency of optimal antibiotic course received at discharge increased from 36% to 81.5%; the discharge antibiotic duration was reduced from 4 (interquartile range [IQR], 3-5) days to 3 (IQR, 2-4) days.[31] There was no difference in clinical success, hospital readmissions, or mortality, however, incidence of serious antibiotic-related adverse events was reduced.[31]

6 | DISCUSSION

This intervention describes a pharmacy practice model shift focused on antimicrobial selection and duration at transition of care that can serve thousands of patients annually across a health system. Implementation science was applied to support optimal uptake of the intervention at TOC. First, prescribing of broad-spectrum antimicrobials at discharge in the health system was examined. Fluoroquinolone indications and durations were often not concordant with recommended practice guidelines.[9] Target units for implementation with high volumes of antimicrobial prescriptions at discharge were identified, at which point physician and pharmacist champions were assigned to be responsible for communications and training. Similar methods were used intermittently throughout the study implementation to disseminate protocol adherence including: notifications from study investigators, commitment letters, and posters that tracked total number of interventions and protocol adherence every month for each study phase. Pharmacists and providers were not individually notified but addressed as teams for each service line.

The most successful models, by protocol adherence, implemented the ASP TOC service in adjunct with collaborative rounds, clinical rounds, and face-to-face communications. Each point of contact offered opportunities to intervene at TOC. It was advantageous to have multiple disciplines involved in the intervention at time of discharge planning to coordinate care; this allowed pharmacists to easily "queue-up" an electronic discharge order for a prescriber to review and cosign. Orders that were already entered could be edited if it were determined that an adjustment would not lead to delays in patient discharge. Collaboration with the institutions' outpatient pharmacy facilitated communication and medication access between the inpatient team. These models were also able to incorporate learners such as residents, fellows, and students to conduct interventions under the supervision and license of another healthcare professional.

One of the major challenges for the TOC models that did not rely on a rounding clinical pharmacist or collaborative rounds was the difficulty in the identification of patients approaching their discharge date. Multiple strategies attempted to remotely identify patients approaching discharge including collaboration with case management to send discharge reports to pharmacists and developing a tool for provider-initiated reporting of anticipated discharge dates into *Epic* columns. However, the columns were frequently invalid and patients identified by case managers with orders for discharge often already had antimicrobial discharge orders prescribed. Thus, additional steps were taken to optimize the outpatient prescription when deemed necessary to change. In resource-limited settings there may be other interventions with possible "low effort/high impact," depending on clinical workflow for entry of discharge prescriptions. Automatic generation of a fixed duration (eg, levofloxacin for 5 days) will likely result in an excessive course, given these electronic orders usually cannot account for the therapy duration received in the hospital. Careful review of all order sets, methods, and practices associated with entry of discharge prescriptions can identify opportunity for intervention from EHR/information technology support.[23] Adaptation of hospital guidelines for antimicrobial selection, dosage, and duration for incorporation into discharge workflows is also a key component in many interventions, as a supplement to audit and feedback.[29,31]

This health system intervention has limitations. Over a third of patients eligible for the intervention did not receive it. However, root-cause analyses was conducted to determine intervention sustainability over 10 months. Multiple factors such as weekend discharges, short lengths of stay (<24 h), and off-shift prescribing contributed to most of the missed opportunities. It was important to not delay discharge, thus increasing workload during these more difficult periods was fit accordingly with available resources. While weekend services were feasible in a limited clinical staffing model at the two hospitals, it was not possible in three community hospitals in phase 3 this likely represents many inpatient clinical pharmacy staffing models with limited resources, and a possible reason for lower protocol adherence in this study phase.

There were valuable lessons learned throughout the implementation of this TOC model and ways to continue to move toward best practice to facilitate antimicrobial stewardship during TOC:

- Evaluate trends in prescribing practices to pave the way for targeted interventions that may be related to a specific antimicrobial, service line, or disease state.
- Collaborate with all healthcare professionals engaged in TOC to expand intervention uptake, responsibility, and dissemination. The TOC team ideally consists of prescribers, case management, information technology, nursing, and clinical pharmacists working in both hospital and ambulatory settings.
- Establish multidisciplinary training, education, and guidelines for transitioning oral antimicrobial transitions with institution-specific criteria for appropriateness based on guidelines and clinical judgment.[37]
- Create mechanisms to identify patients approaching hospital discharge and prospectively validate the tool.
- Share progress, expectations, and successes with all groups involved.

7 | CONCLUSION

Thousands of patients are discharged from health systems with antimicrobials annually, representing a critical opportunity for ASP. There are many approaches to implementing a model for ASP during TOC. Key steps include development of guidelines, gaining support from stakeholders, establishing a reliable system for patient identification, collaborative planning, communication, and ensuring accurate documentation of a plan. We observed sustained pharmacist-driven interventions in a practice model change aimed to improve antimicrobial prescribing at TOC. Careful implementation of training, procedures, communication, and monitoring is necessary to support successful and sustainable large-scale interventions.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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