

REVIEWS OF ANTI-INFECTIVE AGENTS: Louis D. Saravolatz, Section Editor

Antibiotic Overuse and Stewardship at Hospital Discharge: The Reducing Overuse of Antibiotics at Discharge Home Framework

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Though opportunities exist to improve antibiotic prescribing across the care spectrum, discharge from acute hospitalization is an increasingly recognized source of antibiotic overuse. Antimicrobials are prescribed to more than 1 in 8 patients at hospital discharge; approximately half of which could be improved. Key targets for antibiotic stewardship at discharge include unnecessary antibiotics, excess duration, avoidable fluoroquinolones, and improving (or avoiding) intravenous antibiotic therapy. Barriers to discharge antibiotic stewardship include the perceived “high stakes” of care transitions during which patients move from intense to infrequent observation, difficulties in antibiotic measurement to guide improvement at discharge, and poor communication across silos, particularly with skilled nursing facilities. In this review, we discuss what is currently known about antibiotic overuse at hospital discharge, key barriers, and targets for improving antibiotic prescribing at discharge and we introduce an evidence-based framework, the Reducing Overuse of Antibiotics at Discharge Home Framework, for conducting discharge antibiotic stewardship.

Keywords. antibiotic stewardship; care transition; discharge; infection.

Antibiotic prescribing, by nature, has both individual and societal effects. The antibiotic prescribed to one individual may affect the antibiotic resistance pattern of an entire population. Despite this collective effect, antibiotic stewardship programs (ASPs) often operate in silos, predominantly focusing on inpatient settings. However, this pattern is changing as hospital-based ASPs begin to include outpatient, emergency, urgent care, and long-term care clinicians [1]. Hospitals in the same regions, which may compete for patients, are beginning to collaborate to standardize and improve antimicrobial prescribing for entire populations [2–4]. Nonetheless, antibiotic prescribing during care transitions is often not scrutinized in the same way as inpatient prescribing, leading to antibiotic overuse and antibiotic-related harm as patients move between care settings. One care transition particularly prone to antibiotic overuse is discharge from acute hospitalization. In this review, we discuss what is

currently known about antibiotic overuse at hospital discharge and key barriers and targets for improving antibiotic prescribing at discharge and we introduce the ROAD (Reducing Overuse of Antibiotics at Discharge) Home Framework for discharge antibiotic stewardship.

WHAT IS CURRENTLY KNOWN ABOUT ANTIBIOTIC USE AND OVERUSE AT DISCHARGE

Antimicrobials are prescribed to half of all patients during hospitalization and more than 1 in 8 at hospital discharge [5]. For common infections treated in the hospital, up to half of antibiotic days occur after the patient has left the hospital [5–7]. For community-acquired pneumonia, two-thirds of patients receive an excess antibiotic duration (ie, days beyond guideline-recommended durations) at discharge, with each excess day increasing the risk of adverse antibiotic events [6]. Despite recent efforts to reduce fluoroquinolone use and the greater harm associated with fluoroquinolones compared with other effective antibiotics, fluoroquinolones remain the most common antibiotic prescribed at discharge [8]. Up to 80% of fluoroquinolone days prescribed for acute infectious hospitalizations occur after discharge [9], which places patients at increased risk for adverse events (eg, *Clostridioides difficile* infection [CDI]) that may go undetected in their home. In total, up to 70% of antibiotic courses prescribed at discharge from medicine services could be improved by narrowing the spectrum, choosing a safer drug, reducing duration, or stopping antibiotics altogether [2, 10, 11].

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Though data are sparse, surgical patients, who commonly receive antibiotics both for treatment and prophylaxis, could likely also benefit from antibiotic stewardship at discharge, including reducing duration of antibiotic treatment and stopping unnecessary post-operative prophylaxis [12].

Three specific scenarios related to discharge stewardship merit special discussion and are discussed in the following sections.

Discharge to Skilled Nursing Facilities

Convalescing hospitalized patients are commonly transferred to skilled nursing facilities (SNFs) after discharge to receive intravenous antibiotics or other nursing care needs. Antibiotic stewardship during this care transition is critical for many reasons. First, antibiotic use on transition to SNFs is common. In one review of 6701 discharges to long-term care, 22.9% of patients were prescribed antibiotics, most commonly cephalosporins and fluoroquinolones [13]. Second, patients discharged to SNFs are especially vulnerable to developing antibiotic side effects, antibiotic resistance, and infections from multidrug-resistant organisms due to older age, multiple comorbidities, and presence of devices (eg, urinary or intravascular catheters); they are also at high risk of experiencing both true infections and overdiagnosis of infections [14]. Third, antibiotic prescribing that starts in the hospital, even when the diagnosis is wrong, is often continued in nursing facilities due to hesitancy to overturn hospital physician decisions. Communication failure between inpatient and post-acute care facilities exacerbates this problem as does the complexity of antibiotic courses, which are often intravenous. In the end, these issues may lead to an antibiotic prescribing cascade in which long-term residents, such as those with dementia who experience fluctuating mental status, may be repeatedly treated with antibiotics, repeatedly moved between hospitals and SNFs, and develop increasing antibiotic resistance. Already, 25% of urinary tract infections in older adults are caused by resistant pathogens [15]. The burden of antibiotic use during care transitions is often shouldered by SNFs that must manage infection control issues raised by the high prevalence of drug-resistant organisms and *C. difficile* colonization [16, 17]. Finally, tracking antibiotic use (or following laboratory results for clinical care) in patients transferred to SNFs is difficult due to limited antibiotic reporting, common use of “free text” to prescribe intravenous antibiotics, and electronic medical records that often differ from those of discharging facilities.

Emergency Department and Observation Discharges

Patients who arrive at the hospital but are discharged without an inpatient stay are also susceptible to antibiotic overuse after discharge, though data are limited. One small, single-center study found that 79% of patients prescribed an antibiotic on discharge from an observation stay received excess, inappropriate,

or unnecessary antibiotics [18]. Similarly, patients discharged from emergency departments (EDs) have high rates of antibiotic use and overuse. More than 10% of ED visits are related to infection, making antimicrobials the most common class of new drugs prescribed at ED discharge [19]. In one Veterans Affairs (VA) study, 39% of antibiotics prescribed to patients discharged from the ED were inappropriate [20].

Outpatient Intravenous Antibiotic Therapy

Up to 14% of antibiotics prescribed at discharge are parenteral [10]. Outpatient intravenous antibiotic therapy (OPAT) programs have revolutionized antibiotic delivery, allowing patients to defer long inpatient stays for early discharge. However, many patients prescribed OPAT could be treated with oral or no antibiotics, a number likely to rise as evidence increasingly supports oral therapy for diseases historically treated with intravenous antibiotics. Case reviews have found that OPAT was potentially not needed in up to 40% of cases [21]. In one pediatric study, additional OPAT misuse was common: 10.5% of cases had an antibiotic drug–organism mismatch and 11.4% of orders had inappropriate antibiotic dosing [21].

CONSEQUENCES OF ANTIBIOTIC OVERUSE AND BARRIERS TO APPROPRIATE ANTIBIOTIC USE AT DISCHARGE

Data on the consequences of antibiotic overuse at discharge are limited and mostly drawn from what we know about the harm from antibiotic misuse generally. These consequences include post-discharge hospital-associated CDI, antibiotic-associated side effects (up to one-quarter of which occur after hospital discharge) [22], effects on community antibiotic resistance (including SNFs to which patients are discharged) [16], and harms associated with the long-term intravenous devices for OPAT.

Hospital discharge is a difficult but critical area for antibiotic stewardship for 3 additional reasons. First, clinicians may perceive the “stakes” as being higher at discharge. Patients transition from being closely monitored to not being seen by a clinician for long periods of time immediately following a serious illness. Thus, getting “it right” feels more important because the effect of decisions at discharge are hard to monitor. In this light, clinicians, though well-intentioned, may weigh risks incorrectly. For example, some will err on the side of prescribing broad-spectrum or longer antibiotic durations to try to prevent readmissions rather than consider the excess risk those decisions may create [23]. Second, there is the complexity surrounding changes of drug, route, and formulation that are required at discharge. Most clinicians hope to transition a patient from an intravenous antibiotic to a medication in the same drug class. When an oral equivalent is not available, clinicians may choose broader-spectrum oral drugs. Finally, there are medication adherence issues. Appropriately, clinicians often account for ease of dosing and cost when determining what to prescribe

at discharge. Still, patients may not complete antibiotic courses for various reasons including side effects that are discomforting but not critical enough to seek care.

BARRIERS TO ANTIBIOTIC MEASUREMENT AT DISCHARGE

Major barriers exist to improving discharge antibiotic use. Perhaps the most critical is the difficulty in accurately measuring antibiotic use or overuse at discharge. In a study of more than 40 hospitals in Michigan, fewer than 5% of stewardship programs reported having access to data on antibiotic prescribing at discharge [24]. The barriers to measuring antibiotic use at discharge are myriad. First, inpatient and outpatient electronic health record integration remains problematic. Hospitals may have different vendors for their inpatient and outpatient sides or, when vendors are the same, the 2 systems do not easily interact for data analytics and dashboard reporting. The resources required to connect the 2 systems often fall outside the capabilities of most ASPs already challenged with data analytics [25]. Second, some hospitals (or discharges within hospitals) do not use electronic prescribing systems at discharge. Smaller, often rural, hospitals may rely on written or phoned-in prescriptions. Even at larger hospitals, OPAT prescriptions and prescriptions for patients discharged to nursing homes may be entered as free text, which is difficult to capture, interpret, and track. Third, the incentives to measure discharge antibiotics are lacking. For example, the Standardized Antimicrobial Administration Ratio metric reported to the Centers for Disease Control and Prevention's (CDC) National Healthcare Safety Network does not include antibiotics prescribed at discharge. Similarly, many national databases do not include discharge antibiotics and, if they do, require marrying inpatient and outpatient databases to track discharge prescriptions. A notable exception to this rule has been VA databases that have provided some of the first and best data on antibiotic prescribing at discharge (though OPAT and discharges to SNFs still require manual review) [8, 26]. Smaller systems are also beginning to have success measuring discharge antibiotic use. The Duke Antimicrobial Stewardship Outreach Network recently published a process for measuring length of therapy for patients discharged with electronic prescriptions for antibiotics [5].

Finally, similar to inpatient antibiotic use, there are challenges in defining appropriate vs antibiotic overuse at discharge. To date, nearly all studies that have assessed antibiotic overuse at discharge have required case review. Creating a standard algorithm for assessing discharge antibiotic appropriateness, similar to the antimicrobial quality assessment for inpatient antibiotics [27], could help streamline this process and allow hospitals to benchmark and track appropriate antibiotic use at discharge over time.

To improve measurement, standardized methods for describing antibiotic use and overuse at discharge are needed.

There is no consensus on what numerators and denominators should be for a discharge antibiotic metric. Often, studies report the percentage of patients discharged on antibiotics (or discharged with antibiotic overuse) with denominators such as per 100 discharges, per 100 discharges with infection, or per 100 discharges on oral antibiotics. Others have focused on counting calendar days of antibiotic use or overuse after discharge. This lack of standardization has made it difficult for hospitals to benchmark their prescribing rates.

KEY STEWARDSHIP TARGETS FOR DISCHARGE ANTIBIOTICS

Based on what is known, there are at least 4 main targets to improving antibiotic prescribing at discharge (Table 1). First, and perhaps most critical, is stopping unnecessary antibiotics in patients who initially were considered to have a possible infection (eg, pulmonary infiltrates, tachycardia) but were later determined to have a nonbacterial etiology (eg, heart failure, viral pneumonia). If not done at 48–72 hours during a “time-out,” discharge is an ideal time to consolidate the medication list and finalize discharge diagnoses, including removing infectious diagnoses that have been ruled out. Second, for patients who have a confirmed or likely infection, the most common type of antibiotic overuse at discharge is excess duration. As noted by the CDC's Core Elements for ASPs, discharge is a critical time for improving total duration of therapy given that the vast majority of excess duration occurs after hospitalization [28]. For stewardship programs seeking “low hanging fruit” to begin their discharge assessment, community-acquired pneumonia and skin and soft tissue infections are prime targets [2, 7, 11, 18]. Third, reducing fluoroquinolone use at discharge remains a critical target. Despite reductions in fluoroquinolone prescribing during hospitalization, fluoroquinolone use at discharge has only minimally decreased [20, 29]. Primary avoidable causes of fluoroquinolone use at discharge include pneumonia, intraabdominal infections, and perioperative therapy [2, 7]. Finally, patients discharged on OPAT can often be optimized by switching to oral therapy, reducing duration, optimizing dose and agent, or stopping antibiotics altogether. Additional opportunities exist for special populations, most critically improving communication, monitoring, and antibiotic use at discharge to SNFs.

THE ROAD HOME FRAMEWORK

Key Discharge Antibiotic Stewardship Interventions

To develop a framework for improving antibiotic prescribing at discharge, we reviewed the available literature on existing discharge-specific antibiotic stewardship interventions, the CDC's Core Elements of ASPs, as well as inpatient-focused interventions that have effectively improved antibiotic prescribing at discharge [28, 30–34]. The ROAD Home Framework

Table 1. Summary of Targets and Example Interventions for Discharge Stewardship

Key Areas for Discharge Stewardship	Specific High-Priority Targets	Example Interventions
Confirm infectious diagnosis still applies	Asymptomatic bacteriuria still being treated CAP or sepsis as part of differential diagnosis but now known alternative cause	Diagnostic or antibiotic time-out at discharge Pharmacist/stewardship prospective audit and feedback at or prior to discharge
Use shortest effective duration	CAP (typically 3 to 5 days duration) Skin and soft tissue infections (typically 5 to 7 days duration)	Enable easier calculation of duration at discharge (eg, antibiotic grouping in electronic health record, incorporating stop dates, deleting default prescribing durations) Incorporate duration recommendations into local guidelines and order sets Include anticipated total duration in existing pharmacist/stewardship interventions
Confirm appropriate, narrow, safest therapy	Avoid fluoroquinolone when safer alternative exists Outpatient intravenous antibiotic therapy	Incorporate oral deescalation recommendations in local guidelines and existing order sets Continue restriction or prior authorization of key antibiotics at discharge Consider antibiotic stewardship review and/or infectious diseases involvement of patients progressing to outpatient intravenous antibiotic therapy
Improve communication	Communication to subsequent care team Patient education Skilled nursing facilities	Smart set or template for discharge summary: "Patient diagnosed with [disease] based on [symptoms]. Antibiotics started on [date] with planned [duration]-day course to finish on [date]." Create standard patient education documents to include in discharge summary for common diseases and antibiotics Incorporate antibiotics into existing nursing or pharmacy-driven patient education Cooperative antibiotic stewardship and data sharing between hospitals and skilled nursing facilities

Abbreviation: CAP, community-acquired pneumonia.

includes 3 tiers modeled after successful frameworks to improve healthcare-associated infection [35]. Tier 1 strategies provide critical infrastructure required for stewardship in general. Tier 2 strategies (classified as “action” elements in the CDC’s Core Elements of ASPs) are those that target inpatient prescribing but, based on published studies, can have carryover effects to discharge when thoughtfully designed with care transitions in mind. Finally, tier 3 strategies are discharge-specific strategies. For hospitals seeking to improve antibiotic prescribing at discharge, the ROAD Home Framework can be helpful to identify critical elements that are missing (ie, tier 1 strategies), existing inpatient stewardship interventions that could be designed

more thoughtfully with discharge in mind (ie, tier 2 strategies), and to plan specific, stand-alone interventions to improve prescribing at discharge (ie, tier 3 strategies). These strategies are summarized in Figure 1.

Tier 1 Strategies

Tier 1 strategies, or “critical infrastructure,” create a foundation for antibiotic stewardship regardless of the target. For example, the CDC recommends that ASPs have an appointed leader(s) for stewardship [28]. Without protected time for that leader(s), other strategies are unlikely to succeed. Though tier 1 strategies are often insufficient on their own to improve antibiotic

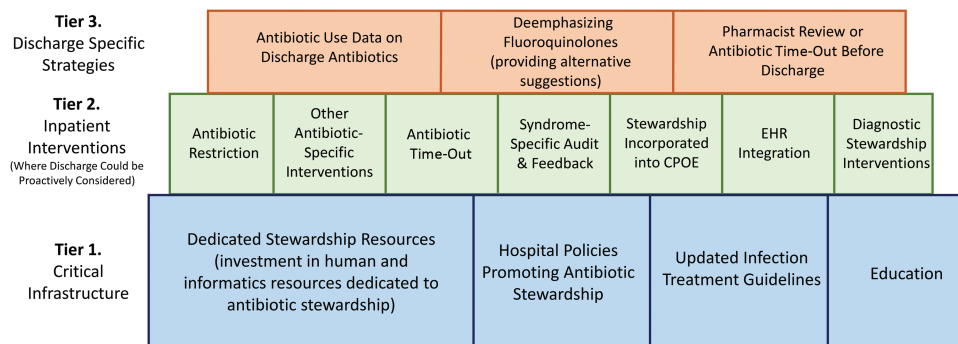


Figure 1. The Reducing Overuse of Antibiotics at Discharge Home Framework for reducing overuse of antibiotics at discharge. Abbreviations: CPOE, computerized order entry; EHR, electronic health record.

prescribing, they provide a foundation for the more directed and “hands-on” tier 2 (and 3) strategies. The key here is integration of antibiotic stewardship across multiple elements of hospital infrastructure. This includes investment in human and informatics resources dedicated to antibiotic stewardship, marrying those resources to policies and guidelines that promote a consistent antibiotic stewardship message, and then educating clinicians on antibiotic stewardship principles, guidelines, and policies.

Tier 2 Strategies

Tier 2 strategies, or “broad inpatient interventions,” include many action elements defined by the CDC’s Core Elements of ASPs [28]. These broad interventions aim to improve inpatient antibiotic prescribing but do not directly target prescribing at discharge. Many inpatient stewardship interventions have obvious potential “carryover” effects at discharge. For example, if an antibiotic time-out or prospective antimicrobial audit at 48–72 hours successfully results in discontinuation of unnecessary antibiotics, then this simultaneously reduces unnecessary antibiotic use at discharge. Other inpatient stewardship interventions have more variable success in improving discharge prescribing. For example, one study found that hospitals with robust inpatient fluoroquinolone stewardship also had less discharge fluoroquinolone use [8]. Another study, however, found that inpatient fluoroquinolone restriction may increase new starts of fluoroquinolone antibiotics at discharge [9]. Thus, the key is thoughtful implementation of inpatient interventions with discharge in mind. For example, many hospitals restrict fluoroquinolone prescribing during hospitalization but not at discharge. In contrast, many VA hospitals restrict both, potentially demonstrating why inpatient fluoroquinolone restriction is more successful at discharge in VA hospitals [8]. Similarly, syndrome-specific interventions that include guidelines, order sets, and/or audit and feedback of inpatient stewardship targets (eg, deescalation, intravenous to oral conversion) and discharge stewardship targets (eg, planned stop date, planned oral discharge medication) as opposed to those that just focus on inpatient targets, may also improve discharge prescribing [33, 36, 37].

Tier 3 Strategies

Finally, tier 3 strategies are those that are discharge specific. A recent systematic review found only 6 studies of discharge-specific antibiotic stewardship interventions [31]. Most published interventions were multifaceted and included a combination of educational, guideline, and interventional strategies. However, 3 evidence-based strategies for improving antibiotic use at discharge can be identified: providing data on discharge antibiotics, targeting fluoroquinolone use at discharge, and having a pharmacist review or antibiotic time-outs focused on discharge.

Though difficult for many hospitals to access, data on antibiotic prescribing at discharge is a critical first step and is necessary to guide stewardship as it may reveal blind spots. The second tier 3 strategy includes interventions that deemphasize fluoroquinolone use at discharge, including strategies borrowed from inpatient stewardship, such as restriction or prior authorization of fluoroquinolones. Often, it is difficult to identify discharge fluoroquinolone prescriptions in real time if inpatient and outpatient electronic health records do not communicate or if prescriptions occur in nonelectronic forms. Behavioral economic or choice architecture interventions can also be powerful in nudging clinicians away from fluoroquinolones at discharge. Examples include incorporating suggestions for discharge antibiotics into order sets or removing fluoroquinolones from common medication lists at discharge [34]. Similarly, changing the “radio buttons” of common discharge durations can reduce the number of pills providers default to at discharge [34]. Institutional treatment guidelines and educational lectures should ensure that recommendations for oral/discharge transition are clear, consistent, and recommend against fluoroquinolone use when avoidable [38].

Finally, prospective antibiotic review or antibiotic time-outs with pharmacists prior to discharge can be powerful [39]. There are multiple ways to structure such a review. In one study, the existing transition-of-care (TOC) pharmacist incorporated basic review of antibiotics at discharge for patients identified as being high risk for readmissions [40]. They found that 14.4% of the TOC pharmacist interventions involved antibiotic recommendations, most often for dosing, duration, and drug interactions. Other studies have involved the ASP or inpatient clinical pharmacists in prospective discharge review by having the stewardship team leave recommendations for discharge prescriptions in the record, having a prospective discharge antibiotic time-out during daily rounds, or incorporating discharge recommendations into syndrome-specific or pharmacist prospective audit and feedback [34, 41]. Similarly, for patients discharged with OPAT, successful stewardship interventions have incorporated ASP or infectious diseases assessment [42].

Remaining Needs

To inform discharge antibiotic stewardship, there remain multiple critical needs. First, we must standardize methods of measuring antibiotic use and overuse at discharge. Days of therapy per 100 discharges would capture true antibiotic use at discharge across diseases. Second, adjusted metrics on antibiotic use at discharge should be incorporated into national reports on antibiotic use, as it has been shown repeatedly that inpatient antibiotic use alone is a limited metric for evaluating a hospital’s true impact on antibiotic use. Third, more work is needed to identify key strategies that have led many hospitals to excel in appropriate antibiotic use at discharge while others have struggled. Finally, prospective discharge stewardship

interventions are needed to identify best practices for diverse hospitals, including those with limited resources. Ideally, such interventions would cross silos to improve prescribing in multiple locations.

CONCLUSIONS

As we increasingly grow aware that antibiotic stewardship requires a team approach that crosses care silos, it is critical to remember hospital discharge as a key opportunity to improve antibiotic use and outcomes for our patients.

Notes

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