Opportunities to Improve Antibiotic Prescribing in Outpatient Hemodialysis Facilities: A Report From the American Society of Nephrology and Centers for Disease Control and Prevention Antibiotic Stewardship White Paper Writing Group

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Antibiotic use is necessary in the outpatient hemodialysis setting because patients receiving hemodialysis are at increased risk for infections and sepsis. However, inappropriate antibiotic use can lead to adverse drug events, including adverse drug reactions and infections with *Clostridioides difficile* and antibiotic-resistant bacteria. Optimizing antibiotic use can decrease adverse events and improve infection cure rates and patient outcomes. The American Society of Nephrology and the US Centers for Disease Control and Prevention created the Antibiotic Stewardship in Hemodialysis White Paper Writing Group, comprising experts in antibiotic stewardship, infectious diseases, nephrology, and public health, to highlight strategies that can improve antibiotic prescribing for patients receiving maintenance hemodialysis. Based on existing evidence and the unique patient and clinical setting characteristics, the following strategies for improving antibiotic use are reviewed: expanding infection and sepsis prevention activities, standardizing blood culture collection processes, treating methicillin-susceptible *Staphylococcus aureus* infections with β-lactams, optimizing communication between nurses and prescribing providers, and improving data sharing across transitions of care. Collaboration among the Centers for Disease Control and Prevention; American Society of Nephrology; other professional societies such as infectious diseases, hospital medicine, and vascular surgery societies; and dialysis provider organizations can improve antibiotic use and the quality of care for patients receiving maintenance hemodialysis.

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Purpose, Focus, and Scope

The discovery of antibiotics has revolutionized the practice of medicine and saved countless lives. However, unnecessary antibiotic use contributes to the spread of antibiotic-resistant bacteria,[1] jeopardizes patient safety, and can lead to adverse drug events[1,2] such as infection with *Clostridioides difficile*[1,3] without the intended clinical benefit. The Centers for Disease Control and Prevention (CDC) estimates that more than 2.8 million people in the United States experience an antibiotic-resistant infection each year, and at least 35,000 people die as a result.[4] Studies have suggested that kidney failure requiring dialysis is an independent risk factor for *C difficile* infections.[5,6] In addition, patients receiving maintenance hemodialysis have a high prevalence of infection and/or colonization with multidrug-resistant organisms[7-9] and substantial mortality resulting from infections and sepsis.[10] Sepsis is a life-threatening organ dysfunction due to a person's dysregulated response to infection.[11] Optimizing antibiotic use can play an important role in improving infection cure rates, preventing sepsis, reducing the unintended negative consequences of antibiotic use, and possibly reducing costs.[12]

The Antibiotic Stewardship in Hemodialysis (ASHD) White Paper Writing Group is a collaboration between CDC and the American Society of Nephrology (ASN). Given nationwide interest in optimizing antibiotic use in various patient populations, the objectives of the writing group were to summarize the current literature on antibiotic use in the outpatient hemodialysis setting and highlight strategies to improve antibiotic prescribing in hemodialysis. We focused on intravenous (IV) antibiotic use because of the lack of published data for oral antibiotic use in the hemodialysis patient population in the United States. This document is not intended as guidelines or recommendations due to limited existing evidence on the topic and is intended for outpatient hemodialysis care, including home hemodialysis, but may also be relevant to inpatient hemodialysis care. The intended target audience includes kidney care providers, public health officials, patient safety officers, health care epidemiologists, and antibiotic stewardship experts.

The ASHD writing group had 8 telephone call meetings over an 18-month period. Initial meetings involved discussing a framework for the white paper and developing an outline of key areas that the white paper would address. A literature search was performed concurrently using PubMed and Google Scholar to identify published articles on antibiotic use or antibiotic stewardship in dialysis settings. A summary of the literature review was presented to the group and generated discussion on study findings, data quality, and strategies to improve antibiotic prescribing. Leaders from several dialysis organizations were invited to present their antibiotic stewardship activities to the writing group. The group members wrote sections of the paper based on their areas of expertise. These sections were collated and synthesized into a cohesive manuscript. The final manuscript was reviewed and approved by writing group members and their respective organizations (ie, CDC and ASN).

Background

In the United States, there are approximately 468,000 patients receiving maintenance hemodialysis and 52,000 patients receiving peritoneal dialysis.[10] Ninety-eight percent of patients receiving maintenance hemodialysis receive dialysis in outpatient dialysis facilities, while the remaining 2% (~9,000 patients) receive dialysis at home.[10] Patients who receive maintenance hemodialysis have a high comorbidity burden from diseases such as diabetes, cardiovascular disease, stroke, and peripheral vascular disease.[13] These comorbid conditions and advanced age place them at increased risk for lower extremity ischemia, ulceration, and skin and soft tissue infection.[14] Patients receiving maintenance hemodialysis are also at increased risk for acquiring infections because of an impaired immune system,[15] frequent accessing of the bloodstream during hemodialysis, and use of hemodialysis central venous catheters (CVCs).[16,17] Infection is the second leading cause of death in this population and sepsis accounts for most of these deaths.[10] Approximately 13,000 patients receiving maintenance hemodialysis died of sepsis from 2015 through 2017.[10] Given this high infection burden, it is not surprising that antibiotic exposure is common among patients receiving maintenance hemodialysis. At least 30% of patients receiving maintenance hemodialysis receive 1 or more doses of IV antibiotics in a given year.[18,19] Improving antibiotic prescribing to ensure that the "right antibiotic is prescribed for the right diagnosis, at the right dose and duration," while avoiding unnecessary antibiotic use, can potentially improve clinical outcomes for patients receiving maintenance hemodialysis.[6]

Antibiotic Stewardship

Antibiotic stewardship is defined as the effort to measure and improve how antibiotics are prescribed by clinicians and used by patients.[20] Improving antibiotic prescribing and antibiotic use is critical to effectively treat infections, protect patients from harms caused by unnecessary antibiotic use, and combat antibiotic resistance.[20] Antibiotic stewardship includes measuring how antibiotics are prescribed and implementing effective strategies to align prescribing practices with evidence-based guidelines[20] (Box 1). Improving antibiotic prescribing intersects with initiatives to improve sepsis detection and treatment such as procedures and tools to enhance identification of causative organisms to optimize antibiotic selection.[11] Interventions designed to improve antibiotic prescribing practices for hospitalized patients have been found to increase compliance with antibiotic use policies, decrease the duration of therapy, and reduce hospital length of stay.[21] A systematic review and meta-analysis of 145 studies examining outcomes of antibiotic stewardship interventions in the hospital setting found that guideline-adherent empirical antibiotic therapy and de-escalation of therapy (ie, streamlining empirical treatment based on culture results)[21] were associated with a reduction in mortality.[22] Another systematic review and meta-analysis demonstrated that antibiotic stewardship programs in hospitals reduced infection caused by *C difficile* and the incidence of infection and colonization with MDROs.[23]

CDC developed the Core Elements of Antibiotic Stewardship to provide a framework for implementing stewardship programs and activities and for monitoring and improving antibiotic use.[24,25] The Core Elements have been developed for different health care settings, including acute care hospitals, nursing homes, and critical access hospitals, to address unique setting characteristics and patient needs.[24-26] In 2016, the Core Elements were adapted for outpatient clinicians and facilities that routinely provide antibiotic treatment but these were not intended to address the outpatient hemodialysis setting.[24] Outpatient hemodialysis facilities and the patient

Box 1. Antibiotic Stewardship Terms and Descriptions

Antibiotic Stewardship
- The effort to measure and improve how antibiotics are prescribed by clinicians and used by patients

Prescribing Protocols
- Evidence-based protocols and standardized checklists for initiating antibiotics
- Antibiotic use protocols can include clinical decision support and prompt clinicians to justify or explain the indication for an antibiotic order (accountable justification)

Postprescription Review
- Reviews of culture results and response to therapy after treatment initiation (antibiotic time out) to determine appropriate treatment and duration needed

Tracking
- Measurement of antibiotic use practices to guide and evaluate interventions

Audit and Feedback
- Assessment and feedback of prescribing practices back to providers to facilitate practice change
- Feedback reports can include comparison of the individual prescriber practices to those of their colleagues (peer comparison)

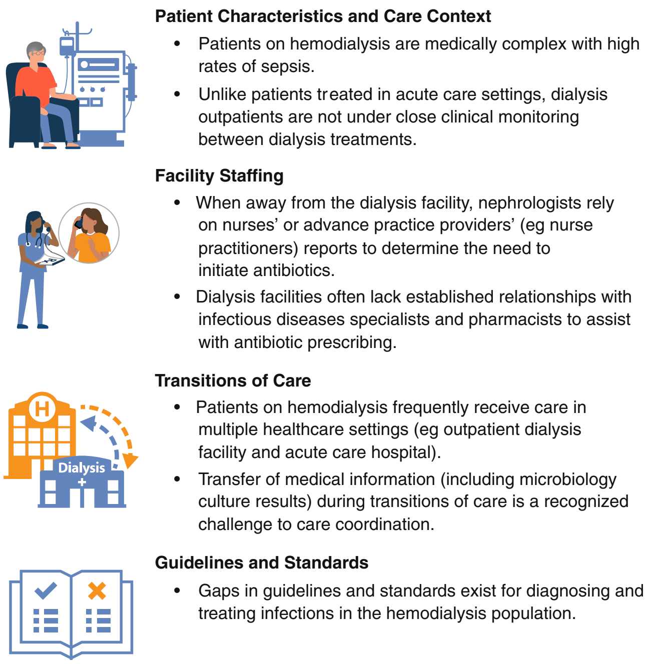


Figure 1. Outpatient hemodialysis setting–specific considerations for antibiotic stewardship interventions. Outpatient hemodialysis facilities and patients receiving maintenance hemodialysis have unique characteristics that may be pertinent when considering antibiotic stewardship activities.

population receiving care in these facilities have unique characteristics that may be pertinent when considering antibiotic stewardship activities such as patient care characteristics and care context, facility staffing, transitions of care, and guidelines and standards (Fig 1).

Evidence Summary: Antibiotic Use and Stewardship in the Hemodialysis Setting—What Is Known?

In the published literature there are 4 studies based on national surveillance data that describe antibiotic use in outpatient hemodialysis facilities in the United States.[7,19,27,28] In addition, there are several small observational studies of a limited number of US outpatient dialysis facilities describing antibiotic use,[18,29] characterizing appropriateness of antibiotic use,[18,30,31] and/or assessing the effectiveness of antibiotic stewardship interventions.[32] Appropriateness of antibiotic use has also been described in the outpatient hemodialysis setting in Canada and Australia[33,34] and an inpatient hemodialysis unit in the United States[35] (Table 1).

Antibiotic Use

Antibiotic use data from the US Renal Data System and a separate small study suggest that 30% of patients receiving maintenance hemodialysis receive at least 1 IV antibiotic dose in US outpatient hemodialysis facilities each year.[18,19] In 2014, data from more than 6,000 outpatient hemodialysis facilities reporting to the National Healthcare Safety Network (NHSN) revealed a facility median of 3.0 IV antimicrobial starts per 100 (interquartile range, 1.91-4.25) patient-months.[7] NHSN captures IV antimicrobial starts only, not all antimicrobial doses. Antibiotic use varies across dialysis facilities, with some facilities having a higher rate of antibiotic use than others.[7,18] Differences in infection rates, prescribing practices, and patient characteristics may play a role in the variations seen in antibiotic start rates in these studies.[7,18] For example, IV antimicrobial starts were higher in patients with CVCs than in those with arteriovenous grafts or fistulas,[7] as would be expected based on the higher infection rates seen in patients with CVCs.

Vancomycin is the most commonly used IV antibiotic in outpatient hemodialysis facilities.[18,19,32] Among US hemodialysis patients who had received outpatient IV antibiotics in 2007, 68% had received vancomycin.[19] Vancomycin also accounts for the highest percentage (>70%) of IV antimicrobial starts.[7,27,28] In contrast, a study conducted in outpatient and inpatient hemodialysis facilities in Hawaii found that cefazolin was the most commonly used IV antibiotic, followed by vancomycin.[29] Third-generation cephalosporins and aminoglycosides are also commonly used in the outpatient dialysis setting.[18,19,29,32]

Appropriateness of Antibiotic Use

Studies assessing the appropriateness of antibiotic use in a small number of outpatient hemodialysis facilities have demonstrated that up to 37% of IV antibiotic courses[33] or 30% of IV antibiotic doses[18] were inappropriate or unnecessary. In a study of 2 dialysis facilities, Snyder et al[30] found that ~60% of patients who received IV antibiotics in a 12-month period received at least 1 dose that was not indicated. They also demonstrated that continued doses (compared with first antibiotic doses and doses for surgical prophylaxis) accounted for the highest proportion of inappropriate antibiotic doses.[18] Similarly, Zvonar et al[33] studied vancomycin prescribing in 3 outpatient dialysis facilities and determined that most (88%) initial or empirical courses of vancomycin were appropriate, but this percentage decreased (to 63%) when assessed after culture and sensitivity results were available. These 2 studies highlighted common reasons that antibiotics were considered inappropriate: failure to meet standard clinical criteria (eg, defined through national guidelines) for bloodstream infections, soft tissue infections, or surgical prophylaxis[18]; failure to discontinue antibiotic therapy based on negative culture results[33]; failure to narrow antibiotic spectrum from vancomycin to β-lactams[18,33] or from third- and fourth-generation cephalosporins to cefazolin when appropriate[18]; and failure to comply with recommended antibiotic duration for surgical prophylaxis.[18]

Table 1. Summary of Studies on Antibiotic Prescribing in Hemodialysis

Study	Setting	Objective	Study Type	Findings
National Surveillance Data				
St. Peter and Solid[19] (2009)	91,000-170,000 patients in all US outpatient HD facilities	Examine IV antibiotic use trends among HD patients	Retrospective study using USRDS claims data from 1995-2007	30%-44% of patients had ≥1 claim for IV antibiotic dose in an outpatient dialysis setting in a given year; vancomycin was predominant antibiotic prescribed
Klevens et al[28] (2008)	32 US outpatient HD facilities	Report rates of bloodstream infections, vascular access infections, and IV antibiotic starts	Prospective surveillance on outpatient dialysis events reported to NHSN for 2006	Overall rate of IV antibiotic starts: 3.48/100 patient-months; vancomycin accounted for 73% of IV antibiotic starts
Patel et al[27] (2016)	193 US outpatient HD facilities	Report rates of bloodstream infections, vascular access infections, and IV antibiotic starts	Prospective surveillance on outpatient dialysis events reported to NHSN for 2007-2011	Overall rate of IV antibiotics starts: 3.12/100 patient-months (6.28 and 1.84/100 patient-months in those with CVC and AVF, respectively); vancomycin accounted for 72% of IV antibiotic starts
Nguyen et al[7] (2017)	6,005 US outpatient HD facilities	Report rates of bloodstream infections, vascular access infections, and IV antibiotic starts	Prospective surveillance on outpatient dialysis events reported to NHSN for 2014	Overall rate of IV antibiotic start: 3.27/100 patient-months (7.91 and 2.07/100 patient-months in those with CVC and AVF, respectively); vancomycin accounted for 76% of IV antibiotic starts
Worth et al[64] (2017)	48 outpatient HD facilities, in Victoria, Australia	Determine the burden of bloodstream and local access-related infections and patterns of IV antibiotic starts	Prospective surveillance on outpatient dialysis events reported to VICNISS for 2008-2015	IV antibiotic start rates: 3.37 and 0.73/100 patient-months in those with tunneled CVC and AVF, respectively; vancomycin accounted for 48.9% of IV antibiotic starts
Observational Studies				
Green et al[35] (2000)	103 patients receiving MHD in 1 hospital in Tennessee	Determine indications for vancomycin use and reasons for inappropriate use in hospitalized MHD patients	Prospective study spanning 3 months	Hospitalized MHD patients received ≥1 dose of vancomycin significantly more often than other hospitalized patients (39% vs 5%); 20% of vancomycin doses judged inappropriate (mostly due to use for β-lactam–sensitive organisms)
Berman et al[29] (2004)	433 patients in 1 inpatient and 4 outpatient dialysis facilities in Hawaii	Examine spectrum of infections in patients receiving maintenance dialysis (including PD and HD)	Retrospective study spanning 9 years	Cefazolin accounted for highest percentage (19.8%) of antibiotic courses in maintenance dialysis patients, followed by vancomycin (18.4%)
Zvonar et al[33] (2008)	105 patients in 3 outpatient HD facilities in Ontario, Canada	Evaluate the appropriateness of vancomycin use in an MHD population	Retrospective study spanning 12 months	88% of vancomycin doses were intitially considered appropriate but this dropped to 63% with culture and sensitivity data availability; most inappropriate vancomycin was use for β-lactam–sensitive organisms
Snyder et al[18] (2013)	278 patients in 2 outpatient HD facilities in Massachusetts	Quantify and characterize antimicrobial use among patients receiving MHD	Retrospective and prospective observational study spanning 35 and 12 months, respectively	Overall rate of IV antibiotic use: 32.9 doses/100 patient-months; vancomycin most commonly prescribed antibiotic, followed by cefazolin and 3rd- and 4th-generation cephalosporins; 29.8% of antibiotic doses classified as inappropriate due to failure to: meet criteria for infection (52.9%), select a more narrow-spectrum antibiotic (26.8%), or meet criteria for surgical prophylaxis (20.3%)

(Continued)

Table 1 (Cont'd). Summary of Studies on Antibiotic Prescribing in Hemodialysis

Study	Setting	Objective	Study Type	Findings
Snyder et al[30] (2016)	278 patients in 2 outpatient HD facilities in Massachusetts	Characterize MHD patients at increased risk for receiving IV antibiotics	Prospective cohort study spanning 12 months	32% of patients got ≥1 dose of IV antibiotics (58% got ≥1 nonindicated antibiotic dose); patients at higher odds of getting IV antibiotics included those with a tunneled dialysis CVC (vs AV access), history of colonization or infection with an MDRO in the year preceding enrollment, or receipt of dialysis during daytime shift; patients with a tunneled dialysis CVC or longer dialysis vintage were at higher odds for receiving nonindicated IV antibiotic dose
Hui et al[34] (2017)	114 patients in 4 outpatient and 2 hospital inpatient HD units in Melbourne, Australia	Describe patterns of use and appropriateness of oral and IV antibiotics prescribed to patients receiving HD	Prospective study spanning 6 months	Vancomycin and piperacillin/tazobactam most common IV antibiotics prescribed; cefazolin and meropenem most common inappropriately prescribed IV antibiotics (due to incorrect dosing frequency)
D'Agata et al[32] (2018)	35-90 patients per facility in 6 outpatient HD facilities in New Jersey	Quantify the effect of a multicomponent antibiotic stewardship intervention (leadership support; antibiotic prescribing educational programs; monthly conference calls with nurse managers, program leaders, and an ID physician; and implementation of positive deviance behavioral process) in reducing antibiotic prescribing	Intervention study and interrupted time-series spanning 12 months	Intervention led to 6% monthly reduction in rate of antibiotic doses per 100 patient-months; de-escalating from vancomycin to cefazolin for MSSA infections most common reason for antibiotic adjustment
Hahn et al[31] (2019)	54 outpatient HD facilities in Philadelphia County, Pennsylvania	Measure the rate of IV antibiotic starts and estimate the proportion that were inappropriate	Analysis of dialysis event data from NHSN in 2018	Rate of IV antibiotic starts: 2.28/100 patient-months; 57.5% of new outpatient IV antibiotic starts classified as inappropriate (using an unvalidated application of surveillance data to estimate appropriateness)
Other Studies				
D'Agata et al[12] (2018)	—	Model the clinical and economic consequences of implementing a nationwide antibiotic stewardship program in US outpatient dialysis facilities	Decision analytical model and cost consequence analysis in a given year	Implementing nationwide antibiotic stewardship program for dialysis patients predicted to decrease infections caused by *Clostridioides difficile* and MDROs and save society $107 million in costs

Abbreviations: AV, arteriovenous; AVF, arteriovenous fistula; CVC, central venous catheter; HD, hemodialysis; ID, infectious diseases; IV, intravenous; MDRO, multidrug-resistant organism; MHD, maintenance hemodialysis; MSSA, methicillin-susceptible *Staphylococcus aureus*; NHSN, National Healthcare Safety Network; PD, peritoneal dialysis; VICNISS, Victorian Healthcare Associated Infection Surveillance System; USRDS, US Renal Data System.

Substantial variations in antibiotic prescribing practices have been observed across facilities. Snyder et al[18] revealed that most inappropriate antibiotic doses for surgical prophylaxis were from 1 of 2 dialysis facilities studied. Vancomycin was the most commonly inappropriately prescribed IV antibiotic, likely reflecting its overall burden of use.[18] In a study involving outpatient and inpatient dialysis facilities in Australia, where vancomycin use was low, cefazolin was found to be the most commonly inappropriately prescribed IV antibiotic among patients receiving hemodialysis.[34] Patient factors associated with receipt of an antibiotic dose that was not indicated included use of dialysis CVC and longer duration of hemodialysis dependence.[30]

Inadequate medical record documentation[18] (eg, antibiotic indication) and failure to obtain blood cultures before initiating antibiotic treatment are recognized barriers to fully evaluating the appropriateness of antibiotic doses.[33] Lack of medical record documentation of infection signs and symptoms may be widespread among dialysis facilities. During 2017, ~50% of true bloodstream infections reported to NHSN (eg, positive blood cultures excluding suspected contaminants) occurred in the absence of reported symptoms of fever, chills, or hypotension (NHSN Dialysis Event Surveillance; P.R.P., unpublished observation, February 27, 2020). Inadequate medical record documentation and/or incomplete NHSN reporting of symptom data might explain the substantial percentage of these apparent asymptomatic infections that prompted blood culture collection.

Stewardship Interventions in the Dialysis Setting

Few studies have examined antibiotic stewardship interventions in the outpatient hemodialysis setting. D'Agata et al[32] introduced into 6 outpatient dialysis facilities an antibiotic stewardship intervention consisting of: (1) leadership support, (2) educational programs, (3) monthly conference calls, and (4) implementation of a social and behavioral change process[32] (Table 1). Monthly audits of antibiotic prescriptions and microbiology data conducted by an infectious diseases physician resulted in adjustment or discontinuation of antibiotic therapy. Overall, a 6% monthly reduction in antibiotic doses per 100 patient-months was observed over a 12-month period, without an identified increase in hospitalization or bloodstream infection rates. Inadequate documentation of antibiotic indication and microbiology data posed a challenge because ~33% of the records did not have adequate data for review.

Implications and Limitations of Studies on Antibiotic Use

Although limited in number, published studies of antibiotic use among patients receiving maintenance hemodialysis highlight potential opportunities to improve prescribing, including consistently obtaining blood cultures before initiating antibiotic therapy, improving documentation of clinical signs of infection and indications for antibiotics, ensuring that patients meet the criteria for treatment of infections or surgical prophylaxis, and adjusting antibiotic therapy based on microbiology results. A common reason that antibiotic prescribing was considered inappropriate was failure to de-escalate vancomycin to a β-lactam for sensitive organisms in the absence of a β-lactam allergy. Studies of methicillin-susceptible *Staphylococcus aureus* (MSSA) infections have shown improved treatment outcomes in patients treated with β-lactams such as cefazolin in comparison to vancomycin,[36] making this a specific area for potential antibiotic optimization.

Studies describing antibiotic use and appropriateness in patients on maintenance hemodialysis are subject to several limitations. First, the results might not be generalizable given the small sample size. Substantial variations in antibiotic prescribing practices observed between 2 facilities in the same study underscore this (eg, 91% of antibiotic doses that were considered inappropriate due to failure to meet criteria for surgical prophylaxis occurred in 1 of the 2 facilities studied).[18]

Second, lack of documentation of clinical signs of infection and/or indications for antibiotic use may have led to misclassification of antibiotic doses as inappropriate, resulting in a falsely elevated proportion of inappropriate antibiotic doses.

Finally, in some instances, there is lack of consensus on infection criteria for this patient population. Although national guidelines for diagnosing and treating infections were applied in developing the appropriateness criteria used in different studies, these guidelines are not always tailored to patients receiving maintenance hemodialysis or the outpatient dialysis setting. For example, Snyder et al[18] lowered the criteria for fever from the standard of ≥100.4 °F to ≥100 °F to address the immune dysfunction observed in patients receiving hemodialysis. Such antibiotic appropriateness criteria, which varied across studies, must be considered when interpreting study results.

Improving Antibiotic Use

Given limited evidence for antibiotic stewardship interventions in the outpatient dialysis setting, the ASHD Writing Group proposed "suggested strategies" based on expert opinion in lieu of evidence-based guidelines (Fig 2). In selecting this group of interventions, which may have broader benefits beyond stewardship, we prioritized interventions already recommended for other patient safety reasons. In addition, we describe additional strategies used in other health care settings that can help inform stewardship efforts in dialysis settings.

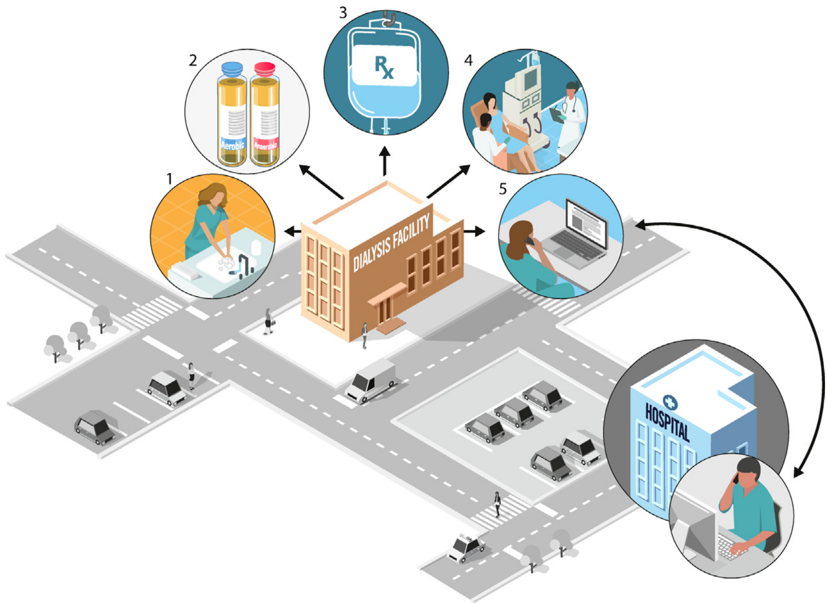
Suggested Strategies for Improving Antibiotic Use in Outpatient Hemodialysis

Invest in Infection Prevention and Sepsis Prevention Efforts

An important strategy to reduce the need for antibiotics is to prevent infections and resultant sepsis from occurring. Dialysis facilities should routinely engage in activities to prevent bloodstream and vascular access infections and maximize delivery of recommended vaccines (eg, influenza and pneumococcal).[37,38] Although few infection prevention intervention studies in this setting have included antibiotic use as an outcome measure, at least 1 large randomized trial demonstrated reductions in rates of catheter-related bloodstream infection and IV antibiotic starts following a catheter care intervention.[39]

Standardize Blood Culture Collection

Collection of blood cultures before delivery of antibiotics for suspected bloodstream infections is a recommended practice[40,41] that allows for the adjustment of empirical



Suggested Strategy	Description	Examples
1. Infection prevention and sepsis prevention efforts	Engage all staff and patients in preventing infections such as bloodstream infection and vascular access infection.	• Conduct routine competency assessments for all dialysis staff involved in catheter care. • Implement influenza vaccine campaign. • Involve patients in hand hygiene observations
2. Blood culture practices	Implement standardized practices to improve blood culture collection.	• Train staff on how blood culture should be obtained (e.g. sites of collection, blood volume). • Evaluate adherence to blood culture collection prior to antibiotic initiation.
3. Treatment of methicillin-susceptible Staphylococcus aureus (MSSA) infections	Treat MSSA infections with ß-lactams instead of vancomycin for better treatment outcomes.	• Incorporate automated alert in electronic medical record to prompt providers to review appropriateness of antibiotic therapy. • Develop a process to receive and notify providers of culture results.
4. Communication with prescribing providers	Implement practices to improve communication between onsite nurses and prescribing physicians or physician extenders.	• Develop a structed method of communicating critical information such as SBAR (Situation, Background, Assessment and Recommendation).
5. Communication across care transitions	Implement practices to improve communication across transitions of care between the outpatient dialysis facility and other healthcare settings.	• Work with local hospitals to establish data sharing agreements for bidirectional communication. • Implement standard transfer form/sign out between dialysis facility and nursing home.

Figure 2. Suggested strategies for improving antibiotic use in outpatient hemodialysis facilities. These strategies for improving antibiotic use in the outpatient hemodialysis setting are based on expert opinion and do not represent evidence-based guidelines. However, they have broader patient care and/or safety benefits beyond stewardship.

antibiotic therapy based on culture results. Written protocols outlining when blood cultures should be obtained and the procedure to obtain them can help ensure that they are collected before antibiotic delivery and that false-positives and false-negatives are minimized. Educating personnel who collect blood samples for culture about recommended procedures and periodically assessing their competency are necessary adjuncts to ensure the implementation of best practice.[42,43]

It is generally recommended that at least 2 sets of cultures of appropriate blood volume be collected, ideally from 2 separate sites, with a set consisting of both aerobic and anaerobic blood culture bottles.[44,45] The collection of more than 1 blood culture set increases the blood volume that is cultured and, when drawn from a different site, helps distinguish contamination from infection.[44,46] For patients receiving hemodialysis, the sites from which cultures are often obtained include the hemodialysis catheter hub(s), the hemodialysis circuit (ie, port within the tubing [blood lines] connected to catheter hub or access needles), and a peripheral vein.[41,44,46] Peripheral venipuncture is often avoided in these patients to preserve peripheral veins for future permanent vascular access creation.[41,47,48] The ASN's Nephrologists Transforming

Dialysis Safety (NTDS) initiative released a guide on standardization of blood culture collection for patients receiving in-center hemodialysis that outlines best blood culturing practices for hemodialysis patients, along with the supporting rationale.[45] The NTDS guide may be a helpful resource for practice improvement in this area.

Treat MSSA Infections With β-Lactams

As highlighted in the evidence summary, a common form of inappropriate antibiotic use is treating β-lactam–susceptible infections such as MSSA infection with vancomycin in the absence of a β-lactam allergy. Cefazolin treatment of MSSA infections has resulted in improved treatment outcomes compared to vancomycin.[36,49,50] Consequently, treating MSSA infections with cefazolin in the absence of a β-lactam allergy can be expected to improve infection cure rates in patients receiving hemodialysis.

Standardize Communication Between Nursing Staff and Prescribing Providers

Standardized protocols and education can assist nurses, advanced practice providers, and other facility staff to identify signs and symptoms of infection and communicate effectively with offsite prescribing physicians/extenders when discussing orders for blood cultures and/or antibiotics. An example of such a communication tool is the SBAR.[51] SBAR is a structured method for communicating critical information that requires immediate attention and action. SBAR has 4 steps: situation, background, assessment, and recommendation. SBAR can improve communication, effective escalation, and safety, and is widely used in many industries including health care, aviation, and the military.[52]

Improve Communication Across Transitions of Care

A central tenet of antibiotic stewardship is the adjustment of empirical antibiotic therapy based on culture results. Obtaining culture results with organism susceptibility profiles is critical for optimal antibiotic selection (eg, de-escalating empirical broad-spectrum antibiotics to narrow-spectrum antibiotics). It follows that access to results of cultures performed is important for multiple clinicians caring for the patient. The initial assessment, collection of blood cultures, and subsequent treatment of an infection episode in a patient may occur in various health care settings, including the emergency department, inpatient hospital ward, physician office, extended care facility, or dialysis unit. Health care facilities frequently use different health record systems and may or may not have a formal association with the dialysis facility. Mechanisms for consistent bidirectional communication of information between the dialysis facility and other health care facilities that share the care of dialysis patients can help ensure use of the correct antibiotic, dose, and duration based on determinants such as culture and susceptibility results, indication for antibiotics, antibiotic start date, and posttreatment diagnostic studies. Bidirectional communication between dialysis facilities and other health care facilities also fosters care coordination and outcome tracking, such as identification of bloodstream infections that are reportable to NHSN.

Strategies Used in Other Health Care Settings

Improve Processes for Detection and Treatment of Common Infections

Several interventions such as accountable justification,[53] prospective audits and feedback,[25,54] and audit and feedback combined with peer comparison[53,55] have been shown to improve antibiotic prescribing in other (nondialysis) health care settings[21,56] (Box 1). Implementing evidence-based clinical decision support protocols for the initiation of antibiotic treatment may be an effective strategy to improve prescribing practices.[57] Providing antibiotic order forms or electronic order sets that incorporate clinical decision support drawn from evidence-based guidelines such as reminders to obtain blood cultures before ordering IV antibiotics, can be considered in the dialysis setting.[18,58,59] Active monitoring or tracking of antibiotic prescribing practices at the local facility level can help identify opportunities for improvement. However, the specifics and effectiveness of these strategies on improving antibiotic use in dialysis settings requires further evaluation. Successful implementation of these and other interventions may result in improvements in antibiotic management but may also require substantial commitment of facility resources. Further, the goals of these efforts, and possibly metrics for evaluation, should include timely initiation of antibiotic therapy for sepsis.

Improve Processes for Antibiotic Adjustment and Discontinuation

Considering that continuing doses, not empirical therapy doses, account for most inappropriate antibiotic doses in dialysis patients,[18] implementing a postprescription review or an antibiotic "time out" may help prevent inappropriate use[60] (Box 1). In addition, evaluating a patient's clinical progress and reassessing antibiotic therapy is a recommended sepsis prevention and management effort.[11] An antibiotic time out is a provider-led reassessment of an antibiotic course after treatment initiation.[25] This allows clinicians to decide whether discontinuation, de-escalation, or adjustment of empirical therapy based on clinical response and the results of diagnostic testing is necessary and determine the duration of therapy. Successful antibiotic time out implementation relies on effective communication across transitions of care so that microbiology results from transferring facilities are available for review.

Establish Relationships With Infectious Diseases Experts

Outpatient dialysis facilities may explore opportunities to establish relationships with infectious diseases physicians or pharmacists who can serve as resources on best antibiotic prescribing practices. These professionals can provide expertise in the diagnosis and treatment of infections and in developing processes and protocols for antibiotic dosing, selection, adjustment, and de-escalation. Whether relationships with such experts are established at the facility or larger organizational level may depend on available resources.

Engage Leadership to Support Antibiotic Stewardship Interventions

Engaging leadership at the local facility and the larger organizational level is important to the success of antibiotic stewardship interventions in the dialysis setting.[32,61] Leadership support can signal that antibiotic stewardship activities are an organizational priority and ensure that needed resources are provided for antibiotic prescribing and stewardship expertise, staff and patient education, and development and promotion of antibiotic prescribing pathways and protocols.

Provide Education on Antibiotic Use

Clinician education is an essential component of any antibiotic stewardship activity.[24] Education topics should include early sepsis prevention and management,[11] blood culture collection procedures,[44] antibiotic selection and dosing for empirical treatment of common infections, and antibiotic adjustment based on microbiology data. However, numerous studies have shown that education alone does not change behavior and should be paired with other interventions to improve prescribing practices.[56] Education through academic detailing (ie, peer-to-peer interactive educational outreach providing evidence-based material and opportunities for dialogue) is more effective than passive didactic-type education.[62] Staff should be given the opportunity to voice concerns, discuss perceived barriers to improving antibiotic prescribing practices, and adapt antibiotic stewardship policies to the needs of the dialysis facility.

Integrate Antibiotic Stewardship Practices With Other Quality Improvement Initiatives

Outpatient dialysis facilities have existing structures and programs to monitor quality measures and conduct quality improvement initiatives. Facilities are incentivized by the Centers for Medicare & Medicaid Services (CMS) to report bloodstream infections to NHSN and are mandated by CMS to have monthly Quality Assessment and Performance Improvement program meetings in which specific health outcome measures, such as bloodstream infection rates, are reviewed by the medical director and clinical staff.[63] Increased bloodstream infection rates or a medical error may prompt a root cause analysis to identify any needed changes in policy, practice, or staff training. Antibiotic stewardship measures and initiatives and sepsis prevention and management activities could potentially be incorporated into this existing structure. Effectively engaging medical directors is important for the success of these efforts and could ensure that the activities receive appropriate attention from clinical staff and leadership.

Box 2. Research Gaps and Future Directions

Measures to Determine Optimal Antibiotic Use

- Identify and refine measures to distinguish optimal vs inadequate or unnecessary antibiotic use in the hemodialysis population

Future Studies Needed

- Comparative effectiveness studies of stewardship interventions
- Cost-effectiveness studies of specific stewardship interventions
- Assessment of patient preferences to inform antibiotic use guidelines and policies

Diagnostic Advancements

- Biomarkers for sepsis in hemodialysis patients to improve early detection of severe infections and assist in targeting empirical antibiotics

Oral Antibiotics and Nondialysis Prescriptions

- Data for all antibiotics (including oral) prescribed to patients receiving dialysis in all health care settings to better target improvement efforts

Guidelines and Standardized Definitions

- Guidelines for evaluation and treatment of common infections in hemodialysis patients and antibiotic prophylaxis for dialysis vascular access procedures to optimize antibiotic use and standardize definitions

Conclusion and Research Gaps

Although immediate actions can be taken to improve antibiotic use among dialysis patients, further research is needed to inform and refine future antibiotic stewardship initiatives (Box 2). The focus of optimizing antibiotic use in the hemodialysis population is on improving cure rates and preventing adverse events from unnecessary antibiotic exposure such as infections caused by *C difficile* and emergence of antibiotic-resistant bacteria. On a national level, antibiotic stewardship programs in outpatient hemodialysis facilities may be cost-effective.[12] Dialysis organizations with strong clinical infrastructure provide an opportunity to evaluate the effectiveness of existing and novel antibiotic stewardship interventions in a formal and robust fashion. Several aspects of stewardship initiatives may be overlapping with infection surveillance, sepsis prevention and management efforts, improving care transitions, and other quality improvement efforts. Cooperative efforts among CDC; ASN; professional organizations such as infectious diseases, hospital medicine, and vascular surgery societies; and dialysis provider organizations can advance the science of antibiotic stewardship and patient safety, and improve the quality of care for patients receiving dialysis.

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