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TRANSPLANT INFECTIOUS DISEASE

ORIGINAL ARTICLE

Outpatient and peri-operative antibiotic stewardship in solid organ transplantation

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Abstract

Background: The consequences of inappropriate antimicrobial use including resistance are increasingly recognized as a global public health threat and many steps have been taken over the last few decades to advance antimicrobial stewardship initiatives with most organ transplant centers currently part of institutions with active antimicrobial stewardship programs.

Methods: A review of the literature was conducted and articles were categorized according to the topic and relevance in the judgment of the two authors.

Results: A summary review of the currently available literature was created with a focus on periprocedural and outpatient antimicrobial stewardship. Limitations in the data were significant and discussed in the review.

Conclusion: The principles of antimicrobial stewardship remain important throughout all phases starting with periprocedural prophylactic antimicrobial selection all the way through to discharge and subsequent healthcare encounters. Despite the broad advances in stewardship initiatives and the rapidly progressing supportive data overall there continue to be significant opportunities for additional research within various special patient populations including recipients of solid organ transplantation (SOT). The recent white paper published in the *American Journal of Transplantation* called to action the transplant and stewardship communities to have an increased focus and awareness of the issues that antimicrobial overuse can present in the SOT patient population. This is an important step that will hopefully generate more data in this group of patients that arguably faces the greatest vulnerability to the consequences of increased antimicrobial resistance.

KEYWORDS
outpatient stewardship, peri-operative stewardship surgical prophylaxis, solid organ transplant, transitions of care

1 | INTRODUCTION

Antimicrobial resistance is among the top global threats to public health as outlined by numerous organizations including the World Health Organization and US Centers for Disease Control and Prevention (CDC).[1] Though there have been significant additions to the antimicrobial pharmacopeia over the past decade, significant concerns remain about the future risk of pathogens developing resistance to all available agents.

As demonstrated clearly in the era of COVID-19, few patient populations are at higher risk for complications of infectious diseases than immunocompromised hosts including those who have undergone solid organ transplantation (SOT).[2]

The negative consequences of resistant organisms as well as other significant adverse effects associated with antibiotic overuse (including secondary infections with *Clostridoides difficile)* reinforce the need for antimicrobial stewardship programs (ASPs).[3] ASPs aim to improve patient outcomes by optimizing antimicrobial usage. This includes treating patients with the right antimicrobial at the right dose for the right duration. While there should be caution taken in broadly applying stewardship interventions that have only been demonstrated to have safety and efficacy in immunocompetent patient populations, there is an important role for stewardship in SOT.[4] There continues to be an unfulfilled need for studies clarifying appropriate durations and routes of antibiotic for many infectious disease processes in SOT patients, but we are slowly identifying more opportunities to reduce unnecessary antimicrobial exposure.

This review aims to identify and evaluate current strategies for antimicrobial stewardship in the perioperative period for SOT patients as well as in the ambulatory setting. It will also identify gaps in the literature and opportunities for future progress.

2 | PERI-OPERATIVE ANTIMICROBIAL STEWARDSHIP

National guidelines from the Infectious Disease Society of America (IDSA), the American Society of Health-System Pharmacists (ASHP), the Surgical Infection Society (SIS) and the Society of Healthcare Epidemiology of America (SHEA) provide recommendations for surgical antimicrobial prophylaxis for SOT;[5] however, high-quality data supporting these recommendations are limited. Despite the common practice of prophylaxis, post-operative infections occur in 3%–53% of SOT recipients and contribute significantly to morbidity and mortality.[6] Rates tend to be lowest with renal transplantation and significantly higher with liver, lung, and multivisceral transplantation.[7,8] While post-surgical infections are often multi-factorial and cannot be prevented only by the administration of broader spectrum or longer duration of peri-operative prophylactic antibiotics, antibiotic selection and administration timing can be potentially powerful tools in reducing rates of infection, particularly surgical site infections.[9]

2.1 | Surgical prophylaxis antibiotic selection

Selection of antibiotics should be tailored based on the transplanted organ type but also need to factor in donor and recipient-specific parameters as well as local epidemiology. IDSA/ASHP/SIS/SHEA guidelines suggest that for some procedure types such as kidney transplant, prophylaxis may be as narrow as cefazolin but is often substantially broader for other transplant types such as liver and lung.[5] Limited evidence exists to guide antibiotic selection for patients known to be colonized with multidrug resistant organisms (MDROs). One study evaluating patients undergoing liver transplantation in the setting of known vancomycin-resistant enterococci (VRE) colonization suggests that there may be benefit in broadening prophylaxis to include the addition of daptomycin.[10] Expert opinion suggests benefit in expansion of coverage to include activity against resistant Gram-negative pathogens when there is known colonization identified prior to transplantation but this has not been substantiated with robust randomized clinical trials.[5] Pre-surgical colonization with methicillin-resistant *Staphylococcus aureus* has been tied to increased risk of surgical site infection in other procedure types and may benefit from the addition of the targeted therapy such as vancomycin.[11] It is quite common for lung transplant recipients to have known colonization with resistant organisms such as *Pseudomonas aeruginosa* and it is considered reasonable to include coverage for such organisms when isolated from either recipient or donor in many cases based on the currently available data.[12]

Another potential factor that may impact antibiotic selection among surgical patients is the history of antibiotic allergy. Numerous studies have identified the beta-lactam allergy label as a significant risk for a variety of negative healthcare outcomes including increased surgical site infection, increased healthcare costs, and increased length of stay.[13,14] Overall, most patients with beta-lactam allergy labels are ultimately found to have little risk of future reaction particularly if utilizing a separate category (i.e., cephalosporin in the setting of a penicillin allergy).[15] Establishment of a clinical pathway for handling beta-lactam allergies can be beneficial in optimizing antibiotic selection for a variety of surgical populations including SOT. Allergen skin testing and oral beta-lactam challenges may help provide further clarity particularly in patients with history of the significant reaction.[16]

2.2 | Pre- and intra-operative antibiotic dosing

The evidence suggests that timing of antibiotic administration prior to incision and during the procedure can be important in limiting surgical site infections.[5,17] It is ideal to maintain antibiotic concentrations at or above the target pharmacodynamic and pharmacokinetic parameters for the selected antibiotic and expected pathogens throughout the procedure. Common guidance is to administer a dose within the 60-min period immediately prior to incision to ensure adequate concentrations and then administration of repeat intra-operative doses should occur between 2 and 2½ times the estimated half-life

of the drug. Further doses are warranted in the setting of significant intra-operative blood loss.[5]

Depending on the antibiotic selected, a single dose may be all that is needed; however, longer procedures such as liver transplants may require several repeat doses of antibiotic to be administered throughout the surgical encounter in order to maintain therapeutic concentrations through surgical closure. Antimicrobial stewardship teams can have valuable input in assessing the available literature and establishing guidelines and order sets to systematically ensure optimal dosing of intra-operative antibiotics in collaboration with other members of the surgical team including the anesthesia service. Electronic alerts within the medical record system may further reinforce the appropriate timing of antibiotic administration during and after the procedure.[18]

2.3 | Post-operative antibiotic durations

Antibiotic durations are increasingly a focus of ASPs as more data confirm that shorter durations of therapy can often achieve equivalent success rates for prevention and treatment of infections while minimizing the risk of adverse consequences such as drug side effects, secondary infections, and colonization with resistant organisms.[19] Many non-transplant surgical procedures now have substantial evidence pointing to a lack of benefit for extending antimicrobial prophylaxis beyond 24–48 h from initial incision.[5] In one recent evaluation of duration of prophylaxis among liver transplant recipients, no benefit was observed in patients undergoing extended prophylaxis (72 h post-procedure) compared to the standard prophylaxis post procedure.[20] Limited additional data exist supporting any particular duration of therapy to another in transplant recipients; however, other non-transplant cardiac procedures have demonstrated no benefit to extending antibiotic duration beyond 48 h.[21] Antimicrobial selection and therapy durations in lung transplant recipients are an area of particularly high variability in clinical practice. Factors affecting selection include donor and recipient colonization, underlying indication for transplant, and local antibiograms. In a survey study of lung transplant centers around the world, recipients with no known colonization of resistant pathogens, durations of prophylaxis tended to 7 days or less; however, recipients with previous colonization typically received at least 14 days of antimicrobial therapy.[22]

The antibiotic duration post-transplant procedure represents a significant research need as there remains significant variability across institutions and expert recommendations around extension of prophylactic therapies in the settings of lung transplantation, colonization with resistant organisms, and infected donor and/or recipient remain poorly supported by the currently available data.

In the absence of high-quality data to support-specific regimens or durations for at least some of the prophylaxis guidance, it is important to monitor process measures (length of stay, rehospitalization), and outcome measures (surgical site infections) as balancing measures, especially when changes to existing regimens are implemented.[23]

2.4 | Transitions of care stewardship opportunity

Transition points between phases of care for patients often represent an opportunity for re-assessment of pharmacotherapy regimens including antimicrobials. This can be particularly true for patients in the immediate post-transplant period when antimicrobials are being started for prophylaxis of common opportunistic infections. The doses of these antimicrobials and other elements of the patient's medication regimen need to be adjusted based on the changing function of transplanted organ and interactions among medications, including immunosuppressants. In a large retrospective study of general inpatients conducted within the Veterans Health Administration, 19.9% of patients were prescribed an oral antibiotic at discharge. These discharge prescriptions ultimately accounted for 39% of the total duration of antimicrobial exposure days for those patient encounters.[24] Other studies have come to similar conclusions regarding the importance of reinforcing stewardship principles at discharge.[25,26] A study conducted at hospital in Australia noted high rates of inappropriate antimicrobial prescribing in review of their discharge prescriptions including an inappropriate total duration of therapy in 79% encounters.[26] Though data specific to solid organ transplant recipients is limited or lacking entirely, transitions of care represent an important timepoint to reinforce antimicrobial stewardship principles not only at discharge from surgical admission but at any subsequent admissions as well.

2.5 | Antimicrobial stewardship in the outpatient setting

Outpatient encounters including medical offices, urgent care centers, and emergency departments continue to generate the majority of antibiotic prescriptions in the United States.[27] According to estimates generated through the Pew Charitable Trust and CDC, as many as 1 in 3 outpatient antibiotic prescriptions, which can equate to as many as 47 million courses of therapy per year are ultimately unnecessary.[28] A national survey of 1550 primary care physicians in 2018 highlighted that while most recognized the issue of antimicrobial resistance as a public health issue and identified the need for antimicrobial stewardship in the outpatient setting, few identified inappropriate antibiotic use in their practice as a problem.[28] The same survey also revealed that physicians felt moderate pressure from their patients or their parents to prescribe antibiotics. Addressing patient education as well as help in implementation of stewardship initiatives was identified as areas of needs by ambulatory care physicians.[28] Despite this need, survey data from a separate study suggest that few institutional ASPs self-identify as fully functional within the ambulatory care setting,[29] indicating an opportunity and necessity for application and consideration of antimicrobial stewardship principles in non-hospitalized patients, including organ transplant recipients.

The breakdown of antibiotic exposure by phase of care in solid organ transplant patients is not clearly delineated in the literature and many

publications that have evaluated various outpatient stewardship initiatives have intentionally excluded immunocompromised patients. Many factors have been reported to lead to overprescription of antibiotics in the outpatient setting. Physicians report patient expectations for antibiotic prescriptions and concern for low patient satisfaction when an antibiotic prescription is not provided to be an important factor in overprescribing. A survey of parents of children with acute respiratory infections identified parents who were given a contingency plan instead of the expected antibiotic prescription to have a higher satisfaction than those without a contingency plan.[30] Recent studies have identified high rates of antibiotic prescribing, particularly in telehealth setting to be associated with higher patient satisfaction rates.[31] Other reported etiologies for overprescription of antibiotics in the outpatient setting include diagnostic uncertainties, high risk of illness versus lower risk of antibiotic treatment, and time pressure are among the most commonly reported reasons.[31,32]

Some of these factors for antibiotic misuse might be exacerbated in solid organ transplant recipients. Emphasis on safe living and prevention of infections to solid organ transplant candidates might lead to increased expectations for antibiotics prescriptions in transplant recipients. Additionally, solid organ transplant recipients have unique and dynamic risks for infection based on organ transplanted, prior infection history, and time since transplantation. The usual timeline of infections in solid organ transplant recipients is also influenced by the graft function and at times higher than the usual immunosuppressive therapy, leading to increased risk of opportunistic infections. [33] Outside the peri-transplant period, most of the care of solid organ transplant recipients is provided by their primary care physicians. Lack of experience in taking care of immunosuppressed patients, and diagnostic uncertainties with additional concerns for atypical presentation of infections, delayed symptoms onset with quick progression to severe disease, as well as worst-case scenarios, such as loss of a precious transplanted organ, progression to severe disease requiring hospitalization or death, especially in the outpatient setting where patients cannot be observed closely may lead to either unwarranted or broader or more prolonged than necessary antibiotic prescriptions. Time pressure is likely to only exacerbate overprescribing in this setting. As many transplant patients may present to their transplant center for serious problems, primary providers might also not consider harm associated with unnecessary antibiotic prescribing during, such as *Clostridium difficile* infections, which are associated with increased mortality and graft loss.[34]

2.6 | Outpatient stewardship best practices

Despite extensive data on antimicrobial stewardship in the acute-care setting, best practices for outpatient stewardship have not been well defined.[32] The outpatient setting presents unique challenges to implementation of certain stewardship initiatives. While traditional stewardship activities of prospective audit and feedback, "handshake stewardship" or antimicrobial restrictions are often not feasible, certain interventions based on behavioral economics have been shown to be effective in outpatient AMS. These include: (1) public commitment letters and posters to declare an intention to prescribe antibiotics only when necessary, signed by prescribers and hung in clinic rooms; (2) feedback and peer comparison with consistent, easily understandable and emotional-laden feedback as well as feedback from a powerful messenger, and (3) justification alerts in which clinicians have to write brief and specific explanation for antibiotic prescribing, making prescribing slightly harder and requiring cognitive effort.[31] Delayed antibiotic prescribing, the practice of providing a prescription with recommendation to initiate antibiotics only in case of worsening symptoms might also be beneficial to address both patient and physician concerns of undertreatment with severe consequences.

CDC core elements of outpatient stewardship published in 2016 focus on commitment and accountability, action with implementation of at least one policy or practice to improve antibiotic prescribing, tracking of antibiotic prescribing practices and reporting at regular intervals to clinicians, and education to clinicians and patients.[35]

2.7 | Commitment and accountability

Studies from acute care settings show that transplant infectious disease involvement in SOT recipient patient care is associated with improved outcomes and stewardship-concordant care,[23] thus transplant infectious disease physicians or pharmacists would serve as ideal stewardship champions in the care of transplant recipients. However, stewardship is a multidisciplinary effort that must involve all members of the healthcare team.

- *Clinical pharmacist role in mitigation of antimicrobial adverse effects*: Integration of clinical pharmacists into the transplant team can have beneficial impact from an antimicrobial stewardship perspective.[36] Clinical pharmacists can play an important role as extenders of ASP efforts and may help provide education to patients and care team members about changes to local policies based on local susceptibility patterns, drug shortages, and new regulatory approvals. Clinical pharmacists in SOT can also play pivotal roles in ensuring appropriate dosing of prophylactic and treatment antimicrobials There are many drug–drug interactions involving immunosuppressive therapies and antimicrobials with demonstrated potential for clinical impact. Though not intended to be an all-inclusive list, Table 1 highlights some high-profile examples.[37] Introduction of new therapies (such as nirmatrelvir–ritonavir for COVID-19), improved dosing strategies, and broader access to pharmacogenomic testing continue to reinforce the importance of pharmacist input in antimicrobial selection and monitoring.
- *Role of nurses in outpatient antimicrobial stewardship in SOT*: Nurses in the outpatient setting can play multiple roles in antimicrobial stewardship, including implementation of diagnostic and antimicrobial stewardship interventions, such as ensuring appropriate collection of testing samples (i.e., instructing patients on appropriate urine collection for cultures), forwarding negative urine culture result of patients who received empiric antibiotics to clinicians for review, notifying patients of plans to discontinue antibiotic therapy.[32]

TABLE 1 Examples of common clinically relevant immunosuppressant-antimicrobial interactions[37]

Antimicrobial category	Examples	Potential patient impact in SOT
Antibiotics	Macrolides	Variably increase CNI and mTORi level
	Rifamycins	Decrease CNI and mTORi level
	Aminoglycosides	Enhance nephrotoxic effect
	Fluoroquinolones	May increase CNI and mTORi level
	Oxazolidinones	Enhance myelosuppression
Antifungals	Azoles	Increase CNI and mTORi level
	Polyenes	Enhance nephrotoxic effect
Antivirals targeting CMV	Ganciclovir	Enhances neutropenia; enhances nephrotoxic effect
	Foscarnet	Enhances nephrotoxic effect
	Letermovir	Increases CNI and mTORi level
	Maribavir	Possibly increases CNI and mTORi level
Antivirals targeting SARS-CoV-2	Nirmatrelvir-ritonavir	Increases CNI and mTORi level

Abbreviations: CNI, calcineurin inhibitor (tacrolimus and/or cyclosporine); CMV, Cytomegalovirus;mTORi, mechanistic target of rapamycin (mTOR) inhibitors (sirolimus and/or everolimus); SOT, solid organ transplantation.

Transplant nurse coordinators, who help coordinate all facets of clinical care of transplant candidates and recipients, can be very especially effective in this role.

- *Communication between transplant centers and primary care providers*: Providing regular information to primary care providers of SOT recipients regarding the patients' degree of immunosuppression, unique risks of infections with an emphasis on time since transplant might ease worst-case scenario concerns and be beneficial to decrease unnecessary antimicrobial use. For patients who have unique clinical scenarios, such as colonization with MDROs or recurrent urinary tract infections, having a treatment plan could decrease use of broad and prolonged antimicrobials.

2.8 | Action for policy and practice

CDC calls for implementation of at least one policy or practice to improve antibiotic prescribing in the outpatient setting with assessment of its efficacy and modification as needed.[35]

Certain syndromes have tended to attract the most attention for antimicrobial stewardship initiatives in the outpatient setting. This includes so-called "never events" such as bronchitis, where antibiotics are not indicated or other common syndromes that often result in inappropriate antibiotic prescribing such as urinary tract infections or acute otitis media.[38] Use of unnecessarily broad-spectrum antibiotic therapy for the site of infection and/or targeted microorganism can often be associated with significant collateral damage. Fluoroquinolones in particular are notable for this potential; the FDA has issued numerous updates to the safety alerts around the fluoroquinolone class to include warnings about adverse effects ranging from blood glucose disturbances and mental health side effects to tendonitis that can potentially progress to tendon rupture. The overall conclusion from the FDA is that fluoroquinolones should be relegated to use in patients with no other alternatives when treating for common (and often mild) infections such as acute bacterial sinusitis and uncomplicated urinary tract infections.[39]

There has also been significant research conducted in shortening durations of therapy for several infectious diagnoses that can oftentimes be treated entirely in the outpatient setting such as genitourinary tract infections and skin and soft tissue infections. Unfortunately, the studies evaluating these shorter courses of therapy oftentimes either intentionally exclude immunocompromised patients or enroll very few such patients in their trials.[40] The lack of robust data specific to SOT recipients for recommended antibiotic spectrum and durations for certain common infectious processes combined with the potential discomfort among general practitioners in assessing infection risk among immunocompromised patients may lead clinicians to opt for longer durations of therapy in this patient population.

Despite the limited numbers, there are some examples of opportunities for application of antimicrobial stewardship principles in outpatients with SOT worth highlighting.

- *Respiratory tract infections*: the diagnosis of respiratory tract infections continues to be subject to significant uncertainty which can lead to substantial overuse of antibiotics for either non-bacterial infections (i.e., viruses) or non-infectious processes entirely.[38] There is increasing data for relatively new diagnostic tools such as multiplex pathogen panels and biomarkers such as procalcitonin that have the potential to aid in stewardship initiatives particularly when paired with effective diagnostic stewardship oversight.[41] A systematic review published in 2014 concluded that procalcitonin maintains reasonable sensitivity and specificity for identifying bacterial infection in patients with history of SOT.[42] The continuation of research and development in this arena can potentially lead to significant reductions in antibiotic exposures in a variety of patient populations including transplant recipients.

- *Urinary tract infections*: overtreatment of asymptomatic bacteriuria continues to be a prominent problem among immunocompetent and immunocompromised patients with significant potential to increase patient exposure to antibiotics and help drive antimicrobial resistance.[43] A study recently conducted in France and Belgium among kidney transplant recipients with asymptomatic bacteriuria at least 2 months after transplantation demonstrated no significant difference in the incidence of symptomatic urinary tract infection over the subsequent 12 months in patients randomly allocated to either antibiotic therapy or no antibiotic therapy.[44] This study reinforced the findings of prior studies and supports guideline recommendations against systematic screening and treatment of asymptomatic bacteriuria in kidney transplant recipients.[43,45,46]
- *Cytomegalovirus (CMV) prophylaxis*: CMV continues to be a problematic opportunistic pathogen for many SOT patient populations which necessitates careful monitoring and adjustment of antiviral therapy. Focused interventions involving multidisciplinary teams have been demonstrated to be effective in optimizing these antiviral therapy regimens in the ambulatory setting. A team at one medical center was able to significantly reduce the number of patients with excessively high CMV viral loads prior to treatment initiation at their institution while also seeing a greater proportion of patients achieve CMV eradication by day 21 of therapy through an intervention involving pharmacist follow-up of labs.[47] Interventions and protocols such as this have the potential to optimize antiviral therapy regimens and thereby reduce the potential for resistance and adverse effects.
- *Clostridioides difficile* infection (CDI) diagnostic stewardship: CDI is a relatively common complication for SOT recipients and antibiotic exposure is a known risk factor. Adherence to antimicrobial stewardship principles and limitation of unnecessary antibiotic exposures can reduce the burden of disease for patients.[48] Another important component of the CDI management is judicious diagnostic testing as there is a substantial percentage of patients that may be positive on high-sensitivity testing who are simply colonized and unlikely to respond to the antibiotic therapy targeted at *Clostridioides difficile*. Overtreatment of colonization can result in increased resistance to antibiotic over the long term but also puts clinicians at risk of overlooking other potential causes of symptoms. Diarrhea, particularly in an SOT recipient, can be indicative of a variety of pathologies. Effective diagnostic stewardship oversight is often a collaboration between multiple sectors within a hospital including infection control, microbiology laboratory, antimicrobial stewardship, and frontline clinicians and produce sizable reductions in CDI testing.[49]

3 | TRACKING AND REPORTING

Tracking and reporting of antimicrobial use in the outpatient setting is limited compared to the acute care setting. Interpretation and application of outpatient antimicrobial use data are difficult in the absence of reliable chart documentation including the indication for the antimicrobial. While some success has been achieved in certain syndrome-based efforts, there remain significant opportunities for improvement in outpatient tracking and reporting, particularly in special populations like SOT. Ideas include: enhanced tracking of antimicrobial resistance in SOT recipients with accumulation of data from various points of care (i.e., transplant center, primary care provider, urgent care center, community hospital, etc.), creation of regional outpatient antibiograms, and mandatory submission of antimicrobial use data in transplant center clinics. Accurate and timely data on antimicrobial use and resistance are imperative for identification of opportunities for targeted interventions and education.

4 | EDUCATION

Education remains an important element of antimicrobial stewardship particularly given the collaborative nature of stewardship efforts. Institutional protocols and recommendations should be readily available, routinely updated, and widely distributed. As discussed above, it is important to utilize any extenders possible including clinical pharmacists, nurses, clinical coordinators, and providers in any clinic in which SOT recipients may be encountered.

5 | RESEARCH GAPS AND FUTURE DIRECTIONS

As highlighted throughout this review, there is very limited data on antimicrobial stewardship in transplant recipients and there are significant limitations in the available data. Best practices for antimicrobial stewardship in SOT recipients in the peri-operative and ambulatory phases of care need to be established with the help of clinical research. Table 2 outlines some proposed areas of the highest need.

6 | CONCLUSION

The consequences of inappropriate antimicrobial use including resistance are increasingly recognized as a global public health threat and many steps have been taken over the last few decades to advance antimicrobial stewardship initiatives. Most organ transplant centers are currently part of institutions with active ASPs.[50]

Despite these advances and the rapidly progressing supportive data for stewardship interventions overall there continue to be significant opportunities for additional research within various special patient populations including recipients of SOT. The recent white paper published in the *American Journal of Transplantation* called to action the transplant and stewardship communities to have an increased focus and awareness of the issues that antimicrobial overuse can present in the SOT patient population.[23] This is an important step that will hopefully generate more data in this group of patients that arguably faces the greatest vulnerability to the consequences of increased antimicrobial resistance.

TABLE 2 Urgent research needs in peri-operative and outpatient antimicrobial stewardship in SOT

Phase of care	Research needs
Peri-operative	• Determination of the impact of antibiotic selection and duration on surgical site infections as balancing parameter of stewardship • Determination of the impact of antibiotic selection in the setting of known colonization with multi-drug resistant organisms in either SOT donor or recipient • Clarification of the impact of duration of post-operative antibiotic prophylaxis particularly for lung transplantation
Outpatient	• Post-approval registry studies to evaluate the utility of novel technologies such as new antimicrobials and rapid diagnostics in the setting of immunocompromised patient populations including SOT recipients • Inclusion of SOT recipients in studies comparing durations of therapy for commonly encountered infectious disease syndromes • Evaluation of provider barriers to implementing and applying stewardship principles in SOT recipients

Abbreviation: SOT, solid organ transplantation.

As data continue to accumulate for a variety of stewardship initiatives including narrower spectrums of therapy, shorter durations of antimicrobials, and other implementation of rapid diagnostics, it will remain important to try to be as inclusive as possible of special patient populations. While studies dedicated to immunocompromised or specific SOT groups may be difficult to achieve high enrollment rates, there is great potential benefit not only for these patients but all patients in need of the societal resource of reliable antibiotic therapy.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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