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Current State of Antimicrobial Stewardship at Solid Organ and Hematopoietic Cell Transplant Centers in the US

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Abstract

Objective—To assess the extent of antimicrobial stewardship programs (ASPs) at solid organ (SOT) and hematopoietic cell transplant (HCT) centers in the United States (US).

Design—An 18-item voluntary survey was developed by Memorial Sloan Kettering Cancer Center and University of Miami to gauge current antimicrobial stewardship practices in transplant patients, examine the availability and perceived usefulness of novel diagnostics and azole levels to guide therapy, and identify challenges for implementation of ASPs at these centers.

Participants—The survey was distributed electronically to Infectious Disease physicians and pharmacists at adult and pediatric SOT and HCT centers during May 1–22, 2015. Facilities were de-identified.

Results—After duplicate removal, 71 (56%) of 127 unique transplant centers in 32 states were analyzed. Forty-four sites (62%) performed 100 SOT annually, and forty (56%) performed 100 HCT annually. Top five stewardship activities encompassing transplant patients included formulary restriction, guideline development, prospective audit & feedback, education, and dose optimization. Respiratory viral panels (100%), azole levels (97%), and serum/BAL galactomannan (88%) were perceived as most useful to guide therapy. Apparent challenges to antimicrobial stewardship included: undefined duration for certain infections (90%), diagnostic uncertainty (80%), the perception that antibiotic-resistant infections required escalation (71%), prescriber opposition (69%), and costly drugs (63%).

Conclusions—ASP activities were performed at many adult and pediatric SOT and HCT centers in the US. Diagnostic and therapeutic uncertainty in transplant patients are challenging for ASPs.

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Collaborative research to examine the impact of antimicrobial stewardship practices in SOT and HCT should be explored.

INTRODUCTION

To tackle the growing problem of antibiotic resistance, an increasingly recognized strategy is to create a formal antimicrobial stewardship program (ASP) that is charged with optimizing antibiotic usage in the hospital.¹ While many hospitals are in the process or have developed an ASP, it is unknown whether stewardship practices are encompassing only the general patient population or whether immunocompromised patients such as cancer and solid organ transplant (SOT) are being included. Antimicrobial stewardship efforts in immunocompromised hosts can be challenging due to the complexity of cases, difficulty with accurate and timely diagnoses, and the high mortality related to invasive bacterial, fungal, and viral infections.²⁻⁴ Established stewardship strategies, such as prospective audit & feedback (PAF) and antimicrobial de-escalation, can be effectively performed in cancer patients.^{5,6} While there are sparse data for hematopoietic cell transplant (HCT) and none for SOT, cost-savings and other benefits of ASPs in the care of transplant patients are thought possible, as transplant recipients can be exposed to prolonged courses of broad-spectrum antimicrobial agents that in turn predispose them to colonization and infection by resistant organisms.⁷ For medical centers where there are established ASPs, it would be helpful to gauge the extent to which these programs are inclusive of transplant patients, how antimicrobial stewardship is being implemented, and what barriers need to be overcome. This is of particular importance as establishment of ASPs across all United States (US) acute care hospitals is one projected goal, as outlined in the *National Action Plan for Combating Antibiotic-Resistant Bacteria* released by the Obama administration in March 2015.⁸ We conducted a cross-sectional survey assessing current antimicrobial stewardship practices, the availability and perceived usefulness of novel diagnostics and azole levels to guide therapy, and implementation barriers of ASPs in hospitals treating SOT and hematopoietic cell transplant (HCT) patients in the US.

MATERIALS AND METHODS

Study Development

Institutional Review Boards at Memorial Sloan Kettering Cancer Center and the University of Miami approved the study. Investigators (LA and SS) jointly designed an 18-item electronic voluntary survey based on an accepted framework for stewardship practices in immunocompromised patients.²⁻⁴ Survey questions encompassed: hospital name and location (state), respondent's position within the hospital (physician, pharmacist, other), number of transplants (SOT, autologous and allogeneic HCT) performed annually, types of organ transplants performed, whether the facility had an ASP in place, years since ASP establishment, stewardship activities performed in hospital areas caring for transplant patients, measured outcomes, available microbiologic tests and their perceived usefulness, and barriers to antimicrobial stewardship for transplant patients. The questionnaire was pilot tested by the Chair and Co-Chair of the American Society of Transplantation (AST)'s

Infectious Disease Community of Practice (IDCOP) for readability, length, and relevance of specific items.

Study Population

One hundred twenty-seven medical centers performing HCT were identified from the National Marrow Donor Program (NMDP)'s "Be the Match" directory.⁹ Of these, 107 also performed SOT, as confirmed by each center's website. The survey was sent to one of the Infectious Disease (ID) physicians or pharmacists, who could then forward it to the person most knowledgeable about antimicrobial stewardship at the center. In addition, an invitation was distributed via electronic mail to the AST IDCOP members comprised of ID physicians and pharmacists involved in the care of SOT patients; only US respondents were included. The survey was open from May 1–22, 2015. Two reminders were sent at one-week intervals until the survey closed. Participation was voluntary, responses were anonymous, and no incentive was provided for completing the survey. Hospital name and location were collected for the purpose of removing duplicate responses. Only one respondent per site was included, and facilities were de-identified prior to analysis.

Data Analysis

Descriptive statistics including frequencies and proportions were computed to summarize the responses to all survey questions. All statistics were generated using SAS (ver.9.3, SAS Institute, Cary, NC).

RESULTS

Data from 87 unique respondents were collected. After duplicate hospital removal, responses from 71 (56%) of 127 unique medical centers from 32 states were analyzed. Twelve of 71 were freestanding children's hospitals. Respondents included 55 physicians, 15 pharmacists, and 1 unknown. Sixty-one medical centers (86%) performed SOT, whereas fifty-nine (83%) did autologous and/or allogeneic HCT. Forty-four sites (62%) performed 100 SOT annually, and forty (56%) performed 100 HCT annually. Types of SOT performed at respondents' sites included: kidney (n=57, 93%), kidney/pancreas (n=47, 77%), pancreas (n=37, 61%), liver (n=50, 82%), lung (n=33, 54%), heart (n=46, 75%), heart/lung (n=22, 36%), intestinal (n=13, 21%), and multi-visceral (n=14, 23%).

Of the 71 medical centers, 62 (87%) had an institutional ASP, as defined by a comprehensive program that functions continuously to monitor antimicrobial use and includes full-time equivalents (FTE) for a dedicated clinical pharmacist and/or adult or pediatric ID specialist; four (6%) were in the process of implementing an ASP, and three (4%) did not have an ASP. At sites with an ASP, 27 (44%) started their ASP 5 years ago, whereas 32 (52%) had longstanding ASPs of >5 years' duration; three (5%) sites were unsure. Of 62 ASPs, the proportion performing stewardship activities that was inclusive of adult SOT, adult HCT, pediatric SOT, and pediatric HCT was 46 (74%), 44 (71%), 29 (47%), and 31 (50%), respectively. Antimicrobial stewardship interventions encompassing transplant patients are shown in Table 1. The top five activities were formulary restriction (SOT: n=48, 77%; HCT: n=47, 76%), guideline development (SOT: n=44, 71%; HCT: n=47, 76%), PAF (n=43, 69%),

education (SOT: n=42, 68%; HCT: n=43, 69%), and dose optimization (SOT: n=43, 69%; HCT: n=42, 68%). Antibiotic cycling (SOT: n=2, 3%; HCT: n=3, 5%) was rarely performed.

The following guidelines were commonly developed at respondents' sites: empiric therapy for fever and neutropenia (F&N) (n=57, 86%), antifungal prophylaxis (n=57, 86%), treatment for invasive fungal infections (IFI) (n=42, 64%), cytomegalovirus (CMV) prophylaxis (n=54, 82%), and CMV treatment (n=46, 70%). Respondents also mentioned other locally developed transplant-specific guidelines, including infection control, management of "routine" infections (e.g., *Clostridium difficile*, pneumonia), management of respiratory viruses (e.g., influenza, respiratory syncytial virus), management and/or prevention of viral reactivations (e.g., BK virus, Epstein-Barr virus, hepatitis B, herpes simplex virus), preoperative prophylaxis for SOT, sepsis, and therapeutic drug level monitoring (e.g., vancomycin, azoles).

Table 1 also shows outcomes measured in transplant patients. Monitoring the rate of *C. difficile* infections was the most common outcome measure for both SOT and HCT, whereas devising transplant ward-specific antibiograms was least commonly done. However, 23% of respondents did not measure outcomes for SOT or HCT at all. Figure 1 shows the percent availability of novel diagnostics and azole levels for transplant patients. If available, respiratory viral panels (100%), azole levels (97%), and serum or bronchoalveolar lavage (BAL) galactomannan antigen (88%) were identified as being most useful to guide therapy. The other tests in order of decreasing utility were as follows: (1-3)-beta-D-glucan assay (BDG) (67%), matrix assisted laser desorption/ionization-time of flight (MALDI-TOF) (64%), multiplex polymerase chain reaction (PCR) (55%), fungal PCR (41%), peptide nucleic acid fluorescence *in situ* hybridization (PNA FISH) (35%), and procalcitonin levels (30%).

Perceived challenges for antimicrobial stewardship in transplant patients included: undefined duration for certain infections (90%), diagnostic uncertainty (80%), the perception that therapeutic escalation was required for suspected antibiotic-resistant infections (71%), prescriber opposition (69%), high-cost drugs (63%), turnaround delay for microbiologic test results (48%), and lack of outcomes data for antimicrobial stewardship in immunocompromised hosts (44%). Lack of ID physician (36%) or pharmacist (24%) staffing or lack of support by hospital administration (17%) rounded out the bottom of the list.

DISCUSSION

To the best of our knowledge, this is the first study to evaluate the extent to which institutional ASPs oversee antimicrobial utilization for both adult and pediatric SOT and HCT patients. Based on the high response rate, we had good geographic representation from transplant centers in the continental US. Although the majority of respondents had an institutional ASP, not all of these established programs were inclusive of adult and pediatric SOT and/or HCT transplant patients. This finding shows that there is still room for improvement in formalizing antimicrobial stewardship to encompass all patient populations, including transplant, across the continuum of care, as advocated by the Infectious Diseases

Society of America (IDSA), the Society for Healthcare Epidemiology of America (SHEA), and the Pediatric Infectious Diseases Society (PIDS).¹⁰ Certainly, significant attention is being placed on antimicrobial stewardship at a national level. In March 2015, the Obama administration released the *National Action Plan for Combating Antibiotic-Resistant Bacteria* that called for the establishment of ASPs in all acute care hospitals by 2020.⁸ In addition, both the Centers for Medicare & Medicaid Services (CMS) and the Leapfrog Group have incorporated a set of questions regarding compliance with the Centers for Disease Control and Prevention (CDC) standards for ASPs into their respective annual hospital surveys.^{11,12} All of these changes will impact SOT and HCT programs within acute care facilities.

Transplant patients are important targets for antimicrobial stewardship. Patients undergoing SOT or HCT are frequently exposed to prolonged courses of prophylactic and therapeutic antibiotics, which may contribute to the occurrence of adverse drug events (e.g., *Clostridium difficile* infection) and colonization and infection by multidrug-resistant organisms.^{13–15} There are also growing reports of antifungal and antiviral resistance occurring in transplant patients.^{16–18} Thus, efforts to optimize the selection, dosing, and duration of antimicrobial therapy both to improve patient outcomes and to minimize selective pressure are extremely relevant to this patient population. In order for stewardship efforts to be effective at a transplant center, ASP staff should be attuned to the complexities of caring for patients with varying degrees of immunosuppression, have expertise over a broad array of anti-infectives, and be informed of new diagnostic and therapeutic modalities that may affect transplant management.^{2,4}

Our study revealed that established ASPs overseeing transplant patients are following the blueprint outlined in the 2016 IDSA/SHEA guideline.¹ There was a slight edge in use of PAF over prior authorization in the transplant setting. While we did not query survey participants on how effective they found either core strategy to be, there is a small but growing body of literature that has reported on the feasibility and benefits of PAF or prior authorization in hematology-oncology units caring for cancer and HCT patients.^{5,19,20} The answer is not yet known as to the effectiveness of PAF or prior authorization in the SOT setting, as there are no dedicated studies to date. We also realized that active ASPs utilized a variety of supplemental stewardship interventions, including formulary restriction, guideline development, education, antimicrobial de-escalation, and intravenous to oral conversion, in the SOT or HCT setting. Because poorer guideline concordance, increased duration of therapy, and higher readmission rates have been reported in immunocompromised patients labeled with a drug allergy, ASPs can also consider initiatives to improve drug allergy assessments.^{1,21} Antimicrobial cycling was rarely performed, a finding compatible with the lack of endorsement by the 2016 IDSA/SHEA guideline.¹

Our survey found that commonly developed institutional guidelines included F&N, prophylaxis and treatment of IFI, and CMV management, all three being well-recognized infectious complications that can occur during the transplant course.^{22–24} Due to the disproportionate use of expensive and potentially toxic antibiotic, antifungal, and antiviral drugs in immunocompromised patients, creation of guidelines to guide prescribing of these agents is fitting. We did not ask our respondents on the specifics of guideline

implementation or the degree of guideline adherence by the transplant teams at their respective hospitals. However, it is worth mentioning that there is some evidence that facility-specific guidelines such as for F&N or IFI can improve antimicrobial utilization and quality of care, even with partial guideline adherence.^{25–29}

Although the role of rapid molecular diagnostic testing for transplant patients has not been clearly established, the fast return of accurate results over standard culture methods is appealing, so as to institute timely and appropriate therapy for documented infections. One trend, however, is the outsourcing of infrequently ordered microbiologic tests to reference laboratories as part of cost-containment and quality-control efforts, and several of these may be disproportionately requested for immunocompromised patients, leading to a delay in results.³⁰ It was interesting to learn that only respiratory viral PCR was available in-house for 97% of responding sites, followed by MALDI-TOF (56%). Microbiologic tests for diagnosis and management of IFI were typically send-outs (azole levels, 79%; BDG, 67%; serum or BAL galactomannan antigen, 50–52%). That being said, respondents felt that tests for diagnosis of respiratory virus or IFI were the most useful in guiding therapy. Diagnostic uncertainty and the turnaround delay in results were two cited barriers for antimicrobial stewardship in immunocompromised hosts. These areas should be further examined in order to find solutions to help us better optimize therapy in transplant and other immunocompromised patients.

Other perceived challenges included undefined duration of therapy for certain infections, the view that antibiotic-resistant infections require further escalation of therapy, and opposition from oncology and surgical colleagues. While we did not delve into this topic, the issue of prescriber opposition was explored in a recent study about stewardship barriers and goals in pediatric oncology and HCT.³¹ Our survey also showed that monitoring is not done robustly in transplant patients with the exception of *C. difficile* rates, followed by antimicrobial costs. According to the 2016 IDSA/SHEA guideline, every ASP should track antimicrobial utilization in order to examine overall consumption or compare usage by unit, provider, or service in the hospital.¹ Additionally, measurement of expenditures based on prescriptions or administrations and use of both process (e.g., guideline compliance) and outcome (e.g., proportion of patients with *C. difficile* related to antibiotic treatment) metrics are important to gauge the effectiveness of stewardship interventions.¹ Efforts dedicated to examining whether antimicrobial stewardship interventions are effective in transplant patients should be strongly encouraged.

One study limitation is that survey respondents were mostly from academic medical centers, so findings may not be generalizable to non-academic centers with transplant capabilities. Another limitation is that the role or position of the respondent was not uniform across centers; it is possible that the respondent may not have been familiar with all aspects of antimicrobial stewardship for transplant patients. We also did not collect formal data by transplant center with regard to antimicrobial use or resistance patterns, and although we have an understanding of what stewardship interventions are being done, the specifics of how these are executed and how these may impact the program were not evaluated. Due to constraints in survey length, factors facilitating antimicrobial stewardship in transplant centers, available resources, and stewardship practices utilized in ambulatory transplant

clinics were not explored. Finally, for questions that allowed for more than one answer, we were unable to verify whether the answers of non-respondents were true negatives versus skipping over the questions, so analyzing results by transplant volume to determine whether larger programs approached antimicrobial stewardship differently from smaller transplant programs was not performed due to an unknown denominator. Strengths of our study were that the survey was anonymous and voluntary, which likely reduced the tendency of respondents to provide “socially desirable” answers. We also had a high response rate, and participants were from well-established, high-volume adult and pediatric SOT and HCT centers located in different geographic regions across the US.

In conclusion, this study provides important information regarding the current state of ASPs in transplantation. ASP activities are performed at many adult and pediatric SOT and HCT centers in the US. However, diagnostic and therapeutic uncertainty in transplant patients are challenging for ASPs. Collaborative research to examine the impact of antimicrobial stewardship practices in SOT and HCT should be explored.

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References

1. Barlam TF, Cosgrove SE, Abbo LM, et al. Implementing an antibiotic stewardship program: guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis*. 2016; 62:e51–e77. [PubMed: 27080992]
2. Mihu, C., Paskovaty, A., Seo, SK. Antimicrobial stewardship considerations for cancer centers. In: Safdar, A., editor. *Principles and Practice of Cancer Infectious Diseases*. Totowa, NJ: Humana Press; 2011. p. 491-498.
3. Tverdek FP, Rolston KV, Chemaly RF. Antimicrobial stewardship in patients with cancer. *Pharmacotherapy*. 2012; 32:722–734. [PubMed: 23307520]
4. Abbo LM, Ariza-Heredia EJ. Antimicrobial stewardship in immunocompromised hosts. *Infect Dis Clin North Am*. 2014; 28:263–279. [PubMed: 24857392]
5. Cosgrove SE, Seo SK, Bolon MK, et al. Evaluation of postprescription review and feedback as a method of promoting rational antimicrobial use: a multicenter intervention. *Infect Control Hosp Epidemiol*. 2012; 33:374–380. [PubMed: 22418633]
6. Paskovaty A, Pastores SM, Gedrimaite Z, Kosteletzky N, Riedel ER, Seo SK. Antimicrobial de-escalation in septic cancer patients: is it safe to back down? *Intensive Care Med*. 2015; 41:2022–2023. [PubMed: 26297120]
7. Aitken SL, Palmer HR, Topal JE, Gabardi S, Tichy E. Call for antimicrobial stewardship in solid organ transplantation. *Am J Transplant*. 2013; 13:2499. [PubMed: 23865747]
8. [Accessed December 1, 2015] National action plan for combating antibiotic-resistant bacteria. The White House website. <https://www.whitehouse.gov/the-press-office/2015/03/27/fact-sheet-obama-administration-releases-national-action-plan-combat-ant>. Published 2015
9. [Accessed March 18, 2015] Be the Match transplant center directory. National Marrow Donor Program website. <https://bethematch.org/TCDirectory/Search>
10. Society for Healthcare Epidemiology of America, Infectious Diseases Society of America, Pediatric Infectious Diseases Society. Policy statement on antimicrobial stewardship by the Society for Healthcare Epidemiology of America (SHEA), the Infectious Diseases Society of America

(IDSA), and the Pediatric Infectious Diseases Society (PIDS). *Infect Control Hosp Epidemiol.* 2012; 33:322–327. [PubMed: 22418625]

11. [Accessed February 3, 2016] Hospital infection control worksheet. Centers for Medicare & Medicaid Services website. <http://go.cms.gov/1B6NCSV>
12. [Accessed February 3, 2016] Changes to the Leapfrog hospital survey. The Leapfrog Group website. http://www.leapfroggroup.org/Hospitals/SurveyInfo/Comment_Form_LF_Survey_2016
13. Cervera C, van Delden C, Gavalda J, et al. Multidrug-resistant bacteria in solid organ transplant recipients. *Clin Microbiol Infect.* 2014; 20(Suppl 7):49–73.
14. Kamboj M, Son C, Cantu S, et al. Hospital-onset *Clostridium difficile* infection rates in persons with cancer or hematopoietic stem cell transplant: a C3IC network report. *Infect Control Hosp Epidemiol.* 2012; 33:1162–1165. [PubMed: 23041818]
15. Macesic N, Morrissey CO, Cheng AC, Spencer A, Peleg AY. Changing microbial epidemiology in hematopoietic stem cell transplant recipients: increasing resistance over a 9-year period. *Transpl Infect Dis.* 2014; 16:887–896. [PubMed: 25298044]
16. Steinmann J, Hamprecht A, Vehreschild MJ, et al. Emergence of azole-resistant invasive aspergillosis in HSCT recipients in Germany. *J Antimicrob Chemother.* 2015; 70:1522–1526. [PubMed: 25630644]
17. Chou S. Approach to drug-resistant cytomegalovirus in transplant recipients. *Curr Opin Infect Dis.* 2015; 28:293–299. [PubMed: 26098499]
18. Frobert E, Burrel S, Ducastelle-Lepretre S, et al. Resistance of herpes simplex viruses to acyclovir: an update from a ten-year survey in France. *Antiviral Res.* 2014; 111:36–41. [PubMed: 25218782]
19. Yeo CL, Chan DS, Earnest A, et al. Prospective audit and feedback on antibiotic prescription in an adult hematology-oncology unit in Singapore. *Eur J Clin Microbiol Infect Dis.* 2012; 31:583–590. [PubMed: 21845470]
20. Standiford HC, Chan S, Tripoli M, Weekes E, Forrest GN. Antimicrobial stewardship at a large tertiary care academic medical center: cost analysis before, during, and after a 7-year program. *Infect Control Hosp Epidemiol.* 2012; 33:338–345. [PubMed: 22418628]
21. Trubiano JA, Leung VK, Chu MY, Worth LJ, Slavin MA, Thursky KA. The impact of antimicrobial allergy labels on antimicrobial usage in cancer patients. *Antimicrob Resist Infect Control.* 2015; 4:23. eCollection 2015. doi: 10.1186/s13756-015-0063-6 [PubMed: 26034582]
22. Tomblyn M, Chiller T, Einsele H, et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. *Biol Blood Marrow Transplant.* 2009; 15:1143–1238. [PubMed: 19747629]
23. Freifeld AG, Bow EJ, Sepkowitz KA, et al. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. *Clin Infect Dis.* 2011; 52:e56–93. [PubMed: 21258094]
24. Blumberg EA, Danziger-Isakov L, Kumar D, Michaels MG, Razonable RR. Foreword: Guidelines 3. *Am J Transplant.* 2013; 13(Suppl 4):1–2.
25. Nucci M, Landau M, Silveira F, Spector N, Pulcheri W. Application of the IDSA guidelines for the use of antimicrobial agents in neutropenic patients: impact on reducing the use of glycopeptides. *Infect Control Hosp Epidemiol.* 2001; 22:651–653. [PubMed: 11776354]
26. Rosa RG, Goldani LZ, dos Santos RP. Association between adherence to an antimicrobial stewardship program and mortality among hospitalised cancer patients with febrile neutropaenia: a prospective cohort study. *BMC Infect Dis.* 2014; 14:286. [PubMed: 24884397]
27. Pakakasama S, Surayuthpreecha K, Pandee U, et al. Clinical practice guidelines for children with cancer presenting with fever to the emergency room. *Pediatr Int.* 2011; 53:902–905. [PubMed: 21418423]
28. Zuckermann J, Moreira LB, Stoll P, Moreira LM, Kuchenbecker RS, Polanczyk CA. Compliance with a critical pathway for the management of febrile neutropenia and impact on clinical outcomes. *Ann Hematol.* 2008; 87:139–145. [PubMed: 17938926]
29. Mondain V, Lieutier F, Hasseine L, et al. A 6-year antifungal stewardship programme in a teaching hospital. *Infection.* 2013; 41:621–628. [PubMed: 23463185]

30. Procop GW, Winn W. Microbiology Resource Committee, College of American Pathologists. Outsourcing microbiology and offsite laboratories. Implications on patient care, cost savings, and graduate medical education. *Arch Pathol Lab Med.* 2003; 127:623–624. [PubMed: 12708912]
31. Wolf J, Sun Y, Tang L, et al. Antimicrobial stewardship barriers and goals in pediatric oncology and bone marrow transplantation: a survey of antimicrobial stewardship practitioners. *Infect Control Hosp Epidemiol.* 2016; 37:343–347. [PubMed: 26639441]

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Figure 1. Availability of novel diagnostics and azole levels for transplant patients

BAL, bronchoalveolar lavage; BDG, (1-3)-beta-D-glucan; MALDI-TOF, matrix assisted laser desorption/ionization-time of flight; PCR, polymerase chain reaction; PNA FISH, peptide nucleic acid fluorescence *in situ* hybridization

Table 1

Antimicrobial stewardship interventions and outcomes encompassing transplant patients

Interventions	Hematopoietic Cell Transplant^I	Solid Organ Transplant^I	Not familiar/Not applicable^I
Formulary restriction	47 (76%)	48 (77%)	11 (18%)
Guideline development	47 (76%)	44 (71%)	12 (19%)
Prospective audit & feedback	43 (69%)	43 (69%)	16 (26%)
Education	43 (69%)	42 (68%)	17 (27%)
Dose optimization	42 (68%)	43 (69%)	17 (27%)
Prior authorization	39 (63%)	40 (65%)	18 (29%)
Antimicrobial de-escalation	36 (58%)	37 (60%)	22 (35%)
Intravenous to oral conversion	35 (56%)	36 (58%)	24 (39%)
Time-sensitive stop orders	23 (37%)	24 (39%)	38 (61%)
Computerized decision support	22 (35%)	23 (37%)	38 (61%)
Antimicrobial order forms	21 (34%)	22 (35%)	38 (61%)
Antimicrobial cycling	3 (5%)	2 (3%)	59 (95%)
None. Transplant patients are excluded.	1 (2%)	1 (2%)	61 (98%)
Outcomes			
Antimicrobial use	21(34%)	17 (27%)	31 (50%)
Antimicrobial costs	32 (52%)	31 (50%)	19 (31%)
Rate of <i>Clostridium difficile</i> infections	40 (65%)	35 (56%)	14 (23%)
Reduction in length-of-stay	13 (21%)	13 (21%)	37 (60%)
Transplant-specific antibiogram	10 (16%)	7 (11%)	42 (68%)
None	14 (23%)	14 (23%)	38 (61%)

^I There were 62 medical centers with antimicrobial stewardship programs responding.