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Risk factors for multidrug-resistant organisms among deceased organ donors

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Abstract

Donor infection or colonization with a multidrug-resistant organism (MDRO) impacts organ utilization and recipient antibiotic management. Approaches to identifying donors at risk of carrying MDROs are unknown. We sought to determine the risk factors for MDROs among transplant donors. A multicenter retrospective cohort study was conducted at four transplant centers between 2015 and 2016. All deceased donors who donated at least one organ were included. Cultures obtained during the donor's terminal hospitalization and organ procurement were evaluated. The primary outcome was isolation of an MDRO on culture. Multivariable Cox regression was used to determine risk factors associated with time to donor MDRO. Of 440 total donors, 64 (15%) donors grew an MDRO on culture. Predictors of an MDRO on donor culture included: hepatitis C viremia (hazard ratio [HR] 4.09, 95% CI 1.71–9.78, *P*=0.002), need for dialysis (HR 4.59, 95% confidence interval [CI] 1.09–19.21, *P*=0.037), prior hematopoietic cell transplant (HR 7.57, 95% CI 1.03–55.75, *P*=0.047), and exposure to antibiotics with a narrow

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the the end of this article.

DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author upon reasonable request.

gram-negative spectrum (HR 1.13, 95% CI 1.00–1.27, *P*=0.045). This is the first study to determine risk factors for MDROs among deceased donors and will be important for risk stratifying potential donors and informing transplant recipient prophylaxis.

1. INTRODUCTION

One of the most significant issues facing solid organ transplantation (SOT) is the limited supply of organ donors. Deceased donors with positive bacterial cultures have been utilized inconsistently in the past due to prior reports of SOT donors transmitting bacteria to their organ recipients via the allograft, causing donor-derived bacterial infections (DDBIs)[1–4]. DDBIs have been linked to poor outcomes including vascular anastomosis dehiscence, overwhelming infection, and death[1–4].

One area of particular concern is the organ donor who carries a multidrug-resistant organism (MDRO), since a DDBI due to an MDRO may be more difficult to treat in the recipient. Indeed, there are several case series describing transmission of MDROs from donors to recipients with poor attendant outcomes[5]. Because of this, the current national transplant guidelines recommend exercising caution when considering the use of organs that may carry an MDRO[6]. Importantly, however, donor cultures are not uniformly finalized prior to donor evaluation, so the presence of an MDRO on donor culture may be discovered after the decision about organ use has been made.

The presence of an MDRO on donor culture not only impacts whether an organ is used, but may also impact the perioperative antibiotic regimen administered to the recipient[7]. Observational studies have suggested that peri- and post-operative antibiotics for the recipient that are active against donor organisms may reduce the risk for DDBIs[8,9]. Standard perioperative prophylaxis regimens for SOT procedures do not target MDROs, however[10,11]. Thus, the ability to identify donors, prior to transplantation, who are at higher risk of carrying an MDRO would be crucial for determining the antibiotic regimen for the recipient. This would be a preferable strategy to broadening perioperative prophylaxis for all transplant recipients, because the antibiotics required to treat MDROs often confer additional toxicities and may themselves promote emergence of MDROs.

Though risk factors for MDROs in the general population have been well-studied, there are no published studies to our knowledge that have determined risk factors associated with MDROs among deceased organ donors specifically. Although all deceased donors are admitted to an intensive care unit (ICU) during their terminal hospitalization (a known risk factor for MDRO colonization[12,13]), deceased organ donors are typically younger, with fewer medical comorbidities, increased rates of injection drug use (IDU), and increased rates of traumatic injuries compared to the general population receiving ICU care[14,15]. In addition, the clinical data available to transplant centers about the organ donor is more limited than that available to clinicians when caring for a hospitalized patient directly[14]. Thus, there is a pressing need to determine the donor factors that are (1) associated with MDROs and (2) can be determined by transplant centers at the time of donor evaluation, so that donors can be risk stratified prior to organ procurement. In this study, we sought to identify risk factors associated with MDROs among deceased SOT donors.

2. MATERIALS AND METHODS

2.1 Study design and setting.

A multicenter retrospective cohort study was performed at four tertiary care transplant centers in Philadelphia: the Hospital of the University of Pennsylvania (HUP) (776 beds), Temple University Hospital (TUH) (722 beds), Hahnemann University Hospital (HUH) (496 beds), and Albert Einstein Medical Center (AEMC) (772 beds).

2.2 Study population.

The initial source population included all deceased donors who were evaluated by the local organ procurement organization (OPO)—the Gift of Life Donor Program (GLDP)—and who ultimately donated at least one organ to a recipient at one of the participating transplant centers between January 1, 2015 and July 1, 2016. Eligible donors were identified by the GLDP, which evaluates all deceased organ donors in eastern Pennsylvania, southern New Jersey, and Delaware. Donors who were imported from outside of the GLDP's region were not included.

2.3 Outcome.

The primary outcome was time to donor MDRO on a bacterial culture that was taken as part of clinical care during the donor's terminal hospitalization (hereafter referred to as a "hospital culture") or at the time of organ procurement (hereafter referred to as an "OPO culture"). We included the following organisms in our definition of MDROs: methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* species (VRE), extended-spectrum cephalosporin-resistant (ESC-R) Enterobacteriaceae (EB), carbapenem-resistant EB (CRE), multidrug-resistant (MDR)-*Pseudomonas* species, and MDR-*Acinetobacter* species[16,17]. Cultures from any anatomic site were considered. The distinction of infection versus colonization with the MDRO pathogen was not determined because (1) this is difficult to determine among organ donors for whom limited clinical data are available; (2) donor infection is not routinely differentiated from colonization by transplant clinicians when determining which organs to accept and what perioperative prophylaxis regimen to administer to the recipient[18,19].

Each donor was included as a subject only once. If an MDRO pathogen was isolated on multiple occasions in the same patient, only the first episode was considered. The study was approved by the Institutional Review Board at each of the participating transplant centers (see Supporting Information [A]).

2.4 Data collection.

Data on donors were abstracted from the GLDP medical record system. Information was collected on the following: donor demographics (e.g., age, gender, race), comorbidities (e.g., diabetes, asthma, hemodialysis, substance use disorders), outpatient medications, IDU, procedures performed during the terminal hospitalization, medications administered during the terminal hospitalization (including all antibiotics and administration of the T4 protocol[20,21]), death mechanism, donor type (donation after circulatory death [DCD] versus donation after brain death [DBD]), whether the donor was a standard criteria donor (SCD) or

expanded criteria donor (ECD), Public Health Service (PHS)-increased risk status[22,23], viral serologies (e.g. for hepatitis C virus [HCV]), donor cultures (including the date of culture, anatomic site of culture, organism(s) that grew on culture, and the organism's *in vitro* susceptibilities).

For the purposes of the analysis, antibiotic exposures were grouped into four major categories: (1) broad Gram-negative (GN) coverage; (2) narrow GN coverage; (3) broad Gram-positive (GP) coverage; and (4) narrow GP coverage (see Supporting Information [B] for details of the antibiotic categories). All antibiotics administered to the donors are included in one of the antibiotic groups above. Antibiotic exposures were evaluated as both binary (any exposure or none) and continuous variables (duration of antibiotic exposures, measured in days).

Following the initial analyses using this antibiotic grouping, we performed three sensitivity analyses where the definition of "narrow GN antibiotics" was revised (see Supporting Information [D.2.] for details).

2.5 Susceptibility testing of bacterial isolates.

Susceptibility testing of donor bacterial isolates was performed at either the donor hospital's microbiology laboratory or the GLDP's reference laboratory (LabsInc, Denver, CO). The *in vitro* susceptibilities were not able to be confirmed due to the retrospective nature of the study and the innumerable different donor hospitals from which the donors originated. The *in vitro* antibiotic susceptibility profile of each organism that grew on hospital or OPO cultures was reviewed by an infectious diseases trained physician (J.A.A.) and was used to categorize donors as having grown an MDRO pathogen or not. The Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network (NHSN) criteria for MDROs was used to define VRE, MRSA, ESC-R EB, CRE, MDR-*Pseudomonas*, and MDR-*Acinetobacter*[17] (see Supporting Information [C] for precise definitions).

2.6 Statistical analysis.

Donors were characterized by potential risk factors, such as demographics, comorbidities, death mechanism, and antibiotic exposures during the terminal hospitalization. Continuous variables were compared using the Student t-test or Wilcoxon rank-sum test, and categorical variables were compared using the χ^2 or Fisher exact test. For the adjusted analysis, a survival analysis was employed. The primary outcome was time to first donor MDRO. The time at risk was measured in days. Time zero was the first day of the donor's terminal hospitalization. The failure event was an MDRO pathogen on culture; the failure date was the day on which the culture that grew an MDRO was collected from the donor. MDRO colonization status before the terminal admission was unknown. Donors were censored when their organs were procured. We ascertained antibiotics administered during the time at risk, and these were modeled as time-varying covariates in order to account for both duration and patterns of use.

A Kaplan Meier curve was plotted to assess the overall time to donor MDRO in this population. To assess whether duration of hospitalization affected the risk for donor MDROs, we evaluated a Hazard Estimate Plot, which shows the instantaneous hazard for an

MDRO during the terminal hospital. Subsequently, bivariable Cox proportional hazard regression was used to examine the relationship between each risk factor and time to MDRO. Variables from bivariable analyses with *P* values <0.20 were considered for inclusion in the final multivariable model. Variables were added to the model in order of biologic plausibility. Variables were retained in the final model if they had a *P* value of <0.05 in the multivariable Cox model. The proportional hazards assumption was verified. A hazard ratio (HR) and 95% confidence interval (CI) were calculated to evaluate the strength of any association.

Subgroup analyses were then performed evaluating (1) time to MRSA, and (2) time to ESC-R EB. These subanalyses were performed to investigate whether the risk factors for the most common MDR-GP organism may be different than the risk factors for the most common MDR-GN organism. The same statistical approach was used for these subgroup analyses as was described for the primary outcome. All analyses were performed using STATA v.14.0 (StataCorp, College Station, Texas).

3. RESULTS

3.1 Study population.

A total of 440 deceased organ donors gave at least one organ to an SOT recipient at one of the four transplant centers during the study period. Of these, 64 (15%) had an MDRO pathogen isolated from a hospital or OPO culture.

Among the entire study cohort, the median age was 37 years (interquartile range [IQR] 27–52), and 183 (41%) were women. Sixty-four (15%) were DCD, 84 (19%) were ECD, and 150 (34%) met the PHS-increased risk criteria. The most common comorbidities included hypertension (124, 28%) and chronic respiratory diseases (e.g. emphysema) (73, 17%). The median number of organs donated per donor was 3 (IQR 2–5). The median length of stay for the terminal hospitalization was 3 days (IQR 2–5, range 1–84). See Table 1 for additional donor baseline characteristics.

3.2 Overview of donor culture results.

Of the 440 donors, 380 (86%) had at least one positive bacterial culture that was obtained during the terminal hospitalization or at the time of organ procurement. The median number of positive cultures per donor was 2 (IQR 1–3, range 0–8). The most common anatomical site of bacterial growth was the respiratory tract, with 337 (76%) donors having a positive sputum culture and 127 (29%) having a positive bronchoalveolar lavage (BAL) culture (not mutually exclusive). There were fewer positive blood (49, 11%) and urine cultures (70, 16%). Among OPO cultures, there were 26 (6%) with a positive ureter culture and 37 (8%) with a positive perfusate culture.

The most common organism isolated on donor cultures was *S. aureus* (183, 42% of donors). This was followed by Enterobacteriaceae (139, 32% of donors) and *Candida* species (127, 29% of donors). The most common MDRO pathogens were MRSA (40, 9% of donors) and ESC-R EB (20, 5% of donors). The most common site of MDRO pathogen growth was the respiratory tract (53, 12% of donors). There were five donors (1%) who were bacteremic

with an MDRO: three with MRSA, one with MDR-*Pseudomonas*, and one with ESC-R EB. There were four donors who grew more than one MDRO species. See Table 2 for additional information on the donor culture results.

3.3 Risk factors for MDRO pathogens on donor cultures.

The time to donor MDRO for the entire cohort is shown in the Kaplan Meier failure curve (Figure 1). Of note, three donors did not contribute any time at risk because they grew an MDRO pathogen on the day of admission. The Kaplan Meier curve shows that 20% of donors were colonized with an MDRO by day 10 (95% CI 7–14), and 33% of donors were colonized with an MDRO by day 15 (95% CI 10–31).

On multivariable analysis (Table 3), we found that there was an increased hazard of MDRO pathogens among donors with HCV viremia (aHR 4.09, 95% CI 1.71–9.78, P=0.002), a prior hematopoietic cell transplant (HCT) (aHR 7.57, 95% CI 1.03–55.76, P=0.047), and need for dialysis (aHR 4.59, 95% CI 1.09–19.21, P=0.037). We also found that any exposure to narrow GN antibiotics during the terminal hospitalization was associated with a significantly increased hazard of donor MDROs (aHR 1.13, 1.00–1.27, P=0.045). Further, there was a significant association between the duration of narrow GN antibiotics and the hazard of donor MDROs (aHR 1.04, 95% CI 1.01–1.07, P=0.018, per day of additional exposure) (Supporting Information Table 1). Finally, we also found that donors who had tetrahydrocannabinol (THC) detected on their toxicology screen at the time of admission to their terminal hospitalization had a borderline increased hazard of MDRO pathogens (aHR 1.90, 95% CI 0.97–3.73, P=0.061).

3.4 Risk factors for MRSA and ESC-R EB growth on donor cultures.

On multivariable analysis, we found that there was an increased hazard of MRSA among donors with HCV viremia (aHR 5.39, 95% CI 2.02–14.36, P=0.001), prior HCT (aHR 18.95, 95% CI 2.43–147.55, P=0.005), receipt of the T4 protocol (aHR 5.12, 95% CI 1.49–17.63, P=0.010), and a positive toxicology screen for THC (aHR 2.88, 95% CI 1.33–6.24, P=0.007) (Table 4). Any exposure to antibiotics with narrow GP coverage during the terminal hospitalization was associated with a reduced hazard of MRSA (aHR 0.80, 95% CI 0.66–0.98, P=0.032) (Table 4), though the duration of exposure to narrow GP antibiotics was not significantly associated with the outcome (data not shown).

Next, we found on multivariable analysis that there was an increased hazard of ESC-R EB among donors who died due to asphyxiation (aHR 5.85, 95% CI 1.86–18.39, P=0.003) and donors who were exposed to narrow GN antibiotics during their terminal hospitalization (aHR 1.17, 95% CI 1.01–1.37, P=0.039) (Table 5). The duration of exposure to narrow GN antibiotics was not significantly associated with the outcome (aHR 1.04, 95% CI 0.99–1.09, P=0.117, data not shown).

3.5 Sensitivity analyses for antibiotic categorization.

Secondarily, three revised categorizations of the “narrow GN antibiotic” group were evaluated, and their association with any donor MDRO and donor ESC-R EB was determined. There were no significant associations between the revised versions of narrow

GN antibiotics and the outcomes. The results are detailed in the Supporting Information (D. 2.).

4. DISCUSSION

In this multicenter cohort study, we found that deceased donors with HCV viremia, a history of dialysis, a history of HCT, and exposure to antibiotics with a narrow GN spectrum during their terminal hospitalization were at increased risk for an MDRO. These findings represent the first evaluation of risk factors for MDROs among deceased organ donors to date, and provide a preliminary framework for a novel, standardized preemptive strategy for (1) risk stratification of potential donors and (2) determining a personalized perioperative antibiotic prophylaxis regimen for recipients. This would represent a significant innovation over the current practice, where donor MDROs are often discovered after transplantation, delaying targeted recipient prophylaxis.

The significant association between donor HCV viremia and growth of an MDRO, particularly MRSA, is a novel finding that is uniquely important in the deceased donor cohort. This association may be related to the direct link between HCV viremia and IDU; it has been shown previously that there is a cumulative increase in risk for HCV infection with increasing duration of IDU[24]. IDU in turn is a well-established risk factor for bacterial infections, particularly MRSA[25–27]. Though a history of IDU was captured as a separate variable in this study, and was not significantly associated with the outcome, the accuracy of the information obtained about IDU is unclear given the reporting by a surrogate and the stigma associated with IDU[14]. Thus, HCV viremia may be an objective measure of IDU activity. Active HCV infection is also known to have immunomodulatory effects, as does the liver dysfunction associated with long-standing HCV viremia, which may increase the risk for MDRO infection[28,29]. With the current opioid and IDU epidemic in the US, as well as the debate in the transplant field about how donors with HCV should be utilized, this is an important finding that merits further study; our study would suggest that an unintended consequence of HCV-positive donation may include an increased risk of MDRO transmission[15,30–33].

The association between medical comorbidities—including dialysis and prior HCT—and risk of MDROs has been well-established in prior studies of the general population[34–38]. It should be noted that both dialysis and prior HCT were infrequent comorbidities among our deceased donor cohort, and thus, further study is required to confirm their significance.

Our study also confirmed an important relationship between exposure to narrow GN antibiotics and donor MDROs, particularly ESC-R EB. We found that with each additional day of narrow GN antibiotic exposure, there was a 4% increase in the hazard of MDROs. This is consistent with prior literature that has shown antibiotic exposures to be a key risk factor for the development of MDROs[39,40]. Notably, however, we also found that *any* exposure to narrow GN antibiotics was associated with an increased risk of donor MDROs, suggesting that prolonged antibiotic exposure is not required to promote the emergence of MDROs among deceased donors.

We also found that recent use of THC was associated with a borderline increased risk of any MDRO pathogen and a significantly increased risk of MRSA on donor culture. It has been previously shown that marijuana smoking can cause chronic respiratory disease and pneumonia, which may increase the risk for MDROs including MRSA in the respiratory tract[41,42]. Further, there have been recent reports documenting abundant bacterial (as well as fungal) colonization of marijuana, including MDRO pathogens[43]. Finally, THC has been shown previously to have immunomodulatory effects[44,45], which could impact the donor's risk for MDRO infection or colonization.

We secondarily performed risk factor analyses for MRSA and ESC-R EB. These subgroup analyses were limited by smaller cohorts, but we identified unique risk factors for each. We observed (1) an increased risk for MRSA associated with administration of the T4 protocol to donors, and (2) a reduced risk for MRSA when donors were administered antibiotics with narrow GP activity. The T4 protocol is typically employed as one component of "aggressive management of brain-dead donors" which also includes pulmonary artery catheterization, intravenous fluid resuscitation, and vasopressor infusions[21]. Such management may increase the risk for bacterial infections, particularly MDROs, due to the extensive central venous access required. Further, the administration of high-dose glucocorticoids as part of the T4 protocol may result in a degree of immune dysfunction that also increases this risk. The association between narrow GP antibiotics and a reduced hazard of MRSA likely relates to the fact that narrow GP agents are the standard perioperative antibiotics used by the GLDP at the time of organ procurement. Thus, narrow GP antibiotics are likely a marker for donors who were not previously known to be colonized with MRSA or went to organ procurement without the need for additional, broader antibiotics (e.g. due to growing an MDRO pathogen).

In the ESC-R EB analysis, we found that there was an increased risk for ESC-R EB among donors who died due to asphyxiation. This association may be related to the fact that all donors with death from asphyxiation (e.g. drowning, hanging) have hypoxic and hypoventilatory respiratory failure and require significant mechanical ventilatory support[46]; respiratory failure and mechanical ventilation are known to increase the risk of respiratory colonization and infection with MDR-GNs including ESC-R EB[47,48].

There are several potential limitations of our study: (1) Since donor hospital cultures were obtained during routine care, donors who did not have infectious symptoms may have had fewer bacterial cultures obtained, which may have limited the detection of an MDRO. The OPO cultures performed by the GLDP are standardized, however, so every donor had the opportunity to have an MDRO detected. Further, any heterogeneity in MDRO surveillance practices between hospitals could impact recovery of MDROs, but none of the MDROs that contributed to the outcomes in this study were obtained from surveillance cultures. (2) We did not capture information about donor travel history and were not able to account for this in the evaluation of risk factors for MDROs. (3) "MDRO pathogens" include a variety of different organisms which may have different risk factors; the size of the study precluded a fully stratified analysis for each organism—or a stratification based on anatomical site of MDRO growth—but we were able to evaluate risk factors for MRSA and ESC-R EB separately so as to partially address this issue. (4) These data were collected from a single

OPO, and the results may not be generalizable to other institutions with dissimilar rates of MDROs among deceased donors. (5) The majority of MDROs were grown on respiratory tract samples, and there is considerable controversy as to the significance of respiratory tract cultures for non-lung recipients. However, we sought to capture both infection and colonization with MDROs in this study, and isolation of an MDRO from the respiratory tract does signify donor colonization with that MDRO. (6) Because clinical data on deceased donors prior to their terminal hospitalization is not available, we are not able to determine the proportion of the donors who were colonized with an MDRO prior to their terminal hospitalization.

In conclusion, the results of our study provide the first determination of donor factors associated with MDRO colonization or infection. We found that 20% of deceased donors are colonized with an MDRO by day 10 of their terminal hospitalization. We identified two novel risk factors for MDRO pathogens, particularly MRSA, that are uniquely important to the deceased donor pool, namely HCV viremia and recent THC use. Although DDBIs are uncommon, the potential for adverse outcomes in recipients with MDRO DDBIs is high due to delayed administration of appropriate antimicrobials. Moreover, the increasing use of expanded criteria donors, including those with HCV, makes it likely that more donors will be infected or colonized with an MDRO in the future. Consequently, this first study identifying risk factors for donor MDROs may aid in earlier administration of appropriate empiric antibiotics for recipients, and will likely be an important tool for improving transplant outcomes. Further studies are needed to determine the impact of MDROs on the donor pool, the true risk for transmission of such MDROs to SOT recipients, and the impact that prophylaxis has on this transmission rate.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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DISCLOSURE

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Abbreviations

AEMC	Albert Einstein Medical Center
BAL	Bronchoalveolar lavage

CRE	Carbapenem-resistant Enterobacteriaceae
CDC	Centers for Disease Control and Prevention
CLSI	Clinical and Laboratory Standards Institute
CI	Confidence interval
DBD	Donation after brain death
DCD	Donation after circulatory death
DDBI	Donor-derived bacterial infection
EB	Enterobacteriaceae
ECD	Expanded criteria donor
ESBL	Extended-spectrum beta-lactamase
ESC-R	Extended-spectrum cephalosporin-resistant
GLDP	Gift of Life Donor Program
GN	Gram-negative
GP	Gram-positive
HUH	Hahnemann University Hospital
HR	Hazard ratio
HCT	Hematopoietic cell transplant
HCV	Hepatitis C virus
HUP	Hospital of the University of Pennsylvania
IDU	Injection drug use
ICU	Intensive care unit
IQR	Interquartile range
MRSA	Methicillin-resistant *Staphylococcus aureus*
MDR	Multidrug-resistant
MDRO	Multidrug-resistant organism
NHSN	National Healthcare Safety Network
OPO	Organ procurement organization
PHS	Public Health Service
SOT	Solid organ transplantation

Spp	Species
SCD	Standard criteria donor
TUH	Temple University Hospital
THC	Tetrahydrocannabinol
T4	Thyroxine
VRE	Vancomycin-resistant *Enterococcus*

REFERENCES

1. Doig RL, Boyd PJ, Eykyn S. Staphylococcus aureus transmitted in transplanted kidneys. Lancet. 1975;2(7928):243–245. [PubMed: 49795]
2. Nelson PW, Delmonico FL, Tolkoff-Rubin NE, et al. Unsuspected donor pseudomonas infection causing arterial disruption after renal transplantation. Transplantation. 1984;37(3):313–314. [PubMed: 6367169]
3. McCoy GC, Loening S, Braun WE, Magnusson MO, Banowsky LH, McHenry MC. The fate of cadaver renal allografts contaminated before transplantation. Transplantation. 1975;20(6):467–472. [PubMed: 1108317]
4. Spees EK, Light JA, Oakes DD, Reinmuth B. Experiences with cadaver renal allograft contamination before transplantation. Br J Surg. 1982;69(8):482–485. [PubMed: 7049310]
5. Lewis JD, Sifri CD. Multidrug-Resistant Bacterial Donor-Derived Infections in Solid Organ Transplantation. Curr Infect Dis Rep. 2016;18(6):18. [PubMed: 27115701]
6. Wolfe CR, Ison MG, Practice ASTIDCo. Donor-derived infections: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant. 2019:e13547. [PubMed: 30903670]
7. Ison MG, Grossi P, Practice ASTIDCo. Donor-derived infections in solid organ transplantation. Am J Transplant. 2013;13 Suppl 4:22–30. [PubMed: 23464995]
8. Mularoni A, Bertani A, Vizzini G, et al. Outcome of Transplantation Using Organs From Donors Infected or Colonized With Carbapenem-Resistant Gram-Negative Bacteria. Am J Transplant. 2015;15(10):2674–2682. [PubMed: 25981339]
9. Miller R, Covington S, Taranto S, et al. Communication gaps associated with donor-derived infections. Am J Transplant. 2015;15(1):259–264. [PubMed: 25376342]
10. Anesi JA, Blumberg EA, Abbo LM. Perioperative Antibiotic Prophylaxis to Prevent Surgical Site Infections in Solid Organ Transplantation. Transplantation. 2018;102(1):21–34. [PubMed: 28614192]
11. Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infect (Larchmt). 2013;14(1):73–156. [PubMed: 23461695]
12. Maechler F, Pena Diaz LA, Schroder C, Geffers C, Behnke M, Gastmeier P. Prevalence of carbapenem-resistant organisms and other Gram-negative MDRO in German ICUs: first results from the national nosocomial infection surveillance system (KISS). Infection. 2015;43(2):163–168. [PubMed: 25395161]
13. Warren DK, Nitin A, Hill C, Fraser VJ, Kollef MH. Occurrence of co-colonization or co-infection with vancomycin-resistant enterococci and methicillin-resistant Staphylococcus aureus in a medical intensive care unit. Infect Control Hosp Epidemiol. 2004;25(2):99–104. [PubMed: 14994932]
14. Nathan HM, Conrad SL, Held PJ, et al. Organ donation in the United States. Am J Transplant. 2003;3 Suppl 4:29–40. [PubMed: 12694048]
15. Goldberg DS, Blumberg E, McCauley M, Abt P, Levine M. Improving Organ Utilization to Help Overcome the Tragedies of the Opioid Epidemic. Am J Transplant. 2016;16(10):2836–2841. [PubMed: 27438538]

16. Boucher HW, Talbot GH, Bradley JS, et al. Bad bugs, no drugs: no ESKAPE! An update from the Infectious Diseases Society of America. Clin Infect Dis. 2009;48(1):1–12. [PubMed: 19035777]
17. Centers for Disease Control and Prevention C. National Healthcare Safety Network (NHSN) Patient Safety Component Manual. Multidrug-Resistant Organism & Clostridioides difficile Infection (MDRO/CDI) Module 2019; https://www.cdc.gov/nhsn/pdfs/pscmanual/pcsmanual_current.pdf.
18. Ruiz I, Gavalda J, Monforte V, et al. Donor-to-host transmission of bacterial and fungal infections in lung transplantation. Am J Transplant. 2006;6(1):178–182. [PubMed: 16433772]
19. Mills JP, Wilck MB, Weikert BC, et al. Successful treatment of a disseminated infection with extensively drug-resistant Klebsiella pneumoniae in a liver transplant recipient with a fosfomycin-based multidrug regimen. Transpl Infect Dis. 2016;18(5):777–781. [PubMed: 27458980]
20. DuBose J, Salim A. Aggressive organ donor management protocol. J Intensive Care Med. 2008;23(6):367–375. [PubMed: 18815202]
21. Salim A, Martin M, Brown C, et al. Using thyroid hormone in brain-dead donors to maximize the number of organs available for transplantation. Clin Transplant. 2007;21(3):405–409. [PubMed: 17488392]
22. Guidelines for preventing transmission of human immunodeficiency virus through transplantation of human tissue and organs. Centers for Disease Control and Prevention. MMWR Recomm Rep. 1994;43(RR-8):1–17.
23. Kucirka LM, Namuyinga R, Hanrahan C, Montgomery RA, Segev DL. Formal policies and special informed consent are associated with higher provider utilization of CDC high-risk donor organs. Am J Transplant. 2009;9(3):629–635. [PubMed: 19191765]
24. Bell J, Batey RG, Farrell GC, Crewe EB, Cunningham AL, Byth K. Hepatitis C virus in intravenous drug users. Med J Aust. 1990;153(5):274–276. [PubMed: 2118227]
25. Millar BC, Prendergast BD, Moore JE. Community-associated MRSA (CA-MRSA): an emerging pathogen in infective endocarditis. J Antimicrob Chemother. 2008;61(1):1–7. [PubMed: 17962214]
26. Saravolatz LD, Markowitz N, Arking L, Pohlod D, Fisher E. Methicillin-resistant Staphylococcus aureus. Epidemiologic observations during a community-acquired outbreak. Ann Intern Med. 1982;96(1):11–16. [PubMed: 7053683]
27. Saravolatz LD, Pohlod DJ, Arking LM. Community-acquired methicillin-resistant Staphylococcus aureus infections: a new source for nosocomial outbreaks. Ann Intern Med. 1982;97(3):325–329. [PubMed: 7114629]
28. Merli M, Lucidi C, Giannelli V, et al. Cirrhotic patients are at risk for health care-associated bacterial infections. Clin Gastroenterol Hepatol. 2010;8(11):979–985. [PubMed: 20621200]
29. Hahn YS. Subversion of immune responses by hepatitis C virus: immunomodulatory strategies beyond evasion? Curr Opin Immunol. 2003;15(4):443–449. [PubMed: 12900277]
30. Gonzalez SA, Trotter JF. The rise of the opioid epidemic and hepatitis C-positive organs: A new era in liver transplantation. Hepatology. 2018;67(4):1600–1608. [PubMed: 29023920]
31. Goldberg DS, Abt PL, Reese PP, Investigators TT. Transplanting HCV-Infected Kidneys into Uninfected Recipients. N Engl J Med. 2017;377(11):1105. [PubMed: 28902585]
32. Goldberg DS, Abt PL, Blumberg EA, et al. Trial of Transplantation of HCV-Infected Kidneys into Uninfected Recipients. N Engl J Med. 2017;376(24):2394–2395. [PubMed: 28459186]
33. Levitsky J, Formica RN, Bloom RD, et al. The American Society of Transplantation Consensus Conference on the Use of Hepatitis C Viremic Donors in Solid Organ Transplantation. Am J Transplant. 2017;17(11):2790–2802. [PubMed: 28556422]
34. Karanika S, Zervou FN, Zacharioudakis IM, Paudel S, Mylonakis E. Risk factors for meticillin-resistant Staphylococcus aureus colonization in dialysis patients: a meta-analysis. J Hosp Infect. 2015;91(3):257–263. [PubMed: 26428959]
35. Zacharioudakis IM, Zervou FN, Ziakas PD, Mylonakis E. Meta-analysis of methicillin-resistant Staphylococcus aureus colonization and risk of infection in dialysis patients. J Am Soc Nephrol. 2014;25(9):2131–2141. [PubMed: 24652802]
36. Calfee DP. Multidrug-resistant organisms in dialysis patients. Semin Dial. 2013;26(4):447–456. [PubMed: 23627545]

37. Collin BA, Leather HL, Wingard JR, Ramphal R. Evolution, incidence, and susceptibility of bacterial bloodstream isolates from 519 bone marrow transplant patients. Clin Infect Dis. 2001;33(7):947–953. [PubMed: 11528564]

38. Oliveira AL, de Souza M, Carvalho-Dias VM, et al. Epidemiology of bacteremia and factors associated with multi-drug-resistant gram-negative bacteremia in hematopoietic stem cell transplant recipients. Bone Marrow Transplant. 2007;39(12):775–781. [PubMed: 17438585]

39. Lautenbach E, Patel JB, Bilker WB, Edelstein PH, Fishman NO. Extended-spectrum beta-lactamase-producing Escherichia coli and Klebsiella pneumoniae: risk factors for infection and impact of resistance on outcomes. Clin Infect Dis. 2001;32(8):1162–1171. [PubMed: 11283805]

40. Ben-Ami R, Rodriguez-Bano J, Arslan H, et al. A multinational survey of risk factors for infection with extended-spectrum beta-lactamase-producing enterobacteriaceae in nonhospitalized patients. Clin Infect Dis. 2009;49(5):682–690. [PubMed: 19622043]

41. Tashkin DP. Smoked marijuana as a cause of lung injury. Monaldi Arch Chest Dis. 2005;63(2):93–100. [PubMed: 16128224]

42. Moore BA, Augustson EM, Moser RP, Budney AJ. Respiratory effects of marijuana and tobacco use in a U.S. sample. J Gen Intern Med. 2005;20(1):33–37. [PubMed: 15693925]

43. Thompson GR 3rd, Tuscano JM, Dennis M, et al. A microbiome assessment of medical marijuana. Clin Microbiol Infect. 2017;23(4):269–270. [PubMed: 27956269]

44. Tashkin DP, Baldwin GC, Sarafian T, Dubinett S, Roth MD. Respiratory and immunologic consequences of marijuana smoking. J Clin Pharmacol. 2002;42(S1):71S–81S. [PubMed: 12412839]

45. Ghasemiesfe M, Ravi D, Vali M, et al. Marijuana Use, Respiratory Symptoms, and Pulmonary Function: A Systematic Review and Meta-analysis. Ann Intern Med. 2018;169(2):106–115. [PubMed: 29971337]

46. Whitson BA, Hertz MI, Kelly RF, et al. Use of the donor lung after asphyxiation or drowning: effect on lung transplant recipients. Ann Thorac Surg. 2014;98(4):1145–1151. [PubMed: 25134859]

47. Trouillet JL, Chastre J, Vuagnat A, et al. Ventilator-associated pneumonia caused by potentially drug-resistant bacteria. Am J Respir Crit Care Med. 1998;157(2):531–539. [PubMed: 9476869]

48. Jones RN. Microbial etiologies of hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia. Clin Infect Dis. 2010;51 Suppl 1:S81–87. [PubMed: 20597676]

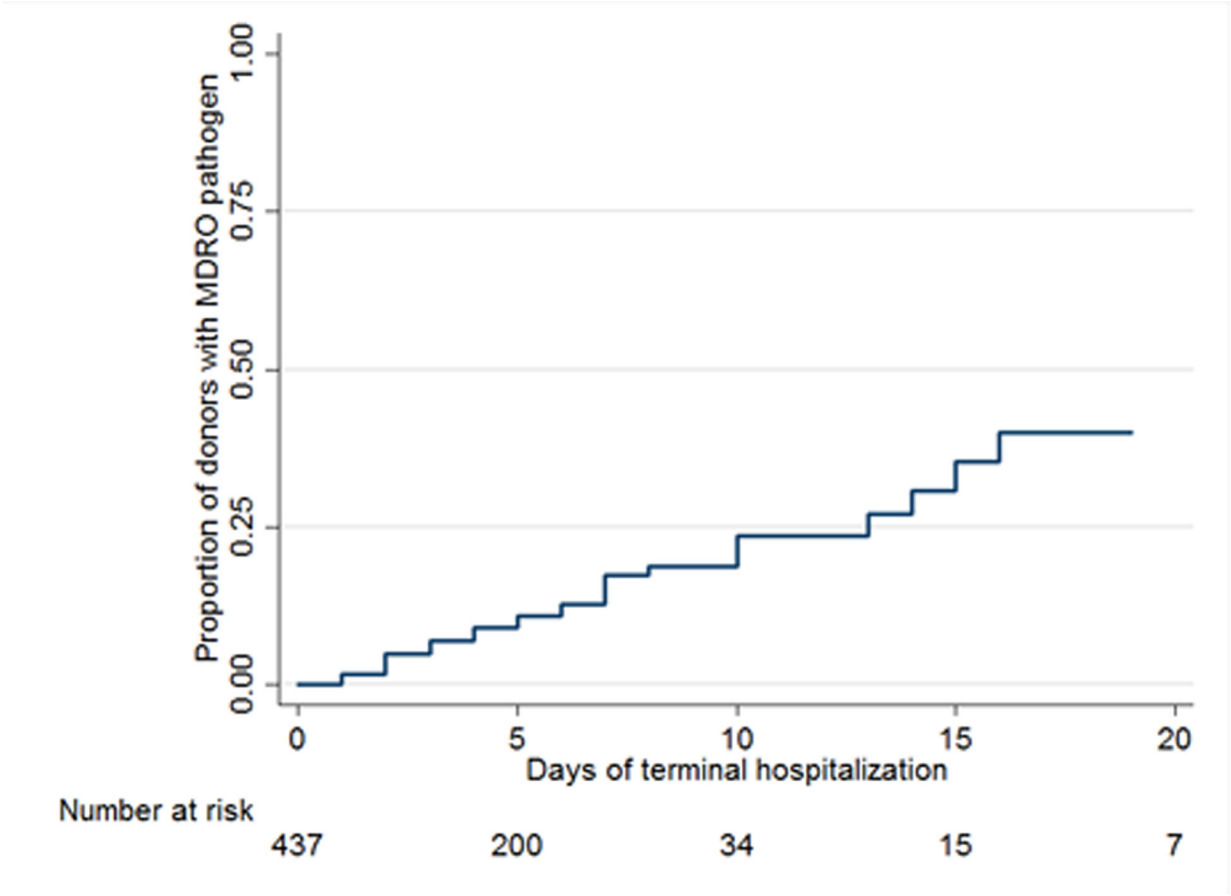

Figure 1. Kaplan Meier failure curve of time to donor MDRO.

Time zero is the day of admission to the terminal hospitalization. The failure event is MDRO colonization/infection. Donors were censored at the time of organ procurement. Plotted through 20 days of follow-up.

Table 1.

Baseline characteristics of the deceased organ donors stratified by MDRO pathogen status.

Donor characteristic[a, b]	No MDRO pathogen (N=376)	MDRO pathogen (N=64)	*P* value
Demographics			
Age (years) (median, IQR)	39 (27–53)	34 (25–50)	0.064
Female gender	150 (40%)	33 (52%)	0.074
Race/Ethnicity			
Black/African American	50 (13%)	9 (14%)	0.171
White/Caucasian	279 (74%)	52 (81%)	
Hispanic	38 (10%)	1 (2%)	
Other	9 (2%)	2 (3%)	
Comorbidities			
Chronic kidney disease	8 (2%)	1 (2%)	0.768
Dialysis	4 (1%)	2 (3%)	0.189
Liver disease	3 (1%)	0 (0%)	0.623
Malignancy	11 (3%)	1 (2%)	0.459
Solid organ transplant	3 (1%)	0 (0%)	0.623
Hematopoietic cell transplant	1 (0.3%)	1 (2%)	0.270
Immunomodulator treatment[c]	31 (8%)	3 (5%)	0.450
Diabetes mellitus	43 (11%)	9 (13%)	0.795
Donor type			
DCD	52 (14%)	12 (19%)	0.294
ECD	73 (19%)	11 (17%)	0.689
PHS-increased risk	128 (34%)	22 (34%)	0.936
Death mechanism			
Drug intoxication	80 (21%)	16 (25%)	0.491
Asphyxiation	22 (6%)	5 (8%)	0.538
Cardiovascular	93 (25%)	16 (25%)	0.946
Gunshot wound	25 (7%)	4 (6%)	0.587
Blunt injury	51 (13%)	8 (13%)	0.829
Intracranial hemorrhage	99 (26%)	13 (20%)	0.317
Drug use			
THC	42 (11%)	11 (17%)	0.166
Opiates (IDU or non-IDU)	104 (28%)	22 (34%)	0.261
IDU	75 (20%)	17 (27%)	0.237
Serologies and laboratory testing			
HCV seropositive	25 (7%)	8 (13%)	0.098
HCV viremia	15 (5%)	6 (10%)	0.083
Procedures during terminal hospitalization			

Donor characteristic[a,b]	No MDRO pathogen (N=376)	MDRO pathogen (N=64)	*P* value
Tracheostomy	5 (1%)	3 (5%)	0.095
Percutaneous endoscopic gastrostomy	4 (1%)	3 (5%)	0.066
Open abdomen	1 (0.3%)	0 (0%)	>0.999
Donor management			
Length of stay of terminal hospitalization (days) (median, IQR)	3 (2–5)	4 (3–7)	<0.001
T4 protocol	312 (83%)	52 (81%)	0.802
Antibiotics			
Any antibiotic	366 (97%)	61 (97%)	0.817
Narrow GP[d]	301 (80%)	40 (63%)	0.003
Broad GP[e]	84 (22%)	19 (30%)	0.191
Narrow GN[f]	36 (10%)	12 (19%)	0.028
Broad GN[g]	249 (66%)	50 (78%)	0.053
Number of antibiotics per donor (median, IQR)	2 (1–2)	2 (2–3)	0.034
Antibiotic days per donor (median, IQR)	4 (3–7)	2 (0–5)	0.001
Length of antibiotics per donor (days) (median, IQR)	3 (2–4)	1 (0–3)	<0.001

[a] Data are presented as numbers (percentages) except where noted.

[b] Only those variables with a P value <0.20 are included in this table, as well as those of notable biologic importance.

[c] Immunomodulators included: abatacept, anakinra, apremilast, azathioprine, cyclophosphamide, cyclosporine, denosumab, hydroxychloroquine, methotrexate, mycophenolate, rituximab, secukinumab, sulfasalazine, tocilizumab, tofacitinib, infliximab, adalimumab, certolizumab, golimumab, etanercept

[d] Narrow GP antibiotics included cefazolin and nafcillin.

[e] Broad GP antibiotics included vancomycin.

[f] Narrow GN antibiotics included ceftriaxone, cefotaxime, ampicillin/sulbactam, and amoxicillin/clavulanate.

[g] Broad GN antibiotics included antibiotics with anti-pseudomonal coverage (cefepime, ceftazidime, piperacillin-tazobactam, meropenem, aztreonam, fluoroquinolones, aminoglycosides).

Abbreviations: DCD, donation after circulatory death; ECD, expanded criteria donor; GN, Gram-negative; GP, Gram-positive; HCV, hepatitis C virus; IDU, injection drug use; IQR, interquartile range; MDRO, multidrug-resistant organism; PHS, Public Health Service; THC, tetrahydrocannabinol

Table 2.

Overview of donor culture results.

Overview of donor cultures		**N (%)**[a]
Donors with a positive hospital or OPO culture		380 (86%)
Donors with a positive OPO culture		322 (73%)
Donors with a positive hospital culture		267 (61%)
Number of positive cultures per donor (median [IQR, range])		2 (1–3, 0–8)
Organisms on culture, stratified by site of growth		
S. aureus	Donors with *S. aureus* on culture	183 (42%)
	Blood cultures with *S. aureus*	8
	Respiratory cultures with *S. aureus*	179
	Urine cultures with *S. aureus*	2
	Ureter cultures with *S. aureus*	2
	Perfusate cultures with *S. aureus*	3
	Abdominal collection cultures with *S. aureus*	1
	Bone cultures with *S. aureus*	1
Candida spp	Donors with *Candida* spp on culture	127 (29%)
	Blood cultures with *Candida* spp	6
	Respiratory cultures with *Candida* spp	110
	Pleural cultures with *Candida* spp	1
	Urine cultures with *Candida* spp	24
	Ureter cultures with *Candida* spp	1
	Perfusate cultures with *Candida* spp	6
	Abdominal collection cultures with *Candida* spp	1
Coagulase-negative staphylococci (CoNS)	Donors with CoNS on culture	52 (12%)
	Blood cultures with CoNS	17
	Respiratory cultures with CoNS	15
	Urine cultures with CoNS	2
	Ureter cultures with CoNS	7
	Perfusate cultures with CoNS	12
	Bone culture with CoNS	1
Klebsiella spp	Donors with *Klebsiella* spp on culture	44 (10%)
	Blood cultures with *Klebsiella* spp	2
	Respiratory cultures with *Klebsiella* spp	39
	Urine cultures with *Klebsiella* spp	3
	Ureter cultures with *Klebsiella* spp	1
	Perfusate cultures with *Klebsiella* spp	2
Haemophilus influenzae	Donors with *H. influenzae* on culture	43 (10%)
	Respiratory cultures with *H. influenzae*	43

Overview of donor cultures		**N (%)**[a]
E. coli	Donors with *E. coli* on culture	38 (9%)
	Blood cultures with *E. coli*	2
	Respiratory cultures with *E. coli*	16
	Urine cultures with *E. coli*	21
	Ureter cultures with *E. coli*	6
	Perfusate cultures with *E. coli*	4
Enterobacter spp	Donors with *Enterobacter* spp on culture	28 (6%)
	Respiratory cultures with *Enterobacter* spp	22
	Urine cultures with *Enterobacter* spp	4
	Ureter cultures with *Enterobacter* spp	2
	Perfusate cultures with *Enterobacter* spp	2
Enterococcus spp	Donors with *Enterococcus* spp on culture	25 (6%)
	Respiratory cultures with *Enterococcus* spp	5
	Urine cultures with *Enterococcus* spp	11
	Ureter cultures with *Enterococcus* spp	7
	Perfusate cultures with *Enterococcus* spp	2
	Chest wound cultures with *Enterococcus* spp	1
Group C and G streptococci	Donors with Group C/G streptococci on culture	23 (5%)
	Respiratory cultures with Group C/G streptococci	22
	Urine cultures with Group C/G streptococci	1
Pseudomonas spp	Donors with *Pseudomonas* spp on culture	22 (5%)
	Blood cultures with *Pseudomonas* spp	1
	Respiratory cultures with *Pseudomonas* spp	21
	Urine cultures with *Pseudomonas* spp	1
MDRO pathogens on culture, stratified by site of growth		
MRSA	Donors with MRSA on culture	40 (9%)
	Blood cultures with MRSA	3
	Respiratory cultures with MRSA	38
	Urine cultures with MRSA	1
ESC-R Enterobacteriaceae (EB)	Donors with ESC-R EB on culture	20 (5%)
	Blood cultures with ESC-R EB	1
	Respiratory cultures with ESC-R EB	13
	Urine cultures with ESC-R EB	4
	Ureter cultures with ESC-R EB	1
	Perfusate cultures with ESC-R EB	1
VRE	Donors with VRE on culture	4 (1%)
	Respiratory cultures with VRE	1
	Ureter cultures with VRE	2
	Perfusate cultures with VRE	1

Overview of donor cultures		**N (%)**[a]
	Chest wound cultures with VRE	1
MDR-*Pseudomonas*[b]	Donors with MDR-*Pseudomonas* on culture	2 (0.5%)
	Blood cultures with MDR- *Pseudomonas*	1
	Respiratory cultures with MDR- *Pseudomonas*	2
CRE	Donors with CRE on culture	1 (0.2%)
	Respiratory cultures with CRE	1
MDR-*Acinetobacter*[b]	Donors with MDR-*Acinetobacter* on culture	1 (0.2%)
	Respiratory cultures with MDR-*Acinetobacter*	1

[a]Data are presented as numbers (percentages) except where noted. The denominator for all percentages is the total number of donors. These events are not mutually exclusive; each donor may have had multiple positive cultures or multiple organisms on a single culture.

[b]The full susceptibility patterns for the three MDR-*Pseudomonas* isolates and single MDR-*Acinetobacter* isolate are given in Supporting Information (C).

Abbreviations: BAL, bronchoalveolar lavage; CRE, carbapenem-resistant Enterobacteriaceae; ESC-R, extended-spectrum cephalosporin-resistant; IQR, interquartile range; MDRO, multidrug-resistant organism; MRSA, methicillin-resistant *S. aureus*; OPO, organ procurement organization; spp, species; VRE, vancomycin-resistant enterococci

Table 3.

Bivariable and multivariable Cox proportional hazard regression model of time to donor MDRO.

Donor characteristic	Bivariable analysis			Multivariable analysis[b]		
	HR	95% CI	*P* value	aHR	95% CI	*P* value
HCV viremia	3.71	1.56–8.82	0.003	4.09	1.71–9.78	0.002
Dialysis	3.50	0.85–14.44	0.084	4.59	1.09–19.21	0.037
Stem cell transplant	5.66	0.78–41.22	0.087	7.57	1.03–55.76	0.047
THC	1.75	0.90–3.40	0.099	1.90	0.97–3.73	0.061
Narrow GN antibiotics[a]	-	-	-	1.13	1.003–1.27	0.045

[a]Antibiotic exposure incorporated as a time-varying covariate in the multivariable analysis. There is no bivariable HR estimate for time-varying covariates.

[b]Proportional hazards test P=0.998

Abbreviations: aHR, adjusted hazard ratio; GN, Gram-negative; HCV, hepatitis C virus; THC, tetrahydrocannabinol

Table 4.

Bivariable and multivariable Cox proportional hazard regression model of time to MRSA on donor culture.

Donor characteristic	Bivariable analysis			Multivariable analysis[b]		
	HR	95% CI	P value	aHR	95% CI	*P* value
HCV viremia	5.04	1.91–13.30	0.001	5.39	2.02–14.36	0.001
Stem cell transplant	8.97	1.21–66.33	0.032	18.95	2.43–147.55	0.005
T4 protocol	3.95	1.17–13.31	0.027	5.12	1.49–17.63	0.010
THC	2.53	1.18–5.43	0.017	2.88	1.33–6.24	0.007
Narrow GP antibiotics[a]	-	-	-	0.80	0.66–0.98	0.032

[a]Antibiotic exposure incorporated as a time-varying covariate in the multivariable analysis. There is no bivariable HR estimate for time-varying covariates.

[b]Proportional hazards test $P=0.944$

Abbreviations: GP, Gram-positive; HCV, hepatitis C virus; THC, tetrahydrocannabinol

Table 5.

Bivariable and multivariable Cox proportional hazard regression model of time to ESC-R EB on donor culture.

Donor characteristic	Bivariable analysis			Multivariable analysis[b]		
	HR	95% CI	*P* value	aHR	95% CI	*P* value
Death from asphyxiation	5.67	1.81–17.82	0.003	5.85	1.86–18.39	0.003
Narrow GN antibiotics[a]	-	-	-	1.17	1.01–1.37	0.039

[a]Antibiotic exposure incorporated as a time-varying covariate in the multivariable analysis. There is no bivariable HR estimate for time-varying covariates.

[b]Proportional hazards test $P=0.679$

Abbreviations: GN, Gram-negative