HHS Public Access

Author manuscript

Am J Transplant. Author manuscript; available in PMC 2025 August 01.

Published in final edited form as:

Am J Transplant. 2024 August ; 24(8): 1427–1439. doi:10.1016/j.ajt.2024.02.022.

Impact of deceased organ donor marijuana use on donor culture positivity and solid organ transplant recipient outcomes

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DISCLOSURES

The authors of this manuscript have conflicts of interest to disclose as described by the *American Journal of Transplantation*.
Emily Blumberg receives research support from Merck, Takeda, Hologic, and Scynexis; was a member of a Data and Safety Monitoring Board (DSMB) for Amplyx; and is a member of Scientific Advisory Committees for Merck and Takeda.
Jennifer Han was affiliated with the University of Pennsylvania during the conduct of this research and is now employed by, and holds shares in, the GlaxoSmithKline group of companies.
Ebbing Lautenbach is a member of a DSMB for Merck and is a member of a scientific advisory committee for Paratek and Shionogi. None of these conflicts are relevant to this article.
All other authors report no disclosures.

Declaration of interests

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Judith Anesi reports financial support was provided by Gift of Life Donor Program. Judith Anesi reports financial support was provided by Antibacterial Resistance Leadership Group. Judith Anesi and Ebbing Lautenbach reports financial support was provided by National Institutes of Health. Ebbing Lautenbach reports financial support was provided by Centers for Disease Control and Prevention. Emily Blumberg reports a relationship with Merck, Takeda, Hologic, and Scynexis that includes: funding grants. Emily Blumberg reports a relationship with Amplyx that includes: consulting or advisory. Emily Blumberg reports a relationship with Merck and Takeda that includes: consulting or advisory. Jennifer Han reports a relationship with GlaxoSmithKline that includes: employment and equity or stocks. Ebbing Lautenbach reports a relationship with Merck & Co Inc that includes: consulting or advisory. Ebbing Lautenbach reports a relationship with Paratek and Shionogi that includes: consulting or advisory. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

SUPPORTING INFORMATION STATEMENT

Additional supporting information may be found online in the Supporting Information section.

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Abstract

With the increasing prevalence of marijuana use in the U.S., many deceased organ donors have a history of marijuana use, raising concerns about infectious risks to transplant recipients. We performed a multicenter retrospective cohort study in which exposed donors were those with recent marijuana use (in the prior 12 months) and unexposed donors were those with no recent marijuana use. Primary outcomes included (1) positive donor cultures for bacteria or fungi, (2) recipient infection due to bacteria or fungi within 3 months post-transplant, and (3) recipient graft failure or death within 12 months post-transplant. Multivariable regression was used to evaluate the relationship between donor marijuana use and each outcome. A total of 658 recipients who received organs from 394 donors were included. Recent marijuana use was not associated with donor culture positivity (aOR 0.84, 95% CI 0.39–1.81, P=0.65), recipient infection (aHR 1.02, 95% CI 0.76–1.38, P=0.90), or recipient graft failure or death (aHR 1.65, 95% CI 0.90–3.02, P=0.11). Our data suggest that organs from donors with a history of recent marijuana use do not pose significant infectious risks in the early post-transplant period.

1. INTRODUCTION

As of November 2022, 37 states have legalized marijuana for medical use, and 21 states have legalized marijuana for recreational use[1]; consequently, the United States has seen a rise in marijuana usage[2,3]. It is likely that a growing proportion of deceased organ donors have a history of marijuana use as well, though this metric has not been specifically reported.

There are concerns surrounding the transmission of pathogens from deceased organ donors with a history of marijuana use to solid organ transplant (SOT) recipients. Marijuana leaves have previously been found to be contaminated with *Aspergillus* spores[4], *Penicillium,* and *Mucor*[5]. In the transplant population, an association between marijuana inhalation and invasive pulmonary aspergillosis has been reported in kidney[6], bone marrow[7], and lung[8] transplant recipients. Additionally, outbreaks of bacterial infection with organisms such as *Salmonella* species[9] and *Mycobacterium tuberculosis*[10] have been associated with marijuana use in the non-transplant population.

Whether a deceased organ donor with a history of marijuana use poses risk for the SOT recipient has not been clearly evaluated. Prior studies examining the impact of SOT donor marijuana use on recipient survival and graft function have shown mixed results[11–13], and no studies have determined the impact of donor marijuana use on donor culture results and risk for donor-derived infection (DDI) among recipients. Consequently, transplant centers have discordant policies surrounding the treatment of these organs[14]. The goal of our study is to better characterize the infectious risks that marijuana use among deceased organ donors may pose to SOT recipients.

2. MATERIALS AND METHODS

2.1 Study Design and Setting.

A multicenter retrospective cohort study was conducted at three transplant centers in Philadelphia, Pennsylvania: The Hospital of the University of Pennsylvania (725 inpatient beds), Temple University Hospital (722 inpatient beds), and Hahnemann University Hospital (496 inpatient beds).

2.2 Study Population.

The cohort included adults who underwent SOT at one of the study centers and received an organ from a deceased donor that was procured by the local organ procurement organization (OPO), the Gift of Life Donor Program, between January 1, 2015 and June 30, 2016. Eligible recipients and their donors were identified by the OPO. Recipients of any organ type were included since donor marijuana use could theoretically lead to infectious complications that extend beyond the lung to include infection of other allograft types.

2.3 Exposure Groups.

Exposed donors were those with “recent marijuana use,” defined as the use of marijuana at any point in the 12 months preceding organ procurement. The exposure status was ascertained by manual review of donor charts maintained by the OPO. These charts contained history abstracted from the donor’s current hospital admission record as well as any known records from past hospitalizations. The OPO transplant coordinator conducted and documented an extensive medical and social history (including the Uniform Donor Risk Assessment Form) with the donor’s next-of-kin/donor informants which included specific questions on drug use. The records were evaluated for report of marijuana use, and this information was cross-referenced with the results of toxicology screens if performed on donors during their terminal hospitalization. We defined “recent marijuana use” as being present if either of the following criteria were met: (1) next-of-kin/donor informant reported a history of marijuana use in the prior 12 months; (2) the toxicology screen was positive for THC regardless of next-of-kin/donor informant report. A 12-month window was used to define “recent marijuana use” in order to exclude those with only remote marijuana use. Donors meeting these criteria were labeled as “exposed” regardless of route of ingestion, due to lack of reliable information regarding route of ingestion. Unexposed donors were those with no recent marijuana use (using the same definition).

The exposed SOT recipients were those who received an organ from a donor with recent marijuana use (as defined above). Unexposed recipients were those who received an organ from a donor with no history of recent marijuana use.

This study was approved by the Institutional Review Board at each of the transplant centers (see Supporting Information section A).

2.4 Study Outcomes.

There were three primary outcomes of the study. The first was donor culture positivity, defined as growth of bacteria or fungi on routine cultures obtained at any point during the

donor's terminal hospitalization or at the time of organ procurement. The OPO collects a standardized set of donor cultures at procurement (including cultures of the blood, sputum, urine, ureter tips, and perfusate/transport solution). "Routine mouth flora" on respiratory cultures and "mixed flora" on urine cultures were excluded, since these were likely contaminants.

The second primary outcome was recipient bacterial or invasive fungal infection (IFI) within three months of transplant, including probable DDIs. Infections were identified using Center for Disease Control and Prevention (CDC)/National Healthcare Safety Network (NHSN) surveillance criteria[15] and were determined via manual chart review by three infectious diseases-trained physicians (JAA at Penn, DHL at Drexel, HC at Temple). Infections at any site, due to any organism, and due to any source (donor-derived or non-donor-derived) were included. Infections were evaluated through three months post-transplant as this is the typical timeframe in which bacterial and fungal donor-derived infections have been reported to occur[16], and this is the primary mechanism by which an effect on post-transplant infections was postulated to occur. A probable DDI was defined using criteria from the Organ Procurement and Transplantation Network (OPTN) Ad Hoc Disease Transmission Advisory Committee (DTAC)[16] as: (a) a bacterial or fungal infection in the recipient, per CDC/NHSN criteria[15], where (b) the infection was caused by an organism with the same species identification and susceptibility pattern as was identified on one of the donor's hospital or organ procurement organization (OPO) cultures. DDIs were evaluated through three months post-transplantation. Probable DDI were determined independently by two transplant infectious diseases-trained physicians (JAA and EAB), and discrepancies were resolved by a third transplant infectious diseases trained physician (DHL). We included positive cultures and infections from any site since the primary mechanism of DDI is microbial transfer via the allograft with subsequent spread to other tissues via the bloodstream.

The third primary outcome was recipient graft failure or death within 12 months post-transplant. Graft failure was defined by re-listing for transplant for any recipient or return to dialysis for kidney transplant recipients.

2.5 Secondary Outcomes.

The following were evaluated as secondary outcomes: (1) positive respiratory donor cultures (for any bacteria or fungi, omitting "normal mouth flora"); (2) multidrug-resistant organisms (MDROs) identified on any donor culture (as defined by CDC/NHSN criteria, see Supporting Information Section B)[17]; (3) fungi on any donor culture (which included mold on any donor culture or *Candida* species [spp] on any non-respiratory donor culture, but did not include *Candida* spp identified solely on respiratory cultures).

We also evaluated subgroups of recipient infections, including (4) respiratory infections; (5) IFI within three months post-transplant (per CDC/NHSN criteria[15]), which included mold infection at any site and invasive candidal infection (which excluded oropharyngeal candidiasis ["thrush"] or candidal vulvovaginitis); and (6) mold infection within three months post-transplant at any site. Invasive fungal disease with mold is typically classified

as “proven”, “probable”, or “possible”[18], but given the small number of infections noted, these categories were combined.

We also evaluated (7) recipient antifungal exposure by determining the days of antifungals administered within 90 days post-transplant. Antifungals included azoles (excluding those administered topically), echinocandins, and amphotericin (both inhaled and intravenous forms). Days of both prophylaxis and treatment with antifungals were collected. Standard antifungal prophylaxis regimens for each transplant center are detailed in Supporting Information Section D, though donor and/or recipient factors (including history of marijuana use) may have impacted the prophylaxis strategy for each recipient.

2.6 Data Collection.

Data on donors and recipients were abstracted from OPO records along with hospital electronic medical records. (See Supporting Information Section C for a complete list of data elements collected.) Notably, data on recipient post-transplant infections included all infections within three months post-transplant, not solely the first infection post-transplant. The standard perioperative antimicrobial prophylaxis employed at each center and approach to treating positive donor cultures is provided in the Supporting Information section D.

2.7 Statistical Analysis.

Exposed and unexposed donors and recipients were characterized by baseline clinical factors. Continuous variables were compared using a t-test or Wilcoxon rank-sum test, and categorical variables were compared using the χ^2 or Fisher exact test.

For the analysis of donor culture positivity, we performed multivariable logistic regression. First, bivariable regression was used to examine the relationship between the primary exposure (recent marijuana use), as well as other baseline donor factors, and the outcome (donor culture positivity). Candidates for the multivariable model were those with a P value <0.20 on bivariable analysis. Variables were retained in the final multivariable model if they were confounders of the primary association (defined by a change in the point estimate of the primary association by more than 15%) or, if after backward elimination, had a P value of <0.05 in the multivariable model. The strength of each association was measured using an odds ratio (OR), and a 95% confidence interval (CI) was calculated for each effect estimate. Each donor was included once in these analyses.

For the analyses of recipient infection and graft failure or death, survival analyses were performed. Time zero was defined as the day of transplantation, and the time at risk was measured in days. For the evaluation of post-transplant infection, the day on which the recipient first met criteria for a bacterial or fungal infection within three months post-transplant was the failure date, and subjects were censored at the time of death or at the end of three months of follow-up (whichever occurred first). Subjects were not censored for graft failure since infection remained possible following graft failure. If a recipient developed multiple infections within three months post-transplant, only the first infection was considered. For the evaluation of post-transplant graft and patient survival, the failure date was the day on which the SOT recipient met criteria for graft failure or died (whichever occurred first), and subjects were censored at 12 months of follow-up. For the unadjusted

analyses, a Kaplan-Meier curve was plotted, stratified by exposure status, and a log rank test was performed. For the adjusted analyses, mixed effects multivariable frailty models using the Weibull distribution were developed for each outcome, with a random effect for donor. This random effect was included in order to account for possible clustering by donor, since several recipients in the cohort received organs from the same donor. For each of the multivariable analyses, bivariable regression was used to examine the relationship between the primary exposure (recent donor marijuana use), as well as other baseline donor and recipient factors, and the outcome. Candidates for the multivariable model were those with a P value <0.20 on bivariable analysis. Variables were retained in the final multivariable model if they were confounders of the primary association (defined by a change in the point estimate of the primary association by more than 15%) or if after backward elimination had a P value of <0.05 in the multivariable model. The strength of each association was measured using a hazard ratio (HR), and a 95% confidence interval (CI) was calculated for each effect estimate.

Of note, we did not adjust our analyses for antimicrobials administered to the donors or recipients peri- or post-transplant, since these antimicrobial administrations would have occurred after the exposure of interest and would thus be on the causal pathway (though we did adjust for antimicrobials given pre-transplantation).

A similar approach was used for all secondary outcomes. All analyses were performed using StataSE v.15.1 (StataCorp, College Station, Texas).

2.8 Subgroup and Sensitivity Analyses.

We performed one subgroup analysis, in which we repeated the above analyses after restricting the cohort to only lung transplant recipients to determine if there was a different relationship between donor marijuana use and outcomes in lung recipients. We also performed one sensitivity analysis, in which we restricted the cohort to those donors/recipients where the donor had a positive toxicology screen for THC; by doing so, the "exposed" group was limited to those donors with confirmed recent use of THC.

3. RESULTS

3.1 Study Population.

The cohort included 394 organ donors, 89 (23%) of whom had a history of recent marijuana use and 49 (12%) of whom had a toxicology screen that was positive for THC. (See Table 1a for further donor baseline characteristics).

These 394 donors provided organs to 658 SOT recipients across the three study sites. Among the recipients, 158 (24%) received organs from a donor with a history of recent marijuana use, and 93 (14%) received organs from a donor with a toxicology screen positive for THC. (See Table 1b for further recipient baseline characteristics).

3.2 Association between recent donor marijuana use and donor culture positivity.

A total of 343 (87%) donors had at least one positive culture obtained during their terminal hospitalization or at the time of organ procurement (see Table 2 for details of donor culture

results). The most common sites of positive donor cultures included the respiratory tract (326, 83%) and genitourinary tract (75, 19%). The most common organisms isolated on donor culture included *Staphylococcus aureus* (167, 42%) and *Candida* spp. (112, 28%). MDROs were isolated in 58 (15%) donors.

Among donors with a history of recent marijuana use, 79 (89%) had at least one positive culture compared to 264 (87%) among those with no history of recent marijuana use (*P*=0.59). On donor respiratory cultures, 76 (85%) donors with a history of recent marijuana use and 250 (82%) donors with no history of recent marijuana use had bacterial or fungal growth on respiratory cultures (*P*=0.45). On both unadjusted analyses and multivariable analyses (Table 3), there was no association between recent donor marijuana use and donor culture positivity (aOR 0.84, 95% CI 0.39–1.81, *P*=0.65).

In evaluating secondary outcomes (Table S1), there was no association between recent donor marijuana use and donor culture positivity on respiratory cultures (aOR 0.93, 95% CI 0.47–1.84, *P*=0.83); no association between recent donor marijuana use and donor culture positivity for MDROs (aOR 0.77, 95% CI 0.38–1.58, *P*=0.48); and no association between recent donor marijuana use and donor culture positivity for fungi (aOR 0.79, 95% CI 0.32–1.96, *P*=0.61).

In the sensitivity analysis, in which we restricted exposed donors to those with a positive toxicology screen for THC, there remained no association between donor toxicology screen positivity for THC and donor culture positivity on either unadjusted analysis (OR 1.07, 95% CI 0.43–2.67, *P*=0.88) or multivariable analysis (aOR 0.74, 95% CI 0.29–1.91, *P*=0.54). No association was found between donor toxicology screen positivity for THC and donor culture positivity for non-respiratory *Candida* or mold on unadjusted analysis (*P*=0.97).

3.3 Association between recent donor marijuana use and recipient infection.

Among the 658 recipients, 294 (45%) developed a bacterial or fungal infection within three months post-transplant. On unadjusted analysis (Figure 1), there was no association between recent donor marijuana use and time to first recipient infection (log rank *P*=0.41). Similarly, on multivariable analysis (Table 4a), there remained no association between recent donor marijuana use and the hazard of bacterial or fungal infection within three months post-transplantation (aHR 1.02, 95% CI 0.76–1.38, *P*=0.90).

Among the 658 recipients, 38 (6%) developed an IFI (including mold and invasive candida infection) and 13 (2%) developed a mold infection within three months post-transplantation. After adjusting for organ type (Table S2), there was no association between recent donor marijuana use and the hazard of recipient IFI (aHR 0.46, 95% CI 0.17–1.19, *P*=0.11) or mold infection (HR 1.35, 95% CI 0.35–5.21, *P*=0.66).

There were 31 (5%) recipients with a probable DDI (see Table S5 for a list of probable DDIs). There was no significant difference in the proportion of recipients who developed a probable DDI among those with a donor with a history of recent marijuana use (9, 6%) and those with no donor history of recent marijuana use (22, 4%) (*P*=0.50).

In our sensitivity analysis, there was again no significant association between donor toxicology screen positivity for THC and time to first recipient bacterial or fungal infection on either unadjusted (HR 1.21, 95% CI 0.84–1.73, P=0.30) or multivariable analysis (aHR 1.11, 95% CI 0.77–1.61, P=0.58). Additionally, no association was found between donor toxicology screen positivity for THC and recipient development of invasive candidal (P>0.99) or mold infection (P>0.99) within 3 months post-transplant.

3.4 Association between recent donor marijuana use and recipient graft failure or death.

Among the 658 recipients, 57 (9%) developed graft failure or death within 12 months post-transplantation. On unadjusted analysis (Figure 2), there was no significant association between recent donor marijuana use and time to graft failure or death (log rank P=0.31). Similarly, on multivariable analysis (Table 4b), there remained no significant association between recent donor marijuana use and the hazard of graft failure or death (aHR 1.65, 95% CI 0.90–3.02, P=0.11).

In our sensitivity analysis, there was no significant association between donor toxicology screen positivity for THC and time to recipient graft failure or death on unadjusted analysis (HR 1.41, 95% CI 0.70–2.83, P=0.33) or multivariable analysis (aHR 1.75, 95% CI 0.86–3.55, P=0.12).

3.5 Association between recent donor marijuana use and recipient infections among lung transplant recipients.

Among 131 lung recipients, 84 (64%) developed a bacterial or fungal infection of which 79 (94% of lung recipient infections) were respiratory infections, 17 (13%) developed an IFI, and 10 (8%) developed a mold infection within three months post-transplantation. On multivariable analysis (Table S3), there was no association between recent donor marijuana use and the development of any infection (aHR 1.01, 95% CI 0.60–1.70, P=0.97) within three months post-lung transplantation. On bivariable analysis (performed due to insufficient numbers for multivariable analysis) (Table S3), there was no significant association between recent donor marijuana use and the development of a respiratory tract infection (HR 0.70, 95% CI 0.37–1.33, P=0.28), IFI (HR 0.78, 95% CI 0.22–2.77, P=0.70), mold infection (HR 1.09, CI 0.22–5.39, P=0.92), or respiratory mold infection (HR 1.15, 95% CI 0.35–3.86, P=0.82) within three months post-lung transplantation.

3.6 Antifungal exposure among organ recipients.

Among 658 recipients, antifungals were administered for a median of 0 days (IQR 0–11 days) during the first 90 days post-transplantation (see Table S4 for details of antifungal exposure). Lung transplant recipients received significantly more days of antifungals (median 31 days, IQR 1–89) than any other organ type, including pancreas (median 15 days, IQR 15–21), liver (median 3 days, IQR 0–13), heart (median 0 days, IQR 0–5), and kidney (median 0 days, IQR 0–0) (P≤0.01) recipients. Among lung transplant recipients, there was a non-significant increase in antifungal exposure among those whose donors had a history of recent marijuana use (median 69 days, IQR 3–90) compared to those whose donors had no history of recent marijuana use (median 20 days, IQR 1–86) (P=0.07).

4. DISCUSSION

Despite concern that donor exposure to marijuana increases the risk of fungal infection in recipients[4–8], our study found that a donor history of marijuana use did not increase (1) the likelihood of donor culture positivity (including respiratory cultures), or (2) the risk of early recipient bacterial or fungal infection, graft failure, or death post-transplantation. Even when evaluating only lung recipients, there remained no association between donor marijuana use and the risk of post-transplant infection.

Previous studies performed in lung transplant recipients have shown mixed results[11–13]: one prior study showed that donors with five or more years of weekly marijuana use were associated with reduced three-year graft survival in the recipient[12], while another study showed similar one- and three-year survival rates for lung recipients with donors with a history of marijuana use compared to those without[13]. Our results likely differed from these studies given we examined only the early-post transplant period, did not account for the amount or duration of marijuana use, and included a smaller cohort of lung transplant recipients.

The optimal strategy for antifungal prophylaxis of lung transplant recipients with a donor history of recent marijuana use is unknown. Given the observational nature of our study, the variable antifungal agents used, and the variable durations of antifungal exposure, we cannot determine the impact of antifungal administration on the risk of IFI. Further study of recipient antifungal prophylaxis in the setting of donor marijuana use is warranted.

There are several limitations to this study: (1) This was a retrospective observational study, so it is possible that unmeasured confounders impacted the outcomes. However, assigning recipients to donors with or without recent marijuana use for the purposes of randomization would not be ethically feasible. (2) The model-building approach used to create multivariable models is susceptible to overfitting of the data and increased Type I error. (3) Misclassification of the exposure was possible, given that donor history of marijuana use is typically gathered from interview of next-of-kin/donor informants, an imperfect measure[19]. We mitigated this by cross-referencing marijuana history with toxicology screen results. When we limited the exposed group to those with a positive toxicology screen for THC, there remained no association with donor culture results or recipient outcomes. Additionally, the route of donor marijuana ingestion was often unknown, so it was assumed to be inhaled given this is how the majority of marijuana is ingested in the United States[20]. Edible and topical formulations may have lower infectious risk; therefore, this may have obscured potential risks of marijuana inhalation. (4) The outcomes described in this study occurred in the context of standardized management of positive donor cultures that exist at the participating institutions (where recipients are given antimicrobials with activity against non-contaminant organisms that grow on donor cultures). The results from this study may not be generalizable to transplant centers with different practices. (5) The data from the study was collected in 2015–2016, possibly impacting the generalizability of the study to current day. (6) Although some fungi were isolated on donor culture in the study, donor specimens are not routinely sent for fungal culture, so some fungal organisms may not have been detected. (7) Diagnosis of IFI in

recipients is challenging[18] and although most donor-derived fungal infections present within three-months post-transplantation[16], it is possible that some later-onset fungal infections may not have been identified using our approach of censoring at three-months post-transplantation. (8) In our evaluation of primary outcomes, we censored recipients when they developed their first post-transplant infection, so it is possible that early infections may have obscured different rates of later-onset infection; however, this would not have occurred in the secondary outcomes focused on only fungal infections. (9) Although our study found no significant associations between donor marijuana use and infectious outcomes, the study may have been limited by lack of power to detect these associations.

In conclusion, our study demonstrates that donors with a history of recent marijuana use are not more likely to have positive donor cultures, and their recipients are not more likely to develop bacterial or fungal infection, graft failure, or death in the early post-transplant period (in the context of current management). These results suggest that organs from donors with a history of recent marijuana use do not pose significant novel infectious risks to recipients in the early post-transplant period.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding:

This work was supported by the Transplant Foundation's Innovative Research Grant Program, an affiliate of the Gift of Life Donor Program (Donation and Transplantation Grant to J.A.A.); the Antibacterial Resistance Leadership Group (grant number 5 UM 1AI104681–05 with a subaward fellowship grant to J.A.A.); the National Institutes of Health (grant numbers K24-AI080942 to E.L., K01-AI137317 to J.A.A.); and by a Centers for Disease Control and Prevention (CDC) Cooperative Agreement FOA#CK16–004-Epicenters for the Prevention of Healthcare Associated Infections (to E.L.). The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ABBREVIATIONS:

aHR	adjusted hazard ratio
aOR	adjusted odds ratio
CDC	Centers for Disease Control and Prevention
CI	confidence interval
CRE	carbapenem-resistant Enterobacterales
DDI	donor-derived infection
DTAC	Disease Transmission Advisory Committee

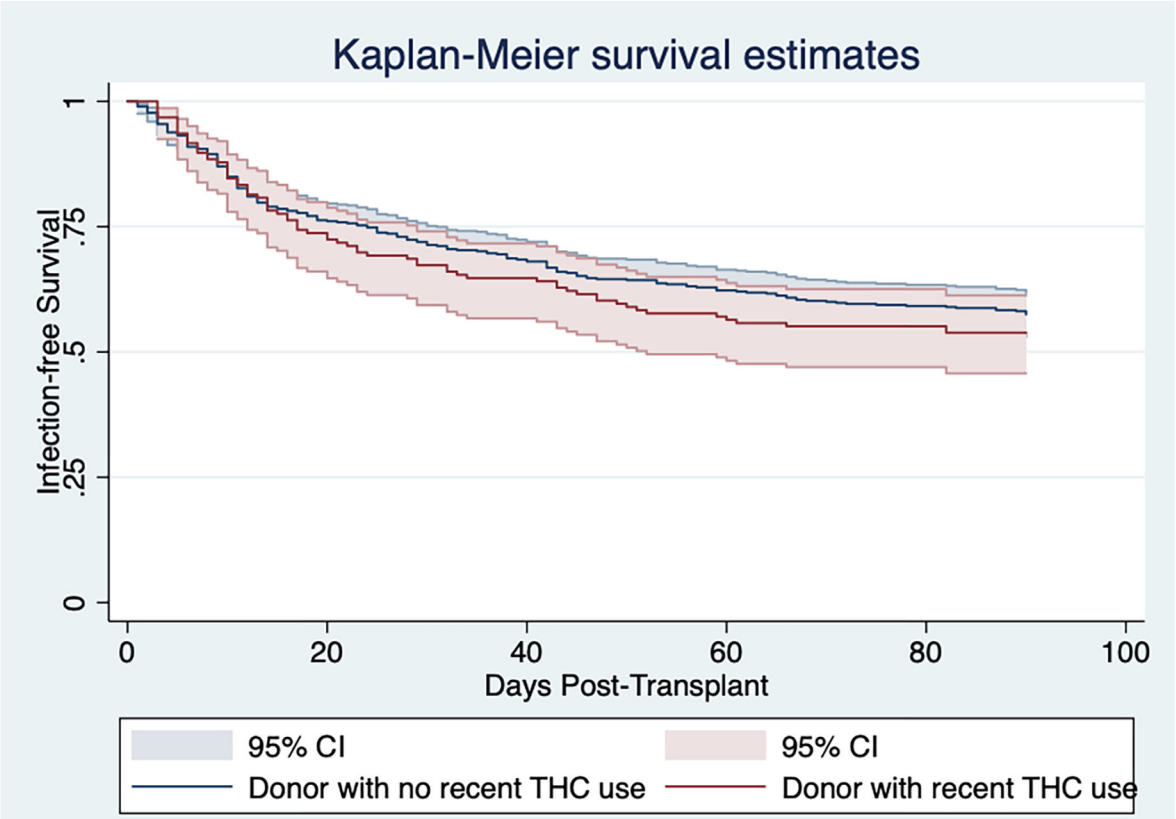
ESBL	extended-spectrum beta-lactamase
IFI	invasive fungal infection
IQR	interquartile range
MDR	multidrug-resistant
MDRO	multidrug-resistant organism
MRSA	methicillin-resistant *Staphylococcus aureus*
NHSN	National Healthcare Safety Network
OPO	organ procurement organization
OR	odds ratio
OPTN	Organ Procurement and Transplantation Network
PHS	Public Health Service
SOT	solid organ transplantation
Spp	species
THC	tetrahydrocannabinol
VRE	vancomycin-resistant *Enterococcus*

REFERENCES:

1. State medical cannabis laws. National Conference of State Legislatures Web site. https://www.ncsl.org/research/health/state-medical-marijuana-laws.aspx#:~:text=MEDICAL-USE%20UPDATE%3A%20As%20of,medical%20use%20of%20cannabis%20products. Updated 2022. Accessed 10/14/, 2022.
2. Key substance use and mental health indicators in the united states: Results from the 2019 national survey on drug use and health. https://www.samhsa.gov/data/sites/default/files/reports/rpt29393/2019NSDUHFFRPDFWHTML/2019NSDUHFFR090120.htm#illi2. Updated 2020. Accessed January 26, 2023.
3. Abuse NIoD. What is the scope of cannabis (marijuana) use in the united states? National Institute on Drug Abuse Web site. https://nida.nih.gov/publications/research-reports/marijuana/what-scope-marijuana-use-in-united-states. Updated −-. Accessed Oct 14, 2022.
4. Kagen SL. Aspergillus: An inhalable contaminant of marihuana. New England Journal of Medicine. 1981;304(8):483–484. [PubMed: 7453776]
5. Kagen SL, Kurup VP, Sohnle PG, Fink JN. Marijuana smoking and fungal sensitization. J Allergy Clin Immunol. 1983;71(4):389–393. Accessed Oct 18, 2022. doi: 10.1016/0091-6749(83)90067-2. [PubMed: 6833678]
6. Marks WH, Florence L, Lieberman J, et al. Successfully treated invasive pulmonary aspergillosis associated with smoking marijuana in a renal transplant recipient. Transplantation. 1996;61(12):1771–1774. https://journals.lww.com/transplantjournal/Fulltext/1996/06270/SUCCESSFULLY_TREATED_INVASIVE_PULMONARY.18.aspx. Accessed Aug 12, 2022. [PubMed: 8685958]
7. Hamadeh R, Ardehali A, Locksley RM, York MK. Fatal aspergillosis associated with smoking contaminated marijuana, in A marrow transplant recipient. CHEST. 1988;94(2):432–433. https://

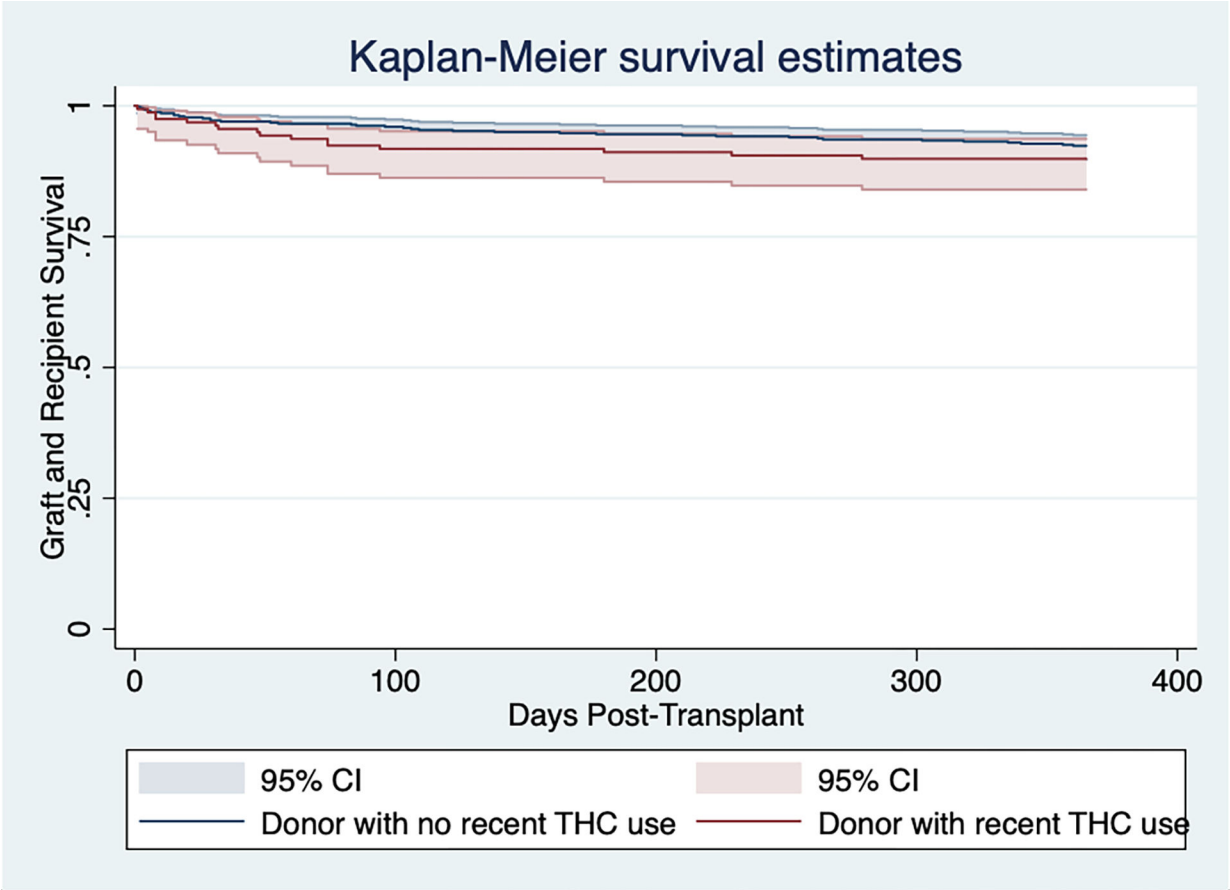
journal.chestnet.org/article/S0012-3692(16)33484-5/abstract. Accessed Aug 12, 2022. doi: 10.1378/chest.94.2.432. [PubMed: 3293934]

8. Faccioli E, Pezzuto F, Dell'Amore A, et al. Fatal early-onset aspergillosis in a recipient receiving lungs from a marijuana-smoking donor: A word of caution. Transpl Int. 2022;36. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8883434/. Accessed Aug 12, 2022. doi: 10.3389/ti.2022.10070.
9. Taylor DN, Wachsmuth IK, Shangkuan YH, et al. Salmonellosis associated with marijuana: A multistate outbreak traced by plasmid fingerprinting. N Engl J Med. 1982;306(21):1249–1253. Accessed Aug 16, 2022. doi: 10.1056/NEJM198205273062101. [PubMed: 7070444]
10. Oeltmann JE, Oren E, Haddad MB, et al. Tuberculosis outbreak in marijuana users, seattle, washington, 2004. Emerg Infect Dis. 2006;12(7):1156–1159. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3291049/. Accessed Aug 16, 2022. doi: 10.3201/eid1207.051436. [PubMed: 16836841]
11. Donahoe LL, Cypel M, de Perrot M, et al. Outcomes of lung transplantation from donors with a history of substance abuse. The Journal of thoracic and cardiovascular surgery. 2023;165(1):384–395.e4. 10.1016/j.jtcvs.2022.08.016. doi: 10.1016/j.jtcvs.2022.08.016. [PubMed: 36216597]
12. Okahara S, Levvey B, McDonald M, et al. Influence of the donor history of tobacco and marijuana smoking on early and intermediate lung transplant outcomes. J Heart Lung Transplant. 2020;39(9):962–969. Accessed Oct 19, 2022. doi: 10.1016/j.healun.2020.05.019. [PubMed: 32593560]
13. Mohite PN, Zeriouh M, Sáez DG, et al. Influence of history of cannabis smoking in selected donors on the outcomes of lung transplantation. Eur J Cardiothorac Surg. 2017;51(1):142–147. Accessed Oct 19, 2022. doi: 10.1093/ejcts/ezw255. [PubMed: 28077504]
14. Levi ME, Montague BT, Thurstone C, Kumar D, Huprikar SS, Kotton CN. Marijuana use in transplantation: A call for clarity. Clinical Transplantation. 2019;33(2):e13456. https://onlinelibrary-wiley-com.proxy.library.upenn.edu/doi/10.1111/ctr.13456. Accessed Aug 12, 2022. doi: 10.1111/ctr.13456. [PubMed: 30506888]
15. CDC/NHSN surveillance definitions for specific types of infections. https://www.cdc.gov/nhsn/PDFs/pscManual/17pscNosInfDef_current.pdf Web site. https://www.cdc.gov/nhsn/PDFs/pscManual/17pscNosInfDef_current.pdf.
16. Kaul DR, Vece G, Blumberg E, et al. Ten years of donor-derived disease: A report of the disease transmission advisory committee. Am J Transplant. 2021;21(2):689–702. https://pubmed.ncbi.nlm.nih.gov/32627325/. Accessed Dec 21, 2021. doi: 10.1111/ajt.16178. [PubMed: 32627325]
17. 2023 NHSN patient safety component manual. CDC Web site. https://www.cdc.gov/nhsn/pdfs/pscmanual/pcsmanual_current.pdf. Updated 2023. Accessed January 4, 2023.
18. Donnelly JP, Chen SC, Kauffman CA, et al. Revision and update of the consensus definitions of invasive fungal disease from the european organization for research and treatment of cancer and the mycoses study group education and research consortium. Clinical infectious diseases. 2020;71(6):1367–1376. https://www.narcis.nl/publication/RecordID/oai:repository.ubn.ru.nl:2066%2F225781. doi: 10.1093/cid/ciz1008. [PubMed: 31802125]
19. Lehrmann E, Afanador ZR, Deep-Soboslay A, et al. CLINICAL STUDY: Postmortem diagnosis and toxicological validation of illicit substance use. Addiction Biology. 2008;13(1):105–117. https://onlinelibrary-wiley-com.proxy.library.upenn.edu/doi/full/10.1111/j.1369-1600.2007.00085.x. Accessed Feb 10, 2022. doi: 10.1111/j.1369-1600.2007.00085.x. [PubMed: 18201295]
20. Schauer GL, Njai R, Grant-Lenzy AM. Modes of marijuana use - smoking, vaping, eating, and dabbing: Results from the 2016 BRFSS in 12 states. Drug Alcohol Depend. 2020;209:107900. Accessed Mar 15, 2023. doi: 10.1016/j.drugalcdep.2020.107900. [PubMed: 32061947]



Days Post-Transplant	0	20	40	60	80
Donors at risk with no recent THC	485	370	332	302	287
Donors at risk with recent THC	156	115	101	89	86

Figure 1.
Kaplan Meier survival curve of time to first bacterial or fungal infection within three months post-transplantation stratified by recent donor marijuana use.



Days Post-Transplant	0	100	200	300
Donors at risk with no recent THC	497	477	470	465
Donors at risk with recent THC	158	145	144	142

Figure 2.
Kaplan Meier survival curve of time to recipient graft failure or death within 12 months post-transplantation stratified by recent donor marijuana use.

Table 1.

Baseline characteristics of (a) deceased organ donors and (b) solid organ transplant recipients stratified by donor history of recent marijuana use.

(a) Deceased organ donors (N=394)			
Baseline characteristic[a,b]	**Donor with recent marijuana use (N=89)**	**Donor with no recent marijuana use (N=305)**	***P* value**
Demographics			
Age (median, IQR), years	30 (23–40)	42 (28–54)	<0.01
Female gender	24 (27%)	140 (46%)	<0.01
Race: Black	14 (16%)	40 (13%)	0.36
Race: White	67 (75%)	228 (75%)	
Ethnicity: Hispanic	8 (9%)	27 (9%)	
Comorbidities			
Diabetes mellitus	4 (4%)	40 (13%)	0.02
Hypertension	15 (17%)	96 (31%)	<0.01
Lung disease	18 (20%)	46 (15%)	0.25
Percutaneous Endoscopic Gastrostomy	2 (2%)	5 (1.64%)	0.66
Donor immunomodulator use[c]	3 (3%)	26 (9%)	0.11
Substance Use			
Injection drug use	16 (18%)	41 (13%)	0.17
Amphetamine use[d]	15 (17%)	14 (5%)	<0.01
Non-intravenous opioid use[d]	32 (36%)	64 (21%)	<0.01
Tobacco use[e]	72 (81%)	167 (55%)	<0.01
Cocaine use[e]	27 (30%)	71 (23%)	0.19
Benzodiazepine use[e]	28 (31%)	72 (24%)	0.14
Death mechanism			
Drug overdose	30 (34%)	49 (16%)	<0.01
Asphyxiation	11 (12%)	12 (4%)	<0.01
Cardiovascular	12 (13%)	89 (29%)	<0.01
Gunshot wound	7 (8%)	21 (7%)	0.75
Blunt injury	12 (13%)	43 (14%)	0.88
Intracranial hemorrhage	16 (18%)	84 (28%)	0.07
Donor type			
Donation after circulatory death	15 (17%)	39 (13%)	0.33
Expanded criteria donor	5 (6%)	69 (23%)	<0.01
PHS-increased risk[f,g]	41 (46%)	90 (30%)	<0.01
Kidney Donor Profile Index, median (IQR)	30 (9.5–48)	51 (23–80)	<0.01
Laboratory values			
CMV seropositive	38 (43%)	164 (54%)	0.07

EBV seropositive	83 (94%)	280 (92%)	0.43
HCV seropositive	5 (6%)	18 (6%)	>0.99
Positive HCV viral load	3 (3%)	10 (3%)	>0.99
HBsAg positive	0 (0%)	1 (0.33%)	>0.99
HBcAb positive	5 (6%)	10 (3%)	0.31
Donor management			
Length of stay during terminal hospitalization (median, IQR), days	4 (3–6)	3 (2–5)	0.53
(b) Solid organ transplant recipients (N=658)			
Baseline characteristic[a,b]	**Donor with recent marijuana use (N=158)**	**Donor with no recent marijuana use (N=500)**	***P* value**
Demographics			
Age (median, IQR), years	57 (46–65)	60 (49–65)	0.03
Female gender	52 (33%)	179 (36%)	0.51
Race: White	91 (58%)	297 (59%)	0.69
Race: Black	56 (35%)	156 (31%)	0.32
Race: Asian	5 (3%)	16 (3%)	>0.99
Race: American Indian/Alaska Native	0 (0%)	1 (0.2%)	>0.99
Race: Pacific Islander	0 (0%)	1 (0.20%)	>0.99
Race: Other	2 (1%)	13 (3%)	0.54
Race: Unknown	4 (3%)	15 (3%)	>0.99
Ethnicity: Hispanic	15 (9%)	33 (7%)	0.22
Organ transplant type			
Kidney	61 (39%)	186 (37%)	0.20
Liver	33 (21%)	141 (28%)	
Pancreas	1 (0.6%)	4 (0.8%)	
Heart	32 (20%)	69 (14%)	
Lung	31 (20%)	100 (20%)	
Comorbidities			
Uncomplicated diabetes mellitus	21 (13%)	84 (17%)	0.29
Complicated diabetes mellitus	27 (17%)	82 (16%)	0.84
Hypertension	101 (64%)	302 (60%)	0.43
Chronic kidney disease	41 (26%)	123 (25%)	0.73
Cirrhosis	34 (22%)	132 (26%)	0.22
Lung Disease	32 (20%)	121 (24%)	0.31
Congestive heart failure	45 (28%)	98 (20%)	0.02
Prior solid organ Transplant	5 (3%)	23 (5%)	0.51
Charlson comorbidity index (median, IQR)	3 (2–6)	4 (2–6)	0.09
Pre-transplant characteristics			
Days on waitlist (median, IQR)	189 (44–653)	236 (51–836)	0.91
Intensive care unit pre-transplantation[g]	23 (15%)	37 (7%)	<0.01

Mechanical ventilation pre-transplantation[g]	7 (4%)	11 (2%)	0.13
Renal replacement therapy pre-transplantation[g,h]	67 (43%)	195 (40%)	0.49
Antimicrobials Administered Pre-transplant			
Vancomycin	19 (12%)	55 (11%)	0.72
Colistin	0 (0%)	2 (0.4%)	>0.99
Cefepime	10 (6%)	35 (7%)	0.77
Piperacillin-tazobactam	12 (8%)	40 (8%)	0.87
Daptomycin	1 (1%)	6 (1%)	>0.99
Laboratory Values			
CMV seropositive	84 (53%)	291 (58%)	0.27
EBV seropositive	140 (89%)	481 (96%)	<0.01
HCV seropositive[h]	12 (10%)	59 (17%)	0.08
HBsAg positive[i]	5 (3%)	3 (0.7%)	0.02
HBsAb positive[j]	71 (49%)	201 (44%)	0.35
HBcAb positive[k]	21 (13%)	57 (11%)	0.53

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

[b] Only those variables with a *P* value <0.20, those of notable biologic importance, and those included in the final multivariable models are shown in this table.

[c] Immunomodulators used within 6 months prior to transplantation. Immunomodulators included: abatacept, anakinra, apremilast, azathioprine, cyclophosphamide, cyclosporine, denosumab, hydroxychloroquine, methotrexate, mycophenolate, rituximab, secukinumab, sulfasalazine, tocilizumab, tofacitinib, infliximab, adalimumab, certolizumab, golimumab, and etanercept (not including corticosteroids). Due to incomplete recipient data, total recipients with recent donor history of marijuana use was 156 and total recipients with no donor history of marijuana use was 490 for this variable.

[d] Due to incomplete donor data, total donors with no history of marijuana use was 302 for this variable.

[e] Due to incomplete donor data, total donors with no history of marijuana use was 303 for this variable.

[f] PHS has since adopted the use of “risk criteria” for infection transmission in place of the term “increased risk donor.” This data was collected prior to this terminology change.

[g] Assessed in the 24 hours prior to transplantation.

[h] Due to incomplete recipient data, total recipients with recent donor history of marijuana use was 119 and total recipients with no donor history of marijuana use was 352 for this variable.

[i] Due to incomplete recipient data, total recipients with recent donor history of marijuana use was 150 and total recipients with no donor history of marijuana use was 461 for this variable.

[j] Due to incomplete recipient data, total recipients with recent donor history of marijuana use was 146 and total recipients with no donor history of marijuana use was 455 for this variable.

[k] Due to incomplete recipient data, total recipients with no donor history of marijuana use was 499 for this variable.

Abbreviations: CMV, cytomegalovirus; EBV, Epstein Barr virus; HBsAb, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; HBcAb, hepatitis B core antibody; HCV, hepatitis C virus; IQR, interquartile range; PHS, Public Health Service

Table 2.

Donor culture results stratified by donor history of recent marijuana use.

Donor Culture[a]	Donor with recent marijuana use (N=89)	Donor with no recent marijuana use (N=305)	*P* value
Any positive culture[b]	79 (89%)	264 (87%)	0.59
Any positive hospital culture[c]	60 (67%)	183 (60%)	0.21
Any positive OPO culture[d]	62 (70%)	229 (75%)	0.31
Sites of Positive Cultures			
Positive blood culture	10 (11%)	33 (11%)	0.91
Positive respiratory culture[e]	76 (85%)	250 (82%)	0.45
Positive genitourinary culture[f]	18 (20%)	57 (19%)	0.75
Positive perfusate culture[g]	8 (9%)	21 (7%)	0.50
Bacterial Organisms Identified on Donor Cultures			
Staphylococcus aureus	39 (44%)	128 (42%)	0.76
Coagulase-Negative *Staphylococcus*	14 (16%)	31 (10%)	0.15
Klebsiella pneumoniae	12 (13%)	26 (9%)	0.16
Escherichia coli	9 (10%)	22 (7%)	0.37
Enterobacter spp	5 (6%)	20 (7%)	>0.99
Enterococcus spp	5 (6%)	17 (6%)	>0.99
Pseudomonas aeruginosa	5 (6%)	17 (6%)	>0.99
Fungal Organisms Identified on Donor Cultures			
Any fungus	27 (30%)	89 (29%)	0.83
Mold spp.[h]	1 (1%)	3 (1%)	>0.99
Candida spp.	26 (29%)	86 (28%)	0.85
Candida albicans	9 (10%)	24 (8%)	0.50
Candida glabrata	2 (2%)	2 (1%)	0.22
Candida parapsilosis	0 (0%)	1 (0.3%)	>0.99
Candida krusei	0 (0%)	1 (0.3%)	>0.99
MDROs identified on donor cultures			
Any MDRO[i]	13 (15%)	45 (15%)	0.86
MRSA	10 (11%)	26 (9%)	0.44
VRE	0 (0%)	3 (1%)	>0.99
ESBL-Enterobacterales	4 (4%)	16 (5%)	>0.99
CRE	0 (0%)	1 (0.3%)	>0.99
MDR-*Pseudomonas*	0 (0%)	2 (1%)	>0.99

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

[b] Routine mouth flora on respiratory cultures and mixed flora on urine cultures were excluded.

[c] Hospital cultures were obtained during the donor's terminal hospitalization and results may have been known prior to organ procurement.

[d] OPO cultures were collected at the time of organ procurement and results would not have been known until after transplantation.

[e] Respiratory cultures included sputum cultures, tracheal aspirate cultures, endotracheal tube aspirate cultures, bronchial cultures, and bronchoalveolar lavage cultures.

[f] Genitourinary cultures included urine cultures and ureter swab cultures.

[g] Perfusate cultures included perfusate fluid cultures, transport fluid cultures, and pump solution cultures.

[h] Mold spp. included *Aspergillus* spp, and *Penicillium* spp.

[i] MDROs included MRSA, ESBL-Enterobacterales, CRE, MDR-*Pseudomonas*, and VRE. MDR-Acinetobacter was also included but there were no donors who had this MDRO identified on culture.

Abbreviations: CRE, carbapenem-resistant Enterobacterales; ESBL, extended-spectrum beta-lactamases; MDR, multidrug-resistant; MDRO, multidrug-resistant organism; MRSA, methicillin-resistant *Staphylococcus aureus*; OPO, organ procurement organization; spp, species; VRE, vancomycin-resistant *Enterococcus*

Table 3.

Multivariable logistic regression model evaluating the association between recent donor marijuana use and donor culture positivity.

Any positive donor culture			
Variable	**aOR**	**95% CI**	***P* value**
History of recent marijuana use	**0.84**	**0.39–1.81**	**0.65**
Donor immunomodulator use[a]	0.16	0.07–0.37	<0.01
Donor tobacco use	6.61	0.86–50.8	0.07
Donor recent injection drug use[b]	3.76	1.08–13.1	0.04
Variable	**OR**	**95%CI**	***P* value**
History of recent marijuana use	1.23	0.59–2.56	0.59

[a]Immunomodulators included: abatacept, anakinra, apremilast, azathioprine, cyclophosphamide, cyclosporine, denosumab, hydroxychloroquine, methotrexate, mycophenolate, rituximab, secukinumab, sulfasalazine, tocilizumab, tofacitinib, infliximab, adalimumab, certolizumab, golimumab, and etanercept (not including corticosteroids).

[b]Defined as report of donor injection drug use within the 12 months prior to organ procurement and/or detection of injectable substances on toxicology screen taken on admission to donor's terminal hospitalization

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio

Table 4.

Mixed-effects multivariable frailty models evaluating the association between recent donor marijuana use and time to (a) first recipient bacterial or fungal infection within three months post-transplant and (b) recipient graft failure or death within 12 months post-transplant.

(a) First recipient bacterial or fungal infection			
Variable	**aHR**	**95% CI**	***P* value**
History of recent marijuana use	**1.02**	**0.76–1.38**	**0.90**
Recipient colistin administration pre-transplantation	5.64	1.24–25.62	0.03
Recipient vancomycin administration pre-transplantation	2.44	1.70–3.49	<0.01
Donor percutaneous endoscopic gastrostomy	2.45	1.00–5.98	0.05
Donor age (per year increase)	0.99	0.98–1.00	0.02
Recipient Charlson comorbidity index (per point increase)	1.16	1.09–1.23	≤0.01
Organ type: kidney	*ref*		
Organ type: liver	0.59	0.39–0.90	0.01
Organ type: pancreas	1.03	0.24–4.42	0.96
Organ type: heart	1.35	0.92–1.98	0.12
Organ type: lung	2.00	1.43–2.78	<0.01
Variable	**HR**	**95% CI**	***P* value**
History of recent marijuana use	1.14	0.87–1.51	0.35
(b) Recipient graft failure or death within 12 months post-transplant			
Variable	**aHR**	**95% CI**	***P* value**
History of recent marijuana use	**1.65**	**0.90–3.02**	**0.11**
Donor death due to drug overdose	0.64	0.29–1.42	0.27
Donor death due to blunt trauma	2.56	1.38–4.73	<0.01
Recipient daptomycin administration pre-transplantation	5.83	1.34–25.37	0.02
Recipient Charlson comorbidity index	1.13	0.99–1.29	0.07
Organ type: kidney	*ref*		
Organ type: liver	0.98	0.41–2.34	0.96
Organ type: pancreas	3.45	0.44–26.90	0.24
Organ type: heart	1.44	0.61–3.39	0.41
Organ type: lung	2.10	1.00–4.38	0.05
Variable	**HR**	**95% CI**	***P* value**
History of recent marijuana use	1.36	0.76–2.42	0.30

Abbreviations: aHR, adjusted hazard ratio; CI, confidence interval; HR, hazard ratio