**SUPPORTING INFORMATION**

1. **Institutional Review Board (IRB) approvals**

The IRB approvals for each participating center are listed below:

1. University of Pennsylvania (parent IRB for all study sites): Protocol #824398
2. Drexel University: Protocol #160400452
3. Albert Einstein Healthcare Network: Executed an IRB Authorization Agreement to serve as relying IRB for Protocol #824398 at the University of Pennsylvania
4. Temple University: Protocol #23715, Executed an IRB Data Use Agreeement to serve as relying IRB for Protocol #824398 at the University of Pennsylvania
5. **Antibiotic categorizations**

For the purposes of the analysis, antibiotic exposures were grouped into five major categories:

(1) Broad Gram-negative (GN) antibiotics: agents with antipseudomonal activity; specifically fluoroquinolones, cefepime, ceftazidime, piperacillin-tazobactam, meropenem, aztreonam, gentamicin, and tobramycin

(2) Narrow GN antibiotics: agents with GN coverage but no antipseudomonal activity; specifically ceftriaxone, cefotaxime, ampicillin-sulbactam, and amoxicillin-clavulanate

(3) Broad Gram-positive (GP) antibiotics: agents active against MRSA and/or VRE; specifically vancomycin

(4) Narrow GP antibiotics: agents active against GP organisms but which do not cover MRSA and/or VRE; specifically cefazolin and nafcillin

(5) Other antibiotics: metronidazole, azithromycin, doxycycline, clindamycin, rifaximin, trimethoprim-sulfamethoxazole, and erythromycin

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

1. **Additional information on isolate susceptibilities**

MDRO definitions:

1. Methicillin-resistant *Staphylococcus aureus* (MRSA): *S. aureus* that has tested resistant to at least one of the following: methicillin, oxacillin, or cefoxitin.
2. Vancomycin-resistant enterococci (VRE): *E. faecalis* or *E. faecium* that has tested resistant to vancomycin.
3. Extended-spectrum cephalosporin-resistant (ESC-R) Enterobacteriaceae (EB): EB that has tested resistant to one of the following: ceftazidime, cefotaxime, ceftriaxone, or cefepime
4. Carbapenem-resistant Enterobacteriaceae (CRE): EB that has tested resistant to at least one of the following: imipenem, meropenem, doripenem, or ertapenem
5. MDR-*Pseudomonas*: *Pseudomonas* species that has tested either intermediate or resistant to at least one of the following: extended-spectrum cephalosporins (cefepime, ceftazidime); fluoroquinolones (ciprofloxacin, levofloxacin); aminoglycosides (amikacin, gentamicin, tobramycin); carbapenems (imipenem, meropenem, doripenem); piperacillin/piperacillin-tazobactam.
6. MDR-*Acinetobacter*: *Acinetobacter* species that has tested either intermediate or resistant to at least one of the following: extended-spectrum cephalosporins (cefepime, ceftazidime, ceftriaxone, cefotaxime); fluoroquinolones (ciprofloxacin, levofloxacin); aminoglycosides (amikacin, gentamicin, tobramycin); carbapenems (imipenem, meropenem, doripenem); piperacillin/piperacillin-tazobactam, ampicillin-sulbactam.

Table 2 Footnote additional information:

One donor had an MDR-*Pseudomonas* on one respiratory tract specimen (Isolate #1 below) and one blood culture (Isolate #2 below). A second donor had MDR- *Pseudomonas* on one respiratory tract specimen (Isolate #3 below). One donor had an MDR-*Acinetobacter* on one respiratory tract specimen (Isolate #4 below).

1. Isolate #1 (respiratory): *Pseudomonas aeruginosa.* Resistant to cefepime, ceftazidime, piperacillin-tazobactam, meropenem, amikacin, gentamicin, tobramycin, levofloxacin.
2. Isolate #2 (blood): *Pseudomonas aeruginosa*. Resistant to amikacin, gentamicin, tobramycin, ciprofloxacin. Intermediate to cefepime, levofloxacin. Susceptible to ceftazidime, meropenem, piperacillin-tazobactam.
3. Isolate #3 (respiratory): *Pseudomonas aeruginosa.* Resistant to aztreonam, cefepime, ceftazidime, piperacillin-tazobactam, meropenem. Intermediate to ciprofloxacin. Susceptible to amikcain, gentamicin, tobramycin.
4. Isolate #4 (respiratory): *Acinetobacter baumannii/calcoaceticus* complex. Resistant to aztreonam, cefepime, cefotaxime, ceftazidime, ceftriaxone, ciprofloxacin, levofloxacin, trimethoprim-sulfamethoxazole, amikacin. Intermediate to piperacillin, gentamicin. Susceptible to imipenem, meropenem, piperacillin-tazobactam, tetracycline, tobramycin.
5. **Sensitivity analyses**

1. Duration of antibiotics

**Supporting Information Table 1.** Multivariable Cox proportional hazard regression model of time to donor MDRO, including duration of exposure to antibiotics with a narrow GN spectrum

|  |  |
| --- | --- |
| **Donor characteristic** | **Multivariable analysis** |
|  | **aHR** | **95% CI** | ***P* value** |
| Hepatitis C (HCV) viremia | 4.32 | 1.81-10.33 | 0.001 |
| Dialysis | 4.35 | 1.04-18.18 | 0.044 |
| Hematopoietic cell transplant | 7.09 | 0.96-52.12 | 0.054 |
| Tetrahydrocannabinol (THC) | 1.80 | 0.91-3.53 | 0.090 |
| Duration of narrow Gram-negative (GN) antibioticsa | 1.04 | 1.01-1.07 | 0.018 |

aDuration measured in days

1. Redefining “narrow GN antibiotics”

We performed three sensitivity analyses in which revised versions of “narrow GN antibiotics” were used: (1) Cefazolin was added to the narrow GN category (thereby including, ceftriaxone, cefotaxime, ampicillin/sulbactam, amoxicillin/clavulanate, and cefazolin); (2) Only ceftriaxone, cefotaxime, and fluoroquinolones were included in the narrow GN category; (3) Fluoroquinolones were added to the narrow GN category (thereby including, ceftriaxone, cefotaxime, ampicillin/sulbactam, amoxicillin/clavulanate, and fluoroquinolones).

When these revised versions of the antibiotic grouping were incorporated into the multivariable analyses, we found the following: First, when narrow GN antibiotics were redefined to include cefazolin in addition to ceftriaxone, cefotaxime, ampicillin/sulbactam, and amoxicillin/clavulanate, there was no longer a significant association between narrow GN antibiotic exposure and donor MDROs (aHR 1.00, 95% CI 0.90-1.10, *P*=0.969) (Supporting Information Table 2). There was similarly not a significant association between narrow GN antibiotic exposure and ESC-R EB with this definition (aHR 1.04, 95% CI 0.90-1.20, *P*=0.570) (Supporting Information Table 3).

 Second, when narrow GN antibiotics were redefined to include only ceftriaxone, cefotaxime, and fluoroquinolones, there was again no longer a significant association between narrow GN antibiotic exposure and donor MDROs (aHR 1.06, 95% CI 0.93-1.21, *P*=0.385) (Supporting Information Table 4). There was similarly not a significant association between narrow GN antibiotic exposure and ESC-R EB with this definition (aHR 0.98, 95% CI 0.77-1.24, *P*=0.843) (Supporting Information Table 5).

Finally, when narrow GN antibiotics were redefined to include fluoroquinolones in addition to ceftriaxone, cefotaxime, ampicillin/sulbactam, and amoxicillin/clavulanate, there was a borderline significant association between narrow GN antibiotic exposure and donor MDROs (aHR 1.10, 95% CI 1.00-1.22, *P*=0.056) (Supporting Information Table 6). There was no significant association between narrow GN antibiotic exposure and ESC-R EB with this definition (aHR 1.11, 95% CI 0.97-1.26, *P*= 0.117) (Supporting Information Table 7).

**Supporting Information Table 2.** Multivariable Cox proportional hazard regression model for time to donor MDRO, where narrow GN antibiotics include ceftriazone, cefotaxime, ampicillin/sulbactam, amoxicillin/clavulonate, and cefazolin

|  |  |
| --- | --- |
| **Donor characteristic** | **Multivariable analysis** |
|  | **aHR** | **95% CI** | ***P* value** |
| HCV viremia | 4.31 | 1.80-10.29 | 0.001 |
| Dialysis | 4.21 | 1.004-17.67 | 0.049 |
| Hematopoietic cell transplant | 7.06 | 0.96-52.08 | 0.067 |
| THC | 1.87 | 0.96-3.66 | 0.067 |
| Narrow GN abx (version 2) | 0.998 | 0.90-1.10 | 0.969 |

**Supporting Information Table 3.** Multivariable Cox proportional hazard regression model for time to donor ESC-R EB, where narrow GN antibiotics include ceftriaxone, cefotaxime, ampicillin/sulbactam, amoxicillin/clavulonate, and cefazolin

|  |  |
| --- | --- |
| **Donor characteristic** | **Multivariable analysis** |
|  | **aHR** | **95% CI** | ***P* value** |
| Death due to asphyxiation | 5.64 | 1.79-17.70 | 0.003 |
| Narrow GN abx (version 2) | 1.04 | 0.90-1.20 | 0.570 |

**Supporting Information Table 4.** Multivariable Cox proportional hazard regression model for time to donor MDRO, where narrow GN antibiotics include ceftriaxone, cefotaxime, and fluoroquinolones

|  |  |
| --- | --- |
| **Donor characteristic** | **Multivariable analysis** |
|  | **aHR** | **95% CI** | ***P* value** |
| HCV viremia | 4.29 | 1.80-10.26 | 0.001 |
| Dialysis | 4.32 | 1.03-18.07 | 0.045 |
| Hematopoietic cell transplant | 6.60 | 0.89-48.88 | 0.065 |
| THC | 1.86 | 0.95-3.64 | 0.069 |
| Narrow GN abx (version 3) | 1.06 | 0.93-1.21 | 0.385 |

**Supporting Information Table 5.** Multivariable Cox proportional hazard regression model for time to donor ESC-R EB, where narrow GN antibiotics include ceftriaxone, cefotaxime, and fluoroquinolones

|  |  |
| --- | --- |
| **Donor characteristic** | **Multivariable analysis** |
|  | **aHR** | **95% CI** | ***P* value** |
| Death due to asphyxiation | 5.60 | 1.78-17.61 | 0.003 |
| Narrow GN abx (version 3) | 0.98 | 0.77-1.24 | 0.843 |

**Supporting Information Table 6.** Multivariable Cox proportional hazard regression model for time to donor MDRO, where narrow GN antibiotics include ceftriaxone, cefotaxime, ampicillin/sulbactam, amoxicillin/clavulonate, and fluoroquinolones

|  |  |
| --- | --- |
| **Donor characteristic** | **Multivariable analysis** |
|  | **aHR** | **95% CI** | ***P* value** |
| HCV viremia | 4.31 | 1.81-10.30 | 0.001 |
| Dialysis | 4.44 | 1.06-18.59 | 0.041 |
| Hematopoietic cell transplant | 6.32 | 0.86-46.67 | 0.071 |
| THC | 1.88 | 0.96-3.68 | 0.065 |
| Narrow GN abx (version 4) | 1.10 | 0.998-1.22 | 0.056 |

**Supporting Information Table 7.** Multivariable Cox proportional hazard regression model for time to donor ESC-R EB, where narrow GN antibiotics include ceftriaxone, cefotaxime, ampicillin/sulbactam, amoxicillin/clavulonate, and fluoroquinolones

|  |  |
| --- | --- |
| **Donor characteristic** | **Multivariable analysis** |
|  | **aHR** | **95% CI** | ***P* value** |
| Death due to asphyxiation | 5.81 | 1.85-18.28 | 0.003 |
| Narrow GN abx (version 4) | 1.11 | 0.97-1.26 | 0.117 |