Epidemiology of ICU-onset bloodstream infection: incidence, pathogens and risk factors among 150,948 ICU patients at 85 U.S. Hospitals

ONLINE SUPPLEMENT

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# Cohort selection and initial data curation

Inpatient encounters in the Cerner Healthfacts Database with missing or implausible admission/discharge dates, no records of medications, laboratory tests or diagnosis codes in the dataset were excluded leading to a cohort of 5.1 million inpatient encounters. After restricting to adult patients (>= 20 years of age) with an admission year between CY 2009 and CY 2015, the subset consisted of 2,529,158 encounters. This smaller but more complete subset contained data from 169 hospitals, but only 10% of those patients were admitted to the ICU and were the subject of this current analysis.

# Detailed definitions

**Pre-ICU antimicrobial exposure**: defined as any inpatient use of antibacterial, antifungal or antiviral agents up to 30 days prior to the BSI of interest during the same hospital stay (1, 2). When applicable, other medications are also considered within the same period. The list of antimicrobial agents was adapted from prior work (3).

**Polymicrobial BSI:** Any episode with more than one clinically important pathogenic species of blood culture isolate detected within 2 days of index bacteremia. If a coagulase-negative staphylococcus was involved, the time-window was increased to 3 days (to allow a 2–day delay after the second coagulase-negative staphylococci positive bacteremia)

# Additional Methods on handling of time varying covariates

The analytic dataset was restricted to those with ICU stays 30 days or fewer.  Global tests for proportional hazards with a dataset of this size are not informative.  In lieu of such, the data were split into two strata that each roughly contained half of the events and the model was then run.  From the two models we compared the z-scores (beta coefficient / standard error) of each variable from the two halves and if they were significant and in opposite directions the final model fitted to all the data would stratify on the flagged variable.  This way we identify variables that behave differently for small times and large times. The final primary and sensitivity analysis models are stratified based on the day of the hospital stay that the patient was admitted to the ICU.

# Detailed variables selection for risk factors and patients’ characteristics

## eTable 1 Patients’ characteristics

|  |  |  |
| --- | --- | --- |
| **Variable Name** | **ICD-9 Codes / Description** | **Values** |
| **Age** | Age in years at admission | Integer values |
| **Gender** | Patient gender | 1 - M2 - F |
| **Race / Ethnicity** |  | Black, White, Unknown, Multiple, Indian/Alaskan |
| **Elixhauser Comorbidity Index** (4–6) | A composite score of patient comorbidities based on ICD-9 | Integer values |
| **Congestive Heart Failure** | 398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4–425.9, 428.x | Yes/No |
| **Cardiac Arrhythmia** | 426.0, 426.13, 426.7, 426.9, 426.10, 426.12, 427.0–427.4, 427.6–427.9, 785.0, 996.01, 996.04, V45.0, V53.3 | Yes/No |
| **Valvular Disease** | 093.2, 394.x–397.x, 424.x, 746.3–746.6, V42.2, V43.3 | Yes/No |
| **Pulmonary Circulation Disorders**  | 415.0, 415.1, 416.x, 417.0, 417.8, 417.9 | Yes/No |
| **Peripheral Vascular Disorders** | 093.0, 437.3, 440.x, 441.x, 443.1– 443.9, 447.1, 557.1, 557.9, V43.4 | Yes/No |
| **Hypertension Uncomplicated**  | 401.x | Yes/No |
| **Hypertension Complicated** | 402.x–405.x | Yes/No |
| **Paralysis** | 334.1, 342.x, 343.x, 344.0– 344.6, 344.9 | Yes/No |
| **Other Neurological Disorders** | 331.9, 332.0, 332.1, 333.4, 333.5, 333.92, 334.x–335.x, 336.2, 340.x, 341.x, 345.x, 348.1, 348.3, 780.3, 784.3 | Yes/No |
| **Chronic Pulmonary Disease** | 416.8, 416.9, 490.x –505.x, 506.4, 508.1, 508.8 | Yes/No |
| **Diabetes Uncomplicated** | 250.0–250.3 | Yes/No |
| **Diabetes Complicated** | 250.4–250.9 | Yes/No |
| **Hypothyroidism** | 240.9, 243.x, 244.x, 246.1, 246.8 | Yes/No |
| **Renal Failure**  | 403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 585.x, 586.x, 588.0, V42.0, V45.1, V56.x | Yes/No |
| **Liver Disease** | 070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 070.6, 070.9, 456.0–456.2, 570.x, 571.x, 572.2–572.8, 573.3, 573.4, 573.8, 573.9, V42.7 | Yes/No |
| **Peptic Ulcer Disease excluding bleeding** | 531.7, 531.9, 532.7, 532.9, 533.7, 533.9, 534.7, 534.9 | Yes/No |
| **AIDS/HIV** | 042.x–044.x | Yes/No |
| **Haematology malignancy** | 200.x–202.x, 203.0, 204.x-208.x, 238.6 | Yes/No |
| **Metastatic Cancer** | 196.x–199.x | Yes/No |
| **Solid/System/Neuroendocrine Tumor without Metastasis** | 140.x–172.x, 173.x, 174.x, 195.x, 196.x-199.x, 209, 235-239 | Yes/No |
| **Rheumatologic / inflammatory diseases** | 135, 277.3, 277.31, 277.39, 340, 341, 357, 422, 446, 495.9, 516, 555-558, 695.4, 710, 711, 712, 714, 720, 725 | Yes/No |
| **Coagulopathy** | 286.x, 287.1, 287.3–287.5 | Yes/No |
| **Obesity** | 278.0 | Yes/No |
| **Weight Loss** | 260.x–263.x, 783.2, 799.4 | Yes/No |
| **Fluid and Electrolyte Disorders** | 253.6, 276.x | Yes/No |
| **Blood Loss Anemia** | 280.0 | Yes/No |
| **Deficiency Anemia** | 280.1–280.9, 281.x | Yes/No |
| **Alcohol Abuse** | 265.2, 291.1–291.3, 291.5–291.9, 303.0, 303.9, 305.0, 357.5, 425.5, 535.3, 571.0–571.3, 980.x, V11.3 | Yes/No |
| **Drug Abuse** | 292.x, 304.x, 305.2–305.9, V65.42 | Yes/No |
| **Psychoses** | 293.8, 295.x, 296.04, 296.14, 296.44, 296.54, 297.x, 298.x | Yes/No |
| **Depression** | 296.2, 296.3, 296.5, 300.4, 309.x, 311 | Yes/No |
| **Admission from acute care facility**  | Hospital or critical access hospital | Yes/No |
| **Admission from non-acute care facility** | Skilled nursing facility or another health care facility | Yes/No |
| **Admission from ambulatory surgery center** | Ambulatory surgery center | Yes/No |
| **Admission from hospice** | Hospice | Yes/No |
| **Insurance status** |  |  |

## eTable 2 Acute care principal diagnosis codes (adapted from (7))

|  |  |  |
| --- | --- | --- |
| **Category** | **ICD-9** | **Presumed Indication for ICU admission**  |
| Pulmonary disease | 460-519 | Pulmonary |
| Diseases of pulmonary circulation | 415 | Pulmonary |
| Infectious diseases | 001-139 | Infectious Diseases/sepsis |
| Metabolic disorder | 240-279 | Renal/Metabolic/Toxic |
| Renal insufficiency | 580-629 | Renal/Metabolic/Toxic |
| Poisoning | 960-989 | Renal/Metabolic/Toxic |
| Digestive disease | 520-579 | Digestive system |
| Diseases of the musculoskeletal system & connective tissue | 710-739 | Skin/Soft tissue/Musculoskeletal |
| Diseases of the skin and subcutaneous tissue | 680-709 | Skin/Soft tissue/Musculoskeletal |
| Other forms of heart disease | 420-429 | Cardiovascular |
| Cerebrovascular disease | 430-438 | Neurologic |
| Neurologic disease | 320-389 | Neurologic |
| Mental disorders | 290-319 | Neurologic |
| Ischemic heart disease | 410 - 414 | Cardiovascular |
| Arteries and veins | 440-459 | Cardiovascular |
| Hypertensive disease | 401-405 | Cardiovascular |
| Chronic rheumatic heart disease | 393-398 | Cardiovascular |
| Acute Rheumatic fever | 390-392 | Cardiovascular |
| Trauma | 800-959 | Trauma/Procedural complication |
| Complications peculiar to certain specified procedures | 996 | Trauma/Procedural complication |
| Neoplasms | 140-239 | Heme-oncology |
| Diseases of the blood and blood-forming organs | 280-289 | Heme-oncology |
| Supplementary classification of factors influencing health status and contact with health services | V01-V86 | Other/unspecified |
| Congenital anomalies | 740-759 | Other/unspecified |
| Symptoms, signs, and ill-defined conditions | 780-799 | Other/unspecified |
| Other complications of procedures, NEC | 998 | Other/unspecified |
| Complications affecting specified body systems, not elsewhere classified | 997 | Other/unspecified |
| Complications of pregnancy, childbirth, and the puerperium | 630-677 | Other/unspecified |
| Complications of medical care, not elsewhere classified | 999 | Other/unspecified |
| Other and unspecified effects of external causes | 990-995 | Other/unspecified |
| Supplementary classification of external causes of injury and poisoning | E800-E999 | Renal/Metabolic/Toxic |

## eTable 3: Transplantation

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable Name** | **Description** | **ICD-9 Codes / Description** | **Values** |
| **Hematopoietic cell transplantation** | Peripheral stem cells | V42.82 | Yes/No |
| Bone marrow transplant | V42.81 |
| **Organ transplant** | Kidney | V42.0 | Yes/No |
| Heart | V42.1 |
| Lung | V42.6 |
| Liver | V42.7 |
| Pancreas | V42.83 |
| Intestines | V42.84 |
| **Organ complications present on admission for transplant** | Kidney | 996.81 | Yes/No |
| Heart | 996.83 |
| Lung | 996.84 |
| Liver | 996.82 |
| Pancreas | 996.86 |
| Intestines | 996.87 |
| **Stem cell transplant status** | Z94.84 | Yes/No |
| **Graft vs. host disease** | 279.50, 279.51, 279.52, 279.53 | Yes/No |

NEC = not elsewhere classified; NOS = not otherwise specified; WBC= white blood cell.

## eTable 4: Immunocompromised definition

|  |
| --- |
| **IMMUNOCOMPROMISED** Defined as positive if:1. HIV/AIDs OR Hematologic Malignancy OR Other Immune Conditions

OR1. (Metastatic Cancer, Solid/System/Neuroendocrine Tumor without Metastasis, Organ Transplant, Organ complications present on admission for transplant, Rheumatology) + Chemo or Immune-Modulating Agent

OR1. Rheumatologic/Inflammatory + Systemic Steroids
 |

## eTable 5: Burn codes

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable Name** | **Description** | **ICD-9 Codes / Description** | **Values** |
| **Burns** | Late effect of burn | 906.5, 906.6, 906.7, 906.8, 906.9 | Yes/No |
| Burn confined to eye | 940.0, 940.1, 940.2, 940.3, 940.4, 940.5, 940.9 |
| Burn of face, head, and neck | 941.0, 941.1, 941.2, 941.3, 941.4, 941.5 |
| Burn of trunk | 942.0, 942.1, 942.2, 942.3, 942.4, 942.5 |
| Burn of upper limb, except wrist and hand | 943.0, 943.1, 943.2, 943.3, 943.4, 943.5 |
| Burn of wrist(s) and hand(s) | 944.0, 944.1, 944.2, 944.3, 944.4, 944.5 |
| Burn of lower limb(s) | 945.0, 945.1, 945.2, 945.3, 945.4, 945.5 |
| Burn of multiple specified sites | 946.0, 946.1, 946.2, 946.3, 946.4, 946.5 |
| Burn of internal organs | 947.0, 947.1, 947.2, 947.3, 947.4, 947.8, 947.9 |
| Extent of body surface involved | 948.0, 948.1, 948.2, 948.3, 948.4, 948.5, 948.6, 948.7, 948.8, 948.9 |
| Burn, unspecified | 949.0, 949.1, 949.2, 949.3, 949.4, 949.5 |

## eTable 6: Trauma codes (adapted from (8))

|  |  |  |
| --- | --- | --- |
| **Variable Name** | **ICD-9 Codes / Description** | **Values** |
| **Trauma** | If any of the ICD-9 codes below is present. | Yes/No |
| **Traumatic Brain Injury** | 851–854, 995.55, 950(.1–.3), 850(.0–.4,.5,.9), [800,801,803,804] (.09–.4,.6–.9,.00–.06,.50–.56, .59) | Yes/No |
| **Other trauma (non TBI)** | Any of the ICD-9 codes below |  |
| **Chest internal injury** | 860–862, 875, 879(.0–.1), 901, 926.19, 953.1 | Yes/No |
| **Abdominal internal injury** | 863–866, 868, 879(.2–.5), 902(.0–.4), 953.2, 953.5 | Yes/No |
| **Uro-genital internal injury** | 867, 877–878, 902(.5, .81–.82), 926(.0, .12), 953.3 | Yes/No |
| **Internal injury** | Chest, abdominal, uro-genital or trunk injury. | Yes/No |
| **Trunk internal injuries** | 879(.6–.7), 926(.8–.9), 954(.1, .8–.9), 876, 926.11 | Yes/No |

## eTable 7: Center level data

|  |  |  |
| --- | --- | --- |
| **Variable Name** | **SAS Variable Type** | **Values** |
| **Urban vs. rural** |  | Urban vs. rural |
| **Teaching vs. non-teaching** |  | Teaching vs. non-teaching |
| **Region** |  | Northeast, South, Midwest, West |
| **Bed size** |  | Large - ≥500 bedsMedium - 200-499 bedsSmall < 200 beds |
| **Volume of ICU-related BSI** | Derived code | Numerical |
| **ICU type** |  | Undifferentiated / Specialty (Medical, Surgical, Cardiac/Coronary, Neurology) |

## eTable 8: Center level data characteristics

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Variables** | **ICU-onset BSI group\*****N=1,306****n (%)** | **ICU–BSIPOA group****N=5,600****n (%)** | **No bacteremia group****N=143,589****n (%)** |
| **Center-level data** | **Urban hospital,** n (%) | 1084 (83.0) | 4720 (84.3) | 107641 (75.0) |
| **Small size hospital,** n (%) | 175 (13.4) | 1160 (20.7) | 26355 (18.4) |
| **Medium size hospital,** n (%) | 800 (61.3) | 3268 (58.4) | 76865 (53.5) |
| **Large size hospital,** n (%) | 331 (25.3) | 1172 (20.9) | 40369 (28.1) |
| **Northeast hospital,** n (%) | 410 (31.4) | 1693 (30.2) | 49531 (34.5) |
| **South hospital,** n (%) | 583 (44.6) | 2194 (39.2) | 56356 (39.2) |
| **Midwest hospital,** n (%) | 201 (15.4) | 906 (16.2) | 20712 (14.4) |
| **West hospital,** n (%) | 112 (8.6) | 807 (14.4) | 16990 (11.8) |
| **Undifferentiated ICU,** n (%) | 841 (64.4) | 3872 (69.1) | 88338 (61.5) |
| **Medical ICU,** n (%) | 112 (8.6) | 555 (9.9) | 13268 (9.2) |
| **Surgical ICU,** n (%) | 159 (12.2) | 468 (8.4) | 16567 (11.5) |
| **Neuro/neurosurgical ICU,** n (%) | 23 (1.8) | 37 (0.66) | 2526 (1.8) |
| **Cardiac ICU,** n (%) | 171 (13.1) | 668 (11.9) | 22890 (15.9) |
| **Academic Teaching Facility,** n (%) | 1047 (80.2) | 3991 (71.4) | 104502 (72.9) |
| **Volume bacteremia per year,** median [IQR] | 268 [118] | 241 [122] | 218 [137] |

\*detected at day 3 or later of ICU stay.

## eTable 9: Organism Distribution Stratified by Infection Onset Timing

|  |  |  |  |
| --- | --- | --- | --- |
|  | **ICU-onset BSI group\*** | **ICU–BSIPOA group** |  |
| **Organism** | **N** | **%** | **N** | **%** | **p-value** |
| *Staphylococcus aureus* | 185 | 14.2% | 1124 | 20.1% | <0.001 |
| *Streptococcus spp* | 65 | 5.0% | 948 | 16.9% | <0.001 |
| Polymicrobial | 188 | 14.4% | 807 | 14.4% | 0.99 |
| *Escherichia coli* | 61 | 4.7% | 925 | 16.5% | <0.001 |
| Coagulase Negative Staphylococcus | 175 | 13.4% | 407 | 7.3% | <0.001 |
| Other | 88 | 6.7% | 395 | 7.1% | 0.69 |
| *Klebsiella spp* | 80 | 6.1% | 324 | 5.8% | 0.64 |
| *Enterococcus spp* | 85 | 6.5% | 192 | 3.4% | <0.001 |
| *Pseudomonas spp* | 67 | 5.1% | 145 | 2.6% | <0.001 |
| *Candida non-albicans* | 118 | 9.0% | 89 | 1.6% | <0.001 |
| *Candida albicans* | 91 | 7.0% | 52 | 0.9% | <0.001 |
| *Enterobacter spp* | 43 | 3.3% | 87 | 1.6% | 0.000031 |
| *Bacteroides spp* | 27 | 2.1% | 73 | 1.3% | 0.037 |
| *Acinetobacter spp* | 33 | 2.5% | 32 | 0.6% | <0.001 |

\*detected at day 3 or later of ICU stay

**eTable 10: Resistant Organism Distribution Stratified by Infection Onset Timing**

|  |  |  |  |
| --- | --- | --- | --- |
|   | **ICU-onset BSI group\*** | **ICU–BSIPOA group** |  |
| **Organism & Resistance** | **N** | **%** | **N** | **%** | **p-value** |
| **Methicillin Resistant** |  |  |  |  |  |
| *Staphylococcus aureus* | 85 | 52.8% | 404 | 42.2% | 0.012 |
| Coagulase Negative *Staphlycoccus* | 104 | 72.2% | 180 | 58.4% | 0.0047 |
| **Vancomycin Resistant** |  |  |  |  |  |
| *Enterococcus* spp | 31 | 34.4% | 37 | 16.5% | 0.00049 |
| **Ceftriaxone Resistant** |  |  |  |  |  |
| *Escherichia coli* | 11 | 28.9% | 75 | 9.4% | 0.0025 |
| *Klebsiella* spp | 17 | 30.2% | 34 | 12.5% | 0.01 |
| *Enterobacter* spp | 16 | 25.0% | 11 | 15.3% | 0.0073 |
| **Carbapenem Resistant** |  |  |  |  |  |
| *Klebsiella* spp | 14 | 20.0% | 22 | 7.9% | 0.00075 |
| *Pseudomonas* spp | 10 | 18.2% | 19 | 15.8% | 0.7 |
| *Escherichia coli* | 7 | 12.7% | 15 | 1.8% | 0.00089 |
| *Enterobacter* spp | 3 | 7.7% | 4 | 5.3% | 0.44 |
| *Acinetobacter* spp | 10 | 34.5% | 2 | 8.0% | 0.02 |

## eTable 11: Organism Distribution Stratified by ICU Admission Timing

|  |  |
| --- | --- |
|  | **ICU–BSIPOA group** |
|  | **Admitted to ICU on day of Hospital Admission**  | **Admitted to ICU after day of Hospital Admission**  |
| **Organism** | **N** | **%** | **N** | **%** |
| *Acinetobacter* spp  | 23 | 0.5% | 9 | 0.7% |
| *Bacteriodes* spp  | 56 | 1.3% | 17 | 1.4% |
| Candida albicans  | 38 | 0.9% | 14 | 1.1% |
| Candida non-albicans  | 49 | 1.1% | 40 | 3.2% |
| Coagulase Negative *Staphylococcus*  | 300 | 6.9% | 107 | 8.6% |
| *Enterobacter* spp  | 62 | 1.4% | 25 | 2.0% |
| *Enterococcus* spp  | 176 | 4.0% | 68 | 5.5% |
| *Escherichia coli*  | 742 | 17.0% | 183 | 14.7% |
| *Klebsiella* spp  | 242 | 5.6% | 82 | 6.6% |
| Other  | 324 | 7.4% | 71 | 5.7% |
| Polymicrobial  | 593 | 13.6% | 162 | 13.1% |
| *Pseudomonas* spp  | 103 | 2.4% | 42 | 3.4% |
| *Staphylococcus aureus*  | 855 | 19.6% | 269 | 21.7% |
| *Streptococcus* spp | 796 | 18.3% | 152 | 12.2% |

## eFigure 1: Blood Culture Sampling by ICU Day



Blood Culture Sampling Date Relative to ICU Day

# Sensitivity Analyses

## eTable 12: Replacing the Elixhauser comorbidity index with individual comorbid conditions that comprise the index (e.g., liver disease, hypertension, coagulopathy, etc.) to evince risk differences by comorbidity type

|  |  |
| --- | --- |
| **Covariate** | **Hazard Ratio (95% CI)** |
| Age | 0.94 (0.91, 0.98) |
| HIV/AIDS | 0.34 (0.15, 0.78) |
| Alcohol Abuse | 1.37 (1.13, 1.65) |
| Pre-ICU Antibacterial Agent Exposure | 3.00 (2.33, 3.87) |
| Pre-ICU Antifungal Agent Exposure | 3.13 (2.76, 3.56) |
| Pre-ICU Antiviral Agent Exposure | 1.01 (0.79, 1.30) |
| Administration of vasopressors | 2.58 (2.27, 2.93) |
| Arterial Line <7 days | 1.01 (0.79, 1.29) |
| Arterial Line >7 days | 1.53 (1.10, 2.14) |
| Blood Loss Anemia | 1.10 (0.74, 1.62) |
| Blood tranfusion/blood product administration | 0.89 (0.74, 1.07) |
| Blood transfusion >7 days | 0.88 (0.68, 1.15) |
| Burns | 2.17 (0.97, 4.88) |
| CPR <7 Days | 1.09 (0.79, 1.50) |
| CPR >7 days | 1.82 (1.12, 2.95) |
| Arrhythmia | 1.14 (1.01, 1.29) |
| Northeast Census Region (vs East) | 1.39 (1.14, 1.69) |
| South Census Region (vs East) | 1.05 (0.88, 1.25) |
| West Census Region (vs East) | 0.83 (0.64, 1.07) |
| Central Line <7 days | 1.14 (0.99, 1.32) |
| Central Line >7 days | 1.70 (1.39, 2.09) |
| Chronic pulmonary disease | 0.91 (0.79, 1.05) |
| Coagulopathy  | 1.41 (1.23, 1.63) |
| Congestive Heart Failure | 1.00 (0.87, 1.15) |
| Iron deficiency anemia | 0.76 (0.55, 1.05) |
| Depression | 0.87 (0.72, 1.07) |
| Diabetes - complicated | 0.74 (0.58, 0.94) |
| Diabetes - uncomplicated | 0.97 (0.84, 1.12) |
| Dialysis Required upon ICU Admission | 0.66 (0.31, 1.40) |
| Drug Abuse | 0.86 (0.66, 1.14) |
| Fluid Electrolyte Disorders | 1.19 (1.05, 1.35) |
| Female (vs Male) | 0.87 (0.77, 0.97) |
| Hematologic malignancy | 0.92 (0.61, 1.39) |
| ECMO/Hearth Circulatory Assistance Required During Admission | 2.12 (1.41, 3.17) |
| Hypertension - complicated | 0.78 (0.61, 0.99) |
| Hypertension - uncomplicated | 0.71 (0.62, 0.82) |
| Hypothyroidism | 0.84 (0.68, 1.03) |
| Cardiac ICU (vs Non-specialty ICU) | 0.89 (0.75, 1.06) |
| Medical ICU (vs Non-specialty ICU) | 0.55 (0.44, 0.68) |
| Neurologic ICU (vs Non-specialty ICU) | 0.68 (0.44, 1.06) |
| Surgical ICU (vs Non-specialty ICU) | 0.77 (0.63, 0.94) |
| Immunocompromised | 1.08 (0.85, 1.37) |
| Healthcare Facility Origin | 1.13 (0.95, 1.34) |
| Liver Disease | 1.36 (1.14, 1.62) |
| Mechanical ventilation during encounter | 3.88 (2.97, 5.07) |
| Metastatic cancer | 0.75 (0.52, 1.08) |
| Neutropenia | 0.71 (0.39, 1.29) |
| Overweight/Obesity | 1.12 (0.94, 1.34) |
| Neurologic Disease | 1.44 (1.27, 1.64) |
| Paralysis | 1.27 (1.01, 1.61) |
| Parenteral Nutrition Required During Admission | 1.22 (0.63, 2.36) |
| Non-bleeding peptic ulcer | 0.88 (0.53, 1.48) |
| Peripheral Vascular Disorders | 1.22 (1.02, 1.45) |
| Psychoses | 0.98 (0.70, 1.36) |
| Pulmonary/Circulatory Disorders | 1.15 (0.94, 1.42) |
| Asian (vs White) | 0.89 (0.50, 1.58) |
| Black (vs White) | 1.32 (1.14, 1.53) |
| Hispanic (vs White) | 1.89 (1.25, 2.85) |
| Other Race (vs White) | 1.80 (1.40, 2.32) |
| Unknown Race (vs White) | 1.09 (0.77, 1.54) |
| Renal Failure | 1.26 (1.00, 1.58) |
| Rheumatologic/Inflammatory Disease | 1.17 (0.96, 1.43) |
| Solid Tumor/Metastasis | 1.04 (0.82, 1.33) |
| Academic Teaching Facility | 1.06 (0.88, 1.28) |
| Trauma (vs None) | 2.33 (1.92, 2.82) |
| Medium Rural Hospital (vs Large Rural Hospital) | 1.68 (1.17, 2.42) |
| Small Rural Hospital (vs Large Rural Hospital) | 1.68 (1.12, 2.51) |
| Large Urban Hospital (vs Large Rural Hospital) | 1.81 (1.31, 2.50) |
| Medium Urban Hospital (vs Large Rural Hospital) | 2.21 (1.65, 2.96) |
| Small Urban Hospital (vs Large rural Hospital | 2.49 (1.74, 3.57) |
| Valvular Disease | 1.12 (0.93, 1.35) |
| Annual Bacteremia Volume | 1.00 (1.00, 1.00) |
| Weight Loss | 1.40 (1.21, 1.61) |

## eTable 13: Counting ICU–onset BSI from ICU-day 3 to ICU Day-4 onwards

|  |  |
| --- | --- |
| **Covariate** | **Hazard Ratio (95% CI)** |
| Age | 0.93 (0.89, 0.97) |
| Pre-ICU Antibacterial Agent Exposure | 2.66 (1.98, 3.58) |
| Pre-ICU Antifungal Agent Exposure | 2.99 (2.57, 3.47) |
| Pre-ICU Antiviral Agent Exposure | 1.04 (0.80, 1.36) |
| Administration of vasopressors | 2.95 (2.55, 3.40) |
| Arterial Line <7 days | 1.02 (0.78, 1.34) |
| Arterial Line >7 days | 1.46 (1.05, 2.03) |
| Blood transfusion <7 days | 0.94 (0.77, 1.14) |
| Blood transfusion >7 days | 0.90 (0.69, 1.18) |
| Burns | 1.33 (0.49, 3.58) |
| CPR <7 Days | 0.91 (0.62, 1.34) |
| CPR >7 days | 1.92 (1.19, 3.11) |
| Arrhythmia | 0.93 (0.80, 1.08) |
| Northeast Census Region (vs East) | 1.44 (1.15, 1.79) |
| South Census Region (vs East) | 1.15 (0.94, 1.40) |
| West Census Region (vs East) | 0.91 (0.69, 1.21) |
| Central Line <7 days | 1.12 (0.96, 1.31) |
| Central Line >7 days | 1.63 (1.32, 2.01) |
| Dialysis Required upon ICU Admission | 0.57 (0.21, 1.53) |
| Gastrointestinal Disease | 1.35 (1.19, 1.54) |
| ECMO/Hearth Circulatory Assistance Required During Admission | 2.36 (1.53, 3.63) |
| Elixhauser comorbidity score | 1.04 (1.00, 1.07) |
| Female (vs Male) | 0.78 (0.69, 0.89) |
| Hematologic malignancy | 1.04 (0.90, 1.20) |
| Cardiac ICU (vs Non-specialty ICU) | 0.94 (0.77, 1.14) |
| Medical ICU (vs Non-specialty ICU) | 0.60 (0.47, 0.77) |
| Neurologic ICU (vs Non-specialty ICU) | 0.65 (0.40, 1.08) |
| Surgical ICU (vs Non-specialty ICU) | 0.89 (0.72, 1.10) |
| Immunocompromised | 0.92 (0.76, 1.13) |
| Infectious Disease/Sepsis | 1.44 (1.20, 1.71) |
| Healthcare Facility Origin | 1.13 (0.93, 1.36) |
| Mechanical ventilation during encounter | 4.77 (3.55, 6.41) |
| Neurologic Disease | 1.03 (0.89, 1.18) |
| Other Trauma/Procedural Complication (vs no Trauma) | 1.86 (1.38, 2.52) |
| Other Unspecified Disease | 0.89 (0.72, 1.10) |
| Parenteral Nutrition Required During Admission | 1.32 (0.66, 2.66) |
| Pulmconary/Circulatory Disorders | 2.32 (1.96, 2.76) |
| Asian (vs White) | 1.07 (0.60, 1.91) |
| Black (vs White) | 1.26 (1.08, 1.48) |
| Hispanic (vs White) | 1.82 (1.15, 2.89) |
| Other Race (vs White) | 1.59 (1.20, 2.12) |
| Unknown Race (vs White) | 1.07 (0.73, 1.58) |
| Renal Failure | 0.74 (0.60, 0.91) |
| Skin-Soft Tissue/Musculoskeletal | 0.99 (0.86, 1.13) |
| Traumatic Brain Injury Alone (vs no Trauma) | 1.33 (0.88, 2.00) |
| Traumatic Brain Injury with Other Complication (vs no Trauma) | 2.64 (1.72, 4.06) |
| Academic Teaching Facility | 1.07 (0.86, 1.32) |
| Other Trauma/Procedural Complication (vs no Trauma) | 1.51 (1.27, 1.78) |
| Medium Rural Hospital (vs Large Rural Hospital) | 2.00 (1.32, 3.05) |
| Small Rural Hospital (vs Large Rural Hospital) | 1.90 (1.21, 3.00) |
| Large Urban Hospital (vs Large Rural Hospital) | 2.29 (1.58, 3.32) |
| Medium Urban Hospital (vs Large Rural Hospital) | 2.41 (1.71, 3.39) |
| Small Urban Hospital (vs Large rural Hospital | 2.81 (1.85, 4.26) |
| Annual Bacteremia Volume | 1.00 (1.00, 1.00) |

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