Appendix 1: Hospital Characteristics

|  |  |  |
| --- | --- | --- |
| Variable | 2011-2013(n= 159,133) | 2014-2016(n= 202,190) |
| **Hospital Region, %(n)** |  |  |
| Northeast | 20.4 (32,243) | 15.3 (30,882) |
| Midwest | 18.5 (30,219) | 21.3 (43,105) |
| South | 37.9 (60,476) | 39.1 (79,121) |
| West | 23.0 (36,195) | 24.3 (49,082) |
| **Hospital Size, %(n)** |  |  |
| Small | 10.1 (15,882) | 15.9 (32,124) |
| Medium | 25.5 (39,697) | 27.8 (56,104) |
| Large | 64.5 (102,306) | 56.4 (113,962) |
| **Hospital Location, %(n)** |  |  |
| Rural | 6.7 (10,411) | 6.4 (12,981) |
| Urban Teaching | 56.7 (89,317) | 69.0 (139,397) |
| Urban Nonteaching | 36.5 (58,157) | 24.7 (49,812) |
| **Hospital Ownership, %(n)** |  |  |
| Government | 12.3 (19,337) | 13.6 (27,412) |
| Private, Investor Owned | 13.9 (21,831) | 14.1 (28,405) |
| Private, Nonprofit | 73.9 (116,717) | 72.4 (146,373) |

All variables with *p* < 0.0001 using chi square.

|  |  |  |
| --- | --- | --- |
|  | **2011-2013 (n=159,003)** | **2014-2016 (n=202,021)** |
| Northeast (%,n) | 25.7 (8,278) | 20.0 (6,163) |
| Midwest (%,n) | 20.3 (6,124) | 16.6 (7,163) |
| South (%,n)  | 23.8 (14,369) | 20.0 (15,838) |
| West (%,n)  | 21.2 (7,676) | 17.1 (8,388) |

Appendix 2: Mortality by Region

All variables with *p* < 0.0001 using chi square.

Appendix 3: Time Series of Severe Sepsis and Septic Shock Mortality

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **2011** | **2012** | **2013** | **2014** | **2015** | **2016** |
| Mortality (%,n) | 23.8 (12,234) | 23.2 (12,528) | 21.7 (11,472) | 20.4 (12,832) | 18.5 (12,766) | 17.1 (12,163) |

Appendix 4: ICD-9 and ICD-10 codes for infection source

|  |  |  |  |
| --- | --- | --- | --- |
| **Infection Category** | **ICD-9-CM Code** | **ICD-9-CM Code Description** | **ICD-10** |
| Parasitic | 001 | Cholera | A00, A00.0 |
|   | 002 | Typhoid/paratyphoid fever | A01.00, A01.1, A01.4, A01.2, A01.3 |
|   | 003 | Other salmonella infection | A02, A02.9, A02.20 |
|   | 004 | Shigellosis | A03,A03.0, A03.1, A03.2, A03.3, A03.8, A03.9 |
|   | 005 | Other food poisoning | T62.91XA, T62.94XA |
|   | 008 | Intestinal infections due to Escherichia coli | A04.0, A04.4 |
|   | 008.1 | Intestinal infections due to Arizona group of paracolon bacillus | A04.8 |
|   | 008.2 | Intestinal infections due to Aerobacter aerogenes | not found |
|   | 008.3 | Intestinal infections due to Proteus (mirabilis morganii) | B96.4 |
|   | 008.4 | Intestinal infections due to unspecified bacteria | A04.8 |
|   | 008.5 | Bacterial enteritis, unspecified | A04.9 |
|   | 009 | Ill-defined intestinal infection | A09 |
|   | 013 | CNS tuberculosis | A17.0 |
|   | 018 | Miliary tuberculosis | A19.2 |
|   | 020 | Plague | A20.0 |
|   | 021 | Tularemia | A21.9 |
|   | 022 | Anthrax | A22.9 |
|   | 023 | Brucellosis | A23.9 |
|   | 024 | Glanders | A24.0 |
|   | 025 | Melioidosis | A23.3, A24.9 |
|   | 026 | Rat-bite fever | A25.0 |
|   | 027 | Other bacterial zoonoses | A32.11, A32.12, A32.7, A32.81, A32.89, A32.9  |
|   | 032 | Diphtheria | A36.0 |
|   | 033 | Whooping cough | A37.00 |
|   | 034 | Streptococcal throat/scarlet fever | J02.0, J03.00 |
|   | 035 | Erysipelas | A46.0 |
|   | 036 | Meningococcal infection | A39.0 |
|   | 037 | Tetanus | A35 |
|   | 038 | Septicemia | A41 |
|   | 039 | Actinomycotic infections | A42.9 |
|   | 040 | Other bacterial diseases | A48.0 |
|   | 041 | Bacterial infection in other diseases not specified | A49.9 |
|   | 098 | Gonococcal infections | A54.00 |
|   | 100 | Leptospirosis | A27.0 |
|   | 101 | Vincent’s angina | A69.1 |
|   | 112 | Candidiasis, of mouth | B37.0 |
|   | 112.4 | Candidiasis, of lung | B37.1 |
|   | 112.5 | Candidiasis, disseminated | B37.7 |
|   | 112.8 | Candidiasis, of other specified sites | B37.89 |
|   | 114 | Coccidioidomycosis | B38.9 |
|   | 115 | Histoplasmosis | B39.5 |
|   | 116 | Blastomycotic infection | B40.9 |
|   | 117 | Other mycoses | B48 |
|   | 118 | Opportunistic mycoses | B48.8 |
| Nervous | 320 | Bacterial meningitis | G00.9 |
|   | 321 | Cryptococcal meningitis | B45.1 |
|   | 321.1 | Meningitis in other fungal diseases | G02 |
|   | 324 | CNS abscess | G06.0 |
|   | 325 | Phlebitis of intracranial sinus | G08 |
|   | 360 | Purulent endophthalmitis | H44.0, H44.001, H44.002, H44.003, H44.009 |
|   | 376 | Acute inflammation of orbit | H05.00, H05.10, H05.0,  |
|   | 380.14 | Malignant otitis externa | H60.23, H60.21, H60.22, H60.90, H60.313 |
|   | 383 | Acute mastoiditis | H70.093, H70.009, H70.091, H70.92, H70.099, H70.003, H70.002, H70.001 |
| Circulatory | 420.99 | Acute pericarditis due to other specified organisms | I30 |
|   | 421 | Acute or subacute endocarditis | I33.9, I33.0, I33.0 |
| Respiratory | 461 | Acute sinusitis | J01.0, J01.00, J01.01, J01.90, J01.91, J01.20, J01.30, J01.10,J01.11, J01.21, J01.31, J01.8, J01.81 |
|   | 462 | Acute pharyngitis | J01, J02.8, J02.9 |
|   | 463 | Acute tonsillitis | J03. J03.01, J03.00, J03.90, J03.90, J03.91, |
|   | 464 | Acute laryngitis/tracheitis | J04, J04.10, J04.1, J04.0, J04.2 |
|   | 465 | Acute upper respiratory infection of multiple sites/not otherwise specified | J06, J06.9 |
|   | 475 | Peritonsillar abscess | J36, J39.0 |
|   | 481 | Pneumococcal pneumonia | J13 |
|   | 482 | Other bacterial pneumonia | J15, J15.6, J15.8, J15.9 |
|   | 485 | Bronchopneumonia with organism not otherwise specified | J18.0 |
|   | 486 | Pneumonia, organism not otherwise specified | J16.8, J18.9 |
|   | 491.21 | Acute exacerbation of obstructive chronic bronchitis | J44.0 |
|   | 494 | Bronchiectasis | J47, J47.1J47.9 |
|   | 510 | Empyema | J86.0, J86.9 |
|   | 513 | Abscess of lung and mediastinum | J85 |
| Digestive | 522.5 | Periapical abscess without sinus | K04.7 |
|   | 522.7 | Periapical abscess with sinus | K04.6 |
|   | 526.4 | Inflammatory conditions of the jaw | M27.2 |
|   | 527.3 | Abscess of the salivary glands | K11.3 |
|   | 528.3 | Cellulitis and abscess of oral soft tissue | K12.2 |
|   | 540 | Acute appendicitis | K35.80 |
|   | 541 | Appendicitis not otherwise specified | K37 |
|   | 542 | Other appendicitis | K36 |
|   | 562.01 | Diverticulitis of the small intestine without hemorrhage | K57.13 |
|   | 562.03 | Diverticulitis of the small intestine with hemorrhage | K57.01 |
|   | 562.11 | Diverticulitis of colon without hemorrhage | K57.33 |
|   | 562.13 | Diverticulitis of colon with hemorrhage | K57.21 |
|   | 566 | Abscess of the anal and rectal regions | K61 |
|   | 567 | Peritonitis | K65, K65.9 |
|   | 569.5 | Intestinal abscess | K63.0 |
|   | 569.61 | Infection of colostomy or enterostomy | K94.12, K94.02 |
|   | 569.83 | Perforation of intestine | K63.1 |
|   | 572 | Abscess of liver | K75.0 |
|   | 572.1 | Portal pyemia | K75.1 |
|   | 575 | Acute cholecystitis | K81.0, K81.2 |
| Genitourinary | 590 | Kidney infection | N11.0 |
|   | 599 | Urinary tract infection not otherwise specified | N39.0 |
|   | 601 | Prostatic inflammation | N41.0 |
|   | 604 | Orchitis and epididymitis | N45.4 |
|   | 614 | Female pelvic inflammation disease | N70.01, N70.02, N70.03 |
|   | 615 | Uterine inflammatory disease | N71.0 |
|   | 616.3 | Abscess of Bartholin’s gland | N75.1 |
|   | 616.4 | Other abscess of vulva | N76.4 |
| Skin | 681 | Cellulitis, finger/toe | L03.019, L03.011, L03.012 L03.039, L03.031, L03.032,  |
|   | 682 | Other cellulitis or abscess | L02.91 |
|   | 683 | Acute lymphadenitis | L04.9 |
|   | 685 | Pilonidal cyst, with abscess | L05.01, L05.02 |
|   | 686 | Other local skin infection | L08.0 |
|   |   |   |   |
| Musculoskeletal | 711 | Pyogenic arthritis | M00.9 |
|   | 728.86 | Necrotizing fasciitis | M72.6 |
|   | 730 | Osteomyelitis | M86 |
| Other | 790.7 | Bacteremia | R78.81 |
|   | 958.3 | Posttraumatic wound infection, not elsewhere classified | T79.8XXA |
|   | 996.6 | Infection or inflammation of device/graft | T85.79XA |
|   | 998.5 | Postoperative infection | T81.40XA |
|   | 999.3 | Infectious complication of medical care not otherwise classified | not found |

ICD-9 codes adopted from Page DB, Donnelly JP, Wang HE. Community-, Healthcare-, and Hospital-Acquired Severe Sepsis Hospitalizations in the University HealthSystem Consortium. *Critical Care Medicine*. 2015; 43(9):1945-1951.

CNS = Central Nervous System

Appendix 5: ICD-9 and ICD-10 codes for organ failure

|  |  |  |  |
| --- | --- | --- | --- |
| **Variables**  |  | **ICD 9 Code** | **ICD 10 Code** |
| Pulmonary  |  |  |  |
|  | Acute respiratory failure | 518.81 | J96.00-02, J96.20-22, J96.90-92 |
|  | ARDS | 518.85 | J80 |
|  | Respiratory Distress | 786.09 | R06.0, R06.09, R06.89 |
|  | Pulmonary insufficiency  | 518.82 | J80 |
|  | Respiratory arrest | 791.1 | R09.2 |
|  | Ventilator Management | 96.7, 96.71, 96.72 | 5A1935Z, 5A1945Z, 5A1955Z  |
| Cardiovascular |  |  |  |
|  | Septic shock  | 785.52 | R65.21 |
|  | Use of vasopressors | 0.17 | 3E033XZ, 3E043XZ |
| Hepatic  |  |  |  |
|  | Acute hepatic failure | 570 | K72.00 |
|  | Hepatic Encephalopathy  | 572.2 | K72.90, K72.91 |
| Hematologic  |  |  |  |
|  | Acquired coagulation factor deficiency  | 286.7 | D68.32, D68.4 |
|  | Coagulopathy, DIC | 286.6, 286.9 | D68.8, D68.9, D65 |
|  | Thrombocytopenia  | 287.4, 287.5 | D69.6 |
| Metabolic  |  |  |  |
|  | Acidosis  | 276.2 | E87.2 |
| Neurologic  |  |  |  |
|  | Altered Consciousness | 780.09 | R40.0, R40.1 |
|  | Acute encephalopathy  | 348.3 | G93.40, G93.41, G93.49 |
|  | Anoxic brain injury | 348.1 | G93.1 |
| Renal  |  |  |  |
|  | Acute kidney injury | 584.5 - 584.9 | N17.0, N17.1, N17.2, N17.8, N17.9 |
|  | Hemodialysis | 39.95 | Z99.2 |
| Procedures  |  |  |  |
|  | Blood transfusion  | 99.03, 99.04 | 30233H1, 30243H1, 30253H1, 30263H1, 30233N1, 30233P1, 30243P1, 30253P1, 30263N1, 30263P1 |
|  | Tracheostomy  | 31.1, 31.2, 31.21, 31.29 | 0B110F4, 0B110Z4, 0B113Z4, 0B114F4, 0B114Z4 |
|  | Ventilator Management | 96.7, 96.71, 96.72 | 5A1935Z, 5A1945Z, 5A1955Z  |
|  | Use of vasopressors | 0.17 | 3E033XZ, 3E043XZ |
| EXCLUSION CRITERIA |  |  |
|  | Kidney Transplant | V42.0, 996.81 | Z94.0 |
|  | Heart Transplant  | V42.1, 996.83 | Z94.1 |
|  | Lung Transplant  | V42.6, 996.84 | Z94.2 |
|  | Liver Transplant | V42.7, 996.82 | Z94.4 |
|  | Stem cell transplant | V42.82 | Z94.84 |
|  | BMT | V42.81, 996.85 | Z94.81 |
|  | ESRD | V56.0-3, V45.1x, V56.2, V56.8 | N18.6 |

ARDS = Acute Respiratory Distress Syndrome

DIC = Disseminated Intravascular Coagulation

BMT = Bone Marrow Transplant

ESRD = End Stage Renal Disease