**Supplementary Information**

**Characteristics, costs, and outcomes associated with central line-associated bloodstream infection and hospital-onset bacteremia and fungemia in US hospitals**

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**Section S1.** Matching for case-matched analysis

For matching of cases to controls (1:5), (1) admissions with potential infections (defined as antibiotic duration ≥72 hours, EHR alert for potential infection, or infection diagnosis-related group) were excluded from the control group (Supplementary Table S1); (2) controls and non-CLABSI HOB cases were limited to the same characteristics as the CLABSI case population including age range, major diagnostic code, and International Classification of Disease 10th revision procedure code system (ICD-10-PCS) code. We matched 5 controls to each case based on the same ICU status and the Agency for Healthcare Research and Quality Clinical Classification Software (CCS) single-level procedure category of the primary ICD-10-PCS procedure code. If cases did not have applicable controls in step 1 and 2, they were excluded (54/403 [13%] CLABSI cases and 402/1574 [26%] of non-CLABSI HOB cases were excluded from the case-matched analyses). We used the same control group for CLABSI and non-CLABSI-HOB to allow comparisons of the incremental burden associated with cases compared with non-BSI controls. Multivariable adjusted regression models were adjusted for patient-level characteristics (age, sex, and AlaRMS comorbidity score) and hospital-level characteristics (payer, staffed bed size, teaching status, and urbanicity).

**Supplementary Table S1.** Analytic cohort matching description

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Inclusion/Exclusion criteria** | **Number of hospitals** | **Number in patient cohort** | **Number of excluded patients** | **Number of patients with CLABSI** | **% of cohort** | **Number of patients with non-CLABSI HOB** | **% of cohort** | **Number of control patients** | **% of cohort** |
| Total hospitalsa, acute care admissions with patient age ≥ 18 yearsb | 85 | 1,149,448 |  |  |  |  |  |  |  |
| At least 1 CLABSI and reporting of blood infection to NHSN of blood NIM | 41 | 756,637 | 392,811 |  |  |  |  |  |  |
| Exclude if LOS >365 days | 41 | 645,315 | 111,322 |  |  |  |  |  |  |
| Cross-sectional cohort | 41 | 645,315 |  | 403 | 0.06% | 1,574 | 0.244% | 643,338 |  |
| Exclude controls with potential infectionc | 41 | 461,888 | 183,427 | 403 | 100.0% | 1,574 | 100.0% | 459,911 | 71.5% |
| Exclude if missing ICU status | 41 | 453,481 | 8,407 | 401 | 99.5% | 1,569 | 99.7% | 451,511 | 70.2% |
| Exclude if age of control is outside of cases | 41 | 453,481 | - | 401 | 99.5% | 1,569 | 99.7% | 451,511 | 70.2% |
| Exclude if control MDC does not match case | 41 | 358,278 | 95,203 | 401 | 99.5% | 1,511 | 96.0% | 356,366 | 55.4% |
| Exclude if primary PCS does not match case | 39 | 164,816 | 193,462 | 358 | 88.8% | 1,200 | 76.2% | 163,258 | 25.4% |
| Case control cohort (1:5 match between CLABSI cases and controls) | 39 | 3,266 | 161,550 | 349 | 86.6% | 1,172 | 74.5% | 1,745 | 0.3% |

aAll sites with appropriate data (defined as at least 3 months of consecutive data with pharmacy, general laboratory, financial, and microbiology data available with a high completion rate)

bAcute care hospitals, excluding children’s long term care facilities and specialty hospitals

cDefined as antibiotic duration ≥72 hours, electronic health record alert for potential infection, or infection diagnosis-related group.

Note. CLABSI, central-line associated bloodstream infection; HOB, hospital-onset bacteremia; ICU, intensive care unit; LOS, length of stay; MDC, major diagnostic code; NHSN, National Health Safety Network; NIM, nosocomial infection marker; PCS, procedure coding system.

**Supplementary Table S2.**  Microorganism definitions. [see separate Excel spreadsheet]

**Supplementary Table S3**. Association of HOB with other specified sites of infection as determined by identification of the same pathogen species from both sources by ICU status. Data are presented as n (%).

| **Other sites of infectionc** | **CLABSIa** | | **Non-CLABSI HOBb** | | **All HOB including CLABSI** | |
| --- | --- | --- | --- | --- | --- | --- |
| **ICU**  **(n=296)** | **No ICU**  **(n=105)** | **ICU**  **(n=977)** | **No ICU**  **(n=592)** | **ICU**  **(n=1273)** | **No ICU**  **(n=697)** |
| None of the below | 268 (90.5%) | 96 (91.4%) | 614 (62.8%) | 452 (76.4%) | 882 (69.3%) | 548 (78.6%) |
| Urine only | 15 (5.1%) | 4 (3.8%) | 118 (12.1%) | 82 (13.9%) | 133 (10.4%) | 86 (12.3%) |
| Respiratory only | 10 (3.4%) | 1 (1.0%) | 152 (15.6%) | 11 (1.9%) | 162 (12.7%) | 12 (1.7%) |
| Skin/soft tissue only | 2 (0.7%) | 3 (2.9%) | 54 (5.5%) | 39 (6.6%) | 56 (4.4%) | 42 (6.0%) |
| Urine and respiratory | 0 | 0 | 15 (1.5%) | 3 (0.5%) | 15 (1.2%) | 3 (0.4%) |
| Urine and skin/soft tissue | 1 (0.3%) | 1 (1.0%) | 8 (0.8) | 2 (0.3%) | 9 (0.7%) | 3 (0.4%) |
| Skin/soft tissue and respiratory | 0 | 0 | 12 (1.2%) | 3 (0.5%) | 12 (0.9% | 3 (0.4%) |
| Urine, respiratory, and skin/soft tissue | 0 | 0 | 4 (0.4%) | 0 | 4 (0.3%) | 0 |

aICU status was unknown for 2 admissions

bICU status was unknown for 5 admissions

cCategories for sites of infection are mutually exclusive

Note. CLABSI, central-line associated bloodstream infection; HOB, hospital-onset bacteremia; ICU, intensive care unit; SSI, surgical site infection.

**Supplementary Table S4**. Association of HOB with other positive cultures from specified HAIs as determined by identification of the same microorganism from both sources. Data are presented as n (%). Categories for HAI are mutually exclusive .

| **HAI** | **CLABSI**  **(N=403)** | **Non-CLABSI HOB**  **(N=1574)** | **All HOB including CLABSI**  **(N=1977)** |
| --- | --- | --- | --- |
| None of the below | 403 (100%) | 1531 (97.3%) | 1934 (97.8%) |
| CAUTI | 0 | 41 (2.6%) | 41 (2.1%) |
| SSI | 0 | 9 (0.6%) | 9 (0.5%) |

Note. CLABSI, central-line associated bloodstream infection; HAI, hospital-acquired infection; HOB, hospital-onset bacteremia; SSI, surgical site infection.

**Supplementary Table S5.** Association of microorganisms in CLABSI or non-CLABSI HOB with the same microorganism from another specified source (urine, respiratory, or skin/soft tissue). Data are presented as n (% of source). Patients could have multiple sources of infection or microorganisms. Percentages may not total to 100 due to rounding.

| **Micro-organism** | **n for CLABSI,**  **non-CLABSI HOB, and all HOBa** | **Urine** | | | **Respiratory** | | | **Skin/soft tissue** | | | **No specified non-blood source** | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **CLABSI**  **(n=21)** | **Non-CLABSI HOB**  **(n=233)** | **All HOBa**  **(n=254)** | **CLABSI**  **(n=11)** | **Non-CLABSI HOB**  **(n=201)** | **All HOBa**  **(n=212)** | **CLABSI**  **(n=7)** | **Non-CLABSI HOB**  **(n=122)** | **All HOBa**  **(n=129)** | **CLABSI**  **(n=379)** | **Non-CLABSI HOB**  **(n=1154)** | **All HOB\***  **(n=1533)** |
| Enterobac-teriaceae | 67  575  642 | 7 (33%) | 149 (64%) | 156 (61%) | 2 (18%) | 56 (27%) | 58 (27%) | 2 (29%) | 29 (24%) | 31 (24%) | 61 (13%) | 385 (32%) | 446 (27%) |
| *S. aureus* | 50  403  453 | 2 (10%) | 25 (11%) | 27 (11%) | 5 (45%) | 85 (41%) | 90 (42%) | 4 (57%) | 65 (53%) | 69 (53%) | 43 (9%) | 263 (22%) | 306 (19%) |
| Entero-coccus spp. | 64  248  312 | 4 (19%) | 15 (6%) | 19 (7%) | 1 (9%) | 3 (1%) | 4 (2%) | 1 (14%) | 9 (7%) | 10 (8%) | 58 (13%) | 226 (19%) | 284 (17%) |
| Environ-mental GNBb | 18  179  213 | 3 (14%) | 35 (15%) | 38 (15%) | 2 (18%) | 50 (24%) | 52 (24%) | 0 | 13 (11%) | 13 (10%) | 29 (6%) | 102 (9%) | 131 (8%) |
| *Candida albicans* and *Candida auris* | 52  123  175 | 1 (5%) | 3 (1%) | 4 (2%) | 0 | 7 (3%) | 7 (3%) | 0 | 1 (1%) | 1 (1%) | 51 (11%) | 114 (10%) | 165 (10%) |
| Other *Candida* sppc | 53  117  170 | 4 (19%) | 6 (3%) | 10 (4%) | 0 | 4 (2%) | 4 (2%) | 0 | 5 (4%) | 5 (4%) | 50 (11%) | 107 (9%) | 157 (10%) |
| CoNSd | 83  0  83 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 83 (18%) | 0 | 83 (5%) |
| Other GPBc | 33  0  33 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 33 (7%) | 0 | 33 (2%) |
| Other GNBc | 18  0  18 | 0 | 0 | 0 | 1 (9%) | 0 | 1 (9%) | 0 | 0 | 0 | 17 (4%) | 0 | 17 (1%) |
| Other commen-salb,d | 17  0  17 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 17 (4%) | 0 | 17 (1%) |
| No pathogen specified | 12  0  12 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 12 (3%) | 0 | 12 (1%) |

aIncluding CLABSI

bPrimarily *Acinetobacter* spp. and *Burkholderia (Pseudomonas)* spp. See Supplementary Table S2 for full list of included microorganisms.

cSee Supplementary Table S2 for full list of included microorganisms.

dAdmissions with CoNS or other commensals were excluded from non-CLABSI HOB events

Note. CLABSI, central-line associated bloodstream infection; CoNS, coagulase-negative staphylococci; GNB, Gram-negative bacteria; GPB, Gram-positive bacteria; HOB, hospital-onset bacteremia; Resp, respiratory; spp., species

**Supplementary Table S6.** Patient and hospital characteristics for matched cases and controls stratified by ICU admission at any point during the specified hospital visit.

| **Characteristic** | **No ICU** | | | | **ICU** | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **CLABSI** | **Non-CLABSI HOB** | **All HOB Including CLABSI** | **Control** | **CLABSI** | **Non-CLABSI HOB** | **All HOB Including CLABSI** | **Control** |
| N | 79 | 391 | 470 | 395 | 270 | 781 | 1051 | 1350 |
| Age group (years) |  |  |  |  |  |  |  |  |
| 18-40 | 16 (20.3%) | 64 (16.4%) | 80 (17.0%) | 53 (13.4%) | 33 (12.2%) | 82 (10.5%) | 115 (10.9%) | 144 (10.7%) |
| 41-64 | 34 (43.0%) | 160 (40.9%) | 194 (41.3%) | 166 (42.0%) | 123 (45.6%) | 339 (43.4%) | 462 (44.0%) | 550 (40.7%) |
| 65-80 | 23 (29.1%) | 118 (30.2%) | 141 (30.0%) | 123 (31.1%) | 93 (34.4%) | 280 (35.9%) | 373 (35.5%) | 484 (35.9%) |
| >80 | 6 (7.6%) | 49 (12.5%) | 55 (11.7%) | 53 (13.4%) | 21 (7.8%) | 80 (10.2%) | 101 (9.6%) | 172 (12.7%) |
| Sex |  |  |  |  |  |  |  |  |
| Male | 35 (44.3%) | 216 (55.2%) | 251 (53.4%) | 187 (47.3%) | 147 (54.4%) | 453 (58.0%) | 600 (57.1%) | 753 (55.8%) |
| Female | 44 (55.7%) | 175 (44.8%) | 219 (46.6%) | 208 (52.7%) | 123 (45.6%) | 328 (42.0%) | 452 (42.9%) | 597 (44.2%) |
| ALaRMS Score |  |  |  |  |  |  |  | 0 (0%) |
| Mean (SD) | 48.0 (20.1) | 50.3 (20.0) | 49.9 (20.0) | 40.6 (17.1) | 65.6 (25.6) | 62.2 (23.5) | 63.1 (24.1) |  |
| Median (Q1, Q3) | 47.0 [36.0, 60.0] | 51.0 [38.0, 63.0] | 50.0 [38.0, 62.0] | 40.0 [29.0, 51.0] | 62.0 [47.0, 83.0] | 60.0 [45.0, 77.0] | 61.0 [45.0, 79.0] | 52.6 (22.5) |
| Missing | 1 (1.3%) | 3 (0.8%) | 4 (0.9%) | 6 (1.5%) | 1 (0.4%) | 3 (0.4%) | 4 (0.4%) | 50.0 [37.0, 67.0] |
| Payor |  |  |  |  |  |  |  |  |
| Medicaid | 13 (16.5%) | 42 (10.7%) | 55 (11.7%) | 32 (8.1%) | 36 (13.3%) | 96 (12.3%) | 132 (12.6%) | 114 (8.4%) |
| Medicare | 42 (53.2%) | 232 (59.3%) | 274 (58.3%) | 221 (55.9%) | 153 (56.7%) | 453 (58.0%) | 606 (57.7%) | 787 (58.3%) |
| Other | 5 (6.3%) | 9 (2.3%) | 14 (3.0%) | 8 (2.0%) | 5 (1.9%) | 31 (4.0%) | 36 (3.4%) | 53 (3.9%) |
| Private | 16 (20.3%) | 93 (23.8%) | 109 (23.2%) | 117 (29.6%) | 62 (23.0%) | 163 (20.9%) | 225 (21.4%) | 331 (24.5%) |
| Uninsured | 3 (3.8%) | 15 (3.8%) | 18 (3.8%) | 16 (4.1%) | 14 (5.2%) | 36 (4.6%) | 50 (4.8%) | 61 (4.5%) |
| Missing | 0 (0%) | 0 (0%) | 0 (0%) | 1 (0.3%) | 0 (0%) | 2 (0.3%) | 2 (0.2%) | 4 (0.3%) |
| Staffed bed size |  |  |  |  |  |  |  |  |
| <100 | 3 (3.8%) | 9 (2.3%) | 12 (2.6%) | 5 (1.3%) | 2 (0.7%) | 22 (2.8%) | 24 (2.3%) | 41 (3.0%) |
| 100-300 | 16 (20.3%) | 85 (21.7%) | 101 (21.5%) | 115 (29.1%) | 58 (21.5%) | 133 (17.0%) | 191 (18.2%) | 372 (27.6%) |
| >300 | 60 (75.9%) | 297 (76.0%) | 357 (76.0%) | 275 (69.6%) | 210 (77.9%) | 626 (80.2%) | 836 (79.5%) | 937 (69.4%) |
| Teaching status |  |  |  |  |  |  |  |  |
| Non-teaching | 16 (20.3%) | 119 (30.4%) | 135 (28.7%) | 133 (33.7%) | 76 (28.1%) | 187 (23.9%) | 263 (25.0%) | 477 (35.3%) |
| Teaching | 63 (79.7%) | 272 (69.6%) | 335 (71.3%) | 262 (66.3%) | 194 (71.9%) | 594 (76.1%) | 788 (75.0%) | 873 (64.7%) |
| Urban status |  |  |  |  |  |  |  |  |
| Rural | 12 (15.2%) | 46 (11.8%) | 58 (12.3%) | 64 (16.2%) | 48 (17.8%) | 107 (13.7%) | 155 (14.7%) | 202 (15.0%) |
| Urban | 67 (84.8%) | 345 (88.2%) | 412 (87.7%) | 331 (83.8%) | 222 (82.2%) | 674 (86.3%) | 896 (85.3%) | 1148 (85.0%) |

Note. ALaRMS, Acute Laboratory Risk of Mortality Score; CLABSI, central-line associated bloodstream infection; HOB, hospital-onset bacteremia; ICU, intensive care unit; SD, standard deviation.

**Supplementary Table S7**. Outcomes for BSI cases and controls. Control data for CLABSI vary slightly from control data for non-CLABSI HOB due to differences in adjustments based on cohort composition.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Outcome** | **CLABSI Analyses** | | **Non-CLABSI HOB Analyses** | | **All HOB Including CLABSI Analyses** | |
| **Control** | **Cases** | **Control** | **Cases** | **Control** | **Cases** |
| N | 1745 | 349 | 1745 | 1172 | 1745 | 1521 |
| Length of stay | | | | | | |
| Adjusteda mean days (95% CI) | 4.7  (4.2, 5.3) | 21.5  (19.3, 23.9) | 4.5  (4.1, 5.0) | 18.3  (16.6, 20.2) | 4.5  (4.1, 5.0) | 19.0  (17.3, 21.0) |
| Difference (case – control) | 16.8  *P* <0.001 | | 13.8  *P* <0.001 | | 14.5  *P* <0.001 | |
| Total hospital cost | | | | | | |
| Adjusteda mean USD | $14,268  (11,325, 17,977) | $63,669  (50,026, 81,032) | $14,285  (13,481, 15,138) | $49,595  (46,835, 52,519) | $14,369  (11,464, 18,011) | $52,755  (42,062, 66,167) |
| Difference (case – control) | $49,400  *P* <0.001 | | $35,310  *P* <0.001 | | $38,386  *P* <0.001 | |
| Mortality rate | | | | | | |
| Unadjusted, n (%) | 134  (7.6%) | 109  (31.2%) | 134  (7.6%) | 320  (27.3%) | 134  (7.6%) | 429  (28.2%) |
| Adjusted %a (95% CI) | 2%  (1, 5) | 9%  (4, 18) | 5%  (3, 7) | 15%  (10, 22) | 4%  (3, 7) | 15%  (10, 21) |
| Relative risk (cases vs controls) | 3.77  *P*<0.001 | | 3.20  *P*<0.001 | | 3.36  *P*<0.001 | |
| 30-day readmission rate | | | | | | |
| Unadjusted, n (%) | 232 (13.3%) | 60 (17.2%) | 232 (13.3%) | 190 (16.2%) | 232 (13.3%) | 250 (16.4%) |
| Adjusted %a (95% CI) | 14%  (10, 19) | 19%  (13, 27) | 13%  (10, 18) | 17%  (13, 22) | 13%  (10, 17) | 18%  (14, 23) |
| Relative risk (cases vs controls) | 1.41  *P*=0.015 | | 1.28  *P*=0.009 | | 1.33  *P*=0.001 | |

aAdjusted for age, sex, ALaRMS value, and hospital-level variables (payer, staffed bed size, teaching status, and urban/rural location)

Note. ALaRMS, Acute Laboratory Risk of Mortality Score; BSI, bloodstream infection; CI, confidence interval; CLABSI, central-line associated bloodstream infection; HOB, hospital-onset bacteremia.