**Supplementary Material**

**Additional text regarding data cleaning:**

Some CLs either did not have a removal date in our dataset or had a line removal date that occurred prior to a documented access to that line. For such lines, we imputed the removal date to be the earliest discharge date from the hospital that (1) followed the date of line insertion and such that (2) no line accesses were documented following the date. Similarly, there were some lines that either had no insertion date in our dataset or had an insertion date that occurred after a documented access to that line. For such lines, we imputed the insertion date to be the latest hospital admission date that occurred before any documented accesses of the line. Lines with no placement or removal times were excluded from the analysis.

**Supplementary Figure 1:** Several examples illustrating methodology regarding central line device day inclusion and outcome definition. Each rectangle represents a separate day for a given patient; these line-days were treated as separate observations. Patient A had a line inserted on day 4 of their stay, and removed on day 9. Patient B had a line inserted on day 4, and a CLABSI was identified on day 9, so days 6, 7, and 8 were considered positive observations. Patient C had a central line inserted in a previous medical encounter; therefore, the first two hospital days did not count as central line days. Patient D had a central line inserted after they contracted a CLABSI, but no line days were assessed for patients after they contracted a CLABSI. Patient E had a line inserted on day 4, and a CLABSI was identified on day 5, so only day 4 was considered an eligible observation (and classified as a positive observation, since it was within 3 days of a CLABSI).

Abbreviations: CLI - central line inserted; CLR - central line removed



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**Supplementary Figure 2:** Pairwise Spearman correlation between each variable, including the outcome variable, considered in the study. Due to the fact that the number of elapsed CL device days and the number of hospital days since admission would be highly correlated for all patients with multiple consecutive CL device days, the number of days since admission was excluded from the multivariate analysis.



**Supplementary Figure 3:** Pairwise Spearman correlation between each variable considered in the multivariate logistic regression analysis.



**Supplementary Figure 4:** Results of the multivariate logistic regression analysis without modeling each patient as a random effect. Shown are adjusted odds ratios, 95% confidence intervals, and *p* values for each variable when regressing on the outcome of confirmed CLABSI in the next 3 days. The use of mixed-effects modelling for this analysis enabled us to model each patient separately. However, the substantial computational resources required for training this model is a barrier to similar research. We found that a relatively simple logistic regression-based approach recapitulated many of the same results as the more intensive mixed effects model. Therefore, logistic regression-based models are useful for exploratory analyses at other institutions that wish to pursue similar analyses. Many of the same conclusions can be drawn from the results of this model as can be drawn from the results of the mixed-effects model (pediatric acute care and peripheral line accesses are associated with lower risk; central line accesses, elapsed central line days, female gender, and stem cell are associated with higher risk).

Abbreviations: CI - confidence interval; Hem/Onc - Hematology/Oncology; CLABSI - central line-associated bloodstream infection

|  |  |  |
| --- | --- | --- |
| **Medication** | **Min. Concentration** | **Route administration details** |
|  |  |  |
| dextrose | 15% | Central line only |
| dobutamine |  | Central line only |
| dopamine |  | Central line only |
| epinephrine |  | Central line only |
| norepinephrine |  | Central line only |
| potassium chloride | 0.4 meq/mL | Central line only |
| TPN |  | Central line only |
| acyclovir |  | Central line preferred |
| alprostadil |  | Central line preferred |
| amiodarone | 6 mg/mL | Central line only |
| amphotericin | 0.25 mg/mL | Central line only |
| anti-thymocyte globulin (lymphocyte) |  | Central line only |
| anti-thymocyte globulin (rabbit) |  | Central line only |
| arginine |  | Central line preferred |
| calcium gluconate | 100 mg/mL | Central line only |
| calcium chloride | 50 mg/mL | Central line only |
| chlorothiazide |  | Central line preferred |
| ciprofloxacin |  | Central line preferred |
| cyclophosphamide |  | Central line preferred |
| dantrolene |  | Central line preferred |
| diltiazem | 1 mg/mL | Central line preferred |
| doxycycline |  | Central line preferred |
| esmolol |  | Central line preferred |
| indomethacin |  | Central line preferred |
| isoproterenol | 20 mcg/mL | Central line only |
| magnesium sulfate | 500 mg/mL | Central line only |
| mannitol |  | Central line preferred |
| melphalan |  | Central line only |
| nafcillin | 20 mg/mL | Central line preferred |
| nicardipine |  | Central line only |
| nitroprusside |  | Central line only |
| pentobarbital |  | Central line preferred |
| phenylephrine | 0.02 mg/mL | Central line only |
| phenytoin |  | Central line preferred |
| promethazine |  | Central line preferred |
| propofol |  | Central line preferred |
| vancomycin | 5 mg/mL | Central line preferred |

**Supplementary Table 1:** List of medications which were classified as "central line (CL) medications" based on the preferred route of access as defined by our pharmacy formulary, which is consistent with the medications’ manufacturer’s directive. All other medications were classified as "peripheral line (PL) medications". For medications with a value in the minimum concentration column, any medication with a concentration lower than the minimum was classified as a PL medication.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Variable** | **Pediatric Acute Care** | **Pediatric ICU** | **Cardiovascular ICU** | **Stem Cell** | **Neonatal ICU** | **Hem/Onc** | **Other Department** | **Total** |
| **N Patients** | 1,487 | 945 | 1,875 | 214 | 1,835 | 788 | 127 | 7,271 |
| **N Patient Hospitalizations** | 2,817 | 1,051 | 2,177 | 364 | 1,862 | 3,529 | 142 | 11,942 |
| **N CL days** | 31,587 | 16,879 | 27,012 | 10,328 | 26,144 | 25,221 | 1,240 | 138,411 |
| **Age on admission, in years** | 9.97 ± 6.66 | 8.08 ± 6.65 | 7.96 ± 11.47 | 11.09 ± 7.25 | 0.04 ± 0.78 | 10.83 ± 6.17 | 16.81 ± 14.58 | 8.26 ± 8.25 |
| **Female (N, %)** | 1,451 (52) | 485 (46) | 998 (46) | 155 (43) | 764 (41) | 1,421 (40) | 94 (66) | 5,368 (45) |
| **CLABSI (N, rate per 1000 CL days)** | 17 (0.538) | 26 (1.54) | 37 (1.37) | 41 (3.97) | 47 (1.8) | 49 (1.94) | 0 (0) | 217 (1.57) |
| **Length of stay in days, median (IQR)** | 8.8 (5-15) | 13 (7.3-26) | 9.3 (5.2-20) | 28 (6.8-47) | 22 (10-46) | 4.9 (3.5-8.7) | 9.4 (4-15) | 8.8 (4.5-20) |
| **CL days per patient, median (IQR)** | 19 (6.1-160) | 8.5 (4.3-26) | 3.3 (0.66-8.6) | 91 (38-170) | 6.4 (4-11) | 92 (31-180) | 7.6 (2.3-17) | 14 (4.6-93) |
| **Number of CLs** | 1.18 ± 0.44 | 1.24 ± 0.48 | 1.43 ± 0.54 | 1.27 ± 0.58 | 1.26 ± 0.40 | 1.19 ± 0.47 | 1.07 ± 0.27 | 1.25 ± 0.48 |
| **Average daily CL accesses** | 6.33 ± 4.15 | 12.54 ± 8.96 | 10.56 ± 7.26 | 10.55 ± 6.74 | 6.77 ± 5.58 | 8.60 ± 4.52 | 5.65 ± 5.01 | 8.51 ± 6.11 |
| **Average daily CL accesses (lab draws)** | 0.76 ± 0.84 | 2.16 ± 2.44 | 1.04 ± 1.39 | 1.40 ± 1.34 | 1.26 ± 1.53 | 1.13 ± 1.02 | 0.48 ± 0.66 | 1.14 ± 1.38 |
| **Average daily CL accesses (CL medications)** | 0.60 ± 0.97 | 0.98 ± 1.16 | 1.70 ± 1.36 | 0.61 ± 0.74 | 0.99 ± 0.82 | 0.27 ± 0.69 | 0.18 ± 0.54 | 0.79 ± 1.10 |
| **Average daily CL accesses (PL medications)** | 4.97 ± 3.69 | 9.40 ± 7.63 | 7.82 ± 5.72 | 8.54 ± 5.66 | 4.51 ± 4.20 | 7.21 ± 4.14 | 4.99 ± 4.72 | 6.58 ± 5.09 |
| **Average daily PL medication accesses** | 1.03 ± 2.01 | 5.34 ± 5.78 | 7.94 ± 5.51 | 0.35 ± 1.23 | 1.02 ± 1.79 | 0.19 ± 0.85 | 0.61 ± 1.40 | 2.39 ± 4.35 |

Unless otherwise noted, values are presented as [mean] ± [standard deviation]

Abbreviations: N - number; ICU - intensive care unit; Hem/Onc - Hematology/Oncology; CL - central line; PL - peripheral line; CLABSI - central line-associated bloodstream infection; IQR - interquartile range

**Supplementary Table 2:** Patient-daily characteristics averaged over individual hospitalizations and broken down by unit.

|  |  |  |  |
| --- | --- | --- | --- |
| **Cardiovascular ICU** | **Hem/Onc** | **Pediatric ICU** | **Stem Cell** |
| **Medication name** | **N** | **Medication name** | **N** | **Medication name** | **N** | **Medication name** | **N** |
| morphine\* | 31,384 | porcine\* | 21,105 | lorazepam (ativan)\* | 26,231 | porcine\* | 17,125 |
| lorazepam (ativan)\* | 22,908 | ondansetron (zofran)\* | 12,483 | fentanyl\* | 18,384 | lorazepam (ativan)\* | 11,087 |
| potassium chloride | 20,217 | cefepime (maxipime)\* | 11,177 | porcine\* | 16,933 | ondansetron (zofran)\* | 10,778 |
| sodium chloride\* | 17,362 | dextrose\* | 11,019 | sodium chloride\* | 15,488 | sodium chloride\* | 10,490 |
| furosemide (lasix)\* | 16,547 | lorazepam (ativan)\* | 8,979 | midazolam\* | 12,919 | cefepime (maxipime)\* | 8,434 |
| acetaminophen (ofirmev)\* | 13,198 | sodium chloride\* | 7,394 | morphine\* | 10,465 | acyclovir (zovirax)\* | 8,403 |
| fat emulsion\* | 12,926 | piperacillin-tazobactam (zosyn)\* | 5,414 | furosemide (lasix)\* | 8,447 | dextrose\* | 7,154 |
| chlorothiazide (diuril)\* | 10,006 | vancomycin (vancocin) | 5,190 | hydromorphone\* | 7,925 | vancomycin (vancocin) | 6,167 |
| midazolam (pf)\* | 9,824 | diphenhydramine (benadryl)\* | 4,246 | acetaminophen (ofirmev)\* | 6,560 | diphenhydramine (benadryl)\* | 5,510 |
| tpn rate | 9,486 | meropenem (merrem)\* | 3,697 | vancomycin (vancocin) | 6,331 | cyclosporine (sandimmune)\* | 4,071 |
| midazolam (lpch)\* | 8,869 | granisetron pf\* | 2,798 | piperacillin-tazobactam (zosyn)\* | 6,303 | tpn rate | 3,555 |
| milrinone (primacor)\* | 8,054 | acetaminophen (ofirmev)\* | 2,749 | fat emulsion\* | 5,648 | meropenem (merrem)\* | 3,549 |
| piperacillin-tazobactam (zosyn)\* | 7,994 | caspofungin (cancidas)\* | 1,811 | tpn rate | 5,524 | granisetron pf\* | 3,427 |
| hydrocortisone sod\* | 7,487 | dexamethasone (decadron)\* | 1,549 | meropenem (merrem)\* | 5,189 | fat emulsion\* | 3,107 |
| vancomycin (vancocin) | 7,297 | dexamethasone (decadron)\* | 1,340 | dextrose\* | 5,157 | mycophenolate (cellcept)\* | 2,852 |
| dopamine | 6,748 | pantoprazole (protonix)\* | 1,299 | hydromorphone (dilaudid)\* | 5,150 | voriconazole (vfend)\* | 2,689 |
| vecuronium (norcuron)\* | 6,450 | tpn rate | 1,250 | potassium chloride | 4,735 | furosemide (lasix)\* | 2,583 |
| fentanyl\* | 6,377 | furosemide (lasix)\* | 1,150 | midazolam (lpch)\* | 4,300 | ceftazidime (fortaz)\* | 2,454 |
| dextrose\* | 6,324 | hydromorphone (dilaudid)\* | 1,147 | aminophylline\* | 3,749 | acetaminophen (ofirmev)\* | 2,401 |
| sodium bicarbonate\* | 5,703 | fat emulsion\* | 1,108 | pantoprazole (protonix)\* | 3,742 | piperacillin-tazobactam (zosyn)\* | 2,345 |
|  |  |  |  |  |  |  |  |
| **Neonatal ICU** | **Pediatric Acute Care** | **Other Department** | **Total** |
| **Medication name** | **N** | **Medication name** | **N** | **Medication name** | **N** | **Medication name** | **N** |
| tpn rate | 16,655 | porcine\* | 56,126 | porcine\* | 2,982 | porcine\* | 119,728 |
| lorazepam (ativan)\* | 15,855 | piperacillin-tazobactam (zosyn)\* | 10,650 | sodium chloride\* | 2,322 | lorazepam (ativan)\* | 93,470 |
| fat emulsion\* | 15,089 | sodium chloride\* | 10,143 | ampicillin\* | 2,226 | sodium chloride\* | 68,330 |
| ampicillin\* | 11,674 | tpn rate | 8,015 | ondansetron (zofran)\* | 2,039 | morphine\* | 53,955 |
| furosemide (lasix)\* | 9,386 | fat emulsion\* | 7,627 | dextrose\* | 1,431 | fat emulsion\* | 46,286 |
| morphine\* | 8,659 | lorazepam (ativan)\* | 7,062 | lorazepam (ativan)\* | 1,348 | tpn rate | 45,378 |
| hydrocortisone sod\* | 6,237 | acetaminophen (ofirmev)\* | 6,138 | tpn rate | 893 | dextrose\* | 41,715 |
| caffeine citrated\* | 5,993 | dextrose\* | 5,679 | dexamethasone (decadron)\* | 825 | furosemide (lasix)\* | 41,357 |
| sodium chloride\* | 5,131 | vancomycin (vancocin) | 5,175 | fat emulsion\* | 781 | acetaminophen (ofirmev)\* | 33,943 |
| dextrose\* | 4,951 | cefepime (maxipime)\* | 4,662 | ranitidine (zantac)\* | 779 | piperacillin-tazobactam (zosyn)\* | 33,805 |
| vancomycin (vancocin) | 3,185 | nafcillin | 4,431 | dexamethasone (decadron)\* | 648 | vancomycin (vancocin) | 33,520 |
| ceftazidime (fortaz)\* | 3,132 | ondansetron (zofran)\* | 4,204 | mesna (mesnex)\* | 511 | cefepime (maxipime)\* | 33,323 |
| cefotaxime (claforan)\* | 2,928 | furosemide (lasix)\* | 3,202 | cefotaxime (claforan)\* | 494 | ondansetron (zofran)\* | 33,084 |
| hydromorphone\* | 2,793 | cefazolin (ancef)\* | 3,191 | meropenem (merrem)\* | 427 | fentanyl\* | 29,158 |
| acetaminophen (ofirmev)\* | 2,721 | diphenhydramine (benadryl)\* | 3,107 | ceftazidime (fortaz)\* | 399 | potassium chloride | 28,860 |
| gentamicin\* | 2,669 | meropenem (merrem)\* | 3,105 | diphenhydramine (benadryl)\* | 342 | meropenem (merrem)\* | 20,746 |
| fentanyl\* | 2,115 | pantoprazole (protonix)\* | 2,954 | ceftriaxone (rocephin)\* | 297 | hydrocortisone sod\* | 19,512 |
| aminophylline\* | 2,038 | hydromorphone (dilaudid)\* | 2,620 | cefazolin (ancef)\* | 232 | ampicillin\* | 17,759 |
| chlorothiazide (diuril)\* | 1,943 | milrinone (primacor)\* | 2,610 | penicillin g\* | 220 | diphenhydramine (benadryl)\* | 16,225 |
| fluconazole in\* | 1,898 | morphine\* | 1,893 | granisetron pf\* | 214 | chlorothiazide (diuril)\* | 15,665 |
|  |  |  |  |  |  |  |  |
| **Legend** |  |  |  |  |  |  |  |
| Neurosedatives/Analgesics |  |  |  |  |  |  |  |
| Antimicrobials |  |  |  |  |  |  |  |
| Dextrose/Electrolytes |  |  |  |  |  |  |  |
| Diuretics |  |  |  |  |  |  |  |
| Parenteral Nutrition |  |  |  |  |  |  |  |
| Miscellaneous |  |  |  |  |  |  |  |
| Anticoagulation/Line maintenance |  |  |  |  |  |  |  |
| **\* = peripheral preferred** |  |  |  |  |  |  |  |

**Supplementary Table 3:** Total number of central line accesses attributed to individual medications, for each unit and in total. Colors denote the type of medication.

\* = medication which can safely be administered through a peripheral line (i.e., peripheral line medication)

|  |  |  |
| --- | --- | --- |
| **Line Name** | **N** | **%** |
| LPCH LDA CENTRAL/MIDLINE CATHETER SINGLE LUMEN | 6571 | 38.64% |
| LPCH LDA CENTRAL/MIDLINE CATHETER DOUBLE LUMEN | 7850 | 46.16% |
| LPCH LDA CENTRAL/MIDLINE CATHETER TRIPLE LUMEN | 1257 | 7.39% |
| LPCH LDA CENTRAL/MIDLINE CATHETER QUADRUPLE LUMEN | 8 | 0.05% |
| LDA HEMODIALYSIS CATH | 220 | 1.29% |
| LDA PORT A CATH | 30 | 0.18% |
| LDA UMBILICAL ARTERY CATH | 847 | 4.98% |
| LPCH G LDA CRRT CIRCUIT | 17 | 0.10% |
| LPCH G LDA ECMO CIRCUIT | 206 | 1.21% |

**Supplementary Table 4:** Total number of central lines of each type considered in the analysis.