Capstone I
Project Report
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BZAN 6360 Capstone Practicum in Business Analytics

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Analysis

Primary BSI in PICU

1. Introduction:

Nosocomial bloodstream infections (BSIs) in Pediatric Intensive Care Units create a significant financial burden for the health care systems. These infections are often caused from medical interventions such as the use of central venous catheters and are linked to increased morbidity, extended hospital stays, and higher medical costs. In pediatric patients, the burden of nosocomial infections remains less well-documented compared to adults. This study, conducted by Elward et al., aims to calculate the additional direct medical costs of nosocomial primary bloodstream infections in PICU patients and understand the broader financial implications associated with these infections.

2. Study Objective:

The goal of this study was to determine the additional costs directly attributable to nosocomial primary bloodstream infections in PICU patients. It focused on comparing the PICU costs of patients with BSIs to those without, controlling for variables such as age, severity of illness (PRISM ||| score), and underlying health conditions. The study provides valuable insight into the financial burden of these infections, potentially informing more cost-effective infection control strategies.

3. Materials & Methods:

<u>Study Design:</u>

> This prospective cohort study was conducted at St. Louis Children's Hospital which is a large academic tertiary care center consisting of 235 beds. All patients who were admitted to the hospital's PICU between September 1, 1999, to May 31, 2000 were included, except those who are older than 18 years, who died within 24 hours of admission, and patients in the NICU unit (a care unit for critically ill newborn, premature babies or born with serious medical conditions.).

<u>Data Collection:</u>

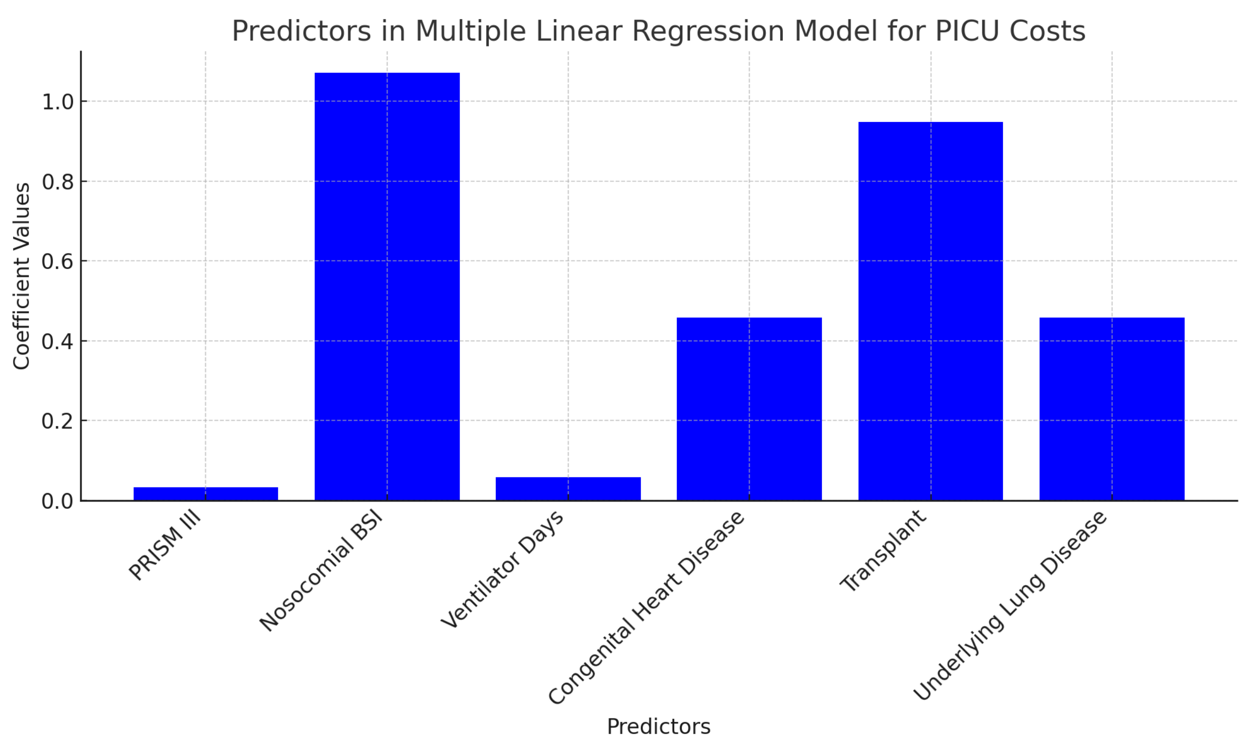
> The study used detailed data from the patients and their demographics which includes severity of illness (measured using the Pediatric Risk of Mortality Score ||| or PRISM ||| score), underlying health conditions such as congenital heart disease and lung disease, usage of ventilator and organ transplants.

<u>Cost Estimation:</u>

The costs were calculated from the perspective of the hospital as a care provider and using data from the hospital cost accounting system. They analyzed two costs which are direct costs (related to the provision of patient care, such as room, board, supplies, and medical treatments) and total costs (which included indirect overhead costs). The study primarily focused on the direct costs to understand the impact of nosocomial infections on the hospital's PICU budget.

Statistical Analysis:

The researchers used multiple regression model to assess the independent predictors of PICU costs. They accounted for multiple factors, such as illness severity and the presence of congenital conditions, to accurately determine the financial impact of BSIs. Statistical analyses were performed to validate the model and remove any potential outliers.



Below is the formula of the attributable direct costs of BSI in the PICU and is demonstrated as the difference in expected costs between infected and noninfected patients:

$$C = exp\ (\beta_0 + \beta_1 x_1 + \ldots + \beta_k x_k) - exp\ (\beta_0 + \beta_1 x_1 + \ldots + \beta_{k-1} x_{k-1})$$

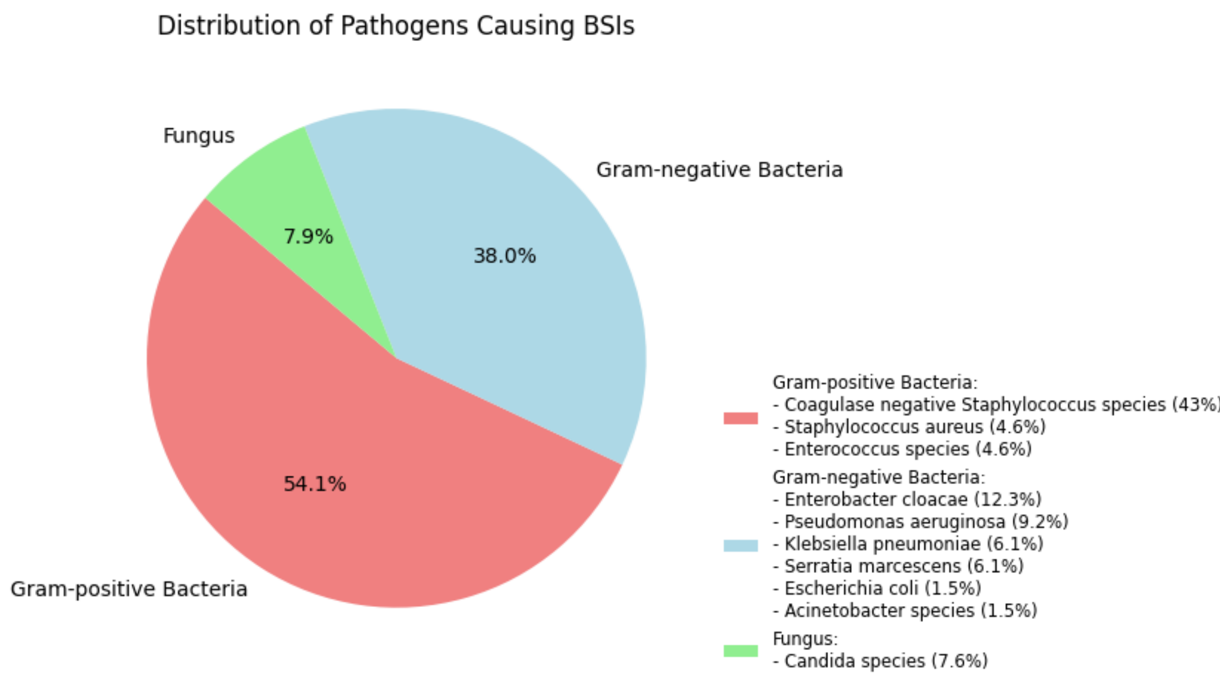
C: Attributable cost of infection

β_i (i = 1…k): estimated regression coefficient

β_k :coefficient for BSI

x_i (i = 1…k): independent variables in the regression

x_k :binary indicator for bloodstream infection



4. Results:

The study included 911 PICU admissions, where 57 children experienced 65 episodes of primary bloodstream infections. This resulted in an infection rate of 13.8 per 1000 central venous catheter days. Most of the infections were attributed to Gram-positive bacteria, with Coagulase-negative staphylococci accounting for 43% of the cases.

Cost Impact: The direct cost of PICU admission for patients with nosocomial BSIs was notably greater, averaging $45,615 compared to $6,396 for those without BSIs. After accounting for other factors, the attributable cost of a BSI was estimated at $39,219, representing the additional financial burden associated with treating infections in the PICU environment.

Predictors of Increased Costs: Several factors were found to independently predict higher PICU costs, including:

- Severity of illness (PRISM III score)
- Congenital heart disease
- Underlying lung disease
- Ventilator days
- Organ transplants

These variables were statistically significant even after excluding outlier cases, reinforcing the robustness of the findings.

5. Discussion:

The study highlights the significant financial burden of nosocomial BSIs in pediatric intensive care units, with an attributable cost of $39,219 per infection. This exceeds prior estimates due to the larger sample size and the use of actual cost data instead of charge-based estimates.

Patients with severe illness, congenital heart or lung conditions, and those on ventilators face a higher risk of increased medical costs. Targeted infection prevention strategies for these high-risk groups could result in substantial hospital cost savings.

Unlike previous studies that relied on charge-based estimates, this study provides more accurate direct cost calculations. Its prospective data collection and rigorous statistical analysis strengthen the validity of the findings.

6. Conclusion:

This study provides a detailed assessment of the financial impact of nosocomial primary bloodstream infections in pediatric ICU patients, showing that these infections lead to an excess cost of $39,219 per patient. The results highlight the importance of effective infection control measures, which could significantly reduce healthcare costs while improving patient outcomes. The findings contribute valuable insights to the limited research on the economic burden of nosocomial infections in pediatric populations.

CLABSI Problem in PICU patients & potential risk factors

Introduction:

Central Line-Associated Bloodstream Infections (CLABSI) are a significant concern in pediatric ICUs due to their impact on patient health, contributing to increased morbidity, mortality, and healthcare costs. The study conducted at Boston Children's Hospital between 2004 and 2007 aimed to identify which factors contribute to the risk of developing CLABSI among pediatric patients. The research examined elements such as central line usage, length of ICU stay, and various health conditions to inform strategies that can improve prevention, patient care, and efficient ICU resource use.

Study Objective:

The primary goal of this study was to identify the key risk factors associated with CLABSI in pediatric ICU settings by analyzing a range of clinical data and patient demographics. By understanding these factors, the research aimed to guide more targeted interventions to prevent infections, optimize ICU resource allocation, and ultimately enhance patient care quality.

Methods and Materials:

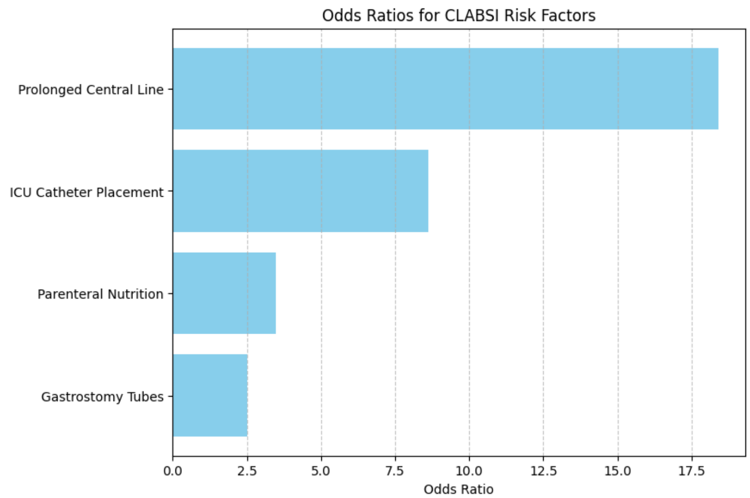
Study Design & Setting: The researchers conducted a retrospective case-control study focused on pediatric ICU patients over a three-year period (2004-2007).

- Data Source: Data was gathered from the hospital's Infection Prevention and Control Program and patient medical records, including information on demographics, medical conditions, catheter usage (type, duration, location), length of ICU stay, and specific interventions like parenteral nutrition and blood transfusions.
- Participants: The study involved 203 pediatric patients who developed CLABSI and 406 control patients who had central venous catheters (CVCs) but did not develop the infection.
- Statistics & Analysis:
    - Univariate Analysis: Initially used to assess individual risk factors for CLABSI.
    - Multivariate Logistic Regression: Performed to identify independent predictors of CLABSI while adjusting for potential confounders.
    - Odds Ratios (ORs) and 95% Confidence Intervals (CIs) were calculated to measure the association strength between risk factors and CLABSI development.

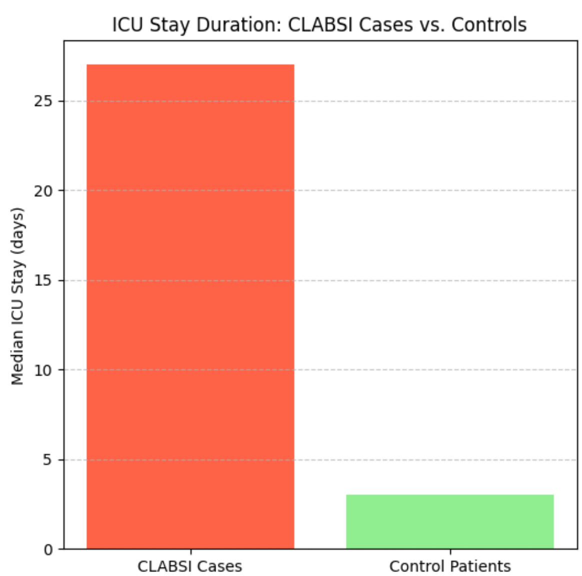
- A predictive model was built using two-thirds of the data for derivation and one-third for validation. The model's performance was assessed using measures like Positive Predictive Value (PPV) and Negative Predictive Value (NPV).
- Software: All analyses were conducted using SAS software (Version 9.2).

Visual Representations:

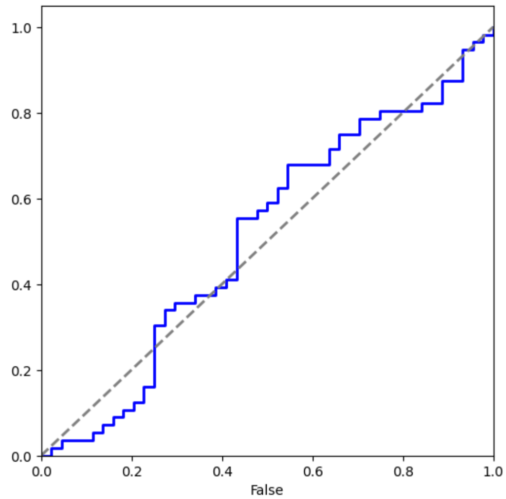
1. **Odds Ratios for Risk Factors**: A **bar chart** illustrated the strength of each risk factor. Longer bars indicated higher odds of developing CLABSI.



2. **ICU Stay Duration (Cases vs. Controls)**: Another **bar chart** compared ICU stays between CLABSI cases (median of **27 days**) and controls (**3 days**), showing significantly longer stays for those with CLABSI.



3. **Predictive Model Performance**: A **Receiver Operating Characteristic (ROC) curve** was used to evaluate the model's ability to identify high-risk CLABSI patients effectively.



Results

The study identified prolonged central line duration (≥15 days) as the strongest independent risk factor for CLABSI, with an OR of 18.41.

- Other risk factors included ICU catheter placement (OR 8.63), parenteral nutrition (OR 3.12), and gastrostomy tubes (OR 2.5).
- Patients with CLABSI had significantly higher mortality rates (20.7%) compared to controls (4.9%), and their ICU stays were much longer (27 days vs. 3 days for controls).
- The predictive model for CLABSI demonstrated moderate performance with a PPV of 54% and an NPV of 79%.

Discussion:

The study's findings highlight that prolonged central line use is a major risk factor for CLABSI, emphasizing the importance of early removal to reduce infection risk. Other factors, such as ICU catheter placement and parenteral nutrition, indicate the need for close monitoring of patients with complex care needs. Given the higher mortality rates and longer ICU stays associated with CLABSI, targeted preventive measures are crucial for improving outcomes and managing healthcare costs. While the predictive model is moderately effective, further validation across multiple hospitals is recommended to confirm these results and improve its predictive accuracy.

Conclusion

In conclusion, the study successfully identified several key risk factors for CLABSI in pediatric ICUs, with **prolonged central line duration** being the most critical predictor. Other significant contributors include **ICU catheter placement** and **parenteral nutrition**. The research underlines the urgency of proactive **management and monitoring** to prevent CLABSI and improve patient care. Although the predictive model is not perfect, it shows potential as a tool for healthcare providers to identify and intervene early in high-risk cases. To enhance its applicability, further **multicenter research** is necessary to refine the model for diverse ICU settings and reduce the burden of CLABSI effectively.

Predicting CLABSI with Machine Learning Based Models

1. Introduction:

Nosocomial bloodstream infections in the ICU, especially central line-associated bloodstream infections (CLABSI), despite advances in healthcare remain a very significant challenge. CLABSI increases the ICU mortality by mani-folds, and thus is considered as a very important mortality factor in ICUs. In the 1990s, it was reported that the mortality rate due to CLABSI was 35% and the ICU stay duration due to CLABSI doubled. In the early 2000s many efforts, such as statistical approaches were taken to predict and treat CLABSI which reduced the mortality by 50%. Though a significant drop was achieved in mortality rates, it was reported that 30,100 deaths still occur in the US, annually due to CLABSI.

Conventional statistical models, although being used to reduce the deaths, have not proved fruitful in identifying the infections as they have multiple factors involved and large data could not be handled properly. Machine Learning models proved to be efficient because they can handle large and complex data very efficiently, which is why 3 machine learning models were used in this study to predict the infections.

Study Objective:

The study aimed to assess three machine learning models: Logistic Regression, Gradient Boosted Trees and Deep Learning (Neural Networks). The models were supposed to predict three outcomes:

1. Central line placement.
2. Central line-associated bloodstream infections (CLABSI).
3. Mortality.

2. Materials and Methods:

Data Source:
The study utilized the Multiparameter Intelligent Systems for analyzing 45,460 records from the time span of 2001 to 2012. This database provided a comprehensive array of patient data, including diagnostic ICD-9-CM codes, laboratory results, vital signs, medication administrations, and mortality data from the Social Security Death Index (SSDI). Additionally, severity of illness scores (e.g., OASIS, SOFA, SAPS, SAPS II, APS III, and LODS) were also available on the first day of each ICU admission.

Variable Selection:
The study identified central venous catheter patients, those diagnosed with CLABSI using ICD-9 codes, and those who received antibiotics or died during their ICU stay. Six different severity of illness scores were calculated to evaluate the patients' conditions on the first day of ICU admission. 30 different Elixhauser comorbidities were also included in this study.
Machine Learning Models:

1. Three predictive models were created for forecasting the three different results (central line placement, CLABSI, and mortality). These models included:
2. Logistic Regression: A conventional statistical model employed for binary classification.
3. Gradient Boosted Trees: An ensemble model based on trees that applies weak classifiers sequentially to generate a sequence of decision trees.
4. Deep Learning (Neural Networks): A multi-layered artificial neural network that imitates the biological nervous system to identify features and make forecasts.

The data was divided into 10 subsets for cross-validation, with each subset being used as a test set while the other 9 subsets were used to train the model. This procedure was repeated to calculate the average performance across all subsets.

The ROC (Receiver Operating Characteristic) curves were used to evaluate the performance of the models, and gradient boosting was used to assess the importance of variables in prediction. Statistical tests conducted had significance levels set at 0.05.

3. Results:
The performance of the three machine learning models in relation to central line placement, CLABSI, and mortality was compared in the study.

Central Line Placement:
The top-performing model for predicting central line placement was Gradient Boosted Trees, surpassing both logistic regression and deep learning models. Its superior sensitivity and accuracy stemmed from its capacity to recognize intricate patterns in the data.

CLABSI Prediction:

Once again, the Gradient Boosted Trees model had the highest AUC (Area Under the ROC Curve) of 0.710 for CLABSI prediction. The model worked well for this result because it could identify the most pertinent clinical variables and interactions.

Because of the possibility of overfitting, the Deep Learning model performed less well in this domain, whereas the Logistic Regression model performed worse because of its simplicity and incapacity to represent intricate non-linear relationships.

Mortality Prediction:

With an AUC of 0.885 as seen in **Fig1 and Table 2 & 3.**, the Deep Learning model outperformed the others in predicting ICU mortality. It was able to model intricate relationships between severity scores and comorbidities because of its capacity to handle big datasets with a variety of features.

Even though logistic regression still had a respectable level of predictive power (AUC of 0.878), it was once more less successful than deep learning.

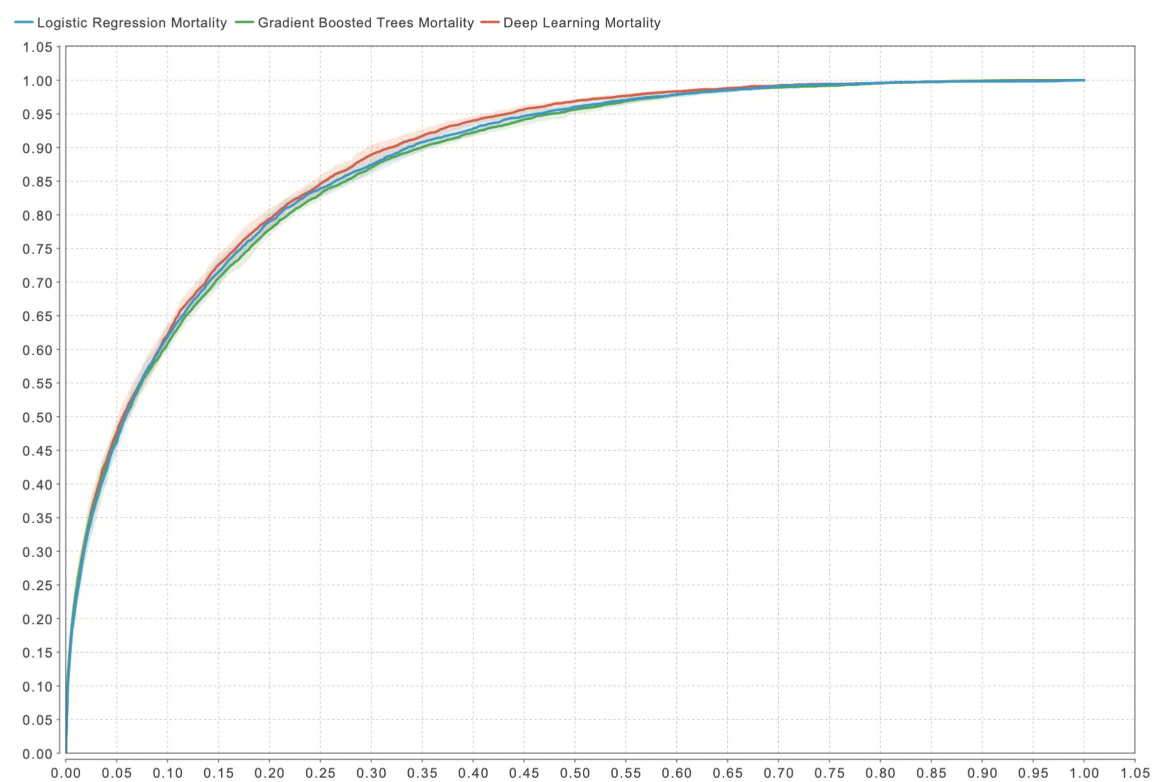


Fig. 1. Mortality classifier performance receiver operating characteristic curve of 10 fold cross validation. Shaded portion represents the range while solid line represents the mean. The x-axis is the false positive rate and the y-axis is the true positive rate.

Table 3
Results of mortality classifier performance presented as mean with standard deviation. AUC = area under the curve, PPV = positive predictive value, NPV = negative predictive value.

	Logistic regression	Gradient boosted trees	Deep learning	F	p
AUC	0.878 ± 0.005	0.874 ± 0.005	0.885 ± 0.010	6.40	<0.01
Accuracy	91.3% ± 0.3%	89.4% ± 0.5%	89.7% ± 0.7%	42.88	<0.01
Precision	65.2% ± 3.9%	47.6% ± 2.2%	49.3% ± 3.2%	105.82	<0.01
Sensitivity	28.5% ± 2.0%	51.5% ± 2.0%	53.3% ± 4.1%	222.95	<0.01
Specificity	98.3% ± 0.2%	93.7% ± 0.5%	93.8% ± 1.0%	166.78	<0.01
PPV	65.2% ± 3.9%	47.6% ± 2.2%	49.3% ± 3.2%	105.82	<0.01
NPV	92.5% ± 0.2%	94.5% ± 0.2%	94.7% ± 0.4%	183.00	<0.01

Table 4
Results of central line classifier performance presented as mean with standard deviation. AUC = area under the curve, PPV = positive predictive value, NPV = negative predictive value.

	Logistic regression	Gradient boosted trees	Deep learning	F	p
AUC	0.811 ± 0.005	0.811 ± 0.008	0.816 ± 0.006	1.89	0.17
Accuracy	74.1% ± 0.5%	71.5% ± 0.7%	73.3% ± 1.1%	50.17	<0.01
Precision	69.8% ± 0.9%	59.9% ± 0.7%	62.6% ± 1.8%	321.85	<0.01
Sensitivity	57.4% ± 0.7%	78.1% ± 1.4%	76.2% ± 2.7%	350.65	<0.01
Specificity	84.5% ± 0.6%	67.4% ± 0.7%	71.5% ± 3.1%	392.40	<0.01
PPV	69.8% ± 0.9%	59.9% ± 0.7%	62.6% ± 1.8%	321.85	<0.01
NPV	76.1% ± 0.3%	83.1% ± 0.9%	82.8% ± 1.2%	177.51	<0.01

4. Pros and Cons of Machine Learning Models:

Pros of logistic regression, include its straightforward, easily understood model and quick computation times. Ideal for variable relationships that are linear in nature. Reduces the amount of processing power needed.
Cons are poor performance when dealing with intricate, non-linear issues. Deals with complex interactions and high-dimensional data. Didn't do as well as other models at predicting CLABSI.

Benefits of Gradient Boosted Trees are Outstanding predictive performance, particularly for complicated outcomes like CLABSI. Manages high-dimensional data and non-linear relationships with efficacy. Enables feature importance analysis, which is useful in identifying important risk factors.
Cons are highly computational, involving additional training time. Inadequate tuning or regularization may cause overfitting. In contrast to more straightforward models like logistic regression, interpretability is decreased.

The advantages of deep learning (Neural Networks) include excellent mortality prediction performance, particularly with big datasets. Can simulate extremely intricate variable interactions and relationships. Able to identify subtle features in the data and non-linear patterns.
Cons are they need a significant amount of training time and processing power. Difficult to interpret, often regarded as a "black box" due to its lack of transparency in feature importance. They also easily overfit, particularly in cases of sparse data.

5. Challenges:

1. Parameter Optimization: To minimize overfitting and maximize performance, model parameters (such as learning rates and tree depths) for gradient boosting and neural networks had to be tuned with great care.
2. Data Quality: ICD-9 codes, which are occasionally erroneous or incomplete and may introduce bias into model training and prediction, were used in this study.
3. Computational Resources: Compared to simpler models like logistic regression, training the deep learning model and gradient boosted trees required more computational resources.

6. Discussion:

The study demonstrated the potential of machine learning models in predicting complex clinical outcomes in ICU patients, particularly with the gradient boosted trees model excelling at predicting central line placement and CLABSI. The models' predictive power was increased by adding severity scores and comorbidities. But when it comes to mortality prediction, the deep learning model performed exceptionally well, suggesting that more intricate models work better with high-dimensional data and nuanced interactions.

By identifying high-risk patients for CLABSI early in their ICU stay, clinicians could implement targeted interventions, reducing the likelihood of infection and improving patient outcomes. There is potential for revolutionizing the way that infection control and patient management are approached through the incorporation of machine learning models into ICU workflows.

7. Conclusion:

There are several benefits to using machine learning models for forecasting clinical outcomes such as CLABSI and ICU mortality. While deep learning proved to be a powerful tool for mortality prediction, gradient boosted trees were found to be the most successful in predicting central line placement and CLABSI. But every model has a unique set of advantages and disadvantages, so depending on the expected result, each one needs to be carefully considered. Subsequent studies ought to concentrate on enhancing these models for immediate clinical implementation and broadening their scope to encompass additional ICU-associated results.

Similarities between Paper 2 & Paper 3:

1. Finding Risk Factors: The main goal of both studies is to find risk factors for bloodstream infections linked to central lines (CLABSI). Paper 3 uses the MIMIC-III database to identify risk factors in a larger population, while Paper 2 examines risk factors in a pediatric intensive care unit setting.

2. Both studies employ data analysis techniques to assess risk factors. To predict the likelihood of CLABSI, Paper 2 uses multivariate conditional logistic regression, and

Paper 3 uses machine learning models (deep learning, gradient boosted trees, and logistic regression).

3. A major risk factor for CLABSI is highlighted in both papers: the central venous catheter (CVC). Paper 2 bases its research exclusively on children with CVCs, and Paper 3 also notes that central line placement is a critical component in the prediction of CLABSI.

4. Models are used in both papers to forecast results. In Paper 2, CLABSI risk factors are predicted using logistic regression models, and in Paper 3, the occurrence of CLABSI and other clinical outcomes are predicted using machine learning algorithms.

Differences Between Paper 2 and Paper 3:

1. Paper 2 highlights the risks related to children by focusing only on pediatric ICU patients at Children's Hospital Boston while paper 3 Examines information from the MIMIC-III database, which covers a larger patient group (adult and pediatric) admitted to the intensive care unit of Beth Israel Deaconess Medical Center.

2. Paper 2 identifies CLABSI risk factors by developing a prediction rule and using conditional logistic regression models. It creates a rating system using the risk factors that have been identified while paper 3 Utilizes machine learning techniques such as logistic regression, gradient boosted forests, and deep learning, it generates predictions. The performance of the models is compared by using cross-validation methods.

3. Paper 2 identifies CLABSI risk factors in pediatric patients using central venous catheters as the main area of focus while paper 3 looks at multiple outcomes involving central line placement, ICU mortality, and CLABSI in a larger patient population.

4. Paper 2 data is restricted to a specific time frame (2004-2007) and is derived from a single children's hospital while paper 3 uses MIMIC-III database, which contains information on a larger and more diverse patient population as well as over 10 years (2001–2012) of data.

5. Paper 2 primarily employs regression, a conventional statistical model, and concentrates on rule-based forecasts while paper 3 uses sophisticated machine learning methods (gradient boosted trees, deep learning), enabling more intricate modeling and predictions for a variety of outcomes.

In conclusion, while identifying risk factors for CLABSI through data-driven methods is the common goal of both articles, there are notable differences between them in terms of the populations examined, the methodologies used, and the prediction tools used. Paper 3 uses machine learning on a larger ICU population, while Paper 2 is primarily concentrated on pediatric patients using conventional statistical methods.

Summary:

This report unifies the findings from the three papers that focus on different aspects related to CLABSI in Pediatric Intensive Care units (PICUs), calculating their financial burden, analyzing risk factors and implementing predictive models using machine learning.

The first study conducted by Edward et al, intended to quantify the direct medical costs attributable to nosocomial bloodstream infections in PICU patients. This prospective cohort study was conducted at St. Louis children's Hospital, and it included a total of 911 PICU patients and compared the costs for patients with and without bloodstream infections. The study identified that there was considerable difference in the costs which is estimated to be $39,219 per infection after adjusting for factors such as congenital heart disease, severity of illness, lung disease and organ transplant. These findings had exceeded prior estimates due to of its larger sample size and usage of actual cost rather than charge-based estimates. The authors have concluded saying that implementation of effective infection prevention strategies could lead to substantial cost savings for hospitals, especially for high-risk patients, such as those with congenital conditions or those needing ventilator support.

The second study was published in Infection Control and Hospital Epidemiology aimed to identify the critical risk factors with CLABSI in PICU patients. This case control study included 203 children with CLABSI and 406 matched control patients. The study discovered several independent risk factors for CLABSIs, which are cardiovascular disease, central line placement within the ICU, extended ICU stays and the presence of a gastrostomy tube. Patients receiving parental nutrition and blood transfusions are also identified as in higher risk of developing CLABSIs. This study showed that the children possessing these risk factors could benefit from targeted interventions, such as use of adjunctive technologies like antibiotic-coated catheters, more aggressive infection prevention techniques. These findings highlight the importance of developing customized prevention strategies that prioritize patients with known risk factors.

The third study looked into how supervised machine learning techniques can be used to predict CLABSIs and mortality among ICU patients. By analyzing data from the Multiparameter Intelligent Monitoring in Intensive Care (MIMIC-III) database, which included information from 57,786 hospital admissions, the researchers created predictive models using logistic regression, gradient-boosted trees, and deep learning algorithms. These models showed high accuracy for predicting mortality, with an AUC of 0.885, and central line placement, with an AUC of 0.816. However, the model for predicting CLABSIs had a lower AUC of 0.722, suggesting that while machine learning can be highly effective in forecasting outcomes like mortality, predicting

CLABSIs is more complex. The study suggests that identifying patients at risk for CLABSIs early on could lead to better patient outcomes and reduce costs by allowing for more timely and focused interventions.

Collectively, these studies highlight the urgent need for continued efforts to prevent CLABSIs in PICUs. The financial impact of these infections is significant, and those with certain risk factors require specialized prevention approaches. Additionally, advances in machine learning hold great promise for identifying at-risk patients early, enabling proactive measures that could improve outcomes and reduce the costs associated with hospital-acquired infections. These findings are key to developing better infection control strategies and optimizing resource use in pediatric ICUs.

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