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Title: Real time forecasting of pediatric intensive care unit length of stay using computerized provider orders

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Abstract: Objective: To develop a model to produce real-time, updated forecasts of patients' intensive care unit length of stay using naturally generated provider orders. The model was designed to be integrated within a computerized decision support system to improve patient flow management.
Design: Retrospective cohort study.
Setting: Twenty-six bed pediatric ICU within an urban, academic children's hospital utilizing a computerized order entry system.
Patients: A total of 2,178 consecutive pediatric ICU admissions during a 16-month time period.
Measurements and Main Results: We obtained unit length of stay measurements, time-stamped provider orders, age, admission source, and readmission status. A joint discrete-time logistic regression model was developed to produce probabilistic length of stay forecasts from continuously updated provider orders. Forecast accuracy was tested using ranked probability scoring and calibration curves. Cross-validation procedures were conducted. The distribution of length of stay was heavily right-skewed with a mean of 3.5 days (95%CI 0.3 to 19.1) Provider orders were highly predictive of LOS in real-time improving forecasts by 33% (i.e., reduction in mean rank probability score) across all patients, 42% for short-stay patients, and 30% for long-stay patients compared to empirical estimates. Seventeen predictive orders were found, grouped by: medication, ventilation, laboratory, diet, activity, foreign body, and extracorporeal membrane oxygenation.
Conclusions: Provider orders reflect dynamic changes in patients' conditions making them useful for real-time length of stay prediction and patient flow management. Patients' length of stay represents a major source of variability in ICU resource utilization and if accurately predicted and communicated, may lead to pro-active bed management and more efficient patient flow.

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Editorial Board, Critical Care Medicine;

We are pleased to submit our manuscript, "Real time forecasting of pediatric intensive care unit length of stay using computerized provider orders" to *Critical Care Medicine*. This manuscript presents a novel approach to ICU length of stay prediction designed to provide real time decision support to improve patient flow management. The design is intended to be generalized to any ICU setting. Thank you for considering our manuscript for publication.

Sincerely,

Scott Levin, PhD
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Title: **Real time forecasting of pediatric intensive care unit length of stay using computerized provider orders**

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Keywords: pediatric intensive care units, length of stay, forecasting, medical order entry systems, logistic model, efficiency organizational

ABSTRACT

Objective: To develop a model to produce real-time, updated forecasts of patients' intensive care unit length of stay using naturally generated provider orders. The model was designed to be integrated within a computerized decision support system to improve patient flow management.

Design: Retrospective cohort study.

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Conclusions: Provider orders reflect dynamic changes in patients' conditions making them useful for real-time length of stay prediction and patient flow management. Patients' length of stay represents a major source of variability in ICU resource utilization and if accurately predicted and communicated, may lead to pro-active bed management and more efficient patient flow.

INTRODUCTION

Quality of care, access to care and financial performance are all impacted by patient flow within hospitals. Accelerating national trends in inpatient volume and hospital-based healthcare expenditures have created an environment where patient flow and length of stay (LOS) management are critical to patient safety, patient satisfaction, and hospital financial viability.[1-2] As hospital system capacity and economic constraints continue to tighten, high priority has been placed on improving the efficiency and timeliness of care.[3-5] Efforts within hospitals, especially large tertiary care facilities, to better manage patient flow are challenged by variability (i.e., uncertainty) in demands for resources, and their complex inter-dependent systems of care.[6-9] These challenges, as recognized by the National Academy of Engineering and Institute of Medicine's joint report, "Building a Better Delivery System: A New Engineering / Healthcare Partnership", lend themselves to systems engineering approaches of study and solution development.[6,10] This study represents the development of a systems engineering tool to be deployed as a real-time decision support application for improved management of patient flow through ICUs and hospitals.

Patient LOS is a major source of variation that determines flow and demand for ICU and hospital resources.[11-15] Obstructions in ICU flow may cause adverse effects within hospital systems through unavailability of services, delays in care, and patients being treated in sub-optimal care areas. ICUs reject admissions with varying rates due to lack of available resources. Critically ill patients are known to have better survival rates when treated in ICUs, with refusal being associated with increased risk of in-hospital mortality.[16] In addition, lack of beds commonly creates delays in the operating room (OR), post-anesthesia care unit, and less frequently may cause surgical case cancellations.[17-18] Delays inconvenience the patient, surgical team, and incur heavy costs for OR idle and staff overtime. Similar access delays are created in the emergency department (ED) where excessive boarding has been associated with significant increases in mortality rate.[19-20] ICUs are not always the root cause of these delays. Most patients exit the ICU to lower level care areas where bed unavailability creates a common barrier to out-going transfers.[9,21] Patients awaiting transition consume valuable ICU resources that may be more beneficially directed toward patients waiting or refused access.[22] Patient flow through the ICU is a major driver of hospital operations impacting patient safety, quality of care, and financial performance.

ICUs are highly integrated into hospital systems stressing the need for effective coordination, communication and timely information transmission. Daily ICU patient flow management requires: ensuring appropriate staffing levels, deciding to accept or refuse patient admissions, and timing and executing admissions and transfers to minimize patient wait time and refusals. These functions require projecting discharge times and future resource needs for patients. In the hospital studied, projections are based on human experience and intuition supplemented by daily status reports available each morning. Information systems such as electronic white-boards or bed-boards are useful in examining the current state of a unit or hospital but do little to assist in projecting the future, which patient flow management is based on.

There has been significant effort in critical care medicine and operations research directed toward predicting patient LOS. From a clinical perspective, LOS is often modeled as an outcome associated with health status and risk of adverse event or mortality (i.e., primary outcome).[23-27] The

Acute Physiology and Chronic Health Evaluation (APACHE) model is a well-known example.[23] Regression models or algorithms are developed using physiologic, diagnosis and demographic information to make predictions on or near arrival. Accuracy of predictions is evaluated through calibration. Mean predicted LOS is compared to mean observed LOS within and across specific ICU patient cohorts. From an operational perspective, LOS is modeled probabilistically. LOS distributions are characterized using Markov models, phase-type, or mixed distributions with the aim of discerning long-stay patients that comprise the long tail often seen in LOS distributions.[27] These models may be incorporated in queuing systems or simulations developed to understand and improve resource allocation and long term strategic planning.[28-29]

The objective of this study is to develop a model to produce real-time forecasts of patients' future ICU LOS using provider orders. Probabilistic forecasts spanning 72 hours into the future are generated from recent orders (i.e., within previous 6-hours) for each patient. Forecasts based on orders are updated to reflect dynamic changes in patients' conditions. An additional study aim was to demonstrate that evaluating probabilistic forecasts for both sharpness and calibration is applicable to real-time LOS prediction. However, the ultimate goal of this research is to create a generalizeable forecasting tool used in clinical practice to support pro-active bed management and improved ICU patient flow.

METHODS

Design and Patient Data Collection

We conducted a retrospective cohort study of 2,178 consecutive pediatric intensive care unit (PICU) patients over a 16-month time period. We excluded 70 (3.2%) patients that died in-hospital and 46 (2.1%) patients with missing or incoherent data. Thus our final cohort consisted of 2,062 patients with an average age of 6.75 years ranging from less than 1 (23%) to 21 years. All patients were cared for in a 26-bed PICU, which is part of a 180-bed children's hospital located within an urban, academic medical center. Patients' source of admission were the OR (39%), pediatric ED (26%), intra-hospital transfers (18%), and referrals from external healthcare facilities (17%). PICU providers use a CPOE system to directly enter all orders including: diets, activity, medication, laboratory tests, radiology tests, and procedures.

PICU LOS, source of admission, readmission status, age and all time-stamped provider orders 6-hours prior to PICU arrival until PICU discharge were collected. An expert panel of three pediatric physicians and one nurse selected key orders hypothesized predictive of LOS. Selected orders fell into the following categories: activity, consults, diet, extracorporeal membrane oxygenation (ECMO), foreign body, laboratory, mechanical ventilation, enteral medications, infused medications (vasoactive, opiate, other), injected medications (electrolytes, sedatives, muscle relaxants, other), and transfusion. Each of the categories was comprised of order groups. In total, 770 unique orders fell into 60 groups recognized by the forecast model. For example, there were 30 unique dietary orders grouped as either: withhold food (NPO), clear liquid diet, full liquid diet, formula/human milk, or regular diet. Additional information such as ventilation frequency (i.e., continuous versus nightly) or laboratory order frequency was also used to stratify order groups. Preliminary discrete-time logistic regression models were displayed to the expert panel in an iterative process to further refine order selection and grouping. Order groups recognized by the model will hereafter be referred to as orders.

Model Development

Patients' future LOS was predicted using survival analysis. Discrete-time logistic regression models were developed to predict the probability of a patient being discharged within each 6-hour interval up to 72 future hours. Twelve separate models (i.e., 72 divided by 6 hours) were used to predict likelihood of discharge across each interval. The models estimate the probability of discharge in a specific interval given the patient will be present the interval prior. The set of model estimates are joined by the following function where: (*a*) represents an individual model's probability estimate, and (*p*) represents the joint probability estimate for the (i_{th}) future time interval:

$$p_i = p_{i-1} * \frac{(1 - a_{i-1})}{a_{i-1}} * a_i$$

This function produces a coherent probability density function profiling a patient's probability of discharge with emphasis on predictions closest to the current time (i.e., i_0) being most accurate.[30]

The joint model is conditioned on fixed information such as a patient's age, source of admission, and readmission status, but is updated in near real-time based on dynamic information such as patient's current LOS, temporal factors, and provider orders. Fixed and dynamic information serve as model predictor variables each time a forecast is made. Patients' current LOS is grouped as either being short stay ($\leq$ 3 days) or long stay at the instant the forecast is made. Temporal information includes the day-of-week, and time-of-day (i.e., grouped by midnight to 6am, 6am to noon, noon to 6pm, and 6pm to midnight) the forecast is made. Dynamic order information is extracted from CPOE in the interval 6 hours prior to forecast time. For each patient's 6-hour order extract, all 60 orders are indicated as either present or not. For example, if a lactic acid laboratory order was placed for a patient within the past 6 hours, this variable was listed as present. Medications were grouped by type and administration method. In addition, counts of medications by administration method (i.e., enteral, infusion, injection) were examined as predictor variables.

An example forecast, at three time points (i.e., sliding window forecasts) during a patient's LOS may be seen in Figure 1. Output forecasts are updated over time to reflect changes in a patient's conditions based on orders. The example forecasts are for an 8 year old patient admitted through the ED, with the leftmost plot representing the patient 6 hours into their PICU stay. Within the previous 6 hours the patient had present orders for: 3 infused medications, 2 injected medications, continuous ventilation, either activated partial thromboplastin time (APTT) or D-Dimer laboratories with a frequency of less than 6 hours, and clear liquid diet (see order set below plot). At this point the patient is likely to be discharged after 3 days, as evident by the forecast density. The middle plot represents this same patient 58 hours into their stay with an order set reflecting a progression in health status, but still uncertainty about future LOS exists. The right plot is again the same patient with an order set indicating further progression and likely discharge within the next 18 hours. The temporal predictor variables (e.g., time-of-day) produce the harmonic peaks most evident in the middle plot. This is designed to account for PICU processes (e.g., rounds, staff shift changes, etc.) that make it most likely for all patients to be discharged during certain portions of the day.

Model Evaluation and Order Selection

Sharpness and calibration are the most important characteristics for evaluating the accuracy of probabilistic forecasts.[31] Sharpness assesses the variance (i.e., uncertainty) of probability estimates around the actual observation (i.e., discharge time). A forecast that places a high concentration around the time of actual observation is sharper and more certain than a density forecast estimate with higher spread. Rank probability scoring (RPS) was used to evaluate the sharpness and accuracy of each patient's sliding window forecasts and also formed the basis for selecting the most highly predictive orders. The RPS is a measure of the difference (i.e., integral) between the cumulative distribution of a forecast and actual observation and has been shown to minimize mean absolute error.[32] An example of how the RPS is measured for a patient discharged between 18 to 24 hours from forecast time may be seen in Figure 2. This measure was calculated for each sliding window forecast (N = 29,749) for all patients in the cohort. Forecasts were also evaluated graphically using calibration curves comparing forecasted mean probability of discharge to observed probability. The utility of orders in predicting LOS was further scrutinized by comparing the order-based forecast model RPS to forecasts created from the empirical LOS distribution and from a model solely relying on fixed and temporal dynamic variables (i.e., order-less model). Empirical sliding window forecasts were constructed by applying the future rescaled empirical distribution given patients' current LOS.

The order selection objective was to determine the most highly predictive set of orders from the 60 hypothesized to influence LOS. Univariate and forward stepwise analysis was used with the objective of minimizing mean RPS across all forecast windows. Fixed predictor variables were initialized in all analysis with univariate and stepwise procedures only conducted on orders. Marginal utility of each final model order was examined with the aim of minimizing orders included (i.e., complexity) while maximizing predictive accuracy.

Cross-validation was used to evaluate the regression model's out-of-sample predictive performance (i.e., mean RPS). Patients were split into 80% training and 20% testing sets. Model parameters were generated from the training set with RPS evaluated against the test set. This process was iterated 100 times to ensure stability of both predictive performance and parameter estimates.

RESULTS

Forecast Estimates

The distribution of PICU LOS was heavily right-skewed with a mean of 3.5 days (95%CI 0.3 to 19.1) and median of 1.7 days (IQR 22.2 to 3.8). The set of orders most predictive of LOS is seen Table 1. Odds ratios estimating patients' likelihood to *remain* in the PICU for the next 6 hours (i.e., first forecast interval) are displayed. Additional orders were predictive, but did not significantly improve model accuracy. All orders evaluated may be seen in Appendix I. Predictive orders included were categorized by: medication, ventilation, activity, laboratory, diet, foreign body and ECMO. Predictive power of orders, defined as their parameter estimates absolute magnitude and significance (p value < 0.05), were associated with frequency of occurrence. Predictive power diminished as forecast horizon increased as depicted in Figure 3. Size and shading of dots reflect the magnitude and direction of discrete-time logistic regression parameter estimates. Dots for the 6 hour (i.e., leftmost) interval correspond to order parameter estimates in Table 1.

Table 1. Forecast model for odds of remaining in the PICU for next 6 hour horizon

Category	Predictor Variable	OR (95% CI)	p value
Age	Age	0.98 (0.97 – 0.99)	< .001
Source	*OR: Reference*	-	-
	ED	1.53 (1.35 – 1.74)	< .001
	Intra-Hospital	1.72 (1.48 – 2.00)	< .001
	Direct Admit	1.42 (1.24 – 1.70)	< .001
Readmission	Readmission Status	1.45 (1.22 – 1.74)	< .001
Timing	Long-Stay (LOS > 3 days)	1.52 (1.37 – 1.69)	< .001
	Monday: Reference	-	-
	Tuesday	1.02 (0.83 – 1.25)	.850
	Wednesday	0.77 (0.64 – 0.93)	.008
	Thursday	0.77 (0.64 – 0.93)	.007
	Friday	0.81 (0.67 – 0.98)	.028
	Saturday	0.87 (0.72 – 1.06)	.163
	Sunday	0.94 (0.77 – 1.14)	.524
	6 am – Noon: Reference	-	-
	Noon – 6 pm	0.23 (0.20 – 0.26)	< .001
	6 pm – Midnight	0.54 (0.46 – 0.62)	< .001
	Midnight – 6 am	3.70 (2.8 – 4.8)	< .001
Medication	Enteral Count[a]	0.91 (0.85 – 0.98)	.016
	Infusion Count[b]	2.38 (1.92 – 2.97)	< .001
	Injection Count[c]	1.45 (1.34 – 1.58)	< .001
Ventilation	Continuous	10.66 (6.25 – 18.17)	< .001
	BIPAP /CPAP, Continuous	7.50 (3.98 – 14.13)	< .001
	BIPAP/ CPAP, Nightly	2.09 (1.34 – 3.25)	< .001
Activity	Activity Age Appropriate	0.23 (0.20 – 0.28)	< .001
	Out of Bed	0.32 (0.25 – 0.42)	< .001
Laboratory	APTT/D-Dimer (freq < 6hrs)	11.63 (5.45 – 10.02)	< .001
	APTT/D-Dimer (freq ≥ 6 hrs)	4.19 (2.39 – 7.35)	< .001
	Lactic Acid Lab	10.46 (4.93 – 22.21)	< .001
Diet	Clear Liquid Diet	1.83 (1.38 – 2.41)	< .001
	Formula/Human Milk	0.67 (0.52 – 0.87)	.002
	Withhold Food (NPO)	2.24 (1.74 – 2.88)	< .001
	Regular Diet	0.61 (0.51 – 0.74)	< .001
Foreign Body	Peripheral Line	0.67 (0.57 – 0.81)	< .001
ECMO	ECMO[d]	-	-

[a] Enteral medication count range: None = 0, Low = 1 to 4, High > 4
[b] Infusion medication count range: None = 0, Low = 1 to 2, High > 2
[c] Injection medication count range: None = 0, Low = 1 to 9, High > 9
[d] ECMO orders supersede joint-forecast model when present

Fixed variables for patients' age, admission source, and readmission status were predictive and significant through all model intervals. Temporal variables characterizing long stay patients and time-of-day were similarly significant. Time-of-day estimates demonstrate the much higher likelihood of discharge between noon and 6 pm compared to other times. Bounded medication counts by administration method were most effective in predicting LOS compared to grouping medications by type as seen in Appendix 1. Ventilation orders for: (1) continuous ventilation, (2) bi-level or continuous positive airway pressure (BIPAP/CPAP), and (3) nightly BIPAP/CPAP were highly predictive of remaining in the PICU. Activity orders allowing patients increased mobility were indicative of a patient becoming ready for discharge. The APTT/D-Dimer laboratory grouped orders were significant and their frequency (i.e., time from last APTT/D-Dimer lab) distinguishable. Mutually exclusive diet orders for NPO and clear liquid decreased likelihood of discharge, while formula/human milk and regular diet orders predicted an increased likelihood. Peripheral line associated orders had a low predictive power, but significantly indicate an increased rate of discharge throughout the forecast horizon. ECMO orders did not demonstrate predictive power because of scarcity, occurring in only 1.1% of patients. However, ECMO orders where highly indicative of remaining in the PICU for this population. If an ECMO associated order was present, the estimated forecast is superseded by the empirical estimate for this population. The ECMO cumulative empirical estimate was linear ranging from a 0% probability of discharge within 6 hours to a 10% chance by 3 days. In this fashion the model is adaptable to orders that are scarce, but are known to be highly predictive.

Model Accuracy

Provider orders were predictive of LOS in real-time improving forecast accuracy (i.e., mean RPS) by 33% across all patients, 42% for short stay patients ($\leq$ 2 days), and 30% for long stay patients compared to empirical estimates. Corresponding order-based forecast accuracy was improved by 30%, 39%, and 27%, respectively compared to models using fixed and temporal predictors (i.e., order-less forecast). Mean RPS scores for all forecast windows for the order-based, empirical, and order-less forecasts were compared over the course of patients' LOS as seen by the sharpness plot in Figure 4. Marked improvements early in patients' LOS were observed because variation in rate of discharge (i.e., 50% patients discharged by 40.3 hours) was highest. Orders were effective in accounting for this variation. Later in patients LOS the rate of discharge declines making empirical estimates more accurate. However, the order-based model still outperforms, keying on orders indicative of discharge. The order-based model forecast calibration curve across all sliding window forecasts may be seen in Figure 4. The model was well calibrated demonstrating correspondence between mean forecasted and observed discharge probability throughout the forecast horizon. Predictive performance and parameter estimates remained stable through all cross-validation procedures.

DISCUSSION

Results suggest that provider orders are useful for real-time prediction of patients' LOS. Orders directly represent provider decision making over time. This capture's a portion of information related to patients' changing conditions, making it useful for prediction. Using provider orders for real-time analysis and application is advantageous. First, all information is likely available in real-time with time-stamps through a single CPOE data source. Comparatively, collecting physiological information from multiple data sources (i.e., electronic medical records, laboratory, radiology) offers more complex data management challenges. Second, orders are naturally generated requiring no user input from providers. In busy healthcare environments, applications designed for minimal maintenance are more likely to succeed.[33] Last, the methods were designed to be generalized to other ICUs and inpatient settings despite varying order patterns and timing of work processes. Models are adaptable in that predictive orders and their parameter estimates may differ, but we hypothesize that orders in most settings provide valuable LOS information.

This study contrasts previous work that generates LOS predictions using demographic, diagnosis and physiological measures.[23-26] This is likely because our objective differs by attempting to capture updates in patients' conditions and project LOS onward. Probabilistic forecasts were well-suited for this task given the variability associated with patients' conditions and hospital work processes. Probability forecasts also allow for easy aggregation and determination of bed availability. For example if 5 patients each have a 20% chance of being discharged between 12 and 18 hours, 2 beds are likely to become available during that future time interval. Density forecasts are useful for many healthcare applications, but methods for evaluation stem from the fields of meteorology and financial risk management.[32,34] The RPS commonly used in these domains captures both accuracy and uncertainty of forecasts. However, accuracy will ultimately be evaluated by application end-users, and their trust in allowing it to support patient flow decisions.

There are several limitations to this research application. Forecast accuracy is highly dependent on the reliability and timeliness of order placement. Orders placed electronically to affect a desired response (e.g., laboratory, medication) are likely reliable. However, other CPOE information may not be. For example, we aimed to track ventilation by initiation (i.e., intubation) and discontinue (i.e., extubation). However, many patients arrive to the PICU already on ventilators and the extubation order was not consistently used. We elected to monitor any order associated with being ventilated or altering settings as a surrogate method of tracking. Forecasts models are able to accommodate uncertainty associated with order information and quantitatively translate this probabilistically. In addition, we know that many types of orders are indicative of LOS. Targeting a sub-set orders most frequently and consistently entered will be most effective in making accurate predictions. Other limitations exist in interpreting the meaning of RPS accuracy measures. It is unknown what level of accuracy is required to support user decision making. Implementation of the forecast application and evaluating its use is the only true means of determining accuracy requirements.

CONCLUSION

Provider orders reflect dynamic changes in patients' conditions making them useful for real-time LOS prediction. This study demonstrates the development and evaluation of a continuously updated LOS forecast model driven by computerized provider orders. Providing accurate and timely LOS forecasts to key personnel may support improved management of patient flow through ICUs and hospitals. Deploying systems engineering tools as informatics applications provides the ability to leverage naturally generated clinical information to perform more evidence based management of ICU resources.

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FIGURE LEGENDS

Figure 1. Patient ICU length of stay forecast over time

Figure 2. Rank probability score (grey area) for example forecast window

Figure 3. Order prediction magnitude over forecast horizon

Figure 4. Forecast model accuracy: sharpness and calibration

Figure 1
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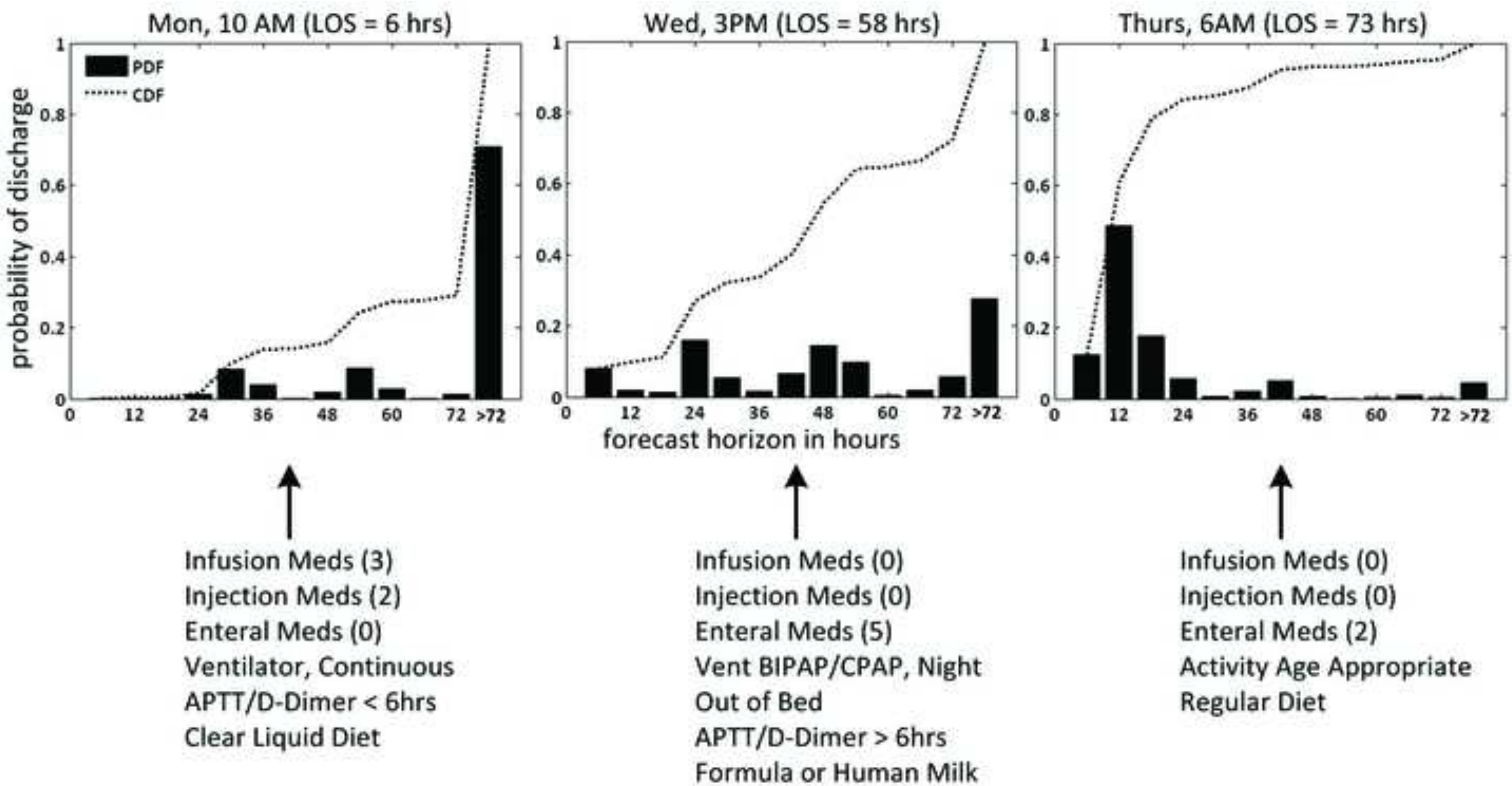

Figure 2

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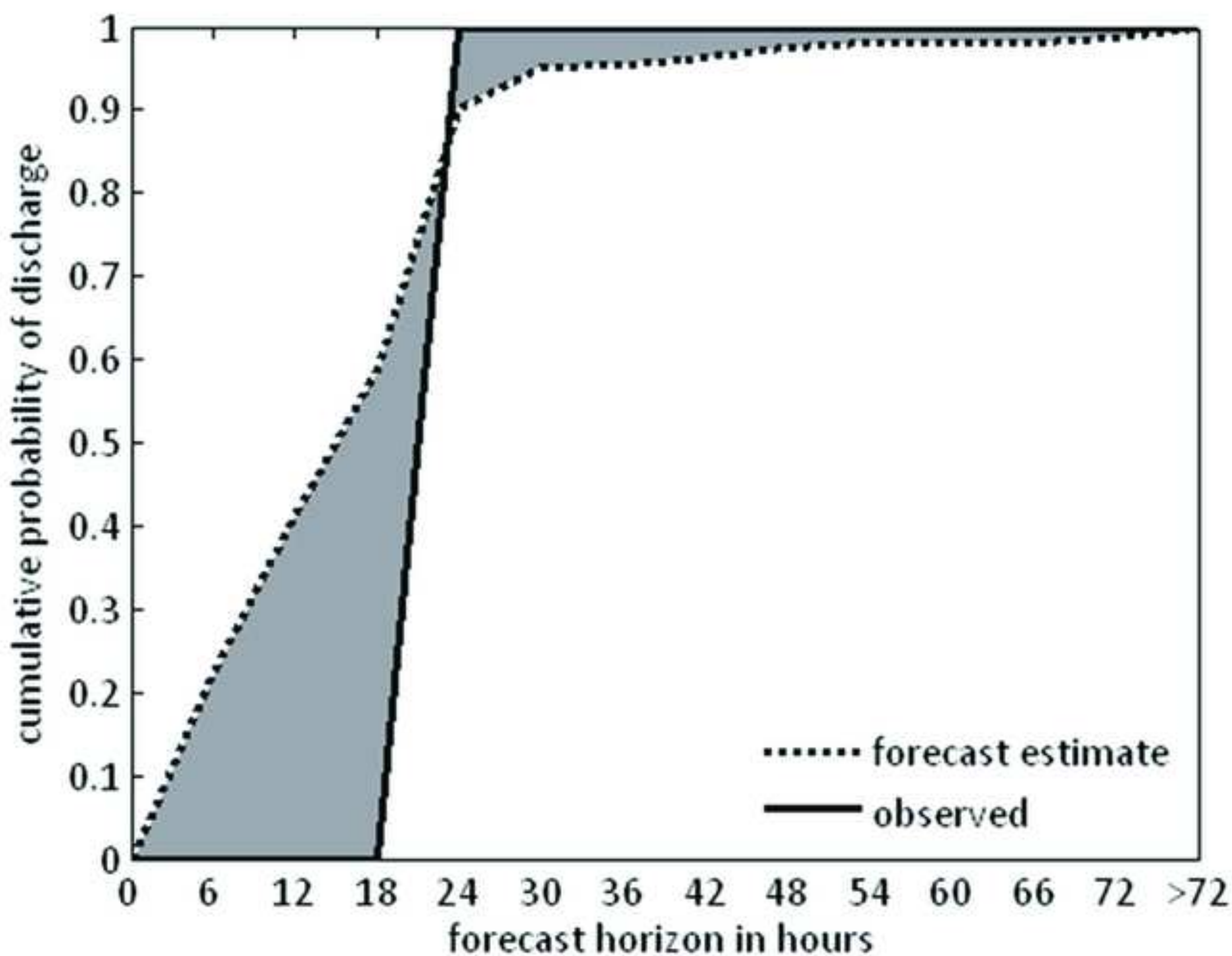

Figure 3

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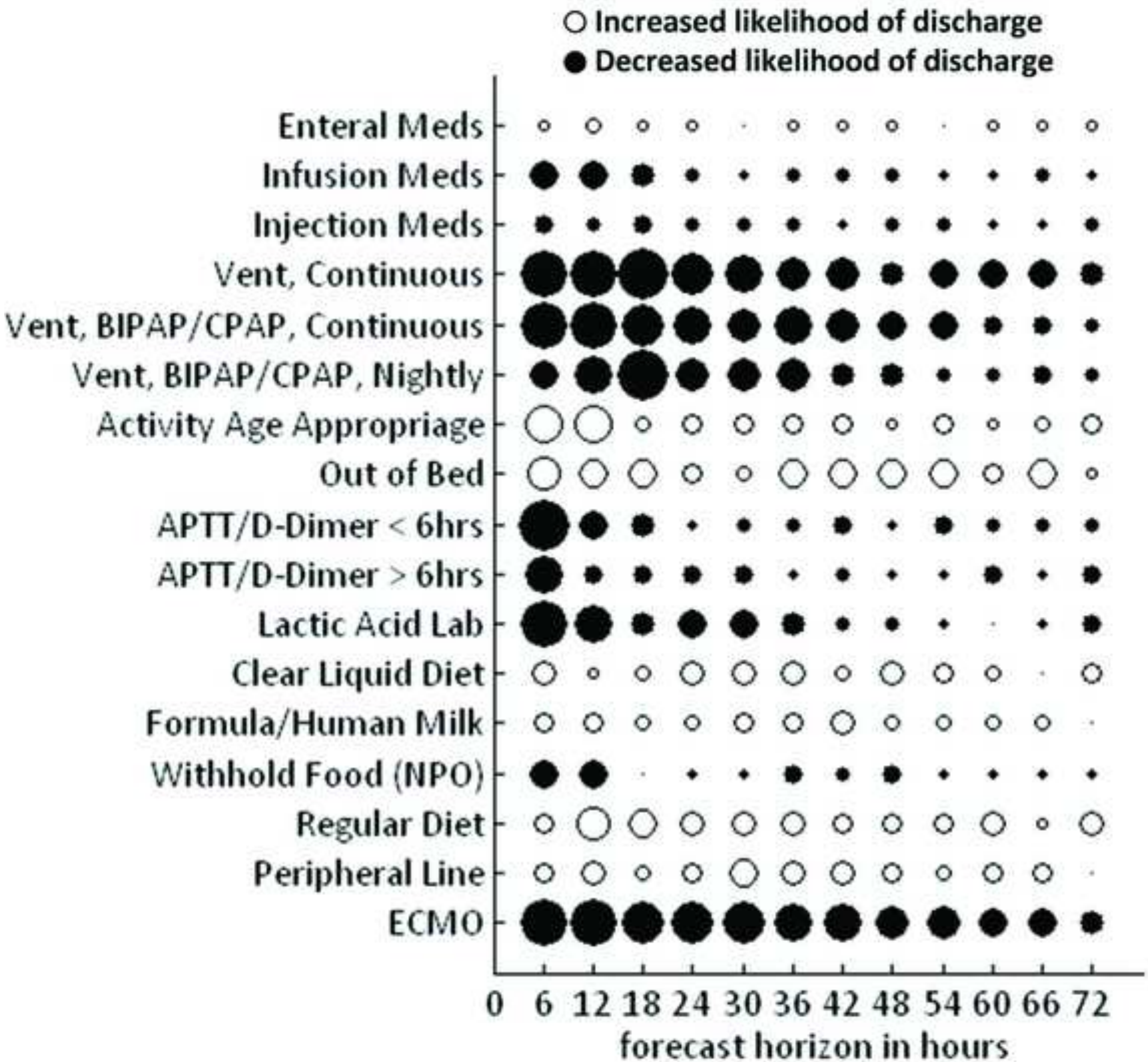

Figure 4

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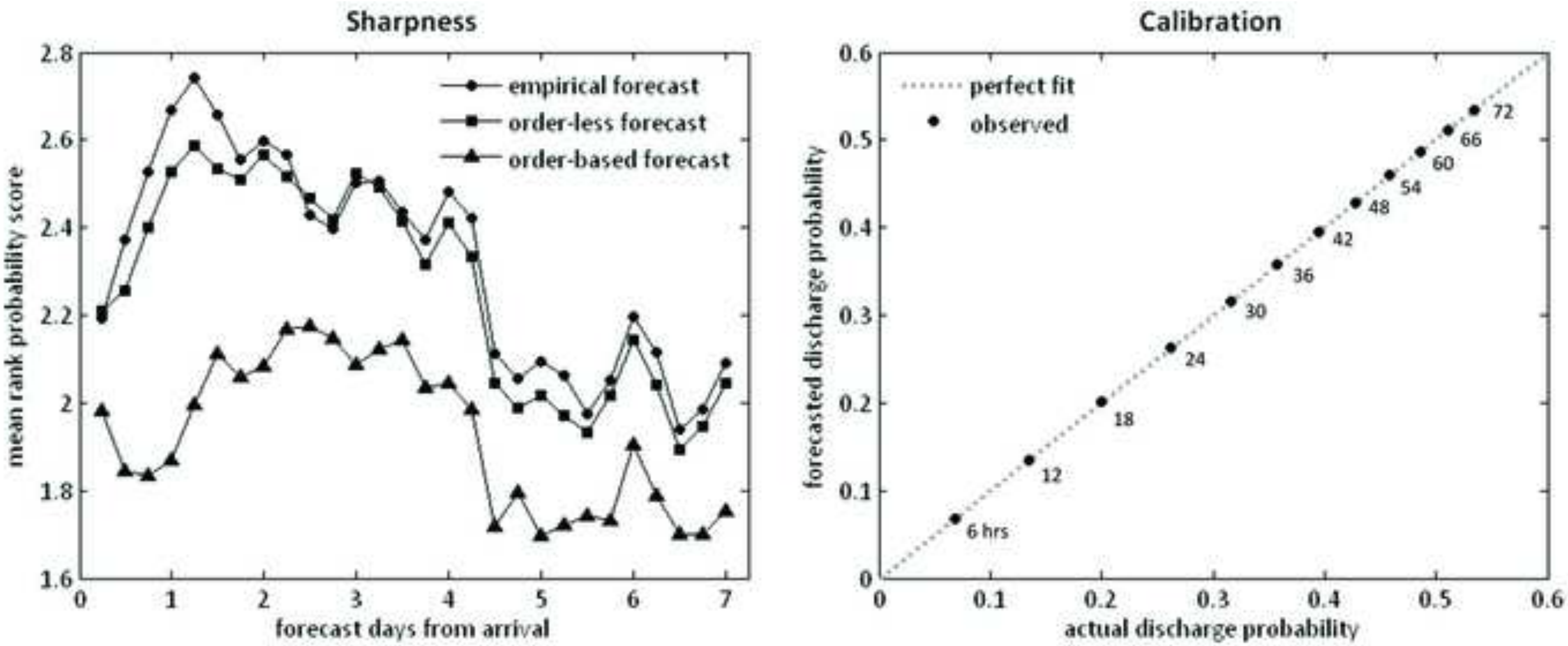

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