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Unsupervised machine learning analysis to identify patterns of ICU medication use for fluid overload prediction

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ABSTRACT

INTRODUCTION: Intravenous (IV) medications are a fundamental cause of fluid overload (FO) in the intensive care unit (ICU); however, the association between IV medication use (including volume), administration timing, and FO occurrence remains unclear.

METHODS: This retrospective cohort study included consecutive adults admitted to an ICU ≥72 hours with available fluid balance data. FO was defined as a positive fluid balance ≥7% of admission body weight within 72 hours of ICU admission. After reviewing medication administration record (MAR) data in three-hour periods, IV medication exposure was categorized into clusters using principal component analysis (PCA) and Restricted Boltzmann Machine (RBM). Medication regimens of patients with and without FO were compared within clusters to assess for temporal clusters associated with FO using the Wilcoxon rank sum test. Exploratory analyses of the medication cluster most associated with FO for medications frequently appearing and used in the first 24 hours was conducted.

RESULTS: FO occurred in 127/927 (13.7%) of the patients enrolled. Patients received a median (IQR) of 31 (13-65) discrete IV medication administrations over the 72-hour period. Across all 47,803 IV medication administrations, ten unique IV medication clusters were identified with 121-130 medications in each cluster. Among the ten clusters, cluster 7 had the greatest association with FO; the mean number of cluster 7 medications received was significantly greater in patients in the FO cohort compared to patients who did not experience FO (25.6 vs.10.9. $p<0.0001$). 51 of the 127 medications in cluster 7 (40.2%) appeared in > 5 separate 3-hour periods during the 72-hour study window. The most common cluster 7 medications included continuous infusions, antibiotics, and sedatives/analgesics. Addition of cluster 7 medications to a prediction model with APACHE II score and receipt of diuretics improved the ability for the model to predict fluid overload (AUROC 5.65, $p =0.0004$).

CONCLUSIONS: Using ML approaches, a unique IV medication cluster was strongly associated with FO. Incorporation of this cluster improved the ability to predict development of fluid overload in ICU patients compared with traditional prediction models. This method may be further developed into real-time clinical applications to improve early detection of adverse outcomes.

KEYWORDS: critical care; fluid overload; prediction; medication regimen complexity; machine learning

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KEY POINTS

Questions: Can machine learning detect the presence of time-dependent medication administration patterns that are associated with risk of fluid overload in critically ill patients?

Findings: Using unsupervised machine learning, a unique IV medication cluster was identified that, when combined with the APACHE II score and diuretic use, improved the ability to predict fluid overload in ICU patients.

Meaning: These findings suggest that machine learning may be an important tool for analyzing IV mediation administration patterns to predict development of fluid overload. Such models may provide insight into areas where medication administration practices could be optimized to mitigate the risk of fluid overload in this patient population.

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INTRODUCTION

While intravenous (IV) medications are integral to the management of critically ill patients, the associated diluent volume contributes to the development of fluid overload (FO) and its sequalae, including mortality, increased intensive care unit (ICU) length of stay (LOS), increased acute kidney injury (AKI), and increased likelihood of mechanical intubation.[1-3] Mitigating fluid overload with timely achievement of euvolemia is associated with improved outcomes.[4-7] Given the complexity and prolific nature of mediation use in the ICU, data driven strategies are increasingly being employed to parse meaningful patterns for fluid overload prediction.[8-10]

While research is ongoing regarding identification of predictors for fluid overload, minimal research has evaluated the impact of medications as potential contributors.[11,12] These studies have shown that medication regimen complexity, as measured by the medication regimen complexity-ICU (MRC-ICU), was related to fluid overload risk, using both traditional regression and supervised machine learning approaches.[8-10] This score has also been shown to predict mortality[13], LOS[14], and prolonged duration of mechanical ventilation.[15-21] Moreover, pharmacophenotyping based approaches including MRC-ICU and employing a common data model (CDM) for ICU medications (ICURx) have previously been created to allow for unsupervised cluster analysis machine learning that showed unique patterns of medication use and ICU complications, including FO.[22,23] Therefore, quantifying patient-specific, medication-related data may be an important strategy in the prediction of fluid overload in critically adults.

No study has evaluated timing of medication administration in relation to fluid overload by reviewing the entire medication administration record (MAR) to identify patterns associated with medication administration. Unsupervised machine learning may be an optimal strategy for identifying factors associated with medication use and timing in relation to fluid overload. The purpose of this study was to employ unsupervised machine learning methods to uncover medication administration patterns that are correlated with the occurrence of FO. We hypothesized that unique clusters of medication use, particularly early in the ICU stay, would have a strong association with FO development.

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MATERIALS AND METHODS

This was a retrospective, observational study of adults admitted to critical care units at the University of North Carolina Health System (UNCHS) who had fluid overload data recorded. The protocol for this study was reviewed and approved by the UNHCS Institutional Review Board (approval number: (Study Number 20-2330); approval date: September 2020). Waivers of informed consent and HIPAA authorization were granted based on study design. All procedures were conducted with ethical standards of the UNHCS Institutional Review Board and the most recent version of the Helsinki Declaration of 1975.[24] The reporting of this study adheres to the STrengthening and reporting of OBservational data in Epidemiology statement (STROBE).[25]

Population

A trained Carolina Data Warehouse (CDW) analyst developed a random sample of 1,000 adult ICU patients (≥18 years) between October 2015 and October 2020 and extracted requested data from electronic health record (EHR) data (Epic Systems, Verona, WI). Patients were excluded if the data provided was not from their index ICU admission. These methods have been previously published.[9,10]

Data Collection and Outcomes

The primary outcome was presence of fluid overload at 72 hours after initial ICU admission. Fluid overload was defined as a positive fluid balance (intake > output) in milliliters (mL) greater than or equal to 7% of the patient's admission body weight in kilograms (kg).[1,3] For example, a patient weighing 80kg at ICU admission with a positive fluid balance at 72 hours of 12,000 mL (or 12kg) would be classified as having fluid overload (positive fluid balance of 12kg is 15% of initial body weight).

Relevant patient demographics were extracted including: age, sex, race, ICU type, admission diagnosis, utilization of end-organ support including mechanical ventilation and renal replacement therapy, presence of AKI, use of vasopressors, Acute Physiology and Chronic Health Evaluation (APACHE) II score at 24 hours, and sequential organ failure assessment (SOFA) score at 24 hours. Additionally, patient outcomes, including in-hospital mortality, maximum fluid overload over 72 hours, and ICU LOS were collected.

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The 72 hour study period was divided into 24 sets of three-hour intervals. Within this timeframe, the frequency of IV medication administration was calculated for each patient. All IV medications (any type of medication) as well as both oral and IV diuretics (e.g., furosemide, torsemide, chlorothiazide) were organized based on time of administration and separated into 3-hour groups (e.g., vancomycin given at hour 1 of ICU admission would be considered a different entity than vancomycin given at hour 12 of ICU admission). This allowed for both the medication and the timing of medication administration to be included in the unsupervised machine learning analysis. Medications were reviewed to combine any listed medications that were the same dose and volume (e.g., cefepime 1000mg/100 mL in normal saline (NS) mini-bag plus and cefepime 1000m/100mL NS infusion would be considered the same drug). Antimicrobials that were infused over an extended interval (e.g., piperacillin-tazobactam) were not combined with the same antimicrobial infused over a standard duration. Additionally, the ICURx CDM was incorporated into analysis to provide additional information regarding specific ICU medications, including medication class and mode of administration (e.g. IV push versus continuous infusion).[17,26]

Data Analysis

Unsupervised machine learning analysis. Principal Component Analysis (PCA) was performed at the patient level to create principal components (PCs) with a cumulative variance of over 85%.[27,28] This dimension reduction approach was essential as it laid a robust foundation for the subsequent stages of our analysis, enabling us to effectively manage the complexity of the dataset.[27,28] PCA helps remove redundant information and reduces the risk of overfitting, making the dimension-reduced representation more robust to noise and irrelevant features.[27,28] Building upon the reduced dimensionality established by the PCA, we proceeded with the implementation of the Restricted Boltzmann Machine (RBM) which allowed us to identify the underlying structure in medication administration.[29,30] By using the insights captured by the PCs, the RBM unveiled concealed layers.[29,30] Following thorough hyperparameter tuning, which included adjustments to the number of neurons (hidden units), learning rate, and other factors, this process culminated in the successful classification of medications into distinct clusters.[31] RBM can learn sparse representations of data, which means that only a subset of neurons (hidden units) is active at any

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given time.[29,30] This sparsity can lead to more robust and interpretable representations, particularly in cases of the medication administration record where there are redundant or noisy features.[29,30]

The entire process is summarized in **Figure 1**.

Test for the association between clusters and fluid overload. The rank sum test was employed to assess association between each cluster and the occurrence of fluid overload. Clusters demonstrating positive correlations were recognized through p-values lower than 0.05, accompanied by higher mean ranks among patients with fluid overload compared to those without fluid overload. Additionally, logistic regression analyses were performed to support the rank sum test, facilitating the identification and examination of the cluster with the highest association. For these ten logistic regression models (which corresponded to the ten medication clusters), the binary dependent outcome was fluid overload and each cluster's standardized medication proportion was the independent variable. All analyses were performed in Python (version 3.0) and R (version 4.2.1).

Predictive modeling: Proportion of medications within the cluster most associated with FO was added to a logistic regression that included APACHE II score & diuretic use to determine if this feature would add to the ability of the model to predict fluid overload in individual patients. This was also done by time period (24, 48, 72 hours) to determine when the proportion of medications matching the cluster most associated with FO was most important in relation to development of fluid overload.

Descriptive characterization of clusters most associated with FO. Upon identification of medication clusters associated with FO, descriptive statistics were planned to explore and characterize these clusters. Analyses included categorization of medications in each cluster by medication class and analysis of frequency of medications occurring within each cluster (ex. Vancomycin appeared within the cluster X times). Additionally, the clusters were split into 24 hour periods to analyze which medications appeared in the cluster within specific ICU days (i.e. medications that appeared only within the first 24 hours of admission versus medications that appeared within the cluster multiple times throughout the 72 hour analysis period) to assess for a temporal relationship between medication administration and fluid overload. An exploratory analysis including variables of timing such as intermittent and bolus administration was also conducted.

RESULTS

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Among the 927 patients included in the study after removal of patients without fluid balance information (see Appendix for consort diagram), a total of 127 individuals (13.7%) experienced fluid overload. In the fluid overload cohort, the median fluid balance at 72 hours was 5934.17mL (3359.3-9156.4mL) vs. 300mL (IQR -894.1-1576.6 mL) in the non-fluid overload cohort. A total of 47,803 medication administrations occurred within the first 72 hours of ICU stay. Of these medication administrations, there were a total of 2,229 distinct combinations of medication plus timing of administration (ex. Cefazolin hours 0-3 of ICU stay, cefazolin hours 4-6 of ICU stay, etc.). Over the first 72 hours of ICU stay, all patients received a median of 31 distinct IV medication administrations (interquartile range: 13-65), with patients in the fluid overload group receiving a higher number of medication administrations compared to the non-fluid overload group (**Table 1**). Patients were mostly cared for in the medical ICU. Patients with fluid overload had a higher severity of illness as demonstrated by the APACHE II and SOFA scores at 24 hours, higher frequency of end-organ support including mechanical ventilation and renal replacement therapy, longer ICU LOS, and worse patient-centered outcomes including morbidity (e.g., AKI) and mortality. Patients in the fluid overload group received more medications overall as well as more vasopressors, sedatives, antibiotics, fluids, analgesics, gastric agents, anticonvulsants, and antidotes/rescue therapy compared to the non-FO group. **Table 1** provides a complete summary of demographics.

The PCA was conducted to identify clusters of medications. While early models of the PCA included patient-specific information including SOFA score, age, sex, etc., these factors were not significant in identifying the clusters and were excluded from the final model, which included only medications and timing of administration. The proposed unsupervised machine learning modeling yielded 10 distinct clusters (**Figure 1**). There were a median of 532 (interquartile range (IQR) 520-539.8) medications in each cluster when medications were associated with an administration time (ex. vancomycin 1g at hour 3 is considered a separate medication than vancomycin 1g at hour 8), and 121-130 medications in each cluster when administration time was not considered. 97 medications were identical in every cluster when timing was not considered, but when timing of medication administration was factored in, the clusters were significantly different with no medication plus timing combinations being identical in all clusters. **Figures 2 & 3** show overlap between clusters when categorizing medications within each cluster by medication administrations (**Figure 2**) and medication names (**Figure 3**). The medications appearing in each cluster are listed in the **Digital Supplementary Materials**. Additionally, medications were categorized by class, and these proportions are reported in **Table 2**.

Clusters 5 and 7 had a positive association with fluid overload based on the rank sum test (**Table 3**). Patients who experienced fluid overload received a higher mean number of Cluster 5 (18.7 medications vs.

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7.7 medications, $p < 0.0001$) and Cluster 7 medications (25.6 medications vs. 10.9 medications, $p < 0.0001$) in comparison to patients who did not experience fluid overload. Ten logistic regression models were employed, yielding similar results to those of the rank sum test (**Table 4**). While Cluster 5 also was associated with fluid overload, its association was weaker than that of Cluster 7. Analyses of Cluster 5 can be found in the **Supplementary Appendix**.

Notably, Cluster 7, which consisted of 127 unique IV medications, exhibited the highest estimated value and the smallest p-value, signifying its substantial contribution to the development of fluid overload. The medications found within Cluster 7 were diverse, with high representation among continuous infusions, antibiotics, as well as sedatives and analgesics (**Table 2).** A total of 51 medications (40%) were administered in >5 separate 3-hour intervals, and fifteen medications within Cluster 7 were administered exclusively within the initial 24 hours of ICU admission (**Table 5**). Patients with fluid overload were more likely to have medications appear within Cluster 7 than patients without fluid overload (**Table 6).** **Table 7** provides a list of medications appearing on each of the first 3 days of ICU admission within Cluster 7. **Figure 4** shows all of the medications within Cluster 7 and how frequently they appeared based on timing of administration. **Figure 5** reveals medications and timing of medication administrations within Cluster 7 ordered from most frequent to least frequent appearance within the Cluster. **Table 6** splits the medications from Cluster 7 into each day of ICU stay (first 72 hours), and **Figure 6** includes timing of medication administrations separated by medication class. **Figure 7** represents the frequency at which each 3-hour time slot appeared within Cluster 7 (ex. 27 medications given within 0-3 hours of ICU admission appeared within Cluster 7 compared to only 17 medications within the 69-72 hour time slot).

Additionally, Cluster 7 improved predictive models for fluid overload. A logistic regression model including Cluster 7, APACHE score at 24 hours of ICU admission, and levels of diuretic administration demonstrated an improvement in the model (**Table 8**). This was evidenced by a reduction in the AIC from 673.6 to 663.43, with a notably significant estimated p-value of <0.0005. Additionally, integrating this feature in the model led to an enhanced ROC curve, elevating the AUC from 0.7193 to 0.7413 (**Figure 8**). An additional visualization of the impact of Cluster 7 on predictive modeling can be seen in **Figure 9**. Additionally, when dividing Cluster 7 into proportion of medications within Cluster 7 given at each day of ICU stay, a higher proportion of Cluster 7 medications on Days 1 and 3 of ICU admission was associated with increased risk of fluid overload (**Table 9**). **Figure 10** shows the distribution of patients in each group (fluid overload and non-fluid overload) based on proportion of their medications that matched Cluster 7. **Figure 11** is an example of the marginal effect of proportion of medications matching Cluster 7

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and association with fluid overload when normalized to APACHE II score of 14 and receipt of no diuretics.

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DISCUSSION

This first of its kind analysis represents the integration of four novel concepts in the domain of data-driven medication use optimization: (1) the application of unsupervised machine learning methods to the entire MAR (including drug and dose), (2) incorporation of temporal data for medication administration, (3) fluid overload prediction in the ICU, and (4) application of the ICURx CDM. These methods identified a cluster of medications that both statistically and clinically correlated with fluid overload and serves as a proof-of-concept for future implementation studies evaluating how machine learning approaches could be integrated with real-time EHR data to provide predictions at the bedside.

Building on unsupervised machine learning methods that analyzed just the names (i.e., excluding dose, formulation, route) of medications received in the first 24 hours[17,23,32], this is first time that unsupervised machine learning methods have been applied to the comprehensive medication regimen (i.e., including dose, formulation, route) up to 72 hours with an intent to explore how patterns in medication use relate to clinically relevant outcomes. These findings bring together two bodies of research: pharmacophenotyping as a means of identifying high risk patients, and fluid overload prediction using machine learning methods. In two prior pharmacophenotyping approaches, six pharmacophenotypes were identified that had unique patterns of associations with patient outcomes; however, these groupings were notably quite large with limited ability for clinical interpretation. Here, we found a more interpretable cluster, particularly when temporal data were added. Indeed, we observed that incorporating timing of medication administration into the unsupervised analysis provided further insight into development of fluid overload and specific medications, which may have a more substantial impact if given early within the ICU stay, and as such, marks an important exploration into the temporal component of medication administration as it relates to outcomes.

The discerned connection between the distinct IV medication cluster and the heightened risk of fluid overload underscores the need for a proactive and precise approach to medication management in the ICU. Such an approach may entail meticulous evaluation of factors such as timing, dosage, and the selection of specific IV medications, especially those falling within the

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identified subgroup. These findings align with other fluid overload prediction algorithms, which showed improvement when using machine learning and also that medications were highly ranked on feature importance graphs.[32-34] While all of the clusters contained a similar list of medications (**Figure 3**), these clusters became more distinct and unique when the timing of medications was included in the original cluster development (**Figure 2**). When including the timing of medications, Cluster 7 was statistically correlated with fluid overload and also improved the prediction model for fluid overload. This may indicate that the timing of medications is more important than we realize and that artificial intelligence may represent the key to discovering these complex relationships. Cluster 7 had a higher number of medications administered within the first 24 hours compared to hours 25-48 or 49-72, which may be reflective of the importance of the first 24 hours of ICU stay. This temporal distribution of medication administration implies a potential association between early medication use and subsequent instances of fluid overload. Additionally, the medications that appeared within Cluster 7 included a large number of medications that clinically would be associated with fluid overload, including fluids themselves and continuous infusions such as vasopressors and inotropes. This adds to the validity of the clustering methods as the results are clinically correlated. As the proportion of medications appearing in Cluster 7 increased, patients were more likely to develop fluid overload as indicated in **Figure 11**, although this association is harder to discern when the proportion of medications appearing in Cluster 7 is >20% due to the limited number of patients who met this criteria. The greatest likelihood of developing fluid overload occurred when patients had between 10% and 20% of their medications matching the Cluster 7 list. Logistic regressions for various breakpoints of proportion of medications matching Cluster 7 can be found in the **Supplementary Appendix**. From a clinical perspective, this could allow for incorporation of clinical decision support by alerting practitioners to patients that have proportions of >10% matching Cluster 7, warranting increased monitoring and evaluation of need for concentrating medications, restricting fluids, or administration of diuretics. Overall, this lends more credence that medication data have a role in improving ICU modeling.[13,35]

Finally, this study represents further application of the ICURx CDM, which was employed to provide the algorithms with further information during the clustering process.[17,36] While information from ICURx CDM was not included in the final methodology for the clustering

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process itself, it was used to provide further information about specific medications that were used for subsequent analyses (IV push versus continuous infusion and sorting of medications into classes). Results from this analysis could not fully evaluate the impact of medications in different volumes of fluid which could be important clinically (e.g., giving cefepime as an IV push medication compared to an intermittent infusion in 100mL of NS over 30 minutes) as the initial data set did not include administration rate.

Our study has several limitations including a small sample size and retrospective data collection. Additionally, due to the retrospective nature of this dataset, we chose a numerical definition for fluid overload as opposed to a clinical assessment which may have under-identified those with clinical fluid overload. Subsequently, bias may exist due to the availability of fluid balance data for the included patients. Causal relationships cannot be assessed by the current study, so it is unknown whether the high fluid overload observed in Patient Cluster 7 was partly caused by the unique distribution of medication patterns versus other factors (although notably, Cluster 7 shared similarities among groups). Additionally, while it is very encouraging that we were able to identify a cluster of medications that was statistically significantly associated with fluid overload through AI methods, at this time, there are multiple limitations in trying to apply this information to a clinical scenario. While there are many hypotheses generated from this information, including which medications may have an undiscovered temporal effect with fluid overload, there must be further research to apply this information at the bedside to have a clinical impact. Even with these limitations, this analysis marks the first time the complete medication profile has been incorporated into outcomes analysis for ICU patients. Future analyses with more granular cluster groupings or more programmed directives incorporating data from a myriad of ICUs and centers may improve the face validity. Artificial intelligence may provide clinical outcome prediction and serve as a supplement to clinicians given its ability to process large amounts of data in real-time.[37-40] Ability to predict events in a critical care setting is highly relevant and desirable given the challenge to predict outcomes in patients with rapidly changing disease states and management.[41,42] Overall, this evaluation is a first step and proof-of-concept exploration into how unsupervised clustering methods may be applied to ICU medications, particularly as it relates to the addition of temporal data.

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CONCLUSION

Unsupervised machine learning uncovered a distinctive cluster of IV medications that exhibited a robust correlation with the occurrence of fluid overload in the ICU setting. Delineating how medications and their administration timing may influence development of fluid overload using data driven methods may support future fluid overload prediction and mitigation strategies.

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Table 1. Study population characteristics

Feature	All (n=927)	Fluid overload (n=127)	No fluid overload (n=800)	p-value
Age, mean (SD)	60.9 (17.5)	55.7 (18.3)	61.7 (17.2)	0.0008
Female, n (%)	398 (42.9)	68 (53.5)	330 (36.7)	0.01
Race, n (%)				
Caucasian	611 (65.9)	72 (56.7)	539 (59.9)	0.04
Black	218 (23.5)	35 (27.6)	183 (20.3)	
Other	98 (10.6)	20 (15.7)	78 (8.7)	
ICU type, n (%)				
Medical	368 (39.7)	58 (45.7)	310 (34.4)	<0.0001
Cardiac	286 (30.8)	14 (11.0)	272 (30.2)	
Surgical	97 (10.5)	34 (26.8)	63 (7)	
Neurosciences	91 (9.8)	7 (5.5)	84 (9.3)	
Burn	65 (7)	11 (8.7)	54 (6.0)	
Other	20 (2.2)	3 (2.4)	17 (1.9)	
Admission diagnosis, n (%)				
Cardiovascular	228 (24.6)	7 (5.5)	221 (24.6)	<0.0001
Neurology	117 (12.6)	9 (7.1)	108 (12)	
Pulmonary	74 (8.0)	11 (8.7)	63 (7)	
Trauma	49 (5.3)	15 (11.8)	34 (3.8)	
Infection including sepsis	70 (7.6)	10 (7.9)	60 (6.7)	
Gastrointestinal	69 (7.4)	18 (14.2)	51 (5.7)	
Neoplasm	49 (5.3)	6 (4.7)	43 (4.8)	
Dermatology	15 (1.6)	5 (3.9)	10 (1.1)	
Renal	23 (2.5)	3 (2.4)	20 (2.2)	
Endocrine	21 (2.3)	4 (3.1)	17 (1.9)	
Other	212 (22.9)	39 (30.7)	273 (30.3)	
Use of mechanical ventilation, n (%)	305 (32.9)	72 (56.7)	233 (25.9)	<0.0001
Renal Replacement Therapy, n (%)	35 (3.8)	16 (12.6)	19 (2.4)	<0.0001
Acute Kidney Injury, n (%)	148 (16)	45 (35.4)	103 (12.9)	<0.0001
Medication Administrations, mean (SD)	51.2 (56.4)	96.4 (81.3)	44 (47.7)	<0.0001
Medication Classes, mean (SD)				
Analgesics	7.9 (12.3)	17.6 (18.6)	6.4 (10.1)	<0.0001
Antiarrhythmics	0.6 (3.5)	0.3 (1.7)	0.6 (3.7)	0.22
Antibiotics	3.2 (5.3)	6.4 (7)	2.7 (4.8)	<0.0001
Anticoagulants	3.1 (9)	3.3 (9.7)	3.1 (8.9)	0.82
Anticonvulsants	0.1 (0.8)	17.6 (1.7)	6.4 (0.4)	<0.0001
Antidotes/ Rescue Therapies	0 (0.1)	0 (0)	0 (0.1)	0.05

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Antifungals	0 (0.3)	0.1 (0.4)	0 (0.3)	0.50
Antihypertensives	1.3 (6.2)	0.5 (5.3)	1.4 (6.3)	0.08
Antiplatelets	0.1 (0.8)	0 (0)	0.1 (0.9)	0.06
Diabetic Agents	2.6 (4.9)	2.7 (4.9)	2.6 (5)	0.84
Diuretics	0 (0.3)	0 (0.1)	0 (0.3)	0.42
Fluids	11.2 (14.2)	20.3 (17.2)	9.7 (13.1)	<0.0001
Gastric Agents	1.6 (2.5)	2.5 (2.6)	1.5 (2.4)	<0.0001
Hypertonic Saline	0.2 (2.4)	0.3 (2.6)	0.2 (2.4)	0.87
Immunosuppressants	0 (0.1)	0 (0.4)	0 (0)	0.32
Inotropic Agents	0.7 (4.4)	0.3 (2.2)	0.8 (4.7)	0.05
Neuromuscular Blocking Agents)	0.1 (0.5)	0.1 (0.3)	0.1 (0.5)	0.49
Sedatives	9.4 (17.7)	19.2 (27.3)	7.8 (15)	<0.0001
Somatostatic Agents	0 (0.1)	0 (0.3)	0 (0.2)	0.27
Total parenteral nutrition	0.1 (1.1)	0.4 (2.7)	0 (0.4)	0.16
Vasopressors	8.9 (23.3)	22.1 (40.6)	6.8 (18.4)	<0.0001
Severity scores at 24 hours of ICU admission				
APACHE II, mean (SD)	14.5 (6.4)	17.4 (6.9)	14 (6.2)	<0.0001
SOFA, mean (SD)	8.1 (3.3)	10.5 (3.4)	7.8 (3.2)	<0.0001
Patient outcomes				
In-hospital Mortality, n (%)	88 (9.5)	23 (18.1)	65 (8.1)	0.0007
Maximum Fluid Overload at 72 h, mL, mean (SD)	2364.9 (3995.5)	9519.9 (5629.2)	1229 (2018.7)	<0.0001
ICU length of stay, days, mean (SD)	2.9 (9.8)	9.7 (13.9)	4.5 (8.7)	<0.0001

Data are presented as n (%) or mean (standard deviation (SD)) unless otherwise stated.
SOFA sequential organ failure assessment, APACHE II Acute Physiology and Chronic Health Evaluation; ICU intensive care unit. P-values from t.test (variables with mean and SD) and chi-square test (variables with count and %).

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Table 2. Distribution of medication classes within each medication cluster

	Cluster									
	1 (N=121)	**2 (N=128)**	**3 (N=130)**	**4 (N=125)**	**5 (N=126)**	**6 (N=127)**	**7 (N=127)**	**8 (N=125)**	**9 (N=123)**	**10 (N=125)**
Analgesic (N=175)	12.4	13.28	14.62	13.6	14.29	14.17	13.39	14.4	14.63	14.4
Antiarrhythmic (N=66)	4.96	5.47	4.62	5.6	5.56	4.72	5.51	4.8	5.69	5.6
Antibiotic (N=248)	20.66	18.75	21.54	20	19.05	20.47	18.9	20.8	19.51	17.6
Anticoagulant (N=109)	9.09	8.59	8.46	8.8	8.73	9.45	8.66	8	8.94	8
Anticonvulsants (N=27)	2.48	2.34	2.31	2.4	2.38	0.79	2.36	2.4	1.63	2.4
Antifungal Agent(N=10)	0.83	0.78	0.77	0.8	0.79	0.79	0.79	0.8	0.81	0.8
Antihypertensive (N=30)	2.48	2.34	2.31	2.4	2.38	2.36	2.36	2.4	2.44	2.4
Antiplatelet (N=10)	0.83	0.78	0.77	0.8	0.79	0.79	0.79	0.8	0.81	0.8
Antifungal (N=9)	0.83	0.78	0.77	0.8	0.79	0.79	0.79	0.8	0	0.8
Diabetic Agents (N=10)	0.83	0.78	0.77	0.8	0.79	0.79	0.79	0.8	0.81	0.8
Diuretic (N=14)	0.83	1.56	0.77	0.8	1.59	1.57	1.57	0.8	0.81	0.8
Fluids (N=143)	11.57	10.94	11.54	12	11.9	11.02	11.02	11.2	11.38	11.2
Gastric Agent (N=40)	3.31	3.13	3.08	3.2	3.17	3.15	3.15	3.2	3.25	3.2
Hypertonic Saline (N=19)	1.65	1.56	1.54	1.6	1.59	1.57	1.57	1.6	0.81	1.6
Inotropic Agent (N=40)	3.31	3.13	3.08	3.2	3.17	3.15	3.15	3.2	3.25	3.2
Neuromuscular blocking agents (N=40)	3.31	3.91	2.31	3.2	2.38	2.36	3.94	3.2	2.44	4.8
Sedative (N=138)	11.57	10.94	10	10.4	11.11	11.02	11.02	11.2	11.38	11.2
Somatostatic Agents (N=10)	0.83	0.78	0.77	0.8	0.79	0.79	0.79	0.8	0.81	0.8
TPN (N=10)	0.83	0.78	0.77	0.8	0.79	0.79	0.79	0.8	0.81	0.8
Vasopressor (N=97)	7.44	7.81	7.69	8	7.14	7.87	7.09	8	8.13	8
Antidotes/ Rescue Therapy (N=5)	0	0.78	0.77	0	0	0.79	0.79	0	0.81	0
Immunosuppressant (N=7)	0	0.78	0.77	0	0.79	0.79	0.79	0	0.81	0.8
N represents the number of medications, with each column summing to 100%										

Table 3. Rank Sum Test for Each Medication Cluster

Rank Sum Test Results for Medication Clusters (Standardized Proportions across Patients) and Fluid Overload

Cluster	Non-fluid overload	Fluid overload	p-value
Cluster 1	0.09 (0.07)	0.08 (0.03)	0.34
Cluster 2	0.11 (0.08)	0.12 (0.04)	0.19
Cluster 3	0.10 (0.07)	0.10 (0.04)	0.93
Cluster 4	0.10 (0.06)	0.10 (0.04)	0.78

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Cluster 5	0.07 (0.06)	0.08 (0.04)	0.0009*
Cluster 6	0.11 (0.07)	0.10 (0.04)	0.13
Cluster 7	0.10 (0.06)	0.11 (0.04)	0.002*
Cluster 8	0.10 (0.06)	0.10 (0.04)	0.90
Cluster 9	0.11 (0.08)	0.11 (0.04)	0.49
Cluster 10	0.10 (0.08)	0.10 (0.05)	0.06

*statistical significance with p ≤0.05

Table 4. Logistic Regression for Each Cluster

Results of 10 Fitted Logistic Regression Models: Dependent Variable - Fluid Overload, Independent Variable - Medication Clusters (Standardized Proportions across Patients).

10 Logistic Regression Models	Estimated Value	P Value
Cluster 1	-2.10	0.22
Cluster 2	0.42	0.73
Cluster 3	-1.41	0.38
Cluster 4	0.16	0.92
Cluster 5	2.68	0.07
Cluster 6	-2.97	0.08
Cluster 7	2.96	0.05*
Cluster 8	-0.87	0.58
Cluster 9	-0.12	0.93
Cluster 10	0.56	0.64

*statistical significance with p ≤0.05

Table 5. Frequency of Medications Appearing in Cluster 7

Medication	Frequency
albumin, human 25 % intravenous solution	6
albumin, human 5 % intravenous solution	8
alteplase 0.81 mg/kg stroke infusion	2
amiodarone 150 mg/100 ml (1.5 mg/ml) in dextrose, iso-osmotic iv	6
amiodarone 360 mg/200 ml (1.8 mg/ml) in dextrose, iso-osmotic iv	6
amiodarone 450 mg/250 ml (1.8 mg/ml) in dextrose 5 % intravenous solution	4

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aztreonam 1 gram solution for iv push	1
aztreonam 2 gram solution for iv push	1
cefazolin 1 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	5
cefazolin 2 gram/100 ml in dextrose(iso-osmotic) intravenous piggyback	3
cefazolin 2 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	4
cefazolin 3 gram/100 ml in 0.9 % sodium chloride intravenous piggyback	3
cefepime 1 gram solution for injection	4
cefepime 2 gram/100 ml in dextrose (iso-osmotic) intravenous piggyback	4
ceftriaxone 1 gram solution for injection	1
ceftriaxone 1 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	1
ceftriaxone 2 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	1
cisatracurium 2 mg/ml intravenous solution	1
clevidipine 25 mg/50 ml intravenous emulsion	10
clindamycin 600 mg/50 ml in 5 % dextrose intravenous piggyback	8
clindamycin 900 mg/50 ml in 5 % dextrose intravenous piggyback	7
cyclosporine 1 mg/ml ns aviva iv	3
dexmedetomidine 200 mcg/50 ml (4 mcg/ml) in 0.9 % sodium chloride iv	3
dexmedetomidine 400 mcg/100 ml (4 mcg/ml) in 0.9 % sodium chloride iv	8
dextrose 10 % in water (d10w) intravenous solution	4
dextrose 10 % iv bolus	3
dextrose 5 % and 0.45 % sodium chloride intravenous solution	4
dextrose 5 % and 0.9 % sodium chloride intravenous solution	3
dextrose 5 % and lactated ringers intravenous solution	6
dextrose 5 % in water (d5w) intravenous solution	6
diazepam 5 mg/ml injection syringe	6
digoxin 250 mcg/ml (0.25 mg/ml) injection solution	2
dobutamine 1,000 mg/250 ml(4,000 mcg/ml) in 5 % dextrose iv	5
dobutamine 250 mg/250 ml (1 mg/ml) in 5 % dextrose intravenous	9
dobutamine 500 mg/250 ml (2,000 mcg/ml) in 5 % dextrose iv	4
dopamine 400 mg/250 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution	3
dopamine 800 mg/500 ml (1,600 mcg/ml) in 5 % dextrose	6

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intravenous solution	
epinephrine hcl 8 mg/250 ml (32 mcg/ml) in 5 % dextrose intravenous	3
eptifibatide 0.75 mg/ml intravenous solution	4
esmolol 2,500 mg/250 ml (10 mg/ml) in sodium chloride (iso-osmotic) iv	2
etomidate 2 mg/ml intravenous solution	3
famotidine (pf) 20 mg/2 ml intravenous solution	6
famotidine (pf) 20 mg/50 ml in 0.9 % sodium chloride (iso) intravenous piggyback	11
famotidine 10 mg/ml inj solution (multi-vial size)	4
fat emulsion 20 % intravenous	6
fentanyl (pf) 10 mcg/ml in 0.9 % sodium chloride intravenous wrapper	6
fentanyl (pf) 2,500 mcg/50 ml (50 mcg/ml) intravenous pca syringe	2
fentanyl (pf) 50 mcg/ml injection solution	8
fentanyl (sublimaze) 100 mcg in ns 50ml (rex or)	1
fluconazole 200 mg/100 ml in sod. chloride (iso) intravenous piggyback	4
fluconazole 400 mg/200 ml in sod. chloride(iso) intravenous piggyback	3
heparin (porcine) 1,000 unit/500 ml in 0.9% sodium chloride iv (combined)	1
heparin (porcine) 1,000 unit/ml injection solution	6
heparin (porcine) 10,000 unit/1,000 ml in 0.9 % sod. chloride iv solution	1
heparin (porcine) 10,000 unit/ml injection solution	2
heparin (porcine) 100 unit/ml bolus from infusion	3
heparin (porcine) 100 unit/ml load from infusion	1
heparin (porcine) 25,000 unit/250 ml in 0.45 % sodium chloride iv solution	4
heparin (porcine) for crrt 25,000 unit/250 ml in 0.45 % sodium chloride iv solution	5
heparin 30,000 units (cell saver) in 1000 ml ns	1
heparin, porcine (pf) 10 unit/ml intravenous syringe	3
heparin, porcine (pf) 100 unit/ml intravenous syringe	4
hydromorphone (pf) 1 mg/ml injection solution	2
hydromorphone 1 mg/ml in ns infusion wrapper	5
hydromorphone 1 mg/ml injection syringe	5
hydromorphone 2 mg/ml injection syringe	9
hydromorphone 50 mg/50 ml (1 mg/ml) in 0.9 % sodium chloride iv pump resevoir	3
insulin u-100 regular human 100 unit/ml injection solution	4
lactated ringers intravenous solution	8

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lactated ringers irrigation solution	1
lactated ringers iv bolus	4
levofloxacin 500 mg/100 ml in 5 % dextrose intravenous piggyback	2
levofloxacin 750 mg/150 ml in 5 % dextrose intravenous piggyback	7
lidocaine (pf) 100 mg/5 ml (2 %) intravenous syringe	2
lidocaine (pf) 4 mg/ml (0.4 %) in 5 % dextrose intravenous solution	4
linezolid in 5% dextrose in water 600 mg/300 ml intravenous piggyback	9
lorazepam 2 mg/ml injection syringe	7
lorazepam 2 mg/ml injection wrapper	6
mannitol 20 % intravenous solution	3
mannitol 25 % intravenous solution	2
meperidine (pf) 25 mg/ml injection syringe	5
metronidazole 500 mg/100 ml-sodium chloride(iso) intravenous piggyback	5
midazolam (pf) 1 mg/ml in 0.9 % sodium chloride intravenous solution	6
midazolam (pf) 1 mg/ml injection solution	3
midazolam (pf) 5 mg/ml injection solution	1
midazolam 1 mg/ml in 0.9 % sodium chloride intravenous	5
midazolam 1 mg/ml injection solution	7
midazolam 5 mg/ml (combined) injection solution wrapper	3
milrinone 20 mg/100 ml(200 mcg/ml) in 5 % dextrose intravenous piggyback	2
morphine (pf) 1 mg/ml in 0.9% sodium chloride intravenous solution	1
morphine 1 mg/ml in 0.9 % sodium chloride injectable pump reservoir	3
morphine 1 mg/ml in dextrose 5 % intravenous solution	6
morphine 10 mg/ml injection solution	5
morphine 2 mg/ml injection pf wrapper	7
morphine 2 mg/ml intravenous cartridge	6
morphine 4 mg/ml intravenous cartridge	7
nitroglycerin 100 mg/250 ml (400 mcg/ml) in 5 % dextrose intravenous	3
nitroglycerin 50 mg/250 ml (200 mcg/ml) in 5 % dextrose intravenous	5
norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in 0.9 % sodium chloride iv	6
norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in dextrose 5 % iv	3
octreotide acetate 100 mcg/ml injection solution	4

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pantoprazole 40 mg intravenous solution	8
pentobarbital 2500mg/50 ml adult infusion	2
pentobarbital sodium 50 mg/ml injection solution	1
phenobarbital sodium 65 mg/ml injection solution	7
phenylephrine 20 mg/250 ml (80 mcg/ml) in 0.9 % sodium chloride iv	6
piperacillin-tazobactam 2.25 gram/50 ml in dextrose(iso) iv piggyback	2
piperacillin-tazobactam 3.375 gm/50ml dextrose (extended duration)	14
piperacillin-tazobactam 3.375 gram/50 ml dextrose(iso-osmotic) iv piggyback	5
piperacillin-tazobactam 4.5 gram/100 ml dextrose(iso-osmotic) iv piggyback	3
propofol 10 mg/ml intravenous emulsion	4
propofol infusion 10 mg/ml	9
rocuronium 10 mg/ml intravenous solution	1
sodium chloride 0.45 % intravenous solution	6
sodium chloride 0.9 % intravenous solution	4
sodium chloride 3 % intravenous bolus solution	1
sodium chloride 3 % intravenous injection solution	4
sodium chloride 4 meq/ml intravenous solution	4
succinylcholine chloride 20mg/ml syringe/vial wrapper	1
vancomycin 1 gram/200 ml in dextrose 5 % intravenous piggyback	8
vancomycin 1.25 gram/250 ml in 0.9 % sodium chloride intravenous	2
vancomycin 1.5 gram/500 ml in 0.9 % sodium chloride intravenous solution	3
vasopressin (pitressin) infusion 40 units/100 ml	7
vasopressin (pitressin) infusion 50 unit/50 ml	1
vasopressin 40 units/50 ml (0.8 unit/ml) ssc premade infusion	4
vecuronium bromide 10 mg intravenous solution	1
vecuronium bromide 20 mg intravenous solution	1

*bolded medications indicate those that only appeared in Cluster 7 if given during the first 24 hours of ICU admission

Table 6. Proportion of Medications Appearing in Cluster 7 by Day and Fluid Overload Status

Proportion of Medications Matching Cluster 7, median	Fluid Overload Group	Non-Fluid Overload Group

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(IQR)		
Hours 0-24 of ICU admission	52.4 (33.9-70.4)	33.3 (14.3-51.2)
Hours 25-48 of ICU admission	50 (22.2-65.4)	18.8 (5.6-40.7)
Hours 49-72 of ICU admission	32.4 (11.8-50)	7.7 (0-22.5)
Hours 0-72 of ICU admission	46.3 (30.4,60.7)	25.2 (11.8-40)

Proportions are calculated on a patient-specific level; the percentage is reported is the median proportion of medications matching Cluster 7 using individual patient data rather than aggregate data. For example, of the medications received in the first 24 hours of ICU stay, 52.4% of those medications were also present in Cluster 7 for the median patient in the fluid overload group, compared to 33.3% of medications in the non-fluid overload group.

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Table 7. Cluster 7 medications by ICU day

Distribution of Medications in Cluster 7 Across ICU Days (Day 1: 0-24 hours, Day 2: 24-48 hours, Day 3: 48-72 hours), N is total number of medications that appeared within that day

DAY1 (N= 190)	DAY2 (N= 179)	DAY3 (N=171)
albumin, human 25 % intravenous solution	albumin, human 25 % intravenous solution	albumin, human 25 % intravenous solution
albumin, human 5 % intravenous solution	albumin, human 5 % intravenous solution	albumin, human 5 % intravenous solution
alteplase 0.81 mg/kg stroke infusion	amiodarone 150 mg/100 ml (1.5 mg/ml) in dextrose, iso-osmotic iv	amiodarone 150 mg/100 ml (1.5 mg/ml) in dextrose, iso-osmotic iv
amiodarone 150 mg/100 ml (1.5 mg/ml) in dextrose, iso-osmotic iv	amiodarone 360 mg/200 ml (1.8 mg/ml) in dextrose, iso-osmotic iv	amiodarone 360 mg/200 ml (1.8 mg/ml) in dextrose, iso-osmotic iv
amiodarone 360 mg/200 ml (1.8 mg/ml) in dextrose, iso-osmotic iv	amiodarone 450 mg/250 ml (1.8 mg/ml) in dextrose 5 % intravenous solution	amiodarone 450 mg/250 ml (1.8 mg/ml) in dextrose 5 % intravenous solution
amiodarone 450 mg/250 ml (1.8 mg/ml) in dextrose 5 % intravenous solution	aztreonam 2 gram solution for iv push	cefazolin 1 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback
aztreonam 1 gram solution for iv push	cefepime 1 gram solution for injection	cefazolin 2 gram/100 ml in dextrose(iso-osmotic) intravenous piggyback
cefazolin 1 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	cefepime 2 gram/100 ml in dextrose (iso-osmotic) intravenous piggyback	cefazolin 2 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback
cefazolin 2 gram/100 ml in dextrose(iso-osmotic) intravenous piggyback	ceftriaxone 2 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	cefepime 1 gram solution for injection
cefazolin 2 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	clevidipine 25 mg/50 ml intravenous emulsion	cefepime 2 gram/100 ml in dextrose (iso-osmotic) intravenous piggyback
cefazolin 3 gram/100 ml in 0.9 % sodium chloride intravenous piggyback	clindamycin 600 mg/50 ml in 5 % dextrose intravenous piggyback	ceftriaxone 1 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback
cefepime 1 gram solution for injection	clindamycin 900 mg/50 ml in 5 % dextrose intravenous piggyback	clevidipine 25 mg/50 ml intravenous emulsion
cefepime 2 gram/100 ml in dextrose (iso-osmotic) intravenous piggyback	cyclosporine 1 mg/ml ns aviva iv	clindamycin 600 mg/50 ml in 5 % dextrose intravenous piggyback
ceftriaxone 1 gram solution for injection	dexmedetomidine 200 mcg/50 ml (4 mcg/ml) in 0.9 % sodium chloride iv	clindamycin 900 mg/50 ml in 5 % dextrose intravenous piggyback
cisatracurium 2 mg/ml intravenous solution	dexmedetomidine 400 mcg/100 ml (4 mcg/ml) in 0.9 % sodium chloride iv	cyclosporine 1 mg/ml ns aviva iv
clevidipine 25 mg/50 ml intravenous emulsion	dextrose 10 % in water (d10w) intravenous solution	dexmedetomidine 200 mcg/50 ml (4 mcg/ml) in 0.9 % sodium chloride iv
clindamycin 600 mg/50 ml in 5 % dextrose intravenous piggyback	dextrose 10 % iv bolus	dexmedetomidine 400 mcg/100 ml (4 mcg/ml) in 0.9 % sodium chloride iv
clindamycin 900 mg/50 ml in 5 % dextrose intravenous piggyback	dextrose 5 % and 0.45 % sodium chloride intravenous solution	dextrose 10 % in water (d10w) intravenous solution
dexmedetomidine 400 mcg/100 ml (4 mcg/ml) in 0.9 % sodium chloride iv	dextrose 5 % and 0.9 % sodium chloride intravenous solution	dextrose 10 % iv bolus
dextrose 5 % and 0.9 % sodium chloride intravenous solution	dextrose 5 % and lactated ringers intravenous solution	dextrose 5 % and 0.45 % sodium chloride intravenous solution
dextrose 5 % and lactated ringers intravenous solution	dextrose 5 % in water (d5w) intravenous solution	dextrose 5 % and lactated ringers intravenous solution
dextrose 5 % in water (d5w) intravenous solution	diazepam 5 mg/ml injection syringe	dextrose 5 % in water (d5w) intravenous solution
diazepam 5 mg/ml injection syringe	dobutamine 250 mg/250 ml (1 mg/ml) in 5 % dextrose intravenous	diazepam 5 mg/ml injection syringe
digoxin 250 mcg/ml (0.25 mg/ml) injection solution	dobutamine 500 mg/250 ml (2,000 mcg/ml) in 5 % dextrose iv	dobutamine 1,000 mg/250 ml(4,000 mcg/ml) in 5 % dextrose iv
dobutamine 1,000 mg/250 ml(4,000 mcg/ml) in 5 % dextrose iv	dopamine 400 mg/250 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution	dobutamine 250 mg/250 ml (1 mg/ml) in 5 % dextrose intravenous
dobutamine 250 mg/250 ml (1 mg/ml) in 5 % dextrose intravenous	dopamine 800 mg/500 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution	dopamine 800 mg/500 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution
dobutamine 500 mg/250 ml (2,000 mcg/ml) in 5 % dextrose iv	epinephrine hcl 8 mg/250 ml (32 mcg/ml) in 5 % dextrose intravenous	epinephrine hcl 8 mg/250 ml (32 mcg/ml) in 5 % dextrose intravenous
dopamine 400 mg/250 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution	eptifibatide 0.75 mg/ml intravenous solution	etomidate 2 mg/ml intravenous solution
dopamine 800 mg/500 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution	esmolol 2,500 mg/250 ml (10 mg/ml) in sodium chloride (iso-osmotic) iv	famotidine (pf) 20 mg/2 ml intravenous solution
epinephrine hcl 8 mg/250 ml (32 mcg/ml) in 5 % dextrose intravenous	etomidate 2 mg/ml intravenous solution	famotidine (pf) 20 mg/50 ml in 0.9 % sodium chloride (iso) intravenous piggyback
eptifibatide 0.75 mg/ml intravenous solution	famotidine (pf) 20 mg/2 ml intravenous solution	famotidine 10 mg/ml inj solution (multi-vial size)
esmolol 2,500 mg/250 ml (10 mg/ml) in sodium chloride (iso-osmotic) iv	famotidine (pf) 20 mg/50 ml in 0.9 % sodium chloride (iso) intravenous piggyback	fat emulsion 20 % intravenous
etomidate 2 mg/ml intravenous solution	fat emulsion 20 % intravenous	fentanyl (pf) 10 mcg/ml in 0.9 % sodium chloride intravenous wrapper

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famotidine (pf) 20 mg/2 ml intravenous solution	fentanyl (pf) 10 mcg/ml in 0.9 % sodium chloride intravenous wrapper	fentanyl (pf) 50 mcg/ml injection solution
famotidine (pf) 20 mg/50 ml in 0.9 % sodium chloride (iso) intravenous piggyback	fentanyl (pf) 2,500 mcg/50 ml (50 mcg/ml) intravenous pca syringe	fluconazole 200 mg/100 ml in sod. chloride (iso) intravenous piggyback
famotidine 10 mg/ml inj solution (multi-vial size)	fentanyl (pf) 50 mcg/ml injection solution	heparin (porcine) 1,000 unit/500 ml in 0.9% sodium chloride iv (combined)
fat emulsion 20 % intravenous	fentanyl (sublimaze) 100 mcg in ns 50ml (rex or)	heparin (porcine) 1,000 unit/ml injection solution
fentanyl (pf) 10 mcg/ml in 0.9 % sodium chloride intravenous wrapper	fluconazole 400 mg/200 ml in sod. chloride(iso) intravenous piggyback	heparin (porcine) 10,000 unit/1,000 ml in 0.9 % sod. chloride iv solution
fentanyl (pf) 2,500 mcg/50 ml (50 mcg/ml) intravenous pca syringe	heparin (porcine) 1,000 unit/ml injection solution	heparin (porcine) 10,000 unit/ml injection solution
fentanyl (pf) 50 mcg/ml injection solution	heparin (porcine) 10,000 unit/ml injection solution	heparin (porcine) 100 unit/ml bolus from infusion
fluconazole 200 mg/100 ml in sod. chloride (iso) intravenous piggyback	heparin (porcine) 100 unit/ml bolus from infusion	heparin (porcine) 25,000 unit/250 ml in 0.45 % sodium chloride iv solution
fluconazole 400 mg/200 ml in sod. chloride(iso) intravenous piggyback	heparin (porcine) 25,000 unit/250 ml in 0.45 % sodium chloride iv solution	heparin (porcine) for crrt 25,000 unit/250 ml in 0.45 % sodium chloride iv solution
heparin (porcine) 1,000 unit/ml injection solution	heparin (porcine) for crrt 25,000 unit/250 ml in 0.45 % sodium chloride iv solution	heparin, porcine (pf) 10 unit/ml intravenous syringe
heparin (porcine) 100 unit/ml bolus from infusion	heparin 30,000 units (cell saver) in 1000 ml ns	heparin, porcine (pf) 100 unit/ml intravenous syringe
heparin (porcine) 100 unit/ml load from infusion	heparin, porcine (pf) 10 unit/ml intravenous syringe	hydromorphone (pf) 1 mg/ml injection solution
heparin (porcine) 25,000 unit/250 ml in 0.45 % sodium chloride iv solution	heparin, porcine (pf) 100 unit/ml intravenous syringe	hydromorphone 1 mg/ml in ns infusion wrapper
heparin (porcine) for crrt 25,000 unit/250 ml in 0.45 % sodium chloride iv solution	hydromorphone 1 mg/ml in ns infusion wrapper	hydromorphone 2 mg/ml injection syringe
heparin, porcine (pf) 10 unit/ml intravenous syringe	hydromorphone 1 mg/ml injection syringe	hydromorphone 50 mg/50 ml (1 mg/ml) in 0.9 % sodium chloride iv pump resevoir
hydromorphone 1 mg/ml in ns infusion wrapper	hydromorphone 2 mg/ml injection syringe	lactated ringers intravenous solution
hydromorphone 1 mg/ml injection syringe	hydromorphone 50 mg/50 ml (1 mg/ml) in 0.9 % sodium chloride iv pump resevoir	lactated ringers iv bolus
hydromorphone 2 mg/ml injection syringe	insulin u-100 regular human 100 unit/ml injection solution	levofloxacin 500 mg/100 ml in 5 % dextrose intravenous piggyback
hydromorphone 50 mg/50 ml (1 mg/ml) in 0.9 % sodium chloride iv pump resevoir	lactated ringers intravenous solution	levofloxacin 750 mg/150 ml in 5 % dextrose intravenous piggyback
lactated ringers intravenous solution	lactated ringers iv bolus	lidocaine (pf) 4 mg/ml (0.4 %) in 5 % dextrose intravenous solution
lactated ringers irrigation solution	levofloxacin 500 mg/100 ml in 5 % dextrose intravenous piggyback	linezolid in 5% dextrose in water 600 mg/300 ml intravenous piggyback
lactated ringers iv bolus	levofloxacin 750 mg/150 ml in 5 % dextrose intravenous piggyback	lorazepam 2 mg/ml injection syringe
levofloxacin 750 mg/150 ml in 5 % dextrose intravenous piggyback	lidocaine (pf) 100 mg/5 ml (2 %) intravenous syringe	lorazepam 2 mg/ml injection wrapper
lidocaine (pf) 100 mg/5 ml (2 %) intravenous syringe	lidocaine (pf) 4 mg/ml (0.4 %) in 5 % dextrose intravenous solution	mannitol 25 % intravenous solution
linezolid in 5% dextrose in water 600 mg/300 ml intravenous piggyback	linezolid in 5% dextrose in water 600 mg/300 ml intravenous piggyback	metronidazole 500 mg/100 ml-sodium chloride(iso) intravenous piggyback
lorazepam 2 mg/ml injection syringe	lorazepam 2 mg/ml injection syringe	midazolam (pf) 1 mg/ml in 0.9 % sodium chloride intravenous solution
lorazepam 2 mg/ml injection wrapper	lorazepam 2 mg/ml injection wrapper	midazolam (pf) 1 mg/ml injection solution
mannitol 20 % intravenous solution	mannitol 25 % intravenous solution	midazolam 1 mg/ml in 0.9 % sodium chloride intravenous
meperidine (pf) 25 mg/ml injection syringe	meperidine (pf) 25 mg/ml injection syringe	midazolam 1 mg/ml injection solution
metronidazole 500 mg/100 ml-sodium chloride(iso) intravenous piggyback	metronidazole 500 mg/100 ml-sodium chloride(iso) intravenous piggyback	midazolam 5 mg/ml (combined) injection solution wrapper
midazolam (pf) 1 mg/ml in 0.9 % sodium chloride intravenous solution	midazolam (pf) 1 mg/ml in 0.9 % sodium chloride intravenous solution	milrinone 20 mg/100 ml(200 mcg/ml) in 5 % dextrose intravenous piggyback
midazolam (pf) 1 mg/ml injection solution	midazolam 1 mg/ml injection solution	morphine 1 mg/ml in dextrose 5 % intravenous solution
midazolam (pf) 5 mg/ml injection solution	morphine (pf) 1 mg/ml in 0.9% sodium chloride intravenous solution	morphine 10 mg/ml injection solution
midazolam 1 mg/ml in 0.9 % sodium chloride intravenous	morphine 1 mg/ml in dextrose 5 % intravenous solution	morphine 2 mg/ml intravenous cartridge
midazolam 1 mg/ml injection solution	morphine 10 mg/ml injection solution	morphine 4 mg/ml intravenous cartridge
midazolam 5 mg/ml (combined) injection solution wrapper	morphine 2 mg/ml injection pf wrapper	norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in 0.9 % sodium chloride iv
milrinone 20 mg/100 ml(200 mcg/ml) in 5 % dextrose intravenous piggyback	morphine 2 mg/ml intravenous cartridge	octreotide acetate 100 mcg/ml injection solution
morphine 1 mg/ml in 0.9 % sodium chloride injectable pump reservoir	morphine 4 mg/ml intravenous cartridge	pantoprazole 40 mg intravenous solution

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morphine 10 mg/ml injection solution	nitroglycerin 100 mg/250 ml (400 mcg/ml) in 5 % dextrose intravenous	pentobarbital 2500mg/50 ml adult infusion
morphine 2 mg/ml injection pf wrapper	nitroglycerin 50 mg/250 ml (200 mcg/ml) in 5 % dextrose intravenous	phenylephrine 20 mg/250 ml (80 mcg/ml) in 0.9 % sodium chloride iv
morphine 2 mg/ml intravenous cartridge	norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in 0.9 % sodium chloride iv	piperacillin-tazobactam 2.25 gram/50 ml in dextrose(iso) iv piggyback
morphine 4 mg/ml intravenous cartridge	norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in dextrose 5 % iv	piperacillin-tazobactam 3.375 gm/50ml dextrose (extended duration)
nitroglycerin 100 mg/250 ml (400 mcg/ml) in 5 % dextrose intravenous	pantoprazole 40 mg intravenous solution	piperacillin-tazobactam 3.375 gram/50 ml dextrose(iso-osmotic) iv piggyback
nitroglycerin 50 mg/250 ml (200 mcg/ml) in 5 % dextrose intravenous	pentobarbital sodium 50 mg/ml injection solution	piperacillin-tazobactam 4.5 gram/100 ml dextrose(iso-osmotic) iv piggyback
norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in 0.9 % sodium chloride iv	phenobarbital sodium 65 mg/ml injection solution	propofol 10 mg/ml intravenous emulsion
norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in dextrose 5 % iv	phenylephrine 20 mg/250 ml (80 mcg/ml) in 0.9 % sodium chloride iv	sodium chloride 0.45 % intravenous solution
octreotide acetate 100 mcg/ml injection solution	piperacillin-tazobactam 3.375 gm/50ml dextrose (extended duration)	sodium chloride 0.9 % intravenous solution
pantoprazole 40 mg intravenous solution	piperacillin-tazobactam 3.375 gram/50 ml dextrose(iso-osmotic) iv piggyback	sodium chloride 3 % intravenous injection solution
phenobarbital sodium 65 mg/ml injection solution	piperacillin-tazobactam 4.5 gram/100 ml dextrose(iso-osmotic) iv piggyback	sodium chloride 4 meq/ml intravenous solution
phenylephrine 20 mg/250 ml (80 mcg/ml) in 0.9 % sodium chloride iv	propofol 10 mg/ml intravenous emulsion	vancomycin 1 gram/200 ml in dextrose 5 % intravenous piggyback
piperacillin-tazobactam 2.25 gram/50 ml in dextrose(iso) iv piggyback	propofol infusion 10 mg/ml	vasopressin (pitressin) infusion 40 units/100 ml
piperacillin-tazobactam 3.375 gm/50ml dextrose (extended duration)	sodium chloride 0.45 % intravenous solution	vasopressin 40 units/50 ml (0.8 unit/ml) ssc premade infusion
piperacillin-tazobactam 3.375 gram/50 ml dextrose(iso-osmotic) iv piggyback	sodium chloride 0.9 % intravenous solution	
propofol infusion 10 mg/ml	sodium chloride 3 % intravenous bolus solution	
rocuronium 10 mg/ml intravenous solution	sodium chloride 3 % intravenous injection solution	
sodium chloride 0.45 % intravenous solution	sodium chloride 4 meq/ml intravenous solution	
sodium chloride 0.9 % intravenous solution	vancomycin 1 gram/200 ml in dextrose 5 % intravenous piggyback	
sodium chloride 3 % intravenous injection solution	vancomycin 1.5 gram/500 ml in 0.9 % sodium chloride intravenous solution	
sodium chloride 4 meq/ml intravenous solution	vasopressin (pitressin) infusion 40 units/100 ml	
succinylcholine chloride 20mg/ml syringe/vial wrapper	vasopressin (pitressin) infusion 50 unit/50 ml	
vancomycin 1 gram/200 ml in dextrose 5 % intravenous piggyback	vecuronium bromide 10 mg intravenous solution	
vancomycin 1.25 gram/250 ml in 0.9 % sodium chloride intravenous		
vancomycin 1.5 gram/500 ml in 0.9 % sodium chloride intravenous solution		
vasopressin (pitressin) infusion 40 units/100 ml		
vasopressin 40 units/50 ml (0.8 unit/ml) ssc premade infusion		
vecuronium bromide 20 mg intravenous solution		

Table 8. Logistic Regressions for Prediction of Fluid Overload with/without Cluster 7 information

Model	Logistic Regression for Fluid Overload with APACHE II Score at 24 hours and Diuretic Level	Logistic Regression for Fluid Overload with APACHE II Score at 24 hours, Diuretic Level, and Proportion of Medications Appearing in Cluster 7

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	Estimated Value	P-value	Estimated Value	P-value
(Intercept)	-3.00	<0.0001	-3.61	<0.0001
APACHE Score at 24 hours	0.095	<0.0001	0.01	<0.0001
Diuretic level (0-5)	-0.46	0.04	-0.42	0.06
Diuretic level (>5)	-17.25	0.98	-17.18	0.98
Proportion of Medications Appearing in Cluster 7			5.65	0.0004

Diuretic level 0-5: the patient received ≤5 doses of a diuretic medication within the first 72 hours of ICU stay
Diuretic level >5: the patient received >5 doses of a diuretic medication within the first 71 hours of ICU stay

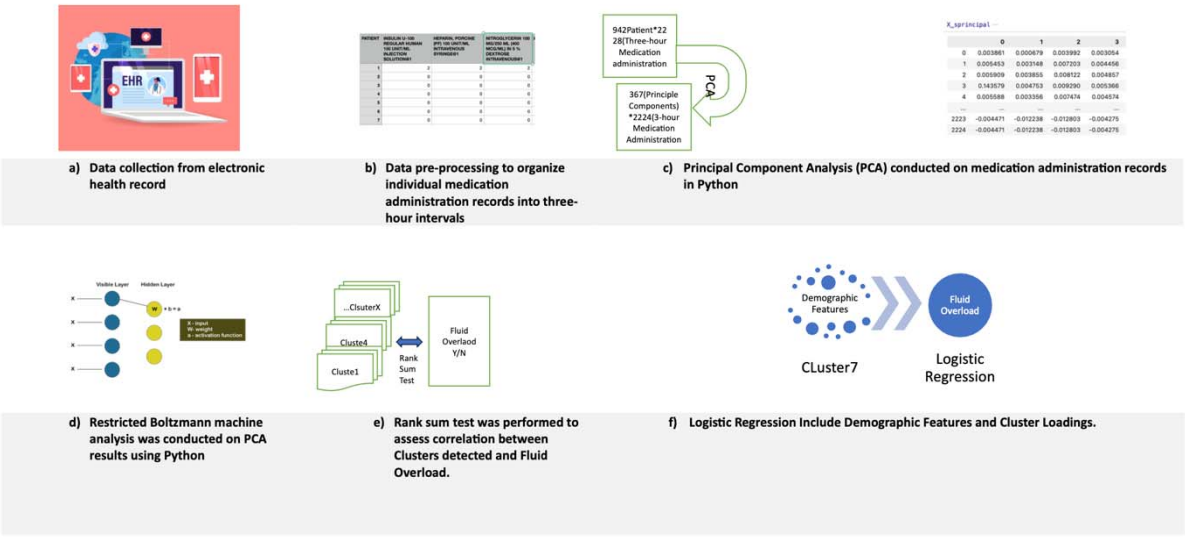
Table 9. Logistic Regressions for Prediction of Fluid Overload Using Proportion of Medications Appearing in Cluster 7 at Specified Time Periods

Model	Logistic Regression for Fluid Overload with APACHE II Score at 24 hours and Diuretic Level	
	Estimated Value	P-value
(Intercept)	-3.34	<0.0001
APACHE Score at 24 hours	0.035	0.052
Diuretic level (0-5)	-0.49	0.037
Diuretic level (>5)	-16.75	0.98
Proportion of Medications Appearing in Cluster 7 in Day 1 of ICU Admission	1.20	0.037
Proportion of Medications Appearing in Cluster 7 in Day 2 of ICU Admission	0.40	0.52
Proportion of Medications Appearing in Cluster 7 in Day 3 of ICU Admission	2.61	<0.0001

Diuretic level 0-5: the patient received ≤5 doses of a diuretic medication within the first 72 hours of ICU stay
Diuretic level >5: the patient received >5 doses of a diuretic medication within the first 71 hours of ICU stay

Figure 1. Workflow for unsupervised analysis of medications for prediction of fluid overload

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a) Data collection from electronic health record

b) Data pre-processing to organize individual medication administration records into three-hour intervals

c) Principal Component Analysis (PCA) conducted on medication administration records in Python

d) Restricted Boltzmann machine analysis was conducted on PCA results using Python

e) Rank sum test was performed to assess correlation between Clusters detected and Fluid Overload.

f) Logistic Regression Include Demographic Features and Cluster Loadings.

Figure 2. Venn diagrams of medication overlap within the 10 clusters by medication name & timing

Venn Diagrams Illustrating Medication Overlaps Between Clusters 1-5 and Clusters 6-10, with Numerical Values Indicating the Count of Shared *Medication Administrations* (Both medication name and time period of administration)

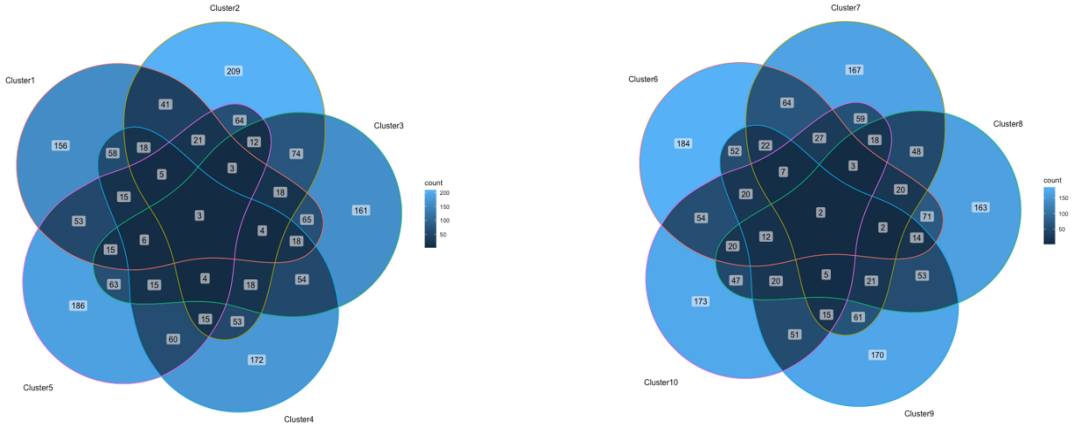
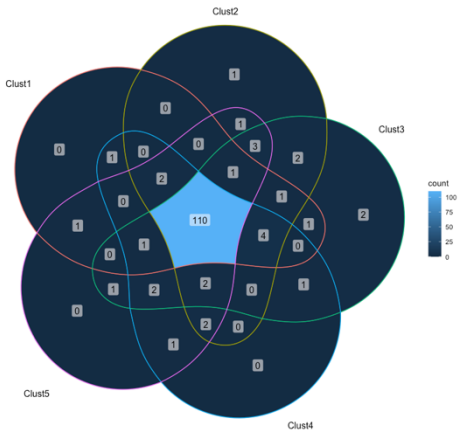
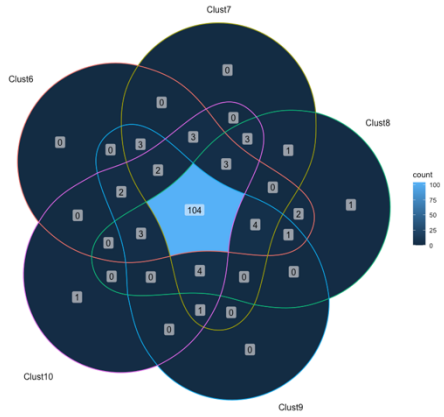


Figure 3. Venn diagrams of medication overlap within the 10 clusters by medication name only

Venn Diagrams Illustrating Medication Overlaps Between Clusters 1-5 and Clusters 6-10, with Numerical Values Indicating the Count of Shared *Medication Names*

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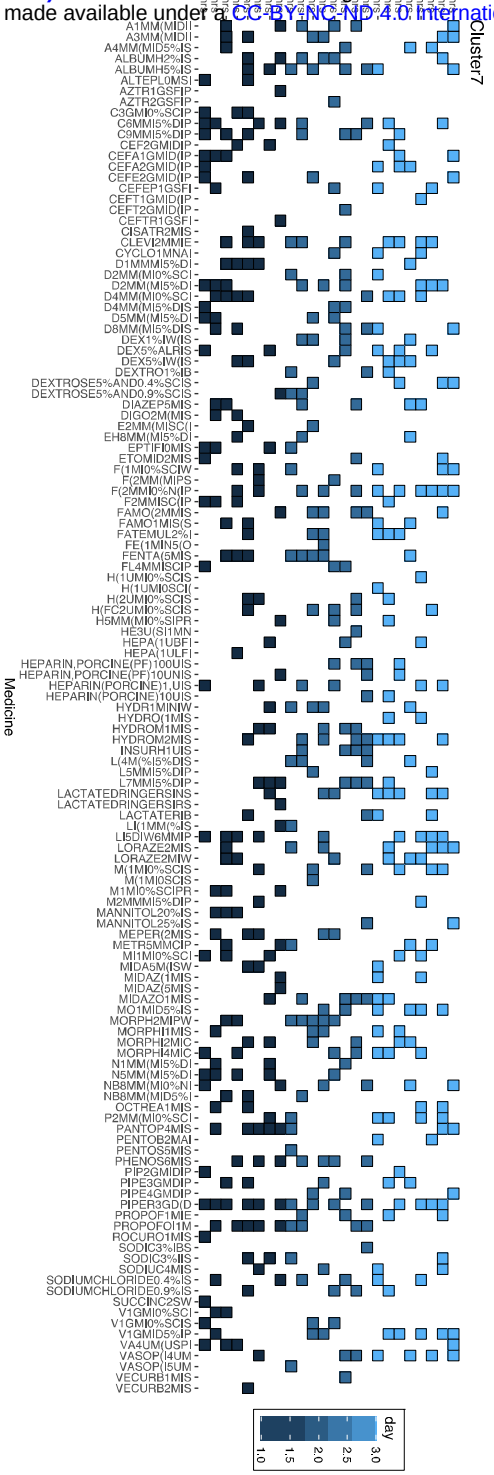


Figure 4. Clus

Medication Re dministration of medication at

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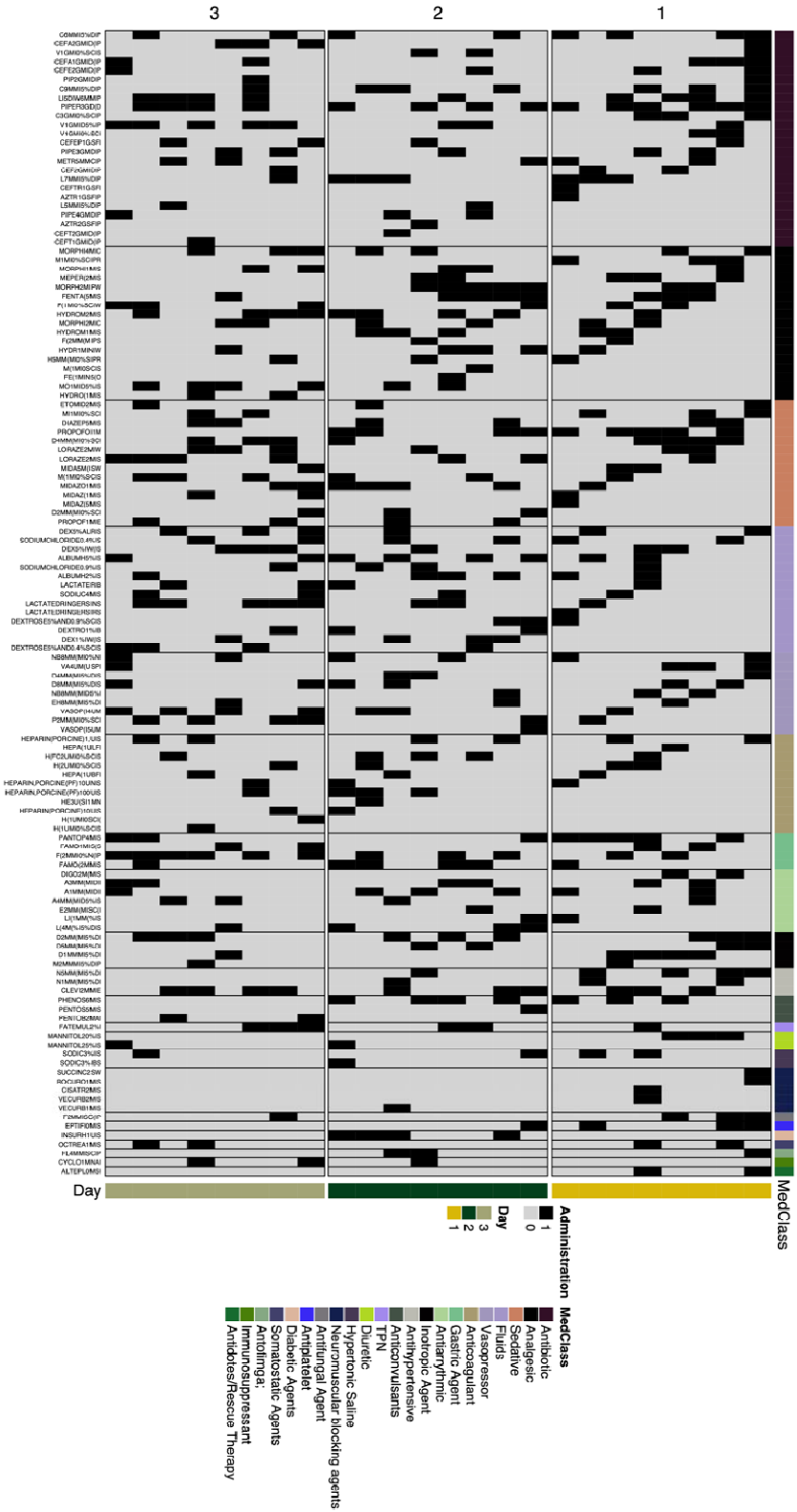
Figure 5. Cluster 7 medica



Distribution of Medication Re ames.
Vertical Axis: Frequency of A

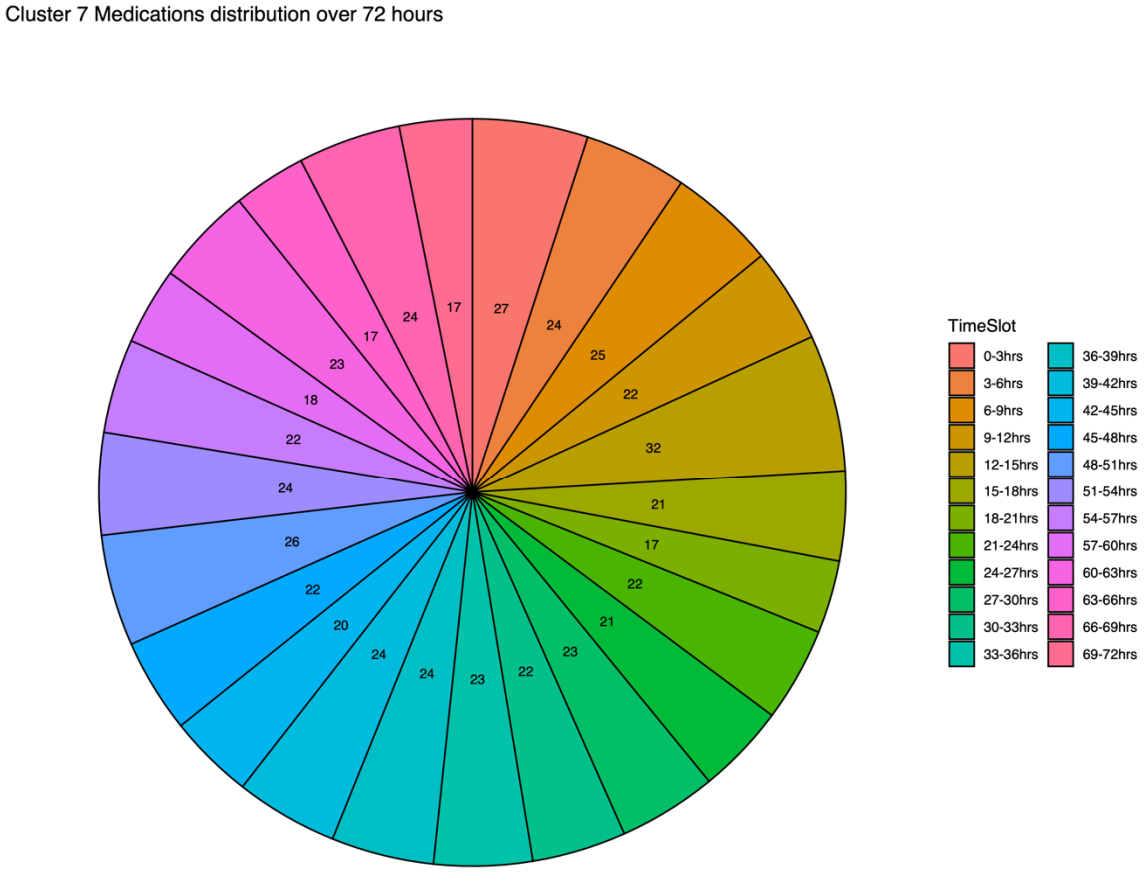
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Figure 6. Cluster 7 medications organized by timing of administration and medication class



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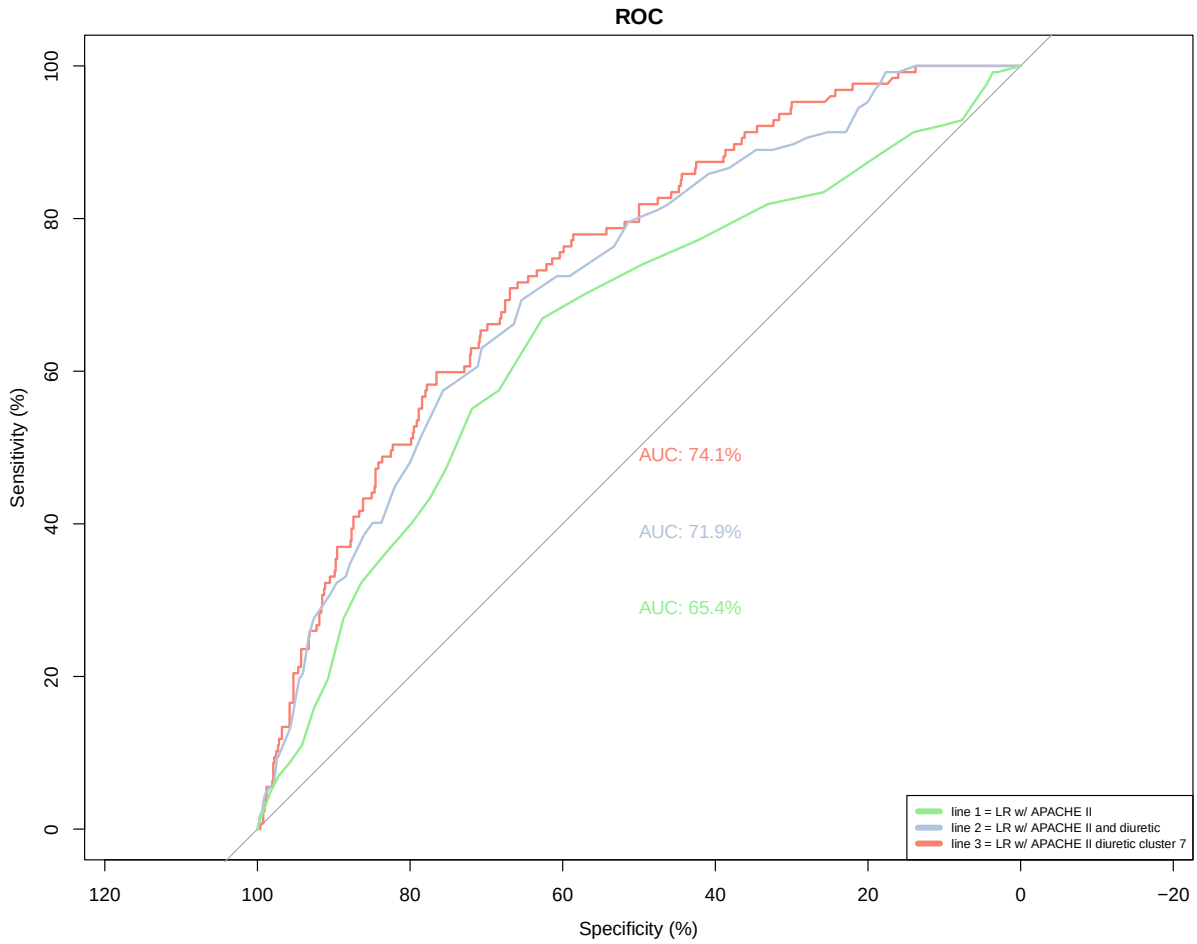
Figure 7. Cluster 7 medications organized by proportion of medications from each 3-hour time period The Custer 7 medication administration is distributed over a span of 72 hours, divided into twenty-four three-hour time slots. These slots are arranged clockwise, starting from the 0-3 hour slot and ending at the 68-72 hour slot. The term "area" represents the quantity of medication detected within each respective time slot.



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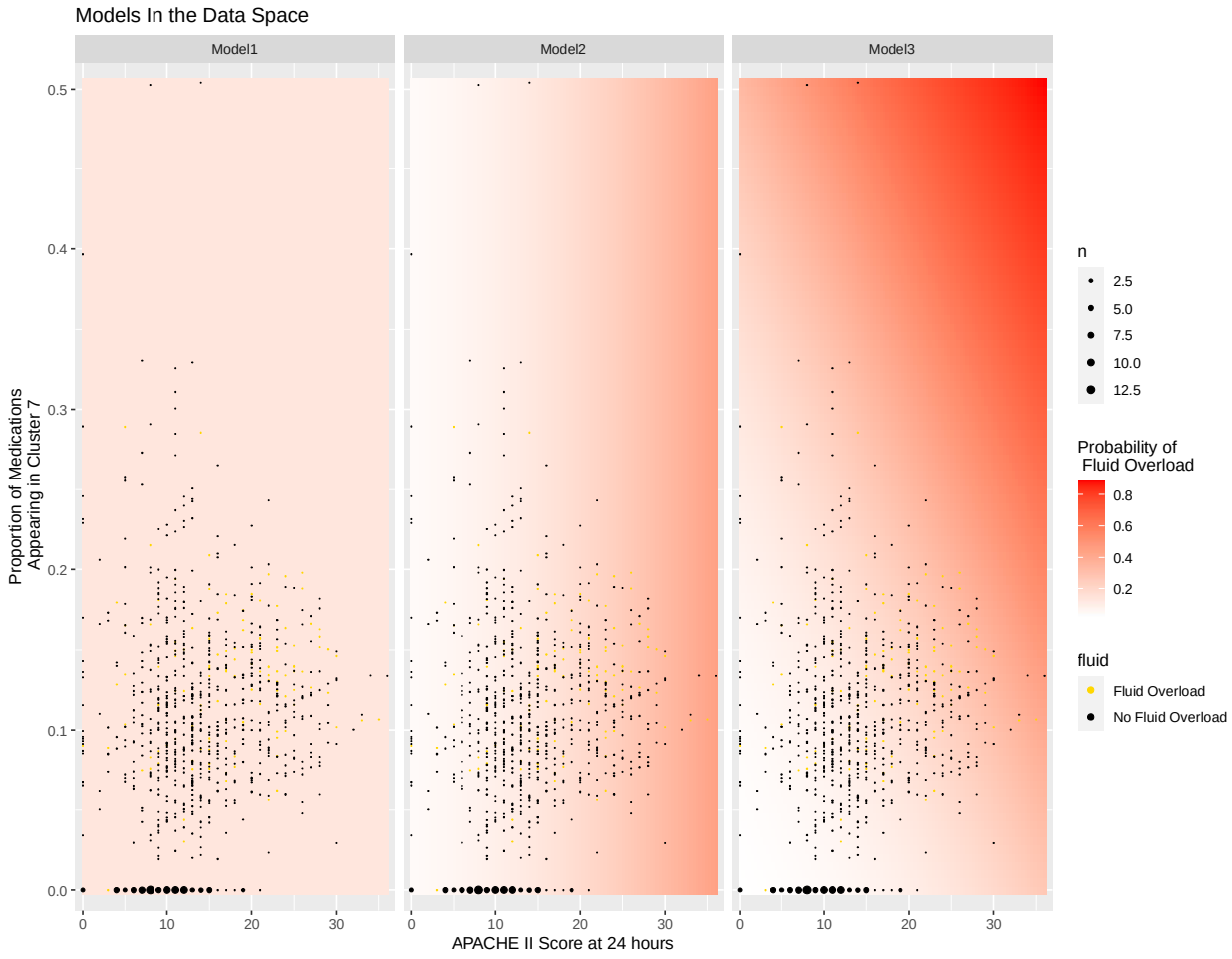
Figure 8 Logistic regression model for Cluster 7

Logistic regression for incidence of fluid overload, including Cluster 7, APACHE II score, and diuretic level



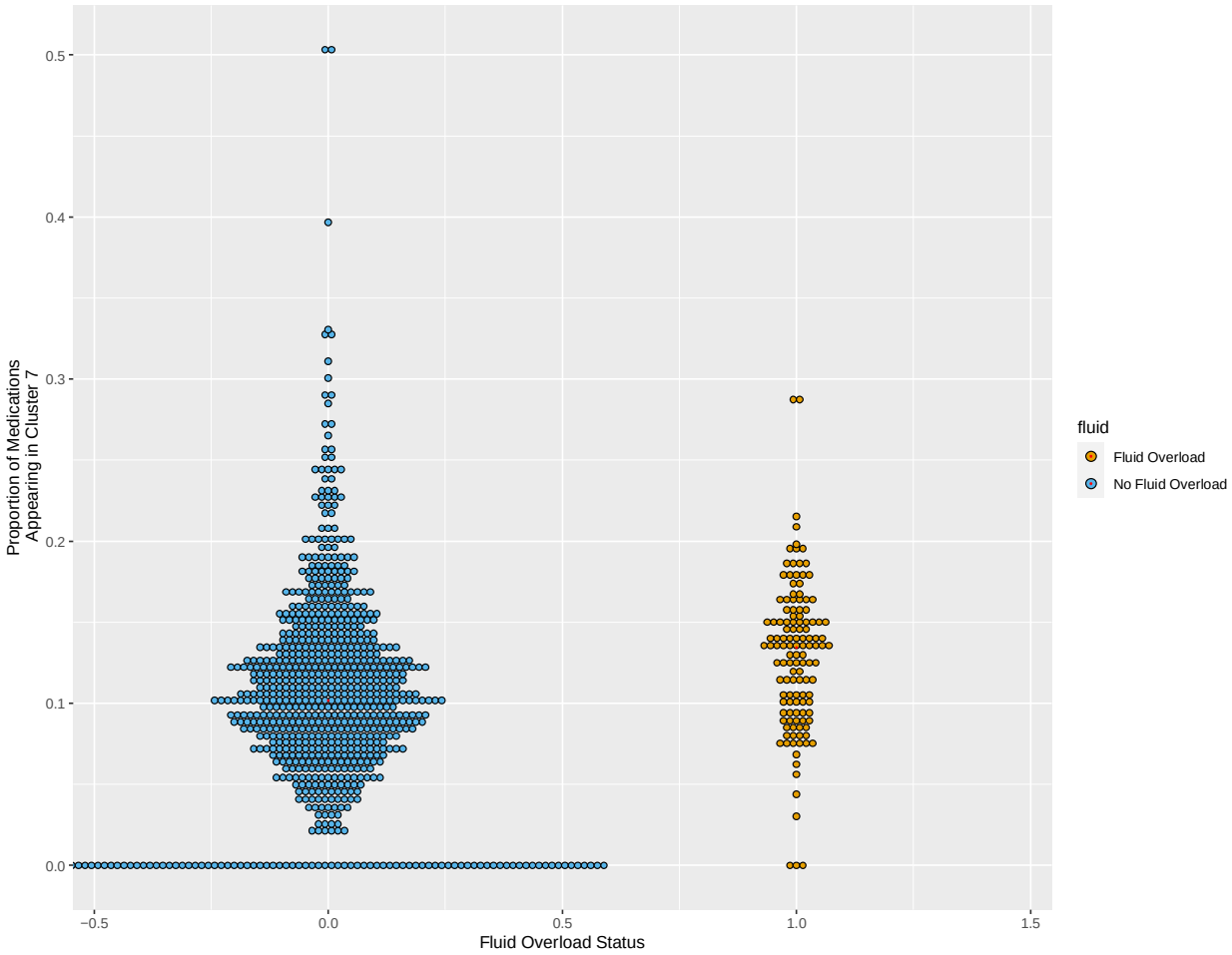
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Figure 9. Visualization of significance of cluster 7 proportion and APACHE II score at 24 hours in logistic regression model in predicting fluid overload.



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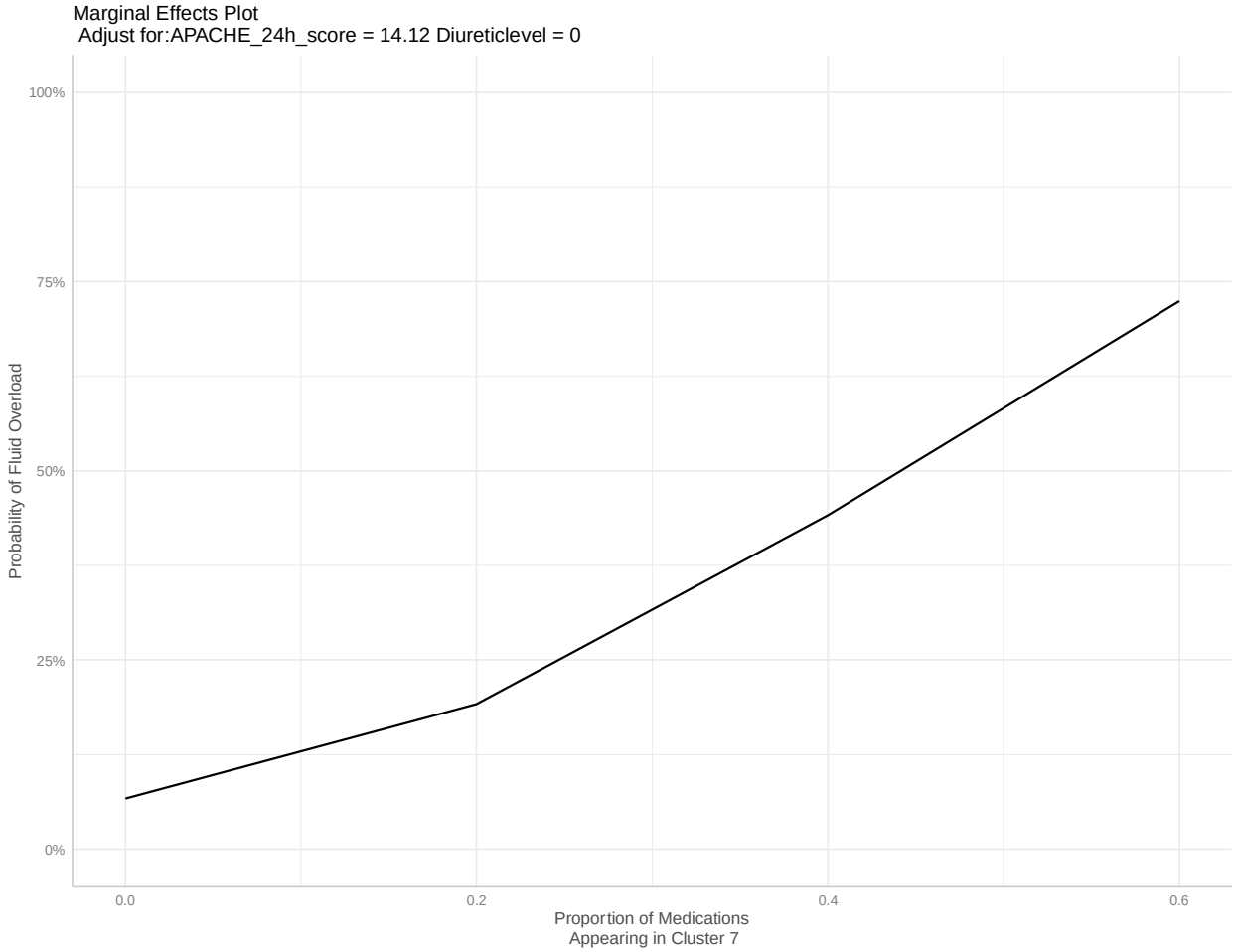
Figure 10. Distribution of patients in each group (non-fluid overload versus fluid overload) based on proportion of individual medications that appeared within Cluster 7



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Figure 11. Marginal effect of cluster 7 proportion on fluid overload

Likelihood of an individual patient developing fluid overload, normalized to APACHE II score of 14 and no receipt of diuretics.



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References

1. Carr JR, Hawkins WA, Newsome AS, et al: Fluid stewardship of maintenance Intravenous fluids. *J Pharm Pract* 2021:8971900211008261

2. Hawkins WA, Smith SE, Newsome AS, et al: Fluid stewardship during critical illness: a call to action. *J Pharm Pract* 2020; 33(6):863-873

3. Bissell BD, Laine ME, Thompson Bastin ML, et al: Impact of protocolized diuresis for de-resuscitation in the intensive care unit. *Crit Care* 2020; 24(1):70

4. Jones TW, Chase AM, Bruning R, et al: Early diuretics for de-resuscitation in septic patients with left ventricular dysfunction. *Clin Med Insights Cardiol* 2022; 16:11795468221095875

5. Hawkins WA, Butler SA, Poirier N, et al: From theory to bedside: implementation of fluid stewardship in a medical ICU pharmacy practice. *Am J Health Syst Pharm* 2022 Jun 7;79(12):984-992.

6. Bissell BD, Donaldson JC, Morris PE, et al: A narrative review of pharmacologic de-resuscitation in the critically ill. *J Crit Care* 2020; 59:156-162

7. Messmer AS, Moser M, Zuercher P, et al: Fluid overload phenotypes in critical illness-a machine learning approach. *J Clin Med* 2022; 11(2)

8. Zhang Z, Ho KM, Hong Y: Machine learning for the prediction of volume responsiveness in patients with oliguric acute kidney injury in critical care. *Crit Care* 2019; 23(1):112

9. Olney WJ, Chase AM, Hannah SA, et al: Medication regimen complexity score as an indicator of fluid balance in critically ill Patients. *J Pharm Pract* 2021:897190021999792

10. Sikora A, Ayyala D, Rech MA, et al: Impact of pharmacists to improve patient care in the critically ill: a large multicenter analysis using meaningful metrics with the medication regimen complexity-ICU (MRC-ICU) score. *Crit Care Med* 2022; 50(9):1318-1328

11. Newsome AS, Smith SE, Olney WJ, et al: Multicenter validation of a novel medication-regimen complexity scoring tool. *Am J Health Syst Pharm* 2020; 77(6):474-478

12. Newsome AS, Anderson D, Gwynn ME, et al: Characterization of changes in medication complexity using a modified scoring tool. *Am J Health Syst Pharm* 2019; 76(Supplement_4):S92-s95

13. Gwynn ME, Poisson MO, Waller JL, et al: Development and validation of a medication regimen complexity scoring tool for critically ill patients. *Am J Health Syst Pharm* 2019; 76(Supplement_2):S34-s40

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14. Al-Mamun MA, Brothers T, Newsome AS: Development of Machine Learning Models to Validate a Medication Regimen Complexity Scoring Tool for Critically Ill Patients. *Ann Pharmacother* 2021; 55(4):421-429

15. Smith SE, Shelley R, Sikora A: Medication regimen complexity vs patient acuity for predicting critical care pharmacist interventions. *Am J Health Syst Pharm* 2022; 79(8):651-655

16. Webb AJ, Rowe S, Newsome AS: A descriptive report of the rapid implementation of automated MRC-ICU calculations in the EMR of an academic medical center. *Am J Health Syst Pharm* 2022; 79(12):979-983

17. Newsome AS, Smith SE, Olney WJ, et al: Medication regimen complexity is associated with pharmacist interventions and drug-drug interactions: A use of the novel MRC-ICU scoring tool. *Journal of the American College of Clinical Pharmacy*. 2020; 3(1):47-56

18. Sanchez P, Voisey JP, Xia T, et al: Causal machine learning for healthcare and precision medicine. *R Soc Open Sci* 2022; 9(8):220638

19. Iwase S, Nakada TA, Shimada T, et al: Prediction algorithm for ICU mortality and length of stay using machine learning. *Sci Rep* 2022; 12(1):12912

20. Beil M, Sviri S, Flaatten H, et al: On predictions in critical care: The individual prognostication fallacy in elderly patients. *J Crit Care* 2021; 61:34-38

21. Lovejoy CA, Buch V, Maruthappu M: Artificial intelligence in the intensive care unit. *Crit Care* 2019; 23(1):7

22. Gutierrez G: Artificial Intelligence in the Intensive Care Unit. *Crit Care* 2020; 24(1):101

23. Goh KH, Wang L, Yeow AYK, et al: Artificial intelligence in sepsis early prediction and diagnosis using unstructured data in healthcare. *Nat Commun* 2021; 12(1):711

24. Hyland SL, Faltys M, Huser M, et al: Early prediction of circulatory failure in the intensive care unit using machine learning. *Nat Med* 2020; 26(3):364-373

25. DeGrave AJ, Janizek JD, Lee SI: AI for radiographic COVID-19 detection selects shortcuts over signal. *medRxiv* 2020

26. Nguyen D, Ngo B, vanSonnenberg E: AI in the Intensive Care Unit: Up-to-Date Review. *J Intensive Care Med* 2021; 36(10):1115-1123

27. Yoon JH, Pinsky MR, Clermont G: Artificial Intelligence in Critical Care Medicine. *Crit Care* 2022; 26(1):75

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28. Farion KJ, Wilk S, Michalowski W, et al: Comparing predictions made by a prediction model, clinical score, and physicians: pediatric asthma exacerbations in the emergency department. *Appl Clin Inform* 2013; 4(3):376-391

29. Feng JZ, Wang Y, Peng J, et al: Comparison between logistic regression and machine learning algorithms on survival prediction of traumatic brain injuries. *J Crit Care* 2019; 54:110-116

30. World Medical Association: World Medical Association Declaration of Helsinki: Ethical principles for medical research involving human subjects. *JAMA* 2023: 312:2191-2194.

31. Von Elm E AD, Egger M, et al: STROBE Initiative: Strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. *BMJ* 2007; 335:806-808.

32. Bouchard J, Soroko SB, Chertow GM, et al: Fluid accumulation, survival and recovery of kidney function in critically ill patients with acute kidney injury. *Kidney Int* 2009; 76(4):422-427

33. Carr JR, Hawkins WA, Newsome AS, et al: Fluid Stewardship of Maintenance Intravenous Fluids. *J Pharm Pract* 2022; 35(5):769-782

34. Malbrain M, Van Regenmortel N, Saugel B, et al: Principles of fluid management and stewardship in septic shock: it is time to consider the four D's and the four phases of fluid therapy. *Ann Intensive Care* 2018; 8(1):66

35. Claure-Del Granado R, Mehta RL: Fluid overload in the ICU: evaluation and management. *BMC Nephrol* 2016; 17(1):109

36. O'Connor ME, Prowle JR: Fluid Overload. *Crit Care Clin* 2015; 31(4):803-821

37. Chen T, Guestrin C. XGBoost: A Scalable Tree Boosting System. In: Proceedings of the 22nd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining [Internet]. New York, NY, USA: ACM; 2016. p. 785–94. Available from: http://doi.acm.org/10.1145/2939672.2939785

38. Cortes C, Vapnik V. Support-vector networks. Machine learning. 1995;20(3):273–97.

39. Ho TK. Random decision forests. In: Proceedings of 3rd international conference on document analysis and recognition. 1995. p. 278–82.

40. Rubin DB: Multiple imputation for nonresponse in surveys. Hoboken, N.J. ;, Wiley-Interscience, 2004

41. Topol EJ: Deep medicine : how artificial intelligence can make healthcare human again. First edition. ed. New York, Basic Books,, 2019, p^pp 1 online resource

medRxiv preprint doi: https://doi.org/10.1101/2024.03.21.24304663; this version posted March 22, 2024. The copyright holder for this preprint
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42. Kahneman D, Sibony O, Sunstein CR: Noise : a flaw in human judgment. First edition. Edition. New York, Little, Brown Spark, 2021

43. D'Hondt E, Ashby TJ, Chakroun I, et al: Identifying and evaluating barriers for the implementation of machine learning in the intensive care unit. *Commun Med (Lond)* 2022; 2(1):162

44. van de Sande D, van Genderen ME, Huiskens J, et al: Moving from bytes to bedside: a systematic review on the use of artificial intelligence in the intensive care unit. *Intensive Care Med* 2021; 47(7):750-760

45. Moss L, Corsar D, Shaw M, et al: Demystifying the Black Box: The Importance of Interpretability of Predictive Models in Neurocritical Care. *Neurocrit Care* 2022; 37(Suppl 2):185-191

46. The Lancet Respiratory M: Opening the black box of machine learning. *Lancet Respir Med* 2018; 6(11):801

47. Malbrain M, Martin G, Ostermann M: Everything you need to know about deresuscitation. *Intensive Care Med* 2022; 48(12):1781-1786

48. Gelbart B, Serpa Neto A, Stephens D, et al: Fluid Accumulation in Mechanically Ventilated, Critically Ill Children: Retrospective Cohort Study of Prevalence and Outcome. *Pediatr Crit Care Med* 2022; 23(12):990-998

49. National Heart L, Blood Institute Acute Respiratory Distress Syndrome Clinical Trials N, Wiedemann HP, et al: Comparison of two fluid-management strategies in acute lung injury. *N Engl J Med* 2006; 354(24):2564-2575

50. Gamble KC, Smith SE, Bland CM, et al: Hidden Fluids in Plain Sight: Identifying Intravenous Medication Classes as Contributors to Intensive Care Unit Fluid Intake. *Hosp Pharm* 2022; 57(2):230-236

51. Branan T, Smith SE, Newsome AS, et al: Association of hidden fluid administration with development of fluid overload reveals opportunities for targeted fluid minimization. *SAGE Open Med* 2020; 8:2050312120979464

52. Mitchell KH, Carlbom D, Caldwell E, et al: Volume Overload: Prevalence, Risk Factors, and Functional Outcome in Survivors of Septic Shock. *Ann Am Thorac Soc* 2015; 12(12):1837-1844

53. Ouchi A, Sakuramoto H, Hoshino H, et al: Association between fluid overload and delirium/coma in mechanically ventilated patients. *Acute Med Surg* 2020; 7(1):e508

54. Murphy CV, Schramm GE, Doherty JA, et al: The importance of fluid management in acute lung injury secondary to septic shock. *Chest* 2009; 136(1):102-109

medRxiv preprint doi: https://doi.org/10.1101/2024.03.21.24304663; this version posted March 22, 2024. The copyright holder for this preprint
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55. Boyd JH, Forbes J, Nakada TA, et al: Fluid resuscitation in septic shock: a positive fluid balance and elevated central venous pressure are associated with increased mortality. *Crit Care Med* 2011; 39(2):259-265

56. Woodward CW, Lambert J, Ortiz-Soriano V, et al: Fluid Overload Associates With Major Adverse Kidney Events in Critically Ill Patients With Acute Kidney Injury Requiring Continuous Renal Replacement Therapy. *Crit Care Med* 2019; 47(9):e753-e760

57. Hawkins WA, Butler SA, Poirier N, et al: From theory to bedside: Implementation of fluid stewardship in a medical ICU pharmacy practice. *Am J Health Syst Pharm* 2022; 79(12):984-992

58. Silversides JA, Perner A, Malbrain M: Liberal versus restrictive fluid therapy in critically ill patients. *Intensive Care Med* 2019; 45(10):1440-1442

59. Goldstein S, Bagshaw S, Cecconi M, et al: Pharmacological management of fluid overload. *Br J Anaesth* 2014; 113(5):756-763

60. Silversides JA, McAuley DF, Blackwood B, et al: Fluid management and deresuscitation practices: A survey of critical care physicians. *J Intensive Care Soc* 2020; 21(2):111-118

61. Burkov A: The hundred-page machine learning book. Quebec City, Canada, Andriy Burkov, 2019

62. Qin X, Zhang W, Hu X, et al: A deep learning model to identify the fluid overload status in critically ill patients based on chest X-ray images. *Pol Arch Intern Med* 2023; 133(2)

medRxiv preprint doi: https://doi.org/10.1101/2024.03.21.24304663; this version posted March 22, 2024. The copyright holder for this preprint
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Bibliography

1. Bouchard J, Soroko SB, Chertow GM, et al. Fluid accumulation, survival and recovery of kidney function in critically ill patients with acute kidney injury. Kidney Int 2009;76(4):422-7. (In eng). DOI: 10.1038/ki.2009.159.
2. Carr JR, Hawkins WA, Newsome AS, et al. Fluid Stewardship of Maintenance Intravenous Fluids. J Pharm Pract 2022;35(5):769-782. (In eng). DOI: 10.1177/08971900211008261.
3. Hawkins WA, Smith SE, Newsome AS, Carr JR, Bland CM, Branan TN. Fluid Stewardship During Critical Illness: A Call to Action. J Pharm Pract 2020;33(6):863-873. (In eng). DOI: 10.1177/0897190019853979.
4. Bissell BD, Donaldson JC, Morris PE, Neyra JA. A narrative review of pharmacologic de-resuscitation in the critically ill. J Crit Care 2020;59:156-162. (In eng). DOI: 10.1016/j.jcrc.2020.07.004.
5. Bissell BD, Laine ME, Thompson Bastin ML, et al. Impact of protocolized diuresis for de-resuscitation in the intensive care unit. Crit Care 2020;24(1):70. (In eng). DOI: 10.1186/s13054-020-2795-9.
6. Hawkins WA, Butler SA, Poirier N, Wilson CS, Long MK, Smith SE. From theory to bedside: Implementation of fluid stewardship in a medical ICU pharmacy practice. Am J Health Syst Pharm 2022;79(12):984-992. (In eng). DOI: 10.1093/ajhp/zxab453.
7. Jones TW, Chase AM, Bruning R, Nimmanonda N, Smith SE, Sikora A. Early Diuretics for De-resuscitation in Septic Patients With Left Ventricular Dysfunction. Clin Med Insights Cardiol 2022;16:11795468221095875. (In eng). DOI: 10.1177/11795468221095875.
8. Olney WJ, Chase AM, Hannah SA, Smith SE, Newsome AS. Medication Regimen Complexity Score as an Indicator of Fluid Balance in Critically Ill Patients. J Pharm Pract 2022;35(4):573-579. (In eng). DOI: 10.1177/0897190021999792.
9. Rafiei A, Rad MG, Sikora A, Kamaleswaran R. Improving irregular temporal modeling by integrating synthetic data to the electronic medical record using conditional GANs: a case study of fluid overload prediction in the intensive care unit. medRxiv 2023:2023.06.20.23291680. DOI: 10.1101/2023.06.20.23291680.
10. Sikora A, Zhang T, Murphy DJ, et al. Machine learning vs. traditional regression analysis for fluid overload prediction in the ICU. medRxiv 2023:2023.06.16.23291493. DOI: 10.1101/2023.06.16.23291493.
11. Messmer AS, Moser M, Zuercher P, Schefold JC, Müller M, Pfortmueller CA. Fluid Overload Phenotypes in Critical Illness-A Machine Learning Approach. J Clin Med 2022;11(2) (In eng). DOI: 10.3390/jcm11020336.
12. Zhang Z, Ho KM, Hong Y. Machine learning for the prediction of volume responsiveness in patients with oliguric acute kidney injury in critical care. Crit Care 2019;23(1):112. (In eng). DOI: 10.1186/s13054-019-2411-z.
13. Sikora A, Devlin JW, Yu M, et al. Evaluation of medication regimen complexity as a predictor for mortality. Sci Rep 2023;13(1):10784. DOI: 10.1038/s41598-023-37908-1.
14. Gwynn ME, Poisson MO, Waller JL, Newsome AS. Development and validation of a medication regimen complexity scoring tool for critically ill patients. Am J Health Syst Pharm 2019;76(Supplement_2):S34-s40. (In eng). DOI: 10.1093/ajhp/zxy054.
15. Murray B, Zhao B, Kong Y, Shen Y, Sikora A. 935: PREDICTING DURATION OF MECHANICAL VENTILATION WITH MEDICATION REGIMEN COMPLEXITY

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VARIABLES. Critical Care Medicine 2023;51(1):460. DOI: 10.1097/01.ccm.0000909468.03569.76.

16. Webb AJ, Rowe S, Sikora Newsome A. A descriptive report of the rapid implementation of automated MRC-ICU calculations in the EMR of an academic medical center. Am J Health Syst Pharm 2022. DOI: 10.1093/ajhp/zxac059.
17. Sikora A, Rafiei A, Rad MG, et al. Pharmacophenotype identification of intensive care unit medications using unsupervised cluster analysis of the ICURx common data model. Crit Care 2023;27(1):167. DOI: 10.1186/s13054-023-04437-2.
18. Chase A AH, Forehand C, Keats K, Taylor A, Wu S, Blotske K, Sikora A. An evaluation of medication regimen complexity's relationship to medication errors in critically ill patients. Hospital Pharmacy 2023;Accepted.
19. Al-Mamun MA, Brothers T, Newsome AS. Development of Machine Learning Models to Validate a Medication Regimen Complexity Scoring Tool for Critically Ill Patients. Ann Pharmacother 2021;55(4):421-429. (In eng). DOI: 10.1177/1060028020959042.
20. Newsome AS, Anderson D, Gwynn ME, Waller JL. Characterization of changes in medication complexity using a modified scoring tool. Am J Health Syst Pharm 2019;76(Supplement_4):S92-s95. (In eng). DOI: 10.1093/ajhp/zxz213.
21. Sikora A, Ayyala D, Rech MA, et al. Impact of Pharmacists to Improve Patient Care in the Critically Ill: A Large Multicenter Analysis Using Meaningful Metrics With the Medication Regimen Complexity-ICU (MRC-ICU) Score. Crit Care Med 2022;50(9):1318-1328. (In eng). DOI: 10.1097/ccm.0000000000005585.
22. Sikora A, Rafiei A, Rad MG, et al. Pharmacophenotype identification of intensive care unit medications using unsupervised cluster analysis of the ICURx common data model. Crit Care 2023;27(1):167. (In eng). DOI: 10.1186/s13054-023-04437-2.
23. Sikora A JH, Yu M, Chen X, Murray B, Kamaleswaran R. Cluster analysis driven by unsupervised latent feature learning of
intensive care unit medications to identify novel pharmacophenotypes of critically ill patients. Research Square 2022. DOI: https://doi.org/10.21203/rs.3.rs-1745568/v1.
24. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. Jama 2013;310(20):2191-4. (In eng). DOI: 10.1001/jama.2013.281053.
25. Elm Ev, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. BMJ 2007;335(7624):806-808. DOI: 10.1136/bmj.39335.541782.AD.
26. Sikora A, Keats K, Murphy DJ, et al. A Common Data Model for the standardization of intensive care unit (ICU) medication features in artificial intelligence (AI) applications. medRxiv 2023:2023.09.18.23295727. DOI: 10.1101/2023.09.18.23295727.
27. Bro R, Smilde AK. Principal component analysis. Analytical Methods 2014;6(9):2812-2831. (10.1039/C3AY41907J). DOI: 10.1039/C3AY41907J.
28. Wold S, Esbensen K, Geladi P. Principal component analysis. Chemometrics and Intelligent Laboratory Systems 1987;2(1):37-52. DOI: https://doi.org/10.1016/0169-7439(87)80084-9.
29. Hinton GE. A Practical Guide to Training Restricted Boltzmann Machines. In: Montavon G, Orr GB, Müller K-R, eds. Neural Networks: Tricks of the Trade: Second Edition. Berlin, Heidelberg: Springer Berlin Heidelberg; 2012:599-619.

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30. Zhang N, Ding S, Zhang J, Xue Y. An overview on Restricted Boltzmann Machines. Neurocomputing 2018;275:1186-1199. DOI: https://doi.org/10.1016/j.neucom.2017.09.065.
31. Deng S. Syuand/unsupervisedfoprediction-: A time-dependent, unsupervised machine learning (ML) analysis was conducted to determine patterns of IV medication use associated with fo. GitHub. (https://github.com/SyuanD/UnsupervisedFOPrediction-.git).
32. Rafiei A, Rad MG, Sikora A, Kamaleswaran R. Improving irregular temporal modeling by integrating synthetic data to the electronic medical record using conditional GANs: a case study of fluid overload prediction in the intensive care unit. medRxiv 2023. DOI: 10.1101/2023.06.20.23291680.
33. Sikora A, Zhang T, Murphy DJ, et al. Machine learning vs. traditional regression analysis for fluid overload prediction in the ICU. medRxiv 2023:2023.06.16.23291493. DOI: 10.1101/2023.06.16.23291493.
34. Olney WJ, Chase AM, Hannah SA, Smith SE, Newsome AS. Medication Regimen Complexity Score as an Indicator of Fluid Balance in Critically Ill Patients. J Pharm Pract 2021:897190021999792. DOI: 10.1177/0897190021999792.
35. Sikora A, Zhao B, Kong Y, Murray B, Shen Y. Machine learning based prediction of prolonged duration of mechanical ventilation incorporating medication data. medRxiv 2023. DOI: 10.1101/2023.09.18.23295724.
36. Sikora A, Keats K, Murphy DJ, et al. A Common Data Model for the standardization of intensive care unit (ICU) medication features in artificial intelligence (AI) applications. medRxiv 2023:2023.09.18.23295727. DOI: 10.1101/2023.09.18.23295727.
37. Goh KH, Wang L, Yeow AYK, et al. Artificial intelligence in sepsis early prediction and diagnosis using unstructured data in healthcare. Nat Commun 2021;12(1):711. (In eng). DOI: 10.1038/s41467-021-20910-4.
38. Gutierrez G. Artificial Intelligence in the Intensive Care Unit. Crit Care 2020;24(1):101. (In eng). DOI: 10.1186/s13054-020-2785-y.
39. Hyland SL, Faltys M, Hüser M, et al. Early prediction of circulatory failure in the intensive care unit using machine learning. Nat Med 2020;26(3):364-373. (In eng). DOI: 10.1038/s41591-020-0789-4.
40. Iwase S, Nakada TA, Shimada T, et al. Prediction algorithm for ICU mortality and length of stay using machine learning. Sci Rep 2022;12(1):12912. (In eng). DOI: 10.1038/s41598-022-17091-5.
41. Beil M, Sviri S, Flaatten H, et al. On predictions in critical care: The individual prognostication fallacy in elderly patients. J Crit Care 2021;61:34-38. (In eng). DOI: 10.1016/j.jcrc.2020.10.006.
42. Lovejoy CA, Buch V, Maruthappu M. Artificial intelligence in the intensive care unit. Crit Care 2019;23(1):7. (In eng). DOI: 10.1186/s13054-018-2301-9.

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Supplemental Digital Information

Table 1. Composition of ten medication clusters identified with Restricted Boltzmann Machine

	Cluster									
	1 (N=498)	**2 (N=561)**	**3 (N=532)**	**4 (N=517)**	**5 (N=539)**	**6 (N=574)**	**7 (N=540)**	**8 (N=518)**	**9 (N=526)**	**10 (N=532)**
1	famotidine 10 mg/ml injection solution (multi-vial size)	morphine 2 mg/ml injection pf wrapper	phenylephrine 20 mg/250 ml (80 mcg/ml) in 0.9 % sodium chloride iv	dextrose 10 % in water (d10w) intravenous solution	lactated ringers irrigation solution	dopamine 400 mg/250 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution	dobutamine 250 mg/250 ml (1 mg/ml) in 5 % dextrose intravenous	insulin u-100 regular human 100 unit/ml injection solution	piperacillin-tazobactam 2.25 gram/50 ml in dextrose(iso) iv piggyback	dopamine 400 mg/250 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution
2	phenylephrine 20 mg/250 ml (80 mcg/ml) in 0.9 % sodium chloride iv	metronidazole 500 mg/100 ml-sodium chloride (iso) intravenous piggyback	heparin (porcine) 10,000 unit/1,000 ml in 0.9 % sod. chloride iv solution	famotidine 10 mg/ml injection solution (multi-vial size)	dopamine 400 mg/250 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution	dobutamine 250 mg/250 ml (1 mg/ml) in 5 % dextrose intravenous	dexmedetomidine 400 mcg/100 ml (4 mcg/ml) in 0.9 % sodium chloride iv	sodium chloride 0.9 % intravenous solution	heparin (porcine) 10,000 unit/1,000 ml in 0.9 % sod. chloride iv solution	metronidazole 500 mg/100 ml-sodium chloride(iso) intravenous piggyback
3	heparin (porcine) 10,000 unit/1,000 ml in 0.9 % sod. chloride iv solution	dobutamine 250 mg/250 ml (1 mg/ml) in 5 % dextrose intravenous	fentanyl (pf) 10 mcg/ml in 0.9 % sodium chloride intravenous wrapper	heparin (porcine) 100 unit/ml load from infusion	fentanyl (pf) 10 mcg/ml in 0.9 % sodium chloride intravenous wrapper	sodium chloride 0.45 % intravenous solution	heparin (porcine) 1,000 unit/ml injection solution	fentanyl (pf) 50 mcg/ml injection solution	levofloxacin 750 mg/150 ml in 5 % dextrose intravenous piggyback	famotidine 10 mg/ml injection solution (multi-vial size)
4	cefepime 2 gram/100 ml in dextrose (iso-osmotic) intravenous piggyback	heparin (porcine) 10,000 unit/1,000 ml in 0.9 % sod. chloride iv solution	sodium chloride 0.9 % intravenous solution	sodium chloride 0.45 % intravenous solution	morphine 1 mg/ml in dextrose 5 % intravenous solution	fentanyl (pf) 10 mcg/ml in 0.9 % sodium chloride intravenous wrapper	clevidipine 25 mg/50 ml intravenous emulsion	propofol infusion 10 mg/ml	cefazolin 2 gram/100 ml in dextrose(iso-osmotic) intravenous piggyback	dexmedetomidine 400 mcg/100 ml (4 mcg/ml) in 0.9 % sodium chloride iv
5	propofol infusion 10 mg/ml	levofloxacin 750 mg/150 ml in 5 % dextrose intravenous piggyback	morphine 1 mg/ml in dextrose 5 % intravenous solution	piperacillin-tazobactam 2.25 gram/50 ml in dextrose(iso) iv piggyback	hydromorphone 2 mg/ml injection syringe	levofloxacin 750 mg/150 ml in 5 % dextrose intravenous piggyback	hydromorphone 2 mg/ml injection syringe	amiodarone 450 mg/250 ml (1.8 mg/ml) in dextrose 5 % intravenous solution	lorazepam 2 mg/ml injection syringe	piperacillin-tazobactam 2.25 gram/50 ml in dextrose(iso) iv piggyback
6	midazolam (pf) 1 mg/ml in 0.9 % sodium chloride intravenous solution	hydromorphone 2 mg/ml injection syringe	clevidipine 25 mg/50 ml intravenous emulsion	insulin u-100 regular human 100 unit/ml injection solution	midazolam (pf) 1 mg/ml in 0.9 % sodium chloride intravenous solution	propofol infusion 10 mg/ml	fentanyl (pf) 10 mcg/ml in 0.9 % sodium chloride intravenous wrapper	phenylephrine 20 mg/250 ml (80 mcg/ml) in 0.9 % sodium chloride iv	cefazolin 2 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	fentanyl (pf) 10 mcg/ml in 0.9 % sodium chloride intravenous wrapper
7	vancomycin 2 gram/500 ml in 0.9 % sodium chloride	vancomycin 2 gram/50 0 ml in 0.9 % sodium chloride	amiodarone 450 mg/250 ml (1.8 mg/ml) in dextrose 5 %	dextrose 5 % and lactated ringers intravenous solution	clevidipine 25 mg/50 ml intravenous emulsion	clevidipine 25 mg/50 ml intravenous emulsion	lactated ringers intravenous solution	dobutamine 1,000 mg/250 ml(4,000 mcg/ml) in 5 % dextrose iv	vasopressin 40 units/50 ml (0.8 unit/ml) in ns infusion	sodium chloride 0.9 % intravenous solution

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	intravenous	intravenous	intravenous solution							
8	midazolam (pf) 1 mg/ml injection solution	clevidipine 25 mg/50 ml intravenous emulsion	vancomycin 2 gram/500 ml in 0.9 % sodium chloride intravenous	dobutamine 250 mg/250 ml (1 mg/ml) in 5 % dextrose intravenous	vasopressin 40 units/50 ml (0.8 unit/ml) in ns infusion	cefazolin 2 gram/100 ml in dextrose(iso-osmotic) intravenous piggyback	propofol 10 mg/ml intravenous emulsion	clevidipine 25 mg/50 ml intravenous emulsion	fentanyl (pf) 10 mcg/ml in 0.9 % sodium chloride intravenous wrapper	hydromorphone 50 mg/50 ml (1 mg/ml) in 0.9 % sod.chloride iv pump resevoir
9	sodium chloride 0.9 % intravenous solution	fentanyl (pf) 10 mcg/ml in 0.9 % sodium chloride intravenous wrapper	cefazolin 2 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	heparin (porcine) 1,000 unit/ml injection solution	fat emulsion 20 % intravenous	midazolam (pf) 1 mg/ml in 0.9 % sodium chloride intravenous solution	heparin (porcine) 10,000 unit/1,000 ml in 0.9 % sod. chloride iv solution	clindamycin 600 mg/50 ml in 5 % dextrose intravenous piggyback	phenylephrine 20 mg/250 ml (80 mcg/ml) in 0.9 % sodium chloride iv	heparin (porcine) 1,000 unit/ml injection solution
10	morphine 1 mg/ml in dextrose 5 % intravenous solution	fat emulsion 20 % intravenous	morphine 10 mg/ml injection solution	fentanyl (pf) 50 mcg/ml injection solution	lactated ringers intravenous solution	norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in 0.9 % nacl iv	phenobarbital sodium 65 mg/ml injection solution	morphine 2 mg/ml intravenous cartridge	propofol 10 mg/ml intravenous emulsion	cefazolin 2 gram/100 ml in dextrose(iso-osmotic) intravenous piggyback
11	eptifibatide 0.75 mg/ml intravenous solution	phenylephrine 20 mg/250 ml (80 mcg/ml) in 0.9 % sodium chloride iv	fat emulsion 20 % intravenous	amiodarone 450 mg/250 ml (1.8 mg/ml) in dextrose 5 % intravenous solution	heparin (porcine) 10,000 unit/1,000 ml in 0.9 % sod. chloride iv solution	vasopressin 40 units/50 ml (0.8 unit/ml) in ns infusion	diazepam 5 mg/ml injection syringe	midazolam (pf) 1 mg/ml injection solution	pantoprazole 40 mg intravenous solution	hydromorphone 2 mg/ml injection syringe
12	morphine 2 mg/ml intravenous cartridge	clindamycin 600 mg/50 ml in 5 % dextrose intravenous piggyback	morphine 2 mg/ml intravenous cartridge	midazolam (pf) 1 mg/ml in 0.9 % sodium chloride intravenous solution	morphine 4 mg/ml intravenous cartridge	fat emulsion 20 % intravenous	morphine 4 mg/ml intravenous cartridge	cefepime 1 gram solution for injection	clindamycin 600 mg/50 ml in 5 % dextrose intravenous piggyback	midazolam (pf) 1 mg/ml in 0.9 % sodium chloride intravenous solution
13	propofol 10 mg/ml intravenous emulsion	phenobarbital sodium 65 mg/ml injection solution	pantoprazole 40 mg intravenous solution	norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in 0.9 % nacl iv	fluconazole 200 mg/100 ml in sod. chloride (iso) intravenous piggyback	dobutamine 1,000 mg/250 ml(4,000 mcg/ml) in 5 % dextrose iv	levofloxacin 500 mg/100 ml in 5 % dextrose intravenous piggyback	propofol 10 mg/ml intravenous emulsion	phenobarbital sodium 65 mg/ml injection solution	vasopressin 40 units/50 ml (0.8 unit/ml) in ns infusion
14	morphine 1 mg/ml in 0.9 % sodium chloride injectable pump reservoir	morphine 4 mg/ml intravenous cartridge	morphine 4 mg/ml intravenous cartridge	clevidipine 25 mg/50 ml intravenous emulsion	heparin (porcine) 10,000 unit/ml injection solution	pantoprazole 40 mg intravenous solution	heparin (porcine) 10,000 unit/ml injection solution	vasopressin (pitressin) infusion 50 unit/50 ml	midazolam 5 mg/ml (combined) injection solution wrapper	fat emulsion 20 % intravenous
15	heparin (porcine) 10,000 unit/1,000 ml in ns (unch cupid)	midazolam 5 mg/ml (combined) injection solution wrapper	lactated ringers intravenous solution	propofol 10 mg/ml intravenous emulsion	morphine 1 mg/ml in 0.9 % sodium chloride injectable pump reservoir	morphine 4 mg/ml intravenous cartridge	morphine 2 mg/ml intravenous cartridge	morphine 4 mg/ml intravenous cartridge	dopamine 400 mg/250 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution	clindamycin 600 mg/50 ml in 5 % dextrose intravenous piggyback

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16	insulin u-100 regular human 100 unit/ml injection solution	eptifibatide 0.75 mg/ml intravenous solution	phenobarbital sodium 65 mg/ml injection solution	heparin (porcine) 10,000 unit/1,000 ml in 0.9 % sod. chloride iv solution	midazolam (pf) 1 mg/ml injection solution	fluconazole 200 mg/100 ml in sod. chloride (iso) intravenous piggyback	midazolam (pf) 1 mg/ml injection solution	dextrose 5 % and 0.45 % sodium chloride intravenous solution	dobutamine 1,000 mg/250 ml(4,000 mcg/ml) in 5 % dextrose iv	clevidipine 25 mg/50 ml intravenous emulsion
17	dextrose 5 % and 0.45 % sodium chloride intravenous solution	morphine 2 mg/ml intravenous cartridge	midazolam (pf) 1 mg/ml injection solution	morphine 4 mg/ml intravenous cartridge	cefepime 1 gram solution for injection	sodium chloride 0.9 % intravenous solution	dobutamine 1,000 mg/250 ml(4,000 mcg/ml) in 5 % dextrose iv	linezolid in 5% dextrose in water 600 mg/300 ml intravenous piggyback	morphine 4 mg/ml intravenous cartridge	midazolam (pf) 1 mg/ml injection solution
18	piperacillin-tazobactam 3.375 gm/50ml dextrose (extended duration)	dexmedetomidine 400 mcg/100 ml (4 mcg/ml) in 0.9 % sodium chloride iv	dextrose 5 % and 0.45 % nacl iv bolus	midazolam (pf) 1 mg/ml injection solution	propofol 10 mg/ml intravenous emulsion	morphine 1 mg/ml in dextrose 5 % intravenous solution	morphine 1 mg/ml in dextrose 5 % intravenous solution	lidocaine (pf) 4 mg/ml (0.4 %) in 5 % dextrose intravenous solution	mannitol 20 % intravenous solution	linezolid in 5% dextrose in water 600 mg/300 ml intravenous piggyback
19	lidocaine (pf) 4 mg/ml (0.4 %) in 5 % dextrose intravenous solution	piperacillin-tazobactam 2.25 gram/50 ml in dextrose (iso) iv piggyback	heparin (porcine) 10,000 unit/ml injection solution	linezolid in 5% dextrose in water 600 mg/300 ml intravenous piggyback	dobutamine 1,000 mg/250 ml(4,000 mcg/ml) in 5 % dextrose iv	morphine 2 mg/ml intravenous cartridge	norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in 0.9 % nacl iv	dopamine 800 mg/500 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution	insulin u-100 regular human 100 unit/ml injection solution	morphine 4 mg/ml intravenous cartridge
20	clindamycin 600 mg/50 ml in 5 % dextrose intravenous piggyback	morphine 1 mg/ml in dextrose 5 % intravenous solution	cefepime 1 gram solution for injection	meperidine (pf) 25 mg/ml injection syringe	norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in 0.9 % nacl iv	midazolam (pf) 1 mg/ml injection solution	mannitol 20 % intravenous solution	famotidine (pf) 20 mg/2 ml intravenous solution	dextrose 5 % and 0.45 % sodium chloride intravenous solution	levofloxacin 500 mg/100 ml in 5 % dextrose intravenous piggyback
21	heparin (porcine) for crrt 25,000 unit/250 ml in 0.45 % sodium chloride iv solution	heparin (porcine) 10,000 unit/1,000 ml in ns (unchcupid)	propofol 10 mg/ml intravenous emulsion	vasopressin (pitressin) infusion 50 unit/50 ml	levofloxacin 500 mg/100 ml in 5 % dextrose intravenous piggyback	cefepime 1 gram solution for injection	morphine 10 mg/ml injection solution	nitroglycerin 100 mg/250 ml (400 mcg/ml) in 5 % dextrose intravenous	piperacillin-tazobactam 4.5 gram/100 ml dextrose(iso-osmotic) iv piggyback	meperidine (pf) 25 mg/ml injection syringe
22	vecuronium bromide 10 mg intravenous solution	morphine 10 mg/ml injection solution	dobutamine 1,000 mg/250 ml(4,000 mcg/ml) in 5 % dextrose iv	dobutamine 1,000 mg/250 ml(4,000 mcg/ml) in 5 % dextrose iv	piperacillin-tazobactam 3.375 gram/50 ml dextrose(iso-os) iv piggyback	meperidine (pf) 25 mg/ml injection syringe	piperacillin-tazobactam 3.375 gm/50ml dextrose (extended duration)	fluconazole 200 mg/100 ml in sod. chloride (iso) intravenous piggyback	piperacillin-tazobactam 3.375 gm/50ml dextrose (extended duration)	vasopressin (pitressin) infusion 50 unit/50 ml
23	lactated ringers intravenous solution	dextrose 5 % and lactated ringers intravenous solution	sodium chloride 3 % intravenous injection solution	fat emulsion 20 % intravenous	linezolid in 5% dextrose in water 600 mg/300 ml intravenous piggyback	propofol 10 mg/ml intravenous emulsion	linezolid in 5% dextrose in water 600 mg/300 ml intravenous piggyback	fat emulsion 20 % intravenous	piperacillin-tazobactam 3.375 gram/50 ml dextrose(iso-os) iv piggyback	dobutamine 1,000 mg/250 ml(4,000 mcg/ml) in 5 % dextrose iv

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24	amiodarone 150 mg/100 ml (1.5 mg/ml) in dextrose, iso-osmotic iv	lactated ringers iv bolus	dextrose 5 % in water (d5w) intravenous solution	phenobarbital sodium 65 mg/ml injection solution	esmolol 2,500 mg/250 ml (10 mg/ml) in sodium chloride (iso-osmotic) iv	heparin, porcine (pf) 10 unit/ml intravenous syringe	fat emulsion 20 % intravenous	dobutamine 250 mg/250 ml (1 mg/ml) in 5 % dextrose intravenous	dextrose 5 % and lactated ringers intravenous solution	heparin, porcine (pf) 10 unit/ml intravenous syringe
25	lorazepam 2 mg/ml injection syringe	nitroglycerin 50 mg/250 ml (200 mcg/ml) in 5 % dextrose intravenous	insulin u-100 regular human 100 unit/ml injection solution	heparin, porcine (pf) 10 unit/ml intravenous syringe	clindamycin 600 mg/50 ml in 5 % dextrose intravenous piggyback	piperacillin-tazobactam 2.25 gram/50 ml in dextrose(iso) iv piggyback	dextrose 5 % and lactated ringers intravenous solution	fentanyl (pf) 2,500 mcg/50 ml (50 mcg/ml) intravenous pca syringe	dopamine 800 mg/500 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution	norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in 0.9 % nacl iv
26	morphine 4 mg/ml intravenous cartridge	lactated ringers intravenous solution	levofloxacin 500 mg/100 ml in 5 % dextrose intravenous piggyback	sodium chloride 3 % intravenous injection solution	nitroglycerin 50 mg/250 ml (200 mcg/ml) in 5 % dextrose intravenous	heparin (porcine) 10,000 unit/1,000 ml in ns (unch cupid)	midazolam 1 mg/ml injection solution	vecuronium bromide 10 mg intravenous solution	famotidine (pf) 20 mg/2 ml intravenous solution	rocuronium 10 mg/ml intravenous solution
27	vasopressin 40 units/50 ml (0.8 unit/ml) ssc premade infusion	hydromorphone 50 mg/50 ml (1 mg/ml) in 0.9 % sod.chloride iv pump resevoir	linezolid in 5% dextrose in water 600 mg/300 ml intravenous piggyback	dextrose 5 % in water (d5w) intravenous solution	sodium chloride 3 % intravenous injection solution	mannitol 20 % intravenous solution	meperidine (pf) 25 mg/ml injection syringe	diazepam 5 mg/ml injection syringe	lactated ringers iv bolus	dextrose 5 % in water (d5w) intravenous solution
28	midazolam 1 mg/ml injection solution	digoxin 250 mcg/ml (0.25 mg/ml) injection solution	clindamycin 900 mg/50 ml in 5 % dextrose intravenous piggyback	piperacillin-tazobactam 3.375 gm/50ml dextrose (extended duration)	hydromorphone 50 mg/50 ml (1 mg/ml) in 0.9 % sod.chloride iv pump resevoir	lidocaine (pf) 4 mg/ml (0.4 %) in 5 % dextrose intravenous solution	albumin, human 5 % intravenous solution	nitroglycerin 50 mg/250 ml (200 mcg/ml) in 5 % dextrose intravenous	lactated ringers intravenous solution	morphine 10 mg/ml injection solution
29	diazepam 5 mg/ml injection syringe	heparin (porcine) for crrt 25,000 unit/250 ml in 0.45 % sodium chloride iv solution	diazepam 5 mg/ml injection syringe	clindamycin 900 mg/50 ml in 5 % dextrose intravenous piggyback	meperidine (pf) 25 mg/ml injection syringe	clindamycin 900 mg/50 ml in 5 % dextrose intravenous piggyback	heparin, porcine (pf) 10 unit/ml intravenous syringe	heparin (porcine) for crrt 25,000 unit/250 ml in 0.45 % sodium chloride iv solution	digoxin 250 mcg/ml (0.25 mg/ml) injection solution	dextrose 5 % and 0.45 % sodium chloride intravenous solution
30	fentanyl (pf) 10 mcg/ml in 0.9 % sodium chloride intravenous wrapper	insulin u-100 regular human 100 unit/ml injection solution	dextrose 5 % and 0.9 % sodium chloride intravenous solution	dopamine 800 mg/500 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution	heparin, porcine (pf) 10 unit/ml intravenous syringe	clindamycin 600 mg/50 ml in 5 % dextrose intravenous piggyback	cefazolin 1 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	heparin (porcine) 100 unit/ml bolus from infusion	heparin (porcine) for crrt 25,000 unit/250 ml in 0.45 % sodium chloride iv solution	lidocaine (pf) 4 mg/ml (0.4 %) in 5 % dextrose intravenous solution
31	cefazolin 1 gram/50 ml in dextrose (iso-osmotic) intravenou	fentanyl (pf) 2,500 mcg/50 ml (50 mcg/ml) intraven	heparin (porcine) for crrt 25,000 unit/250 ml in 0.45 %	famotidine (pf) 20 mg/2 ml intravenous solution	lorazepam 2 mg/ml injection syringe	famotidine (pf) 20 mg/2 ml intravenous solution	heparin (porcine) for crrt 25,000 unit/250 ml in 0.45 %	morphine 1 mg/ml in 0.9 % sodium chloride injectable pump	amiodarone 150 mg/100 ml (1.5 mg/ml) in dextrose, iso-	clindamycin 900 mg/50 ml in 5 % dextrose intravenous

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	s piggyback	ous pca syringe	sodium chloride iv solution				sodium chloride iv solution	reservoir	osmotic iv	piggyback
32	nitroglycerin 100 mg/250 ml (400 mcg/ml) in 5 % dextrose intravenous	rocuronium 10 mg/ml intravenous solution	lactated ringers iv bolus	diazepam 5 mg/ml injection syringe	vancomycin 1.25 gram/250 ml in 0.9 % sodium chloride intravenous	heparin (porcine) for crrt 25,000 unit/250 ml in 0.45 % sodium chloride iv solution	fentanyl (pf) 2,500 mcg/50 ml (50 mcg/ml) intravenous pca syringe	piperacillin-tazobactam 3.375 gm/50ml dextrose (extended duration)	vasopressin 40 units/50 ml (0.8 unit/ml) ssc premade infusion	heparin (porcine) 10,000 unit/ml injection solution
33	heparin (porcine) 1,000 unit/ml injection solution	midazolam 1 mg/ml in 0.9 % sodium chloride intravenous	cefazolin 1 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	heparin (porcine) for crrt 25,000 unit/250 ml in 0.45 % sodium chloride iv solution	vasopressin 40 units/50 ml (0.8 unit/ml) ssc premade infusion	dextrose 5 % and lactated ringers intravenous solution	lorazepam 2 mg/ml injection syringe	vancomycin 1.5 gram/500 ml in 0.9 % sodium chloride intravenous solution	fentanyl (pf) 2,500 mcg/50 ml (50 mcg/ml) intravenous pca syringe	dopamine 800 mg/500 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution
34	dexmedetomidine 200 mcg/50 ml (4 mcg/ml) in 0.9 % sodium chloride iv	vasopressin (pitressin) infusion 50 unit/50 ml	amiodarone 150 mg/100 ml (1.5 mg/ml) in dextrose, iso-osmotic iv	heparin (porcine) 100 unit/ml bolus from infusion	pentobarbital 2500mg/50 ml adult infusion	diazepam 5 mg/ml injection syringe	vancomycin 1 gram/200 ml in dextrose 5 % intravenous piggyback	morphine 1 mg/ml in dextrose 5 % intravenous solution	diazepam 5 mg/ml injection syringe	famotidine (pf) 20 mg/2 ml intravenous solution
35	dextrose 5 % and 0.9 % sodium chloride intravenous solution	albumin, human 25 % intravenous solution	fentanyl (pf) 2,500 mcg/50 ml (50 mcg/ml) intravenous pca syringe	lactated ringers iv bolus	sodium chloride 0.45 % intravenous solution	dextrose 5 % and 0.9 % sodium chloride intravenous solution	octreotide acetate 100 mcg/ml injection solution	lorazepam 2 mg/ml injection syringe	vancomycin 1 gram/200 ml in dextrose 5 % intravenous piggyback	lactated ringers iv bolus
36	dobutamine 250 mg/250 ml (1 mg/ml) in 5 % dextrose intravenous	vancomycin 1 gram/200 ml in dextrose 5 % intravenous piggyback	lorazepam 2 mg/ml injection syringe	lorazepam 2 mg/ml injection syringe	heparin (porcine) 1,000 unit/ml injection solution	midazolam 1 mg/ml injection solution	sodium chloride 0.9 % intravenous solution	cefazolin 1 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	pentobarbital 2500mg/50 ml adult infusion	heparin (porcine) for crrt 25,000 unit/250 ml in 0.45 % sodium chloride iv solution
37	sodium chloride 4 mEq/ml intravenous solution	cefepime 2 gram/100 ml in dextrose (iso-osmotic) intravenous piggyback	vasopressin 40 units/50 ml (0.8 unit/ml) ssc premade infusion	fentanyl (pf) 2,500 mcg/50 ml (50 mcg/ml) intravenous pca syringe	phenylephrine 20 mg/250 ml (80 mcg/ml) in 0.9 % sodium chloride iv	phenylephrine 20 mg/250 ml (80 mcg/ml) in 0.9 % sodium chloride iv	dexmedetomidine 200 mcg/50 ml (4 mcg/ml) in 0.9 % sodium chloride iv	vancomycin 1.25 gram/250 ml in 0.9 % sodium chloride intravenous	sodium chloride 0.45 % intravenous solution	nitroglycerin 50 mg/250 ml (200 mcg/ml) in 5 % dextrose intravenous
38	heparin 30,000 units (cell saver) in 1000 ml ns	norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in 0.9 % nacl iv	heparin (porcine) 1,000 unit/ml injection solution	midazolam 1 mg/ml injection solution	midazolam 1 mg/ml injection solution	heparin (porcine) 100 unit/ml bolus from infusion	amiodarone 360 mg/200 ml (1.8 mg/ml) in dextrose, iso-osmotic iv	amiodarone 150 mg/100 ml (1.5 mg/ml) in dextrose, iso-osmotic iv	heparin (porcine) 1,000 unit/ml injection solution	morphine 1 mg/ml in 0.9 % sodium chloride injectable pump reservoir
39	norepinephrine bitartrate 8	lorazepam 2 mg/ml	amiodarone 360 mg/200 ml	midazolam 1 mg/ml in 0.9 %	morphine 2 mg/ml injection pf	morphine 1 mg/ml in 0.9 %	mannitol 25 % intravenou	midazolam 1 mg/ml in 0.9 %	vasopressin (pitressin)	albumin, human 5 % intravenou

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	mg/250 ml (32 mcg/ml) in 0.9 % nacl iv	injection wrapper	(1.8 mg/ml) in dextrose, iso-osmotic iv	sodium chloride intravenous	wrapper	sodium chloride injectable pump reservoir	s solution	sodium chloride intravenous	infusion 40 units/100 ml	s solution
40	epinephrine hcl 8 mg/250 ml (32 mcg/ml) in 5 % dextrose intravenous	propofol infusion 10 mg/ml	sodium chloride 0.45 % intravenous solution	fentanyl (pf) 10 mcg/ml in 0.9 % sodium chloride intravenous wrapper	vasopressin (pitressin) infusion 50 unit/50 ml	lactated ringers intravenous solution	hydromorphone 1 mg/ml in ns infusion wrapper	fentanyl (pf) 10 mcg/ml in 0.9 % sodium chloride intravenous wrapper	amiodarone 450 mg/250 ml (1.8 mg/ml) in dextrose 5 % intravenous solution	heparin (porcine) 100 unit/ml bolus from infusion
41	clevidipine 25 mg/50 ml intravenous emulsion	heparin (porcine) 1,000 unit/ml injection solution	lorazepam 2 mg/ml injection wrapper	cefazolin 1 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	heparin 30,000 units (cell saver) in 1000 ml ns	cefazolin 1 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	propofol infusion 10 mg/ml	vasopressin 40 units/50 ml (0.8 unit/ml) ssc premade infusion	vasopressin (pitressin) infusion 50 unit/50 ml	piperacillin-tazobactam 3.375 gm/50ml dextrose (extended duration)
42	famotidine (pf) 20 mg/2 ml intravenous solution	dextrose 10 % iv bolus	dextrose 5 % and lactated ringers intravenous solution	octreotide acetate 100 mcg/ml injection solution	dextrose 10 % iv bolus	insulin u-100 regular human 100 unit/ml injection solution	dextrose 5 % in water (d5w) intravenous solution	vasopressin (pitressin) infusion 40 units/100 ml	cefepime 2 gram/100 ml in dextrose (iso-osmotic) intravenous piggyback	lactated ringers intravenous solution
43	sodium chloride 0.45 % intravenous solution	midazolam (pf) 1 mg/ml injection solution	ceftriaxone 2 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	epinephrine hcl 8 mg/250 ml (32 mcg/ml) in 5 % dextrose intravenous	heparin (porcine) for crrt 25,000 unit/250 ml in 0.45 % sodium chloride iv solution	dopamine 800 mg/500 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution	levofloxacin 750 mg/150 ml in 5 % dextrose intravenous piggyback	octreotide acetate 100 mcg/ml injection solution	dextrose 5 % and 0.9 % sodium chloride intravenous solution	lorazepam 2 mg/ml injection syringe
44	sodium chloride 3 % intravenous injection solution	epinephrine hcl 8 mg/250 ml (32 mcg/ml) in 5 % dextrose intravenous	fentanyl (pf) 50 mcg/ml injection solution	pentobarbital 2500mg/50 ml adult infusion	lorazepam 2 mg/ml injection wrapper	vancomycin 1 gram/200 ml in dextrose 5 % intravenous piggyback	famotidine (pf) 20 mg/50 ml in 0.9 % nacl (iso) intravenous piggyback	sodium chloride 0.45 % intravenous solution	dextrose 10 % iv bolus	amiodarone 150 mg/100 ml (1.5 mg/ml) in dextrose, iso-osmotic iv
45	piperacillin-tazobactam 4.5 gram/100 ml dextrose(iso-osmotic) iv piggyback	vancomycin 1.25 gram/250 ml in 0.9 % sodium chloride intravenous	famotidine (pf) 20 mg/2 ml intravenous solution	nitroglycerin 50 mg/250 ml (200 mcg/ml) in 5 % dextrose intravenous	nitroglycerin 100 mg/250 ml (400 mcg/ml) in 5 % dextrose intravenous	nitroglycerin 100 mg/250 ml (400 mcg/ml) in 5 % dextrose intravenous	piperacillin-tazobactam 3.375 gram/50 ml dextrose(iso-os) iv piggyback	pentobarbital 2500mg/50 ml adult infusion	famotidine (pf) 20 mg/50 ml in 0.9 % nacl (iso) intravenous piggyback	midazolam 1 mg/ml injection solution
46	lactated ringers irrigation solution	piperacillin-tazobactam 3.375 gram/50 ml dextrose (iso-os) iv piggyback	vancomycin 1,000 mg intravenous injection	dextrose 5 % and 0.9 % sodium chloride intravenous solution	morphine 10 mg/ml injection solution	vasopressin (pitressin) infusion 40 units/100 ml	cisatracurium 2 mg/ml intravenous solution	piperacillin-tazobactam 3.375 gram/50 ml dextrose(iso-os) iv piggyback	epinephrine hcl 8 mg/250 ml (32 mcg/ml) in 5 % dextrose intravenous	propofol 10 mg/ml intravenous emulsion
47	vasopressi	fentanyl	heparin,	albumin,	hydromorp	lactated	dobutamin	cefepime 2	clevidipine	pentobarbit

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	n (pitressin) infusion 50 unit/50 ml	(pf) 50 mcg/ml injection solution	porcine (pf) 100 unit/ml intravenous syringe	human 25 % intravenous solution	hone 1 mg/ml injection syringe	ringers iv bolus	e 500 mg/250 ml (2,000 mcg/ml) in 5 % dextrose iv	gram/100 ml in dextrose (iso-osmotic) intravenous piggyback	25 mg/50 ml intravenous emulsion	al 2500mg/50 ml adult infusion
48	piperacillin-tazobactam 3.375 gram/50 ml dextrose(iso-os) iv piggyback	dobutamine 500 mg/250 ml (2,000 mcg/ml) in 5 % dextrose iv	hydromorphone 2 mg/ml injection syringe	cefepime 2 gram/100 ml in dextrose (iso-osmotic) intravenous piggyback	piperacillin-tazobactam 4.5 gram/100 ml dextrose(iso-osmotic) iv piggyback	hydromorphone 1 mg/ml in ns infusion wrapper	famotidine (pf) 20 mg/2 ml intravenous solution	hydromorphone (pf) 1 mg/ml injection solution	hydromorphone 1 mg/ml injection syringe	nitroglycerin 100 mg/250 ml (400 mcg/ml) in 5 % dextrose intravenous
49	fluconazole 400 mg/200 ml in sod. chloride(iso) intravenous piggyback	famotidine (pf) 20 mg/2 ml intravenous solution	piperacillin-tazobactam 2.25 gram/50 ml in dextrose(iso) iv piggyback	hydromorphone 1 mg/ml in ns infusion wrapper	dextrose 5 % and lactated ringers intravenous solution	heparin 30,000 units (cell saver) in 1000 ml ns	amiodarone 150 mg/100 ml (1.5 mg/ml) in dextrose, iso-osmotic iv	levofloxacin 500 mg/100 ml in 5 % dextrose intravenous piggyback	cisatracurium 2 mg/ml intravenous solution	sodium chloride 0.45 % intravenous solution
50	dextrose 10 % in water (d10w) intravenous solution	vancomycin 1,000 mg intravenous injection	lactated ringers irrigation solution	famotidine (pf) 20 mg/50 ml in 0.9 % nacl (iso) intravenous piggyback	fentanyl (pf) 2,500 mcg/50 ml (50 mcg/ml) intravenous pca syringe	sodium chloride 3 % intravenous injection solution	piperacillin-tazobactam 4.5 gram/100 ml dextrose(iso-osmotic) iv piggyback	norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in 0.9 % nacl iv	nitroglycerin 50 mg/250 ml (200 mcg/ml) in 5 % dextrose intravenous	vasopressin (pitressin) infusion 40 units/100 ml
51	cefepime 1 gram solution for injection	cefazolin 1 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	fluconazole 400 mg/200 ml in sod. chloride(iso) intravenous piggyback	nitroglycerin 100 mg/250 ml (400 mcg/ml) in 5 % dextrose intravenous	cefazolin 1 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	vasopressin (pitressin) infusion 50 unit/50 ml	dextrose 5 % and 0.45 % sodium chloride intravenous solution	famotidine (pf) 20 mg/50 ml in 0.9 % nacl (iso) intravenous piggyback	heparin (porcine) 100 unit/ml bolus from infusion	epinephrine hcl 8 mg/250 ml (32 mcg/ml) in 5 % dextrose intravenous
52	hydromorphone 50 mg/50 ml (1 mg/ml) in 0.9 % sod.chloride iv pump resevoir	ceftriaxone 1 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	albumin, human 5 % intravenous solution	amiodarone 150 mg/100 ml (1.5 mg/ml) in dextrose, iso-osmotic iv	dextrose 5 % and 0.45 % sodium chloride intravenous solution	piperacillin-tazobactam 3.375 gram/50 ml dextrose(iso-os) iv piggyback	cefepime 2 gram/100 ml in dextrose (iso-osmotic) intravenous piggyback	lorazepam 2 mg/ml injection wrapper	fentanyl (pf) 50 mcg/ml injection solution	amiodarone 450 mg/250 ml (1.8 mg/ml) in dextrose 5 % intravenous solution
53	ceftriaxone 1 gram solution for injection	heparin (porcine) 100 unit/ml bolus from infusion	dobutamine 500 mg/250 ml (2,000 mcg/ml) in 5 % dextrose iv	phenylephrine 20 mg/250 ml (80 mcg/ml) in 0.9 % sodium chloride iv	heparin (porcine) 100 unit/ml bolus from infusion	heparin (porcine) 1,000 unit/ml injection solution	albumin, human 25 % intravenous solution	hydromorphone 2 mg/ml injection syringe	dexmedetomidine 400 mcg/100 ml (4 mcg/ml) in 0.9 % sodium chloride iv	mannitol 25 % intravenous solution
54	lactated ringers iv bolus	etomidate 2 mg/ml intravenous solution	famotidine (pf) 20 mg/50 ml in 0.9 % nacl (iso) intravenous	dexmedetomidine 400 mcg/100 ml (4 mcg/ml) in 0.9 % sodium	albumin, human 25 % intravenous solution	hydromorphone 1 mg/ml injection syringe	dextrose 10 % in water (d10w) intravenous solution	albumin, human 25 % intravenous solution	linezolid in 5% dextrose in water 600 mg/300 ml intravenous	morphine 2 mg/ml intravenous cartridge

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			piggyback	chloride iv					piggyback	
55	hydromorphone 1 mg/ml injection syringe	sodium chloride 0.45 % intravenous solution	heparin (porcine) 10,000 unit/1,000 ml in ns (unch cupid)	dextrose 5 % and 0.45 % sodium chloride intravenous solution	albumin, human 5 % intravenous solution	famotidine (pf) 20 mg/50 ml in 0.9 % nacl (iso) intravenous piggyback	etomidate 2 mg/ml intravenous solution	cefazolin 2 gram/100 ml in dextrose(iso-osmotic) intravenous piggyback	lactated ringers irrigation solution	sodium chloride 4 mEq/ml intravenous solution
56	vancomycin 1 gram/200 ml in dextrose 5 % intravenous piggyback	dextrose 5 % in water (d5w) intravenous solution	dobutamine 250 mg/250 ml (1 mg/ml) in 5 % dextrose intravenous	morphine 2 mg/ml injection pf wrapper	dextrose 10 % in water (d10w) intravenous solution	nitroglycerin 50 mg/250 ml (200 mcg/ml) in 5 % dextrose intravenous	lidocaine (pf) 100 mg/5 ml (2 %) intravenous syringe	lactated ringers iv bolus	cefazolin 1 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	propofol infusion 10 mg/ml
57	dobutamine 1,000 mg/250 ml(4,000 mcg/ml) in 5 % dextrose iv	dopamine 400 mg/250 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution	cefazolin 3 gram/100 ml in 0.9 % sodium chloride intravenous piggyback	fluconazole 400 mg/200 ml in sod. chloride(iso) intravenous piggyback	heparin (porcine) 10,000 unit/1,000 ml in ns (unch cupid)	etomidate 2 mg/ml intravenous solution	cefazolin 2 gram/100 ml in dextrose(iso-osmotic) intravenous piggyback	hydromorphone 1 mg/ml in ns infusion wrapper	ceftriaxone 1 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	dextrose 5 % and lactated ringers intravenous solution
58	hydromorphone (pf) 1 mg/ml injection solution	clindamycin 900 mg/50 ml in 5 % dextrose intravenous piggyback	cefazolin 2 gram/100 ml in dextrose(iso-osmotic) intravenous piggyback	morphine 1 mg/ml in 0.9 % sodium chloride injectable pump reservoir	propofol infusion 10 mg/ml	fentanyl (pf) 50 mcg/ml injection solution	ceftriaxone 1 gram solution for injection	dextrose 5 % and 0.9 % sodium chloride intravenous solution	dexmedetomidine 200 mcg/50 ml (4 mcg/ml) in 0.9 % sodium chloride iv	lorazepam 2 mg/ml injection wrapper
59	midazolam 5 mg/ml (combined) injection solution wrapper	dextrose 5 % and 0.9 % sodium chloride intravenous solution	albumin, human 25 % intravenous solution	lidocaine (pf) 100 mg/5 ml (2 %) intravenous syringe	dextrose 5 % and 0.9 % sodium chloride intravenous solution	linezolid in 5% dextrose in water 600 mg/300 ml intravenous piggyback	amiodarone 450 mg/250 ml (1.8 mg/ml) in dextrose 5 % intravenous solution	esmolol 2,500 mg/250 ml (10 mg/ml) in sodium chloride (iso-osmotic) iv	morphine 2 mg/ml intravenous cartridge	cisatracurium 2 mg/ml intravenous solution
60	meperidine (pf) 25 mg/ml injection syringe	amiodarone 450 mg/250 ml (1.8 mg/ml) in dextrose 5 % intravenous solution	dopamine 400 mg/250 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution	sodium chloride 0.9 % intravenous solution	cefazolin 2 gram/100 ml in dextrose(iso-osmotic) intravenous piggyback	vancomycin 1,000 mg intravenous injection	fluconazole 400 mg/200 ml in sod. chloride(iso) intravenous piggyback	vasopressin 40 units/50 ml (0.8 unit/ml) in ns infusion	lidocaine (pf) 100 mg/5 ml (2 %) intravenous syringe	phenylephrine 20 mg/250 ml (80 mcg/ml) in 0.9 % sodium chloride iv
61	clindamycin 900 mg/50 ml in 5 % dextrose intravenous piggyback	dobutamine 1,000 mg/250 ml(4,000 mcg/ml) in 5 % dextrose iv	norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in dextrose 5 % iv	cefepime 1 gram solution for injection	lactated ringers iv bolus	lactated ringers irrigation solution	norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in dextrose 5 % iv	sodium chloride 3 % intravenous injection solution	sodium chloride 0.9 % intravenous solution	lactated ringers irrigation solution
62	heparin, porcine (pf) 100 unit/ml intravenou	fluconazole 400 mg/200 ml in sod.	vasopressin 40 units/50 ml (0.8 unit/ml) in	morphine 1 mg/ml in dextrose 5 % intravenou	dextrose 5 % in water (d5w) intravenou	cefepime 2 gram/100 ml in dextrose (iso-	morphine 1 mg/ml in 0.9 % sodium chloride	lactated ringers irrigation solution	morphine 1 mg/ml in dextrose 5 % intravenou	piperacillin-tazobactam 3.375 gram/50

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	s syringe	chloride (iso) intravenous piggyback	ns infusion	s solution	s solution	osmotic) intravenous piggyback	injectable pump reservoir		s solution	ml dextrose(iso-os) iv piggyback
63	linezolid in 5% dextrose in water 600 mg/300 ml intravenous piggyback	morphine 1 mg/ml in 0.9 % sodium chloride injectable pump reservoir	fluconazole 200 mg/100 ml in sod. chloride (iso) intravenous piggyback	cefazolin 2 gram/100 ml in dextrose(iso-osmotic) intravenous piggyback	clindamycin 900 mg/50 ml in 5 % dextrose intravenous piggyback	morphine 2 mg/ml injection pf wrapper	cefazolin 2 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	milrinone 20 mg/100 ml(200 mcg/ml) in 5 % dextrose intravenous piggyback	heparin (porcine) 10,000 unit/1,000 ml in ns (unch cupid)	morphine 2 mg/ml injection pf wrapper
64	lorazepam 2 mg/ml injection wrapper	fluconazole 200 mg/100 ml in sod. chloride (iso) intravenous piggyback	norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in 0.9 % nacl iv	hydromorphone 50 mg/50 ml (1 mg/ml) in 0.9 % sod.chloride iv pump resevoir	fluconazole 400 mg/200 ml in sod. chloride(iso) intravenous piggyback	midazolam 1 mg/ml in 0.9 % sodium chloride intravenous	milrinone 20 mg/100 ml(200 mcg/ml) in 5 % dextrose intravenous piggyback	meperidine (pf) 25 mg/ml injection syringe	lorazepam 2 mg/ml injection wrapper	heparin (porcine) 10,000 unit/1,000 ml in ns (unch cupid)
65	pantoprazole 40 mg intravenous solution	dextrose 10 % in water (d10w) intravenous solution	nitroglycerin 50 mg/250 ml (200 mcg/ml) in 5 % dextrose intravenous	heparin (porcine) 10,000 unit/1,000 ml in ns (unch cupid)	dobutamine 250 mg/250 ml (1 mg/ml) in 5 % dextrose intravenous	albumin, human 25 % intravenous solution	clindamycin 900 mg/50 ml in 5 % dextrose intravenous piggyback	digoxin 250 mcg/ml (0.25 mg/ml) injection solution	hydromorphone 1 mg/ml in ns infusion wrapper	dobutamine 500 mg/250 ml (2,000 mcg/ml) in 5 % dextrose iv
66	ceftriaxone 1 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	cefazolin 2 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	piperacillin-tazobactam 3.375 gram/50 ml dextrose(iso-os) iv piggyback	vasopressin 40 units/50 ml (0.8 unit/ml) ssc premade infusion	lidocaine (pf) 4 mg/ml (0.4 %) in 5 % dextrose intravenous solution	ceftriaxone 1 gram solution for injection	dopamine 800 mg/500 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution	eptifibatide 0.75 mg/ml intravenous solution	heparin (porcine) 25,000 unit/250 ml in 0.45 % sodium chloride iv solution	etomidate 2 mg/ml intravenous solution
67	dopamine 800 mg/500 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution	linezolid in 5% dextrose in water 600 mg/300 ml intravenous piggyback	hydromorphone 1 mg/ml injection syringe	vasopressin (pitressin) infusion 40 units/100 ml	mannitol 25 % intravenous solution	heparin (porcine) 25,000 unit/250 ml in 0.45 % sodium chloride iv solution	vasopressin (pitressin) infusion 40 units/100 ml	hydromorphone 50 mg/50 ml (1 mg/ml) in 0.9 % sod.chloride iv pump resevoir	esmolol 2,500 mg/250 ml (10 mg/ml) in sodium chloride (iso-osmotic) iv	dextrose 5 % and 0.9 % sodium chloride intravenous solution
68	morphine 2 mg/ml injection pf wrapper	milrinone 20 mg/100 ml(200 mcg/ml) in 5 % dextrose intravenous piggyback	digoxin 250 mcg/ml (0.25 mg/ml) injection solution	clindamycin 600 mg/50 ml in 5 % dextrose intravenous piggyback	fentanyl (sublimaze) 100 mcg in ns 50ml (rex or)	eptifibatide 0.75 mg/ml intravenous solution	heparin (porcine) 100 unit/ml bolus from infusion	midazolam 1 mg/ml injection solution	eptifibatide 0.75 mg/ml intravenous solution	dobutamine 250 mg/250 ml (1 mg/ml) in 5 % dextrose intravenous
69	norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in	hydromorphone 1 mg/ml injection syringe	heparin (porcine) 100 unit/ml bolus from infusion	midazolam 5 mg/ml (combined) injection solution wrapper	hydromorphone 1 mg/ml in ns infusion wrapper	fluconazole 400 mg/200 ml in sod. chloride(iso)	pantoprazole 40 mg intravenous solution	dextrose 5 % in water (d5w) intravenous solution	hydromorphone 2 mg/ml injection syringe	vasopressin 40 units/50 ml (0.8 unit/ml) ssc

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	dextrose 5 % iv					intravenous piggyback				premade infusion
70	fluconazole 200 mg/100 ml in sod. chloride (iso) intravenous piggyback	meperidine (pf) 25 mg/ml injection syringe	heparin (porcine) 25,000 unit/250 ml in 0.45 % sodium chloride iv solution	norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in dextrose 5 % iv	famotidine (pf) 20 mg/50 ml in 0.9 % nacl (iso) intravenous piggyback	cefazolin 2 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	lorazepam 2 mg/ml injection wrapper	fentanyl (sublimaze) 100 mcg in ns 50ml (rex or)	dobutamine 250 mg/250 ml (1 mg/ml) in 5 % dextrose intravenous	cefepime 2 gram/100 ml in dextrose (iso-osmotic) intravenous piggyback
71	succinylcholine chloride 20mg/ml syringe/vial wrapper	midazolam 1 mg/ml injection solution	hydromorphone 1 mg/ml in ns infusion wrapper	digoxin 250 mcg/ml (0.25 mg/ml) injection solution	amiodarone 150 mg/100 ml (1.5 mg/ml) in dextrose, iso-osmotic iv	piperacillin-tazobactam 3.375 gm/50ml dextrose (extended duration)	alteplase 0.81 mg/kg stroke infusion	dexmedetomidine 200 mcg/50 ml (4 mcg/ml) in 0.9 % sodium chloride iv	morphine 1 mg/ml in 0.9 % sodium chloride injectable pump reservoir	heparin (porcine) 25,000 unit/250 ml in 0.45 % sodium chloride iv solution
72	vancomycin 1.5 gram/500 ml in 0.9 % sodium chloride intravenous solution	vasopressin (pitressin) infusion 40 units/100 ml	epinephrine hcl 8 mg/250 ml (32 mcg/ml) in 5 % dextrose intravenous	eptifibatide 0.75 mg/ml intravenous solution	dexmedetomidine 200 mcg/50 ml (4 mcg/ml) in 0.9 % sodium chloride iv	dextrose 5 % in water (d5w) intravenous solution	eptifibatide 0.75 mg/ml intravenous solution	dextrose 10 % in water (d10w) intravenous solution	midazolam 1 mg/ml in 0.9 % sodium chloride intravenous	esmolol 2,500 mg/250 ml (10 mg/ml) in sodium chloride (iso-osmotic) iv
73	famotidine (pf) 20 mg/50 ml in 0.9 % nacl (iso) intravenous piggyback	pantoprazole 40 mg intravenous solution	mannitol 20 % intravenous solution	dopamine 400 mg/250 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution	ceftriaxone 1 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	vancomycin 1.5 gram/500 ml in 0.9 % sodium chloride intravenous solution	morphine 2 mg/ml injection pf wrapper	norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in dextrose 5 % iv	dextrose 10 % in water (d10w) intravenous solution	digoxin 250 mcg/ml (0.25 mg/ml) injection solution
74	metronidazole 500 mg/100 ml-sodium chloride(iso) intravenous piggyback	heparin (porcine) 25,000 unit/250 ml in 0.45 % sodium chloride iv solution	dextrose 5 % and 0.45 % sodium chloride intravenous solution	vancomycin 1.75 gram/500 ml in 0.9 % sodium chloride intravenous	diazepam 5 mg/ml injection syringe	dexmedetomidine 200 mcg/50 ml (4 mcg/ml) in 0.9 % sodium chloride iv	clindamycin 600 mg/50 ml in 5 % dextrose intravenous piggyback	dexmedetomidine 400 mcg/100 ml (4 mcg/ml) in 0.9 % sodium chloride iv	succinylcholine chloride 20mg/ml syringe/vial wrapper	phenobarbital sodium 65 mg/ml injection solution
75	hydromorphone 1 mg/ml in ns infusion wrapper	amiodarone 360 mg/200 ml (1.8 mg/ml) in dextrose, iso-osmotic iv	dextrose 10 % in water (d10w) intravenous solution	ceftriaxone 1 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	piperacillin-tazobactam 3.375 gm/50ml dextrose (extended duration)	alteplase 0.81 mg/kg stroke infusion	cyclosporine 1 mg/ml ns aviva iv	heparin (porcine) 10,000 unit/1,000 ml in 0.9 % sod. chloride iv solution	meperidine (pf) 25 mg/ml injection syringe	hydromorphone 1 mg/ml injection syringe
76	cefazolin 2 gram/100 ml in dextrose(iso-osmotic) intravenous piggyback	midazolam (pf) 5 mg/ml injection solution	midazolam 1 mg/ml in 0.9 % sodium chloride intravenous	propofol infusion 10 mg/ml	vancomycin 1 gram/200 ml in dextrose 5 % intravenous piggyback	dextrose 10 % in water (d10w) intravenous solution	cefepime 1 gram solution for injection	metronidazole 500 mg/100 ml-sodium chloride(iso) intravenous piggyback	midazolam 1 mg/ml injection solution	heparin, porcine (pf) 100 unit/ml intravenous syringe
77	albumin, human 25 % intravenous solution	albumin, human 5 % intravenous solution	hydromorphone 50 mg/50 ml (1 mg/ml) in 0.9 % sod.chlorid	heparin, porcine (pf) 100 unit/ml intravenous syringe	dobutamine 500 mg/250 ml (2,000 mcg/ml) in 5 %	norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in	nitroglycerin 100 mg/250 ml (400 mcg/ml) in 5 %	famotidine 10 mg/ml injection solution (multi-vial size)	fentanyl (sublimaze) 100 mcg in ns 50ml (rex or)	fentanyl (pf) 50 mcg/ml injection solution

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			e iv pump resevoir		dextrose iv	dextrose 5 % iv	dextrose intravenous			
78	amiodarone 360 mg/200 ml (1.8 mg/ml) in dextrose, iso-osmotic iv	alteplase 0.81 mg/kg stroke infusion	midazolam 1 mg/ml injection solution	lactated ringers intravenous solution	heparin, porcine (pf) 100 unit/ml intravenous syringe	dexmedetomidine 400 mcg/100 ml (4 mcg/ml) in 0.9 % sodium chloride iv	lidocaine (pf) 4 mg/ml (0.4 %) in 5 % dextrose intravenous solution	vancomycin 1 gram/200 ml in dextrose 5 % intravenous piggyback	midazolam (pf) 5 mg/ml injection solution	vancomycin 1.75 gram/500 ml in 0.9 % sodium chloride intravenous
79	piperacillin-tazobactam 2.25 gram/50 ml in dextrose(iso) iv piggyback	lorazepam 2 mg/ml injection syringe	cyclosporine 1 mg/ml ns aviva iv	vancomycin 1.5 gram/500 ml in 0.9 % sodium chloride intravenous solution	famotidine (pf) 20 mg/2 ml intravenous solution	amiodarone 150 mg/100 ml (1.5 mg/ml) in dextrose, iso-osmotic iv	heparin, porcine (pf) 100 unit/ml intravenous syringe	vancomycin 2 gram/500 ml in 0.9 % sodium chloride intravenous	propofol infusion 10 mg/ml	morphine 1 mg/ml in dextrose 5 % intravenous solution
80	dextrose 10 % iv bolus	heparin, porcine (pf) 100 unit/ml intravenous syringe	fentanyl (sublimaze) 100 mcg in ns 50ml (rex or)	vancomycin 1 gram/200 ml in dextrose 5 % intravenous piggyback	sodium chloride 4 mEq/ml intravenous solution	heparin (porcine) 10,000 unit/1,000 ml in 0.9 % sod. chloride iv solution	fentanyl (sublimaze) 100 mcg in ns 50ml (rex or)	dobutamine 500 mg/250 ml (2,000 mcg/ml) in 5 % dextrose iv	alteplase 0.81 mg/kg stroke infusion	heparin (porcine) 10,000 unit/1,000 ml in 0.9 % sod. chloride iv solution
81	heparin, porcine (pf) 10 unit/ml intravenous syringe	dextrose 5 % and 0.45 % sodium chloride intravenous solution	vasopressin (pitressin) infusion 40 units/100 ml	metronidazole 500 mg/100 ml-sodium chloride(iso) intravenous piggyback	levofloxacin 750 mg/150 ml in 5 % dextrose intravenous piggyback	metronidazole 500 mg/100 ml-sodium chloride(iso) intravenous piggyback	sodium chloride 4 mEq/ml intravenous solution	cefazolin 2 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	dextrose 5 % in water (d5w) intravenous solution	midazolam (pf) 5 mg/ml injection solution
82	cisatracurium 2 mg/ml intravenous solution	amiodarone 150 mg/100 ml (1.5 mg/ml) in dextrose, iso-osmotic iv	vancomycin 1 gram/200 ml in dextrose 5 % intravenous piggyback	ceftriaxone 1 gram solution for injection	cefepime 2 gram/100 ml in dextrose (iso-osmotic) intravenous piggyback	amiodarone 450 mg/250 ml (1.8 mg/ml) in dextrose 5 % intravenous solution	aztreonam 1 gram solution for iv push	aztreonam 1 gram solution for iv push	heparin, porcine (pf) 100 unit/ml intravenous syringe	hydromorphone 1 mg/ml in ns infusion wrapper
83	pentobarbital 2500mg/50 ml adult infusion	sodium chloride 0.9 % intravenous solution	vancomycin 1.75 gram/500 ml in 0.9 % sodium chloride intravenous	heparin 30,000 units (cell saver) in 1000 ml ns	amiodarone 360 mg/200 ml (1.8 mg/ml) in dextrose, iso-osmotic iv	cyclosporine 1 mg/ml ns aviva iv	sodium chloride 0.45 % intravenous solution	dextrose 5 % and lactated ringers intravenous solution	clindamycin 900 mg/50 ml in 5 % dextrose intravenous piggyback	dextrose 10 % in water (d10w) intravenous solution
84	dopamine 400 mg/250 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution	diazepam 5 mg/ml injection syringe	dopamine 800 mg/500 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution	fentanyl (sublimaze) 100 mcg in ns 50ml (rex or)	mannitol 20 % intravenous solution	phenobarbital sodium 65 mg/ml injection solution	vasopressin (pitressin) infusion 50 unit/50 ml	mannitol 20 % intravenous solution	metronidazole 500 mg/100 ml-sodium chloride(iso) intravenous piggyback	norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in dextrose 5 % iv
85	levofloxacin 750 mg/150 ml in 5 % dextrose intravenous	nitroglycerin 100 mg/250 ml (400 mcg/ml) in 5 %	pentobarbital sodium 50 mg/ml injection solution	sodium chloride 4 mEq/ml intravenous solution	vancomycin 1.75 gram/500 ml in 0.9 % sodium chloride	dobutamine 500 mg/250 ml (2,000 mcg/ml) in 5 % dextrose iv	midazolam 5 mg/ml (combined) injection solution wrapper	amiodarone 360 mg/200 ml (1.8 mg/ml) in dextrose, iso-	amiodarone 360 mg/200 ml (1.8 mg/ml) in dextrose, iso-	cyclosporine 1 mg/ml ns aviva iv

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	piggyback	dextrose intravenous			intravenous			osmotic iv	osmotic iv	
86	midazolam 1 mg/ml in 0.9 % sodium chloride intravenous	piperacillin-tazobactam 3.375 gm/50ml dextrose (extended duration)	cisatracurium 2 mg/ml intravenous solution	vancomycin 2 gram/500 ml in 0.9 % sodium chloride intravenous	dopamine 800 mg/500 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution	lorazepam 2 mg/ml injection syringe	pentobarbital sodium 50 mg/ml injection solution	midazolam (pf) 1 mg/ml in 0.9 % sodium chloride intravenous solution	famotidine 10 mg/ml injection solution (multi-vial size)	vancomycin 1 gram/200 ml in dextrose 5 % intravenous piggyback
87	dexmedetomidine 400 mcg/100 ml (4 mcg/ml) in 0.9 % sodium chloride iv	cefazolin 2 gram/100 ml in dextrose (iso-osmotic) intravenous piggyback	metronidazole 500 mg/100 ml-sodium chloride(iso) intravenous piggyback	lactated ringers irrigation solution	midazolam 5 mg/ml (combined) injection solution wrapper	heparin (porcine) 10,000 unit/ml injection solution	nitroglycerin 50 mg/250 ml (200 mcg/ml) in 5 % dextrose intravenous	heparin, porcine (pf) 100 unit/ml intravenous syringe	cefepime 1 gram solution for injection	vancomycin 2 gram/500 ml in 0.9 % sodium chloride intravenous
88	nitroglycerin 50 mg/250 ml (200 mcg/ml) in 5 % dextrose intravenous	lactated ringers irrigation solution	levofloxacin 750 mg/150 ml in 5 % dextrose intravenous piggyback	levofloxacin 750 mg/150 ml in 5 % dextrose intravenous piggyback	insulin u-100 regular human 100 unit/ml injection solution	vancomycin 1.25 gram/250 ml in 0.9 % sodium chloride intravenous	hydromorphone 1 mg/ml injection syringe	levofloxacin 750 mg/150 ml in 5 % dextrose intravenous piggyback	heparin 30,000 units (cell saver) in 1000 ml ns	levofloxacin 750 mg/150 ml in 5 % dextrose intravenous piggyback
89	fat emulsion 20 % intravenous	famotidine (pf) 20 mg/50 ml in 0.9 % nacl (iso) intravenous piggyback	clindamycin 600 mg/50 ml in 5 % dextrose intravenous piggyback	milrinone 20 mg/100 ml(200 mcg/ml) in 5 % dextrose intravenous piggyback	pentobarbital sodium 50 mg/ml injection solution	hydromorphone 50 mg/50 ml (1 mg/ml) in 0.9 % sod.chloride iv pump resevoir	pentobarbital 2500mg/50 ml adult infusion	heparin (porcine) 1,000 unit/ml injection solution	vancomycin 2 gram/500 ml in 0.9 % sodium chloride intravenous	cefazolin 2 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback
90	dextrose 5 % and lactated ringers intravenous solution	dopamine 800 mg/500 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution	dexmedetomidine 200 mcg/50 ml (4 mcg/ml) in 0.9 % sodium chloride iv	vasopressin 40 units/50 ml (0.8 unit/ml) in ns infusion	cisatracurium 2 mg/ml intravenous solution	hydromorphone 4 mg/ml injection syringe	dextrose 5 % and 0.9 % sodium chloride intravenous solution	piperacillin-tazobactam 2.25 gram/50 ml in dextrose(iso) iv piggyback	lidocaine (pf) 4 mg/ml (0.4 %) in 5 % dextrose intravenous solution	octreotide acetate 100 mcg/ml injection solution
91	heparin (porcine) 100 unit/ml bolus from infusion	dexmedetomidine 200 mcg/50 ml (4 mcg/ml) in 0.9 % sodium chloride iv	octreotide acetate 100 mcg/ml injection solution	hydromorphone 4 mg/ml injection syringe	aztreonam 2 gram solution for iv push	amiodarone 360 mg/200 ml (1.8 mg/ml) in dextrose, iso-osmotic iv	hydromorphone 50 mg/50 ml (1 mg/ml) in 0.9 % sod.chloride iv pump resevoir	heparin 30,000 units (cell saver) in 1000 ml ns	vancomycin 1.75 gram/500 ml in 0.9 % sodium chloride intravenous	amiodarone 360 mg/200 ml (1.8 mg/ml) in dextrose, iso-osmotic iv
92	morphine 10 mg/ml injection solution	pentobarbital sodium 50 mg/ml injection	lidocaine (pf) 4 mg/ml (0.4 %) in 5 % dextrose	cefazolin 2 gram/50 ml in dextrose (iso-osmotic)	midazolam 1 mg/ml in 0.9 % sodium chloride intravenou	famotidine 10 mg/ml injection solution (multi-vial size)	midazolam 1 mg/ml in 0.9 % sodium chloride intravenou	morphine 2 mg/ml injection pf wrapper	octreotide acetate 100 mcg/ml injection solution	fluconazole 200 mg/100 ml in sod. chloride (iso)

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		solution	intravenous solution	intravenous piggyback	s		s			intravenous piggyback
93	milrinone 20 mg/100 ml(200 mcg/ml) in 5 % dextrose intravenous piggyback	cisatracurium 2 mg/ml intravenous solution	milrinone 20 mg/100 ml(200 mcg/ml) in 5 % dextrose intravenous piggyback	hydromorphone 1 mg/ml injection syringe	cefazolin 3 gram/100 ml in 0.9 % sodium chloride intravenous piggyback	morphine 10 mg/ml injection solution	midazolam (pf) 1 mg/ml in 0.9 % sodium chloride intravenous solution	morphine 10 mg/ml injection solution	fluconazole 200 mg/100 ml in sod. chloride (iso) intravenous piggyback	pantoprazole 40 mg intravenous solution
94	heparin (porcine) 25,000 unit/250 ml in 0.45 % sodium chloride iv solution	sodium chloride 3 % intravenous bolus solution	vancomycin 1.25 gram/250 ml in 0.9 % sodium chloride intravenous	hydromorphone (pf) 1 mg/ml injection solution	sodium chloride 3 % intravenous bolus solution	milrinone 20 mg/100 ml(200 mcg/ml) in 5 % dextrose intravenous piggyback	dextrose 10 % iv bolus	lactated ringers intravenous solution	vecuronium bromide 10 mg intravenous solution	pentobarbital sodium 50 mg/ml injection solution
95	dobutamine 500 mg/250 ml (2,000 mcg/ml) in 5 % dextrose iv	sodium chloride 3 % intravenous injection solution	hydromorphone 4 mg/ml injection syringe	lorazepam 2 mg/ml injection wrapper	eptifibatide 0.75 mg/ml intravenous solution	midazolam 5 mg/ml (combined) injection solution wrapper	heparin 30,000 units (cell saver) in 1000 ml ns	cisatracurium 2 mg/ml intravenous solution	heparin, porcine (pf) 10 unit/ml intravenous syringe	midazolam 5 mg/ml (combined) injection solution wrapper
96	albumin, human 5 % intravenous solution	lidocaine (pf) 4 mg/ml (0.4 %) in 5 % dextrose intravenous solution	piperacillin - tazobactam 3.375 gm/50ml dextrose (extended duration)	piperacillin - tazobactam 4.5 gram/100 ml dextrose(iso-osmotic) iv piggyback	hydromorphone 4 mg/ml injection syringe	cisatracurium 2 mg/ml intravenous solution	famotidine 10 mg/ml injection solution (multi-vial size)	piperacillin - tazobactam 4.5 gram/100 ml dextrose(iso-osmotic) iv piggyback	albumin, human 25 % intravenous solution	midazolam 1 mg/ml in 0.9 % sodium chloride intravenous
97	cefazolin 2 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	vasopressin 40 units/50 ml (0.8 unit/ml) in ns infusion	morphine 2 mg/ml injection pf wrapper	piperacillin - tazobactam 3.375 gram/50 ml dextrose(iso-os) iv piggyback	famotidine 10 mg/ml injection solution (multi-vial size)	mannitol 25 % intravenous solution	vancomycin 1.5 gram/500 ml in 0.9 % sodium chloride intravenous solution	epinephrine hcl 8 mg/250 ml (32 mcg/ml) in 5 % dextrose intravenous	fat emulsion 20 % intravenous	dexmedetomidine 200 mcg/50 ml (4 mcg/ml) in 0.9 % sodium chloride iv
98	vasopressin (pitressin) infusion 40 units/100 ml	hydromorphone 4 mg/ml injection syringe	sodium chloride 3 % intravenous bolus solution	amiodarone 360 mg/200 ml (1.8 mg/ml) in dextrose, iso-osmotic iv	vasopressin (pitressin) infusion 40 units/100 ml	dextrose 5 % and 0.45 % sodium chloride intravenous solution	fentanyl (pf) 50 mcg/ml injection solution	heparin (porcine) 100 unit/ml load from infusion	milrinone 20 mg/100 ml(200 mcg/ml) in 5 % dextrose intravenous piggyback	sodium chloride 3 % intravenous bolus solution
99	heparin (porcine) 100 unit/ml load from infusion	famotidine 10 mg/ml injection solution (multi-vial size)	heparin (porcine) 100 unit/ml load from infusion	pentobarbital sodium 50 mg/ml injection solution	heparin (porcine) 25,000 unit/250 ml in 0.45 % sodium chloride iv solution	hydromorphone 2 mg/ml injection syringe	heparin (porcine) 25,000 unit/250 ml in 0.45 % sodium chloride iv solution	dextrose 10 % iv bolus	vancomycin 1,000 mg intravenous injection	cefepime 1 gram solution for injection
100	vecuronium bromide 20 mg intravenous solution	hydromorphone 1 mg/ml in ns infusion wrapper	alteplase 0.81 mg/kg stroke infusion	vecuronium bromide 20 mg intravenous solution	cefazolin 2 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	sodium chloride 3 % intravenous bolus solution	insulin u-100 regular human 100 unit/ml injection solution	heparin, porcine (pf) 10 unit/ml intravenous syringe	morphine (pf) 1 mg/ml in 0.9% sodium chloride intravenous solution	dextrose 10 % iv bolus

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101	digoxin 250 mcg/ml (0.25 mg/ml) injection solution	vancomycin 1.5 gram/500 ml in 0.9 % sodium chloride intravenous solution	meperidine (pf) 25 mg/ml injection syringe	sodium chloride 0.9 % iv bolus (cath lab)	vancomycin 1,000 mg intravenous injection	dextrose 10 % iv bolus	heparin (porcine) 100 unit/ml load from infusion	morphine 10 mg/ml injection syringe	morphine 2 mg/ml injection pf wrapper	albumin, human 25 % intravenous solution
102	fentanyl (pf) 50 mcg/ml injection solution	vecuronium bromide 10 mg intravenous solution	morphine 10 mg/ml injection syringe	pantoprazole 40 mg intravenous solution	amiodarone 450 mg/250 ml (1.8 mg/ml) in dextrose 5 % intravenous solution	heparin, porcine (pf) 100 unit/ml intravenous syringe	sodium chloride 3 % intravenous bolus solution	vecuronium bromide 20 mg intravenous solution	nitroglycerin 100 mg/250 ml (400 mcg/ml) in 5 % dextrose intravenous	diazepam 5 mg/ml injection syringe
103	phenobarbital sodium 65 mg/ml injection solution	mannitol 25 % intravenous solution	vancomycin 1.5 gram/500 ml in 0.9 % sodium chloride intravenous solution	dextrose 10 % iv bolus	lidocaine (pf) 100 mg/5 ml (2 %) intravenous syringe	morphine 10 mg/ml injection syringe	fluconazole 200 mg/100 ml in sod. chloride (iso) intravenous piggyback	heparin (porcine) 25,000 unit/250 ml in 0.45 % sodium chloride iv solution	norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in 0.9 % nacl iv	hydromorphone 4 mg/ml injection syringe
104	amiodarone 450 mg/250 ml (1.8 mg/ml) in dextrose 5 % intravenous solution	esmolol 2,500 mg/250 ml (10 mg/ml) in sodium chloride (iso-osmotic) iv	dexmedetomidine 400 mcg/100 ml (4 mcg/ml) in 0.9 % sodium chloride iv	morphine 10 mg/ml injection solution	morphine 2 mg/ml intravenous cartridge	lorazepam 2 mg/ml injection wrapper	vecuronium bromide 20 mg intravenous solution	sodium chloride 0.9 % iv bolus (cath lab)	sodium chloride 3 % intravenous injection solution	piperacillin-tazobactam 4.5 gram/100 ml dextrose(iso-osmotic) iv piggyback
105	pentobarbital sodium 50 mg/ml injection solution	lidocaine (pf) 100 mg/5 ml (2 %) intravenous syringe	nitroglycerin 100 mg/250 ml (400 mcg/ml) in 5 % dextrose intravenous	heparin (porcine) 25,000 unit/250 ml in 0.45 % sodium chloride iv solution	heparin (porcine) 100 unit/ml load from infusion	piperacillin-tazobactam 4.5 gram/100 ml dextrose(iso-osmotic) iv piggyback	dopamine 400 mg/250 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution	sodium chloride 3 % intravenous bolus solution	hydromorphone (pf) 1 mg/ml injection solution	vecuronium bromide 10 mg intravenous solution
106	mannitol 20 % intravenous solution	mannitol 20 % intravenous solution	aztreonam 2 gram solution for iv push	albumin, human 5 % intravenous solution	metronidazole 500 mg/100 ml-sodium chloride(iso) intravenous piggyback	vancomycin 2 gram/500 ml in 0.9 % sodium chloride intravenous	sodium chloride 3 % intravenous injection solution	dopamine 400 mg/250 ml (1,600 mcg/ml) in 5 % dextrose intravenous solution	vancomycin 1.5 gram/500 ml in 0.9 % sodium chloride intravenous solution	lidocaine (pf) 100 mg/5 ml (2 %) intravenous syringe
107	midazolam (pf) 5 mg/ml injection solution	morphine 10 mg/ml injection syringe	dextrose 10 % iv bolus	mannitol 20 % intravenous solution	morphine 10 mg/ml injection syringe	aztreonam 2 gram solution for iv push	digoxin 250 mcg/ml (0.25 mg/ml) injection solution	pantoprazole 40 mg intravenous solution	vancomycin 1.25 gram/250 ml in 0.9 % sodium chloride intravenous	vecuronium bromide 20 mg intravenous solution
108	hydromorphone 2 mg/ml injection syringe	midazolam (pf) 1 mg/ml in 0.9 % sodium chloride intraven	morphine 1 mg/ml in 0.9 % sodium chloride injectable pump	morphine 2 mg/ml intravenous cartridge	sodium chloride 0.9 % iv bolus (cath lab)	midazolam (pf) 5 mg/ml injection solution	phenylephrine 20 mg/250 ml (80 mcg/ml) in 0.9 % sodium	clindamycin 900 mg/50 ml in 5 % dextrose intravenous	sodium chloride 4 mEq/ml intravenous solution	famotidine (pf) 20 mg/50 ml in 0.9 % nacl (iso) intravenous

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		ous solution	reservoir				chloride iv	piggyback		piggyback
109	octreotide acetate 100 mcg/ml injection solution	cyclosporine 1 mg/ml ns aviva iv	pentobarbital 2500mg/50 ml adult infusion	dobutamine 500 mg/250 ml (2,000 mcg/ml) in 5 % dextrose iv	digoxin 250 mcg/ml (0.25 mg/ml) injection solution	albumin, human 5 % intravenous solution	aztreonam 2 gram solution for iv push	albumin, human 5 % intravenous solution	morphine 10 mg/ml injection solution	vancomycin 1.25 gram/250 ml in 0.9 % sodium chloride intravenous
110	dextrose 5 % in water (d5w) intravenous solution	pentobarbital 2500mg/50 ml adult infusion	etomidate 2 mg/ml intravenous solution	lidocaine (pf) 4 mg/ml (0.4 %) in 5 % dextrose intravenous solution	midazolam (pf) 5 mg/ml injection solution	ceftriaxone 1 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	vancomycin 1.25 gram/250 ml in 0.9 % sodium chloride intravenous	fluconazole 400 mg/200 ml in sod. chloride(iso) intravenous piggyback	aztreonam 2 gram solution for iv push	sodium chloride 3 % intravenous injection solution
111	vancomycin 1.25 gram/250 ml in 0.9 % sodium chloride intravenous	hydromorphone (pf) 1 mg/ml injection solution	ceftriaxone 1 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	dexmedetomidine 200 mcg/50 ml (4 mcg/ml) in 0.9 % sodium chloride iv	octreotide acetate 100 mcg/ml injection solution	vancomycin 1.75 gram/500 ml in 0.9 % sodium chloride intravenous	metronidazole 500 mg/100 ml-sodium chloride(iso) intravenous piggyback	vancomycin 1,000 mg intravenous injection	midazolam (pf) 1 mg/ml in 0.9 % sodium chloride intravenous solution	cefazolin 1 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback
112	vancomycin 1.75 gram/500 ml in 0.9 % sodium chloride intravenous	cefepime 1 gram solution for injection	esmolol 2,500 mg/250 ml (10 mg/ml) in sodium chloride (iso-osmotic) iv	levofloxacin 500 mg/100 ml in 5 % dextrose intravenous piggyback	phenobarbital sodium 65 mg/ml injection solution	epinephrine hcl 8 mg/250 ml (32 mcg/ml) in 5 % dextrose intravenous	hydromorphone (pf) 1 mg/ml injection solution	ceftriaxone 1 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	albumin, human 5 % intravenous solution	milrinone 20 mg/100 ml(200 mcg/ml) in 5 % dextrose intravenous piggyback
113	levofloxacin 500 mg/100 ml in 5 % dextrose intravenous piggyback	vasopressin 40 units/50 ml (0.8 unit/ml) ssc premade infusion	hydromorphone (pf) 1 mg/ml injection solution	cefazolin 3 gram/100 ml in 0.9 % sodium chloride intravenous piggyback	hydromorphone (pf) 1 mg/ml injection solution	digoxin 250 mcg/ml (0.25 mg/ml) injection solution	cefazolin 3 gram/100 ml in 0.9 % sodium chloride intravenous piggyback	phenobarbital sodium 65 mg/ml injection solution	midazolam (pf) 1 mg/ml injection solution	ceftriaxone 1 gram solution for injection
114	fentanyl (pf) 2,500 mcg/50 ml (50 mcg/ml) intravenous pca syringe	levofloxacin 500 mg/100 ml in 5 % dextrose intravenous piggyback	vasopressin (pitressin) infusion 50 unit/50 ml	sugammadex 100 mg/ml intravenous solution	pantoprazole 40 mg intravenous solution	cefazolin 3 gram/100 ml in 0.9 % sodium chloride intravenous piggyback	epinephrine hcl 8 mg/250 ml (32 mcg/ml) in 5 % dextrose intravenous	cefazolin 3 gram/100 ml in 0.9 % sodium chloride intravenous piggyback	dobutamine 500 mg/250 ml (2,000 mcg/ml) in 5 % dextrose iv	insulin u-100 regular human 100 unit/ml injection solution
115	cefazolin 3 gram/100 ml in 0.9 % sodium chloride intravenous piggyback	heparin, porcine (pf) 10 unit/ml intravenous syringe	sodium chloride 4 mEq/ml intravenous solution	fluconazole 200 mg/100 ml in sod. chloride (iso) intravenous piggyback	ceftriaxone 1 gram solution for injection	fentanyl (pf) 2,500 mcg/50 ml (50 mcg/ml) intravenous pca syringe	piperacillin-tazobactam 2.25 gram/50 ml in dextrose(iso) iv piggyback	etomidate 2 mg/ml intravenous solution	cefazolin 3 gram/100 ml in 0.9 % sodium chloride intravenous piggyback	fentanyl (pf) 2,500 mcg/50 ml (50 mcg/ml) intravenous pca syringe
116	sodium chloride 3 % intravenous bolus solution	norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in	propofol infusion 10 mg/ml	succinylcholine chloride 20mg/ml syringe/vial wrapper	epinephrine hcl 8 mg/250 ml (32 mcg/ml) in 5 % dextrose intravenou	succinylcholine chloride 20mg/ml syringe/vial wrapper	vasopressin 40 units/50 ml (0.8 unit/ml) ssc premade infusion	heparin (porcine) 10,000 unit/ml injection solution	etomidate 2 mg/ml intravenous solution	heparin (porcine) 100 unit/ml load from infusion

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		dextrose 5 % iv			s					
117	vancomycin 1,000 mg intravenous injection	sodium chloride 4 mEq/ml intravenous solution	morphine (pf) 1 mg/ml in 0.9% sodium chloride intravenous solution	vancomycin 1.25 gram/250 ml in 0.9 % sodium chloride intravenous	fentanyl (pf) 50 mcg/ml injection solution	vasopressin 40 units/50 ml (0.8 unit/ml) ssc premade infusion	lactated ringers irrigation solution	morphine (pf) 1 mg/ml in 0.9% sodium chloride intravenous solution	hydromorphone 4 mg/ml injection syringe	sugammadex 100 mg/ml intravenous solution
118	aztreonam 1 gram solution for iv push	sugammadex 100 mg/ml intravenous solution	succinylcholine chloride 20mg/ml syringe/vial wrapper	hydromorphone 2 mg/ml injection syringe	sodium chloride 0.9 % intravenous solution	morphine (pf) 1 mg/ml in 0.9% sodium chloride intravenous solution	esmolol 2,500 mg/250 ml (10 mg/ml) in sodium chloride (iso-osmotic) iv	succinylcholine chloride 20mg/ml syringe/vial wrapper	norepinephrine bitartrate 8 mg/250 ml (32 mcg/ml) in dextrose 5 % iv	succinylcholine chloride 20mg/ml syringe/vial wrapper
119	heparin (porcine) 1,000 unit/500 ml in 0.9% sodium chloride iv (combined)	propofol 10 mg/ml intravenous emulsion	piperacillin-tazobactam 4.5 gram/100 ml dextrose(iso-osmotic) iv piggyback	cisatracurium 2 mg/ml intravenous solution	sugammadex 100 mg/ml intravenous solution	octreotide acetate 100 mcg/ml injection solution	morphine (pf) 1 mg/ml in 0.9% sodium chloride intravenous solution	midazolam (pf) 5 mg/ml injection solution	hydromorphone 50 mg/50 ml (1 mg/ml) in 0.9 % sod.chloride iv pump resevoir	morphine (pf) 1 mg/ml in 0.9% sodium chloride intravenous solution
120	esmolol 2,500 mg/250 ml (10 mg/ml) in sodium chloride (iso-osmotic) iv	heparin 30,000 units (cell saver) in 1000 ml ns	midazolam (pf) 1 mg/ml in 0.9 % sodium chloride intravenous solution	sodium chloride 3 % intravenous bolus solution	etomidate 2 mg/ml intravenous solution	esmolol 2,500 mg/250 ml (10 mg/ml) in sodium chloride (iso-osmotic) iv	lactated ringers iv bolus	hydromorphone 1 mg/ml injection syringe	heparin (porcine) 10,000 unit/ml injection solution	vancomycin 1.5 gram/500 ml in 0.9 % sodium chloride intravenous solution
121	ketamine 10 mg/ml injection solution	octreotide acetate 100 mcg/ml injection solution	eptifibatide 0.75 mg/ml intravenous solution	vancomycin 1,000 mg intravenous injection	vancomycin 1.5 gram/500 ml in 0.9 % sodium chloride intravenous solution	levofloxacin 500 mg/100 ml in 5 % dextrose intravenous piggyback	succinylcholine chloride 20mg/ml syringe/vial wrapper	ceftriaxone 2 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	levofloxacin 500 mg/100 ml in 5 % dextrose intravenous piggyback	aztreonam 1 gram solution for iv push
122		piperacillin-tazobactam 4.5 gram/100 ml dextrose (iso-osmotic) iv piggyback	aztreonam 1 gram solution for iv push	heparin (porcine) 10,000 unit/ml injection solution	piperacillin-tazobactam 2.25 gram/50 ml in dextrose(iso) iv piggyback	cefepime 2 gram solution for iv push'	midazolam (pf) 5 mg/ml injection solution	vancomycin 1.75 gram/500 ml in 0.9 % sodium chloride intravenous	heparin (porcine) 1,000 unit/500 ml in 0.9% sodium chloride iv (combined)	fluconazole 400 mg/200 ml in sod. chloride(iso) intravenous piggyback
123		cefazolin 3 gram/100 ml in 0.9 % sodium chloride intravenous piggyback	heparin, porcine (pf) 10 unit/ml intravenous syringe	esmolol 2,500 mg/250 ml (10 mg/ml) in sodium chloride (iso-osmotic) iv	vecuronium bromide 10 mg intravenous solution	heparin (porcine) 1,000 unit/500 ml in 0.9% sodium chloride iv (combined)	vecuronium bromide 10 mg intravenous solution	midazolam 5 mg/ml (combined) injection solution wrapper	cyclosporine 1 mg/ml ns aviva iv	eptifibatide 0.75 mg/ml intravenous solution
124		ceftriaxone 2 gram/50 ml in	ceftriaxone 1 gram solution for	midazolam (pf) 5 mg/ml injection	cyclosporine 1 mg/ml ns aviva iv	hydromorphone (pf) 1 mg/ml injection	heparin (porcine) 1,000 unit/500	pentobarbital sodium 50 mg/ml injection		hydromorphone (pf) 1 mg/ml injection

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		dextrose (iso-osmotic) intravenous piggyback	injection	solution		solution	ml in 0.9% sodium chloride iv (combined)	solution		solution
125		vancomycin 1.75 gram/500 ml in 0.9 % sodium chloride intravenous	heparin (porcine) 1,000 unit/500 ml in 0.9% sodium chloride iv (combined)	cefepime 2 gram solution for iv push'	ketamine 10 mg/ml injection solution	sodium chloride 4 mEq/ml intravenous solution	ceftriaxone 2 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback	cefepime 2 gram solution for iv push'		fentanyl (sublimaze) 100 mcg in ns 50ml (rex or)
126		heparin (porcine) 100 unit/ml load from infusion	vecuronium bromide 10 mg intravenous solution		milrinone 20 mg/100 ml(200 mcg/ml) in 5 % dextrose intravenous piggyback	heparin (porcine) 100 unit/ml load from infusion	rocuronium 10 mg/ml intravenous solution			
127		succinylcholine chloride 20mg/ml syringe/ vial wrapper	cefepime 2 gram/100 ml in dextrose (iso-osmotic) intravenous piggyback			rocuronium 10 mg/ml intravenous solution	ceftriaxone 1 gram/50 ml in dextrose (iso-osmotic) intravenous piggyback			
128		heparin (porcine) 1,000 unit/500 ml in 0.9% sodium chloride iv (combined)	midazolam (pf) 5 mg/ml injection solution							
129			famotidine 10 mg/ml injection solution (multi-vial size)							
130			cefepime 2 gram solution for iv push'							
N represents the number of individual medication administrations										

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Table 2. Distribution of medication classes within each medication cluster by total medication administrations

		Cluster									
Medication Class		1 (N=498)	2 (N=561)	3 (N=532)	4 (N=517)	5 (N=539)	6 (N=574)	7 (N=540)	8 (N=518)	9 (N=526)	10 (N=532)
1	Analgesic (N=7348)	15.46	14.62	16.73	15.28	15.21	13.76	15.00	15.25	14.45	13.35
2	Antiarrhythmic (N=511)	3.61	5.35	6.02	4.64	5.38	3.83	4.81	5.02	5.70	5.26
3	Antibiotic (N=2992)	21.89	18.72	19.74	18.18	18.18	20.73	19.07	18.15	19.96	20.11
4	Anticoagulant (N=2915)	6.43	6.24	6.77	7.54	8.35	6.45	5.74	7.14	7.60	7.71
5	Anticonvulsants (N=55)	3.21	1.96	1.50	1.74	1.86	1.05	1.85	1.74	1.52	1.13
6	Antifungal Agent (N=29)	0.40	0.89	0.94	0.77	0.93	0.87	0.74	1.16	0.76	0.94
7	Antihypertensive (N=1195)	2.61	2.32	2.82	2.51	2.41	4.18	3.33	2.70	2.85	3.57
8	Antiplatelet (N=46)	1.00	0.71	0.38	0.39	0.74	0.52	0.74	0.39	0.95	0.38
9	Antifungal (N=14)	1.00	0.71	0.75	1.35	0.37	0.35	0.56	0.19	0.00	0.38
10	Diabetic Agents (N=16)	1.00	1.25	1.13	1.55	0.56	1.39	0.74	1.16	0.95	0.38
11	Diuretic (N=)	0.20	0.36	0.19	0.19	0.56	0.52	0.93	0.19	0.19	0.38
12	Fluids (N=10364)	10.44	14.80	12.59	15.09	14.29	12.37	12.41	11.78	13.88	11.65
13	Gastric Agent (N=1494)	5.02	4.99	3.57	3.09	3.34	3.83	5.37	4.05	4.94	3.38
14	Hypertonic Saline (N=230)	1.20	1.60	1.13	1.16	1.30	2.09	0.93	1.74	0.76	1.13
15	Inotropic Agent (N=687)	3.21	3.92	3.38	4.06	2.04	3.66	3.70	2.90	2.28	3.01
16	Neuromuscular blocking agents (N=62)	1.41	1.25	1.13	0.97	0.74	0.87	0.93	1.16	1.52	1.88
17	Sedative (N=8700)	13.25	11.94	11.28	10.64	11.69	11.85	13.15	13.90	11.79	14.10
18	Somatostatic Agents (N=11)	0.40	0.18	0.38	0.58	0.74	0.35	0.74	0.77	0.57	0.56
19	Total parenteral nutrition (N=59)	0.80	0.53	0.75	1.16	1.11	0.52	1.11	1.35	0.57	1.13
20	Vasopressor (N= 8270)	7.43	7.31	8.27	9.09	10.02	10.45	7.22	9.27	8.37	9.21
21	Antidotes/Rescue Therapy	0.00	0.18	0.19	0.00	0.00	0.17	0.37	0.00	0.19	0.00

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	(N=4)										
22	Immunosuppressant (N=4)	0.00	0.18	0.38	0.00	0.19	0.17	0.56	0.00	0.19	0.38
N represents the number of medication administrations, with each column summing up to 100%.											

Table 3 Logistic Regressions for Incidence of Fluid Overload with Varying Proportions of Medication Administrations Matching Cluster 7

Model	Logistic Regression for Fluid Overload with APACHE II Score at 24 hours and Diuretic Level	
	Estimated Value	P-value
Greater than 10% of Medication Administrations Matching Cluster 7	0.68	0.00183
Greater than 15% of Medication Administrations Matching Cluster 7	0.63	0.00481
Greater than 20% of Medication Administrations Matching Cluster 7	-0.29	0.601
Greater than 30% of Medication Administrations Matching Cluster 7	-16.2	0.9941

Table 4. Logistic Regressions for Prediction of Fluid Overload with/without Cluster 5 information

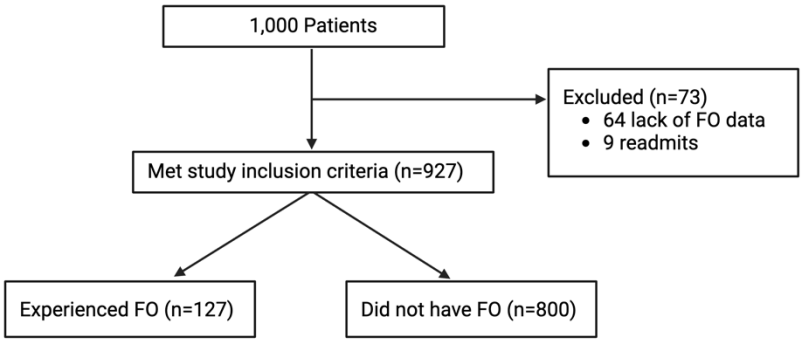
Model	Logistic Regression for Fluid Overload with APACHE II Score at 24 hours and Diuretic Level		Logistic Regression for Fluid Overload with APACHE II Score at 24 hours, Diuretic Level, and Proportion of Medications Appearing in Cluster 5	
	Estimated Value	P-value	Estimated Value	P-value
(Intercept)	-3.00	<0.0001	-3.42	<0.0001
APACHE Score at 24 hours	0.095	<0.0001	0.09343	<0.0001
Diuretic level (0-5)	-0.46	0.04	-0.486	0.03
Diuretic level (>5)	-17.25	0.98	-17.26	0.98
Proportion of Medications Appearing in Cluster 5			5.406	0.0007

Diuretic level 0-5: the patient received ≤5 doses of a diuretic medication within the first 72 hours of ICU stay

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Diuretic level >5: the patient received >5 doses of a diuretic medication within the first 71 hours of ICU stay

Figure 1. Consort Diagram of the Data Process Procedures



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Figure 2. Cluster 7 medication administrations organized by timing of administration and medication class

Black boxes indicate medication administration at specific time slots, while the width of column indicates amount of medications appearing within that class within the cluster

Alternative version of Figure 6 from the main text

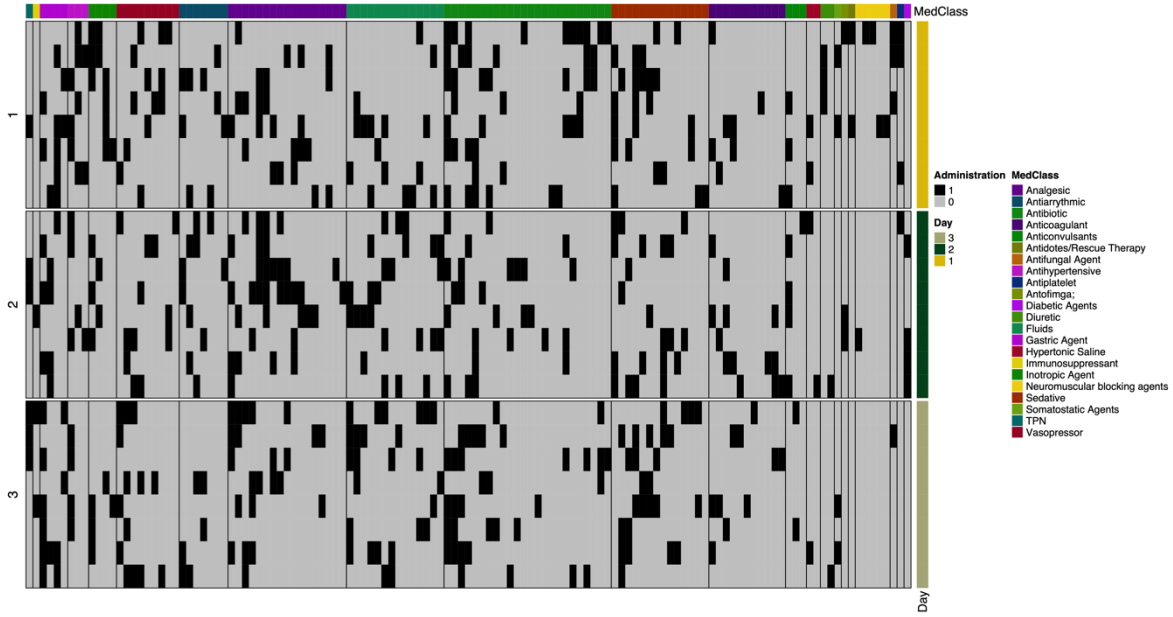


Figure 3. Cluster 7 medication administrations organized by timing of administration and medication class with classes in alphabetical order

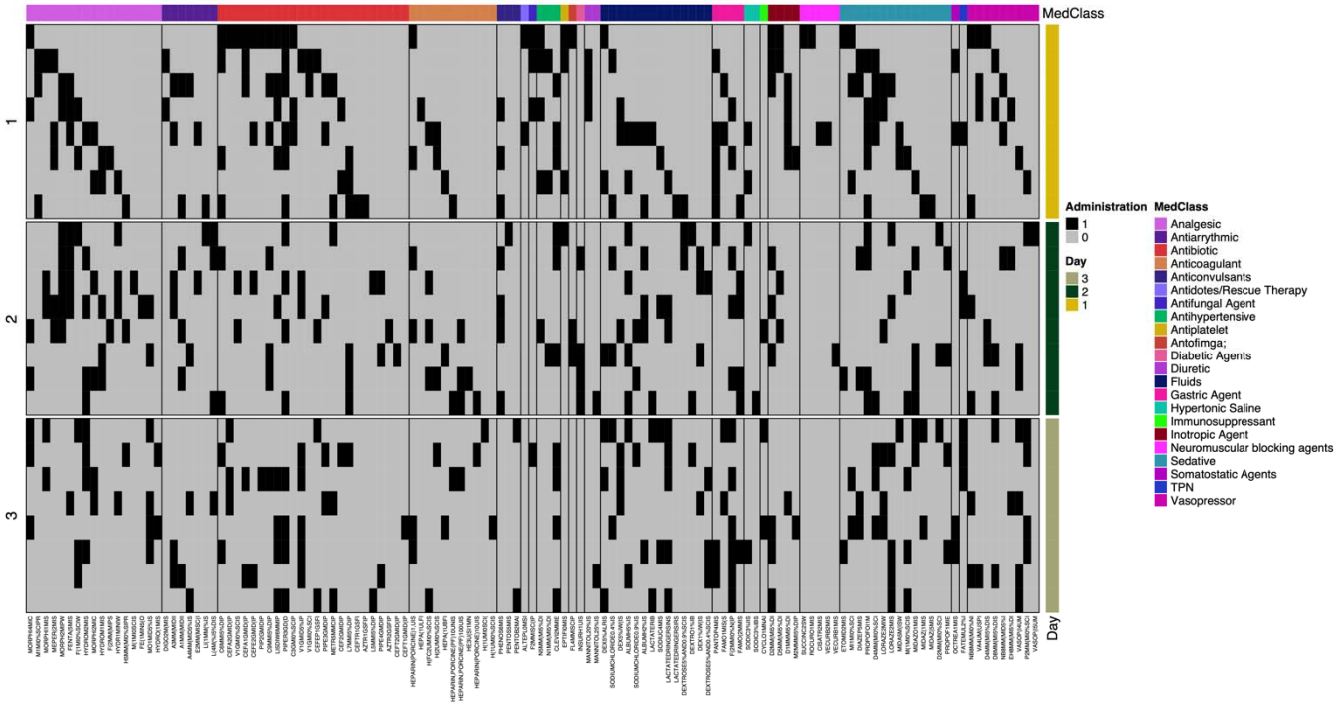
Black boxes indicate medication administration at specific time slots, while the width of column indicates amount of medications appearing within that class within the cluster

Alternative version of Figure 6 from the main text

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Figure 4. Logistic regression model for Cluster 5



Logistic regression for incidence of fluid overload, including Cluster 5, APACHE II score, and diuretic level

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