



Mortality Prediction with Adaptive Feature Importance Recalibration for Peritoneal Dialysis Patients:

a retrospective study on a real-world longitudinal follow-up dataset

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PD is one of the most widely used life-supporting therapies for ESRD

Clinical Background

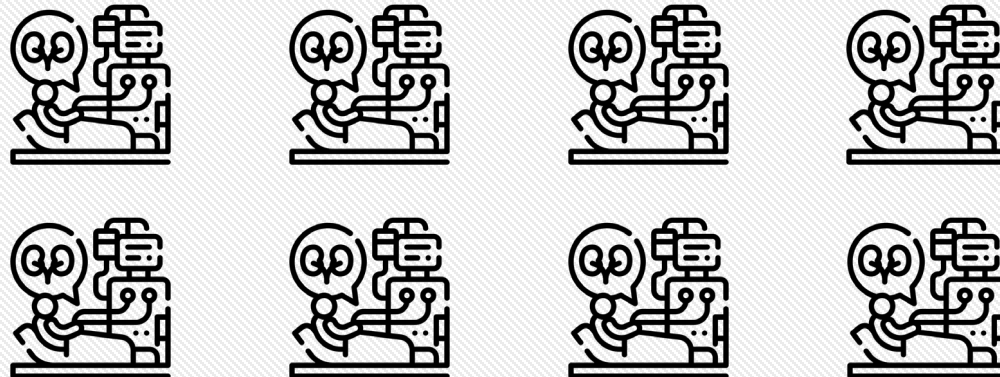
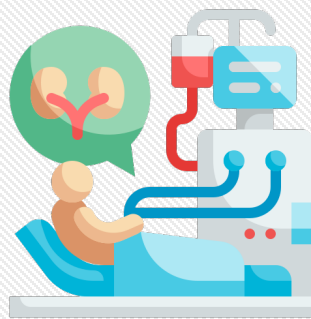
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- Mortality Prediction
- Challenge Issues

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- The prevalence of **End-Stage Renal Disease (ESRD)** continues to increase and has become a significant healthcare burden worldwide.
 - Approximately 3.8 million people currently rely on some form of dialysis for the treatment of ESRD worldwide
- ESRD is a long-term chronic disease, and patients need continuous medical care and treatment for years or even decades.

➤ **Peritoneal Dialysis (PD)** is a well-established Renal Replacement Therapy (RRT) modality and the leading form of home-based life-supporting dialysis therapy for patients with ESRD





Performing dynamic mortality prediction for PD patients

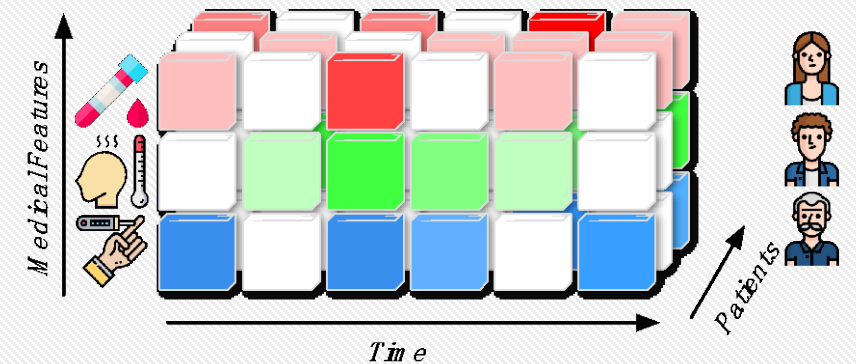
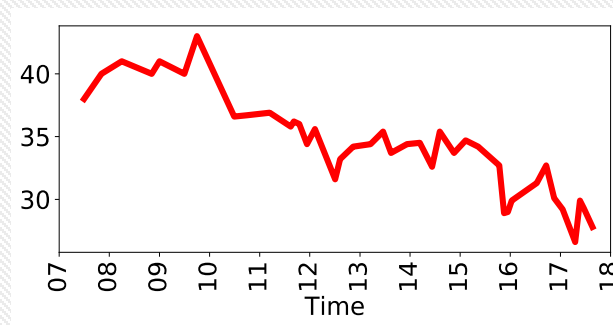
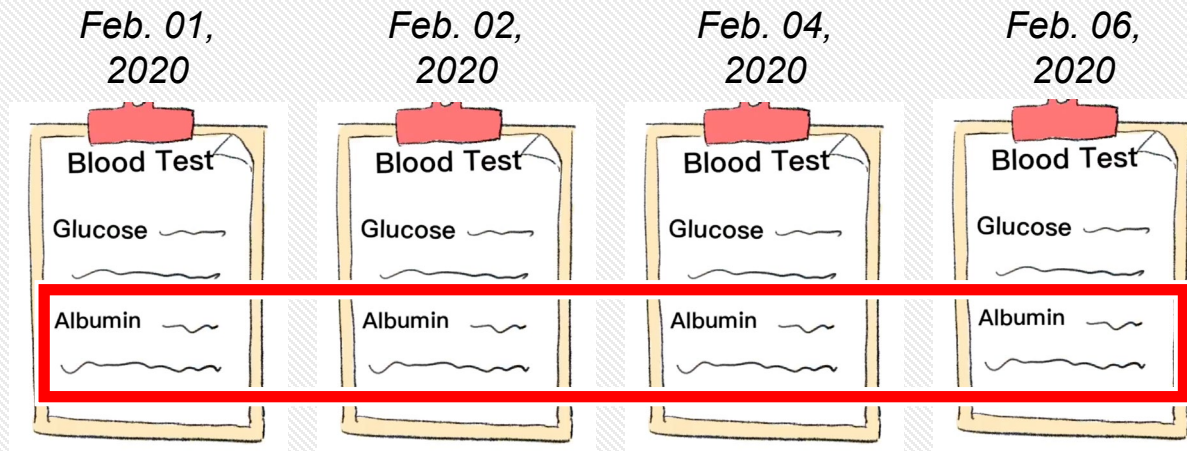
- PD patients need lifelong treatment with periodic follow-up visits to monitor their health status.

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Performing dynamic mortality prediction for PD patients

- Predicting mortality risk and identifying modifiable risk factors from routine clinic visit records are of great importance for personalized medicine and early intervention to prevent adverse outcomes and improve the survival of long-term PD patients.

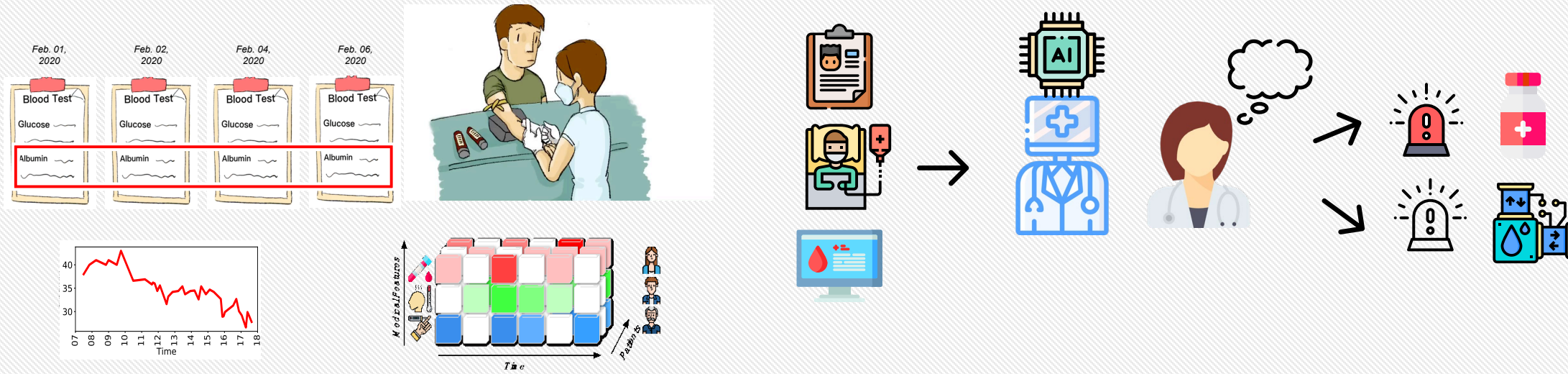
- **Input:** Time series of laboratory tests; Demographics; etc
- **Output:** Mortality risk at each follow-up visit

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Multivariate time-series electronic medical records



Issues that have not yet been thoroughly addressed

- Recent studies have attempted to utilize machine learning and deep learning techniques to evaluate the health status of patients.

Author/Year	Published Journal	Patient Cohort	Prediction Task	Prediction Model	Information	Dynamic Monitor	Interpret Method	Ante-Hoc Interpret	Adaptive Importance
Noh 2020 [12]	Nature Sci. R.	PD	Mortality	Decision Tree	Static	×	Tree	✓	×
Zhou 2021 [9]	Aging Alb. NY	PD	Premature Mortality	ANN	Static	×	Permutation	×	×
Chaudhuri 2021 [6]	IJMI	HD	Hospitalization	XGboost	Static	×	×	×	×
Radovic 2021 [10]	CMBBE	HD	Mortality	SVM	Static	×	Permutation	×	×
Akbilgic 2019 [7]	Kidney Int. R.	ESRD	Postdialysis Mortality	Random Forest	Static	×	Tree	✓	×
Bai 2022 [67]	Nature Sci. R.	CKD	ESRD	Naive Bayes	Static	×	×	×	×
Makino 2019 [20]	Nature Sci. R.	DKD	Aggravation	CAE + LR	Sequential	✓	Inverse	×	×
Schena 2021 [13]	Kidney Int.	IgAN	ESRD	ANN	Static	×	×	×	×
Srinivas 2017 [16]	Ame. Jour. Trans.	Kidney Trans.	Graft Loss/Mortality	LR	Both	×	×	×	×
Liu 2021 [8]	PLOS ONE	AKI in ICU	Mortality	XGBoost	Static	×	Tree	✓	×
Kang 2020 [11]	Critical Care	CRRT for AKI	In-hospital Mortality	XGBoost	Static	×	Tree	✓	×
Ravizza 2019 [5]	Nature Medicine	Diabetes	CKD Early Risk	LR	Static	×	×	×	×
Xu 2019 [4]	MEDINFO	ICU	AKI	GBDT	Static	×	×	×	×
Hyland 2020 [18]	Nature Medicine	ICU	Circulatory Failure	lightGBM	Sequential	✓	SHAP	×	×
Thorsen 2020 [19]	Lancet Digi. Heal.	ICU	Mortality	LSTM	Both	✓	SHAP	×	×
Sung 2021 [24]	JMIR Med. Info.	ICU	Mortality/AKI	biLSTM	Both	✓	×	×	×
Tomasev 2019 [15]	Nature	In-Patient	AKI	Multitask RHN	Sequential	✓	×	×	×
Yan 2020 [17]	Nature Mach. Int.	COVID-19	In-hospital Mortality	XGBoost	Static	×	Tree	✓	×
Meyer 2018 [22]	Lancet Res. Med.	Cardiosurgical	Complications	GRU	Sequential	✓	×	×	×
Raket 2020 [68]	Lancet Digi. Heal.	Schizophrenia	Psychosis	RNN	Sequential	✓	×	×	×
Nitski 2021 [23]	Lancet Digi. Heal.	Liver Trans.	Mortality	Transformer	Sequential	✓	Gradient	×	×
Rank 2020 [14]	NPJ Digital Med.	Cardiosurgical	AKI	RNN	Sequential	✓	×	×	×
Ours 2022	-	PD (HD)	Mortality	AICare	Both	✓	AICare	✓	✓

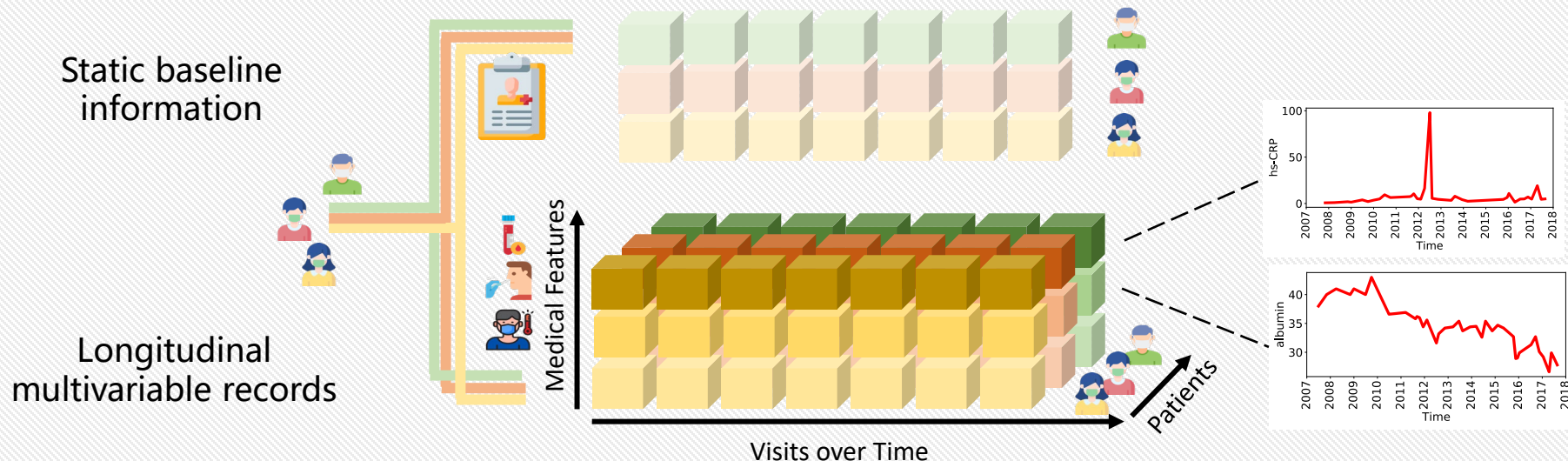
- However, there are still some critical issues that have not yet been thoroughly addressed by existing works.

- Clinical Background**
- Peritoneal Dialysis
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- Challenge Issues**
- AICare Framework**
- Results**



Issue 1: Utilization of sequential records and demographics

- Most AI-based EMR analysis research on kidney disease patients only use static baseline information to perform one-time health prediction based on traditional machine learning methods.
 - Some other research model the disease process by incorporating sequential EMR. However, these works cannot effectively embed the baseline information and the sequential records together, and capture the interaction between them, which leads to limited prediction performance.
- Issue 1: Perform **dynamic mortality prediction** at each follow-up visit based on the effective utilization of both **sequential medical records** and the **baseline demographic information**.



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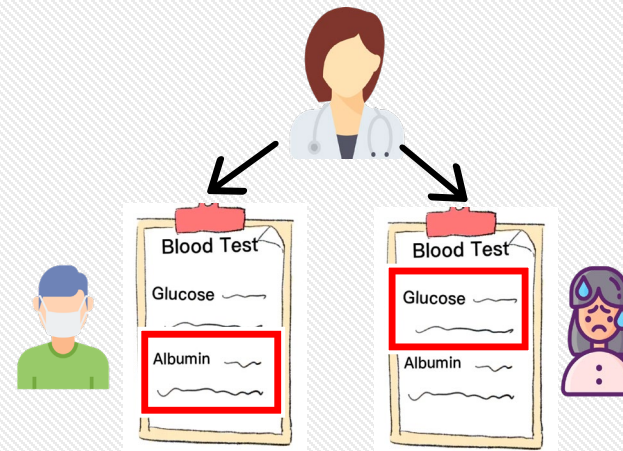
AIcare Framework

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Issue 2: Identifying the most indicative feature for each patient

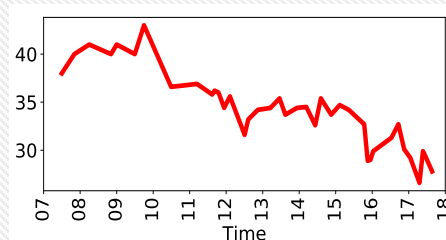
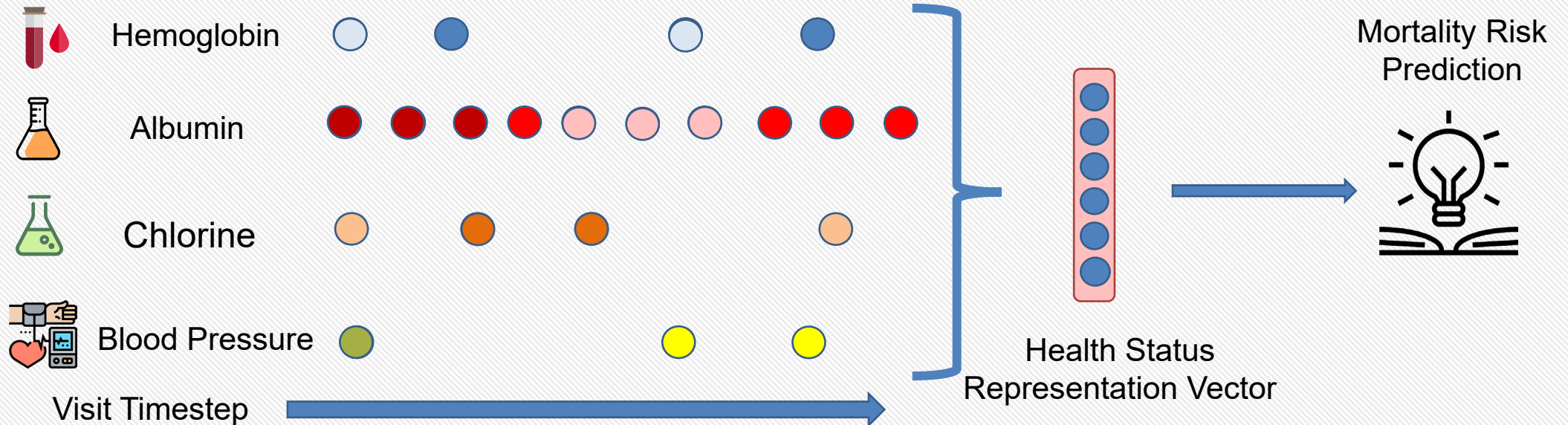
- Key factors that strongly indicate health risk are different among patients. Medical experts need to ***understand how a model makes a specific decision for a particular patient.***
 - It will also remind physicians of the previously unknown correlation between the biomarker and the cause of death.
 - This requires sufficient model interpretability to ensure that prediction results are trustworthy for developing bespoke interventions and extracting medical knowledge.
- However, most existing works fail to ensure the model's trustworthiness in providing verifiable interpretations, and may suffer the tradeoff between the interpretability and the prediction performance.
- Issue 2: Provide ***fine-grained interpretability*** for each patient individually by selecting key features which contribute the most to mortality prediction (patient-level interpretability) and achieve high prediction performance simultaneously.





Issue 3: Analyzing the changes of feature importance with its value

- The way of attending to the medical feature in the prediction process should be flexible and individualized according to its value and the specific health condition of the patient
- Issue 3: Adaptively analyze **the importance of each feature** along with the **variation of its value** (feature-level interpretability) to provide medical advice and extract knowledge.



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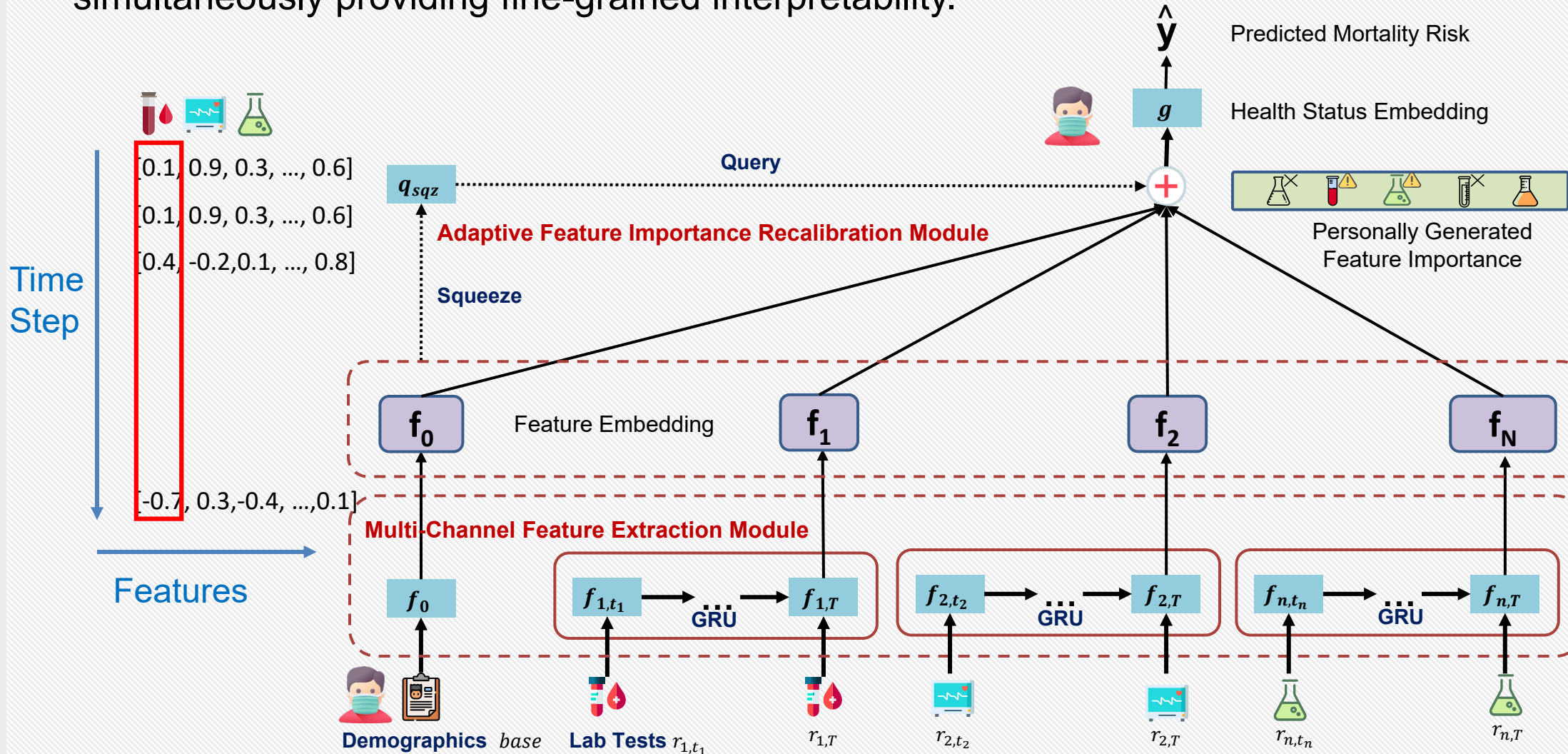
AI Care Framework

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We propose a deep learning framework for interpretable EMR analysis

- To address the above challenges, we propose a novel end-to-end deep-learning-based framework, **AICare**, to model the health trajectory based on multivariate EMR data, while simultaneously providing fine-grained interpretability.



Clinical Background

AICare Framework

● AICare Model

○ Dataset

Results



Real-World Longitudinal EMR of PD Patients with Regular Clinical Follow-ups

- This study has collected **13,091 clinical follow-up visits** and demographic data of 656 PD patients from Peking University Third Hospital, covering more than 12 years.
- This long-term real-world clinical electronic medical record (EMR) dataset consists of static baseline information, longitudinal multi-variable records and clinical outcomes.
 - Peritoneal Dialysis (PD) patients were followed up **every 3 months**. There are about **20 visits** recorded for each patient.
 - There are 39.8% patients, unfortunately, who died before the final follow-up.
 - The age range of patients enrolled is from 16 to 98 years old.

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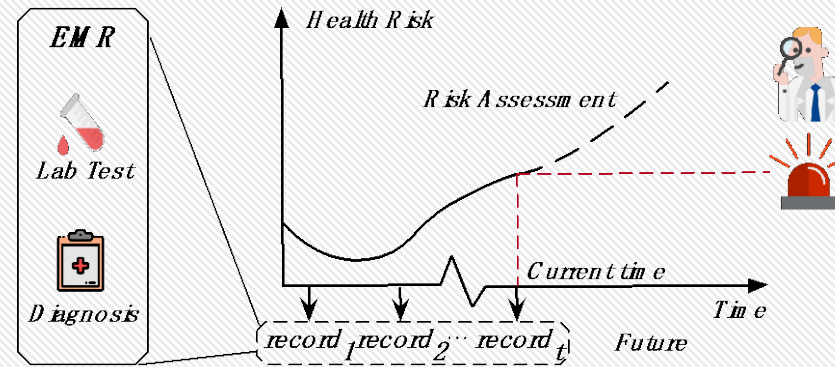
Statistic	Avg.	Med.	Max.	Min.	Std.
Age (year)	58.55	60.70	97.45	16.79	15.81
Visits per Patient	19.95	16	69	1	13.53
High Risk Visits per Patient	2	0	29	0	2.95
Duration of Follow-up (year)	3.98	3.43	10.44	0.1	2.67
Visit Interval (month)	2.73	2.48	29.87	-	2.67

	Total	Mortality (%)	Survival (%)
# Patients	656	261 (39.8%)	395(60.2%)
# Visits	13091	1196 (9.1%)	11895 (90.9%)
Age			
16-40	96 (14.6%)	10 (10.4%)	86 (89.6%)
40-60	217 (33.1%)	64 (29.5%)	153 (70.5%)
60-80	297 (45.3%)	153 (51.5%)	144 (48.5%)
80-98	44 (6.7%)	33 (75.0%)	11 (25.0%)
Diabetes			
# Diabetes	244 (37.2%)	120 (49.2%)	124 (50.8%)
Gender			
# Female	327 (49.8%)	125 (38.2%)	202 (61.8%)
# Male	328 (50.2%)	136 (41.5%)	192 (58.5%)



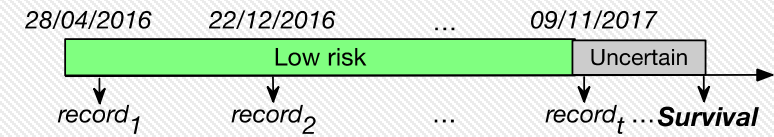
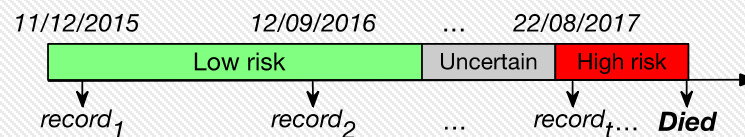
Problem Formulation: 1-year Mortality Prediction

- Given a patient's visit records with visits, the binary classification task is to predict the mortality risk in the future one year at each visit.



Label Assignment

- Clinical visits within 1 year before death are labeled as **high risk**.
- Visits recorded 2 years before death are labeled as **low risk**.
- Other visits are labeled as **uncertain** status and will not be included in the training process.





Features used in the mortality prediction for PD patients

- This dataset comprises 16 dynamic features recorded at each clinical visit and 4 static baseline features recorded at the first visit.

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Abbreviation	Full Name	Unit	High Risk Visits ($y = 1$)			Low Risk Visits ($y = 0$)			% Missing
			Mean	Std	Median	Mean	Std	Median	
Dynamic Features									
Albumin	Albumin	g/L	33.81	4.437	34.3	37.87	4.337	38	25%
DBP	Diastolic Blood Pressure	mmHg	70.28	14.71	70	78.59	13.79	80	18%
SBP	Systolic Blood Pressure	mmHg	125.3	25.19	127	134.4	21.61	135	14%
Cl	Chlorine	mmol/L	96.02	4.155	96	98.21	4.923	98	17%
Cr	Creatinine	umol/L	779.6	250.3	741	868.9	270.3	853	10%
Urea	Urea	mmol/L	18.12	5.545	17.8	20.09	5.363	19.8	11%
Ca	Calcium	mmol/L	2.358	0.277	2.345	2.406	0.341	2.39	12%
Na	Sodium	mmol/L	137.1	4.262	137.9	138.5	4.617	139	21%
K	Potassium	mmol/L	4.240	0.783	4.17	4.320	0.718	4.25	11%
P	Phosphorus	mmol/L	1.549	0.450	1.5	1.606	0.430	1.57	13%
CO ₂ CP	CO ₂ Combining Power	mmol/L	27.45	3.562	27.5	27.38	3.630	27.4	8%
Hb	Hemoglobin	g/L	111.4	19.54	113	114.6	17.05	115	12%
Weight	Body Weight	kg	59.98	11.05	59.59	62.26	11.07	62	41%
Glucose	Glucose	mmol/L	7.758	3.665	6.7	6.689	3.089	5.7	30%
hs-CRP	Hypersensitive C-Reactive Protein	mg/L	17.57	28.07	8.49	7.954	13.96	3.19	29%
WBC	White Blood Cell Count	$\times 10^9/L$	8.238	2.767	7.895	7.773	2.754	7.43	10%
Baseline Features									
Age	Age	year	66.12	13.01	67.82	53.30	15.54	54.53	0%
Gender	Female (0) or Male (1)	-	0.53	0.50	1	0.49	0.50	0	0%
Height	Height	m	162.2	9.95	160.5	164.1	10.98	163.8	0%
Diabetes	Is (1) or Not (0) Has Diabetes	-	0.45	0.50	0	0.31	0.46	0	0%



Prediction Performance

- *AICare* achieves 47.2% AUPRC (the area under the precision-recall curve), which is relatively 11.8% higher than the comparative baseline model.

Method	AUPRC	AUROC
GRU [22]	0.422 (0.109)	0.781 (0.047)
Transformer [23]	0.406 (0.097)	0.789 (0.047)
MT-RHN [15]	0.413(0.107)	0.777(0.063)
LSTM [19]	0.395(0.100)	0.782(0.065)
biLSTM-FC [24]	0.398(0.089)	0.758(0.067)
LR [5]	0.370 (0.084)	0.610 (0.044)
XGBoost [17]	0.379 (0.087)	0.597 (0.033)
DT [12]	0.319 (0.040)	0.607 (0.027)
LightGBM [18]	0.405 (0.082)	0.604 (0.028)
AICare	0.472** (0.075)	0.816** (0.033)

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Case Study

Indicative Features

Importance Variation

Recommendation



We release our code at <https://github.com/Accountable-Machine-Intelligence/AICare> .



Health Trajectory Interactive Visualization System

Case Study I: 66-year-old male, diabetic nephropathy

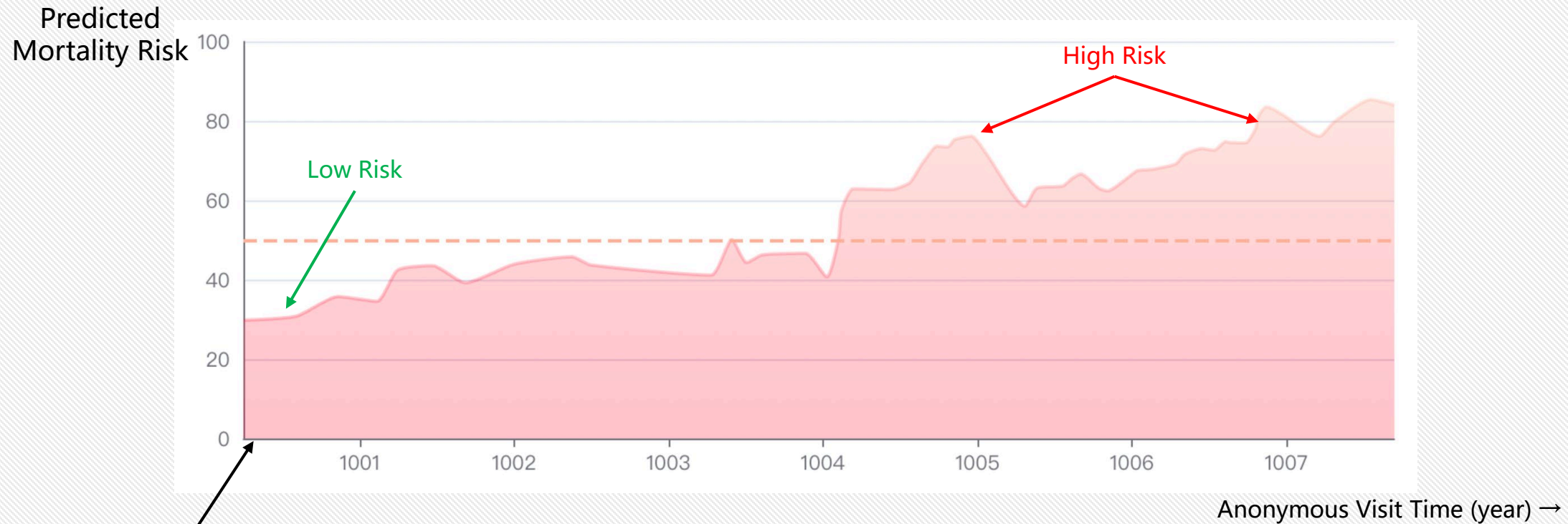
- We develop an **AI-Doctor online system** with an interactive interface to visualize the patient's health trajectory with the importance weights of features at each timestep.

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The patient initiated PD therapy.



Case Study I: 66-year-old male, diabetic nephropathy

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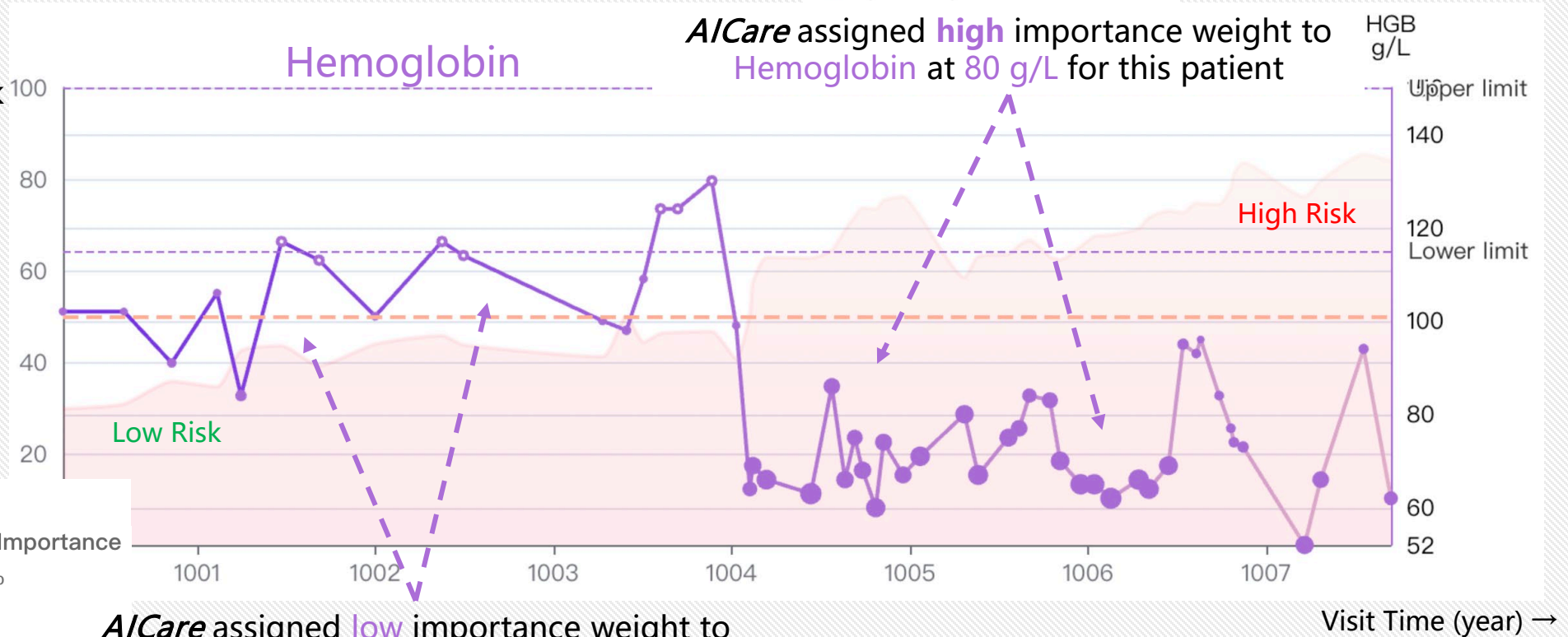
- 16 -

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Adaptive Feature Importance

- HGB: 54.5%
- Diastolic pressure: 36.1%
- Albumin: 5.4%
- Systolic pressure: 4.0%

Predicted Mortality Risk



1002-01-01

Adaptive Feature Importance

- Albumin: 23.6%
- SCR: 19.7%
- hs-CRP: 11.8%
- Glucose: 10.8%
- Weight: 10.1%
- Calcium: 7.9%
- Systolic pressure: 5.6%
- HGB: 4.5%



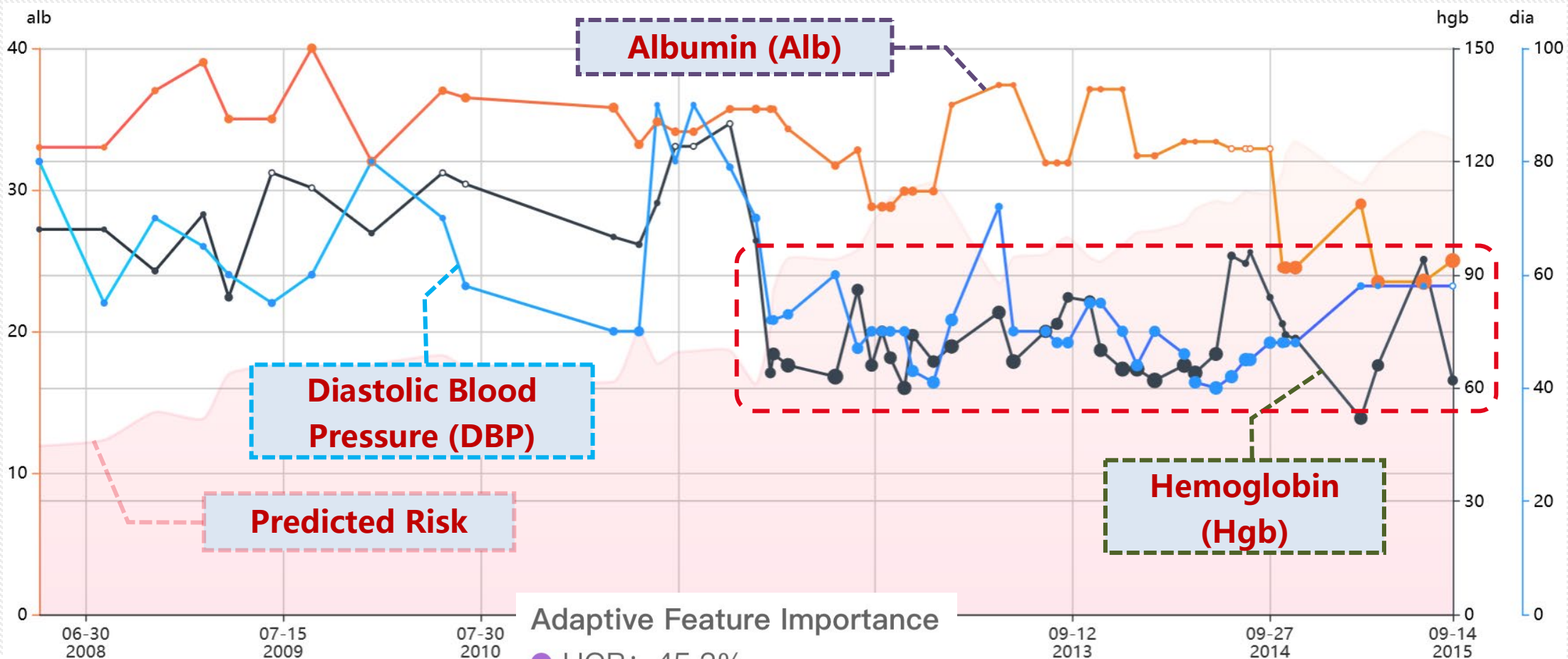
Case Study I: 66-year-old male, diabetic nephropathy

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The patient died of multiple organ failure and prostate cancer, unfortunately.

(The health trajectory interactive visualization system is publicly deployed at <http://47.93.42.104/a8>.)





Health Trajectory Interactive Visualization System

Case Study I: 66-year-old male, diabetic nephropathy

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-



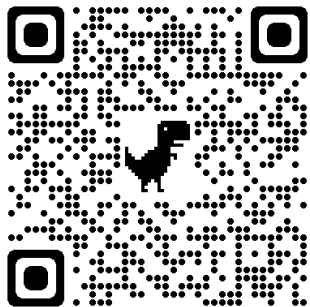
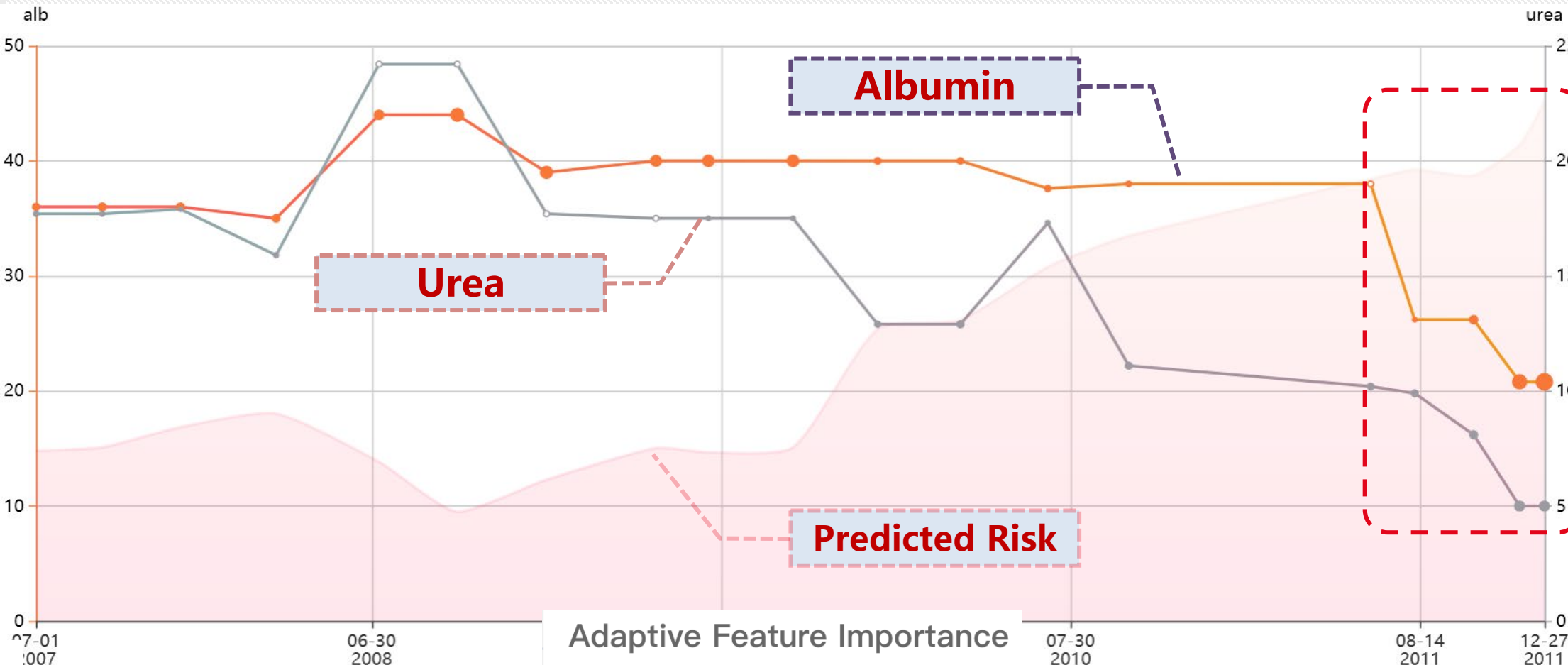
Case Study II: 68-year-old female, ischemic kidney disease

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Patient-level interpretability: Relationship between causes of death and features

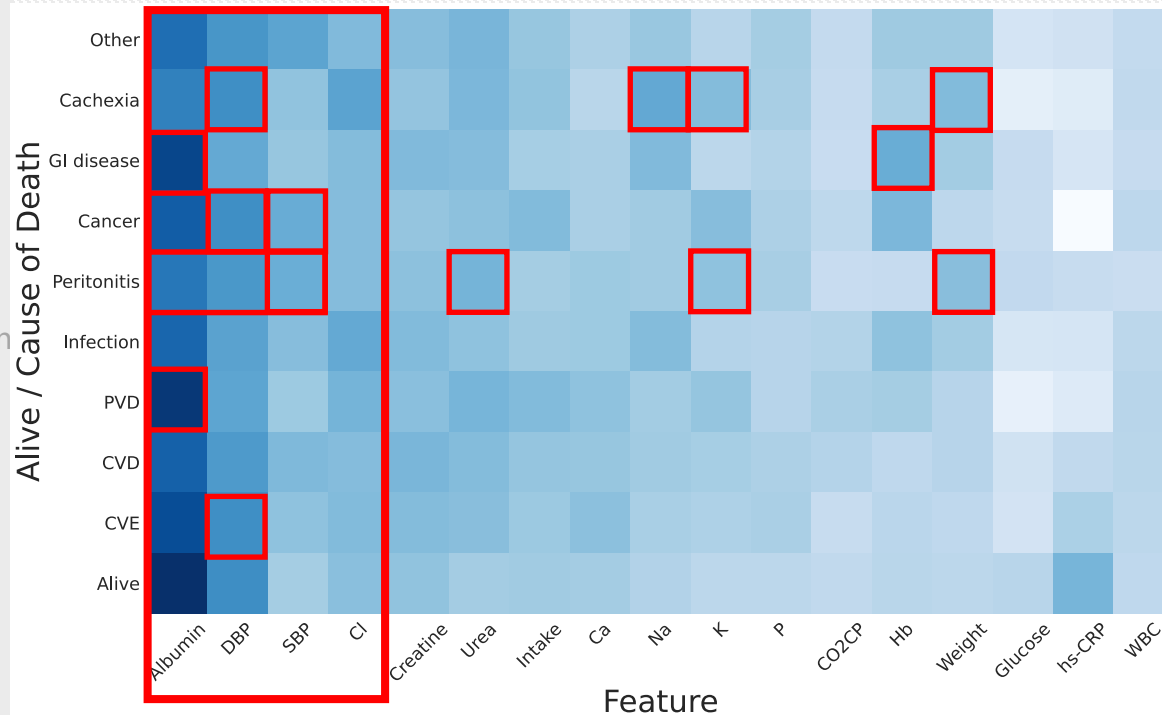
- AICare provides the **first** comprehensive elucidation of the relationship between the causes of mortality in patients with PD and clinical features based on an end-to-end deep learning model.
- The model explicitly emphasizes indicative features based on a recalibration module.

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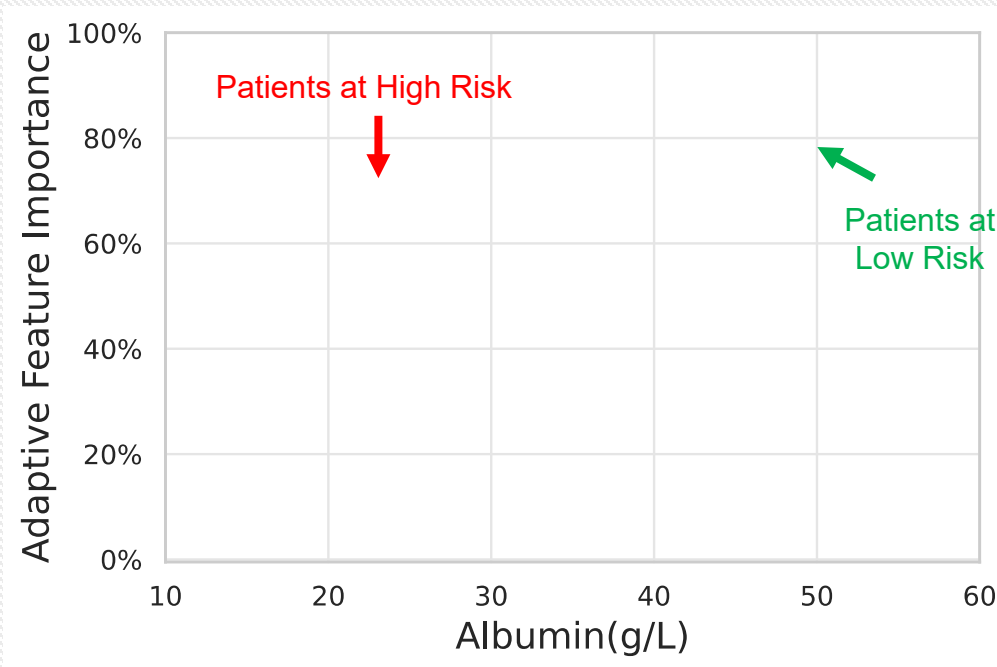
- Serum albumin, diastolic blood pressure, and chlorine are the most important indicators for most PD patients.
- Albumin has a strong indication for patients who died of gastrointestinal disease and peripheral vascular disease.
- Diastolic blood pressure (DBP) has an indication for patients who died of cachexia, cancer, and cerebrovascular disease.
- Systolic Blood Pressure (SBP) is indicative of cancer and peritoneal dialysis-associated peritonitis deaths.
- Sodium (Na), potassium (K) and body weight are important indicators for cachexia deaths.
- Hemoglobin (Hb) is an important indicator for Gastrointestinal (GI) disease deaths.
- Urea, body weight, potassium (K), albumin, DBP and SBP are important indicators for PD-related peritonitis deaths.



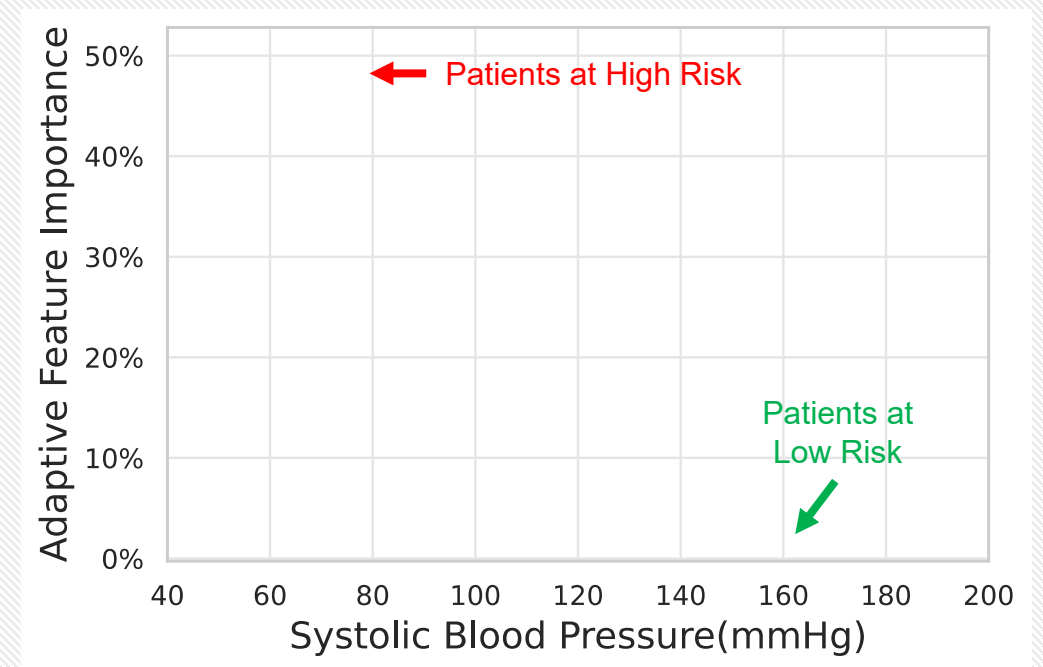
Feature-level interpretability: Variation of Feature Importance

- AICare **first** reveals the variation pattern in each feature's importance for PD patient's mortality prediction task based on the built-in interpretability, without any injection of human physicians' knowledge.
- There are two variation patterns of importance in medical features

V-shaped parabolic curves
(e.g., albumin, diastolic blood pressure)



L-shaped fold lines
(e.g., systolic blood pressure, hemoglobin)



Each dot represents the follow-up visit of a patient. The color represents the predicted risk.



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Albumin: V-shaped curve with 32 g/L as a turning point

- AICare believes that the albumin's importance attention weight appears to be a V-shaped curve with 32 g/L as a turning point.

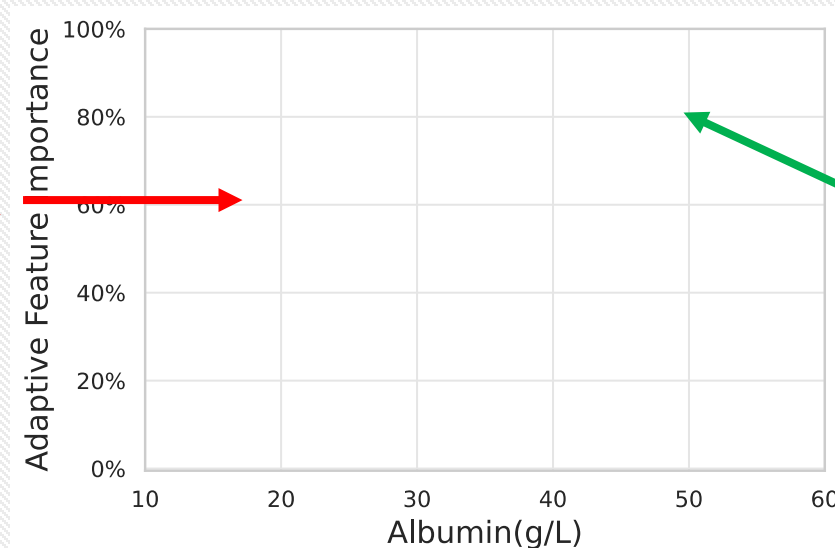
- The variation of albumin in a descending or ascending manner always gets the model's attention.

- Albumin **lower than 32 g/L**

- Patients tend to have a high importance weight and poor prognosis.
- When the albumin level is lower than 23 g/L, more than 50% attention weight is given, which means that the albumin level becomes the most critical indicator for mortality outcome.

- Albumin **higher than 32 g/L**

- Between the range of 32-57 g/L, a high albumin value also causes high importance weight and indicates a significant improvement in the patient's health.
- When the albumin level is higher than 40 g/L, it often occupies about 50% to even 100% of the feature importance weight, which means the model can predict the high survival expectation of the patient using just this feature.



Patients with **high importance weight of Albumin** at **high risk**

Patients with **high importance weight of Albumin** at **low risk**

As a result, AICare recommends **raising the albumin level to above 32 g/L** as much as possible for most PD patients.





Albumin's Importance: V-shaped curve with 32 g/L as a turning point

Clinical Background

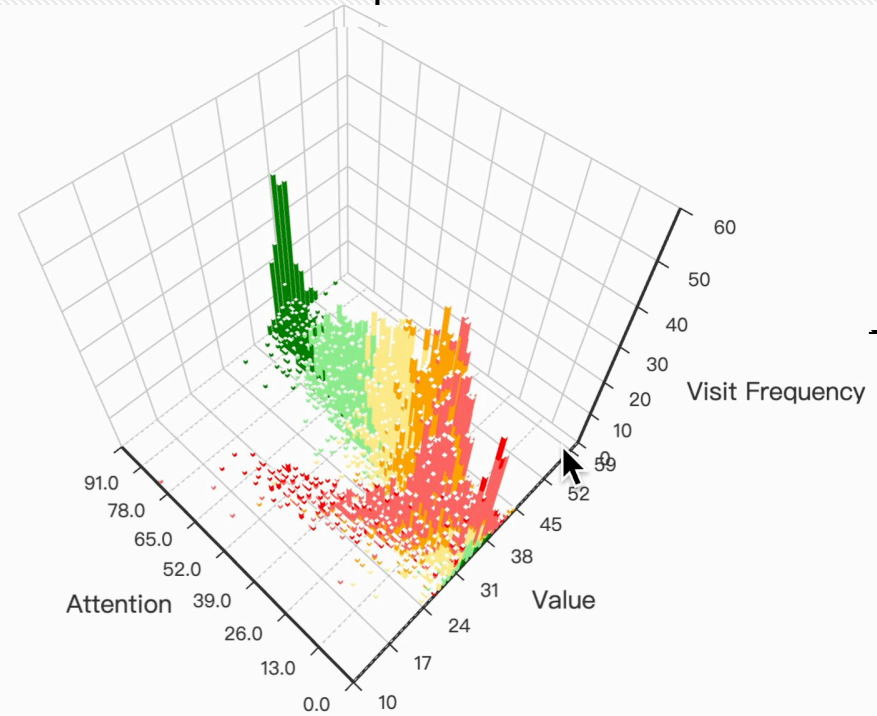
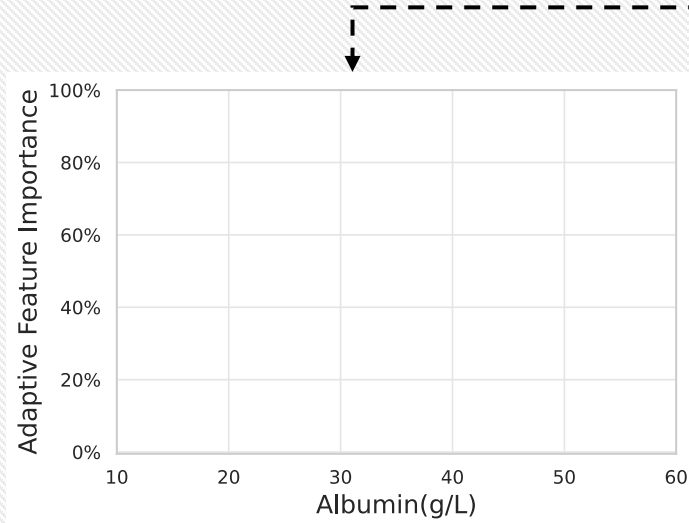
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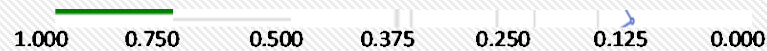
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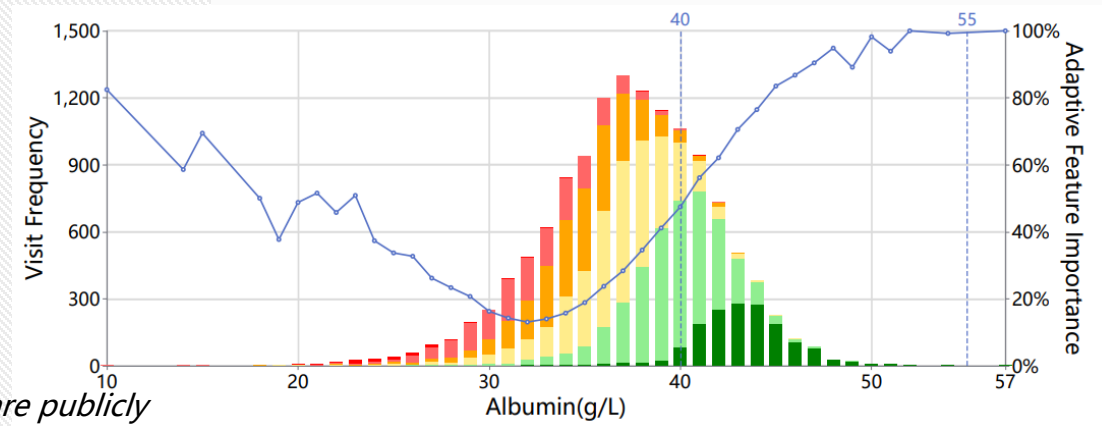
(Vertical View)



Each dot represents a follow-up visit of a patient.
The color represents the predicted risk.



(Horizontal View)



(The feature importance visualization results are publicly deployed at <http://47.93.42.104/statistics/feature>.)

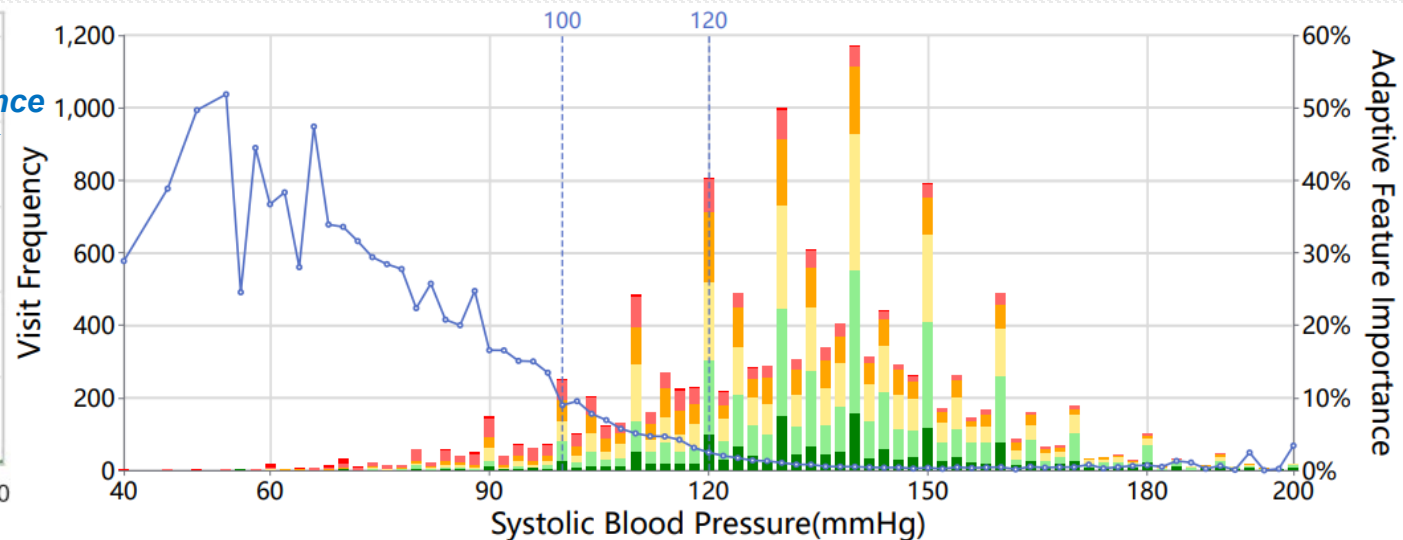
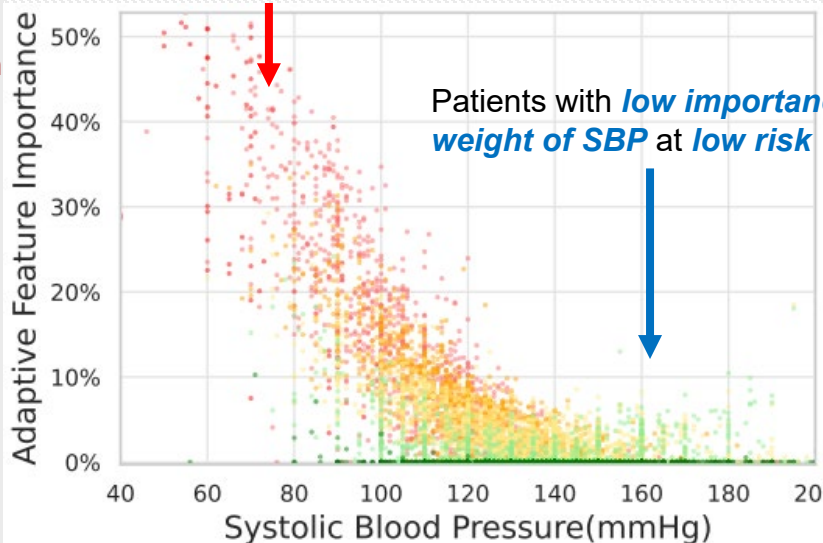


SBP: L-shaped curve with 130 mmHg as a turning point

- *AICare* believes that **Systolic Blood Pressure (SBP)** is a typical feature whose importance weights vary in an **L-shaped** fold line with 130mmHg as a turning point.
 - The importance weights decrease as the value increases.
- SBP **lower than 130 mmHg**
 - The lower the SBP level, the **more attention** the model pays.
 - When the SBP level drops below 60 mmHg, *AICare* gives more than 50% attention, and in most cases, patients are likely to be predicted with **poor outcomes** presented.
- SBP **higher than 130 mmHg**
 - *AICare* pays nearly **no attention** to SBP, which means that SBP does not affect the health status representation learning.

As a result, *AICare* recommends **raising the SBP level at least 130 mmHg** for most PD patients. **But further increments may not bring many benefits.**

Patients with **high importance weight of SBP** at **high risk**



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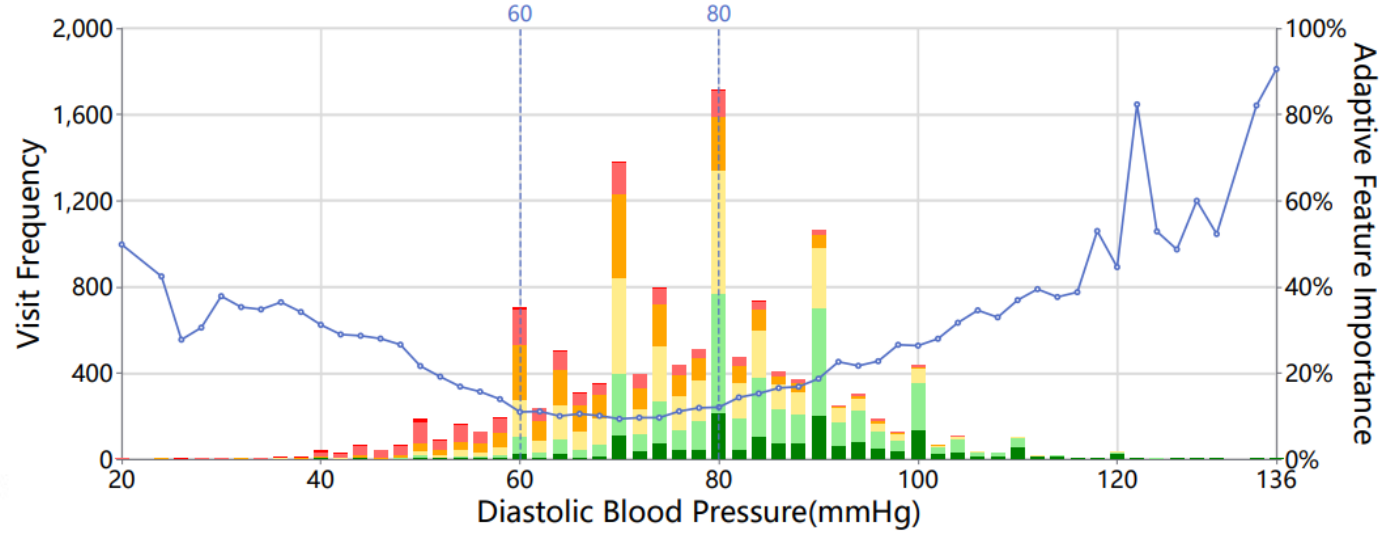
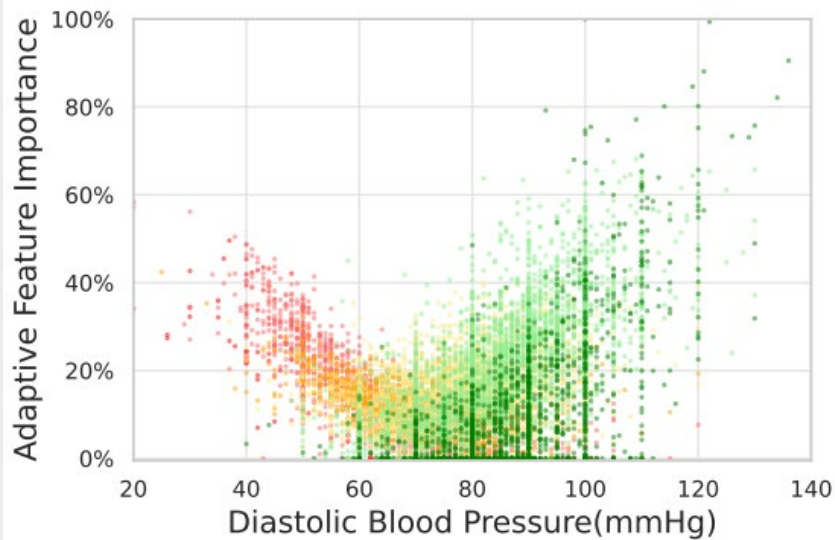


Clinical Background

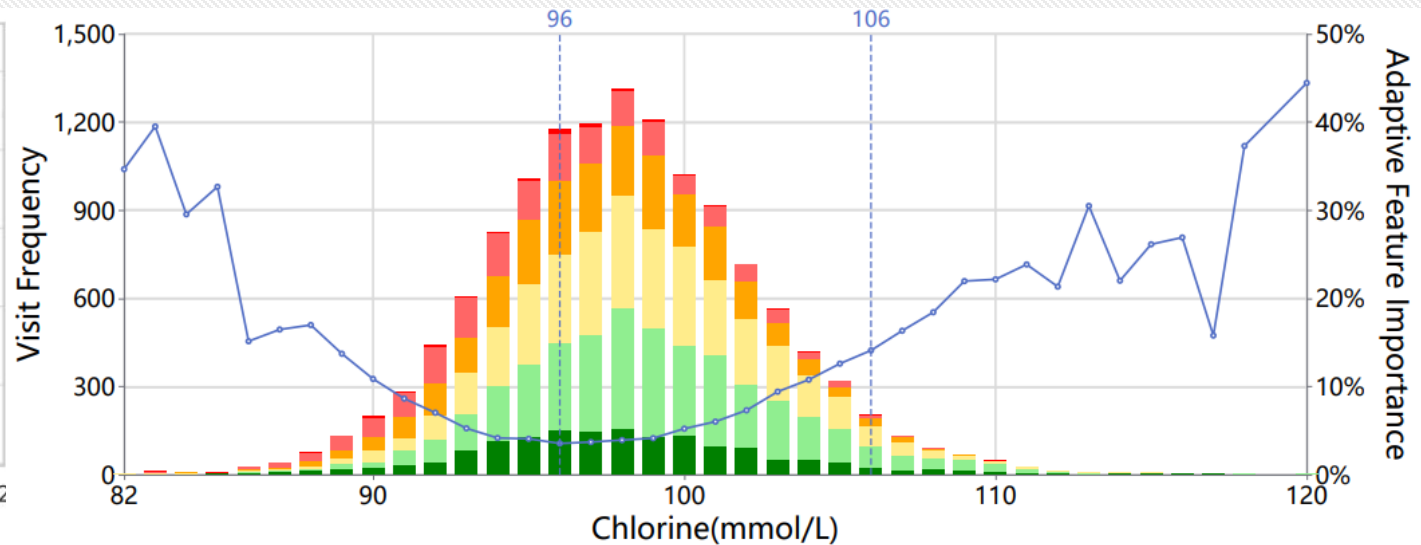
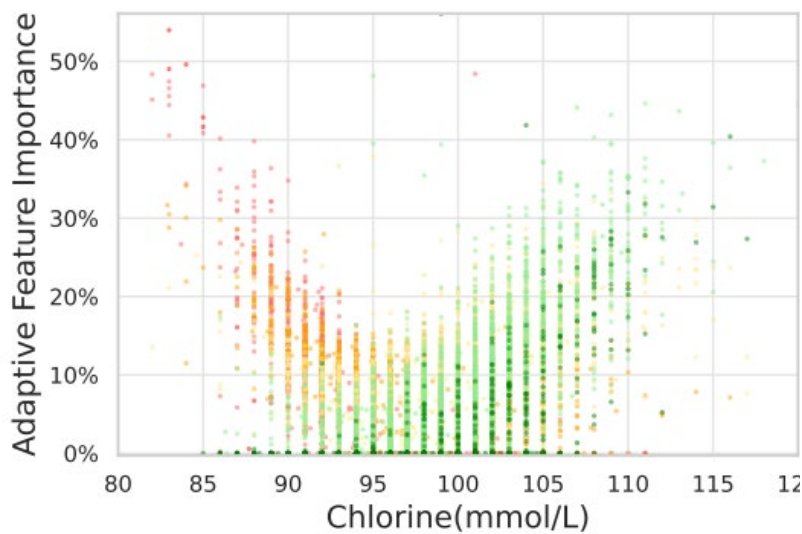
AICare Framework

Results

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Diastolic Blood Pressure (DBP): **V-shaped**.
AICare recommends increasing the DBP level to **above 70 mmHg** for most PD patients.



Chlorine (Cl): **V-shaped**.
AICare recommends increasing the Cl level to **above 96 mmol/L** for most PD patients.



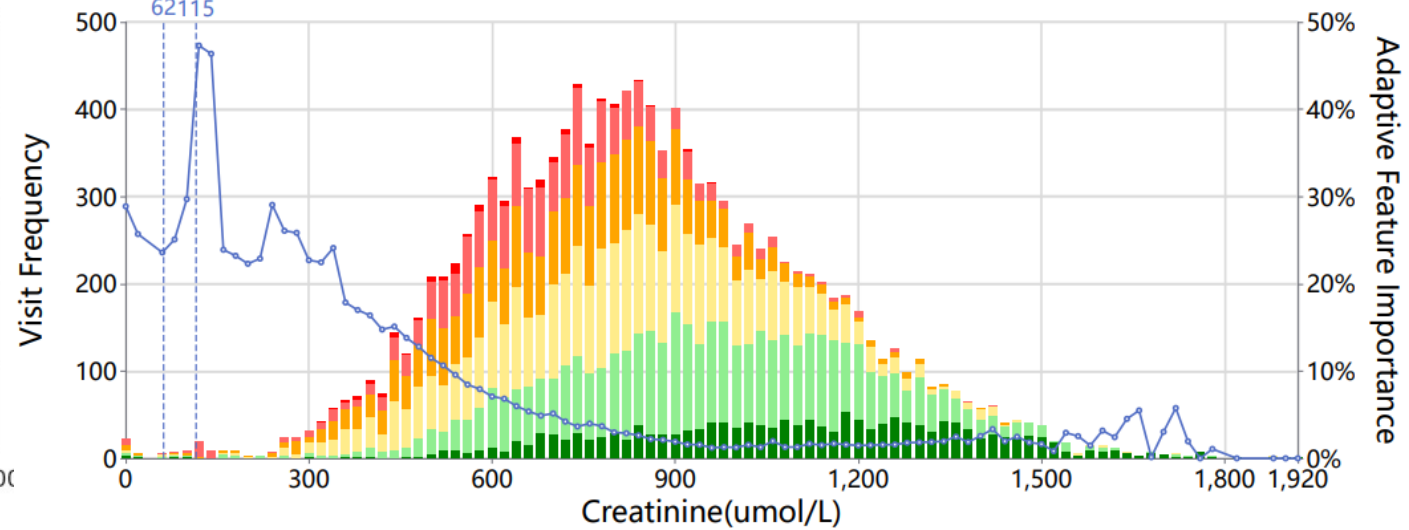
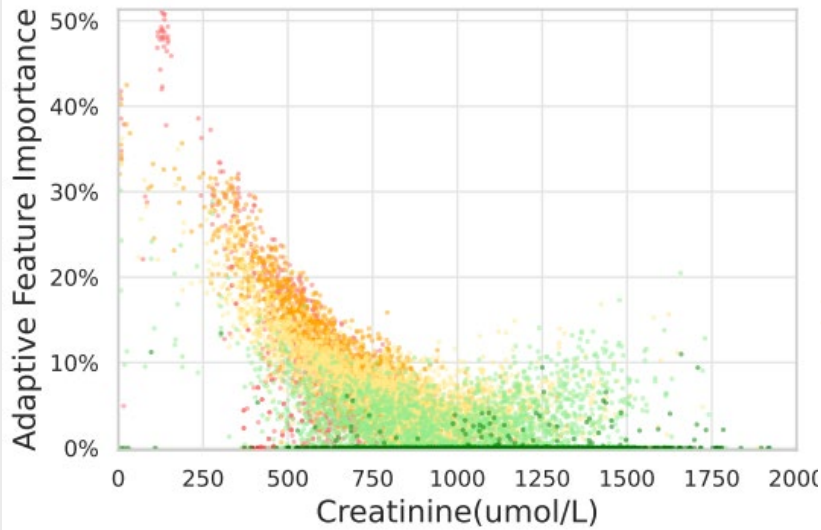


Clinical Background

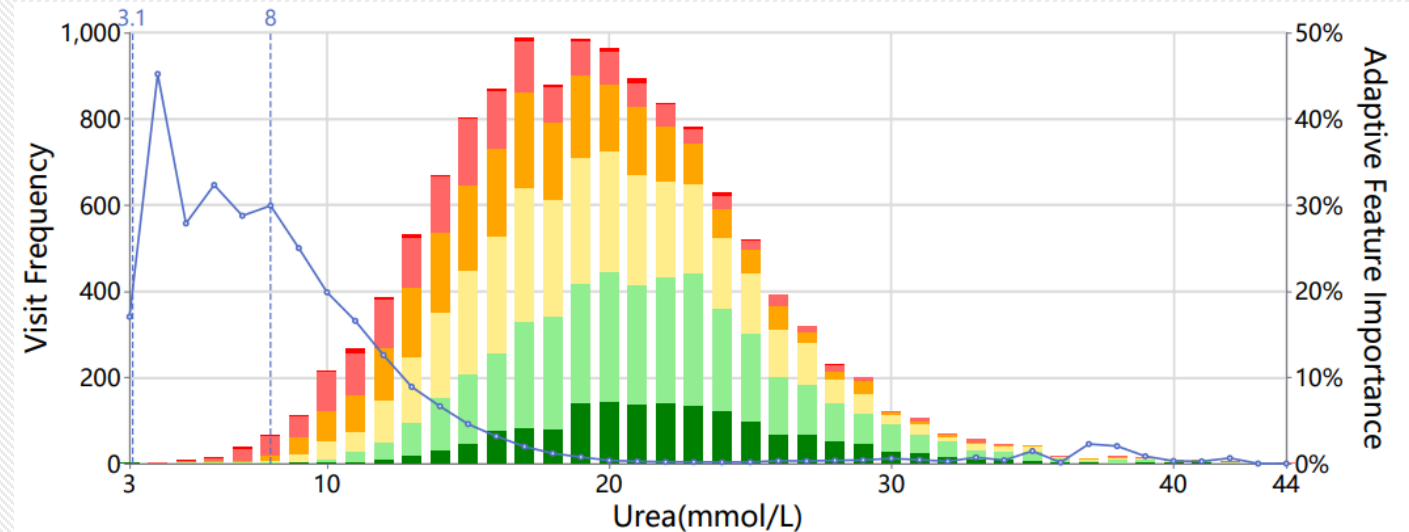
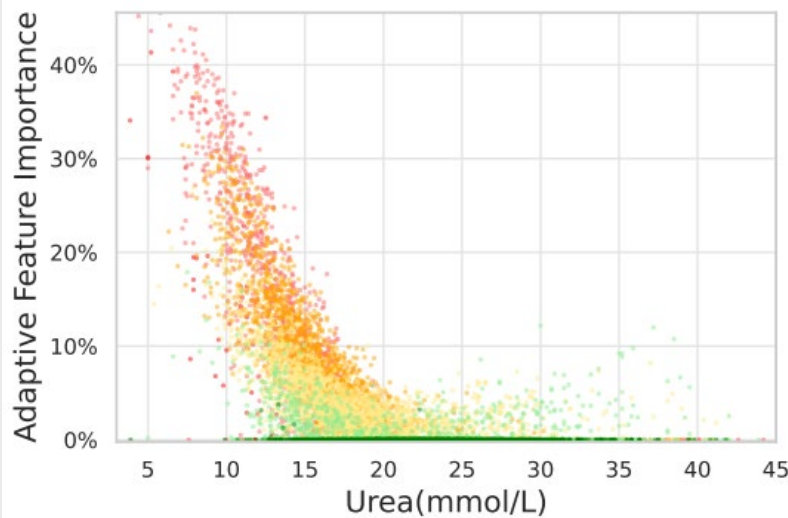
AICare Framework

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Creatinine (Cr): **L-shaped**. *AICare* recommends maintaining the Cr level **at least 900 umol/L**. This is a rough recommendation for most PD patients in this dataset. We will specify this finding for different cohorts (e.g., different gender) in future work.



Urea: **L-shaped**.

AICare recommends maintaining the Urea level **at least 20 mmol/L** for most PD patients. *But further increments may not bring many benefits.*

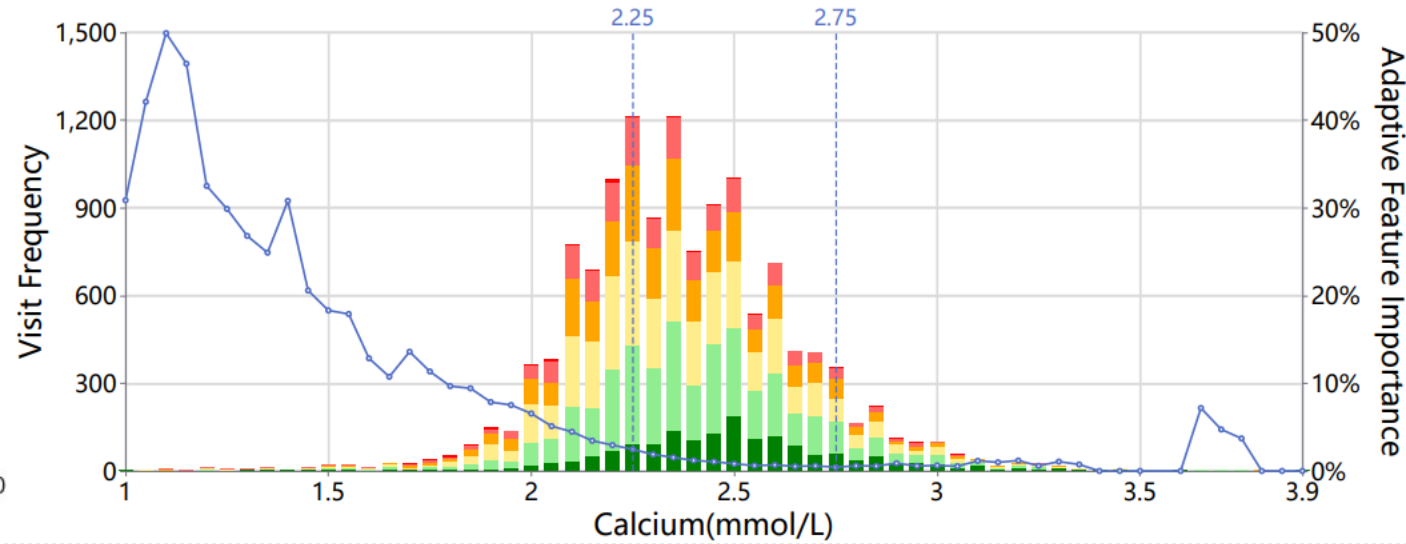
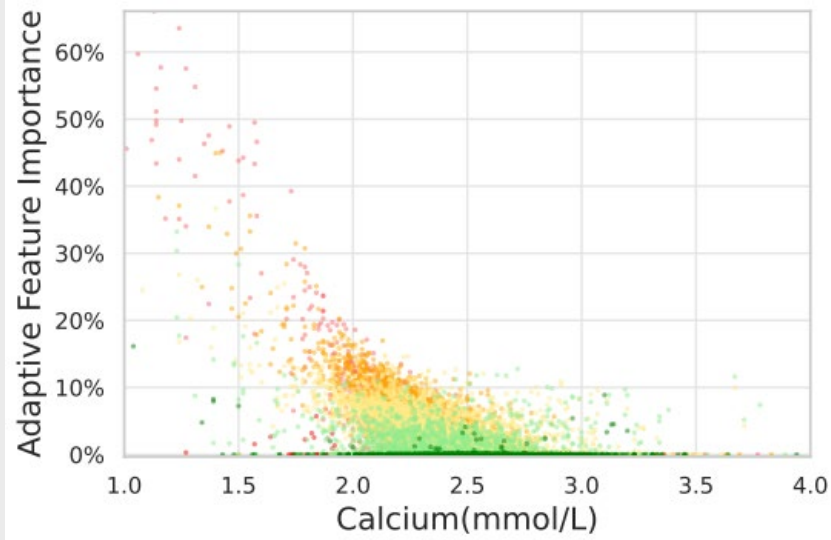


Clinical Background

AICare Framework

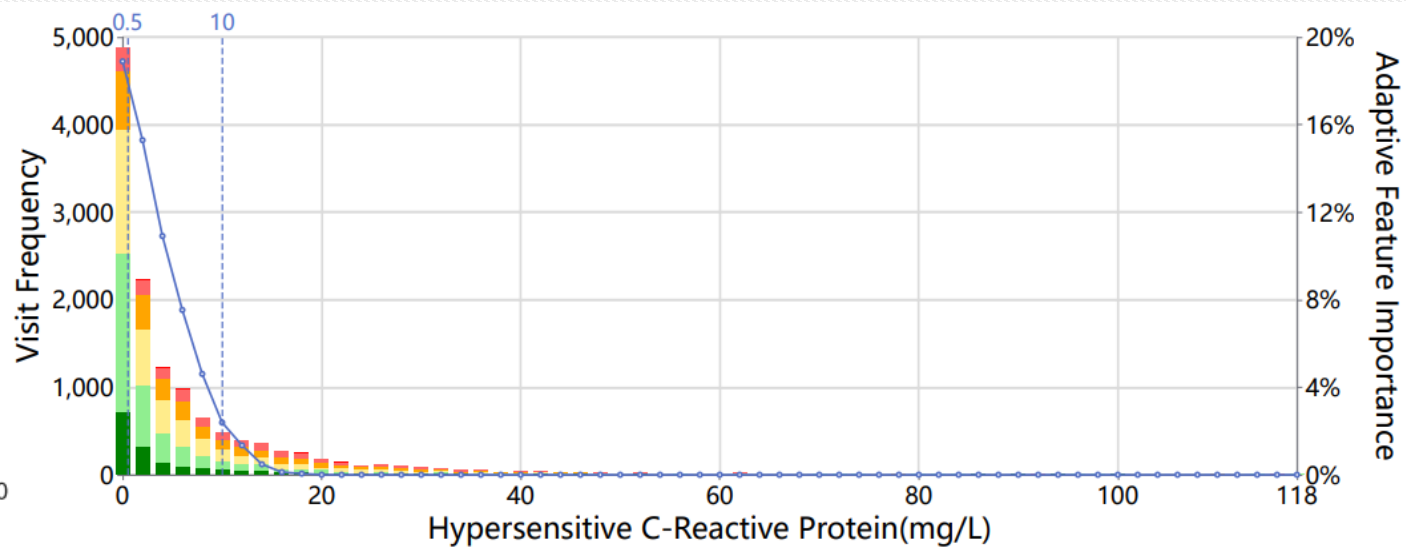
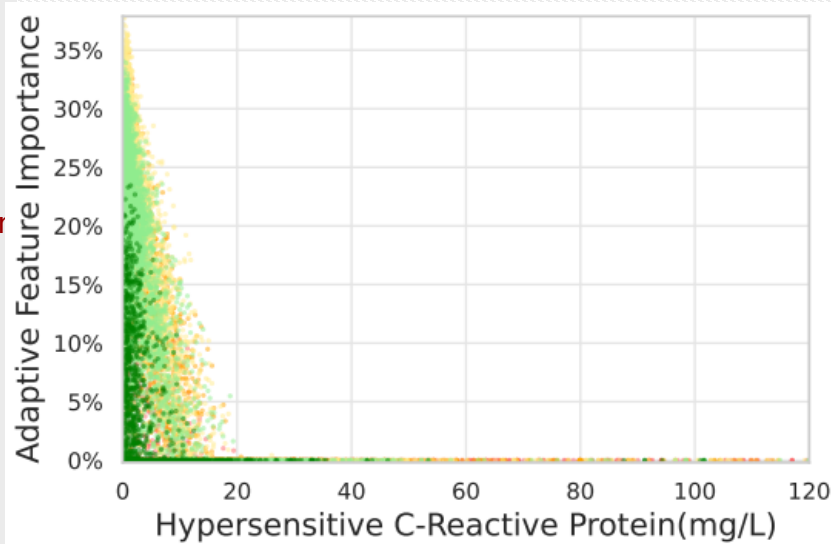
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Calcium (Ca): **L-shaped**.

AICare recommends maintaining the Ca level **at least 2.5 mmol/L** for most PD patients.
But further increments may not bring many benefits.



Hypersensitive C-Reactive Protein (Hs-CRP): **L-shaped**.

AICare recommends maintaining the Hs-CRP level **not exceed 16 mg/L** for most PD patients.



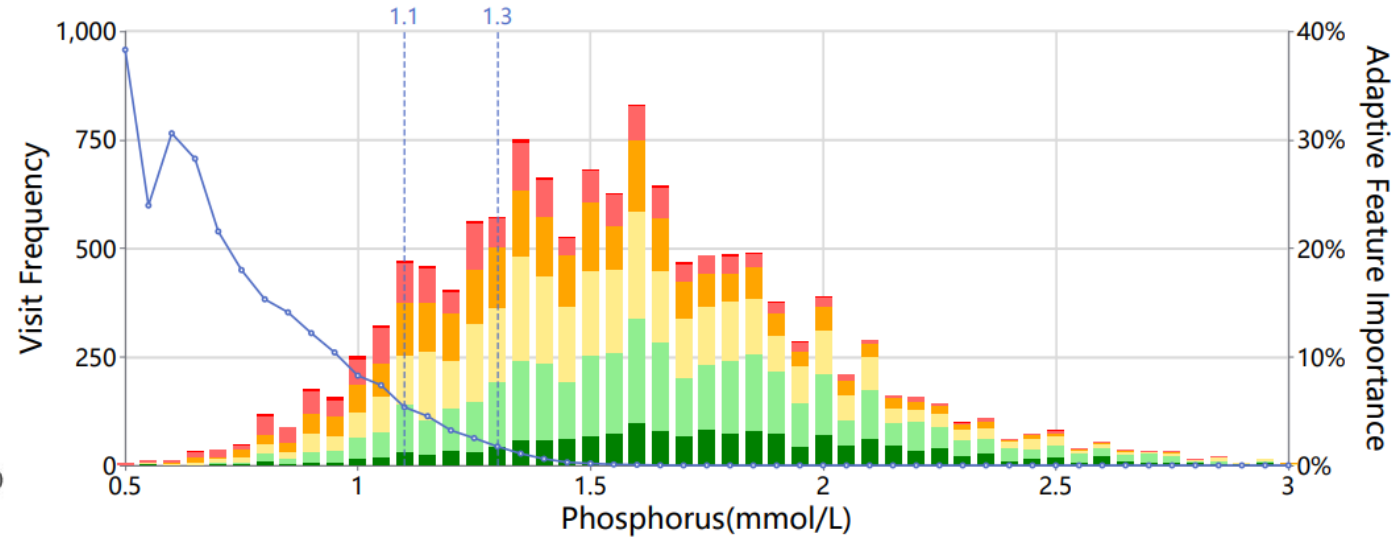
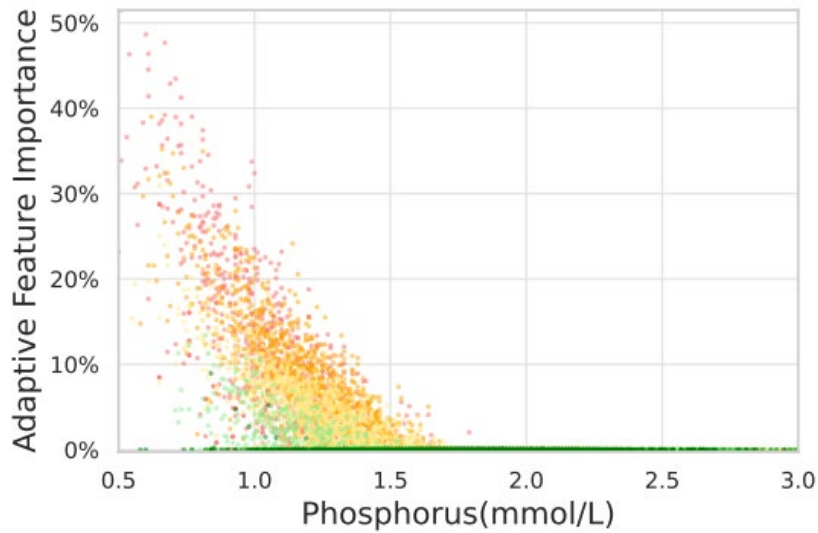
Clinical Background

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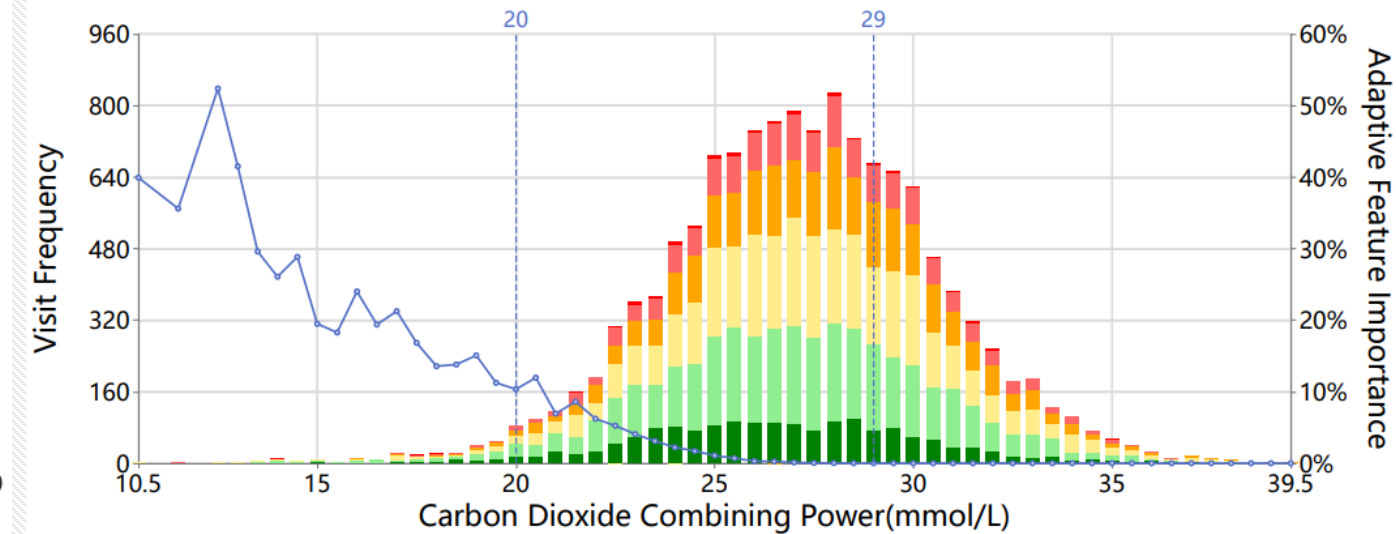
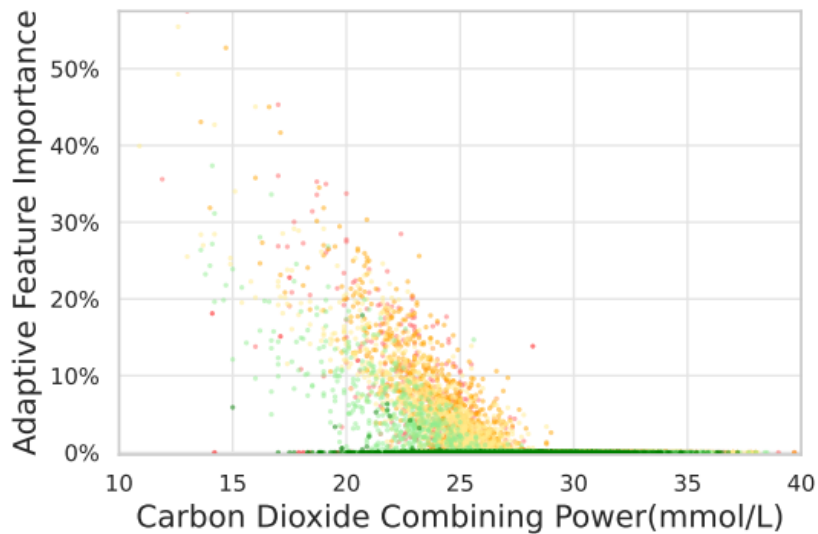
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Phosphorus (P): **L-shaped**.

AICare recommends maintaining the P level **at least 1.5 mmol/L** for most PD patients.
But further increments may not bring many benefits.



Carbon Dioxide Combining Power (CO2CP): **L-shaped**.

AICare recommends maintaining the CO2CP level **at least 25 mmol/L** for most PD patients.
But further increments may not bring many benefits.



Importance Variation Pattern and Recommended Reference Value (Turning Point) Learned by AICare for PD Patients

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Feature	Unit	Importance Variation Learned by AICare			Traditional Reference Range		Consistency
		Variation Type	Recommendation	Turning Point	Lower Limit	Upper Limit	
Albumin	g/L	V-Shape	Higher	>32	40	55	✓
DBP	mmHg	V-Shape	Higher	>70	60	80	~
SBP	mmHg	L-Shape	At Least	>130	100	120	×
Chlorine	mmol/L	V-Shape	Higher	>96	96	106	✓
Creatinine	umol/L	L-Shape	At Least	>900	62	115	×
Urea	mmol/L	L-Shape	At Least	>20	3.1	9	×
Calcium	mmol/L	L-Shape	At Least	>2.5	2.25	2.75	~
Sodium	mmol/L	L-Shape	At Least	>135.5	135	145	✓
Potassium	mmol/L	L-Shape	At Least	>4	3.5	5.5	✓
Phosphorus	mmol/L	L-Shape	At Least	>1.5	1.1	1.3	×
CO2CP	mmol/L	L-Shape	At Least	>25	20	29	~
Hemoglobin	g/L	L-Shape	At Least	>114	115	150	✓
Weight	kg	L-Shape	At Least	>59	-	-	-
Glucose	mmol/L	L-Shape	Not Exceed	<6	3.9	6.1	✓
Hs-CRP	mg/L	L-Shape	Not Exceed	<16	0.5	10	✓
WBC	x10 ⁹ /L	Irregular	Unknown	-	3.5	9.5	-



We publicly release the source code and AI-Doctor Interaction System

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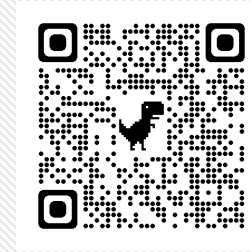
Results

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- Scan the QR code to try the visualization prototype system!

- Source code of *AICare*

- <https://github.com/Accountable-Machine-Intelligence/AICare>



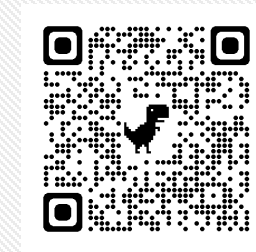
- Case Study

- <http://47.93.42.104/A1>
- <http://47.93.42.104/A2>
- <http://47.93.42.104/A3>
- <http://47.93.42.104/A4>
- <http://47.93.42.104/A5>
- <http://47.93.42.104/A6>
- <http://47.93.42.104/A7>
- <http://47.93.42.104/A8>
- <http://47.93.42.104/A9>
- <http://47.93.42.104/A10>



- Variation of Feature Importance

- <http://47.93.42.104/statistics/feature>





Thanks for you attention!