

Supplementary Material

Title: Early Fluid Therapy Trajectories in Acute Pancreatitis: A Retrospective Cohort Study

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Table S1. Statistics for choosing the best number of trajectories.

G	Conv	AIC	BIC	SABIC	Entropy	PP 1	PP 2	PP 3	PP 4	PP 5	PP 6
2	1	73983.73	74074.51	74026.85	0.66	0.91	0.91	NA	NA	NA	-
3	1	73147.09	73268.15	73204.60	0.69	0.81	0.90	0.87	NA	NA	-
4	1	72837.25	72988.57	72909.13	0.67	0.85	0.76	0.88	0.83	NA	-
5	1	72641.96	72823.54	72728.21	0.79	0.86	0.91	0.80	0.84	0.72	-
6	2	76367.56	76524.93	76442.32	0.54	0.76	0.62	0.61	0.53	0.82	0.65

AIC, Akaike information criterion; BIC, Bayesian information criteria; SABIC, sample-adjusted information criteria; PP, posterior probability.

Table S2. Baseline characteristics of included acute pancreatitis grouped by quartile of CumFWR.

Variables	Total (n = 3142)	Quartile 1 (n = 786)	Quartile 2 (n = 785)	Quartile 3 (n = 785)	Quartile 4 (n = 786)	<i>p</i>
Male, n (%)	2050 (65.2)	621 (79)	531 (67.6)	475 (60.5)	423 (53.8)	< 0.001
Age (years)	47.3 ± 13.4	44.8 ± 12.7	47.3 ± 13.1	48.6 ± 13.4	48.8 ± 14.0	< 0.001
BMI (kg/m ²)	24.7 ± 4.1	27.3 ± 4.0	25.2 ± 3.8	24.3 ± 3.6	22.9 ± 3.6	< 0.001
Etiology, n (%)						< 0.001
Biliary	1394 (44.4)	273 (34.7)	392 (49.9)	354 (45.1)	375 (47.7)	
HTG	1081 (34.4)	307 (39.1)	251 (32)	263 (33.5)	260 (33.1)	
Alcoholism	237 (7.5)	71 (9)	52 (6.6)	62 (7.9)	52 (6.6)	

Others	430 (13.7)	135 (17.2)	90 (11.5)	106 (13.5)	99 (12.6)	
Smoking, n (%)	911 (29.0)	268 (34.1)	228 (29)	219 (27.9)	196 (24.9)	< 0.001
Drinking, n (%)	959 (30.5)	262 (33.3)	221 (28.2)	238 (30.3)	238 (30.3)	0.169
Diabetes, n (%)	387 (12.3)	85 (10.8)	85 (10.8)	108 (13.8)	109 (13.9)	0.089
Body						
temperature	37.0 ± 0.7	37.0 ± 0.6	37.0 ± 0.7	37.0 ± 0.7	37.1 ± 0.7	0.076
(°C)						
Heart rate (bpm)	94.5 ± 20.3	91.6 ± 17.2	93.3 ± 18.1	95.4 ± 20.3	97.6 ± 24.3	< 0.001
Respirations						
	22.3 ± 5.5	20.8 ± 3.0	21.9 ± 5.0	22.7 ± 5.9	23.6 ± 6.9	< 0.001
(bpm)						
Mean Arterial						
Pressure	98.6 ± 19.8	100.3 ± 13.9	100.3 ± 20.9	98.9 ± 26.2	94.9 ± 15.2	< 0.001
(mmHg)						
NEU (%)	83.5 ± 9.7	81.2 ± 10.6	83.2 ± 10.1	84.9 ± 8.5	84.7 ± 8.9	< 0.001
HCT (%)	41.1 ± 7.9	41.2 ± 8.0	40.8 ± 7.4	40.8 ± 8.0	41.8 ± 8.1	0.041
TBIL (umol/L)	18.3 (11.7, 30.9)	17.0 (10.9, 26.5)	19.0 (11.9, 32.0)	18.8 (12.2, 32.0)	18.6 (11.8, 35.3)	0.007
ALB (g/L)	39.0 ± 6.1	41.0 ± 5.1	39.0 ± 5.8	38.2 ± 6.1	38.0 ± 6.7	< 0.001
LDH (U/L)	295.5 (209.0, 446.0)	251.2 (183.2, 350.8)	285.2 (199.3, 411.2)	328.0 (228.2, 529.6)	354.6 (231.1, 629.2)	< 0.001
TG (mmol/L)	2.0 (0.9, 8.0)	2.3 (1.2, 8.3)	1.7 (0.8, 6.4)	1.8 (0.8, 8.3)	1.8 (0.9, 8.8)	< 0.001

AMY (U/L)	383.0 (132.0, 871.0)	222.0 (84.1, 593.6)	353.0 (134.2, 778.0)	497.0 (185.0, 1038.0)	507.0 (165.1, 1030.5)	< 0.001
BUN (mmol/L)	5.0 (3.7, 6.7)	4.7 (3.7, 6.3)	4.8 (3.6, 6.4)	5.0 (3.7, 6.8)	5.4 (3.9, 7.6)	< 0.001
Cr (mmol/L)	67.3 (54.7, 82.7)	70.0 (57.3, 80.5)	66.0 (54.6, 78.0)	65.6 (53.0, 85.5)	68.8 (54.2, 91.6)	< 0.001
Ca (mmol/L)	2.1 ± 0.3	2.2 ± 0.3	2.1 ± 0.3	2.1 ± 0.3	2.0 ± 0.4	< 0.001
PaO ₂ /FiO ₂	376.0 ± 117.0	386.3 ± 103.4	376.9 ± 114.0	366.2 ± 113.9	376.1 ± 131.9	0.063
SIRS	1.4 ± 1.1	1.2 ± 1.0	1.4 ± 1.1	1.5 ± 1.1	1.6 ± 1.1	< 0.001
APACHEII	7.1 ± 4.7	5.6 ± 4.0	6.4 ± 4.5	7.5 ± 4.5	9.0 ± 5.1	< 0.001
ALB used, n (%)	781 (24.9)	73 (9.3)	157 (20)	245 (31.2)	306 (38.9)	< 0.001
LMWH used, n (%)	630 (20.1)	160 (20.4)	150 (19.1)	161 (20.5)	159 (20.2)	0.897
Insulin used, n (%)	1666 (53.0)	317 (40.3)	365 (46.5)	432 (55)	552 (70.2)	< 0.001
FWR day1, (mL/kg)	41.9 ± 19.0	26.7 ± 6.9	35.0 ± 8.3	44.1 ± 11.5	61.9 ± 22.5	< 0.001
FWR day2, (mL/kg)	46.6 ± 19.4	27.5 ± 5.1	38.4 ± 4.5	48.9 ± 6.5	71.4 ± 19.0	< 0.001
FWR day3, (mL/kg)	44.1 ± 17.9	27.1 ± 6.1	37.0 ± 6.6	46.6 ± 8.5	65.6 ± 17.6	< 0.001

CumFWR,
 89.6 ± 33.8 54.4 ± 8.3 74.4 ± 5.0 94.2 ± 6.7 135.2 ± 29.1 < 0.001
(mL/kg)

Abbreviations: FWR, fluid therapy-to-body weight ratio; BMI, Body Mass Index; NEU, neutrophil; HCT, hematocrit; TBIL, total bilirubin; ALB, albumin; TG, triglyceride; BUN, blood urea nitrogen; Cr, creatinine; Ca, calcium; SIRS, systemic inflammatory response syndrome; APACHEII, Acute Physiology and Chronic Health Evaluation II; LMWH, Low Molecular Weight Heparin.

Table S3. The clinical outcomes of included acute pancreatitis grouped by quartile of CumFWR.

Variables	Total (n = 3142)	Quartile 1 (n = 786)	Quartile 2 (n = 785)	Quartile 3 (n = 785)	Quartile 4 (n = 786)	<i>p</i>
Severity, n (%)						< 0.001
MAP, n (%)	1338 (42.6)	410 (52.2)	348 (44.3)	277 (35.3)	303 (38.5)	
MSAP, n (%)	1100 (35.0)	293 (37.3)	288 (36.7)	282 (35.9)	237 (30.2)	
SAP, n (%)	704 (22.4)	83 (10.6)	149 (19)	226 (28.8)	246 (31.3)	
APFC, n (%)	786 (25.0)	182 (23.2)	212 (27)	209 (26.6)	183 (23.3)	0.142
PPC, n (%)	69 (2.2)	16 (2)	17 (2.2)	18 (2.3)	18 (2.3)	0.983
WON, n (%)	272 (8.7)	33 (4.2)	55 (7)	79 (10.1)	105 (13.4)	< 0.001
ANC, n (%)	720 (22.9)	108 (13.7)	161 (20.5)	220 (28)	231 (29.4)	< 0.001
IPN, n (%)	145 (4.6)	13 (1.7)	21 (2.7)	43 (5.5)	68 (8.7)	< 0.001

Respiratory failure, n (%)	1001 (31.9)	165 (21)	219 (27.9)	297 (37.8)	320 (40.7)	< 0.001
Persistent respiratory failure, n (%)	677 (21.5)	78 (9.9)	143 (18.2)	218 (27.8)	238 (30.3)	< 0.001
Renal failure, n (%)	283 (9.0)	24 (3.1)	41 (5.2)	88 (11.2)	130 (16.5)	< 0.001
Persistent renal failure, n (%)	189 (6.0)	9 (1.1)	21 (2.7)	59 (7.5)	100 (12.7)	< 0.001
Circulatory failure, n (%)	169 (5.4)	7 (0.9)	14 (1.8)	50 (6.4)	98 (12.5)	< 0.001
Persistent circulatory failure, n (%)	144 (4.6)	7 (0.9)	13 (1.7)	40 (5.1)	84 (10.7)	< 0.001
Organ failure, n (%)	1049 (33.4)	175 (22.3)	230 (29.3)	311 (39.6)	333 (42.4)	< 0.001
Persistent Organ Failure, n (%)	704 (22.4)	83 (10.6)	149 (19)	226 (28.8)	246 (31.3)	< 0.001
Persistent MOF, n (%)	230 (7.3)	9 (1.1)	23 (2.9)	70 (8.9)	128 (16.3)	< 0.001
LOS (days)	9.0 (6.0, 14.0)	7.0 (5.0, 10.0)	9.0 (6.0, 14.0)	10.0 (6.0, 16.0)	10.0 (7.0, 17.0)	< 0.001
LOS in ICU (days)	0.0 (0.0, 3.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 5.0)	0.0 (0.0, 7.0)	< 0.001
Mortality, n (%)	101 (3.2)	3 (0.4)	9 (1.1)	31 (3.9)	58 (7.4)	< 0.001

79 Abbreviations: AP, acute pancreatitis; MAP, mild acute pancreatitis; MSAP, moderately
80 severe acute pancreatitis; SAP, severe acute pancreatitis; APFC, acute peripancreatic fluid
81 collection; PPC, pancreatic pseudocyst; WON, walled-off necrosis; ANC, acute necrotic

82 collection; IPN, infected pancreatic necrosis; LOS, length of hospital stay; MOF, multiple

83 organ failure; ICU, intensive care unit.

84

85 **Table S4.** Multicollinearity evaluation of predictor variables through variance inflation factor

86 (VIF) analysis.

Feature	VIF
SEX	2.078
Age	1.942
BMI	1.615
Smoking	1.794
Drinking	2.183
Diabetes	1.289
Body temperature	1.362
Heart rate	1.788
Respirations	1.541
Mean arterial pressure	1.1
NEU	1.265
HCT	1.378
TG	1.561
BUN	2.851
Cr	2.974

Ca 1.577

87 Abbreviations as in Table S2.

88

89 **Table S5:** Proportion of missing data per variable in the final regression model

Variable	Missing frequent	Missing percentage %
SEX	0	0
Age	0	0
Smoking	0	0
Drinking	0	0
Body temperature	0	0
Heart rate	1	0.0318
HCT	111	3.5328
BUN	93	2.9599
TG	483	15.3724

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91 Abbreviations as in Table S2.

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93 **Table S6.** Standardized mean difference (SMD) for each variable before and after propensity

94 score matching.

Variables	Before PSM			After PSM		
	LMVT (2642)	HVT (500)	SMD	LMVT (483)	HVT (483)	SMD

Sex	1747 (66.1)	303 (60.6)	0.115	305 (63.1)	292 (60.5)	0.055
Drinking	781 (29.6)	178 (35.6)	0.129	166 (34.4)	169 (35.0)	0.013
BMI	24.51 (3.45)	23.88 (3.78)	0.174	24.05 (3.73)	23.94 (3.80)	0.029
Body temperature	37.00 (0.66)	37.12 (0.81)	0.167	37.09 (0.71)	37.10 (0.80)	0.018
Heart rate	92.63 (19.05)	104.26 (23.53)	0.543	101.92 (22.68)	103.17 (22.86)	0.055
Respirations	21.83 (4.93)	24.49 (7.37)	0.424	24.10 (7.15)	24.23 (7.28)	0.018
HCT	40.87 (7.66)	42.64 (8.24)	0.223	42.66 (8.23)	42.52 (8.19)	0.017
TG	5.75 (7.98)	8.59 (10.48)	0.305	8.44 (10.87)	8.31 (10.34)	0.012
BUN	5.65 (3.71)	7.06 (4.72)	0.334	6.90 (4.92)	6.97 (4.71)	0.015
SIRS	1.34 (1.06)	1.79 (1.11)	0.423	1.71 (1.09)	1.76 (1.10)	0.05
APACHE II	6.53 (4.41)	10.36 (4.99)	0.813	10.28 (4.98)	9.99 (4.49)	0.061

95 Abbreviations as in Table S2.

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97 **Table S7.** Hazard ratio (HR) of propensity score matching - related models

Models	HR (95%CI)	P value
Unmatched crude	3.19 (2.14~4.76)	<0.001
Multivariable adjusted	2.57 (1.68~3.93)	<0.001
Propensity Score adjusted	2.11 (1.39~3.21)	<0.001
Propensity Score Matched	2.31 (1.36~3.94)	0.002
Weighted IPTW	1.64 (1.04~2.6)	0.038
Weighted SMRW	1.74 (1.28~2.37)	0.03

Weighted PA 1.66 (0.99~2.77) 0.026

Weighted Ow 1.64 (0.88~3.08) 0.028

HR, hazard ratio; SMD, standardized mean difference; IPTW, inverse probability of treatment weighting; SMRW, stabilized inverse probability of treatment weighting; PA, propensity score adjustment; Ow, Overlap Weighting.

Table S8. Comparisons of baseline characteristics of the AP patients with LMVT and HVT group before and after propensity score matching.

Variables	Before PSM				After PSM		
	Total	LMVT	HVT	<i>p</i>	LMVT	HVT	<i>p</i>
	(n = 3142)	(n = 2642)	(n = 500)		(n = 483)	(n = 483)	
Male, n (%)	2050 (65.2)	1747 (66.1)	303 (60.6)	0.017	305 (63.1)	292 (60.5)	0.389
Age (years)	47.3 ± 13.4	47.3 ± 13.2	47.4 ± 14.2	0.888	48.8 ± 13.7	47.5 ± 14.3	0.128
BMI (kg/m ²)	24.7 ± 4.1	24.9 ± 4.1	23.9 ± 4.0	< 0.001	24.1 ± 4.1	23.9 ± 4.0	0.521
Etiology, n (%)				0.001			0.971
Biliary	1394 (44.4)	1202 (45.5)	192 (38.4)		187 (38.7)	187 (38.7)	
HTG	1081 (34.4)	873 (33)	208 (41.6)		196 (40.6)	200 (41.4)	
Alcoholism	237 (7.5)	207 (7.8)	30 (6)		29 (6)	30 (6.2)	
Others	430 (13.7)	360 (13.6)	70 (14)		71 (14.7)	66 (13.7)	
Smoking, n (%)	911 (29.0)	775 (29.3)	136 (27.2)	0.335	157 (32.5)	132 (27.3)	0.079

Drinking, n (%)	959 (30.5)	781 (29.6)	178 (35.6)	0.007	166 (34.4)	169 (35)	0.839
Diabetes, n (%)	387 (12.3)	298 (11.3)	89 (17.8)	<	88 (18.2)	84 (17.4)	0.737
				0.001			
Body temperature (°C)	37.0 ± 0.7	37.0 ± 0.7	37.1 ± 0.8	<	37.1 ± 0.7	37.1 ± 0.8	0.776
				0.001			
Heart rate (bpm)	94.5 ± 20.3	92.6 ± 19.1	104.3 ± 23.5	<	101.9 ± 22.7	103.2 ± 22.9	0.391
				0.001			
Respirations (bpm)	22.3 ± 5.5	21.8 ± 4.9	24.5 ± 7.4	<	24.1 ± 7.2	24.2 ± 7.3	0.775
				0.001			
Mean Arterial Pressure (mmHg)	98.6 ± 19.8	99.0 ± 20.5	96.7 ± 15.6	0.021	100.5 ± 15.7	97.0 ± 15.6	<
							0.001
NEU (%)	83.5 ± 9.7	83.3 ± 9.9	84.5 ± 8.6	0.013	84.9 ± 8.8	84.6 ± 8.5	0.607
HCT (%)	41.1 ± 7.9	40.8 ± 7.7	42.7 ± 8.5	<	42.6 ± 8.3	42.6 ± 8.4	0.974
				0.001			
DBIL (umol/L)	5.5 (3.1, 12.2)	5.5 (3.2, 11.8)	5.2 (2.9, 13.8)	0.525	5.1 (2.9, 10.6)	5.3 (3.0, 13.9)	0.278
ALB (g/L)	39.0 ± 6.1	39.4 ± 5.7	37.7 ± 7.1	<	38.4 ± 6.4	37.8 ± 7.0	0.267
				0.001			
LDH (U/L)	295.5 (209.0, 446.0)	285.1 (202.1, 413.1)	377.3 (250.0, 643.0)	<	374.6 (256.5, 661.2)	363.9 (247.0, 635.0)	0.792

TG (mmol/L)	2.0 (0.9, 8.0)	1.9 (0.9, 7.0)	3.1 (1.1, 12.9)	<	2.9 (1.0, 13.9)	2.9 (1.1, 12.6)	0.884
							0.001
AMY (U/L)	383.0 (132.0, 871.0)	358.6 (126.2, 837.0)	507.0 (182.0, 1001.0)	<	433.0 (156.0, 884.0)	503.7 (178.4, 961.2)	0.07
BUN (mmol/L)	5.0 (3.7, 6.7)	4.9 (3.6, 6.5)	5.7 (4.2, 8.6)	<	5.5 (4.0, 7.8)	5.6 (4.2, 8.4)	0.365
							0.001
Cr (mmol/L)	67.3 (54.7, 82.7)	67.0 (54.2, 80.5)	73.1 (57.1, 107.8)	<	70.2 (54.0, 102.5)	72.3 (57.0, 101.0)	0.255
Ca (mmol/L)	2.1 ± 0.3	2.1 ± 0.3	2.0 ± 0.4	<	2.1 ± 0.3	2.0 ± 0.4	0.073
							0.001
PaO ₂ /FiO ₂	376.0 ± 117.0	375.9 ± 112.3	376.4 ± 136.2	0.946	360.5 ± 117.8	379.2 ± 133.1	0.049
SIRS	1.4 ± 1.1	1.3 ± 1.1	1.8 ± 1.1	<	1.7 ± 1.1	1.8 ± 1.1	0.43
							0.001
APACHEII	7.1 ± 4.7	6.5 ± 4.4	10.4 ± 5.0	<	10.3 ± 5.0	10.0 ± 4.5	0.409
							0.001
CumFWR, (mL/kg)	89.6 ± 33.8	81.2 ± 24.4	133.6 ± 41.6	<	88.0 ± 25.6	132.4 ± 39.7	<
							0.001

Abbreviations as in Table S2.

Table S9. The clinical outcomes of the AP patients with LMVT and HVT group before and after propensity score matching.

Variables	Before PSM				<i>p</i>	After PSM		
	Total (n =	LMVT	HVT	LMVT		HVT	<i>p</i>	
	3142)	(n = 2642)	(n = 500)	(n = 483)		(n = 483)		
Severity, n (%)				<			0.364	
				0.001				
MAP, n (%)	1338 (42.6)	1195 (45.2)	143 (28.6)		144 (29.8)	143 (29.6)		
MSAP, n (%)	1100 (35.0)	950 (36)	150 (30)		167 (34.6)	149 (30.8)		
SAP, n (%)	704 (22.4)	497 (18.8)	207 (41.4)		172 (35.6)	191 (39.5)		
APFC, n (%)	786 (25.0)	671 (25.4)	115 (23)	0.256	134 (27.7)	110 (22.8)	0.076	
PPC, n (%)	69 (2.2)	59 (2.2)	10 (2)	0.744	9 (1.9)	10 (2.1)	0.817	
WON, n (%)	272 (8.7)	178 (6.7)	94 (18.8)	<	67 (13.9)	86 (17.8)	0.094	
				0.001				
ANC, n (%)	720 (22.9)	516 (19.5)	204 (40.8)	<	158 (32.7)	194 (40.2)	0.016	
				0.001				
IPN, n (%)	145 (4.6)	89 (3.4)	56 (11.2)	<	35 (7.2)	55 (11.4)	0.027	
				0.001				
Respiratory failure, n (%)	1001 (31.9)	750 (28.4)	251 (50.2)	<	212 (43.9)	235 (48.7)	0.138	
				0.001				
Persistent respiratory failure, n (%)	677 (21.5)	477 (18.1)	200 (40)	<	168 (34.8)	185 (38.3)	0.256	
				0.001				

Renal failure, n (%)	283 (9.0)	165 (6.2)	118 (23.6)	<	82 (17)	106 (21.9)	0.051
				0.001			
Persistent renal failure, n (%)	189 (6.0)	96 (3.6)	93 (18.6)	<	47 (9.7)	82 (17)	<
				0.001			0.001
Circulatory failure, n (%)	169 (5.4)	88 (3.3)	81 (16.2)	<	34 (7)	73 (15.1)	<
				0.001			0.001
Persistent circulatory failure, n (%)	144 (4.6)	75 (2.8)	69 (13.8)	<	31 (6.4)	61 (12.6)	0.001
				0.001			
Organ failure, n (%)	1049 (33.4)	787 (29.8)	262 (52.4)	<	221 (45.8)	246 (50.9)	0.107
				0.001			
Persistent Organ Failure, n (%)	704 (22.4)	497 (18.8)	207 (41.4)	<	172 (35.6)	191 (39.5)	0.207
				0.001			
Persistent MOF, n (%)	230 (7.3)	119 (4.5)	111 (22.2)	<	59 (12.2)	101 (20.9)	<
				0.001			0.001
LOS (days)	9.0 (6.0, 14.0)	8.0 (6.0, 13.0)	11.0 (7.0, 21.0)	<	10.0 (6.0, 18.0)	11.0 (7.0, 20.0)	0.05
				0.001			
Mortality, n (%)	101 (3.2)	46 (1.7)	55 (11)	<	19 (3.9)	49 (10.1)	<
				0.001			0.001

Abbreviations as in Table S3.

Table S10. Unmeasured confounding E-value calculation.

Item	point	lower	upper
HR	2.31	1.36	3.94
E-values	4.05	2.06	-

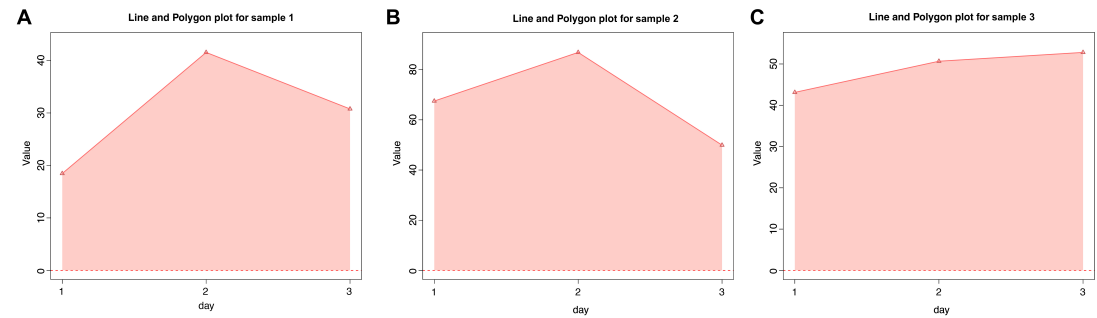


Figure S1. The area under the curve (AUC) of the exposure (Three patients: A-C).

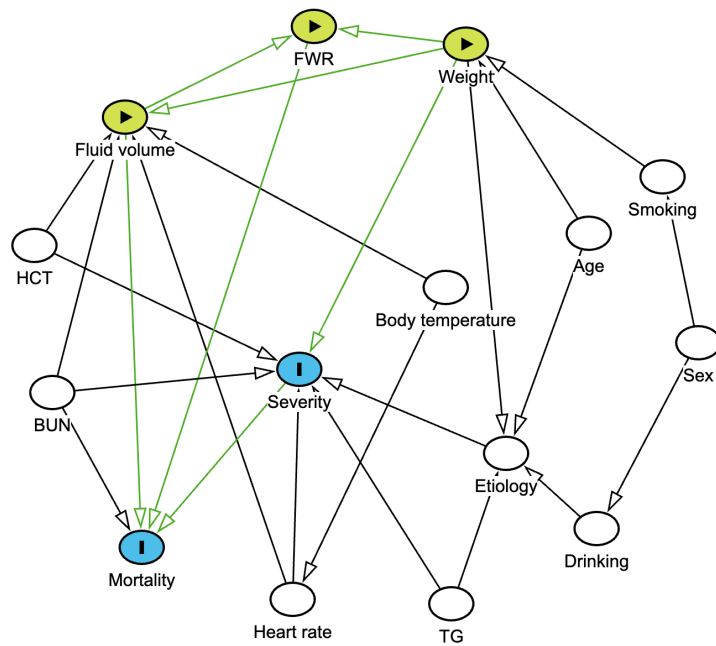


Figure S2. Variables included in the directed acyclic graph (DAG). This figure lists the variables considered in the DAG analysis to assess potential confounders and mediators between fluid therapy-to-body weight ratio (FWR) and in-hospital mortality.

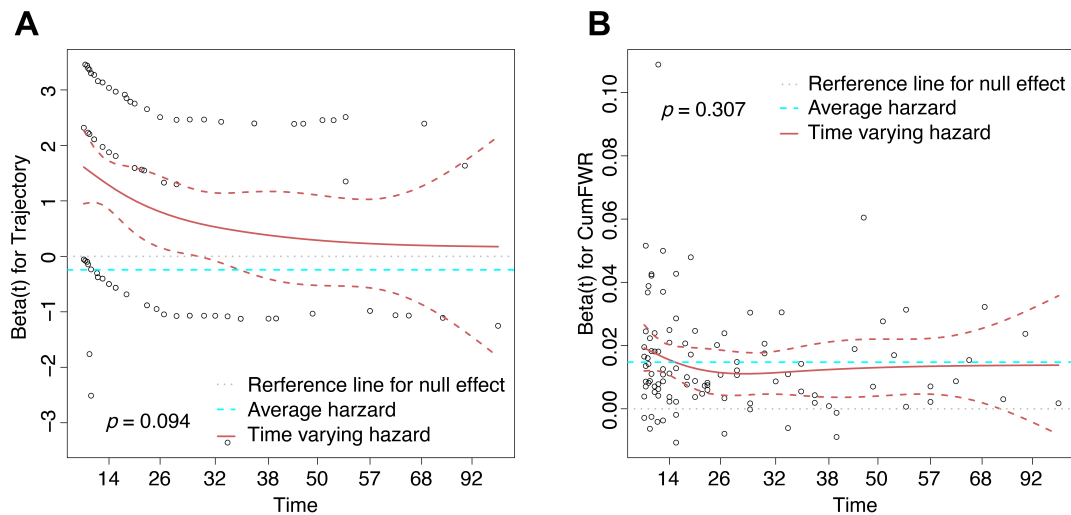


Figure S3. Time-dependent risk. (A-B) Schoenfeld residual tests showed that CumFWR ($p=0.094$) and FWR trajectory ($p=0.307$) satisfied the Cox proportional hazards assumption.

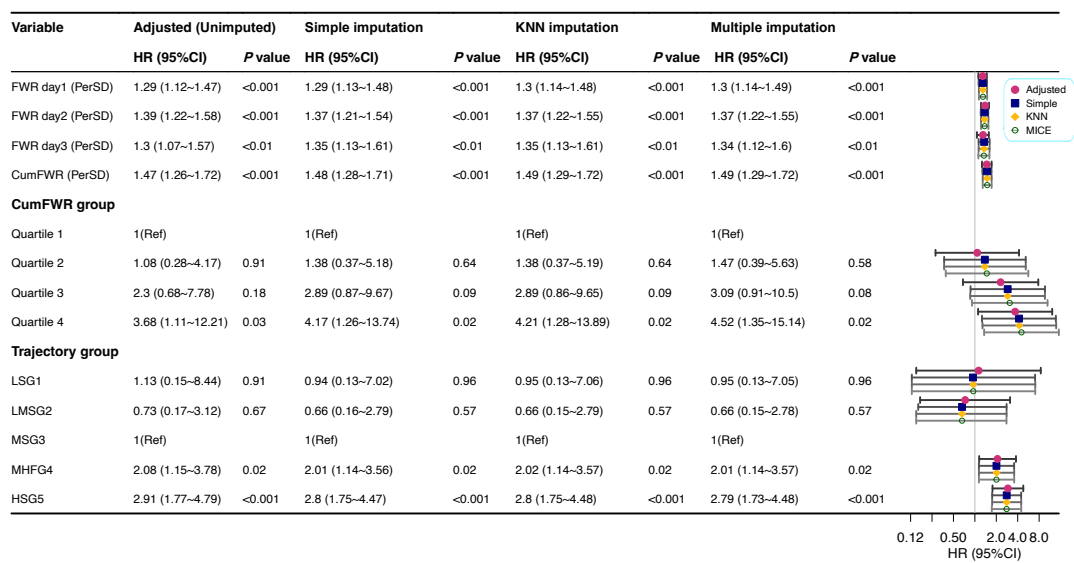


Figure S4. Robustness test of imputation methods used Cox regression. A fully adjusted model was used: adjusted for gender, age, smoking history, drinking history, etiology, body temperature, heart rate, HCT, BUN, and TG.

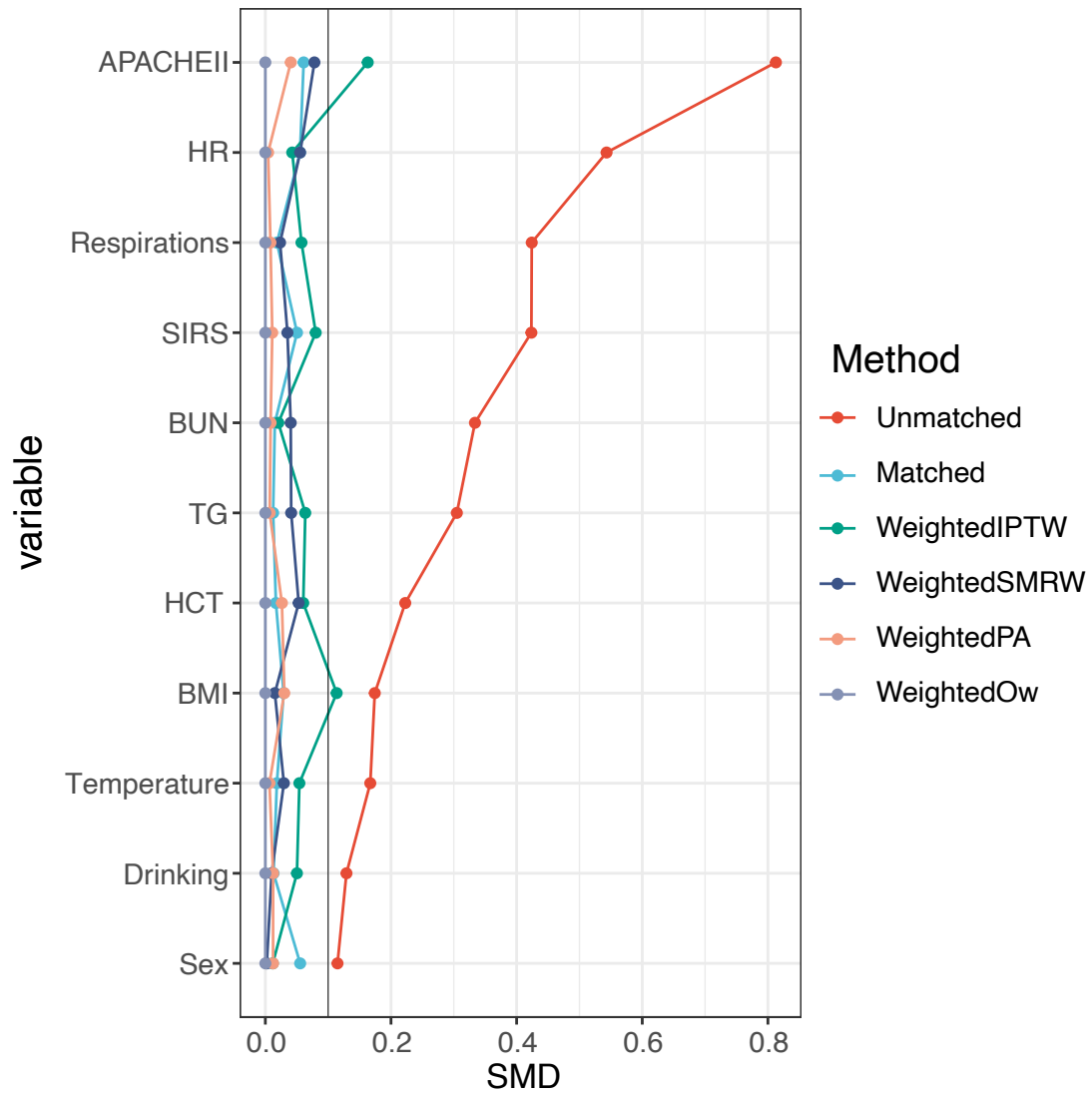


Figure S5. Standardized mean difference (SMD) of baseline covariates before and after matching.

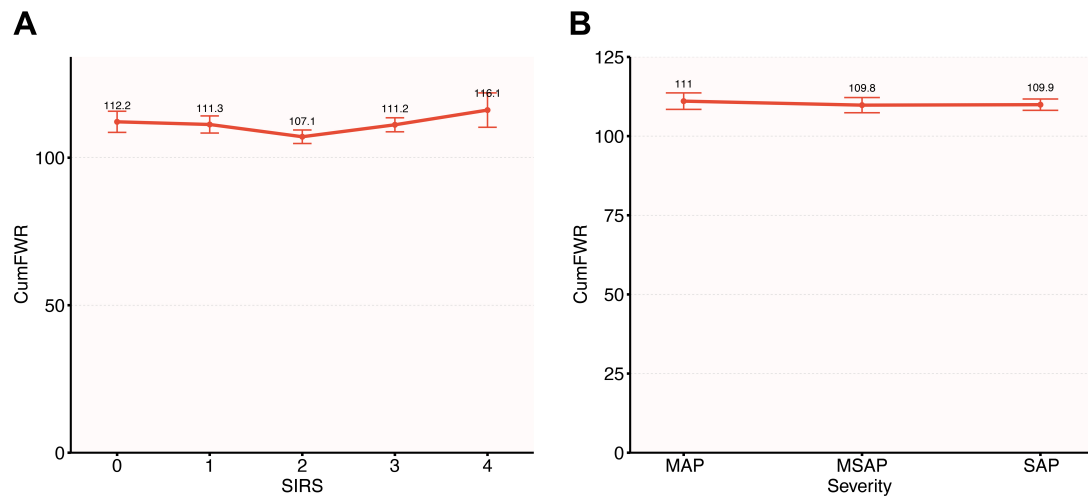


Figure S6. Distribution of CumFWR in the matched cohort. (A) Different SIRS statuses; (B.) Disease severity stratification (MAP/MSAP/SAP).

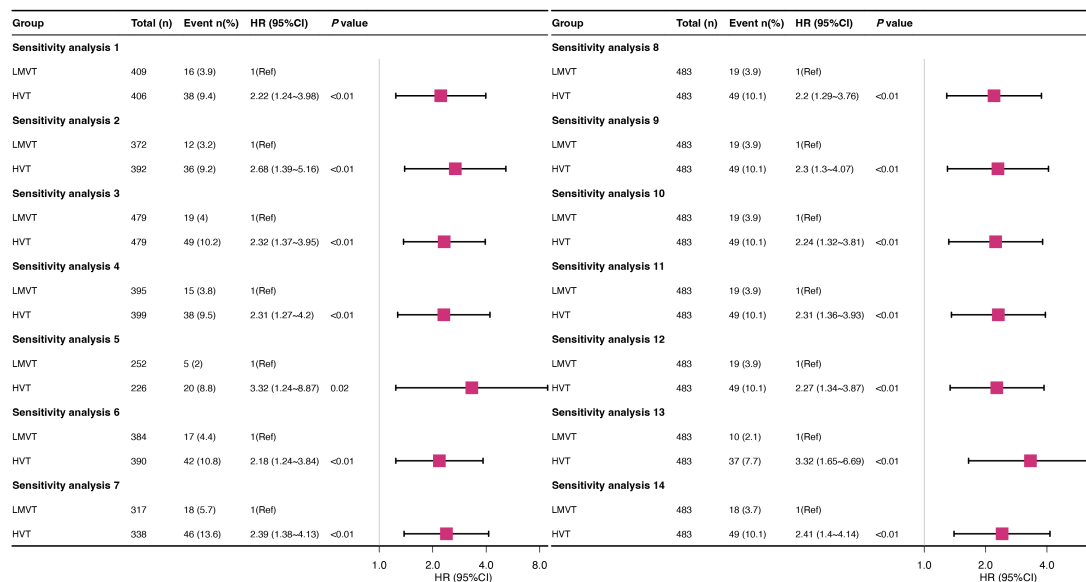


Figure S7. Sensitivity analyses. Patients admitted in the first 9 years of the study were excluded, and data from the most recent 9 years were analyzed (Sensitivity analyses 1). Patients with hypertension (Sensitivity analyses 2), COPD (Sensitivity analyses 3), diabetes (Sensitivity analyses 4) were excluded. Patients admitted within 24 hours after onset were included (Sensitivity analyses 5). Patients with a first episode of AP were included, excluding those with recurrent episodes (Sensitivity analyses 6). Patients with APACHE II >8 at

admission were included (Sensitivity analyses 7). In the Cox model, further adjustments were made for mean arterial pressure (Sensitivity analyses 8), oxygenation index PaO2/FiO2 (Sensitivity analyses 9) and treatment measures (such as use of albumin (Sensitivity analyses 10), low-molecular-weight heparin (Sensitivity analyses 11), insulin (Sensitivity analyses 12)). The definition of the primary outcome was modified, such as considering 28-day mortality (Sensitivity analyses 13) or 90-day mortality (Sensitivity analyses 14).

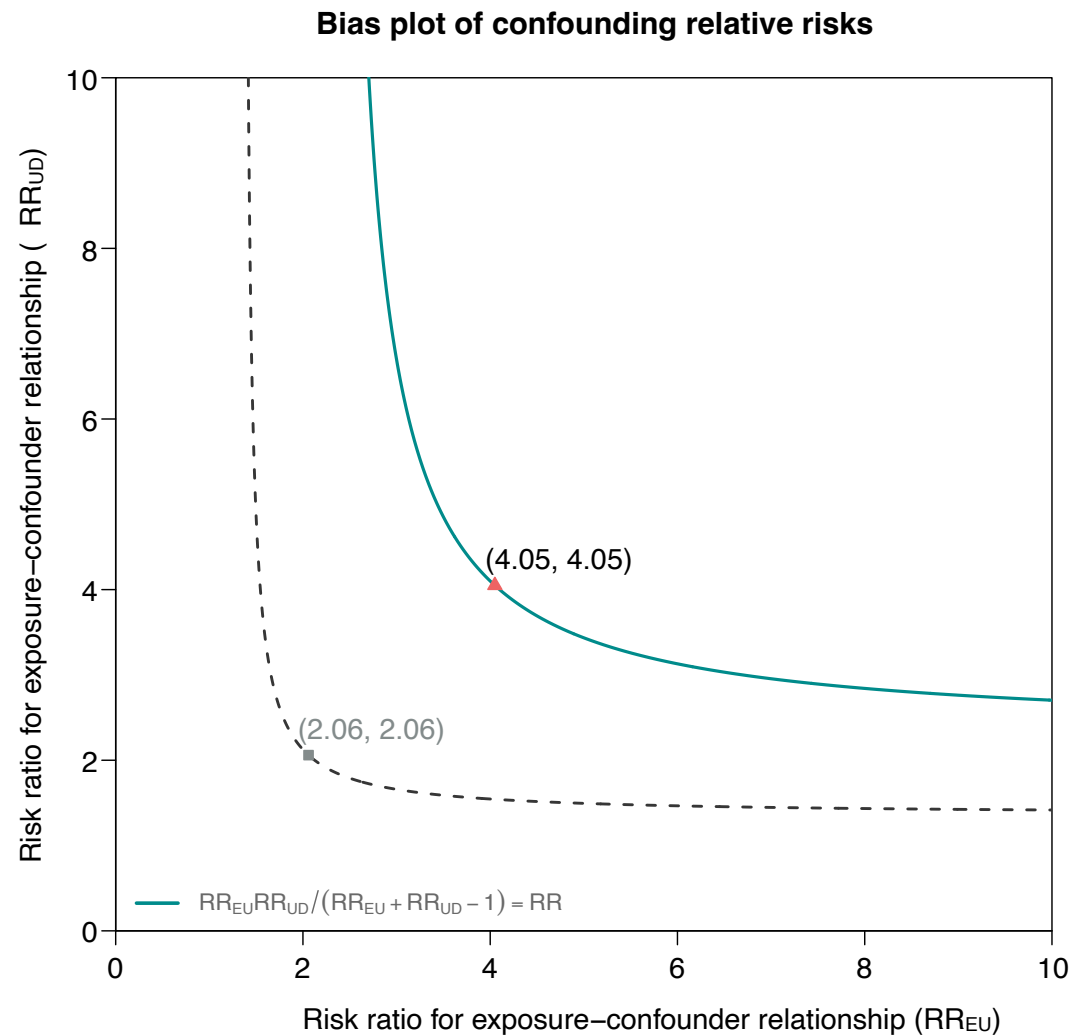


Figure S8. E-value analysis for unmeasured confounding. The bias plot illustrates the sensitivity of the CumFWR-mortality association to potential unmeasured confounders.

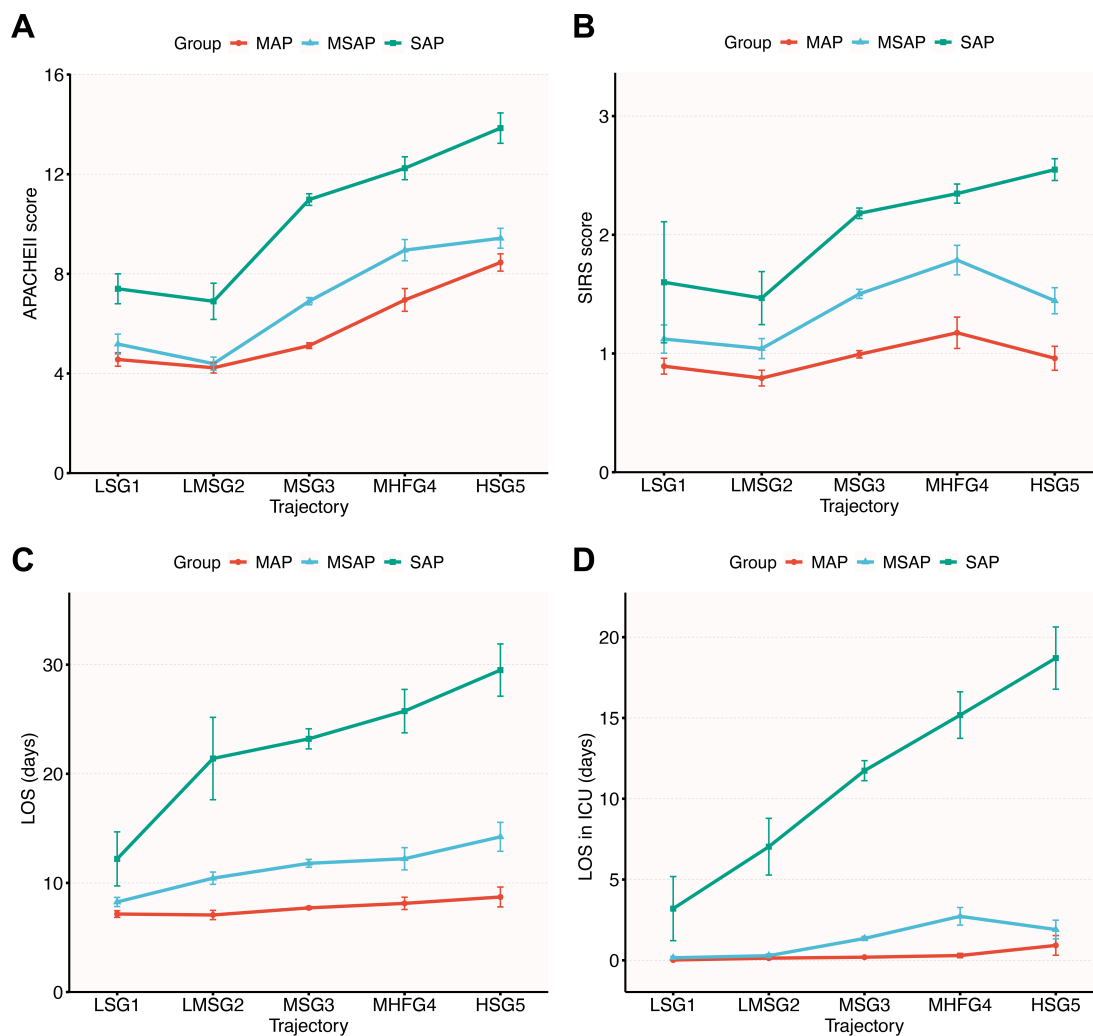


Figure S9. Distribution of disease severity stratified by FWR trajectories. (A) APACHE II score; (B) SIRS score; (C) LOS, length of hospital stay; (D) LOS in ICU.

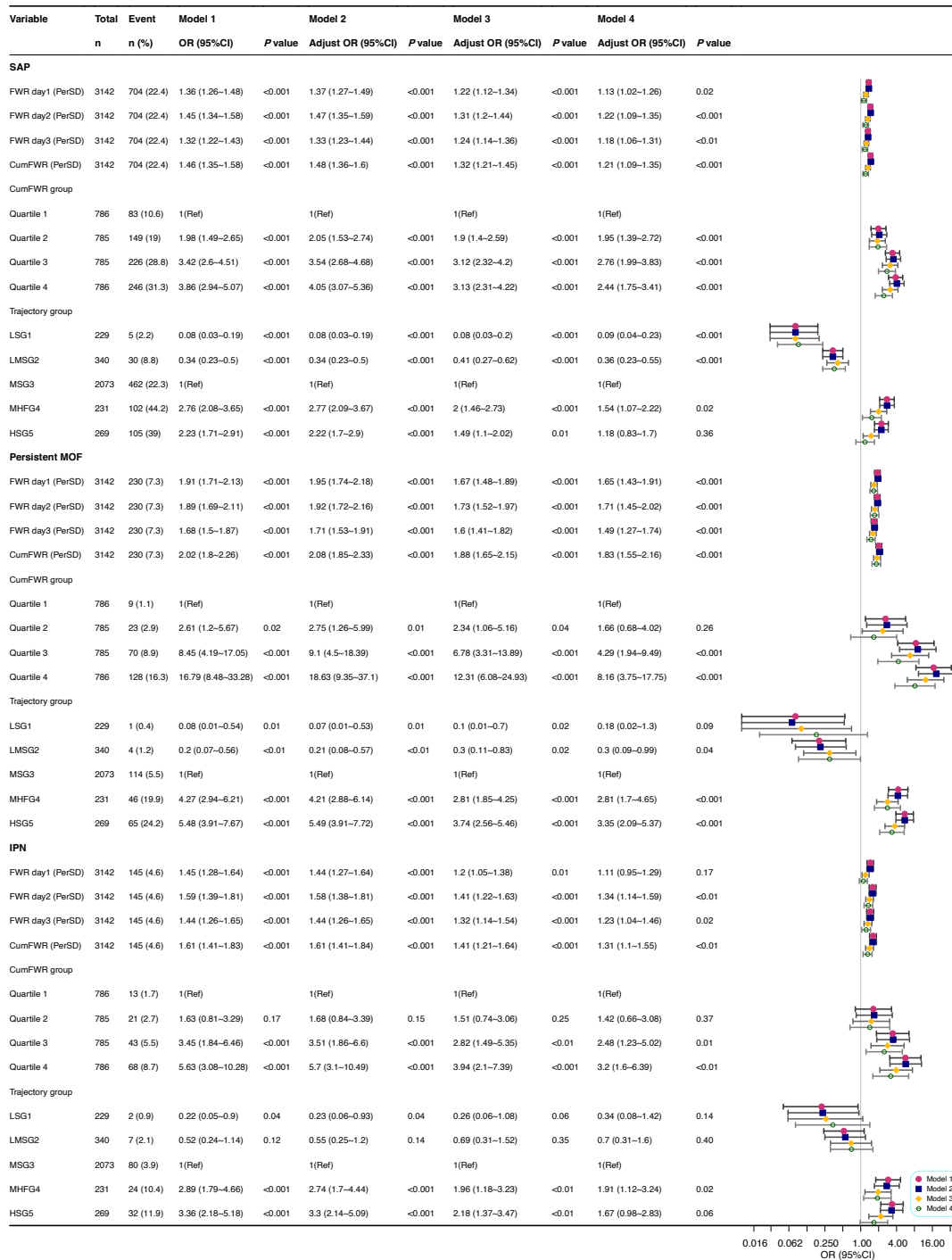


Figure S10. Forest plot of logistic regression.

Multiple models were constructed using a stratified adjustment strategy: Model 1: non adjustment. Model 2: Model 1 + gender, age, smoking history, drinking history. Model 3: Model 2 + etiology (biliary, alcoholic, hypertriglyceridemic, other/idiopathic), body

temperature, heart rate. Model 4: Model 3 + baseline laboratory indicators (e.g., admission
HCT, BUN, TG).

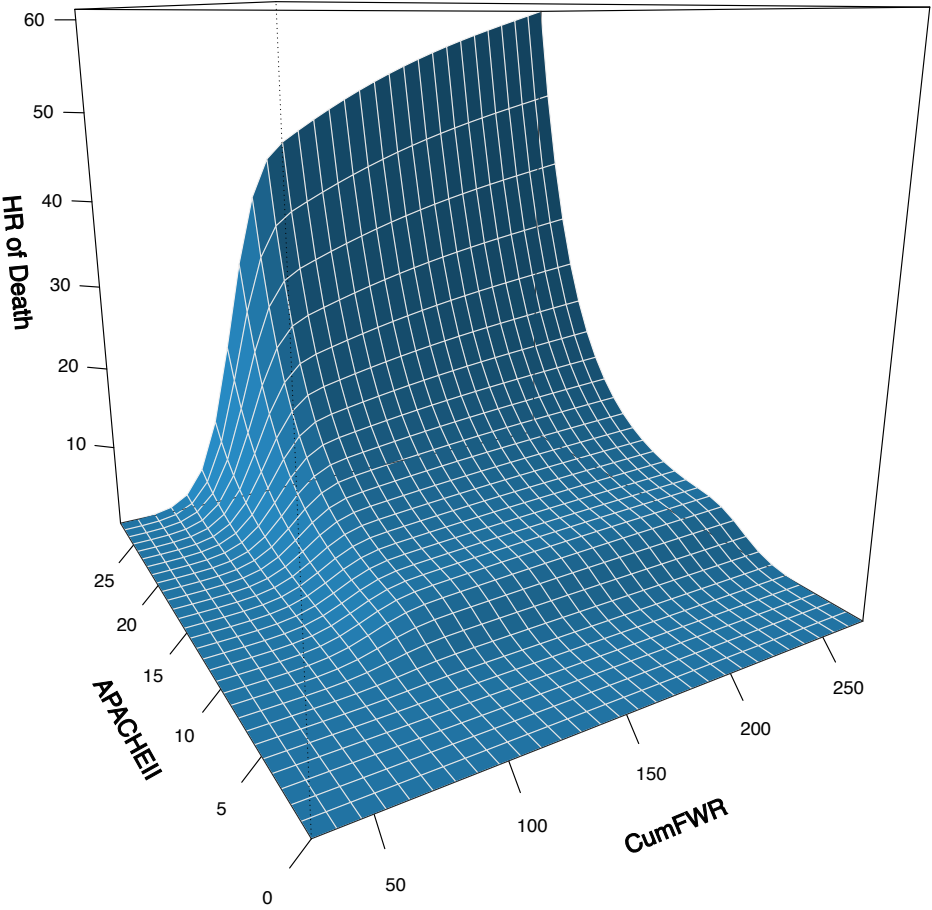


Figure S11. Three-dimensional surface plots exhibited the combined effect of APACHE II
score and CumFWR on the risk of death.

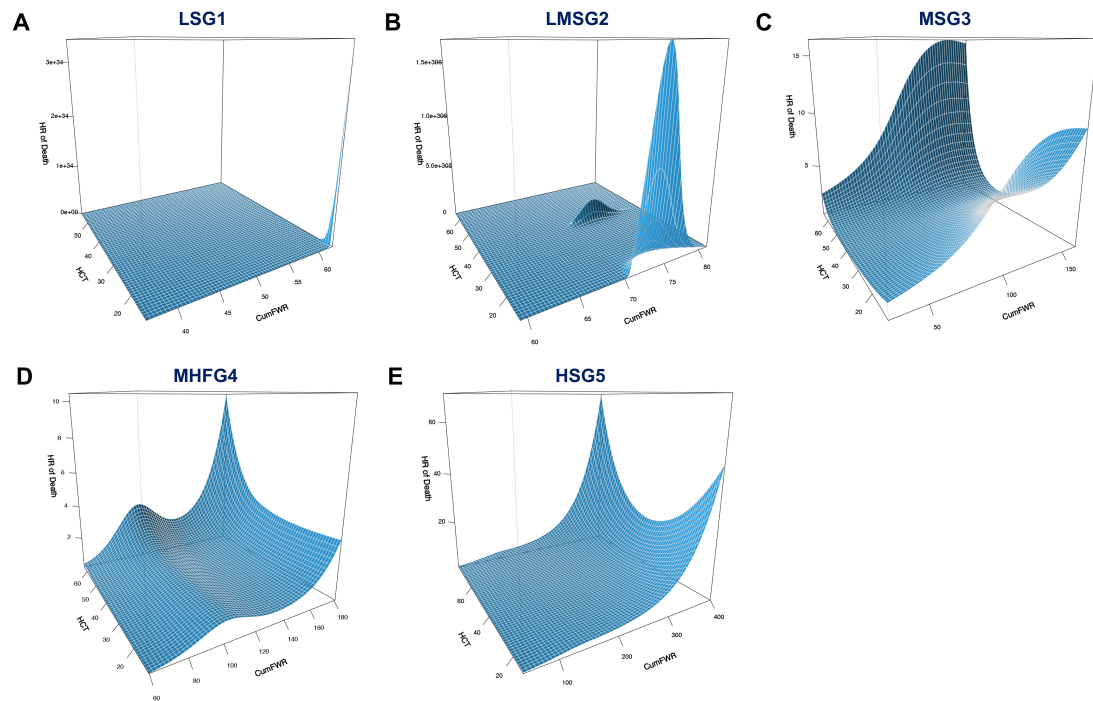


Figure S12. Interaction between CumFWR and HCT on the risk of death in different trajectory groups (LSG1 to HSG5) (A-E).