Supplemental Digital Content

eTable 1.

Title: Patient characteristics at baseline and after propensity score matching.

Legend: Statistically significant baseline differences in demographics, Elixhauser comorbidities, and co-interventions prior to matching *are noted in italics** (all p-values <0.01). Propensity score matching controlled for all of the listed baseline differences and resulted in complete equivalence of the two cohorts. Prior to matching, in-hospital mortality differed significantly while ICU LOS differed statistically but not clinically. After matching only ***in-hospital mortality*** differed significantly.

Characteristics	'No Balanced Fluids' by Day 2 (N = 50,052)	'Balanced Fluids' by Day 2 (N = 3,396)	Propensity Matched 'No Balanced Fluids' group (N = 3365)	Propensity Matched 'Balanced Fluids' group (N = 3365)
Demographics				
*Age; Median [IQR] **	68 [56, 79]	64 [52, 76]	64 [52, 76]	64 [53, 77]
*Male Gender (%) **	50.47	48.47	48.65	48.38
White Race *(%)*	64.69	62.49	61.10	62.56
*Black Race (%) **	13.36	12.49	13.08	12.57
Hispanic Race *(%)*	5.99	10.13	10.58	10.10
Other Race/Unknown *(%)*	15.96	14.90	15.25	14.77
Smoker (current) *(%)*	5.40	5.48	6.30	5.50
Elixhauser Comorbidities (% Patients with each comorbidity)				
*Congestive heart failure **	32.90	23.76	23.06	23.80
*Valvular disease **	9.34	7.16	7.76	7.19
Pulmonary circulation disease	7.00	6.12	6.24	6.18
*Peripheral vascular disease**	8.55	6.89	7.25	6.84
Hypertension	31.27	32.69	32.90	32.75
*Hypertension with complications **	21.54	16.25	16.97	16.37
Paralysis	7.70	7.36	7.64	7.31

*Other neurological disorders**	16.59	14.96	15.16	14.98
*Chronic pulmonary disease **	32.33	25.56	24.31	25.71
Diabetes w/o chronic complications	27.53	26.35	26.51	26.33
*Diabetes w/ chronic complications**	8.08	6.15	6.66	6.18
Hypothyroidism	14.18	13.25	13.22	13.31
*Renal failure**	27.87	20.32	20.77	20.45
Liver disease	6.93	7.24	7.61	7.28
Metastatic cancer	5.19	4.86	5.20	4.87
Obesity	11.02	11.63	12.30	11.65
Weight loss	21.71	21.23	21.34	21.31
*Deficiency anemias**	40.69	37.37	36.82	37.38
*Alcohol abuse **	6.40	7.71	7.67	7.67
*Psychoses**	6.31	5.33	4.61	5.35
Depression	10.95	10.81	10.64	10.76
Co-Interventions (% Patients with intervention)				
*Mechanical Ventilation by Day 2 **	39.96	43.32	44.70	43.27
*Dialysis by Day 2 (excluded in ARF matching model) **	6.55	3.91	4.96	4.67
Sodium Bicarbonate by Day 2	28.01	28.59	29.51	28.62
*Hydrocortisone by Day 2 **	23.03	27.71	27.61	27.61
*Thiamine by Day 2 **	6.11	7.80	8.80	7.73
Psychotropics by Day 2	8.55	7.60	7.93	7.64
*Tube feed by Day 2 **	3.98	5.36	5.38	5.35
*Nutritional Supplements by Day 2 **	26.93	35.19	35.93	35.04
*Statins by Day 2 **	12.97	9.69	9.63	9.69
*Foley Catheter by Day 2 **	35.18	40.40	40.86	40.42

*CVP Monitor by Day 2 **	51.60	59.69	59.55	59.64
*Arterial Line by Day 2 with ICD-9 Codes **	11.95	17.96	18.37	18.04
*Echocardiography by Day 2**	37.82	34.01	34.32	33.03
Beta Blockers by Day 2	13.67	14.16	14.95	14.09
Calcium Channel Blockers by Day 2	8.73	7.98	7.13	8.02
Red Blood Cell/Whole Blood Transfusion by Day 2	20.75	21.88	21.69	21.78
*Diuretics by Day 2**	24.47	19.85	19.05	19.94
*Colloids by Day 2**	19.14	23.91	23.57	23.77
Total Crystalloid Amount by Day 2	5000 [3500, 8000]	7000 [5000, 10000]	7000 [5000, 10,500]	7000 [5000, 10,000]
Type of Colloid-Albumin by Day 2	16.01	19.26	19.58	19.14
Outcomes				
In-Hospital Mortality * (%patients that died after day 2)	**22.74% (11,384 out of 50,052)**	**19.49% (662 out of 3,396)**	**22.82 % (768 out of 3,365)**	**19.58 % (659 out of 3,365)**
ARF with Dialysis ***(% dialysis after day 2)***	4.16% (1861 out of 44,694)	4.50% (143 out of 3,175)	4.74% (149 out of 3144)	4.52% (142 out of 3,144)
ARF without the Dialysis ***(% with ARF after day 2)***	6.49% (2408 out of 37,177)	7.09% (190 out of 2,679)	7.50% (199 out of 2,655)	7.12% (159 out of 2,655)
ICU Length of Stay (in days) for Survivors beyond day 2 *	**4 [2, 7]**	**4 [2, 7]**	**4 [2, 7]**	**4 [2, 7]**
Hospital Length of Stay (in days) for Survivors beyond day 2	9 [6, 14]	9 [6, 14]	9 [6, 14]	9 [6, 14]

eTable 2.

Title - Fluid Types

Legend -Types of crystalloids in each of the two groups being compared (received over hospital days 1 and 2)

Group	Fluid	Percent	Cumulative Percent
Balanced Fluids by Day 2; PSM Cohort	LR1000ML	76.84	76.84
	D5% LR 1000ML	8.99	85.83
	LR 500ML	6.97	92.80
	NORMOSOL-R 7.4% 1000ML (Hospira)	1.21	94.01
	PLASMA-LYTE 148 1000ML (Baxter)	1.14	95.16
No Balanced Fluids by Day 2; PSM Cohort	IS 1000ML	54.67	54.67
	IS 500ML	21.60	76.27
	½ Normal Saline 1000ML	6.35	82.62
	D5% IS 1000ML	5.30	87.92
	D5% ½ Normal Saline 1000ML	4.49	92.41
	0.9% NACL+KCL 20MEQ 1000ML	2.98	95.40

eTable 3.

Title: Total fluid volume quintiles

Legend: Patients categorized (by quintile) based on the total amount of intravenous fluids received over hospital days 1 and 2.

Quintile	N	Minimum	Median	Maximum
1	11,998	2,000	2,500	3,000
2	9,302	3,010	4,000	4,530
3	11,216	5,000	5,500	6,000
4	9,144	6,005	7,000	8,100
5	11,788	8,500	10,500	20,000+

eTable 4.

Title. Balanced fluid proportions.

Legend. Patients categories based on the proportion of 'balanced fluids' received (total balanced fluid volume divided by the total fluid volume over hospital days 1 and 2).

Group	N = 3,396	Percent of patients receiving Balanced Fluids by Day 2 (Total n= 3,396)	N =3,365	**Percent of patients receiving Balanced Fluids by Day 2 in the propensity-matched sample (Total n=3365)**
< 20% Balanced	1,118	32.92%	1,107	32.90%
>20% and ≤ 40% Balanced	1,063	31.30%	1,055	31.35%
>40% and ≤ 60% Balanced	592	17.43%	590	17.53%
>60% and ≤ 80% Balanced	317	9.33%	312	9.27%
>80% and ≤ 100% Balanced	306	9.01%	301	8.95%

eTable 5.

Title: Dose-response effects by mortality risk.

Legend: Change in outcomes per 10% change in exposure (balanced fluid proportion) within and across quintiles of predicted mortality.

Quintile based on Mortality Risk; Quintile and then Raw Mortality Rate (%)	Mortality Odds Ratio per 10% Change Balanced Fluid to Total by Day 2;	ARF with Dialysis Odds Ratio per 10% Change Balanced Fluid to Total by Day 2	ARF without Dialysis Odds Ratio per 10% Change Balanced Fluid to Total by Day 2	LOS for Survivors per 10% Change Balanced Fluid to Total by Day 2;	ICU LOS for Survivors per 10% Change Balanced Fluid to Total by Day 2;
1 (5.29%)	**0.925 (0.858, 0.998)**	0.980; 95% CI(0.866 to 1.108)	1.016; 95% CI (0.941 to 1.097)	-0.065 (-0.146, 0.015)	-0.065 (-0.115, -0.014)
2 (11.91%)	0.976 (0.916, 1.040)	1.002; 95% CI (0.888 to 1.130)	1.003; 95% CI (0.918 to 1.096)	-0.045 (-0.170, 0.079)	-0.043 (-0.124, 0.038)
3 (20.06%)	0.969 (0.920, 1.020)	1.001; 95% CI (0.905 to 1.106)	1.024; 95% CI (0.939 to 1.117)	-0.135 (-0.297, 0.026)	**-0.180 (-0.264, -0.095)**
4 (29.05%)	0.942 (0.895, 0.992)	0.953; 95% CI (0.862 to 1.054)	0.962; 95% CI (0.818 to 1.054)	0.215 (-.042, 0.473)	-.0.116 (-0.030, 0.262)
5 (46.39%)	1.001 (0.948, 1.057)	1.022; 95% CI (0.941 to 1.111)	1.037; 95% CI (0.956 to 1.125)	-0.070 (-0.316, 0.175)	-0.001 (-0.184, 0.183)

eTable 6.

Title: Dose-response effects by total fluid volume quintile.

Legend: Change in outcomes per 10% change in exposure (balanced fluid proportion) across quintiles of total fluid volume.

Quintiles of Total Fluid Volume	Mortality Odds Ratio per 10% Change Balanced Fluid to Total by Day 2	ARF with Dialysis Odds Ratio per 10% Change Balanced Fluid to Total by Day 2	ARF without Dialysis Odds Ratio per 10% Change Balanced Fluid to Total by Day 2	LOS for Survivors 10% Change Balanced Fluid to Total by Day 2;	ICU LOS for Survivors 10% Change Balanced Fluid to Total by Day 2;
1	**0.935 (0.895, 0.978**)	0.998; 95% CI (0.921 to 1.082)	1.007; 95% CI (0.931 to 1.090)	-0.021 (-0.108, 0.065)	-0.031 (-0.085, 0.022)
2	0.969 (0.916, 1.025)	0.988; 95% CI (0.858 to 1.138)	1.024; 95% CI (0.936 to 1.121)	-0.084 (-0.227, 0.060)	-0.076 (-0.176, 0.024)
3	0.991 (0.938, 1.046)	1.020; 95% CI (0.903 to 1.152)	0.994; 95% CI (0.908 to 1.087)	-0.041 (-0.209, 0.128)	-0.086 (-0.181, 0.010)
4	0.954 (0.898, 1.013)	1.020; 95% CI (0.920 to 1.130)	1.036; 95% CI (0.944 to 1.137)	0.077 (-0.120, 0.274)	-0.022 (-0.126, 0.083)
5	**0.953 (0.910, 0.999)**	0.965; 95% CI (0.888 to 1.049)	1.002; 95% CI (0.927 to 1.084)	**-0.141 (-0.280, -0.001)**	**-0.085 (-0.162, -0.007)**

eTable 7.

Title: Sensitivity analysis for unmeasured confounding.

Legend: Modeling effects of a hypothetical unmeasured confounder on inpatient mortality.

Relative Mortality Risk of the unmeasured confounder	Prevalence in the No Balanced Fluid by Day 2 group	Prevalence in the Balanced Fluid by Day 2 group	Adjusted RR: Original is 0.858 95% CI (0.782, 0.942)
1.1	10%	0%	0.867 (0.790, 0.951)
1.1	20%	0%	0.875 (0.798, 0.961)
1.1	40%	0%	0.892 (0.813, 0.980)
1.5	10%	0%	0.901 (0.821, 0.989)
1.5	**20%**	**0%**	**0.944 (0.860, 1.036)**
1.5	**40%**	**0%**	**1.030 (0.938, 1.130)**
2.0	10%	0%	0.944 (0.860, 1.036)
2.0	20%	0%	1.030 (0.938, 1.130)
2.0	40%	0%	1.201 (1.095, 1.319)

eTable 8.

Title: Effect of balanced fluid utilization on outcomes occurring early during hospitalization.

Legend: Results of sensitivity analyses showing effects when including outcomes that occurred earlier than Day 2. Results of main analyses were confirmed and the difference in ICU LOS became statistically significant (lower LOS with balanced fluid exposure).

Outcome	Marginal Effect in the 'Balanced Fluid by Day 2' Matched Sample	Marginal Effect in the 'No Balanced Fluid by Day 2' Matched Sample	Relative Risk among patients treated with balanced fluids	95% CI
In-hospital mortality (after day 2)	**19.6% (659 out of 3365)**	**22.8% (768 out of 3365)**	**0.86**	**(0.78, 0.94) P = 0.001**
ARF with dialysis	4.52% (142 out of 3144)	4.74% (149 out of 3144)	0.95	(0.76, 1.19)
ARF without dialysis	7.12% (189 out of 2655)	7.50% (199 out of 2655)	0.95	(0.79, 1.15)
	Marginal Effect for Balanced Fluid by Day 2 on Matched Sample	Marginal Effect for No Balanced Fluid by Day 2 on Matched Sample	Coefficient for Balanced Fluid by Day 2	95% CI
HLOS (Survivors)	11.26	11.37	-0.11	(-0.55, 0.34)
HLOS (Survivors Day 1 Sensitivity Analysis	10.92	10.47	-0.45	(-1.02, 0.11)
Day 1 Sensitivity Analysis	***Marginal Effect in the 'Balanced Fluid by Day 1' Matched Sample***	***Marginal Effect in the 'No Balanced Fluid by Day 1' Matched Sample***	***Relative Risk among patients treated with balanced fluids by day 1***	***95% CI***
Mortality Rate for Patients who died On or After Day 2	**18.7% (478 out of 2,562)**	**23.7% (606 out of 2,562)**	**0.79**	**(0.71, 0.88)**
Mortality Rate for Patients who died On or	**21.7% (478 out of 2206)**	**26.4% (581 out of 2206)**	**0.82**	**(0.74, 0.91)**

After Day 2 (after excluding patients with LOS = 1 Day)				
ARF with Dialysis on the Day 1 Sensitivity Set	5.89% (143 out of 2427)	6.47% (157 out of 2427)	0.91	(0.74, 1.13)
ARF without Dialysis on the Day 1 Sensitivity Set	6.76% (138 out of 2043)	6.80% (139 out of 2043)	1.04	(0.82, 1.31)
	Marginal Effect for Balanced Fluid by Day 1 on Matched Sample	Marginal Effect for No Balanced Fluid by Day 1 on Matched Sample	Coefficient for Balanced Fluid by Day 1	95% CI
ICU LOS (Survivors)	5.39	5.50	-0.11	(-0.37, 0.15)
ICU LOS (Survivors Day 1 Sensitivity Analysis	**5.08**	**5.51**	**-0.43**	**(-0.75, -0.10) P = 0.009**