

## Supplementary Digital Content 1

### Supplemental Methods

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## Supplemental Methods

### 1. Generalized Additive Model (GAM)

GAM is an extension of GLM. Unlike Generalized Linear Model (GLM), GAM does not assume a linear relationship between outcome variable and predicted variable. As shown in the mathematical representation  $y = \alpha + f(X)$ , GAM does not specify anything about the shape of the function connect  $X$  and  $y$ ; it only allows so-called smooth terms  $f(X)$  which can be “loess”, “splines” or other very flexible link functions. The smoothing parameters are decided based on cross-validation or maximum likelihood estimation.

### 2. Generalized Additive Mixed Model (GAMM)

GAMM is to GAM as Generalized Linear Mixed Model (GLMM) to GLM. GAMM allows random effects and random smooths by group random variation. Random smooth is like random slope, but random smooth is more flexible. Random smooth can deal with by group variation in non-linear effect while random slope can account for by group variation in linear form.

### 3. E-Value

The e-value is defined as the minimum strength of association that an unmeasured confound would need to have to explain away the exposure-outcome association. An e-value of 137.488 implies considerable unmeasured confounding would be required to explain away the timing and mortality association.

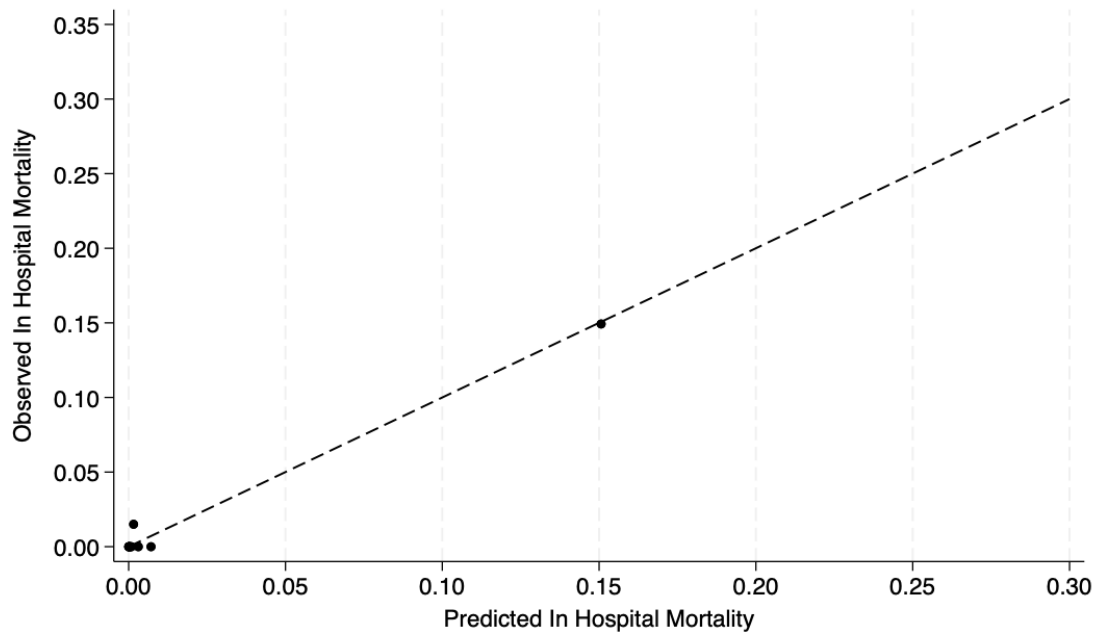
VanderWeele TJ, Ding P. Sensitivity analysis in observational research: introducing the E-value. *Ann Intern Med.* 2017;167(4):268-274. doi:10.7326/M16-2607

Mathur MB, Ding P, Riddell CA, VanderWeele TJ. Web site and R package for computing E-values. *Epidemiology.* 2018;29(5):e45-e47. doi:10.1097/EDE.0000000000000864

**eTable 1: Demographics and characteristics of study population and time to operating room quintiles**

Time Quintile	All Groups	1-252 minutes	253-399 minutes	400-641 minutes	642-1465 minutes	1467-4257 minutes	
N	1,199	242	237	240	239	239	
Age, median (IQR)	63 (49-73)	63 (50-73)	64 (54-75)	62.5 (47.5-73)	61 (44-71)	62 (47-73)	
Sex, female, No.(%)	617 (51.5%)	128 (52.9%)	118 (49.8%)	134 (55.8%)	113 (47.3%)	124 (51.9%)	
Frail, No.(%)	523 (43.7%)	66 (27.3%)	102 (43%)	97 (40.4%)	112 (46.9%)	146 (61.1%)	
SOFA Score, median (IQR)	1 (1-3)	2 (1-6)	1 (1-3)	1 (1-3)	1 (0-3)	1 (0-2)	
Initial HR, median (IQR)	90 (75-103)	90 (78-109)	90 (74-105)	85 (71-97)	92 (79-104)	86 (73-102)	
Initial WBC, median (IQR)	9.6 (7-13.3)	10.75 (7.8-15.8)	10.3 (7.3-14.3)	9.75 (6.9-13.5)	9.3 (6.9-12.2)	8.75 (6.5-12.2)	
SBP Low, median (IQR)	83 (74-92)	81 (70-90)	83 (75-92)	83 (74-92)	84 (74-93)	84.5 (75.5-92)	
Temperature High, median (IQR)	37.11 (36.83)	37.11 (36.88-37.5)	37.1 (36.83-37.44)	37.1 (36.78-37.5)	37.11 (36.83-37.5)	37.11 (36.89-37.5)	
Temperature Low, median (IQR)	35.4 (34-36)	35.2 (33.6-35.8)	35.5 (34.1-36)	35.5 (34.25-36)	35.4 (33.9-36)	35.3 (34-36)	
RR High, median (IQR)	26 (22-32)	27.5 (23-35)	27 (22-33)	26 (22-32)	25 (21-30)	25 (21-31)	
Laparotomy, No.(%)	615 (51.4%)	173 (71.5%)	154 (65.0%)	124 (51.7%)	75 (31.4%)	89 (37.2%)	
Transfer, No.(%)	384 (32.1%)	151 (62.4%)	67 (28.3%)	52 (21.7%)	55 (23.0%)	59 (24.7%)	
Sepsis, No.(%)	190 (15.9%)	66 (27.3%)	34 (14.3%)	34 (14.2%)	27 (11.3%)	29 (12.1%)	
Ventilator, No.(%)	65 (5.4%)	25 (10.3%)	10 (4.2%)	10 (4.2%)	12 (5.0%)	8 (3.3%)	
EGS Diagnosis, No.(%)							
	Incarcerated Hernia	218 (21.2%)	23 (10.2%)	39 (18.9%)	48 (22.3%)	61 (31.0%)	47 (25.3%)
	Volvulus	25 (2.4%)	5 (2.2%)	9 (4.4%)	10 (4.7%)	1 (0.5%)	0 (0.0%)
	Toxic C Diff	42 (4.1%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	3 (1.5%)	3 (1.6%)
	Perforated SB	96 (9.3%)	7 (3.1%)	4 (1.9%)	11 (5.1%)	12 (6.1%)	8 (4.3%)
	Ischemic Bowel	75 (7.3%)	39 (17.3%)	26 (12.6%)	16 (7.4%)	7 (3.6%)	8 (4.3%)
	NSTI	171 (16.6%)	26 (11.6%)	12 (5.8%)	19 (8.8%)	9 (4.6%)	9 (4.8%)
	Perforated LB	99 (9.6%)	32 (14.2%)	32 (15.5%)	34 (15.8%)	44 (22.3%)	29 (15.6%)
	Bowel Obstruction	59 (5.7%)	22 (9.8%)	25 (12.1%)	18 (8.4%)	12 (6.1%)	22 (11.8%)
	Surgical Rescue	148 (14.4%)	13 (5.8%)	13 (6.3%)	16 (7.4%)	8 (4.1%)	9 (4.8%)
In-hospital Mortality, No. (%)	75 (6.27%)	32 (13.2%)	13 (5.49%)	11 (4.58%)	9 (3.77%)	10 (4.18%)	
30-day Mortality, No. (%)	87 (7.27%)	34 (14.05%)	16 (6.75%)	15 (6.25%)	11 (4.6%)	11 (4.6%)	

SOFA, sequential organ failure assessment; HR, Heart Rate; WBC, White blood count; SBP, Systolic Blood Pressure; RR, Respiratory Rate; C Diff, clostridium difficile; SB, Small Bowel; LB Large Bowel; Time in Minutes

**eFigure 1: Calibration Curve**

Calibration graph for the primary outcome of in-hospital mortality logistic regression model depicting predicted mortality from the model versus observed mortality across deciles of predicted mortality. The dotted line indicates a perfect association between predicted and observed mortality. The C-statistic of 0.971 indicates excellent discrimination.

**eTable 2: Adjusted odds ratio and 95% Confidence Interval for 30-day mortality from logistic regression model**

Adjusted odds ratio and 95% Confidence Interval for 30-day mortality from logistic regression model				
	aOR	95%CI Lower Bound	95%CI Upper Bound	p value
Time to OR				
0-4.2 (Reference)				
4.2-6.7	1.835	0.391	8.619	0.442
6.7-10.7	3.540	0.858	14.602	0.080
10.8-24.4	2.244	0.428	11.764	0.339
24.5-70.9	2.373	0.470	11.979	0.296
Age	1.028	0.989	1.069	0.163
Frailty	2.128	0.695	6.519	0.186
Initial HR	1.001	0.980	1.022	0.948
WBC	0.994	0.928	1.065	0.864
SBP Low	0.974	0.940	1.009	0.144
Laparotomy	1.599	0.575	4.448	0.369
SOFA Score	1.338	1.172	1.528	0.000
Temperature High	0.477	0.244	0.931	0.030
Temperature Low	0.977	0.900	1.062	0.589
RR High	1.021	0.996	1.046	0.102
Transfer	3.928	0.514	30.024	0.187
Sepsis	8.163	1.302	51.186	0.025

SOFA, sequential organ failure assessment; HR, Heart Rate; WBC, White blood count; SBP, Systolic Blood Pressure; RR, Respiratory Rate; Time in Minutes

**eTable 3: Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality from logistic regression model with varying SOFA score**

Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality from logistic regression model with SOFA $\geq 1$				
	aOR	95%CI Lower Bound	95%CI Upper Bound	p value
Time to OR				
0-4.2 (Reference)				
4.2-6.7	5.691	0.643	522.583	0.089
6.7-10.7	62.981	6.890	6108.439	0.002
10.8-24.4	14.463	1.692	4168.549	0.026
24.5-70.9	65.197	4.012	11571.530	0.008
Age	1.072	1.002	1.177	0.046
Frailty	1.586	0.399	27.482	0.268
Initial HR	0.987	0.948	1.021	0.389
WBC	0.986	0.839	1.066	0.359
SBP Low	0.951	0.861	0.999	0.047
Laparotomy	1.310	0.125	9.557	0.936
SOFA Score	1.603	1.346	2.283	0.000
Temperature High	0.210	0.018	0.340	0.001
Temperature Low	1.112	0.849	1.444	0.451
RR High	1.013	0.996	1.046	0.102
Transfer	2.213	0.514	30.024	0.187
Sepsis	7.040	1.302	51.186	0.025

SOFA, sequential organ failure assessment; HR, Heart Rate; WBC, White blood count; SBP, Systolic Blood Pressure; RR, Respiratory Rate; Time in Minutes

**eTable 4: Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality from logistic regression model including only intraabdominal pathology**

Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality from logistic regression model including only intraabdominal pathology				
	aOR	95%CI Lower Bound	95%CI Upper Bound	p value
Time to OR				
0-4.2 (Reference)				
4.2-6.7	18.337	0.643	522.583	0.089
6.7-10.7	205.157	6.890	6108.439	0.002
10.8-24.4	83.974	1.692	4168.549	0.026
24.5-70.9	215.451	4.012	11571.530	0.008
Age	1.086	1.002	1.177	0.046
Frailty	3.310	0.399	27.482	0.268
Initial HR	0.984	0.948	1.021	0.389
WBC	0.945	0.839	1.066	0.359
SBP Low	0.928	0.861	0.999	0.047
Laparotomy	1.092	0.125	9.557	0.936
SOFA Score	1.753	1.346	2.283	0.000
Temperature High	0.079	0.018	0.340	0.001
Temperature Low	1.108	0.849	1.444	0.451
RR High	1.021	0.996	1.046	0.102
Transfer	3.928	0.514	30.024	0.187
Sepsis	8.163	1.302	51.186	0.025

SOFA, sequential organ failure assessment; HR, Heart Rate; WBC, White blood count; SBP, Systolic Blood Pressure; RR, Respiratory Rate; Time in Minutes

**eTable 5: Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality including interfacility transfer time**

Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality from logistic regression model with added total transfer time

	aOR	95%CI Lower Bound	95%CI Upper Bound	p value
Time to OR				
0-4.3 (Reference)				
4.4-6.9	6.124	0.308	121.828	0.235
6.9-11.1	68.985	4.608	1032.657	0.002
11.2-25.7	15.723	0.686	360.582	0.085
25.8-149.4	69.670	2.968	1635.382	0.008
Age	1.072	1.002	1.147	0.044
Frailty	1.619	0.302	8.683	0.574
Initial HR	0.987	0.955	1.019	0.415
WBC	0.986	0.898	1.083	0.768
SBP Low	0.950	0.895	1.007	0.085
Laparotomy	1.358	0.243	7.589	0.727
SOFA Score	1.617	1.302	2.007	0.000
Temperature High	0.204	0.068	0.611	0.005
Temperature Low	1.115	0.875	1.420	0.379
RR High	1.013	0.994	1.033	0.185
Transfer	2.238	0.473	10.587	0.310
Sepsis	7.336	1.584	33.986	0.011

SOFA, sequential organ failure assessment; HR, Heart Rate; WBC, White blood count; SBP, Systolic Blood Pressure; RR, Respiratory Rate; Time in Minutes



**eTable 6a: Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality with 4 knot spline model**

Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality from logistic regression model with splines

	aOR	95%CI Lower Bound	95%CI Upper Bound	p value
Time to OR				
Spline 1 <sup>1</sup>	1.017	1.005	1.028	0.005
Spline 2	0.770	0.622	0.954	0.017
Spline 3	1.489	1.066	2.080	0.020
Age	1.058	0.994	1.126	0.078
Frailty	2.056	0.391	10.806	0.394
Initial HR	0.991	0.960	1.024	0.597
WBC	0.961	0.871	1.059	0.418
SBP Low	0.963	0.909	1.020	0.202
Laparotomy	2.399	0.487	11.804	0.282
SOFA Score	1.679	1.330	2.119	0.000
Temperature High	0.209	0.072	0.604	0.004
Temperature Low	1.134	0.920	1.399	0.238
RR High	1.017	0.997	1.038	0.101
Transfer	2.235	0.500	9.999	0.293
Sepsis	7.145	1.620	31.510	0.009

SOFA, sequential organ failure assessment; HR, Heart Rate; WBC, White blood count; SBP, Systolic Blood Pressure; RR, Respiratory Rate; Time in Minutes

<sup>1</sup> 4 evenly spaced knot model with knots at 2.1, 5.1, 13.5, 48.1 hours.

**eTable 6b: Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality with clinical splines**

Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality from logistic regression model with splines

	aOR	95%CI Lower Bound	95%CI Upper Bound	p value
Time to OR				
Spline 1 <sup>2</sup>	0.950	0.887	1.017	0.140
Spline 2	1.726	1.050	2.837	0.031
Spline 3	0.413	0.189	0.901	0.026
Age	1.065	0.997	1.137	0.062
Frailty	2.856	0.513	15.899	0.231
Initial HR	0.992	0.960	1.024	0.610
WBC	0.968	0.881	1.063	0.495
SBP Low	0.948	0.890	1.011	0.104
Laparotomy	2.297	0.478	11.034	0.299
SOFA Score	1.650	1.309	2.080	0.000
Temperature High	0.242	0.089	0.660	0.006
Temperature Low	1.157	0.926	1.446	0.200
RR High	1.019	1.000	1.039	0.052
Transfer	2.417	0.526	11.100	0.257
Sepsis	8.033	1.780	36.252	0.007

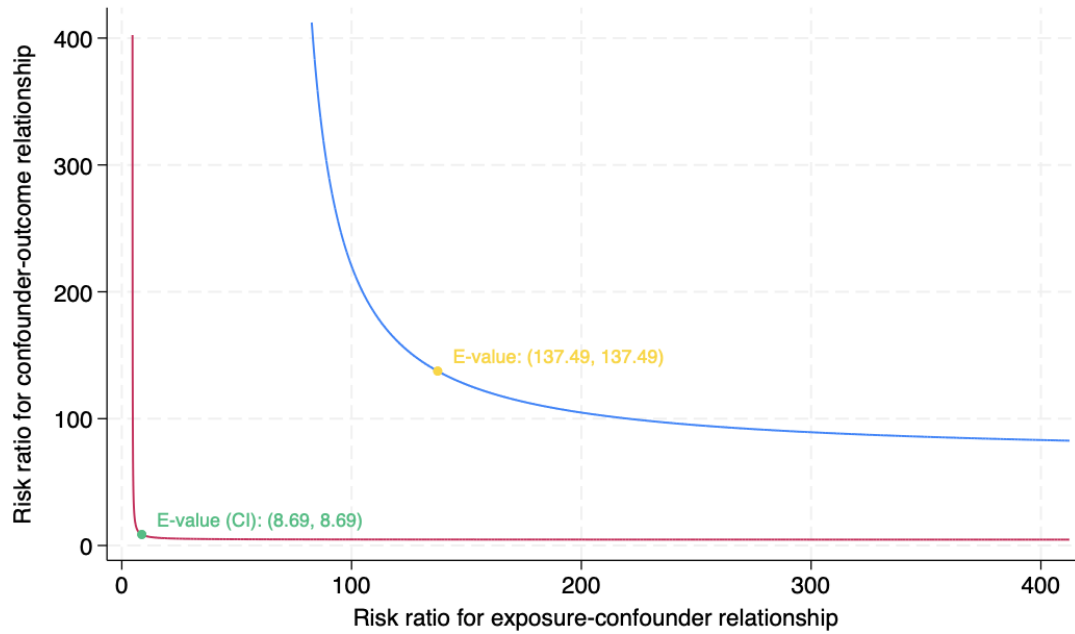
SOFA, sequential organ failure assessment; HR, Heart Rate; WBC, White blood count; SBP, Systolic Blood Pressure; RR, Respiratory Rate; Time in Minutes

<sup>2</sup> 4 knot model derived from institutional guidelines at 1, 2, 4, 8 hours.

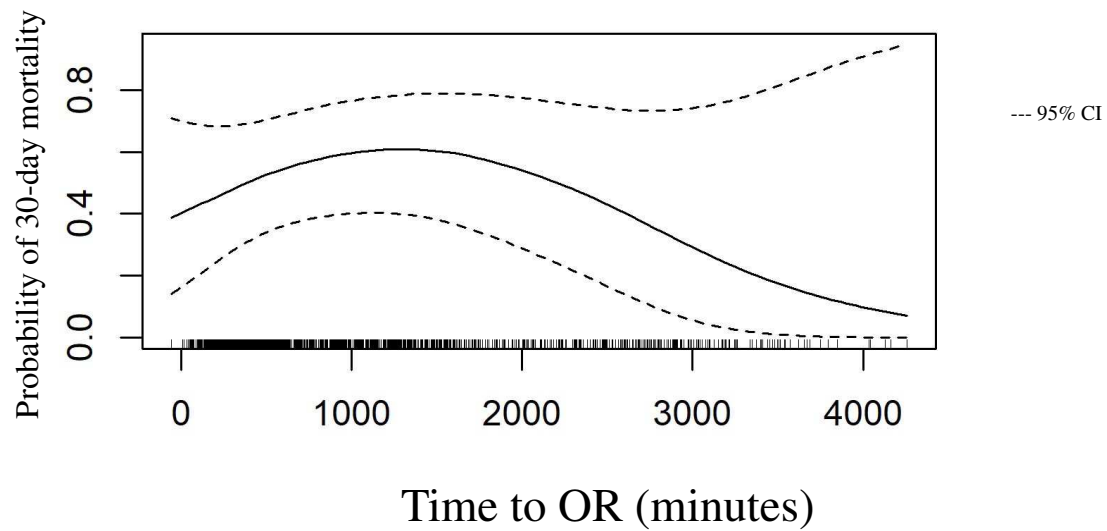
**eFigure 2: E-value calculation for primary analysis**

E-value (point estimate): 137.488

E-value (CI): 8.686



**eFigure 3:** Generalized additive mixed model (GAMM) of probability of 30-day mortality versus time to operating room. Solid line represents effect estimates, dotted lines represent 95% confidence interval.



**eTable 7: Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality with ESS included in model**

Adjusted odds ratio and 95% Confidence Interval for in-hospital mortality from logistic regression model

	aOR	95%CI Lower Bound	95%CI Upper Bound	p value
Time to OR				
0-4.3 (Reference)				
4.4-6.9	2.067	0.131	32.583	0.606
6.9-11.1	31.992	2.994	341.901	0.004
11.2-25.7	7.638	0.437	133.512	0.164
25.8-149.4	23.638	1.594	350.581	0.022
Age	1.077	1.005	1.155	0.035
Initial HR	1.005	0.972	1.039	0.783
WBC	0.927	0.838	1.026	0.142
SBP Low	0.924	0.872	0.979	0.008
Laparotomy	1.805	0.339	9.622	0.489
Temperature High	0.159	0.049	0.514	0.002
Temperature Low	1.016	0.870	1.186	0.842
RR High	1.009	0.996	1.022	0.168
Transfer	1.342	0.315	5.726	0.691
Sepsis	18.454	4.374	77.856	0.000
ESS Score	1.950	1.389	2.737	0.000

HR, Heart Rate; WBC, White blood count; SBP, Systolic Blood Pressure; RR, Respiratory Rate; ESS, Emergency Surgery Score; Time in Minutes