

Table of Contents

eTables

eTable 1. Background literature table of studies	5
eTable 2. Inclusion/exclusion criteria and limitations	11

eFigures

eFigure 1. VAE criteria, including VAC, IVAC, PVAP	14
eFigure 2. Different ventilator requirement scenarios.	15
eFigure 3. Difference between calendar day and 24-hour time intervals.	18
eFigure 4. Time definition between calendar days and 24-hour periods	20
eFigure 5. Additional examples of explorations	21
eFigure 5a. Using calendar day time intervals, $\Delta_{\min}\text{FiO}_2 \geq 40\%$, $\Delta_{\min}\text{PEEP} \geq 3$.	21
eFigure 5b. Using 24 hour time intervals, $\Delta_{\min}\text{FiO}_2 \geq 20\%$, $\Delta_{\min}\text{PEEP} \geq 3$.	23
eFigure 5c. Using CDC VAC criteria ($\Delta_{\min}\text{FiO}_2 \geq 20\%$, $\Delta_{\min}\text{PEEP} \geq 3$, calendar day time intervals) for late VAC (VAC developed on day 7 or later)	25
eFigure 5d. Using CDC VAC criteria ($\Delta_{\min}\text{FiO}_2 \geq 20\%$, $\Delta_{\min}\text{PEEP} \geq 3$, calendar day time intervals) for respiratory SOFA score ≥ 3 (implying P/F ratio < 200)	27

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eTables

eTable 1. Background literature table of studies

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eTable 1: Background Literature Table of Studies: Ventilator Associated Events

Citation	Sample Method Years	2013/2017 HNSN Definitions	VAE	VAC	IVAC	PVAP	VAP 2008 HNSN Definition	Measured outcomes	Severity of illness score	Results	Data-Driven Surveillance Model	Comments
He et al. (2021) The epidemiology and clinical outcomes of ventilator-associated events among 20,769 mechanically ventilated patients at intensive care units: an observational study. <i>Crit Care</i> . 2021 2;25(1):44.	20,769 MV patients 11,697 MV days. N= 6,252 >4 days MV. 1882 VAC 712 IVAC 185 PVAP Retrospective Registry Single Center, 5 ICUs (China) Years April 2015-Dec 2018	Yes	X	X	X	X	No	Mortality VAE Non-VAE	APACHE II score	VAC rate: 16.7 per 1000 MV days. IVAC rate: 6.4 per 1000 MV days. PVAP rate: 1.64 per 1000 MV days. Hospital mortality with a VAE was more than 3-times higher than non-VAE. VAE rates varied by ICU. VAE typically occurred early in MV course.	No	Retrospective analysis of prospectively collected hospital acquired infections registry. Some MV patients had more than one VAC event: 1780 patients with 1882 VAC events. Compared VAEs with non-VAEs.
Fang et al. (2020) Risk factors and associated outcomes of ventilator-associated events developed in 28 days among sepsis patients admitted to intensive care unit. <i>Sci Rep</i> . 2020, 29;10(1):12702.	2,295 admissions N=453 consecutive MV patients with sepsis. 118 VAE 33 <u>Early-VAE</u> onset <7 days MV. 85 <u>Late-VAE</u> onset 7-28 days MV. Retrospective Single Center, 3 medical ICUs (Taiwan) Years: Aug 2013-to-Jan 2016	Yes	X				No	Mortality Early VAE Late VAE	APACHE II score SOFA score and sub-scores Charleston Comorbidity Index (CCI)	Early VAE (n = 33) associated with higher mortality than non-VAE. Late VAE had longer MV days than non-VAE.	No	Compared early-VAE and Late-VAE with non-VAE in patients with sepsis. VAE rate per 1000 MV days not reported
Wolffers et al. (2021) An automated retrospective	N=22,442 MV admissions (37,221 ventilator days) 592 VAE 194 IVAC	Modified	X	X	X		No	Model Tested	Not reported	VAE rate 15.9 per 1000 MV days (95% CI, 14.7–17.2).	Yes	Study aim was to create and evaluate an automated VAE surveillance program.

Citation	Sample Method Years	2013/2017 HNSN Definitions	VAE	VAC	IVAC	PVAP	VAP 2008 HNSN Definition	Measured outcomes	Severity of illness score	Results	Data-Driven Surveillance Model	Comments
VAE-surveillance tool for future quality improvement studies. <i>Sci Rep.</i> 2021,15;11(1):22264.	Retrospective Years 2008-2016 (Switzerland)									VAE rate: 10.1–22.1 per 1000 MV days depending on the year (2008-2016). Mortality not reported		All ICU patients with MV were included to develop the model (median MV was 1 day). Three different sub-samples were used to test the model. Included manual surveillance.
Wu et al (2020) Prevalence, Clinical Characteristics, and Outcomes Related to VAE Events in Neurocritically Ill Patients. <i>Neurocrit Care.</i> 2020;33(2):499-507.	Neurocritical care N=855 ≥ 3 days MV. 147 VAE in 130 patients. 85 VAC 33 IVAC 29 VAP Retrospective Single Center (USA) Years 2014-2018	Modified	X	X	X	X	No	Mortality VAE LOS-ICU	Glasgow Coma Scale (GCS)	VAE rate: 13/1000 MV days. VAE prolonged MV and ICU-LOS but did not increase in-patient mortality.	No	VAE trigger event 84% increase in PEEP 16% increase in FIO2
Meagher et al. (2019) VAE not VAP Is Associated with Higher Mortality in Trauma Patients. <i>J Trauma Acute Care Surg.</i> 2019;87(2):307-314.	Trauma non-head injury with ≥ 3 days MV: N=1,537 total 124 VAE 114 VAP 63 VAE & VAP Retrospective Single Center (USA) Years: 2012-2017	Modified	X				Yes	Mortality VAE VAP LOS-ICU LOS-Hosp Discharge home	Injury Severity Score (ISS)	Trauma patients have higher mortality with VAE than VAP	No	Data from hospital trauma registry and VAE registry. VAE rate per 1000 MV days not reported. Days of MV are below the ≥ 4 days NHSN threshold.
Shenoy et al. (2018) Real-Time, Automated Detection of Ventilator-	Two ICU Cohorts <u>Development cohort</u> 1,325 ICU admissions 479 MV patients 2,539 MV days	Yes	X	X	X	X	No	FIO2 change PEEP change LOS	Not Reported	<u>Development Cohort:</u> For manual surveillance sensitivity 40%, specificity 89%, PPV 70%.	Yes	Aim was to develop and validate an algorithm model to detect VAE in real time from the EHR

Citation	Sample Method Years	2013/2017 HNSN Definitions	VAE	VAC	IVAC	PVAP	VAP 2008 HNSN Definition	Measured outcomes	Severity of illness score	Results	Data-Driven Surveillance Model	Comments
Associated Events: Avoiding Missed Detections, Misclassifications, and False Detections Due to Human Error. 2018;39(7):826-833.	47 VAE 28 VAC 12 IVAC 7 PVAC Year: Jan-March 2015 <u>Validation cohort</u> 1,234 ICU admissions 431 MV patients 2,604 MV days 56 VAE 44 VAC 12 IVAC 0 PVAP Year: Jan-March 2016 Single Center 4 ICUs (USA)							VAE		For automated surveillance sensitivity 100%, specificity 100% PPV 100%. <u>Validation Cohort:</u> For manual surveillance sensitivity 71%, specificity 98% PPV 100%. For automated surveillance sensitivity 85%, specificity 99% PPV 100%.		using the NHSN 2017 definition. Compared manual and automated surveillance methods in two cohorts. <u>Development Cohort MV:</u> 1.9 MV days (median) <u>Validation Cohort MV:</u> 2.2 MV days (median) Number of patients with MV ≥ 4 days not reported VAE rate per 1000 MV days not reported.
Younan et al. (2017) Trauma patients meeting both CDC definitions for VAP had worse outcomes than those meeting only one. <i>J Surg Res.</i> 2017;216:123-128.	Trauma ≥ 2 days MV: N=1,165 total: 78 PVAP 361 VAP 68 PVAP & VAP. Retrospective Single Center (USA) Years: 2013-2014	Modified				X	Yes	Mortality PVAC VAP LOS-ICU LOS-Hosp MV days	Injury Severity Score (ISS)	Longer LOS if patients met both PVAC & VAP criteria. No difference in mortality between patients with PVAC versus VAP	No	Aim was to compare two NHSN definitions for VAP and PVAP. VAE rate per 1000 MV days not reported. Days of MV are below the > 4 days NHSN threshold.
Magill et al. (2016) Incidence and Characteristics of Ventilator-Associated Events Reported to the National Healthcare	1,824 adult healthcare facilities reported 32,772 months of VAE surveillance data to NHSN. 19,676 VAE 12,474 VAC	Yes	X	X	X	X	No	Mortality VAC IVAC PVAC	Not Reported	In critical care units the highest VAE pooled mean rates per 1,000 MV days were trauma (11.79) and neurology (8.92).	No	First national report of VAE rates. Comprehensive table of pooled mean for multiple types of VAE by location (Table 1).

Citation	Sample Method Years	2013/2017 HNSN Definitions	VAE	VAC	IVAC	PVAP	VAP 2008 HNSN Definition	Measured outcomes	Severity of illness score	Results	Data-Driven Surveillance Model	Comments
Safety Network in 2014. <i>Crit Care Med.</i> 2016;44(12):2154-2162.	4,002 IVAC 3,200 PVAP Multicenter (USA) Year: 2014 – May 2015											
Bouadma et al. (2015) Ventilator Associated Events: Prevalence, Outcome, and Relationship with VAP. <i>Crit Care Med.</i> 2015;43(9):1798-1806.	ICU ≥ 5 days MV N=3,028 total 2,331 VAC 869 IVAC Years: 1996-2012 Retrospective, Multicenter (France)	Modified		X	X		Yes	Mortality LOS-ICU MV Days	SOFA SAPS II GCS	VAC Rate: 107 per 1000 MV days. IVAC Rate: 35 per 1000 MV days. Rates and incidence were similar across all ICUs VAE and VAC are a frequent occurrence in the ICU	No	Practice changes for PEEP and FIO2 were based on P/F ratio which differs from the CDC criteria. Data obtained from French multicenter OUTCOMEREA database (1996-2012).
Kobayashi et al. (2017) The Impact of VAE in Critically Ill Subjects with Prolonged MV. <i>Respir Care.</i> 2017;62(11):1379-1386.	ICU ≥ 4 days MV N=404 total 54 VAC 23 IVAC 20 VAP Retrospective Single Center (Japan) Years: 2010-2013	Yes		X	X		Yes	Mortality LOS-ICU LOS-Hosp Vent days	APACHE II (IQR)	IVAC associated with higher hospital mortality than VAP	No	VAE rate per 1000 MV days not reported.
Klouwenberg et al. (2014) Electronic Implementation of a Novel Surveillance Paradigm for Ventilator-associated Events: Feasibility and Validation. <i>Am J Respir Crit Care Med.</i> 2014;189(8):947-55.	N=2080 ICU MV pts. 158 VAC 66 IVAC 51 PVAP 127 VAP (prior criteria) Prospective Cohort. Multicenter (Netherlands) Years: Jan 2011-to-July 2012	Yes	X	X	X		Yes	Mortality VAE VAP		VAC Rate: VAE rate per 1000 MV days not reported. Most VACs were identified by a PEEP increase. All types of VAE and VAP increased mortality. The VAE algorithm detected at most 32% of VAP that was identified by prospective surveillance.	Yes	

Citation	Sample Method Years	2013/2017 HNSN Definitions	VAE	VAC	IVAC	PVAP	VAP 2008 HNSN Definition	Measured outcomes	Severity of illness score	Results	Data-Driven Surveillance Model	Comments
Ramírez-Estrada et al. (2018) Assessing predictive accuracy for outcomes of ventilator-associated events in an international cohort: the EUVAE study. <i>Intensive Care Med.</i> 2018;44(8):1212-1220.	ICU pts ≥ 2 days MV: N=244 total 117 (VAE) 4 (VAC) 113 (IVAC) 64 (PVAP) 33 (VAP) 51 (VAT) Prospective Cohort Multicenter 13 ICUs in multiple countries. (Australia, France, Greece, Iran, Italy, Slovenia, Spain, Turkey) Years: not given	Modified	X	X	X		Yes	Mortality LOS-ICU LOS-Hosp	APACHE II	ICU mortality higher in patients with VAT than VAP	No	Cites the CDC criteria but uses alternative definitions ie: VAT & VARI. Notes new CDC criteria miss VAEs that occur without oxygenation deficits. Same research-group as Bouadma et al. (2015) in table above.
Pouly et al. (2020) Accuracy of VAE for the diagnosis of ventilator-associated lower respiratory tract infections (VA-LRTI). <i>Ann Intensive Care.</i> 2020;10(1):6.	ICU ≥ 5 days MV: N=189 Years: not given 6 MV Patients 15,029 MV Days 227 (VAE) 227 (VAC) 123 (IVAC) 62 (PVAP) 99 (VAT) 215 (VAP) 314 (VA-LRTI) Prospective Single Center	Yes	X	X	X	X	Yes	Mortality VAE VAT VAP LOS-ICU LOS-Hosp MV Days	SOFA SAPS II	VAE Rate: 17.4 per 1000 MV Days VAT Rate: 8.5 per 1000 MV Days VAP Rate: 17.8 per 1000 MV Days Poor agreement between VAE & VAP No difference in mortality across groups	No	Aim of study was to examine concordance between VAE and lower respiratory tract VAP. incidence numbers listed are from the Flow diagram, Figure 1.

eTable 2. Inclusion/exclusion criteria and limitations

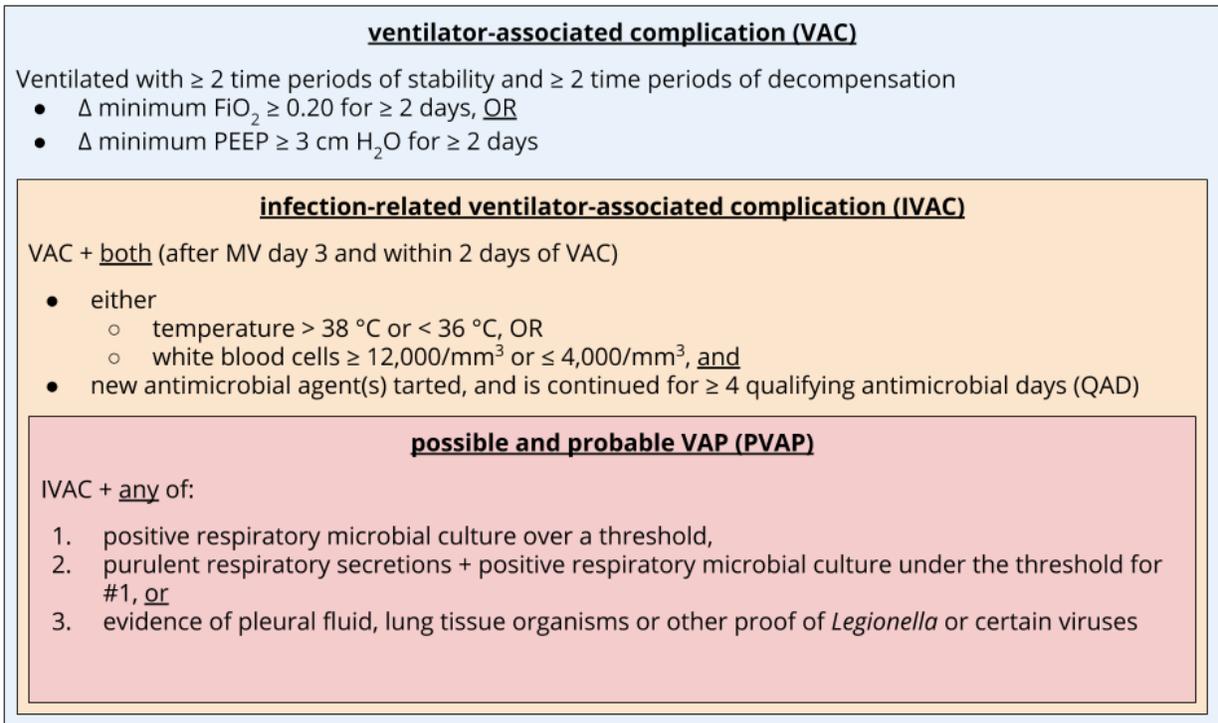
inclusion	exclusion
<ul style="list-style-type: none">● ICU stay \geq 4 days● MV \geq 4 days, consecutive	<ul style="list-style-type: none">● missing \geq 1 day data on PEEP, FiO₂● age < 18● subsequent episodes of MV within the same ICU stay

16.5% (n=1,344) of patients in the eICU-CRD database and 19.7% (n=1,632) of patients in the MIMIC-III database had multiple instances of MV during a single ICU stay and those subsequent episodes were excluded from the analyses so that each episode of MV was in the ICU stay only once.

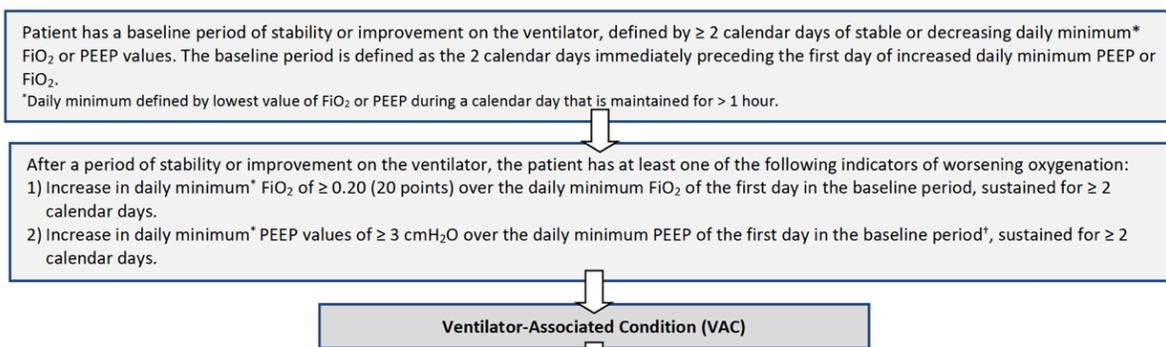
eFigures

eFigure 1. VAE criteria, including VAC, IVAC, PVAP

The VAE criteria build infection-related ventilator-associated complications (IVAC) and possible and probable VAP (PVAP) on top of the definition for the ventilator-associated complication (VAC). As such, IVAC is a subset of VAC, and PVAP is a subset of IVAC.



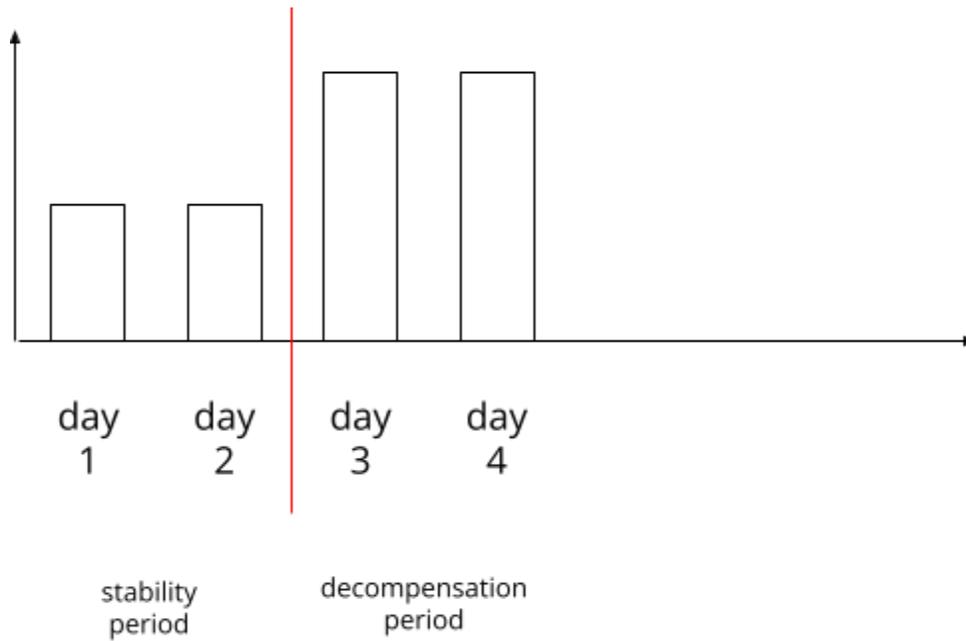
The VAC algorithm definition is explained in detail below.



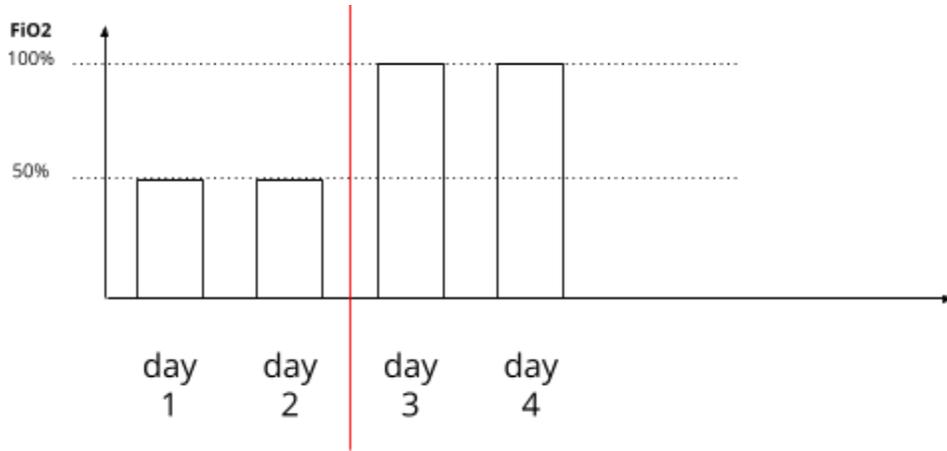
eFigure 2. Different ventilator requirement scenarios.

The red line indicates the completion of the stability period. Increasing bar height implies higher requirements, either of FiO₂ or PEEP.

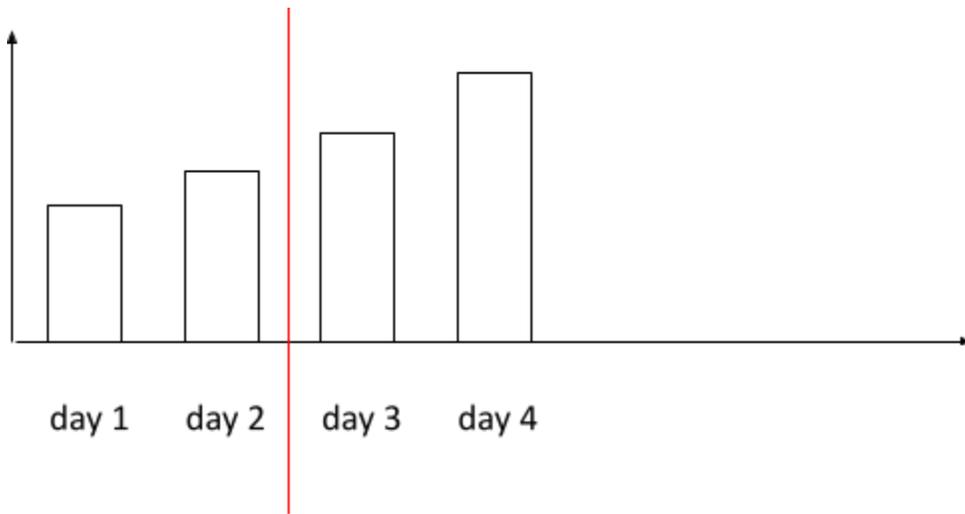
eFigure 2a. Classic example of VAC



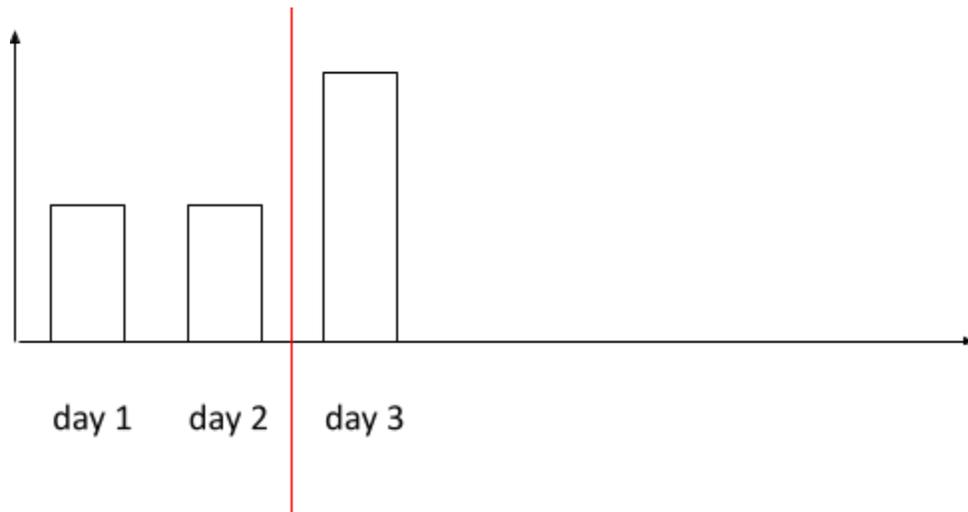
eFigure 2b. By this situation, this would be defined as a VAC if Δ_{minFiO_2} is $\leq 50\%$. For $\Delta_{\text{minFiO}_2} > 50\%$, this situation by definition cannot be defined as a VAC by Δ_{minFiO_2} criteria, as the resultant minFiO_2 cannot surpass 100%.



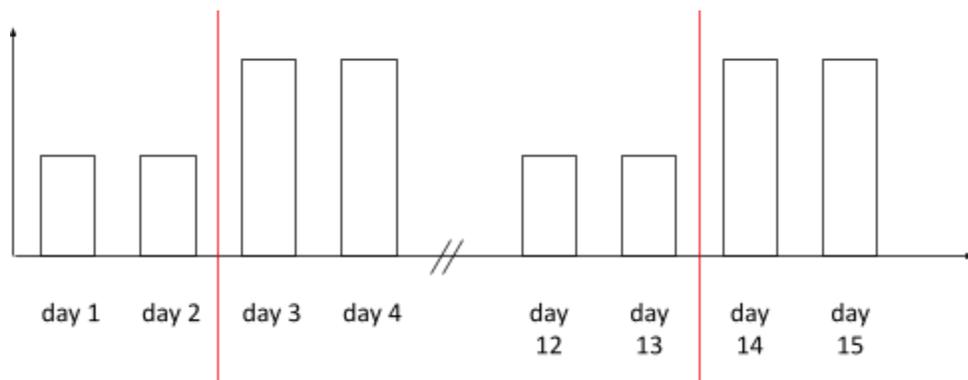
eFigure 2c. Would not satisfy stability requirement



Supplemental Figure 2d. Died too early

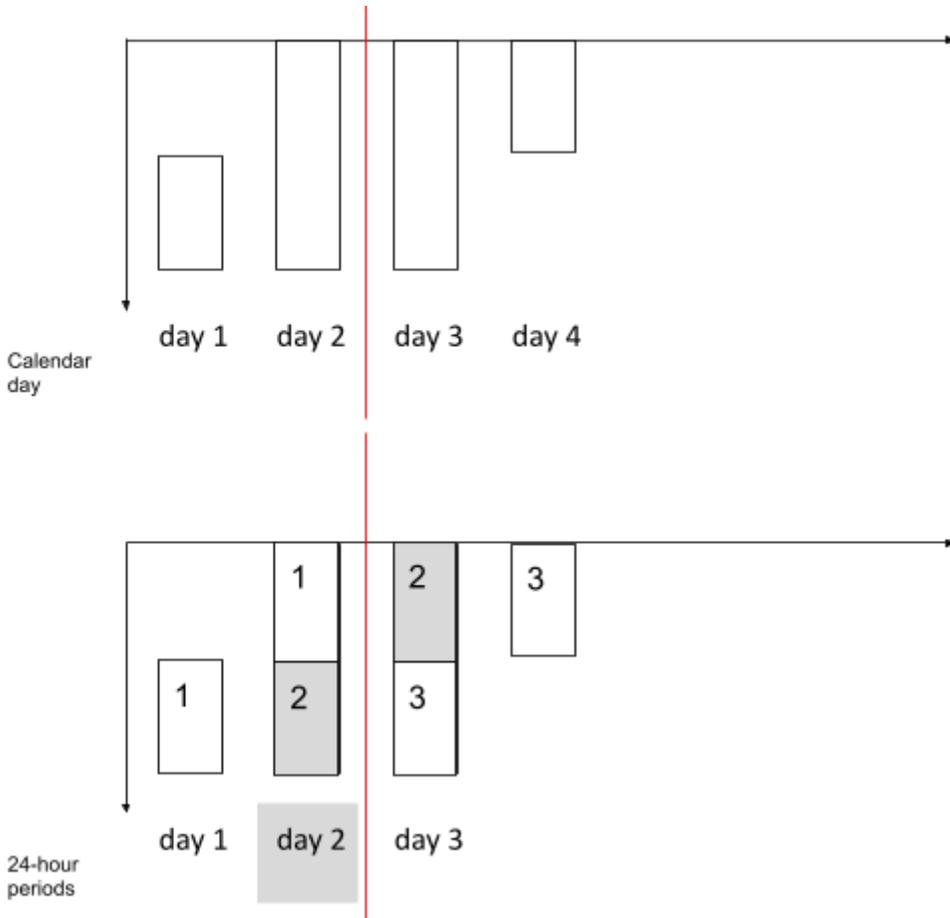


Supplemental Figure 2e. New event too soon

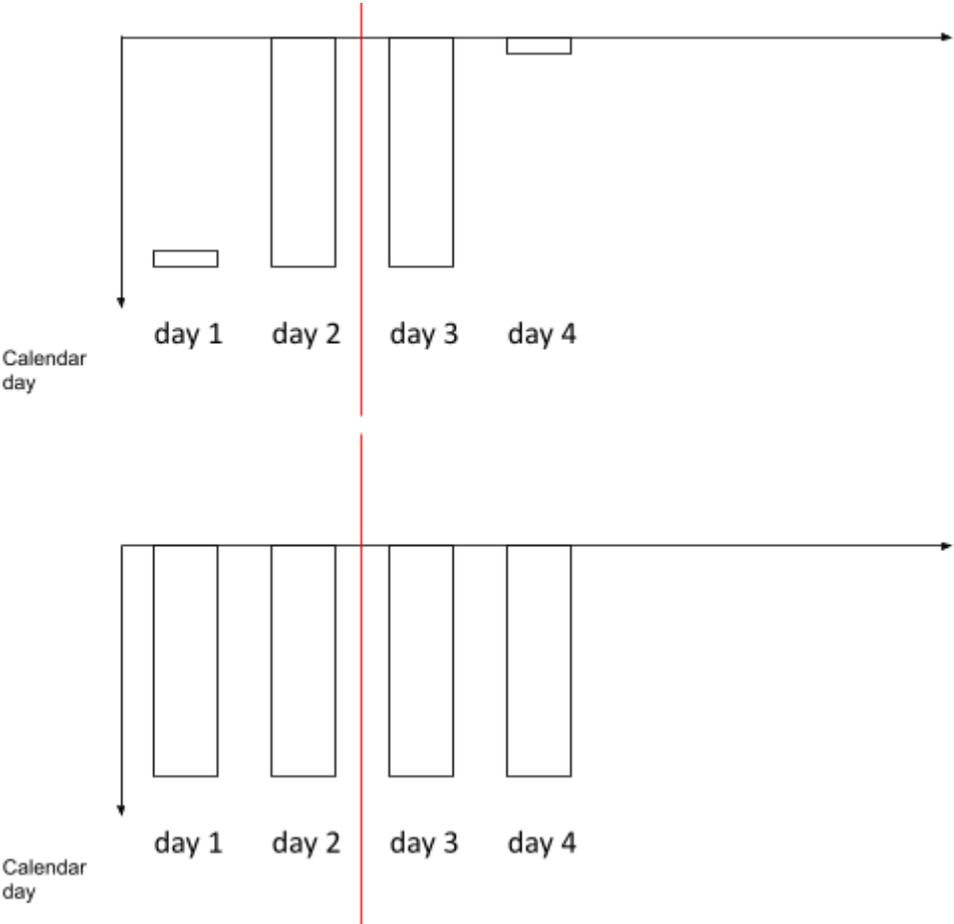


eFigure 3. Difference between calendar day and 24-hour time intervals.

eFigure 3a. Comparing calendar day notation versus 24-hour periods. In this example, this patient would have 4 calendar days but 3 sets of 24-hour time-intervals.

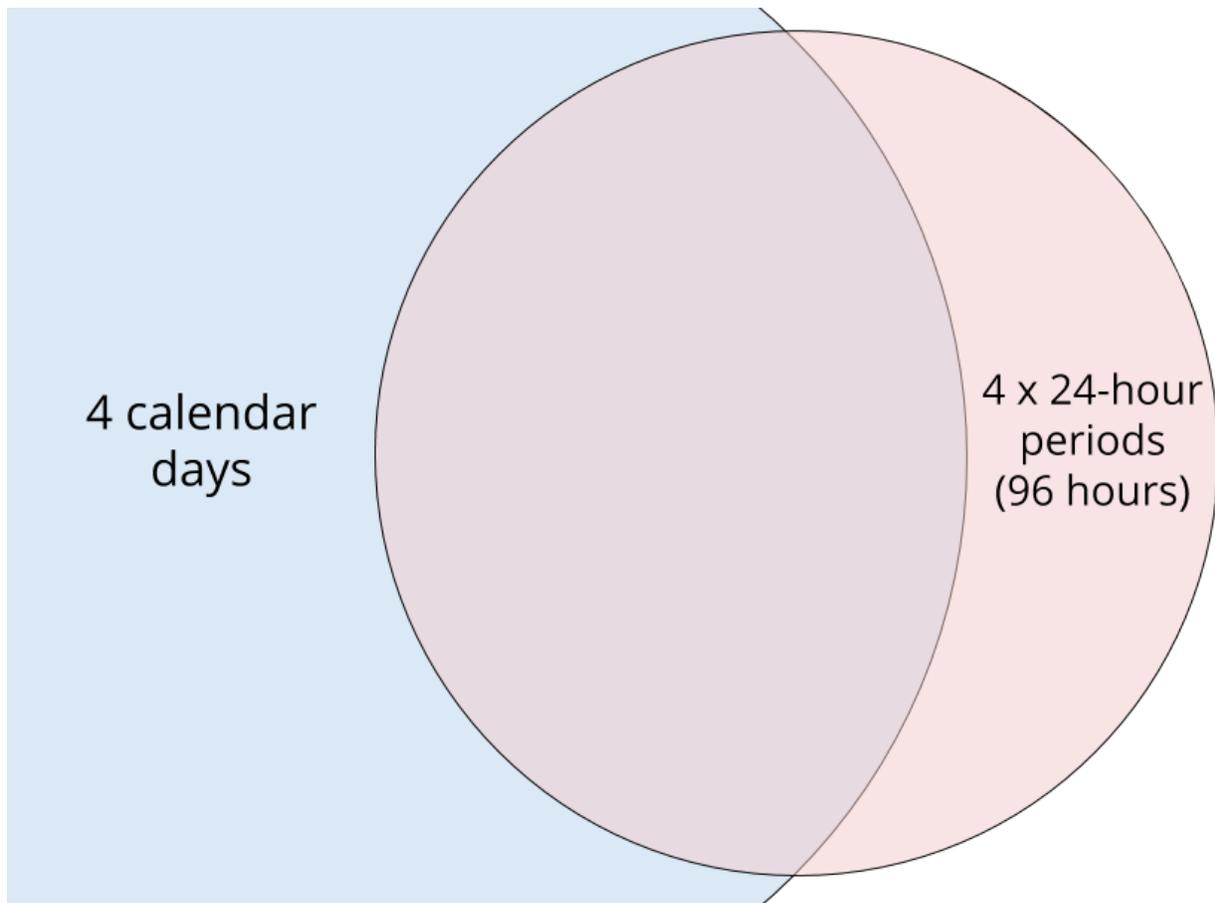


eFigure 3b. Comparing MV variability for 4 calendar days. Both the top figure (50 hours) and bottom figure (96 hours) are considered as having 4 calendar days of MV. However, only the bottom would qualify for 96 hours of MV.



eFigure 4. Time definition between calendar days and 24-hour periods

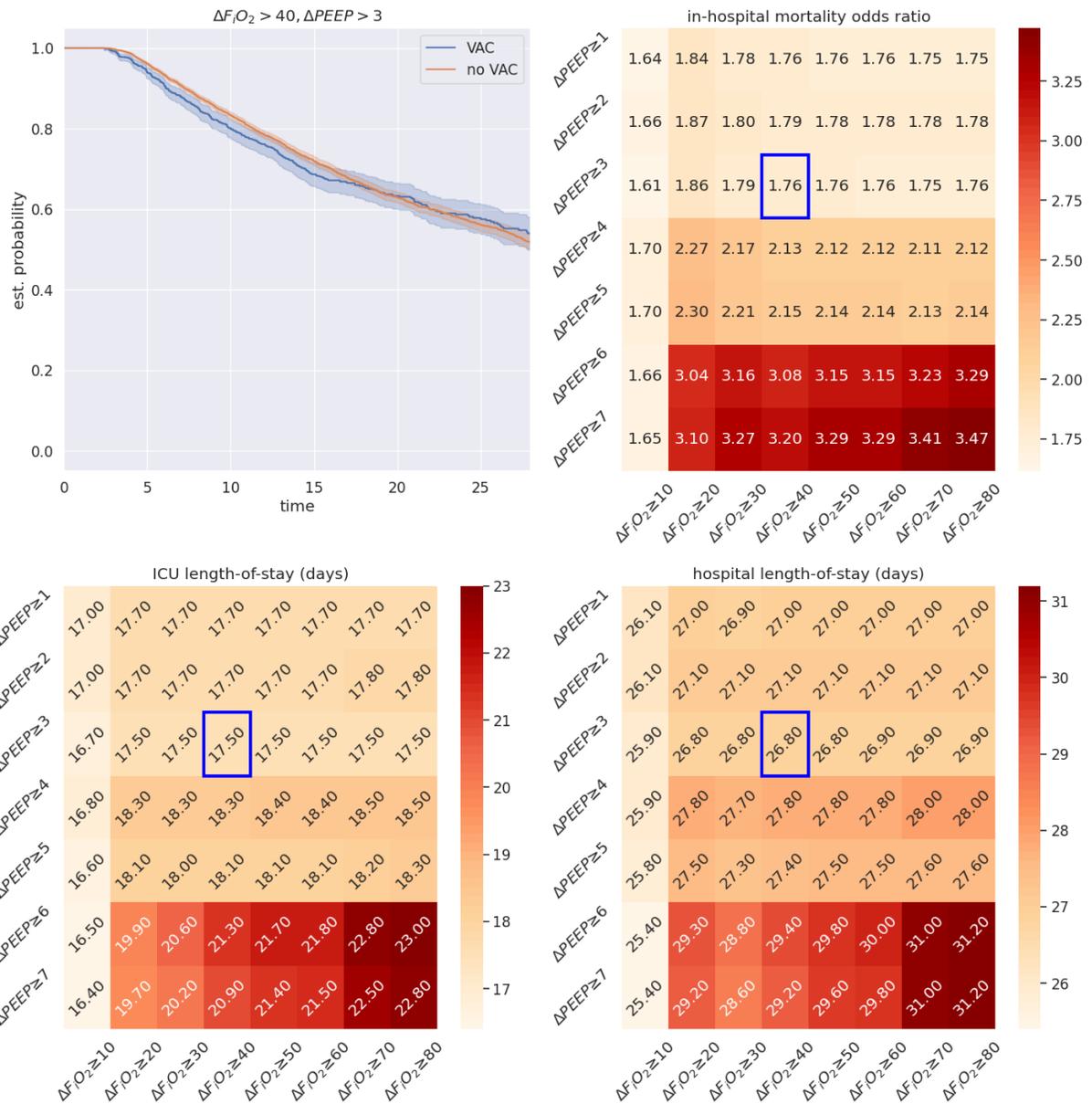
The purple overlap includes most patients who fit both criteria (> 4 calendar days and > 96 hours of MV).



eFigure 5. Additional examples of explorations

These examples present similar situations as those explored in the manuscript. However, screenshots from the interactive tool are also included for further context - both to describe settings and to illustrate the comparative tables generated for each example.

eFigure 5a. Using calendar day time intervals, $\Delta F_{iO_2} \geq 40\%$, $\Delta PEEP \geq 3$.



dataset(s): all

time definiti... calendar day

$\Delta \text{minFiO}_2 >$ 40

$\Delta \text{minPEEP}$ 3

VAC timing any

ICU type(s): all

rSOFA any

event: in-hospital mortality

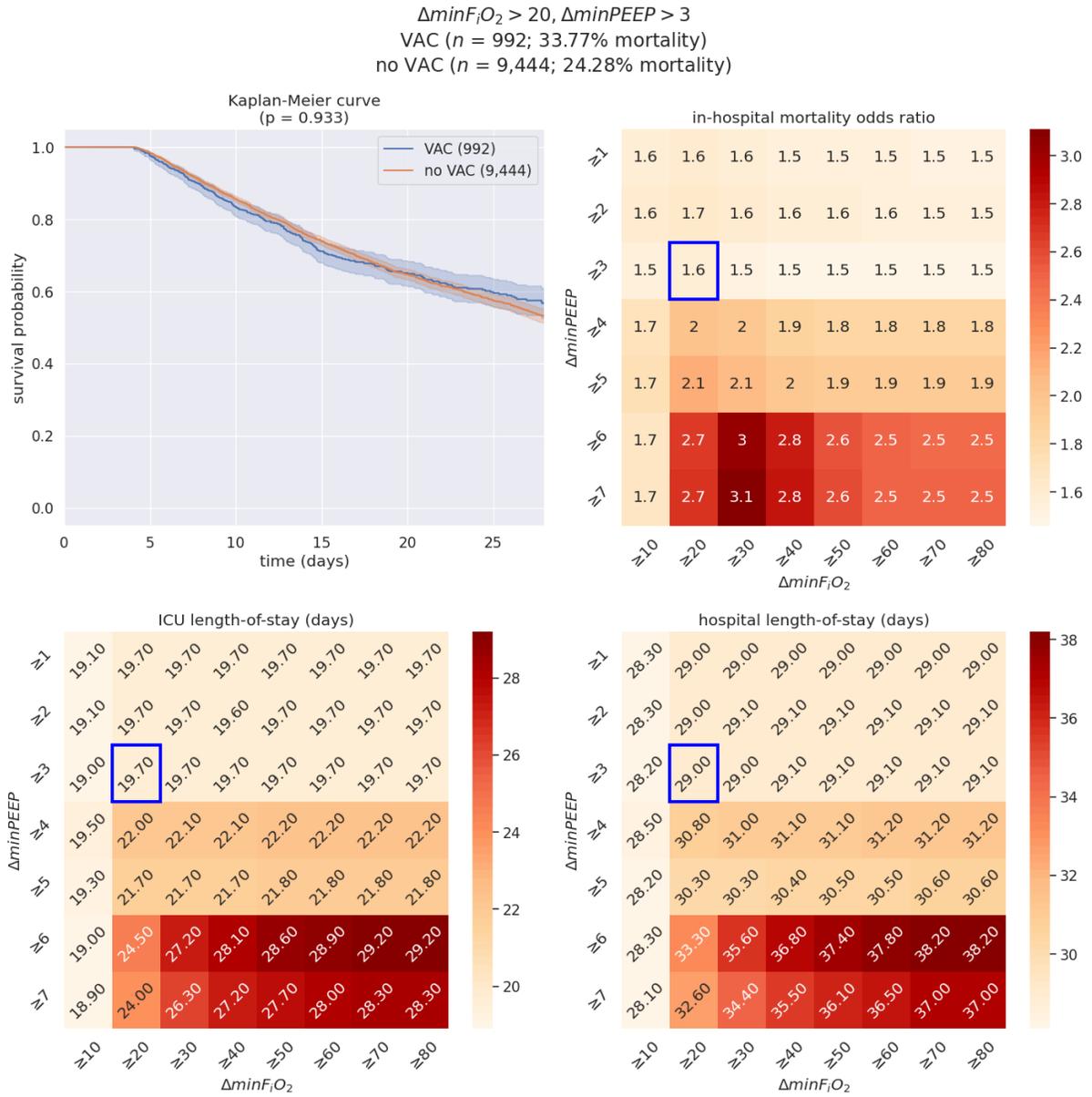
	VAC	no VAC	all
n	1,261	13,256	14,517
# vent days	14,521.00	102,902.00	117,423.00
VAC/1000 vent days			10.74
# events	422	2929	3351
event rate	33.47%	22.10%	23.08%

Comparison between patients with a VAC (+) and without a VAC (-), with stratifications by in-hospital mortality

	column-value	count (VAC)	% (VAC)	count (no VAC)	% (no VAC)	count (all)	mean \pm std (VAC)	mean \pm std (no VAC)	p	statistic	mean \pm std (both)	median (VAC)	median (no VAC)
0	All-raw	1261.0	8.69%	13256.0	91.31%	14517.0							
1	==(los-hospital: survivors)==	836.0	100.0%	10244.0	100.0%		(VAC)	(no VAC)				(VAC)	(no VAC)
2	los-hospital						26.84 \pm 18.31	21.09 \pm 17.34	1.69e-35	5387805.0	21.52 \pm 17.48	22.46	16.9
3	==(los-hospital: non - survivors)==	422.0	100.0%	2929.0	100.0%		(VAC)	(no VAC)				(VAC)	(no VAC)
4	los-hospital						16.28 \pm 15.0	17.1 \pm 17.3	0.1147	588710.5	17.0 \pm 17.03	11.5	12.38
5	==(los-icu: survivors)==	836.0	100.0%	10244.0	100.0%		(VAC)	(no VAC)				(VAC)	(no VAC)
6	los-icu						17.47 \pm 11.58	11.83 \pm 9.11	5.03e-82	5987982.0	12.26 \pm 9.44	14.08	9.03
7	==(los-icu: non - survivors)==	422.0	100.0%	2929.0	100.0%		(VAC)	(no VAC)				(VAC)	(no VAC)
8	los-icu						12.07 \pm 10.05	11.54 \pm 9.92	0.594	627923.0	11.61 \pm 9.94	8.89	8.79

eFigure 5b. Using 24 hour time intervals, $\Delta\text{minFiO}_2 \geq 20\%$, $\Delta\text{minPEEP} \geq 3$.

Note that the total number of patients has changed from 14,517 to 10,436.



dataset(s): all

time definiti... 24hr day

$\Delta \text{minFiO}_2 >$ 20

$\Delta \text{minPEEP}$ 3

VAC timing any

ICU type(s): all

rSOFA any

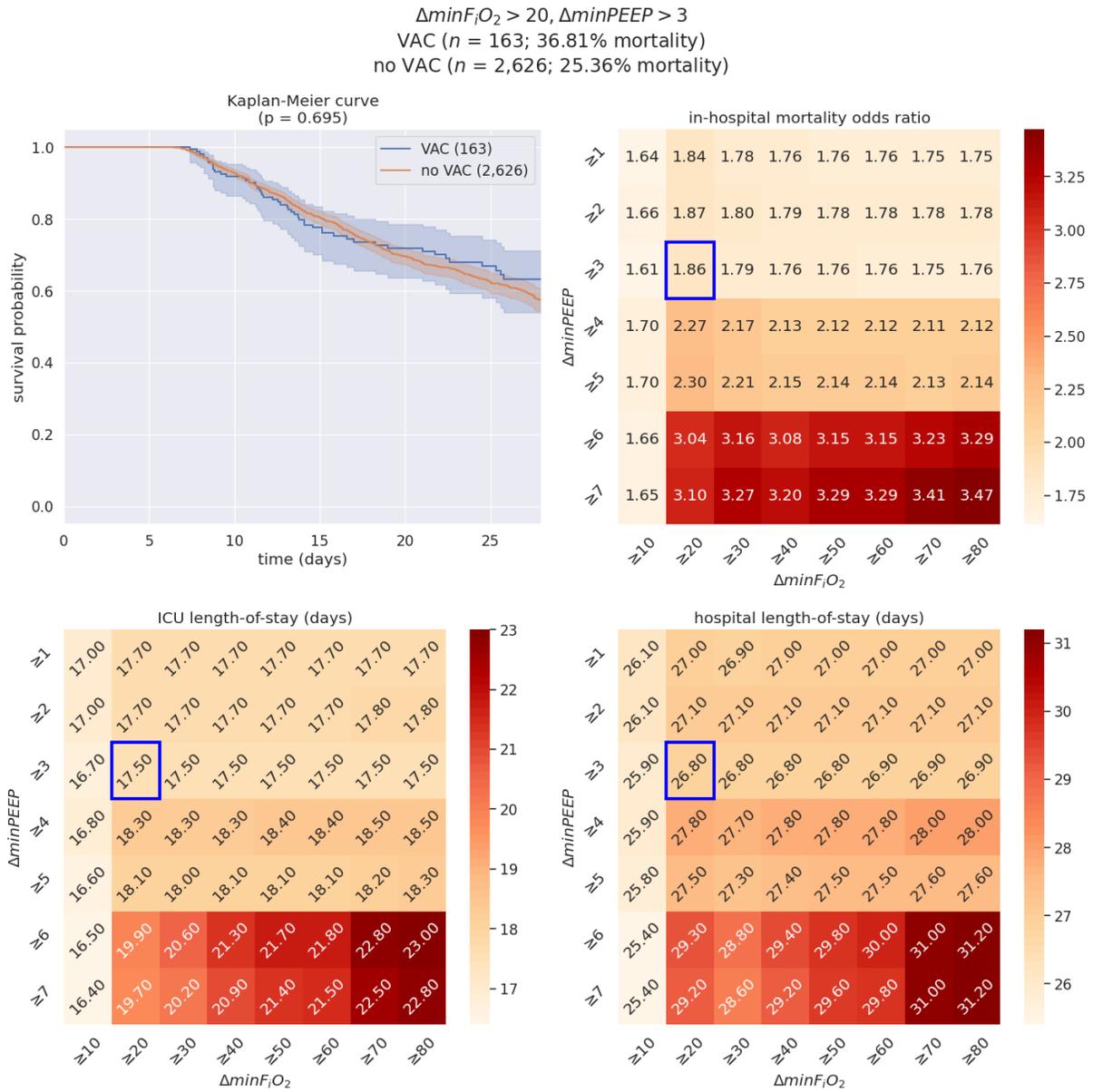
event: in-hospital mortality

	VAC	no VAC	all
n	992	9,444	10,436
# vent days	12,250.16	81,353.74	93,603.90
VAC/1000 vent days			10.60
# events	335	2293	2628
event rate	33.77%	24.28%	25.18%

Comparison between patients with a VAC (+) and without a VAC (-), with stratifications by in-hospital mortality

	column-value	count (VAC)	% (VAC)	count (no VAC)	% (no VAC)	count (all)	mean \pm std (VAC)	mean \pm std (no VAC)	p	statistic	mean \pm std (both)	median (VAC)	median (no VAC)
0	All-raw	992.0	9.51%	9444.0	90.49%	10436.0							
1	==(los-hospital: survivors)==	654.0	100.0%	7088.0	100.0%		(VAC)	(no VAC)				(VAC)	(no VAC)
2	los-hospital						28.99 \pm 17.9	23.25 \pm 17.33	4.22e-27	2907411.5	23.73 \pm 17.45	24.37	18.96
3	==(los-hospital: non - survivors)==	335.0	100.0%	2293.0	100.0%		(VAC)	(no VAC)				(VAC)	(no VAC)
4	los-hospital						17.5 \pm 14.06	18.27 \pm 17.99	0.5554	376428.0	18.18 \pm 17.54	13.07	13.24
5	==(los-icu: survivors)==	654.0	100.0%	7088.0	100.0%		(VAC)	(no VAC)				(VAC)	(no VAC)
6	los-icu						19.72 \pm 12.12	13.89 \pm 9.56	5.46e-55	3171956.0	14.38 \pm 9.94	16.38	11.06
7	==(los-icu: non - survivors)==	335.0	100.0%	2293.0	100.0%		(VAC)	(no VAC)				(VAC)	(no VAC)
8	los-icu						13.51 \pm 9.83	12.74 \pm 10.4	0.1071	404981.5	12.84 \pm 10.33	10.66	9.96

eFigure 5c. Using CDC VAC criteria ($\Delta\text{minFiO}_2 \geq 20\%$, $\Delta\text{minPEEP} \geq 3$, calendar day time intervals) for late VAC (VAC developed on day 7 or later)



dataset(s): all

time definiti... calendar day

$\Delta \text{minFiO}_2 >$ 20

$\Delta \text{minPEEP}$ 3

VAC timing >=7d

ICU type(s): all

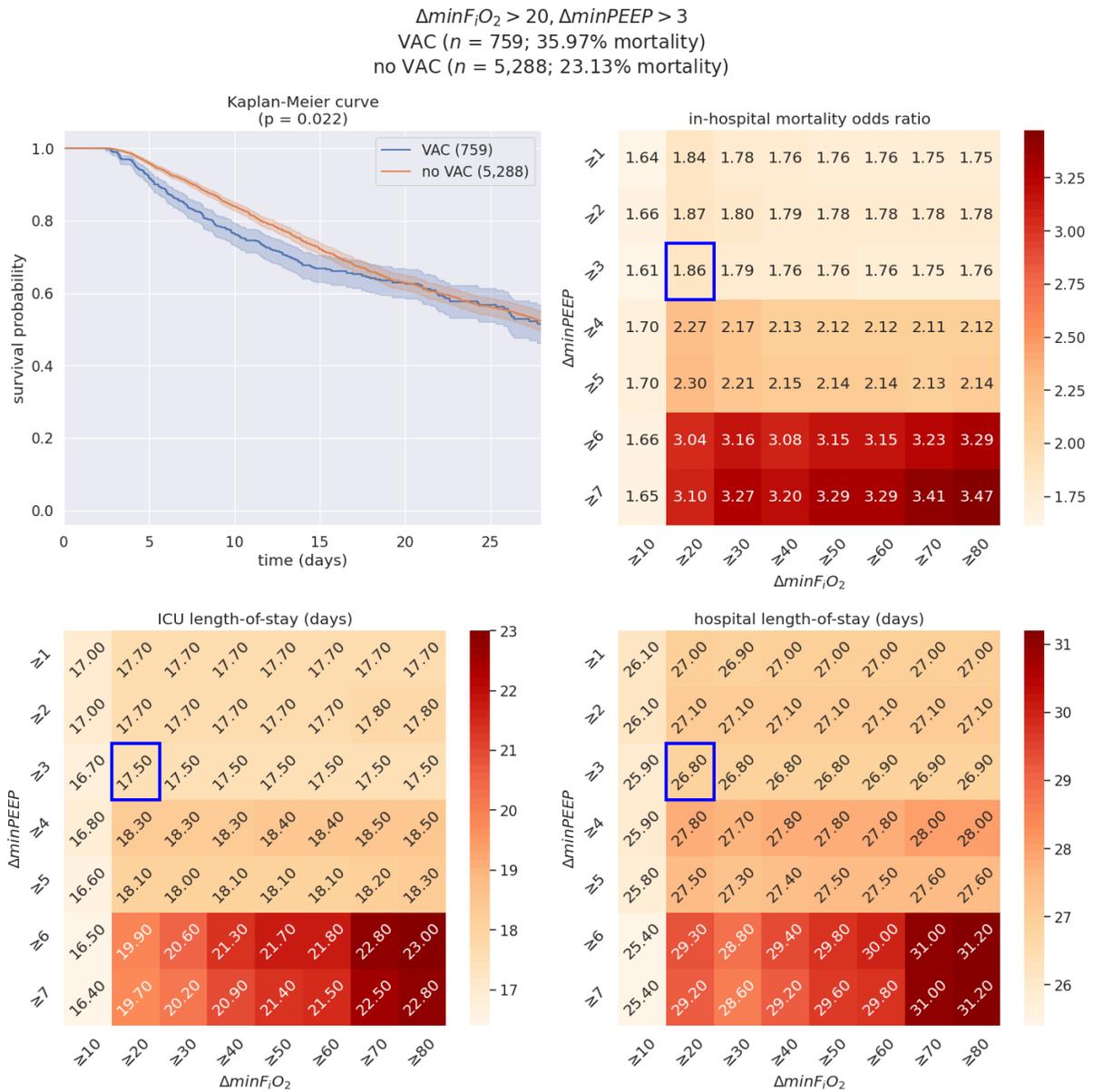
rSOFA any

event: in-hospital mortality

	VAC	no VAC	all
n	163	2,626	2,789
# vent days	2,743.00	30,882.00	33,625.00
VAC/1000 vent days			4.85
# events	60	666	726
event rate	36.81%	25.36%	26.03%

	column-value	count (VAC)	% (VAC)	count (no VAC)	% (no VAC)	count (all)	mean \pm std (VAC)	mean \pm std (no VAC)	p	statistic	mean \pm std (both)	median (VAC)	median (no VAC)
0	All-raw	163.0	5.84%	2626.0	94.16%	2789.0							
1	==(los-hospital: survivors)==	103.0	100.0%	1934.0	100.0%		(VAC)	(no VAC)				(VAC)	(no VAC)
2	los-hospital						33.58 \pm 17.3	27.29 \pm 18.81	4.52e-07	128949.0	27.6 \pm 18.79	29.82	22.27
3	==(los-hospital: non - survivors)==	60.0	100.0%	666.0	100.0%		(VAC)	(no VAC)				(VAC)	(no VAC)
4	los-hospital						22.33 \pm 15.84	23.35 \pm 20.32	0.6098	19185.5	23.27 \pm 19.98	15.47	17.39
5	==(los-icu: survivors)==	103.0	100.0%	1934.0	100.0%		(VAC)	(no VAC)				(VAC)	(no VAC)
6	los-icu						24.76 \pm 13.11	17.13 \pm 10.43	2.56e-13	142151.5	17.52 \pm 10.71	22.56	13.97
7	==(los-icu: non - survivors)==	60.0	100.0%	666.0	100.0%		(VAC)	(no VAC)				(VAC)	(no VAC)
8	los-icu						18.48 \pm 11.87	16.63 \pm 13.59	0.1944	21999.5	16.78 \pm 13.46	13.75	13.25

eFigure 5d. Using CDC VAC criteria ($\Delta\text{minFiO}_2 \geq 20\%$, $\Delta\text{minPEEP} \geq 3$, calendar day time intervals) for respiratory SOFA score ≥ 3 (implying P/F ratio < 200)



dataset(s): all

time definiti... calendar day

$\Delta \text{minFiO}_2 >$ 20

$\Delta \text{minPEEP}$ 3

VAC timing any

ICU type(s): all

rSOFA $>=3$

event: in-hospital mortality

	VAC	no VAC	all
n	759	5,288	6,047
# vent days	8,679.00	42,533.00	51,212.00
VAC/1000 vent days			14.82
# events	273	1223	1496
event rate	35.97%	23.13%	24.74%

Comparison between patients with a VAC (+) and without a VAC (-), with stratifications by in-hospital mortality

	column-value	count (VAC)	% (VAC)	count (no VAC)	% (no VAC)	count (all)	mean \pm std (VAC)	mean \pm std (no VAC)	p	statistic	mean \pm std (both)	median (VAC)	median (no VAC)
0	All-raw	759.0	12.55%	5288.0	87.45%	6047.0							
1	==(los-hospital: survivors)==	484.0	100.0%	4034.0	100.0%		(VAC)	(no VAC)				(VAC)	(no VAC)
2	los-hospital						27.1 \pm 18.4	21.43 \pm 18.77	3.83e-23	1244903.5	22.04 \pm 18.81	22.98	17.09
3	==(los-hospital: non - survivors)==	273.0	100.0%	1223.0	100.0%		(VAC)	(no VAC)				(VAC)	(no VAC)
4	los-hospital						15.69 \pm 15.02	17.27 \pm 15.71	0.0038	148237.0	16.98 \pm 15.59	10.36	13.08
5	==(los-icu: survivors)==	484.0	100.0%	4034.0	100.0%		(VAC)	(no VAC)				(VAC)	(no VAC)
6	los-icu						17.87 \pm 11.49	12.39 \pm 9.41	1.26e-44	1356264.0	12.98 \pm 9.8	14.81	9.5
7	==(los-icu: non - survivors)==	273.0	100.0%	1223.0	100.0%		(VAC)	(no VAC)				(VAC)	(no VAC)
8	los-icu						11.32 \pm 10.03	11.93 \pm 9.3	0.0135	151002.5	11.82 \pm 9.43	8.17	9.25