

**Supplemental Table 1: VAC and IVAC bivariate risk factor analysis over 3-day and 7-day periods prior to VAC onset**

	VAC Cases	Controls	OR (95% CI)	p-value	IVAC Cases	Controls	OR (95% CI)	p-value
<b>Classic VAP Bundle: mean % adherence over 3 days prior to VAC (SD)</b>								
Head of bed elevation	77 (28)	74 (32)	1.01 (1.00-1.02)	NS	73 (34)	75 (35)	1.00 (0.98-1.01)	NS
Oral care with chlorhexidine	77 (26)	82 (30)	1.01 (1.00-1.02)	NS	75 (29)	75 (33)	1.00 (0.98-1.02)	NS
Deep vein thrombosis prophylaxis	80 (27)	74 (31)	1.01 (1.00-1.02)	NS	77 (32)	77 (32)	1.00 (0.98-1.02)	NS
Stress ulcer prophylaxis	<b>85 (24)</b>	<b>79 (28)</b>	<b>1.01 (1.00-1.02)</b>	<b>0.08</b>	83 (28)	80 (29)	1.01 (0.98-1.02)	NS
Sedative interruption	47 (38)	45 (35)	1.00 (0.99-1.01)	NS	44 (39)	49 (37)	1.00 (0.98-1.01)	NS
Spontaneous breathing trial	22 (31)	21 (30)	1.00 (0.99-1.01)	NS	21 (30)	22 (31)	1.00 (0.98-1.02)	NS
Measure the Rapid Spontaneous Breathing Index	<b>60 (38)</b>	<b>51 (40)</b>	<b>1.01 (1.00-1.02)</b>	<b>0.08</b>	54 (41)	45 (39)	1.01 (0.99-1.02)	NS
<b>Classic VAP Bundle: mean % adherence over 7 days prior to VAC (SD)</b>								
Head of bed elevation	73 (27)	71 (29)	1.00 (0.99-1.02)	NS	67 (31)	70 (33)	1.00 (0.98-1.01)	NS
Oral care with chlorhexidine	73 (25)	70 (27)	1.01 (0.99-1.02)	NS	70 (26)	73 (31)	0.99 (0.97-1.01)	NS
Deep vein thrombosis prophylaxis	75 (27)	73 (29)	1.00 (0.99-1.01)	NS	72 (31)	76 (31)	1.00 (0.98-1.01)	NS
Stress ulcer prophylaxis	80 (24)	78 (26)	1.00 (0.99-1.01)	NS	79 (28)	79 (27)	1.00 (0.98-1.02)	NS
Sedative interruption	44 (35)	44 (34)	1.00 (0.99-1.01)	NS	40 (36)	49 (36)	0.99 (0.97-1.00)	NS
Spontaneous breathing trial	19 (26)	20 (26)	1.00 (0.99-1.01)	NS	17 (23)	20 (28)	1.00 (0.98-1.01)	NS
Measure the Rapid Spontaneous Breathing Index	55 (36)	50 (38)	1.00 (1.00-1.01)	NS	49 (37)	47 (37)	1.00 (0.99-1.02)	NS
Mean RSBI over 3 days prior to VAC	102 (76)	110 (85)	1.00 (0.99-1.00)	NS	105 (99)	92 (82)	1.00 (0.99-1.01)	NS
Mean RSBI over 7 days prior to VAC	103 (75)	107 (70)	1.00 (0.99-1.00)	NS	107 (97)	101 (80)	1.00 (0.99-1.01)	NS
<b>Nutrition over 3 days prior to VAC (%)</b>								
Nothing by mouth 100% of the time	36 (33%)	36 (33%)	1.00 (0.49-2.06)	NS	10 (26%)	11 (29%)	0.86 (0.28-2.58)	NS
Tube feeding – any exposure	59 (54%)	68 (62%)	0.64 (0.34-1.19)	NS	26 (68%)	26 (68%)	1.00 (0.34-2.92)	NS
Parenteral nutrition – any exposure	15 (14%)	11 (10%)	1.50 (0.62-3.83)	NS	2 (5.3%)	3 (7.9%)	0.67 (0.09-4.02)	NS
<b>Nutrition over 7 days prior to VAC (%)</b>								
Nothing by mouth 100% of the time	36 (33%)	36 (33%)	1.00 (0.49-2.06)	NS	10 (26%)	11 (29%)	0.86 (0.28-2.58)	NS
Tube feeding – any exposure	60 (55%)	69 (63%)	0.64 (0.34-1.19)	NS	26 (68%)	26 (68%)	1.00 (0.34-2.92)	NS
Parenteral Nutrition – any exposure	15 (14%)	13 (12%)	1.20 (0.52-2.82)	NS	2 (5.3%)	5 (13%)	0.40 (0.06-1.86)	NS
<b>Blood products: mean units over 3 days (SD)</b>								
Red blood cells	0.63 (1.3)	0.56 (1.6)	1.04 (0.85-1.30)	NS	0.7 (1.5)	0.7 (2.3)	1.01 (0.75-1.36)	NS
Fresh frozen plasma	0.44 (1.3)	0.40 (1.4)	1.03 (0.81-1.31)	NS	0.5 (1.3)	0.7 (2.1)	0.92 (0.61-1.28)	NS
Platelets	0.13 (0.4)	0.15 (0.6)	0.92 (0.50-1.64)	NS	0.1 (0.3)	0.3 (1.0)	0.70 (0.20-1.47)	NS
<b>Blood products: mean units over 7 days (SD)</b>								
Red blood cells	0.68 (1.3)	0.56 (1.3)	1.08 (0.87-1.37)	NS	0.8 (1.5)	0.7 (1.9)	1.01 (0.74-1.40)	NS
Fresh frozen plasma	0.55 (1.4)	0.43 (1.2)	1.10 (0.86-1.45)	NS	0.7 (1.4)	0.8 (1.8)	0.95 (0.63-1.38)	NS
Platelets	0.14 (0.37)	0.16 (0.61)	0.93 (0.47-1.75)	NS	0.2 (0.3)	0.3 (1.0)	0.64 (0.14-1.43)	NS
<b>Sedative medications: mean total dose over 7 days (SD)</b>								
Total sedative (propofol + benzodiazepines) – mg midazolam equivalents/kg	<b>4.7 (5.5)</b>	<b>5.9 (6.7)</b>	<b>0.96 (0.91-1.01)</b>	<b>0.10</b>	6.1 (6.8)	7.0 (7.4)	0.98 (0.91 -1.05)	NS
Total Benzodiazepine – mg midazolam equivalents/kg	1.0 (1.2)	1.0 (1.5)	1.00 (0.85-1.18)	NS	0.9 (1.1)	0.9 (1.2)	1.01 (0.67-1.53)	NS
Propofol – mg midazolam equivalents/kg	3.7 (5.2)	4.9 (6.6)	0.96 (0.91-1.01)	NS	5.2 (6.8)	6.1 (7.5)	0.98 (0.91-1.05)	NS
Total sedative (propofol + benzodiazepines) – mg midazolam equivalents/kg/day	1.1 (1.3)	1.2 (1.3)	0.68 (0.71-1.14)	NS	1.4 (1.6)	1.4 (1.3)	1.02 (0.73-1.44)	NS
Total Benzodiazepine – mg midazolam equivalents/kg/day	0.2 (0.6)	0.2 (0.3)	1.03 (0.51-2.09)	NS	0.2 (0.3)	0.2 (0.2)	1.45 (0.19-13)	NS
Propofol – mg midazolam equivalents/kg/day	0.9 (1.2)	1.0 (1.3)	0.91 (0.71-1.13)	NS	1.3 (1.6)	1.2 (1.4)	1.01 (0.73-1.39)	NS
Total opioid – 100 mcg fentanyl equivalents/kg	0.66 (0.95)	0.62 (0.89)	1.06 (0.77-1.50)	NS	<b>0.67 (0.64)</b>	<b>0.49 (0.54)</b>	<b>2.64 (0.90-9.6)</b>	<b>0.08</b>
Total fentanyl – 100 mcg fentanyl/kg	0.54 (0.63)	0.48 (0.57)	1.23 (0.77-2.04)	NS	0.63 (0.63)	0.48 (0.54)	2.42 (0.80-8.9)	NS
Total morphine – mcg fentanyl equivalents/kg	0.2 (1.2)	0.4 (3.9)	0.97 (0.81-1.07)	NS	0.2 (0.6)	0.0 (0.2)	4.24 (0.72-610)	NS
Total opioid – 100 mcg fentanyl equivalents/kg/day	0.13 (0.15)	0.12 (0.15)	1.30 (0.19-9.5)	NS	0.14 (0.13)	0.10 (0.10)	54 (0.44-1.7E4)	NS

Total fentanyl – mcg fentanyl/kg/day	0.11 (0.12)	0.10 (0.11)	2.65 (0.21-1.04)	NS	0.13 (0.13)	0.10 (0.10)	36 (0.29-1.1E4)	NS
Total morphine – mcg fentanyl equivalents/kg/day	0.0 (0.2)	0.1 (0.6)	0.82 (0.25-1.63)	NS	0.0 (0.1)	0.0 (0.0)	3.7x10 <sup>4</sup> (0.19-2.9x10 <sup>17</sup> )	NS
Dexmedetomidine – mg/kg	0.3 (1.5)	0.7 (4.6)	0.95 (0.82-1.04)	NS	0.1 (1.3)	1.2 (7.1)	0.95 (0.68-1.05)	NS
Dexmedetomidine – mcg/kg/day	0.1 (0.6)	0.1 (0.7)	0.98 (0.62-1.53)	NS	0.0 (0.2)	0.2 (1.0)	0.69 (0.06-1.43)	NS
Cisatracurium – mg/kg	0.3 (1.3)	0.4 (1.4)	0.98 (0.80-1.19)	NS	0.6 (1.9)	0.5 (1.9)	1.02 (0.79-1.35)	NS
Cisatracurium – mg/kg/day	0.1 (0.3)	0.1 (0.3)	0.95 (0.37-2.38)	NS	0.1 (0.5)	0.1 (0.3)	1.65 (0.46-8.99)	NS
Daily minimum RASS: 3-day mean (SD)	-2.8 (1.5)	-2.7 (1.5)	0.93 (0.70-1.22)	NS	-3.1 (1.3)	-3.1 (1.3)	0.93 (0.60-1.43)	NS
Daily minimum RASS: 7-day mean (SD)	-2.8 (1.4)	-2.6 (1.7)	0.85 (0.64-1.08)	NS	-3.1 (1.2)	-2.9 (1.3)	0.75 (0.44-1.19)	NS
<b>Fluid balance: 3-day mean/day (SD)</b>								
Ins – L	<b>4.9 (3.7)</b>	<b>3.8 (2.6)</b>	<b>1.20 (1.05-1.41)</b>	<b>0.003</b>	4.7 (3.8)	4.3 (3.1)	1.07 (0.90-1.31)	NS
Outs – L	2.5 (2.1)	2.5 (1.4)	1.01 (0.85-1.21)	0.89	<b>2.4 (1.5)</b>	<b>2.8 (1.5)</b>	<b>0.66 (0.36-1.07)</b>	<b>0.10</b>
Net balance – L	<b>2.4 (3.4)</b>	<b>1.5 (2.3)</b>	<b>1.20 (1.06-1.40)</b>	<b>0.004</b>	2.4 (3.8)	1.6 (2.5)	1.13 (0.95-1.43)	0.18
<b>Fluid balance: 7-day mean/day (SD)</b>								
Ins – L	<b>4.8 (3.5)</b>	<b>3.8 (2.5)</b>	<b>1.19 (1.05-1.38)</b>	<b>0.004</b>	4.7 (3.8)	4.1 (3.0)	1.08 (0.92-1.31)	NS
Outs – L	2.4 (1.6)	2.3 (1.3)	1.07 (0.87-1.34)	NS	2.4 (1.4)	2.6 (1.4)	0.79 (0.46-1.25)	NS
Net balance – L	<b>2.4 (3.3)</b>	<b>1.6 (2.1)</b>	<b>1.16 (1.03-1.35)</b>	<b>0.015</b>	2.3 (3.7)	1.6 (2.3)	1.10 (0.93-1.36)	NS
<b>Ventilator: 7-day mean (SD)</b>								
Minimum tidal volume – L/kg	5.3 (1.6)	5.1 (1.4)	1.12 (0.91-1.39)	NS	<b>5.5 (1.3)</b>	<b>5.1 (1.4)</b>	<b>1.51 (0.95-2.59)</b>	<b>0.08</b>
Maximum tidal volume – L/kg	7.7 (2.4)	7.6 (2.4)	1.01 (0.89-1.15)	NS	8.0 (1.9)	7.5 (2.3)	1.14 (0.89-1.48)	NS
% days on mandatory vent modes at min TV	<b>62 (40)</b>	<b>54 (38)</b>	<b>1.01 (1.00-1.02)</b>	<b>0.05</b>	61 (37)	54 (37)	1.01 (0.99-1.02)	NS
% days on mandatory vent modes at max TV	<b>54 (41)</b>	<b>42 (37)</b>	<b>1.01 (1.00-1.02)</b>	<b>0.007</b>	52 (37)	44 (37)	1.01 (0.99-1.02)	NS
Mandatory vent modes 100% of days at min TV	<b>48 (44)</b>	<b>35 (32)</b>	<b>2.00 (1.05-4.02)</b>	<b>0.04</b>	13 (34)	10 (26)	1.50 (0.54-4.47)	NS
Mandatory vent modes 100% of days at max TV	<b>40 (36)</b>	<b>21 (19)</b>	<b>2.73 (1.41-5.69)</b>	<b>0.003</b>	10 (26)	7 (18)	1.60 (0.53-5.29)	NS

**Abbreviations:** NS – non-significant, RASS – Richmond Agitation and Sedation Scale, RSBI – rapid shallow breathing index, SD – standard deviation, TV – tidal volume, VAP – ventilator-associated pneumonia