

Supplementary Online Content

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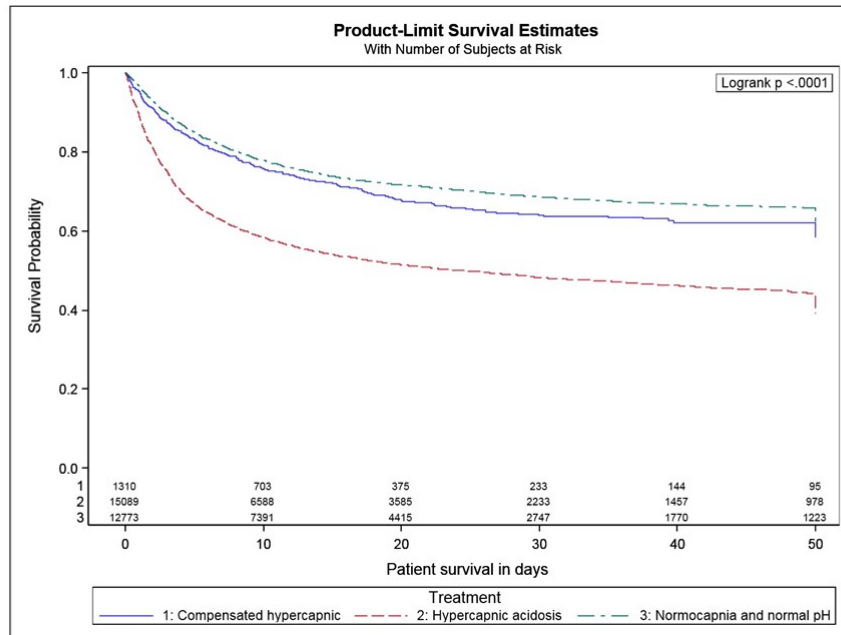
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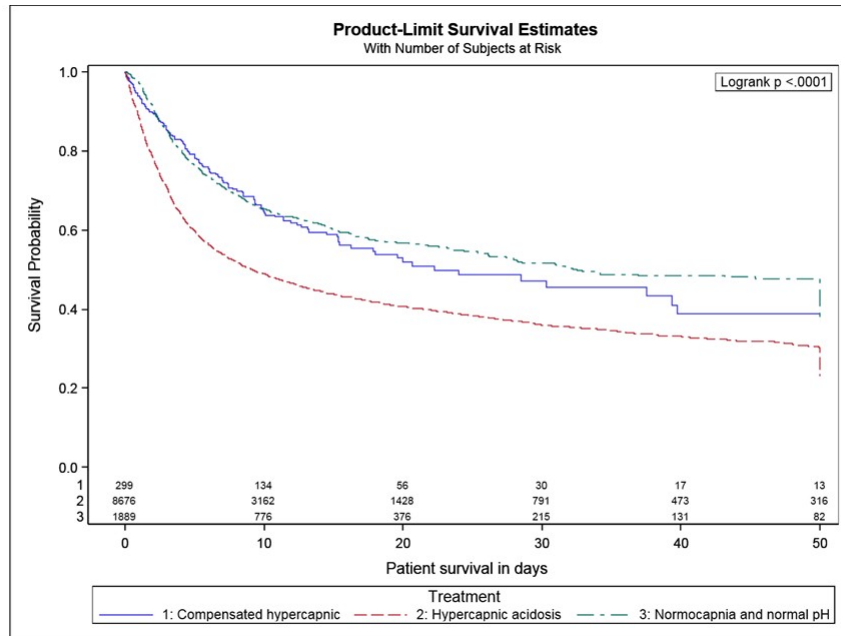
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This supplementary material has been provided by the authors to give readers additional information about their work.

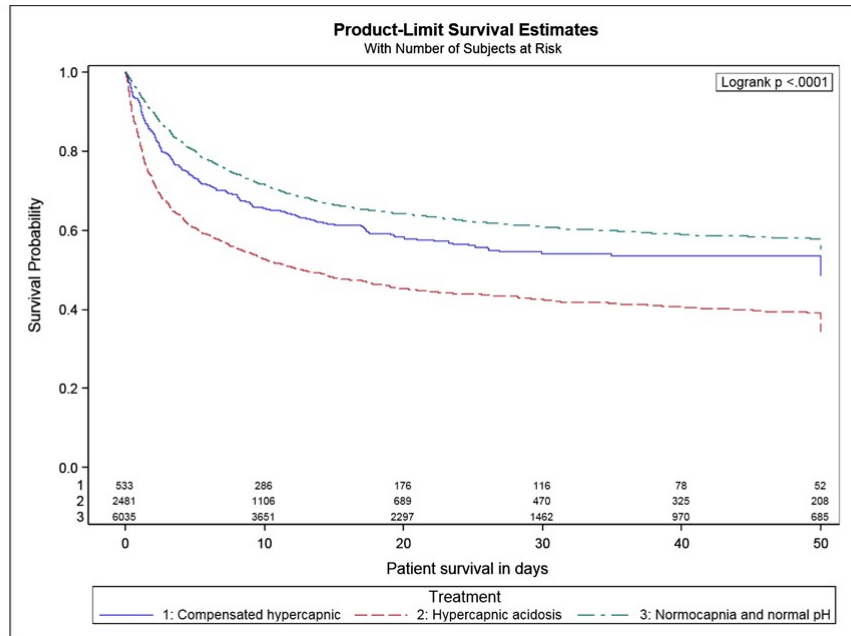
eFigure 1 : Kaplan-Meier survival curves all cerebral injury patients



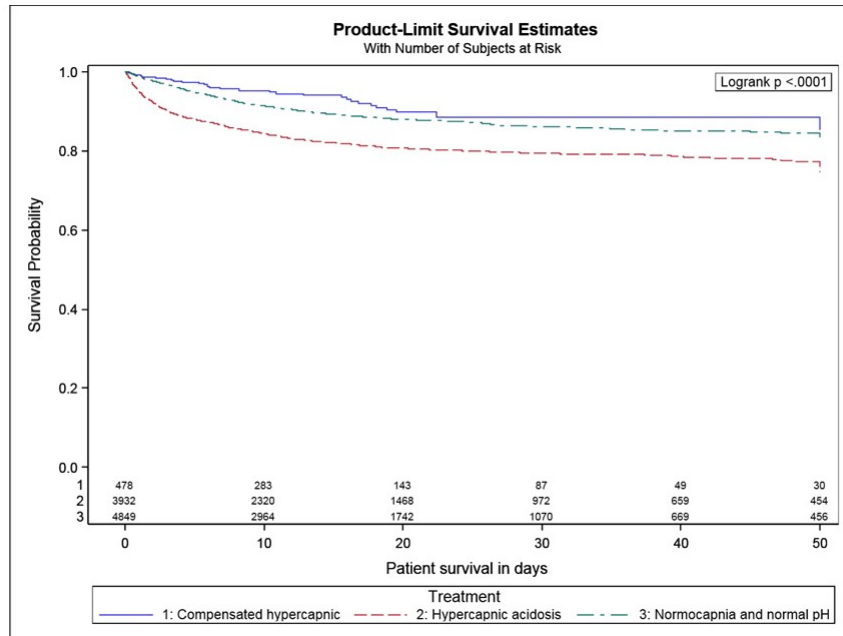
eFigure 2 Kaplan-Meier survival curves for cardiac arrest patients



eFigure 3 Kaplan-Meier survival curves for stroke patients



eFigure 4 Kaplan-Meier survival curves for traumatic brain injury patients



e Table 1. Prediction model to determine each patient’s probability to present to intensive care units with Hypercapnic Acidosis

Category	Hypercapnic Acidosis		Odds Ratio
	No	Yes	95%CI
Age			
1.<=44	33.9%(4879)	26.7%(4364)	1
2.45-64	30.4%(4371)	33.5%(5470)	1.28(1.2-1.36)
3.65-84	31.9%(4597)	35.8%(5860)	1.19(1.12-1.27)
4.>=85	3.8%(543)	4%(658)	1.08(0.95-1.23)
Chronic renal failure			
No	98.7%(14196)	97.1%(15880)	1
Yes	1.3%(194)	2.9%(472)	1.78(1.49-2.13)
Diabetes			
No	98.7%(14200)	97.5%(15949)	1
Yes	1.3%(190)	2.5%(403)	1.43(1.19-1.72)
Immunotherapy			
No	98.8%(14223)	98.1%(16040)	1
Yes	1.2%(167)	1.9%(312)	1.58(1.3-1.93)
Gender			
Female	30.8%(4438)	27%(4418)	1
Male	69.2%(9952)	73%(11934)	1.29(1.22-1.36)
Admission Source			
Chronic care	0.6%(84)	0.8%(137)	0.99(0.74-1.32)
Home	52.9%(7611)	67.8%(11082)	1
Other Hospital	32%(4607)	22.6%(3695)	0.55(0.51-0.58)
Other ICU	3.5%(508)	1.7%(284)	0.39(0.33-0.46)
Unknown	11%(1580)	7.1%(1154)	0.86(0.75-0.99)
Hospital Level			
Metropolitan	7.9%(1135)	17%(2782)	2.1(1.56-2.82)
Private	3%(435)	2.8%(462)	1
Rural	4.4%(630)	8.7%(1427)	1.89(1.4-2.55)
Tertiary	84.7%(12190)	71.4%(11681)	1.01(0.77-1.33)

*All variables were significant p<0.0001

AUC= 0.683 (0.677-0.689)

Hosmer Lemmeshow p=0.11

eTable 2. Prediction model to determine each patient's probability to present to intensive care units with compensated hypercapnia

Variable	Compensated Hypercapnia		Odds Ratio (95%CI)
	No	Yes	
Diagnosis			
Cardiovascular	38.9%(11450)	23%(308)	1
Neurological	30.4%(8929)	41%(548)	2.43(2.09-2.83)
Trauma	30.7%(9025)	36%(482)	2.15(1.84-2.51)
Day Shift admission			
No	55.5%(16305)	53.1%(710)	0.86(0.77-0.96)
Yes	44.5%(13099)	46.9%(628)	1
Admission Source			
Chronic Care	0.7%(209)	0.9%(12)	1.53(0.85-2.77)
Home	61.1%(17968)	54.2%(725)	1
Other Hosp	26.7%(7863)	32.8%(439)	1.28(1.13-1.44)
Other ICU	2.5%(735)	4.3%(57)	1.8(1.35-2.39)
Unknown	8.9%(2629)	7.8%(105)	0.85(0.68-1.07)
Hospital Type			
Metropolitan	12.7%(3749)	12.6%(168)	1.25(0.87-1.8)
Private	2.9%(857)	3%(40)	1
Rural	6.7%(1966)	6.8%(91)	1.19(0.81-1.75)
Tertiary	77.6%(22832)	77.7%(1039)	0.87(0.62-1.21)
Indigenous status			
No	68.1%(20038)	66%(883)	1
Yes	5.3%(1549)	3.7%(49)	0.76(0.56-1.02)
Unknown	26.6%(7817)	30.3%(406)	1.28(1.13-1.46)
Location (Australian states and New Zealand)			
ACT	3.1%(916)	3.1%(42)	1.64(1.11-2.41)
NSW	25.6%(7530)	28.8%(385)	1.85(1.45-2.36)
NT	1.4%(399)	1%(13)	0.93(0.5-1.73)
NZ	9.9%(2913)	6.9%(92)	1
QLD	15.5%(4570)	13.1%(175)	1.31(1-1.72)
SA	11%(3225)	13.2%(177)	2(1.53-2.6)
TAS	2.3%(676)	2.6%(35)	1.65(1.1-2.48)
VIC	25.6%(7513)	26.7%(357)	1.66(1.31-2.12)
WA	5.7%(1662)	4.6%(62)	1.41(0.99-2)
Gender			
Female	29%(8515)	25.5%(341)	1
Male	71%(20889)	74.5%(997)	1.23(1.08-1.39)

*All variables were significant $p < 0.01$

AUC=0.632 (0.617-0.647)

Hosmer Lemmeshow $p = 0.30$

eTable 3: Adjusted hospital mortality for cohort of cerebral injury patients matched for admission severity scores

N	Diagnostic categories	Logistic regression analysis	
		OR (95% CI)	P Value
Cardiac arrest			
	Hypercapnic group		<0.0001
307	Normocapnia and normal pH	1	
307	Compensated hypercapnia vs Normocapnia and normal pH	0.97 (0.67-1.41)	
307	Hypercapnic acidosis vs Normocapnia and normal pH	2.16 (1.48-3.15)	
Stroke			
	Hypercapnic group		p=0.06
547	Normocapnia and normal pH	1	
547	Compensated hypercapnia vs Normocapnia and normal pH	1.05 (0.8-1.37)	
547	Hypercapnic acidosis vs Normocapnia and normal pH	1.34 (1.03-1.74)	
Traumatic Brain Injury			
	Hypercapnic group		p=0.13
481	Normocapnia and normal pH	1	
481	Compensated hypercapnia vs Normocapnia and normal pH	0.99 (0.6-1.64)	
481	Hypercapnic acidosis vs Normocapnia and normal pH	1.48 (0.96-2.28)	

eTable 4 Adjusted Hospital Mortality** (logistic regression) in patients with cerebral injury stratified based on Glasgow Coma Scale (GCS)

N	Baseline GCS	Logistic regression analysis*	
		OR (95% CI)	P-value
Cardiac arrest			
	Hypercapnic group GCS3-7		<0.001
1260	Normocapnia and normal pH	1	
192	Compensated vs Normocapnia and normal pH	1.11 (0.79-1.56)	
7522	Hypercapnic acidosis vs Normocapnia and normal pH	1.53 (1.33-1.76)	
	Hypercapnic group GCS8-12		0.21
198	Normocapnia and normal pH	1	
38	Compensated hypercapnia vs Normocapnia and normal pH	0.7 (0.29-1.68)	
562	Hypercapnic acidosis vs Normocapnia and normal pH	1.29 (0.85-1.94)	
	Hypercapnic group GCS13-15		0.04
430	Normocapnia and normal pH	1	
71	Compensated hypercapnia vs Normocapnia and normal pH	1.08 (0.51-2.29)	
1180	Hypercapnic acidosis vs Normocapnia and normal pH	1.5 (1.08-2.1)	
Stroke			
	Hypercapnic group GCS3-7		<0.001
3098	Normocapnia and normal pH	1	
280	Compensated hypercapnia vs Normocapnia and normal pH	0.96 (0.73-1.27)	
1737	Hypercapnic acidosis vs Normocapnia and normal pH	1.45 (1.25-1.67)	
	Hypercapnic group GCS8-12		0.03
1616	Normocapnia and normal pH	1	
136	Compensated hypercapnia vs Normocapnia and normal pH	1.25 (0.84-1.88)	
461	Hypercapnic acidosis vs Normocapnia and normal pH	1.37 (1.07-1.76)	
	Hypercapnic group GCS13-15		0.11
1424	Normocapnia and normal pH	1	
123	Compensated hypercapnia vs Normocapnia and normal pH	0.81 (0.47-1.4)	
469	Hypercapnic acidosis vs Normocapnia and normal pH	1.3 (0.98-1.74)	
Traumatic Brain Injury			
	Hypercapnic group GCS3-7		<0.001
2104	Normocapnia and normal pH	1	
15	Compensated hypercapnia vs Normocapnia and normal pH	0.61 (0.37-1.03)	
1866	Hypercapnic acidosis vs Normocapnia and normal pH	1.39 (1.17-1.66)	
	Hypercapnic group GCS8-12		0.11
1356	Normocapnia and normal pH	1	
116	Compensated hypercapnia vs Normocapnia and normal pH	1.42 (0.61-3.29)	
912	Hypercapnic acidosis vs Normocapnia and normal pH	0.72 (0.5-1.04)	
	Hypercapnic group GCS13-15		0.72
1383	Normocapnia and normal pH	1	
204	Compensated hypercapnia vs Normocapnia and normal pH	0.82 (0-939)	
1276	Hypercapnic acidosis vs Normocapnia and normal pH	1.2 (0.06-25.4)	

*p-value for interaction between neurological severity and hypercapnic group- Cardiac arrest: 0.88; Stroke:0.22; Traumatic brain injury: 0.03

** all analyses are adjusted for GCS, patient severity (ANZROD with oxygen, pH and GCS components removed), propensity to present with hypercapnic acidosis, propensity to present with compensated hypercapnia and year of admission

eTable 5 **Adjusted Hospital Mortality ** (logistic regression) in subgroups of cerebral injury based on diagnostic subgroups**

N	Diagnostic Subgroups	Logistic regression analysis*	
		OR (95% CI)	P Value
Ischaemic Stroke			
	Hypercapnic group		0.16
1233	Normocapnia and normal pH	1	
151	Compensated hypercapnia vs Normocapnia and normal pH	0.94 (0.64-1.37)	
613	Hypercapnic acidosis vs Normocapnia and normal pH	1.23 (0.98-1.54)	
Intracerebral haemorrhage			
	Hypercapnic group		0.001
2402	Normocapnia and normal pH	1	
228	Compensated hypercapnia vs Normocapnia and normal pH	0.9 (0.65-1.25)	
989	Hypercapnic acidosis vs Normocapnia and normal pH	1.42 (1.18-1.72)	
Subarachnoid haemorrhage			
	Hypercapnic group		<0.001
1781	Normocapnia and normal pH	1	
108	Compensated hypercapnia vs Normocapnia and normal pH	1.13 (0.7-1.83)	
875	Hypercapnic acidosis vs Normocapnia and normal pH	1.6 (1.3-1.98)	
Subdural or extradural haemorrhage			
	Hypercapnic group		0.29
803	Normocapnia and normal pH	1	
61	Compensated hypercapnia vs Normocapnia and normal pH	1.03 (0.52-2.03)	
233	Hypercapnic acidosis vs Normocapnia and normal pH	1.36 (0.93-2)	
Isolated Traumatic Brain Injury			
	Hypercapnic group		0.65
779	Normocapnia and normal pH	1	
64	Compensated hypercapnia vs Normocapnia and normal pH	0.71 (0-195.65)	
500	Hypercapnic acidosis vs Normocapnia and normal pH	1.14 (0.11-12.45)	
Traumatic Brain Injury associated with other injuries			
	Hypercapnic group		0.002
4123	Normocapnia and normal pH	1	
418	Compensated hypercapnia vs Normocapnia and normal pH	0.74 (0.47-1.18)	
3623	Hypercapnic acidosis vs Normocapnia and normal pH	1.28 (1.08-1.5)	

*p-value for interaction between diagnostic subgroup and hypercapnic group- Ischaemic stroke, intracerebral haemorrhage, subarachnoid haemorrhage and subdural or extradural haemorrhage:0.49; Isolated Traumatic brain injury and Traumatic brain injury associated with other injuries :0.81

** all analyses are adjusted for GCS, patient severity (ANZROD with oxygen, pH and GCS components removed), propensity to present with hypercapnic acidosis, propensity to present with compensated hypercapnia and year of admission

eTable 6. **Adjusted Hospital Mortality** (logistic regression) in subgroups of cerebral injury patients who required neurosurgical intervention and who did not require neurosurgical intervention**

N	Diagnostic Subgroups	Logistic regression analysis*	
		OR (95% CI)	P Value
Stroke- Nonoperative			
	Hypercapnic group		<0.001
3612	Normocapnia and normal pH	1	
381	Compensated hypercapnia vs Normocapnia and normal pH	0.93 (0.73-1.19)	
1953	Hypercapnic acidosis vs Normocapnia and normal pH	1.44 (1.25-1.65)	
Stroke- Operative			
	Hypercapnic group		0.02
2607	Normocapnia and normal pH	1	
167	Compensated hypercapnia vs Normocapnia and normal pH	1.12 (0.76-1.66)	
757	Hypercapnic acidosis vs Normocapnia and normal pH	1.32 (1.08-1.62)	
Traumatic Brain Injury- Non operative			
	Hypercapnic group		0.02
3429	Normocapnia and normal pH	1	
339	Compensated hypercapnia vs Normocapnia and normal pH	0.79 (0.47-1.31)	
2767	Hypercapnic acidosis vs Normocapnia and normal pH	1.25 (1.04-1.51)	
Traumatic Brain Injury- Operative			
	Hypercapnic group		0.15
1473	Normocapnia and normal pH	1	
143	Compensated hypercapnia vs Normocapnia and normal pH	0.68 (0.34-1.34)	
1356	Hypercapnic acidosis vs Normocapnia and normal pH	1.18 (0.93-1.5)	

*No patient in cardiac surgery diagnostic category had neurosurgical intervention.

** p-value for interaction between diagnostic subgroup and hypercapnic group- Stroke:0.24, Traumatic brain injury:0.81

*** all analyses are adjusted for GCS, patient severity (ANZROD with oxygen, pH and GCS components removed), propensity to present with hypercapnic acidosis, propensity to present with compensated hypercapnia and year of admission