

Supplementary Appendix:

Electronic supplementary material prepared for: Dysnatraemia and 6-month functional outcomes in critically ill patients with aneurysmal subarachnoid haemorrhage. A prospective cohort study.

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Table S1: Inclusion/Exclusion Criteria

The following inclusion criteria were applied:

- a) age > 18 years
- b) aneurysm confirmed on computed tomography angiography (CTA) or digital subtraction angiography (DSA) of the intra-cranial arteries
- c) admitted under the care of an intensive care specialist during their initial hospital stay
- d) consent for participation was obtained from the patient or their legally authorized substitute decision maker.

Ethical approval to undertake the study was obtained at each participating site (QLD, SA, NSW; HREC/16/QRBW/204 &, VIC; HREC/15/Alfred/8, WA; HREC/16/SCGG/74, NZ; 16/NTB/172).

Patients were excluded if the SAH was from another cause (such as an arterio-venous malformation or trauma) or the diagnosis was unclear

Figure S1: Patient Enrolment and Follow Up

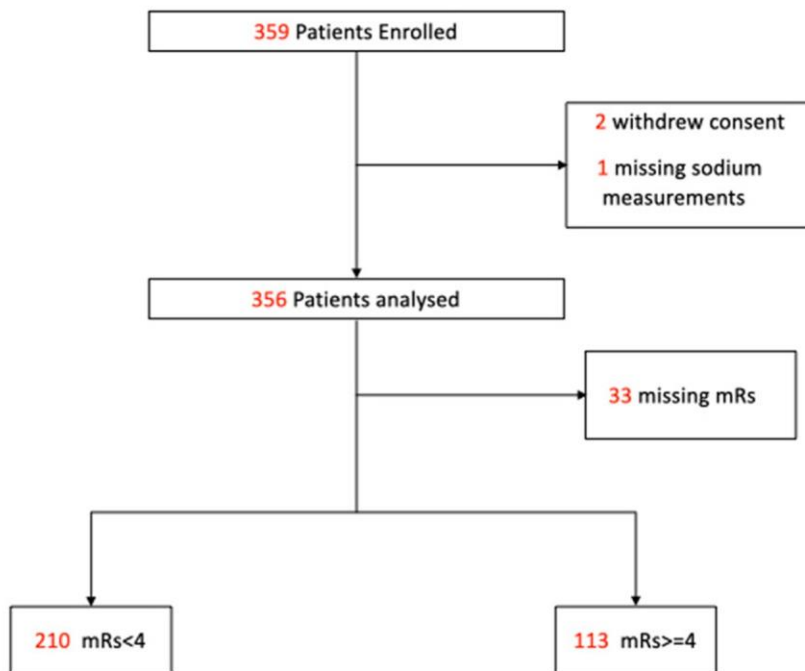


Table S2: Adjusted association of mean and standard deviation of sodium concentrations with the incidence of delayed cerebral ischaemia - Multivariable logistic model

	OR	95% confidence interval	P-value
Mean sodium	0.95	(0.86, 1.04)	0.287
Standard deviation of sodium	1.06	(0.82, 1.37)	0.654
Male	0.84	(0.44, 1.62)	0.610
Age	0.99	(0.97, 1.01)	0.464
High WFNS	1.18	(0.56, 2.50)	0.668
APACHE III score	1.01	(0.99, 1.02)	0.369
Hours from admission to neurovascular intervention	1.00	(1.00, 1.01)	0.403
Surgical Clipping	0.99	(0.48, 2.05)	0.977
Treated with sodium tablets*	0.95	(0.37, 2.46)	0.918
Treated with fludrocortisone*	0.58	(0.20, 1.71)	0.325
Treated with Sodium Fluids*	1.32	(0.56, 3.11)	0.532

APACHE III is Acute Physiology and Chronic Health Score

WFNS is World Federation of Neurosurgeons Score

*Patients could receive multiple treatment modalities during the ICU admission.

Table S3: Adjusted association of mean and standard deviation of sodium concentrations

with ICU length of stay and length of stay in the hospital – multivariable negative binomial model

	Length of stay - ICU		Length of stay - Hospital	
	MLR (95% CI)	P-value	MLR (95% CI)	P-value
Mean sodium	1.00 (0.98, 1.02)	0.956	0.98 (0.96, 1.01)	0.181
Standard deviation of sodium	1.13 (1.07, 1.20)	>0.001	1.08 (1.01, 1.15)	0.018
Male	0.89 (0.78, 1.02)	0.091	0.94 (0.81, 1.08)	0.375
Age	1.00 (0.99, 1.01)	0.942	1.01 (1.00, 1.01)	0.030
High WFNS	1.32 (1.13, 1.53)	>0.001	1.25 (1.06, 1.46)	0.007
APACHE III score	1.00 (0.99, 1.00)	0.572	1.01 (1.00, 1.01)	0.128
Hours from admission to neurovascular intervention	1.002 (1.00, 1.004)	0.006	1.00 (1.00, 1.01)	0.051
Surgical Clipping	1.24 (1.07, 1.43)	0.004	1.34 (1.14, 1.56)	>0.001
Treated with sodium tablets*	1.12 (0.91, 1.39)	0.273	1.14 (0.92, 1.42)	0.225
Treated with fludrocortisone*	0.97 (0.77, 1.22)	0.809	0.82 (0.64, 1.05)	0.124
Treated with Sodium Fluids*	1.10 (0.93, 1.30)	0.256	1.02 (0.86, 1.22)	0.783

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Table S4: Sensitivity analysis for missing mRS values

	Original analysis	Sensitivity 1 (missing mRS >= 4)	Sensitivity 2 (missing mRS < 4)
mRS values:	mRS < 4 = 210 mRS ≥ 4 = 113	mRS < 4 = 210 mRS ≥ 4 = 146	mRS < 4 = 243 mRS ≥ 4 = 113
	OR (95% CI)		
Mean sodium	1.17 (1.05, 1.29)	1.10 (1.01, 1.20)	1.16 (1.06, 1.28)
Standard deviation of sodium	1.53 (1.17, 1.99)	1.51 (1.19, 1.91)	1.47 (1.14, 1.88)
Male	1.41 (0.72, 2.79)	1.08 (0.60, 1.96)	1.58 (0.83, 3.02)
Age	1.06 (1.03, 1.09)	1.04 (1.01, 1.06)	1.06 (1.03, 1.09)
High WFNS	1.79 (0.88, 3.68)	1.50 (0.81, 2.79)	2.00 (1.02, 3.93)
APACHE III score	1.02 (1.00, 1.04)	1.02 (1.00, 1.04)	1.02 (1.01, 1.04)
Hours from admission to neurovascular intervention	1.01 (1.00, 1.02)	1.01 (1.00, 1.02)	1.01 (1.00, 1.03)
Surgical Clipping	1.78 (0.86, 3.66)	1.71 (0.91, 3.21)	1.71 (0.86, 3.39)
Treated with sodium tablets*	0.47 (0.16, 1.40)	0.33 (0.12, 0.90)	0.49 (0.17, 1.45)
Treated with fludrocortisone*	1.93 (0.55, 6.76)	2.65 (0.93, 7.51)	1.34 (0.43, 4.22)
Treated with Sodium Fluids*	0.93 (0.39, 2.24)	0.73 (0.33, 1.60)	1.08 (0.46, 2.51)

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Multivariable logistic models used for mRS>=4 vs <4.

Model sensitivity 1 imputes all missing mRS values to be less than 4.

Model sensitivity 2 imputes all missing mRS values to be 4 or more.

OR is Odds Ratio

CI is Confidence Intervals

Table S5: Sensitivity analysis for sodium summarization method

	Original analysis	Min and max sodium	Min and max sodium quadratics	Area outside clinical thresholds
AIC/BIC of model	272.03/319.70	263.10/310.76	263.77/318.76	292.39/336.31
OR (95% CI)				
Mean sodium	1.17 (1.05, 1.29)	-	-	-
Standard deviation of sodium	1.53 (1.17, 1.99)	-	-	-
Minimum sodium	-	1.25 (1.15, 1.35)	1.22 (1.11, 1.33)	-
Maximum sodium	-	0.96 (0.87, 1.05)	0.96 (0.87, 1.06)	-
Minimum sodium squared	-	-	1.01 (0.99, 1.02)	-
Maximum sodium squared	-	-	1.01 (1.00, 1.01)	-
Area outside thresholds	-	-	-	1.08 (0.79, 1.49)
Male	1.41 (0.72, 2.79)	1.49 (0.75, 2.97)	1.50 (0.74, 3.03)	1.63 (0.85, 3.11)
Age	1.06 (1.03, 1.09)	1.06 (1.03, 1.09)	1.06 (1.03, 1.09)	1.04 (1.01, 1.06)
High WFNS	1.79 (0.88, 3.68)	1.72 (0.83, 3.58)	1.87 (0.89, 3.95)	2.53 (1.28, 5.01)
APACHE III score	1.02 (1.00, 1.04)	1.03 (1.01, 1.04)	1.03 (1.01, 1.04)	1.03 (1.01, 1.05)
Hours from admission to neurovascular intervention	1.01 (1.00, 1.02)	1.01 (1.00, 1.03)	1.02 (1.00, 1.03)	1.01 (1.00, 1.02)
Surgical Clipping	1.78 (0.86, 3.66)	1.62 (0.78, 3.38)	1.75 (0.83, 3.67)	1.71 (0.85, 3.44)
Treated with sodium tablets*	0.47 (0.16, 1.40)	0.40 (0.13, 1.25)	0.39 (0.13, 1.21)	0.34 (0.12, 0.96)
Treated with fludrocortisone*	1.93 (0.55, 6.76)	2.07 (0.57, 7.45)	1.85 (0.49, 7.01)	1.63 (0.49, 5.46)
Treated with Sodium Fluids*	0.93 (0.39, 2.24)	0.84 (0.34, 2.05)	0.84 (0.34, 2.09)	1.27 (0.57, 2.82)

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Table S6: Sensitivity analysis for deaths within 48 hours

mRS values:	Original analysis	Sensitivity (deaths within 48 hours)
	mRS < 4 = 210 mRS ≥ 4 = 113	mRS < 4 = 210 mRS ≥ 4 = 84
OR (95% CI)		
Mean sodium	1.17 (1.05, 1.29)	1.10 (0.99, 1.23)
Standard deviation of sodium	1.53 (1.17, 1.99)	1.58 (1.19, 2.09)
Male	1.41 (0.72, 2.79)	1.47 (0.73, 2.93)
Age	1.06 (1.03, 1.09)	1.06 (1.03, 1.09)
High WFNS	1.79 (0.88, 3.68)	2.30 (1.08, 4.89)
APACHE III score	1.02 (1.00, 1.04)	1.02 (1.00, 1.04)
Hours from admission to neurovascular intervention	1.01 (1.00, 1.02)	1.02 (1.00, 1.03)
Surgical Clipping	1.78 (0.86, 3.66)	2.20 (1.07, 4.53)
Treated with sodium tablets*	0.47 (0.16, 1.40)	0.45 (0.16, 1.27)
Treated with fludrocortisone*	1.93 (0.55, 6.76)	1.45 (0.40, 5.28)
Treated with Sodium Fluids*	0.93 (0.39, 2.24)	0.85 (0.35, 2.05)

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Multivariable logistic models used for mRS ≥ 4 vs < 4.

Model sensitivity 1 imputes all missing mRS values to be less than 4.

Model sensitivity 2 imputes all missing mRS values to be 4 or more.

OR is Odds Ratio

CI is Confidence Intervals

Figure S2: Residual vs predicted values from the GAM model for the change in sodium concentrate over time for the two outcome groups. Left mRS < 4 and right mRS >=4.

