Influence of sodium bicarbonate on mortality in general intensive care patients with metabolic acidosis

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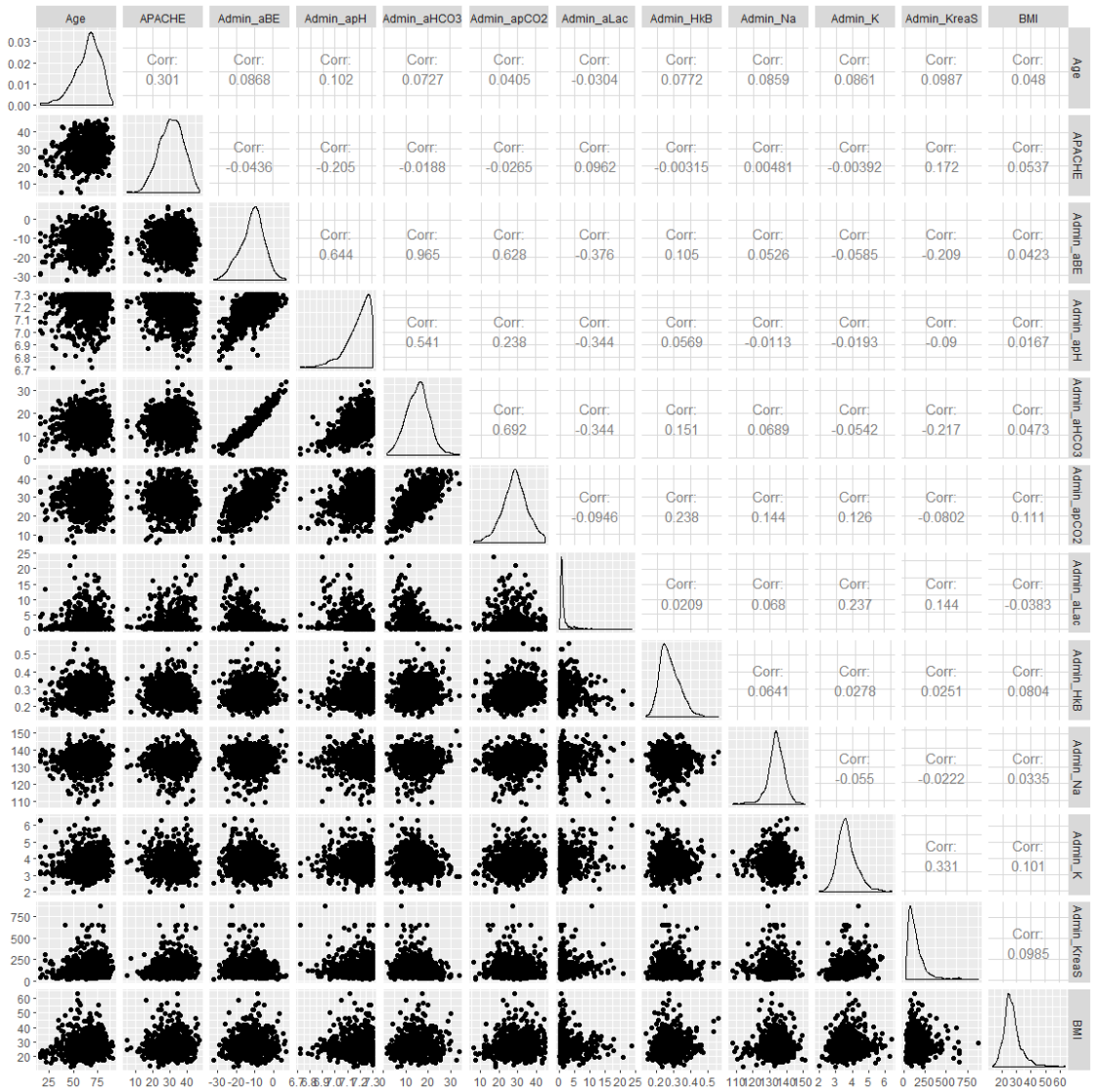
Online-Supplement



Suppl. Figure 1: Marginal distributions of continuous variables in the full sample.

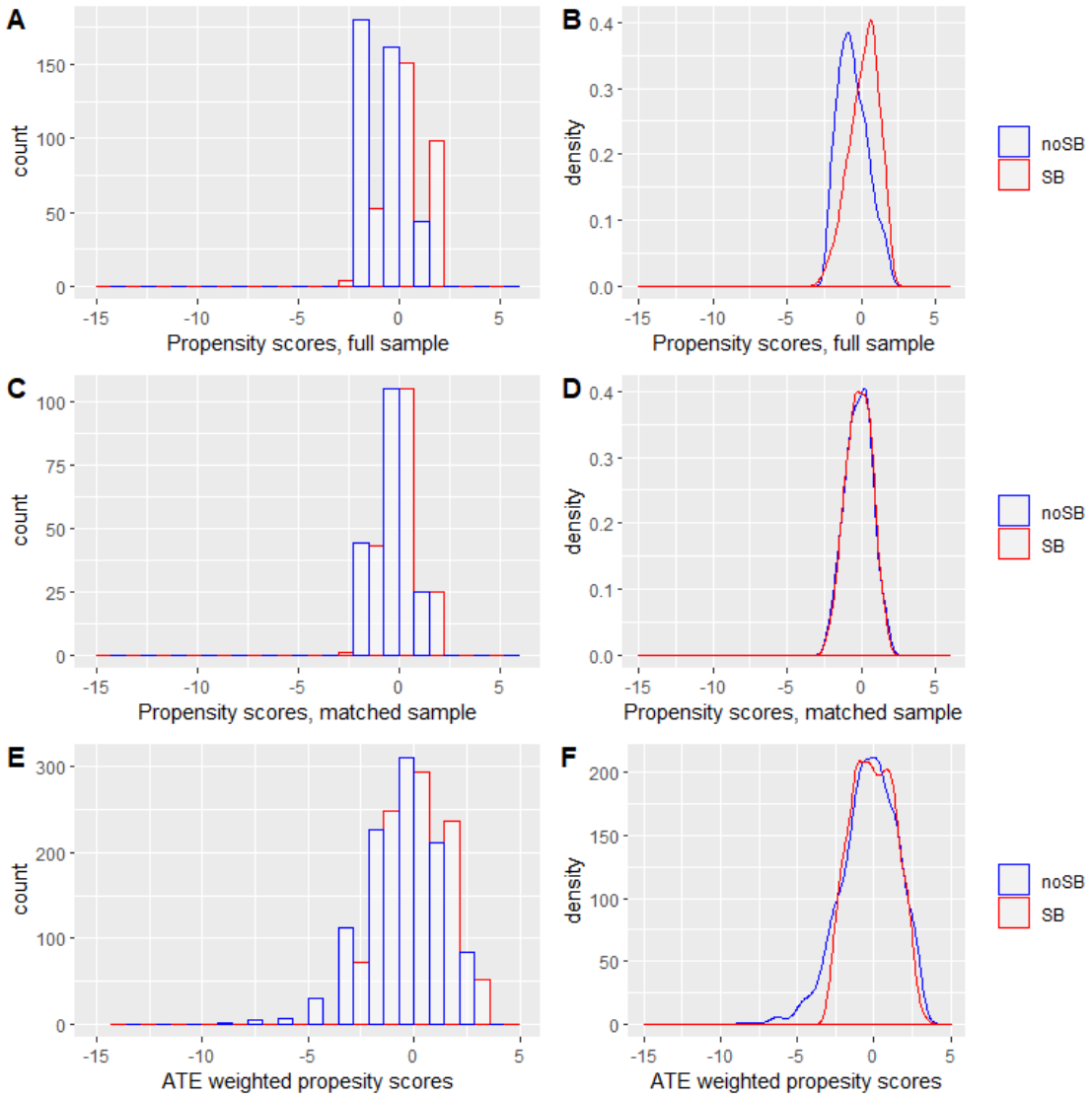
Correlations are in the upper triangle, univariate estimated densities on the diagonal and bivariate clouds in the lower triangle.

	ATE ("crude" sample), n=971	p-value	ATT("crude" sample), n=971	p-value
ICU mortality	1.54 (1.26, 1.88)	**<.001**	1.56 (1.17, 2.07)	**.002**
Hospital death	0.81 (0.60, 1.08)	.15	0.67 (0.43, 1.03)	.07
30d death	0.63 (0.45, 0.87)	**.005**	0.52 (0.32, 0.84)	**.007**
Death d31 to 365	1.43 (0.99, 2.05)	.06	1.31 (0.74, 2.31)	.36
Death at last follow-up*	0.83 (0.63, 1.09)	.18	0.72 (0.47, 1.09)	.12

Suppl. Table 1: Odds ratios (OR) for treatment effects for mortality in the "crude" dataset.

Reported are the odds ratios (OR) for the treatment effects for mortality at various stages in presence of sodium bicarbonate treatment for the "crude" dataset. Estimated by logit logistic regressions, regressing mortality outcome on SB treatment status, sex, age, BMI and APACHE. * Last follow up: September 2019.

ATE Average Treatment Effect, ATT Average Treatment effect in Treated



Supplement Figure 2: Distributions of the constructed propensity scores.

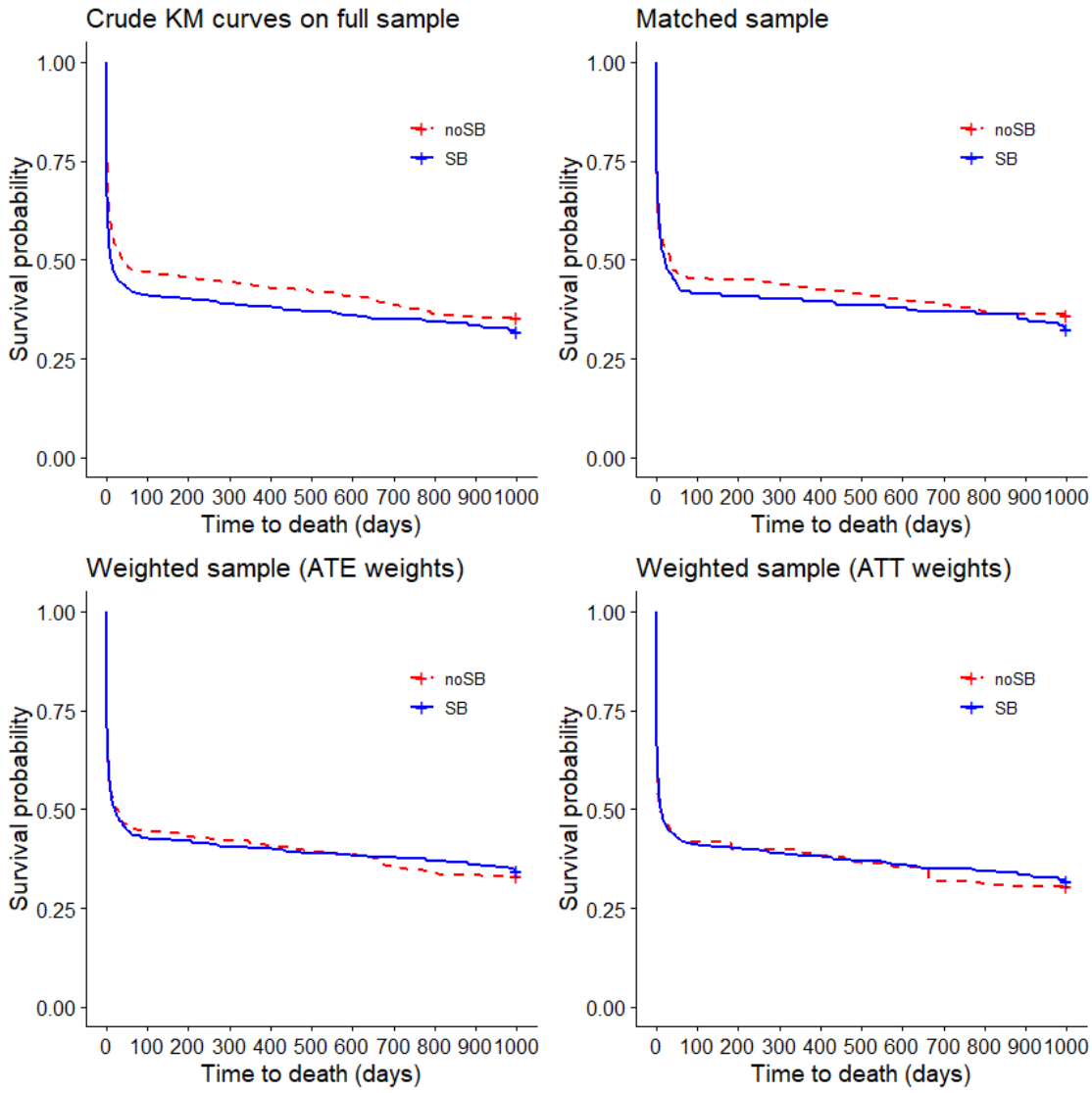
Distributions are given on the log scale. A and B - in the original sample; C and D - in the matched sample; E and F- with inverse weighting by ATE weights. ATE Average Treatment Effect.

Variable	n(no SB) =356	n(SB) =267	p
Gender	female: 109 (31%)	female: 104 (39%)	**.04**
BMI (kg/m2)	26.23 [23.65, 29.39]	25.95 [23.2, 29.38]	.51
Age (years)	67 [57.75, 74]	64 [53.5, 72]	.08
APACHE II	32 [27, 35]	30 [25, 36]	.11
DG Cardiovasc.	123 (35%)	96 (36%)	.78
DG Respiratory	96 (27%)	29 (11%)	**<.001**
DG Gastroint.	22 (6%)	32 (12%)	**.02**
DG Neurological	48 (13%)	7 (3%)	**<.001**
DG Trauma&TBI	6 (2%)	33 (12%)	**<.001**
DG Metabolic& Intox	10 (6%)	33 (12%)	.67
DG Haemat. disease	6 (2%)	5 (2%)	1
DG Renal	4 (1%)	6 (2%)	.43
DG Sepsis	25 (7%)	41 (15%)	**<.001**
apH	7.24 [7.19, 7.28]	7.12 [7.05, 7.18]	**<.001**
aHCO3 (mmol/l)	19.15 [17, 21.5]	10.6 [8.1, 12.5]	**<.001**
aLactate (mmol/l)	0.9 [0.7, 1.2]	1.4 [0.8, 4.55]	**<.001**
apCO2 (mmHg)	32.1 [28.08, 36.4]	24.8 [20, 28.5]	**<.001**
BE	-6.6 [-9.22, -3.68]	-17.4 [-21.3, -14.35]	**<.001**
Hc	0.28 [0.24, 0.33]	0.26 [0.23, 0.3]	**<.001**
Na (mmol/l)	134 [131, 137]	134 [131, 137]	.54
K (mmol/l)	3.6 [3.3, 3.9]	3.6 [3.27, 4.1]	.35
CreaS (mmol/l)	90.5 [59.75, 144]	116 [80.75, 174]	**<.001**
Adrenaline (y/n)	117 (33%)	162 (61%)	**<.001**
Adrenaline CD (µg)	1238.38 [183.3, 3818.12]	6658.19 [2575.14, 13312.91]	**<.001**
Noradrenaline (y/n)	231 (65%)	201 (75%)	**.01**
Noradrenaline CD (µg)	1838.96 [358.17, 7252.5]	4790.74 [1491.42, 17500.32]	**<.001**
Ventilation (y/n)	246 (69%)	157 (59%)	**.01**
Blood Products (y/n)	143 (40%)	167 (63%)	**<.001**
RRT (y/n)	44 (12%)	91 (34%)	**<.001**
ICU days	2.51 [1.07, 5.38]	2.26 [0.9, 5.73]	.34
Hospital days	8 [3, 16]	8 [2, 18]	.08
ICU Mortality	109 (31%)	130 (49%)	**<.001**
InHospital death	41 (12%)	22 (8%)	.23
30d death	34 (10%)	19 (7%)	.35
Death d31 to 365	28 (8%)	14 (5%)	.26
Death at last follow up*	48 (13%)	25 (9%)	.15
Time to death(days)	9.01 [1.28, 285.47]	2.03 [0.33, 22.07]	**<.001**

Suppl Table 2: Patient demographics, ICU treatment, and follow-up data of patients dropped during matching (n=623).

Median values [interquartile ranges] or counts (percentages) are given. ‘p’ refers to Kolmogorov-Smirnov test for continuous variables, or to chi-squared test for categorical variables (for the null hypothesis of equal categorical frequencies between two groups). Laboratory data are at admission to

ICU. DG Diagnosis Group is referring to the APACHE IV-classification of diagnosis ad admission with a separate sepsis group (all groups include operative and non-operative diagnoses). NoSB non sodium bicarbonate recipients, SB sodium-bicarbonate recipients, APACHE II Acute Physiology and Chronic Health Evaluation II Score, Cardiovasc. Cardiovascular, Gastroint. Gastrointestinal, Haemat. Haematological, Hc hematocrit, Na sodium, K potassium, CreaS serum creatinine, TBI traumatic brain injury, CD cumulative dose, RRT renal replacement therapy, ICU intensive care unit. * Last follow up was in September 2019.



Supplement Figure 3: Kaplan–Meier survival curves (until last follow-up) obtained using different propensity score methods.

In the top-left panel crude Kaplan–Meier survival curves for treated and untreated subjects in the "crude" original sample (n=971) are reported (log-rank test: p = 0.047). In the top right panel Kaplan–Meier survival curves for treated and untreated subjects in the propensity score matched sample (n=348) are described (stratified log-rank test p = 0.75). In the bottom-left and bottom-right panels survival curves in the sample weighted using the ATE weights (n=971) and the sample weighted using

the ATT weights (n=971) are reported (adjusted log-rank test with p-values 0.82 and 0.84). ATE Average Treatment Effect, ATT Average Treatment effect in Treated.