

Supplementary Information

Association of first-24-hour hypernatremia and hyperkalemia co-occurrence with 30-day mortality in critically ill adults: a retrospective cohort study

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Supplementary Methods

The 2018–2020 TW-CORE workbook contained 16,692 ICU episodes. Analysis worksheets were joined one-to-one by the registry record identifier after separating metadata rows. Source column comments provided the code dictionary. The stored APACHE II total reconciled exactly to its 14 components in every episode. Age 999.9 represented age above 89 years and was retained in the ≥ 90 category. No individual-level identifiers or predictions are included in the reproducibility files.

Model priority and revision transparency

M2 is the principal benchmark for incremental information beyond complete APACHE II. M3 is complementary and replaces total APACHE II with total minus its stored sodium/potassium component points. This clarifies interpretation; no dated prospective statistical plan establishing model priority is claimed. The revised M1 explicitly includes all listed chronic indicators and five-level diabetes coding. The original report did not provide sufficient detail to recover its exact chronic-condition coding, so M1 was recalculated rather than preserving an unverifiable specification. The main cohort and M0/M2/M3 regression estimates reproduced the submitted results. All additional reviewer-requested analyses are post hoc.

Cross-validation and uncertainty

Twenty five-fold patient-grouped cross-validations used seeds 20260905 through 20260924. All records for one patient remained in one fold; paired models used identical folds, and model fitting used training data only. M1–M3 AUCs use pooled held-out predictions within each repeat. M0 uses an admission-weighted average of within-fold AUCs so that differing training prevalences across folds do not create an artificial intercept-only ranking; its baseline AUC is exactly 0.5. Brier scores are averaged across held-out admissions. Means and 2.5th–97.5th percentiles across repeats describe split variability, not population confidence intervals. An additional deterministic GroupKFold allocation is reported separately with 1,000 paired patient-cluster bootstrap resamples of fixed held-out predictions. These bootstrap intervals are conditional on the fitted predictions and omit model-refitting uncertainty; they must not be attached to the repeated-CV mean as if they shared one estimand.

Observation weighting

A logistic model for known binary 30-day status was fitted in 15,012 complete-covariate admissions, including 1,701 with unknown status. Predictors were phenotype, categorical age, sex, ICU type/source, pre-ICU cardiac arrest, baseline DNR, total APACHE II and ICU year. The stabilized observed-outcome weight was $\text{Pr}(\text{observed})/\text{Pr}(\text{observed} \mid \text{predictors})$. In 500 patient bootstrap resamples (seed 20260905), both the observation and outcome models were refitted; all 500 completed. Bootstrap percentile intervals therefore account for weight estimation. Correct specification, positivity and conditional outcome-observation assumptions remain necessary. No weighting of unavailable electrolyte records was attempted.

Penalization and influence

Firth logistic regression maximized the Bernoulli log likelihood plus one-half $\log|X^T W X|$ in the deterministic one-record-per-patient sample. Profile intervals constrained each contrast while retaining the full design-matrix penalty. Full and constrained fits passed adjusted-score and profile-deviance checks. No cluster correction was claimed for Firth; there was only one record per patient. Influence analysis removed all eligible admissions of each complete-case co-occurrence patient and refitted the ordinary clustered model. The analysis script retains numerical checks and no patient identifiers.

Table S1. Traditional adjustment and repeat-admission sensitivities

Analysis	N	Na only OR (95% CI)	K only OR (95% CI)	Both OR (95% CI)	Global P
Omit baseline DNR (M2)	13,383	1.05 (0.85–1.29)	0.85 (0.64–1.13)	1.86 (1.05–3.31)	0.109
Omit baseline DNR (M3)	13,383	1.22 (0.99–1.50)	1.14 (0.86–1.51)	2.65 (1.50–4.67)	0.002
One record per patient (M2)	11,877	0.99 (0.78–1.25)	0.86 (0.64–1.17)	1.66 (0.94–2.93)	0.240
One record per patient (M3)	11,877	1.16 (0.92–1.46)	1.17 (0.87–1.58)	2.37 (1.35–4.15)	0.013
M1: age ≥90 assigned 90 (M1)	13,311	3.15 (2.63–3.78)	3.02 (2.32–3.93)	15.69 (8.82–27.92)	<0.001
M1 + non-electrolyte components (M1)	13,311	1.28 (1.02–1.60)	1.15 (0.85–1.55)	2.26 (1.22–4.20)	0.013
Add ICU year and campus (M3)	13,311	1.21 (0.98–1.50)	1.15 (0.87–1.52)	2.71 (1.52–4.83)	0.002

Neither abnormality is the reference. Ordinary models use patient-clustered sandwich intervals and a 3-df global Wald test. The one-record sample is selected before complete-case exclusions by earliest recorded ICU year, then lowest numeric registry identifier. This cannot identify the true earliest admission within a year or hospitalization. The revised M1 chronic-condition specification is detailed in Table S10. Component and year/campus analyses use their explicit revised specification. The prior age-top-code deletion error audit is not presented as an inferential sensitivity analysis.

Table S2. Exploratory multiplicative interaction

Contrast	OR (95% CI)	P
Hypernatremia when hyperkalemia absent	1.22 (0.99–1.51)	0.065
Hyperkalemia when hypernatremia absent	1.15 (0.87–1.52)	0.340
Multiplicative sodium-by-potassium interaction	1.93 (1.01–3.70)	0.048
Joint both-versus-neither contrast	2.70 (1.53–4.75)	<0.001

Same covariates and sample as M3. The interaction contrast is $\beta_{\text{both}} - \beta_{\text{Na-only}} - \beta_{\text{K-only}}$, with the patient-clustered covariance propagated through the contrast. Results are exploratory, uncorrected for multiple testing, and do not establish biological synergy or clinical predictive value.

Table S3A. Outcome availability: demographics and presentation

Characteristic	Known 30-day status	Unknown 30-day status
Admissions	13,383	1,707
Distinct patients within status group	11,942	1,354
Total APACHE II	14.0 [10.0, 22.0]	17.0 [12.0, 23.0]
APACHE II excluding Na/K points	14.0 [9.0, 21.0]	17.0 [12.0, 22.0]
Peak sodium, mmol/L	138.7 [136.0, 141.0]	137.9 [135.0, 140.6]
Peak potassium, mmol/L	3.9 [3.5, 4.3]	4.0 [3.6, 4.5]
ICU length of stay, days	4.0 [3.0, 7.0]	5.0 [3.0, 8.0]
Hospital length of stay, days	14.0 [8.0, 26.0]	23.0 [13.0, 43.0]
Age 20–39	1,010/13,383 (7.5%)	32/1,707 (1.9%)
Age 40–59	3,656/13,383 (27.3%)	346/1,707 (20.3%)
Age 60–74	4,681/13,383 (35.0%)	622/1,707 (36.4%)
Age 75–89	3,506/13,383 (26.2%)	603/1,707 (35.3%)
Age ≥90 (top-coded)	530/13,383 (4.0%)	104/1,707 (6.1%)
Female	5,127/13,383 (38.3%)	691/1,707 (40.5%)
Medical ICU	6,666/13,383 (49.8%)	897/1,707 (52.5%)
Surgical ICU	5,415/13,383 (40.5%)	681/1,707 (39.9%)
Mixed ICU	1,302/13,383 (9.7%)	129/1,707 (7.6%)
Operating/recovery room	3,014/13,383 (22.5%)	492/1,707 (28.8%)
Emergency department	9,626/13,383 (71.9%)	1,099/1,707 (64.4%)
Ward	743/13,383 (5.6%)	116/1,707 (6.8%)
Pre-ICU cardiac arrest	259/13,383 (1.9%)	20/1,707 (1.2%)
Baseline DNR	1,240/13,311 (9.3%)	244/1,701 (14.3%)
Post-admission DNR	2,930/13,311 (22.0%)	1,189/1,701 (69.9%)
Recorded in-hospital death (code 2)	2,108/13,383 (15.8%)	39/1,707 (2.3%)
Neither abnormality	12,097/13,383 (90.4%)	1,531/1,707 (89.7%)
Hypernatremia only	841/13,383 (6.3%)	109/1,707 (6.4%)
Hyperkalemia only	367/13,383 (2.7%)	64/1,707 (3.7%)
Both abnormalities	78/13,383 (0.6%)	3/1,707 (0.2%)

Continuous values are median [25th, 75th percentile]. Denominators reflect available records. Status-group patient counts can overlap because one patient may contribute admissions to both groups. Observed differences do not identify the missingness mechanism: MCAR is implausible, while conditional MAR is untestable. Recorded in-hospital non-death is not evidence of 30-day survival.

Table S3B. Outcome availability: recorded chronic conditions

Recorded variable	Known 30-day status	Unknown 30-day status
Respiratory chronic-health flag	1,410/13,383 (10.5%)	295/1,707 (17.3%)
Cardiovascular chronic-health flag	4,555/13,383 (34.0%)	877/1,707 (51.4%)
Liver chronic-health flag	1,667/13,383 (12.5%)	345/1,707 (20.2%)
Renal chronic-health flag	744/13,383 (5.6%)	221/1,707 (12.9%)
Immune-disease flag	2,286/13,383 (17.1%)	573/1,707 (33.6%)
Immunosuppressive-therapy flag	3,374/13,383 (25.2%)	738/1,707 (43.2%)
AIDS	20/13,383 (0.1%)	1/1,707 (0.1%)
Hepatic failure	166/13,383 (1.2%)	46/1,707 (2.7%)
Lymphoma	68/13,383 (0.5%)	15/1,707 (0.9%)
Metastatic cancer	788/13,383 (5.9%)	213/1,707 (12.5%)
Leukaemia/myeloma	53/13,383 (0.4%)	9/1,707 (0.5%)
Hypertension	4,899/13,383 (36.6%)	935/1,707 (54.8%)
Coronary artery disease	1,372/13,383 (10.3%)	274/1,707 (16.1%)
COPD	736/13,383 (5.5%)	166/1,707 (9.7%)
Dementia	575/13,383 (4.3%)	112/1,707 (6.6%)
Diabetes code 1: type 1	33/13,383 (0.2%)	3/1,707 (0.2%)
Diabetes code 2: type 2	3,364/13,383 (25.1%)	681/1,707 (39.9%)
Diabetes code 3: gestational	5/13,383 (0.0%)	0/1,707 (0.0%)
Diabetes code 4: other/prediabetes	80/13,383 (0.6%)	4/1,707 (0.2%)
Diabetes code 5: never diagnosed	9,901/13,383 (74.0%)	1,019/1,707 (59.7%)

Chronic-health flags and comorbidity indicators retain their source definitions; overlapping conditions are not mutually exclusive. These comparisons are descriptive, not significance tests or evidence that conditional MAR holds.

Table S4A. Repeated grouped-CV AUC

M	N	Covariates only	Covariates + phenotype	Paired change
M0	13383	0.50000 [0.50000, 0.50000]	0.58335 [0.58282, 0.58375]	0.08335 [0.08282, 0.08375]
M1	13311	0.74138 [0.73959, 0.74294]	0.76932 [0.76764, 0.77048]	0.02794 [0.02736, 0.02855]
M2	13311	0.87035 [0.86989, 0.87069]	0.87041 [0.86996, 0.87083]	0.00007 [-0.00012, 0.00020]
M3	13311	0.86933 [0.86890, 0.86964]	0.86970 [0.86926, 0.87011]	0.00037 [0.00017, 0.00050]

Each cell gives the mean and [2.5th, 97.5th percentile] across 20 randomized patient-grouped five-fold splits. These are split-variability ranges, not population confidence intervals. Positive Δ AUC and negative Δ Brier favor the phenotype model. Model definitions are in S10. M0 uses admission-weighted within-fold AUC; M1–M3 use pooled out-of-fold AUC per repeat. Brier scores use all held-out admissions. The original single-split estimates are replaced by these documented repeated runs.

Table S4B. Repeated grouped-CV Brier score

M	N	Covariates only	Covariates + phenotype	Paired change
M0	13383	0.124020 [0.124000, 0.124056]	0.118363 [0.118292, 0.118437]	-0.005658 [-0.005728, -0.005587]
M1	13311	0.110299 [0.110125, 0.110570]	0.106679 [0.106477, 0.106923]	-0.003620 [-0.003717, -0.003514]
M2	13311	0.086386 [0.086302, 0.086486]	0.086392 [0.086272, 0.086518]	0.000006 [-0.000038, 0.000059]
M3	13311	0.086271 [0.086183, 0.086373]	0.086163 [0.086034, 0.086297]	-0.000108 [-0.000156, -0.000050]

Each cell gives the mean and [2.5th, 97.5th percentile] across 20 randomized patient-grouped five-fold splits. These are split-variability ranges, not population confidence intervals. Positive Δ AUC and negative Δ Brier favor the phenotype model. Model definitions are in S10. M0 uses admission-weighted within-fold AUC; M1–M3 use pooled out-of-fold AUC per repeat. Brier scores use all held-out admissions. The original single-split estimates are replaced by these documented repeated runs.

Table S4C. Conditional uncertainty from a fixed grouped split

M	Metric	Covariates only	Covariates + phenotype	Paired change [95% interval]
M0	AUC	0.50000	0.58339	0.08339 [0.07326, 0.09297]
M0	Brier	0.124002	0.118353	-0.005650 [-0.006832, -0.004292]
M1	AUC	0.74126	0.76911	0.02785 [0.02186, 0.03407]
M1	Brier	0.110255	0.106601	-0.003654 [-0.004789, -0.002505]
M2	AUC	0.87038	0.87032	-0.00006 [-0.00037, 0.00027]
M2	Brier	0.086343	0.086423	0.000080 [-0.000092, 0.000247]
M3	AUC	0.86939	0.86963	0.00024 [-0.00023, 0.00076]
M3	Brier	0.086239	0.086192	-0.000048 [-0.000293, 0.000196]

A separate deterministic five-fold GroupKFold run, without shuffling, supplies these point estimates. Intervals use 1,000 paired patient-level resamples of its fixed held-out predictions, with all records for sampled patients retained. They are conditional on those predictions and do not account for refitting the training models. Both paired intervals cross zero for M2 and M3. M0 uses weighted within-fold AUC as described above.

Table S5. Data completeness and exclusion audit

Requirement or variable	Available / denominator	Missing
Binary 30-day status after age eligibility	13,826/16,691 (82.8%)	2,865
Complete extrema after binary 30-day status	13,383/13,826 (96.8%)	443
Baseline DNR in primary cohort	13,311/13,383 (99.5%)	72
BMI in primary cohort	10,084/13,383 (75.3%)	3,299
ICU outcome in primary cohort	13,291/13,383 (99.3%)	92
Hospital outcome in primary cohort	13,383/13,383 (100%)	0
Hospital length of stay	13,382/13,383 (>99.9%)	1

Mutually exclusive missing-extrema patterns among 443 exclusions

Missing variables	Records
Sodium maximum + minimum and potassium maximum + minimum	385
Sodium maximum + minimum only	53
Potassium maximum + minimum only	5
Usable sodium/potassium maxima but one/both minima missing	0

Sodium maxima and minima were each missing in 438 excluded records; potassium maxima and minima were each missing in 390. Counts overlap across electrolytes. Requiring maxima alone restores zero additional admissions: N=13,383 and M2/M3 estimates are identical. Minima were not required scientifically for exposure classification. The original complete-extrema restriction is retained only for cohort comparability.

Table S6A. Inverse-probability-of-observation analysis

M	Contrast vs neither	Observed N	Weighted OR (95% bootstrap CI)
M2	Hypernatremia only	13,311	1.04 (0.84–1.28)
M2	Hyperkalemia only	13,311	0.87 (0.63–1.16)
M2	Both abnormalities	13,311	1.91 (1.07–3.32)
M3	Hypernatremia only	13,311	1.21 (0.97–1.49)
M3	Hyperkalemia only	13,311	1.17 (0.84–1.55)
M3	Both abnormalities	13,311	2.70 (1.56–4.76)

Eligible complete-extrema cohort: 15,090. Observation-model complete cases: 15,012, comprising 13,311 observed and 1,701 unknown outcomes; 78 baseline-DNR values were missing. Stabilizer: 0.886691. Fitted observation probabilities: 0.608–0.996. Stabilized observed weights: 0.891–1.458; 99th percentile 1.178. Effective sample size: 13,265.5. No truncation. Intervals are percentile intervals from 500 patient-level bootstrap samples refitting both models; zero failures. No bootstrap global P value is claimed.

Interpretation

Weighted estimates closely resemble unweighted estimates under the specified measured-variable observation model. This does not establish absence of selection bias. Conditional MAR, correct functional form and adequate positivity remain assumptions; unmeasured determinants of outcome availability and missing electrolyte data are not resolved.

Table S6B. Recorded in-hospital mortality sensitivity

Cohort/model	N	Na only OR (95% CI)	K only OR (95% CI)	Both OR (95% CI)	Global P
Known 30-day cohort (M2)	13,311	1.11 (0.90–1.37)	0.83 (0.62–1.13)	1.62 (0.89–2.93)	0.175
Known 30-day cohort (M3)	13,311	1.29 (1.04–1.58)	1.11 (0.83–1.49)	2.28 (1.28–4.06)	0.005
Irrespective of 30-day status (M2)	15,012	1.14 (0.94–1.39)	0.83 (0.63–1.09)	1.83 (1.03–3.26)	0.042
Irrespective of 30-day status (M3)	15,012	1.32 (1.09–1.60)	1.09 (0.83–1.43)	2.55 (1.46–4.46)	<0.001
Expanded; exclude terminal discharge (M2)	14,826	1.20 (0.99–1.46)	0.80 (0.60–1.06)	2.18 (1.23–3.89)	0.005
Expanded; exclude terminal discharge (M3)	14,826	1.39 (1.15–1.69)	1.07 (0.81–1.42)	3.07 (1.75–5.37)	<0.001

The expanded eligible cohort has 15,090 admissions with complete extrema and recorded hospital outcome, including 1,707 without interpretable 30-day status. Complete covariates yield 15,012 admissions and 2,124 recorded hospital deaths; excluding terminal-discharge code 11 yields 14,826 admissions and the same 2,124 deaths. The known-30-day complete-case cohort has 13,311 admissions and 2,085 recorded hospital deaths. Hospital outcome code 2 is recorded death; other documented codes are non-death events in this registry endpoint, not verified later survival. Code 11 is terminal discharge and was therefore excluded in a separate sensitivity. These outcomes do not have the same follow-up horizon as 30-day mortality.

Table S6C. Extreme-assumption crude mortality bounds

Phenotype	Unknown status	All eligible N	Crude mortality logical range
Neither abnormality	1531	13628	10.9%–22.1%
Hypernatremia only	109	950	29.8%–41.3%
Hyperkalemia only	64	431	27.8%–42.7%
Both abnormalities	3	81	71.6%–75.3%

Within each phenotype, all unknown outcomes are assigned first to survival and then to death. These are assumption-extreme arithmetic ranges, not estimated probabilities or confidence intervals. Joint extremes give a crude both-versus-neither OR range of 8.89–25.03. They do not bound the adjusted OR, address missing electrolyte data, or validate mortality ascertainment after discharge. They demonstrate why the crude risk contrast and the adjusted prognostic interpretation require separate discussion.

Table S7A. Firth penalized logistic regression

M	Contrast vs neither	Firth OR (95% profile CI)	P
M2	Hypernatremia only	0.99 (0.80–1.22)	0.922
M2	Hyperkalemia only	0.86 (0.63–1.18)	0.367
M2	Both abnormalities	1.64 (0.90–3.09)	0.108
M3	Hypernatremia only	1.16 (0.94–1.44)	0.162
M3	Hyperkalemia only	1.17 (0.85–1.60)	0.324
M3	Both abnormalities	2.34 (1.29–4.36)	0.005

One deterministically selected record per patient before complete-case exclusion; 11,877 patients, 1,712 deaths, 73 co-occurrence records (54 deaths). M2 and M3 use the same one-record sample. Intervals use profile penalized likelihood and P values use penalized likelihood-ratio tests. Same-sample ordinary co-occurrence ORs are 1.66 (0.94–2.93) for M2 and 2.37 (1.35–4.15) for M3. M2 therefore does not show a precise residual contrast in this reduced sample. Final adjusted scores are below 1.4×10^{-12} and profile-deviance endpoint residuals below 3.1×10^{-8} .

Table S7B. Delete-one-co-occurrence-patient influence analysis

M	Patients deleted in turn	Full-sample OR	OR range after deletion	Largest relative change
M2	77	1.90	1.76–2.08	9.2%
M3	77	2.70	2.50–2.94	9.0%

Each deletion removes all eligible admissions of the selected patient, not only their co-occurrence record. The complete-case primary sample contains 77 co-occurrence patients; refit N ranges from 13,308 to 13,310. Finite estimates were obtained in every fit. This diagnostic evaluates single-patient influence within the observed data; it does not eliminate sparse-data bias or assess population transportability.

Table S8. Alternative sodium and potassium thresholds

Na, mmol/L	K, mmol/L	Co-occurrence deaths/N	M2 both OR (95% CI)	M3 both OR (95% CI)
>145	>5.5	58/78 (74.4%)	1.90 (1.07–3.39)	2.70 (1.53–4.75)
>145	>5	82/129 (63.6%)	1.47 (0.95–2.28)	1.84 (1.19–2.84)
>150	>5.5	25/34 (73.5%)	1.60 (0.66–3.85)	2.63 (1.09–6.31)
>145	>6	39/45 (86.7%)	2.28 (0.85–6.16)	3.77 (1.39–10.24)
>150	>6	18/19 (94.7%)	4.23 (0.38–46.78)	8.72 (0.79–96.30)

All inequalities are strict. Phenotype counts refer to the full N=13,383 primary cohort; M2/M3 use N=13,311 complete cases. Reference is neither abnormality under that row's thresholds. These post hoc choices examine clinically plausible definitions rather than selecting a favorable result. The >150/>6.0 group has only 19 admissions and one survivor, yielding a very wide M3 interval; threshold robustness is not uniformly precise or statistically significant. Full three-contrast estimates and global tests are supplied in the aggregate reproducibility files.

Table S9. Timing and ascertainment: what the source supports

Data element	Availability	Analytical consequence
Individual specimen timestamps	Unavailable	Cannot determine simultaneity, ordering relative to treatment/death, or exact exposure onset.
Sodium/potassium measurement counts	Unavailable	Cannot compare or adjust testing intensity.
Exact ICU admission and death timestamps	Unavailable	Cannot enumerate deaths before hour 24 or implement a valid 24-hour landmark.
Recorded ICU length of stay	Integer days; rounding convention not documented	Cannot substitute for exact hours or establish survival at a 24-hour landmark.
Hospital encounter identifier	Unavailable	Cannot distinguish same-hospitalization ICU readmission from separate hospitalizations.
ICU admission diagnosis	No validated diagnosis field in analysis extract	Cannot provide diagnosis-based case-mix adjustment.
Treatment and laboratory sequence	Not time resolved	Cannot separate treatment-induced electrolyte changes from pretreatment or evolving disease.
DNR timing category	Before/after ICU admission codes available	Only pre-ICU codes used as baseline; missing status not assumed absent.

No early-death exclusion was imposed by the documented primary eligibility criteria. Stored first-24-hour extrema were used, but the extract cannot independently verify that every measurement up to early death was incorporated. Lack of serial timing does not mean that all physiological measurements (for example stored APACHE acid–base components) were absent. No duration proxy is presented as a valid landmark analysis.

Table S10A. Exact model and variable coding

Variable/model	Specification
Unit of analysis	ICU admission; repeated admissions linked through a patient cluster identifier.
Phenotypes	NAHI>145 and KHI>5.5 mmol/L; neither, Na only, K only, both. NALO/KLO required by original complete-extrema cohort; no added records with peak-only restriction.
30-day outcome	SURVIVAL_RATE_30_DAY: 0=death, 1=alive; all other/missing values excluded from primary endpoint.
Sex	SEX=F indicator; male reference.
Age	20–39 reference, 40–59, 60–74, 75–89, ≥90; AGE=999.9 included in ≥90.
ICU type	ICU_TYPE: 1 medical (reference), 2 surgical, 3 mixed.
Admission source	ICU_SRCE: 1 operating/recovery room (reference), 2 emergency department, 3 ward.
Cardiac arrest	CARDARREST indicator for pre-ICU arrest.
Baseline DNR	DNR_STATUS 1/2=before ICU admission; 0/3=no baseline order; missing remains missing. Code 3 is post-admission.
Complete APACHE II	APACH_II_score, continuous.
APACHE II remainder	APACH_II_score – A2_NA_SCORE_9 – A2_K_SCORE_10, continuous; not a validated score.
M0	Three phenotype indicators + intercept.
M1	Phenotype + age category + sex + ICU type + source + arrest + baseline DNR + chronic indicators and diabetes category (S10B).
M2 benchmark	Phenotype + sex + ICU type + source + arrest + baseline DNR + total APACHE II.
M3 complementary	M2 specification replacing total APACHE II with remainder.
Year/campus sensitivity	ICU year entered categorically; CAREUNIT codes 1–5=Taipei, 6–9=Tamsui (source comment dictionary).

Table S10B. Chronic-condition specification and software

M1 chronic variables	Coding
RESPIRATORY, CARDIOVASCULAR, LIVER, RENAL, IMMUNE_DISEASE, IMMUNE_THERAPY, AIDS, HEPATIC_FAILURE, LYMPHOMA, METASTATIC_CANCER, LEUKAEMIA_MYELOMA, HYPERTENSION, CAD, COPD, DEMENTIA	Each source indicator entered separately as recorded binary 0/1. Aggregate CHRON/COMORB strings are not added as duplicate predictors.
DIABETES	Five nominal categories: 1 type 1 (reference); 2 type 2; 3 gestational; 4 other/prediabetes; 5 never diagnosed.
Non-electrolyte acute-physiology sensitivity	Revised M1 plus ten stored APACHE II acute-physiology components other than sodium/potassium; age/chronic health remain explicit baseline covariates rather than duplicated total-score terms.

Software and reproducibility

Python 3.12.13; NumPy 2.3.5; pandas 2.2.3; SciPy 1.17.0; scikit-learn 1.8.0. Ordinary logistic models used unpenalized likelihood and a patient-clustered sandwich covariance with finite-sample correction. Firth fitting, score checks and profile intervals are implemented in the accompanying script. Cross-validation seeds: 20260905–20260924. Conditional prediction-bootstrap seeds: M0 20270905, M1 20270906, M2 20270907, M3 20270908. Observation-weight bootstrap seed: 20260905. The original split seed was not documented; revised runs use the explicit seeds above.

Source workbook SHA-256: f49bf4afa2171b64175c183661a977b6c96c2ae17f33651bcaa4d9c97053065d

The reproducibility archive contains the code, code dictionary, aggregate model estimates, performance metrics, sensitivity results, source hash and numerical QA. It excludes the source patient-level workbook, patient identifiers and individual predictions. Access to source data remains governed by the institution and the manuscript Data availability statement.

Methods references

Seaman, S. R. & White, I. R. Review of inverse probability weighting for dealing with missing data. *Stat. Methods Med. Res.* 22, 278–295 (2013). <https://doi.org/10.1177/0962280210395740>

Firth, D. Bias reduction of maximum likelihood estimates. *Biometrika* 80, 27–38 (1993). <https://doi.org/10.1093/biomet/80.1.27>