

Supplementary Data

SUPPLEMENTARY TABLE S1. COBRIT BASELINE PATIENT FEATURES INCLUDED IN UNSUPERVISED LEARNING ANALYSIS

<i>Feature category</i>	<i>Feature name</i>	<i>Raw data format</i>	<i>Cleaned data format (dummy coded where more than 2 values)</i>	<i>Number of missing values (type of missingness)</i>	<i>Imputed values (if any)</i>	<i>Included or excluded in data set</i>
Demographics	Age	Numerical	Numerical	0	None	Included
	Gender	Female; male	Female; male	0	None	Included
	Hand preference	Both hands; left hand; right hand	Right-handed; left-handed	73 (MCAR)	MI	Included
	Marital partner status	Divorced or separated; married (common or civil law); single	Single; married; divorced/widowed	1 (MCAR)	MI	Included
	Pre-injury living situation	Homeless/lives in shelter; lives alone; lives in a group home/assisted living; lives with friend(s) or roommate(s) or co-habiting; lives with spouse and/or other family member(s); other	Alone; with family; co-habiting	2 (MCAR)	MI	Included
	Pre-injury employment	Employed full-time; employed part-time; full-time student (and unemployed); homemaker; part-time student (and unemployed); retired; unemployed/disabled	Employed; unemployed	13 (MCAR)	MI	Included
	U.S. education level	College graduate; graduate school completed; high school graduate/GED; none; some college; some elementary school; some graduate school; some high school; technical	High school or less; some college or trade school; college graduate or higher	19 (MCAR)	MI	Included
	Race	American Indian or Alaskan Native; Asian; black or African American; more than one race; Native Hawaiian or other Pacific Islander; white	White; black; another race	5 (MCAR)	MI	Included
	Ethnicity	Hispanic; non-Hispanic	Hispanic; non-Hispanic	0	MI	Included
	Annual income pre-injury	\$10,000–\$29,999 per year; \$30,000–\$49,999 per year; \$50,000–\$99,999 per year; < \$10,000 per year; > \$100,000 per year; none	None	593 (MNAR)	MI	Excluded

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SUPPLEMENTARY TABLE S1. (CONTINUED)

<i>Feature category</i>	<i>Feature name</i>	<i>Raw data format</i>	<i>Cleaned data format (dummy coded where more than 2 values)</i>	<i>Number of missing values (type of missingness)</i>	<i>Imputed values (if any)</i>	<i>Included or excluded in data set</i>	
Medical history (3 months prior to injury)	Cardiovascular disease	Yes; No	Yes; No	9 (MCAR)	MI	Included	
	Chronic headache/migraine	Yes; No	Yes; No	10 (MCAR)	MI	Included	
	Diabetes	Yes; No	Yes; No	8 (MCAR)	MI	Included	
	HIV infection	Yes; No	Yes; No	10 (MCAR)	MI	Included	
	Hard of hearing	Yes; No	Yes; No	9 (MCAR)	MI	Included	
	Hepatitis	Yes; No	Yes; No	11 (MCAR)	MI	Included	
	Learning disability (ADHD/dyslexia)	Yes; No	Yes; No	9 (MCAR)	MI	Included	
	Non-CNS malignancy	Yes; No	Yes; No	10 (MCAR)	MI	Included	
	Previous TBI	Yes; No	Yes; No	9 (MCAR)	MI	Included	
	Renal failure	Yes; No	Yes; No	9 (MCAR)	MI	Included	
	Respiratory disease	Yes; No	Yes; No	7 (MCAR)	MI	Included	
	Seizures	Yes; No	Yes; No	9 (MCAR)	MI	Included	
	Treated hypertension	Yes; No	Yes; No	8 (MCAR)	MI	Included	
	Treated psychiatric problem	Yes; No	Yes; No	9 (MCAR)	MI	Included	
	Another condition	Yes; No	Yes; No	11 (MCAR)	MI	Included	
	Medication use 3 months prior to injury	Yes; No	Yes; No	98 (MNAR)	None	Excluded	
	Injury information	Mechanism of injury	Assault; fall from a moving object (bike/skateboard/horse); fall from stationary object (roof/ladder); individual struck by any type of vehicle; motor vehicle (driver/passenger); motorcycle/ATV/golf cart (driver/passenger); sports (football/gymnastics); struck on head by object, not assault (tree); assault	Motor vehicle; fall; other	0	None	Included
		Time of injury (24h clock)	00:00–02:59; 03:00–05:59; 06:00–08:59; 09:00–11:59; 12:00–14:59; 15:00–17:59; 18:00–20:59; 21:00–23:59	Early morning: 0:00–5:59; Morning: 6:00–11:59; afternoon: 12:00–17:59; evening: 18:00–11:59	0	None	Included

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SUPPLEMENTARY TABLE S1. (CONTINUED)

<i>Feature category</i>	<i>Feature name</i>	<i>Raw data format</i>	<i>Cleaned data format (dummy coded where more than 2 values)</i>	<i>Number of missing values (type of missingness)</i>	<i>Imputed values (if any)</i>	<i>Included or excluded in data set</i>	
Computed tomography (CT)	Epidural lesion anatomic site	Left supratentorial; no epidural areas involved; posterior fossa; right supratentorial	Dummy coded each anatomic site	0	None	Included	
	Epidural lesion volume category	No involvement; ≤ 25 cc; > 25cc; evacuated	No involvement; ≤ 25 cc; > 25cc; evacuated	328 (MAR)	MI	Included	
	Intraparenchymal lesion anatomic site	Brainstem/diencephalon/CC; cerebellar; left frontal; left occipital; left parietal; left temporal; no intraparenchymal areas involved; right frontal; right occipital; right parietal; right temporal	Dummy coded each anatomic site	0	None	Included	
	Intraparenchymal lesion volume category	No involvement; ≤ 25 cc; > 25cc	No involvement; ≤ 25 cc; > 25cc	328 (MAR)	MI	Included	
	Lesions of high or mixed density indicator	Absent; present	Absent; present	0	None	Included	
	Mesencephalic cisterns type	Abnormal - blood in cisterns but no compression; abnormal - effaced/compressed but visible (regardless if there is blood); abnormal - obliterated/absent (regardless if there is blood); normal	Abnormal; normal	0	None	Included	
	Midline shift measurement category	None; 0–5 mm; 6–10 mm; > 10 mm	None; 0–5 mm; 6–10 mm; > 10 mm	4 (MAR)	MI	Included	
	Subarachnoid hemorrhage type	Absent; present cisterns only; present convexities/sulci and cisterns; present convexities/sulci only	Absent; present	0	None	Included	
	Subdural lesion anatomic site	Falcine; interhemispheric; left supratentorial; no subdural areas involved; posterior fossa; right supratentorial; tentorial	Dummy coded each anatomic site	0	None	Included	
	Subdural lesion volume category	No involvement; ≤ 25 cc; > 25 cc; evacuated	No involvement; ≤ 25 cc; > 25 cc; evacuated	328 (MAR)	MI	Included	
	Hydrocephalus present indicator	Yes; no	Yes; No	0	None	Included	
	Intraventricular hemorrhage status	Absent; indeterminate; pre-morbid; present	Absent; present	0	None	Included	
	Laboratory tests	Platelets (1000/ μ L)	Numerical	Numerical	8 (MCAR)	MI	Included
		Hemoglobin (g/dL)	Numerical	Numerical	5 (MCAR)	MI	Included
Hematocrit (%)		Numerical	Numerical	6 (MCAR)	MI	Included	
White blood cell count (1000/ μ L)		Numerical	Numerical	7 (MCAR)	MI	Included	

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SUPPLEMENTARY TABLE S1. (CONTINUED)

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	Absolute neutrophil count (1000/ μ L)	Numerical	Replaced with indicator feature for completion of differential blood test	308 (MNAR)	None	Excluded
	Neutrophils (%)	Numerical (%)	Replaced with indicator feature for completion of differential blood test	373 (MNAR)	None	Excluded
	Absolute lymphocyte count (1000/ μ L)	Numerical	Replaced with indicator feature for completion of differential blood test	275 (MNAR)	None	Excluded
	Lymphocytes (%)	Numerical (%)	Replaced with indicator feature for completion of differential blood test	341 (MNAR)	None	Excluded
	Creatinine (mg/dL)	Numerical	Numerical	16 (MCAR)	MI	Included
	Glucose (mg/dL)	Numerical	Numerical	7 (MCAR)	MI	Included
	Potassium (mM/L)	Numerical	Numerical	5 (MCAR)	MI	Included
	Sodium (mM/L)	Numerical	Numerical	3 (MCAR)	MI	Included
	Aspartate aminotransferase (IU/L)	Numerical	None	105 (MNAR)	Replaced with indicator feature for completion of hepatic blood test	Excluded
	Alanine aminotransferase (IU/L)	Numerical	None	127 (MNAR)	Replaced with indicator feature for completion of hepatic blood test	Excluded
	Bilirubin (mg/dL)	Numerical; highest and lowest daily measurements recorded	None	517 (MNAR)	Replaced with indicator feature for completion of hepatic blood test	Excluded
	Lactate (mEq/L)	Numerical; highest and lowest daily measurements recorded	None	420 (MNAR)	Replaced with indicator feature for completion of bilirubin test	Excluded
Baseline Assessments	Weight (kg)	Numerical	Numerical	5 (MCAR)	MI	Included
	Clinical signs of neuroworsening	Yes; no	Numerical	20 (MNAR)	MI	Excluded
	Transfusion	Yes; No	Yes; No	1 (MCAR)	MI	Included
	Ins/outs- total volume in (mL)	Numerical	Numerical; combined with total volume out to create net fluid intake (mL) feature	37 (MCAR)	MI	Included

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SUPPLEMENTARY TABLE S1. (CONTINUED)

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	Ins/outs- total volume out (mL)	Numerical	Numerical; combined with total volume out to create net fluid intake (mL) feature	56 (MCAR)	MI	Included
	Temperature (Celsius)	Numerical; highest and lowest daily measurements recorded	Numerical; daily average of high/low measurements	9 (MCAR)	MI	Included
	Systolic blood pressure (mmHg)	Numerical; highest and lowest daily measurements recorded	Numerical; daily average of high/low measurements	1 (MCAR)	MI	Included
	Diastolic blood pressure (mmHg)	Numerical; highest and lowest daily measurements recorded	Numerical; daily average of high/low measurements	13 (MCAR)	MI	Included
	Heart rate (BPM)	Numerical; highest and lowest measurements recorded	Numerical; daily average of high/low measurements	3 (MCAR)	MI	Included
	Respiratory rate (RPM)	Numerical; highest and lowest measurements recorded	Numerical; daily average of high/low measurements	6 (MCAR)	MI	Included
	Blood oxygen saturation level (%)	Numerical; Highest and lowest daily measurements recorded	Numerical; daily average of high/low measurements	7 (MCAR)	MI	Included
	PaO ₂ (mmHg)	Numerical; highest and lowest daily measurements recorded	Replaced with indicator feature for completion of arterial blood gas test	525 (MNAR)	None	Excluded
	PCO ₂ (mmHg)	Numerical; highest and lowest daily measurements recorded	Replaced with indicator feature for completion of arterial blood gas test	504 (MNAR)	None	Excluded
	FiO ₂ (%)	Numerical; highest and lowest daily measurements recorded	Replaced with indicator feature for completion of arterial blood gas test	441 (MNAR)	None	Excluded
	Arterial pH	Numerical; highest and lowest daily measurements recorded	Replaced with indicator feature for completion of arterial blood gas test	504 (MNAR)	None	Excluded
	Prothrombin time (sec)	Numerical; highest and lowest daily measurements recorded	Numerical; daily average of high/low measurements	27 (MCAR)	MI	Included
	Partial thromboplastin time (sec)	Numerical; highest and lowest daily measurements recorded	Numerical; daily average of high/low measurements	30 (MCAR)	MI	Included
	PT international normalized ratio	Numerical; highest and lowest daily measurements recorded	Numerical; daily average of high/low measurements	28 (MCAR)	MI	Included
	Toxicology drug screen completed	Yes; no	Yes; no	356 (MAR)	MI	Included
	Toxicology alcohol screen completed	Yes; no	Yes; no	161 (MAR)	MI	Included
	Drug screen: amphetamines	Positive; negative	Positive; negative	440 (MNAR)	None	Excluded
	Drug screen: barbiturates	Positive; negative	Positive; negative	391 (MNAR)	None	Excluded
	Drug screen: benzo-diazapines	Positive; negative	Positive; negative	391 (MNAR)	None	Excluded

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SUPPLEMENTARY TABLE S1. (CONTINUED)

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Study treatment arm	Drug screen: cocaine (BZE)	Positive; negative	Positive; negative	447 (MNAR)	None	Excluded
	Drug screen: marijuana (THC)	Positive; negative	Positive; negative	719 (MNAR)	None	Excluded
	Drug screen: methadone	Positive; negative	Positive; negative	856 (MNAR)	None	Excluded
	Drug screen: methamphetamine amines	Positive; negative	Positive; negative	895 (MNAR)	None	Excluded
	Drug screen: opiates	Positive; negative	Positive; negative	453 (MNAR)	None	Excluded
	Drug screen: phencyclidine (PCP)	Positive; negative	Positive; negative	550 (MNAR)	None	Excluded
	Drug screen: another drug	Positive; negative	Positive; negative	899 (MNAR)	None	Excluded
	Treatment arm	Citicoline; placebo	Citicoline; placebo	0	None	Included

Baseline patient features that were collected within 24h of injury were input into unsupervised machine learning schema. (Column 1) Baseline feature category, (Column 2) feature name, (Column 3) feature values in the raw data format (categorical features were dummy coded if feature contained >2 values), (Column 4) feature values in the cleaned data format, (Column 5) number of missing values in the original data set with the type of missingness indicated in parentheses, (Column 6) method of imputing missing values, and (Column 7) whether the feature was included in the final data set.

COBRIT, Citicoline Brain Injury Treatment Trial; MAR, missing at random; MCAR, missing completely at random; MNAR, missing not at random; MI, multiple imputation with random forest method; GED, general education diploma; ADHD, attention-deficit/hyperactivity disorder; CNS, central nervous system; TBI, traumatic brain injury; ATV, all-terrain vehicle; CC,; BPM, beats per minute; RPM, respirations per minute; BZE, benzodiazepines; THC, tetrahydrocannabinol.