Supplementary Online Content

Hawryluk GWJ, Nielson JL, Huie JR, et al. Analysis of normal high-frequency intracranial pressure values and treatment threshold in neurocritical care patients. *JAMA Neurol*. Published online June 15, 2020. doi:10.1001/jamaneurol.2020.1310

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

eMethods: Primer on Principal Component Analysis

Principal component analysis is an increasingly utilized technique that has particular utility in the analysis of large datasets. Principal components are mathematical entities which can explain inter-relationships between variables and they can ultimately be used to reduce the number of variables in a dataset by combining those that share a certain amount of explained variance. Moreover, they can be grouped into new composite or multivariate outcomes. Additionally, principal components are completely independent of each other – in other words they are non-overlapping or 'orthogonal'.

An easy way to understand how principal components work is to liken them to the domains of an Intelligence Quotient (IQ) test. Although numerous individual tests are administered as part of an IQ test, these tests are ultimately viewed as measuring *verbal IQ* or *performance IQ*. Said differently, one's verbal IQ is felt to explain performance on some tests while one's performance IQ explains accomplishment on the others. Principal components are similar 'underlying factors' which can be used to explain patterns of change across multiple variables in a dataset.

Under different conditions of the dataset, different principal components can have varying degrees of influence. A loading for a particular value in a principal component reflects a correlation of that variable on the entire composite measure. Loading values can range from -1 to +1 to help explain the relationship of the variables that are used to interpret the identity of each component, with a threshold set to only include loadings greater than or equal to the absolute value of 0.4 for interpretation. Variable with loadings that fall below this threshold are not considered to be significant loaders on the principal component, and therefore are not used to describe what that principal component represents. Loadings with a positive loading have been colored red, and those with a negative loading are colored blue in *Figure 3*, to denote positive and negative correlations on the principal component, respectively.

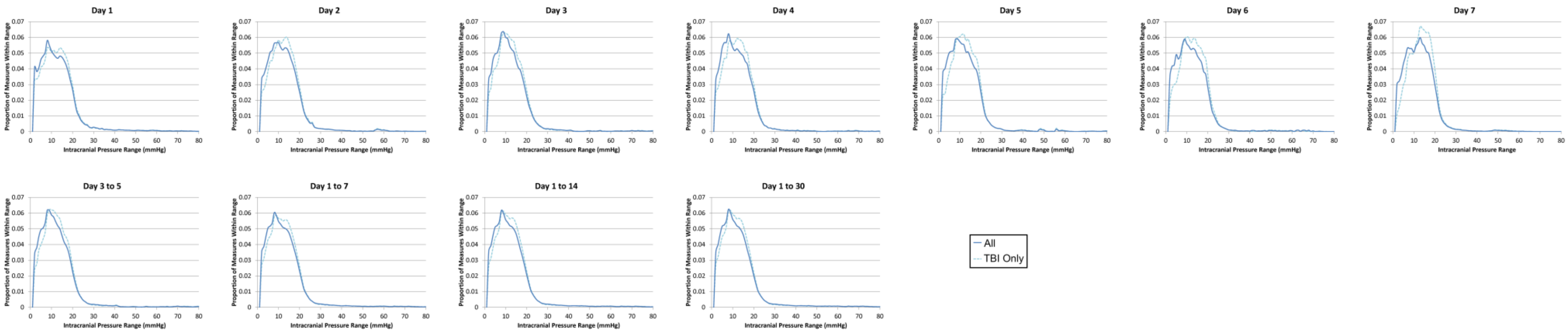
In *Figure 3* on the left, the loading values for 5 identified principal components are displayed for different ICP values. The influence of principal component 1 explains the variance for measures above approximately 24 mmHg, wherease principal component 2 explains variance for ICP values below 19 mmHg, while principal component 3 explains the variance for ICP values between 19 and 24 mmHg. Each principal component reflects a pattern of change between physiologic variables.

eTable. Characteristics of Included Patients In Relation to Neurological Insult

	All Patients	Traumatic Brain Injury	Non-Traumatic Brain Injury	p-value
Age	46.4 ± 19.7	43.9 ± 20.3	53.3 ± 16.0	0.038
Sex (M:F)	370:153	292:91	78:62	<0.001
Mean GOS Score	2.4 ± 1.0	2.5 ± 1.0	2.4 ± 1.1	0.774
Surgery (Y:N)	261:262	209:175	52:87	0.001
Craniectomy (Y:N)	212:307	175:209	37:98	<0.001
Total Hospital Days	34.5 ± 41.3	34.3 ± 41.3	35.0 ± 41.4	0.865
Total Measurements	8070.4 ± 6794.9	7798.7 ± 6580.7	8772.4 ± 7296.6	0.144

Legend: Values presented represent mean ± standard deviation; values separated by a colon are numbers of patients. Continuous data were analyzed by ANOVA with brain injury type as the independent variable. Dichotomous data was analyzed with binomial logistic regression with brain injury type as the independent variable. P<0.05 was considered statistically significant and denoted with red font.

Supplementary eFigure 1

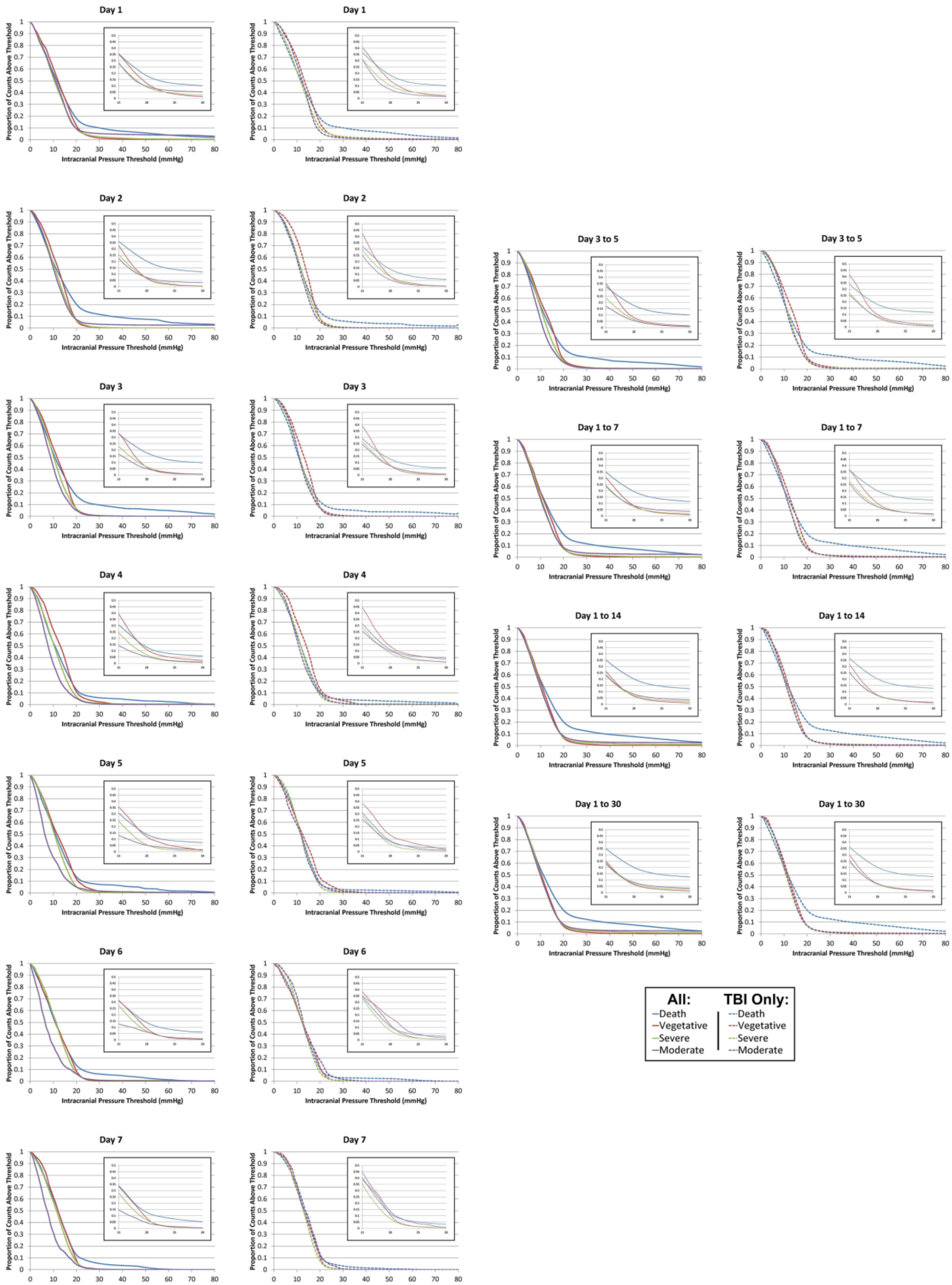


Supplementary eFigure 1 Legend: Here we provide a detailed analysis of ICP distributions for all examined epochs – both cumulative (*bottom row*) and non-cumulative (*top row*). The distribution of intracranial pressure measures is plotted for all patients (dark blue solid line) and for TBI patients only (light blue dotted line).

TBI = traumatic brain injury

For All, n=523; for TBI only, n=383

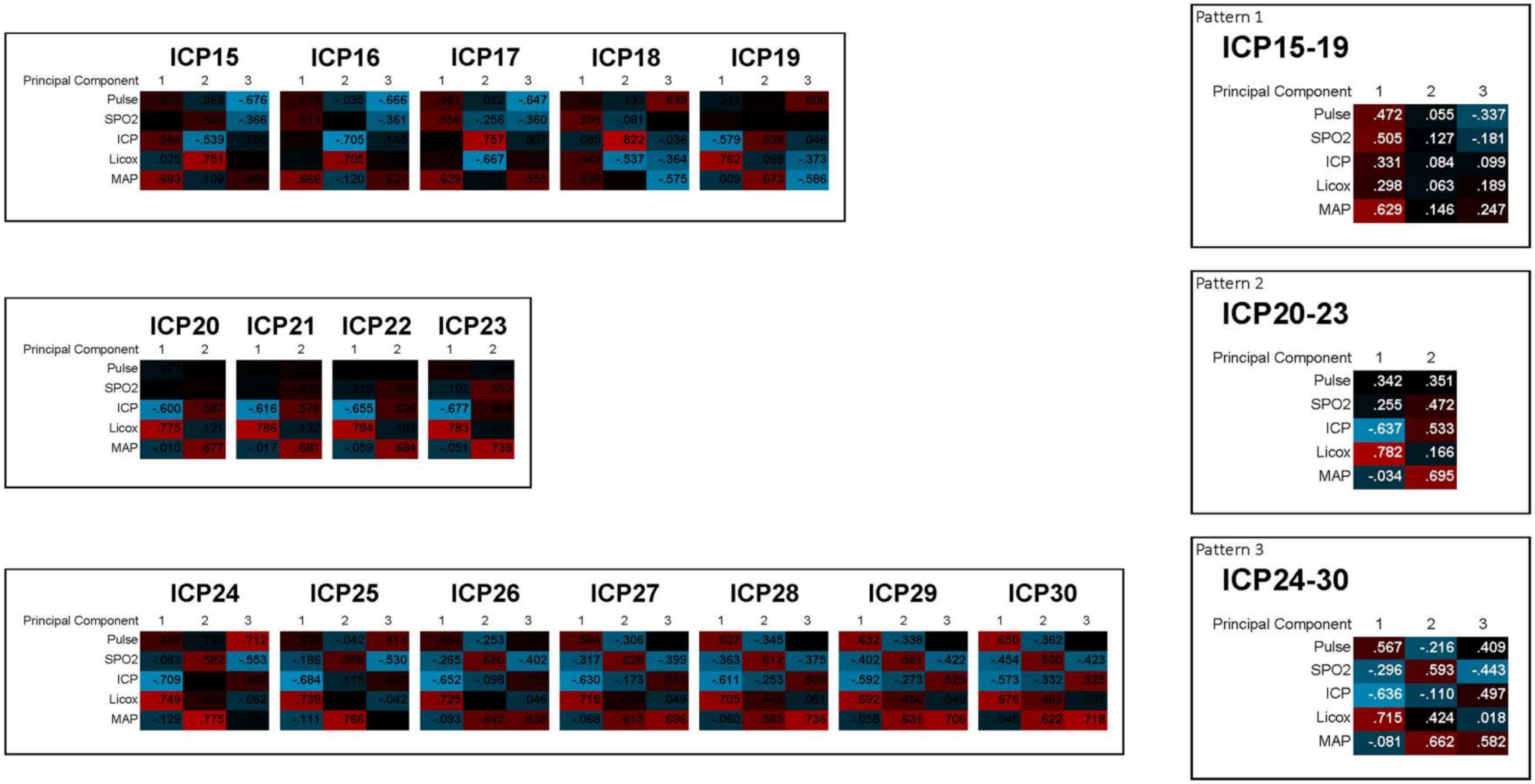
Supplementary eFigure 2



Supplementary eFigure 2 Legend: Here we provide plots of the relationship between time spent above ICP thresholds and outcome for all examined epochs. Plots of the time patients spent with ICP values above 79 different ICP thresholds (1 to 80 in 1 mmHg increments) are shown for outcome groups based on discharge Glasgow Outcome Scale scores. Non-cumulative analyses are shown on the left while cumulative analyses are shown of the right. In the insets the region of each graph is replotted for the range of ICP values between 15 and 30 mmHg to improve visualization.

TBI = traumatic brain injury

Supplementary eFigure 3:



Supplementary eFigure 3: Here we provide more extensive results of principal component analyses performed for each examined ICP threshold. This more extensive data clearly demonstrates the consistency of the physiological relationships for ICP threshold from 15-19, 20-23 and 24-30 mmHg which is presented in summary form in *Figure 3*.