Supplementary Appendix

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Supplementary Methods

Definitions

If adult patients satisfied at least 2 of 4 SIRS criteria within the 12 hours preceding a blood culture order for the suspicion of infection, we looked for evidence of end-organ dysfunction within 12 hours before or after the time of blood culture order.

Physiologic Data Acquisition

The bedside monitors were connected to either a Bernoulli Enterprise (Cardiopulmonary Corp, Milford, Connecticut) or a BedMasterEx (Excel Medical, Jupiter, Florida) patient monitoring system, each of which records vital signs and waveform data. These data were downloaded and warehoused daily on a custom grid-computing cluster (1). When available, we favored invasive rather than noninvasive blood pressure recordings.

Statistical Analysis

Measurements beyond physiologic ranges (<0.25% for any given variable), which could represent spurious or illegitimate readings, were truncated to either the minimum or maximum integer value as determined by the 0.1 and 99.9 percentiles respectively (2). The most commonly missing variable was respiratory rate (Resp; up to 39.2%), which is likely a reflection of chest impedance leads that are vulnerable to displacement and extraneous noise. Incomplete data (mean 7.4%; range: <0.5 – 39.2%) were multiply imputed under the fully conditional specification with chained equations using predictive mean matching using the mice R package (3, 4). We created and analyzed 5 multiply imputed datasets for each unit-illness cohort. Model parameters were estimated with logistic regression applied to each imputed dataset separately. These estimates and their standard errors were combined. We adjusted the look-back time window in 2-hour increments to optimize the predictive accuracy. Candidate predictors that did not have any significant nonlinear terms in any of the models were constrained to be linear. Nonmonotonic associations were modeled with restricted cubic splines using 3 knots fixed at equally spaced quantiles (i.e. 10%, 50%, 90%) of a predictor's marginal distribution.

Supplementary Figures

Supplementary Figure 1: Predictor Effects

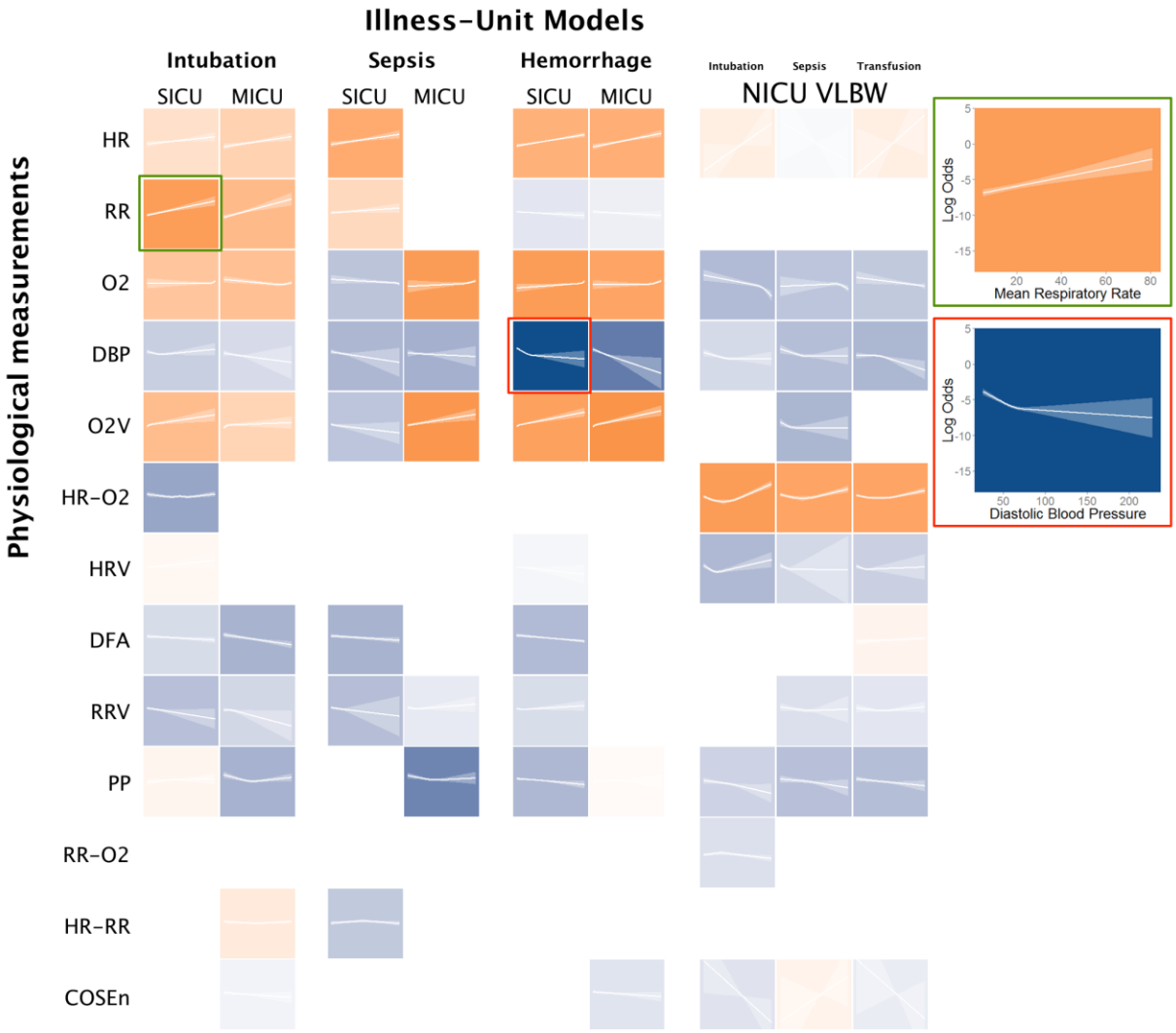

Figure 2 with the additional features analyzed. MICU: medical intensive care unit; SICU: surgical intensive care unit; NICU: neonatal intensive care unit. HR: heart rate; RR: respiratory rate; O2: pulse oxygen saturation; DBP: diastolic blood pressure; O2V: pulse oxygen saturation variability; HR-O2: cross correlation coefficient of heart rate and pulse oxygen saturation; HRV: heart rate variability; DFA: detrended fluctuation analysis; RRV: respiratory rate variability; PP: pulse pressure; RR-O2: cross-correlation coefficient of respiratory rate and oxygen saturation; HR-RR: cross-correlation coefficient of heart rate and respiratory rate; COSEn: coefficient of sample entropy.

Supplementary References

1. Clark MT, Rusin CG, Hudson JL, et al: Breath-by-breath analysis of cardiorespiratory interaction for quantifying developmental maturity in premature infants. *J Appl Physiol (1985)* 2012;112:859-867

2. Osborne JW, Overbay A: The power of outliers (and why researchers should always check for them).

3. van Buuren S, Groothuis-Oudshoorn K: Mice: Multivariate imputation by chained equations in R. 2011

4. van Buuren S: Flexible imputation of missing data. Boca Raton, Florida, CRC Press, 2012