

# Supplementary figures and tables

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Figure S1

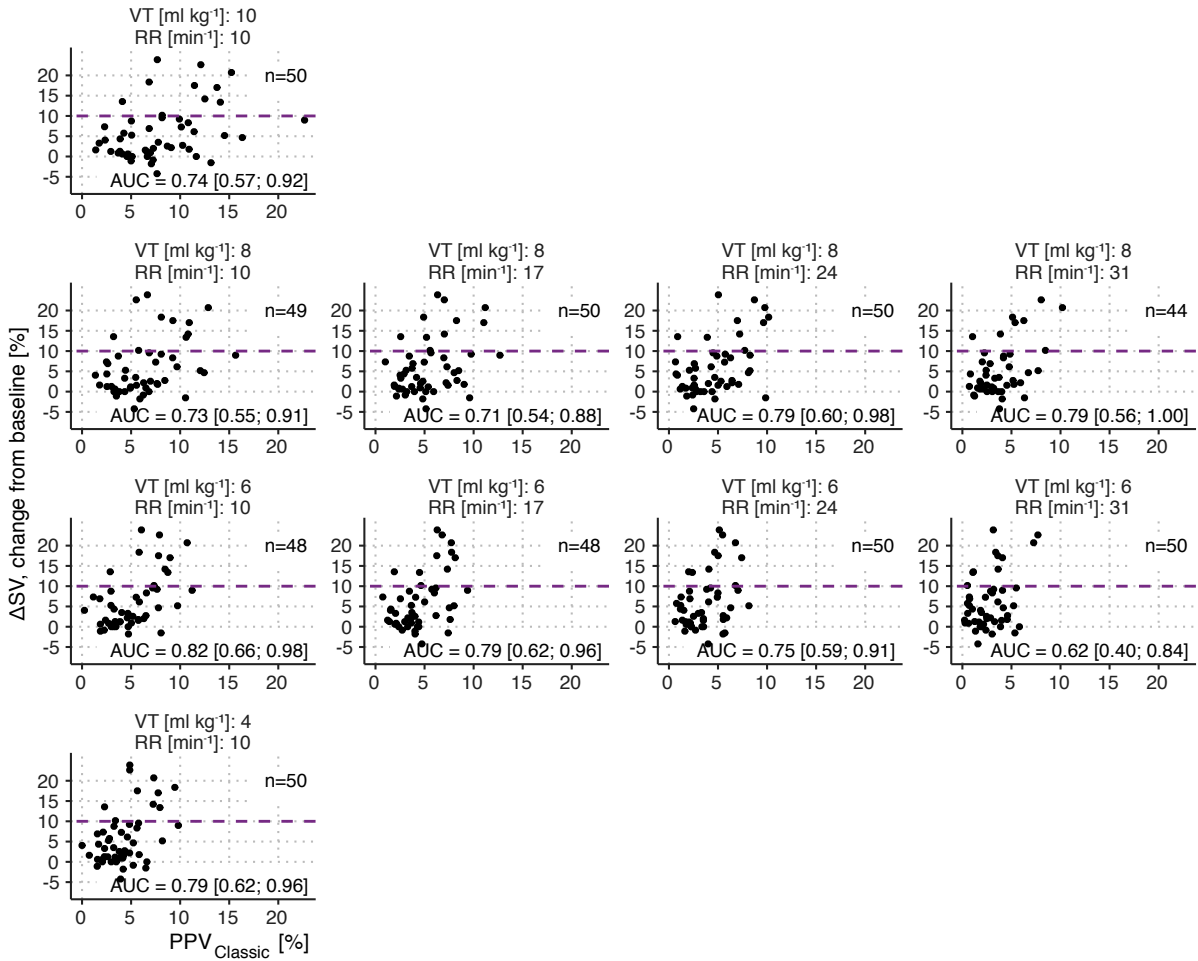


Figure S1: Scatter plots of the relation between PPV calculated with the classic algorithm ( $PPV_{Classic}$ ) and the stroke volume response ( $\Delta SV$ ) to a 250 ml fluid challenge. Panels are arranged with tidal volumes (VT) in rows and respiratory rates (RR) in columns. One fluid challenge was evaluated for each subject ( $n = 50$ ), while  $PPV_{Classic}$  was calculated for each of the 10 ventilator settings.

Figure S2

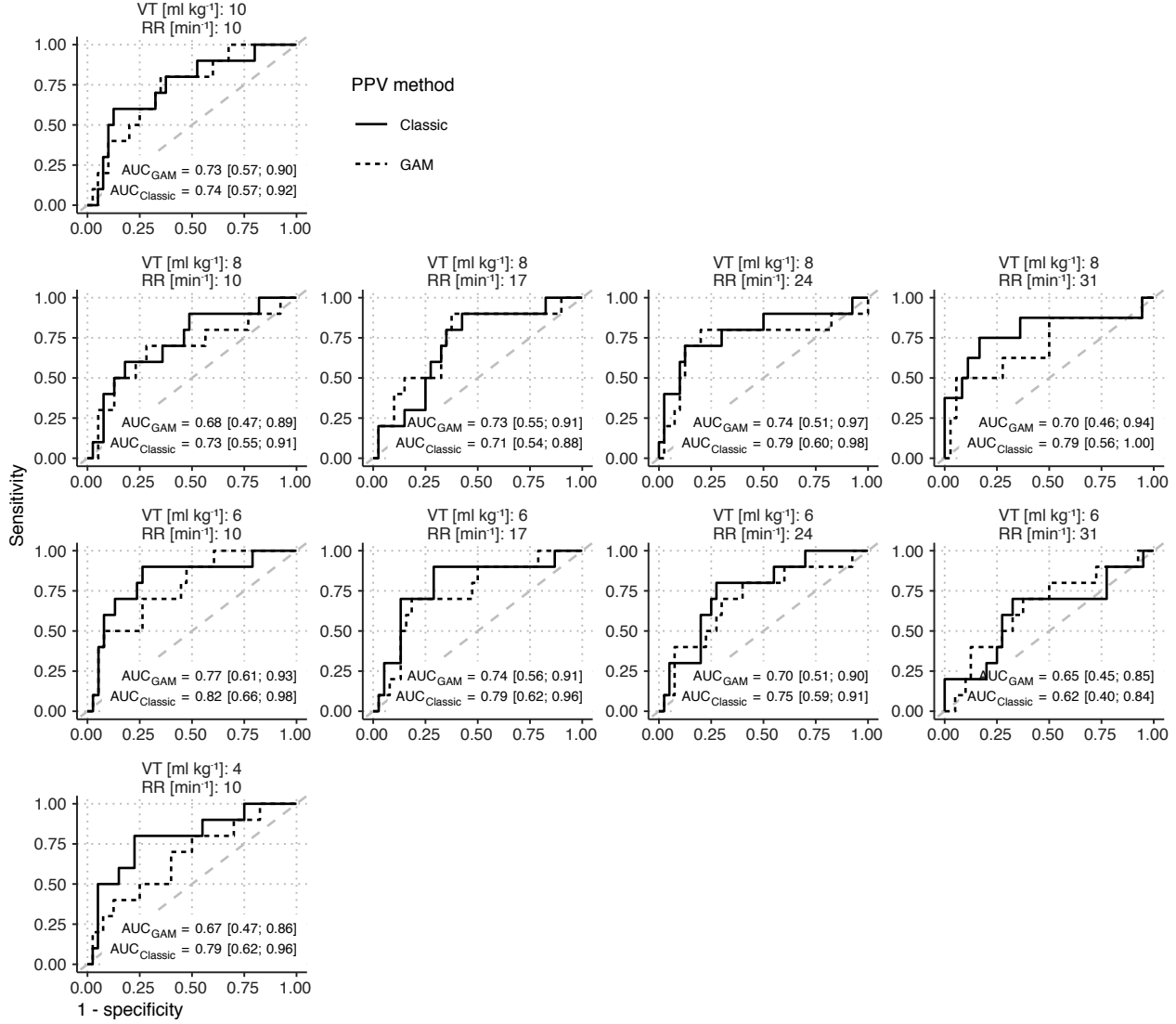


Figure S2: Receiver operating characteristic (ROC) curves for capacity of pulse pressure variation (PPV) to classify fluid responsiveness (stroke volume change > 10%). Panels are arranged with tidal volumes (VT) in rows and respiratory rates (RR) in columns. One fluid challenge was evaluated for each subject (n = 50), while  $PPV_{GAM}$  and  $PPV_{Classic}$  was calculated for each of the 10 ventilator settings.

Figure S3

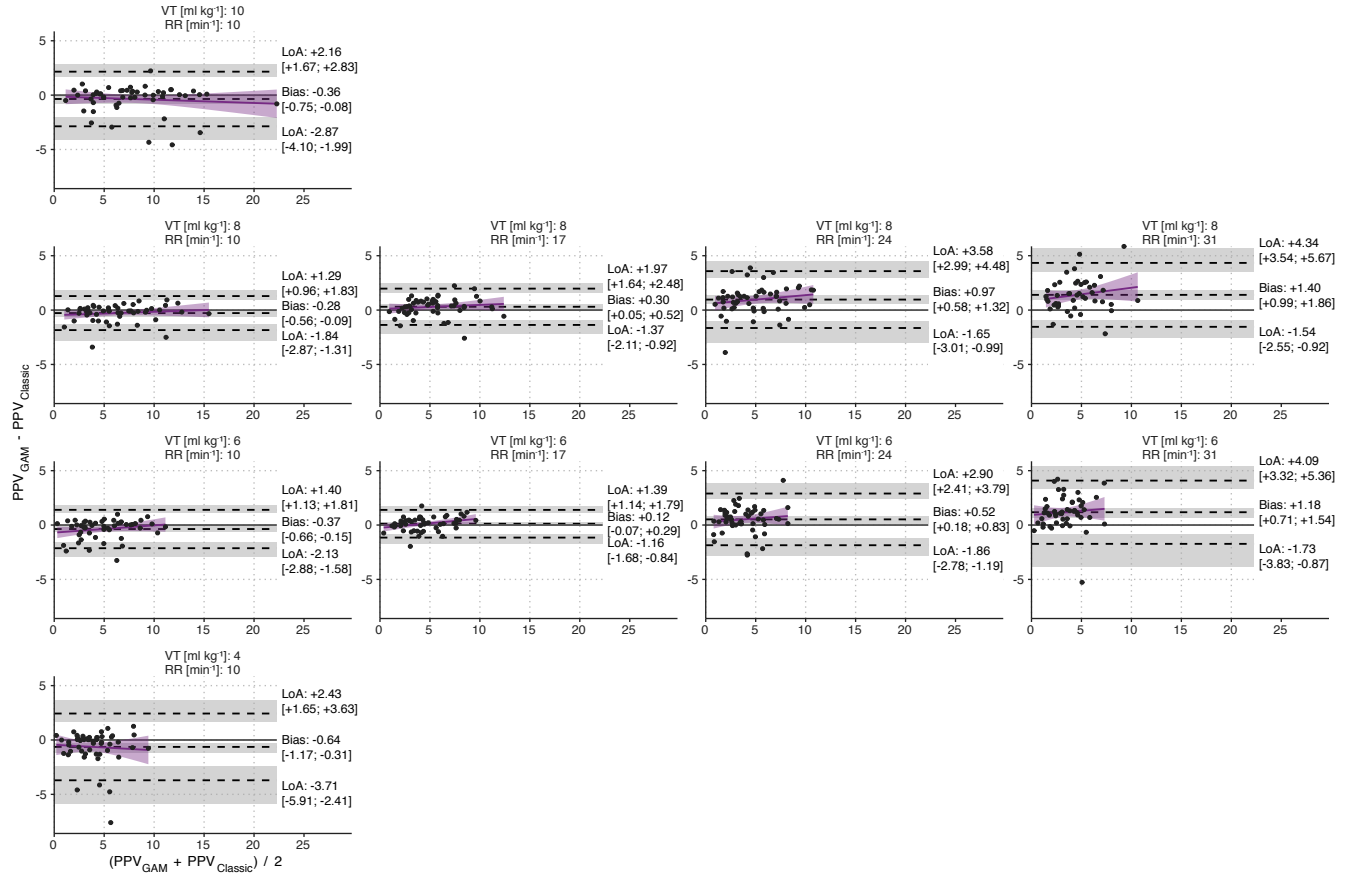


Figure S3: Bland-Altman plots showing the relation between  $PPV_{GAM}$  and  $PPV_{Classic}$ . The outer dashed lines represent 95% limits of agreement (LoA). Grey areas are 95% confidence intervals for bias and LoA. The purple lines and areas are linear regression fits with 95% confidence intervals. Panels are arranged with tidal volumes (VT) in rows and respiratory rates (RR) in columns.

Figure S4

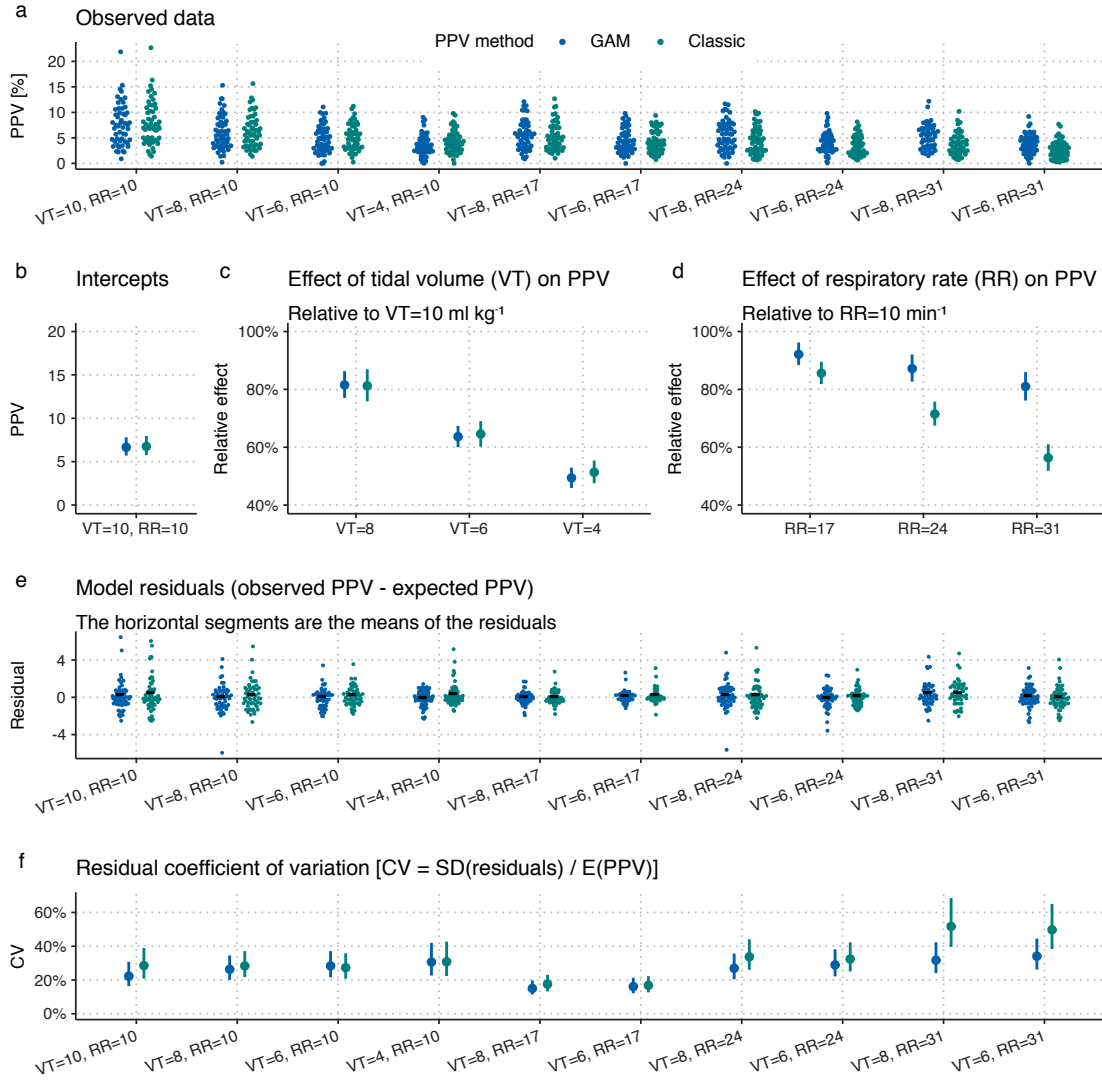


Figure S4: (Extended version of the paper's Fig. 5): Parameter estimates for a Bayesian mixed-effects model, describing the effect of tidal volume (VT) and respiratory rate (RR) on pulse pressure variation (PPV). Parameters are estimated for both PPV derived using a generalized additive model (GAM) and using a classic approach (Classic). Panel **a** presents the observed PPV values (outcomes) using each method (n=507 for both GAM and Classic). Vertical bars are 95% compatibility intervals. Panel **b**, **c** and **d** present parameter estimates. Vertical bars are 95% compatibility intervals. Panel **e** shows model residuals, and panel **f** shows the residual variation relative to the estimated value of PPV.

Table S1

Receiver operating characteristic analysis of fluid-responsiveness prediction using pulse pressure variation (PPV). A positive fluid response was a >10% increase in stroke volume from a 250 ml fluid bolus. PPV was calculated using a classic method and derived from a generalized additive model (GAM). Results are presented as *estimate* [95% confidence interval].

| Tidal volume<br>[ml<br>kg <sup>-1</sup> ] | Respiratory rate [min <sup>-1</sup> ] | GAM PPV                        |                     |                     |                     | Classic PPV                    |                     |                     |                     |
|---|---------------------------------------|--------------------------------|---------------------|---------------------|---------------------|--------------------------------|---------------------|---------------------|---------------------|
|   |                                       | Optimal threshold <sup>†</sup> | Sensitivity         | Specificity         | AUC                 | Optimal threshold <sup>†</sup> | Sensitivity         | Specificity         | AUC                 |
| 10  | 10                                    | 7.9%                           | 0.80<br>[0.50;1.00] | 0.65<br>[0.50;0.80] | 0.73<br>[0.57;0.90] | 11.4%                          | 0.60<br>[0.30;0.90] | 0.88<br>[0.78;0.97] | 0.74<br>[0.57;0.92] |
| 8   | 10                                    | 6.9%                           | 0.70<br>[0.40;1.00] | 0.72<br>[0.56;0.85] | 0.68<br>[0.47;0.89] | 8.1%                           | 0.60<br>[0.30;0.90] | 0.82<br>[0.69;0.92] | 0.73<br>[0.55;0.91] |
| 6   | 10                                    | 5.9%                           | 0.70<br>[0.40;1.00] | 0.74<br>[0.61;0.87] | 0.77<br>[0.61;0.93] | 5.8%                           | 0.90<br>[0.70;1.00] | 0.74<br>[0.61;0.87] | 0.82<br>[0.66;0.98] |
| 4   | 10                                    | 3.1%                           | 0.80<br>[0.50;1.00] | 0.50<br>[0.35;0.68] | 0.67<br>[0.47;0.86] | 4.9%                           | 0.80<br>[0.50;1.00] | 0.78<br>[0.62;0.90] | 0.79<br>[0.62;0.96] |
| 8   | 17                                    | 5.7%                           | 0.90<br>[0.70;1.00] | 0.62<br>[0.47;0.78] | 0.73<br>[0.55;0.91] | 4.9%                           | 0.90<br>[0.70;1.00] | 0.57<br>[0.42;0.72] | 0.71<br>[0.54;0.88] |
| 6   | 17                                    | 5.7%                           | 0.70<br>[0.40;1.00] | 0.82<br>[0.68;0.92] | 0.74<br>[0.56;0.91] | 4.4%                           | 0.90<br>[0.70;1.00] | 0.71<br>[0.58;0.84] | 0.79<br>[0.62;0.96] |
| 8   | 24                                    | 7.2%                           | 0.80<br>[0.50;1.00] | 0.80<br>[0.68;0.93] | 0.74<br>[0.51;0.97] | 6.7%                           | 0.70<br>[0.40;1.00] | 0.88<br>[0.78;0.97] | 0.79<br>[0.60;0.98] |
| 6   | 24                                    | 4.6%                           | 0.70<br>[0.40;1.00] | 0.70<br>[0.55;0.85] | 0.70<br>[0.51;0.90] | 4.1%                           | 0.80<br>[0.50;1.00] | 0.72<br>[0.57;0.85] | 0.75<br>[0.59;0.91] |
| 8   | 31                                    | 7.7%                           | 0.50<br>[0.12;0.88] | 0.94<br>[0.86;1.00] | 0.70<br>[0.46;0.94] | 5.0%                           | 0.75<br>[0.38;1.00] | 0.83<br>[0.69;0.94] | 0.79<br>[0.56;1.00] |
| 6   | 31                                    | 4.3%                           | 0.70<br>[0.40;1.00] | 0.62<br>[0.47;0.78] | 0.65<br>[0.45;0.85] | 3.1%                           | 0.70<br>[0.40;1.00] | 0.68<br>[0.53;0.82] | 0.62<br>[0.40;0.84] |

<sup>†</sup> Threshold with maximum Youden index.