

## Understanding Patients' Perceived Health After Critical Illness

### Analysis of Two Prospective, Longitudinal Studies of ARDS Survivors

*Alison E. Turnbull, DVM, MPH, PhD; Hongkai Ji, PhD; Victor D. Dinglas, MPH;  
Albert W. Wu, MD; Pedro A. Mendez-Tellez, MD; Cheryl Dennison Himmelfarb, PhD, RN;  
Carl B. Shanholtz, MD; Megan M. Hosey, PhD; Ramona O. Hopkins, PhD; and  
Dale M. Needham, MD, PhD*

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**e-Table 1: Self-reported measures of health used to predict perception of health**

Domain	Instrument	Questions
Physical Functioning	SF-36v2	10 questions about physical activities ranging from dressing oneself to running.
	EQ-5D-3L	2 questions about walking and self-care.
Role limitations due to physical health problems	SF-36v2	4 questions about the impact of physical health on work and other regular daily activities
	EQ-5D-3L	1 question about usual activities, for example work, study, housework, family or leisure.
Bodily Pain	SF-36v2	2 questions about the impact of bodily pain on regular activities
	EQ-5D-3L	1 question about pain
Social Functioning	SF-36v2	2 questions about how physical health and emotional problems have affected social activities with family, friends, neighbors, or groups.
Mental Health	SF-36v2	5 questions about mental health symptoms
	EQ-5D-3L	1 question about mental health symptoms
Role limitations due to emotional problems	SF-36v2	3 questions about the impact of mental health symptoms on work and other regular daily activities
Vitality, energy or fatigue	SF-36v2	4 questions about fatigue

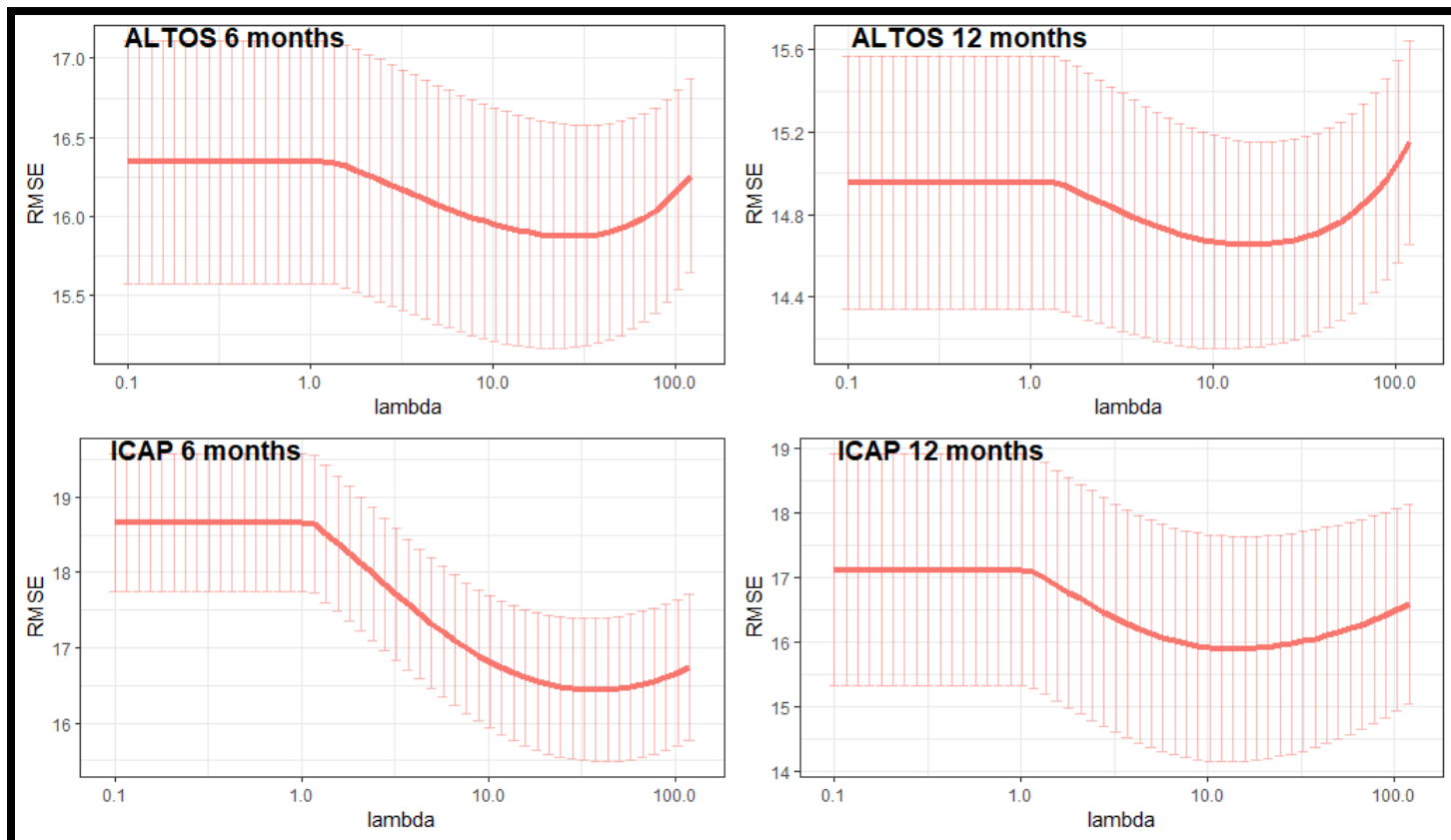
**e-Table 2: Techniques used to estimate perception of health**

Technique	Approach	Features/variables	Hyper-parameters via cross-validation†	
Dimension Reduction	Simple linear regression (glm)	7 transformed domain scores excluding the “General health perceptions” domain (7 features)	Link function = identify Distribution = Gaussian	
	LASSO (glmnet)	EQ5D items and 30 of the SF-36 items (35 features)	Regularization parameter $\lambda = 0.625$	
Shrinkage Methods**	Ridge Regression* (glmnet)	EQ5D items and 30 of the SF-36 items (35 features)	ALTOS* Regularization parameters 6 months: $\lambda = 28.2$ 12 months: $\lambda = 15.8$	ICAP* Regularization parameters 6 months: $\lambda = 37.7$ 12 months: $\lambda = 18.3$
	Elastic Net (glmnet)	EQ5D items and 30 of the SF-36 items (35 features)	Mixture of $l_1$ and $l_2$ penalty $\alpha = 0.903$ Tuning parameter $\lambda = 0.605$	
Tree-Based Methods	Random forest (ranger)	EQ5D items and 30 of the SF-36 items (35 features)	6 months: Number of candidate variables for splitting at in each node(mtry)= 2 Minimum node size (min_n)= 1 trees = 2,000  12 months: Number of candidate variables for splitting at in each node(mtry)= 7 Minimum node size (min_n)= 10 trees = 2,000	
	Extreme gradient boosting (xgboost)	EQ5D items and 30 of the SF-36 items (35 features)	The number of trees (trees)= 955 Number of splits in each tree(tree_depth)= 1 Shrinkage parameter $\lambda$ (learn_rate)= 0.005	

Abbreviations: LASSO, Least Absolute Shrinkage and Selection Operator; QoL, Quality of Life; VAS, Visual Analogue Scale; †Hyper-parameters were tuned using 10-fold cross-validation. Optimal combinations of parameters were selected based on the lowest root mean squared error. For some approaches, different combinations were chosen for the 6 month and 12 month time-points.

\* Because the central tendency of EQ-5D-VAS scores in the ICAP cohort was substantially lower than in ALTOS, we fit a second ICAP-specific prediction model with hyper-parameters tuned using 10-fold cross-validation.

\*\* Shrinkage methods regularize or “shrink” coefficient estimates thereby reducing their variance. In LASSO and ridge regression models, the regularization parameter lambda ( $\lambda$ ) controls the impact of the shrinkage penalty. When  $\lambda=0$ , the penalty term has no effect and the model produces least squares estimates. Conversely, as  $\lambda$  grows coefficient estimates approach zero. In situations where the number of independent variables (predictors) is large relative to the number of observations ( $n$ ), the least squares estimates become extremely variable, while shrinkage methods are less so. The LASSO and Ridge Regression methods use slightly different shrinkage penalties, referred to as  $l_1$  and  $l_2$  respectively. While the  $l_1$  penalty allows some coefficients to be minimized to 0, the  $l_2$  penalty prevents any coefficients from being removed from the model. The Elastic Net technique includes both the  $l_1$  and  $l_2$  penalties, and the hyperparameter  $\alpha$  ranges between 0 and 1 and determines how much weight is given to each.

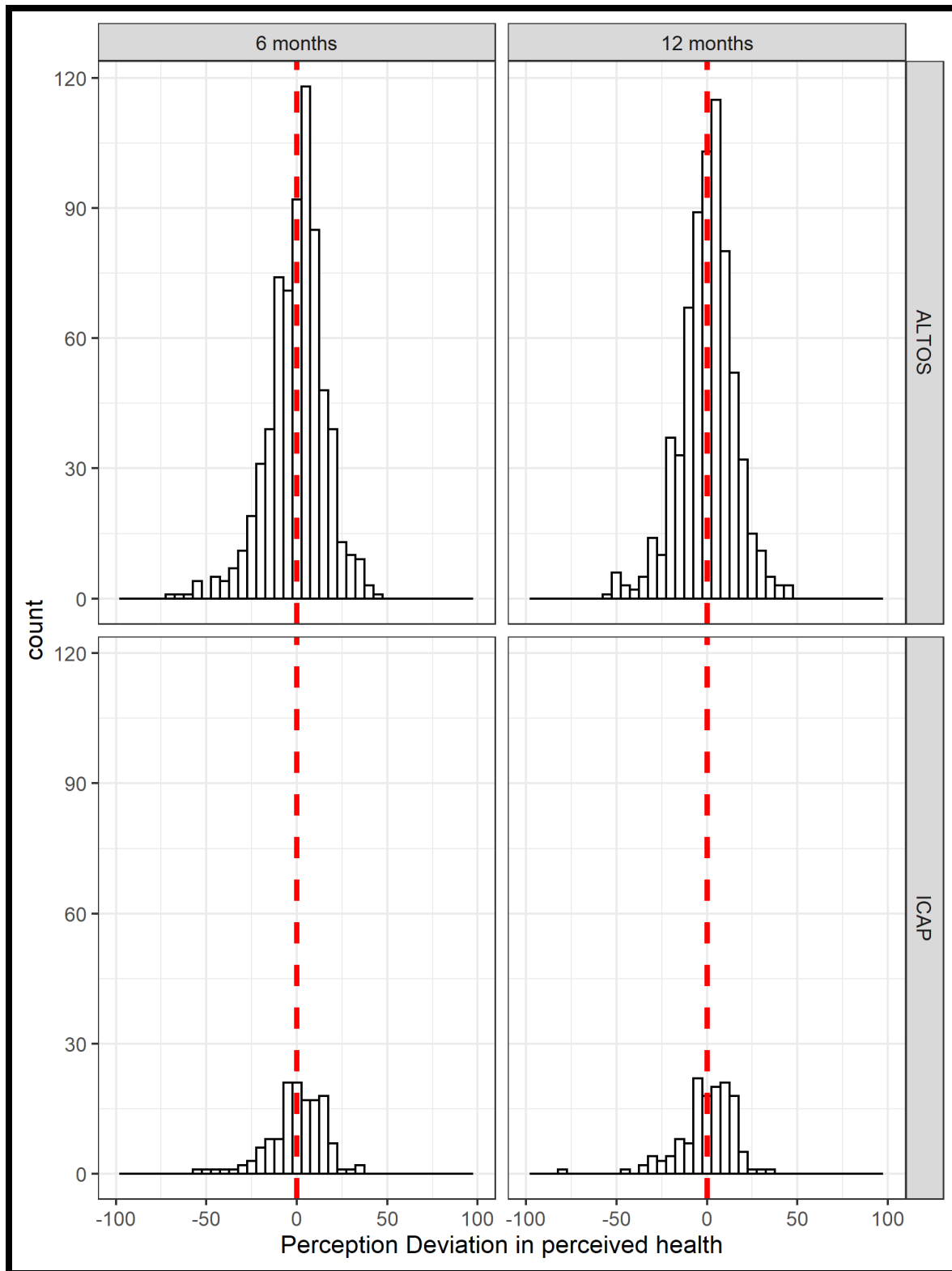


**e-Figure 1: Root Mean Squared Error (RMSE) for ridge regression predictions as a function of the regularization parameter lambda ( $\lambda$ )** The model for which RMSE of predictions is smallest is used to identify the optimal value of  $\lambda$ . The x-axis is on a log<sub>10</sub> scale.

**e-Table 3: Mean squared error of candidate prediction models using validation data**

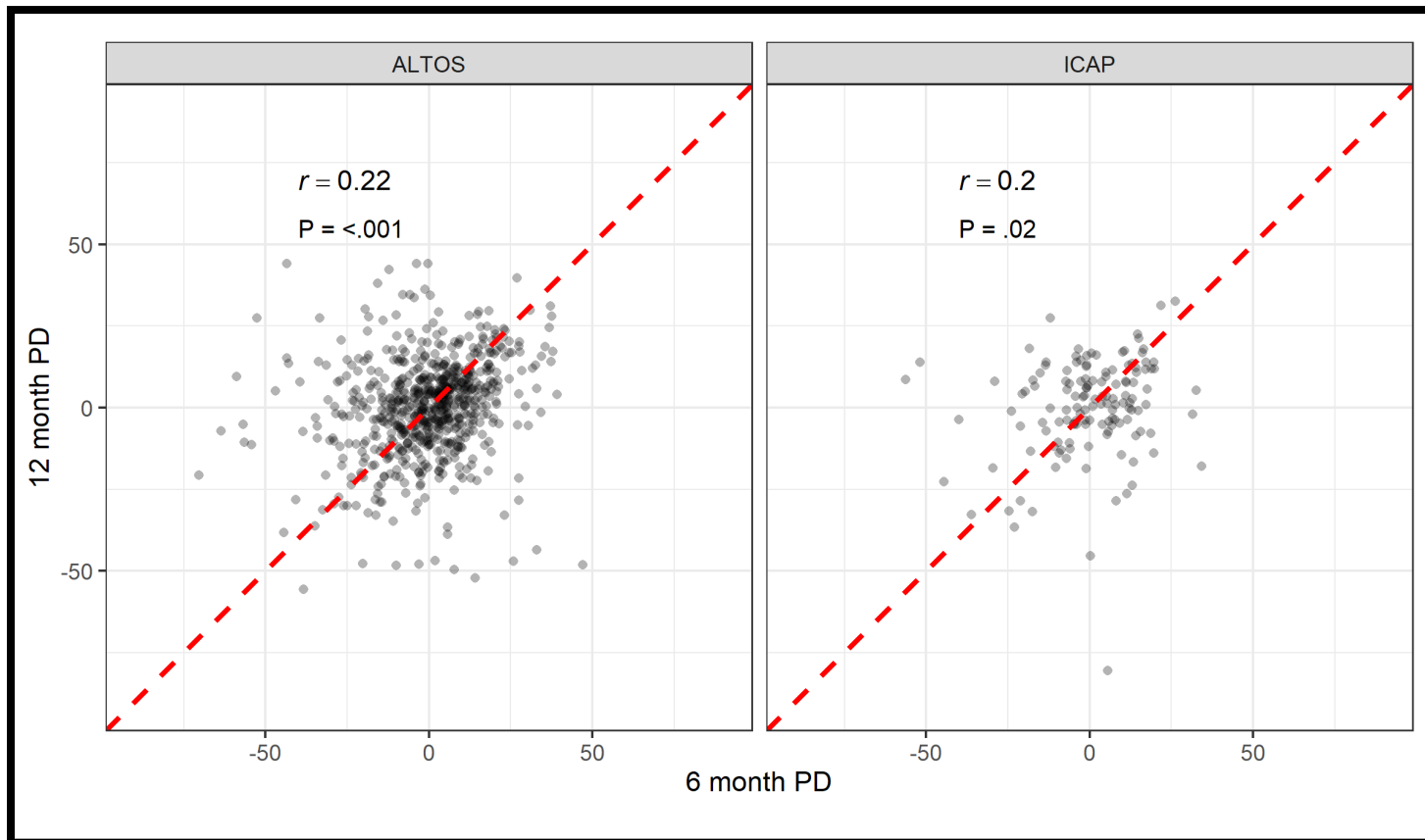
	Simple linear regression	LASSO	Ridge regression	Elastic net	Random Forest	Extreme gradient boosting
6 month VAS score	274	270	264	270	275	320
12 month VAS score	277	277	273	278	281	331

Abbreviations: LASSO, Least Absolutely Shrinkage and Selection Operator; VAS, Visual Analogue Scale

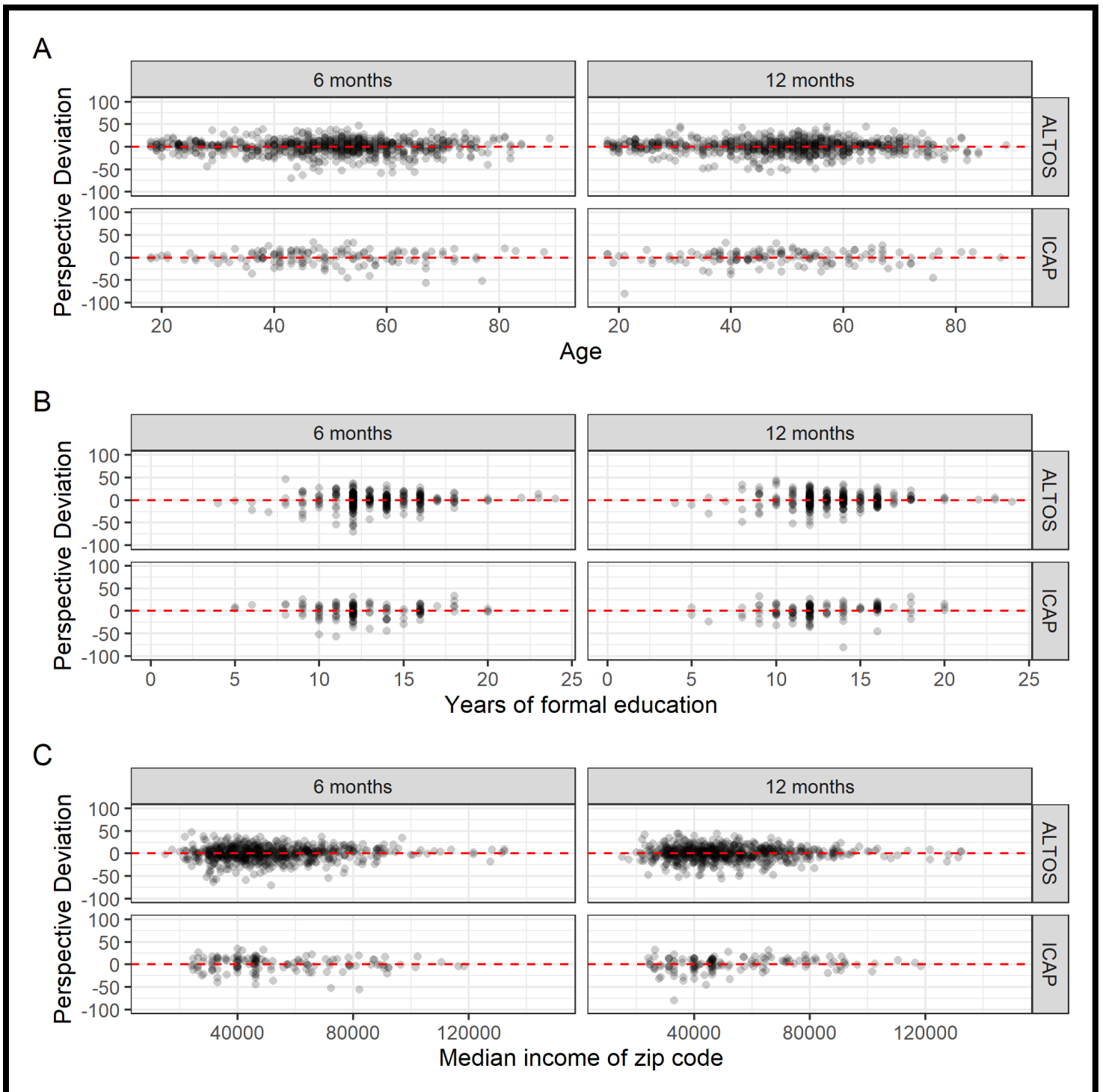


**e-Figure 2: Histograms of estimated perspective deviation** Abbreviations: ALTOS = ARDSNET Long Term Outcomes Study; ICAP = The Improving Care of Acute Lung Injury Patients study

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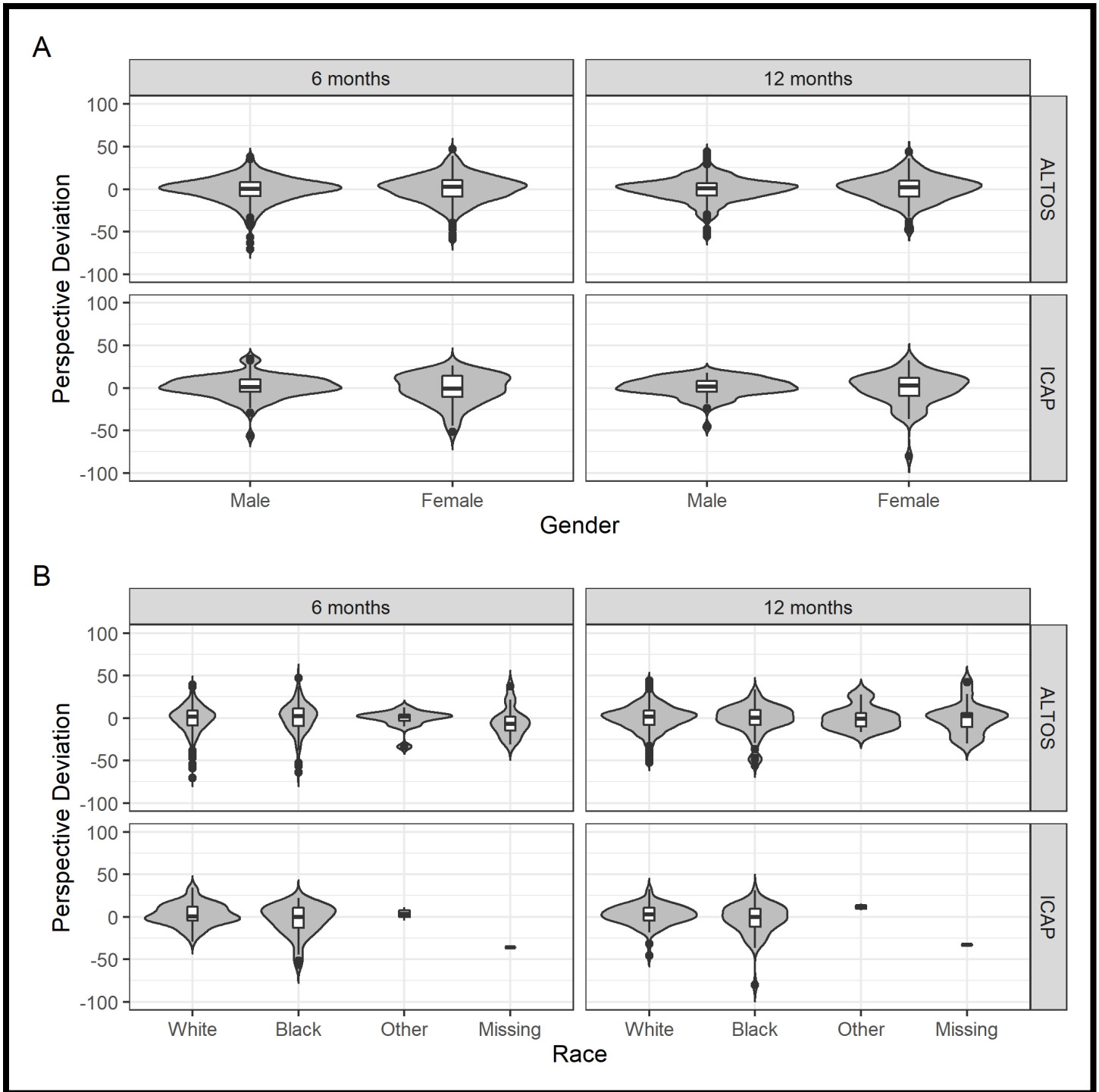
**e-Figure 3: Correlation between 6 month and 12 month perspective deviation** Pearson's correlation coefficients reported. P-values for the null hypothesis that  $r = 0$ . **Abbreviations:** ALTOS = ARDSNET Long Term Outcomes Study; ICAP = The Improving Care of Acute Lung Injury Patients study



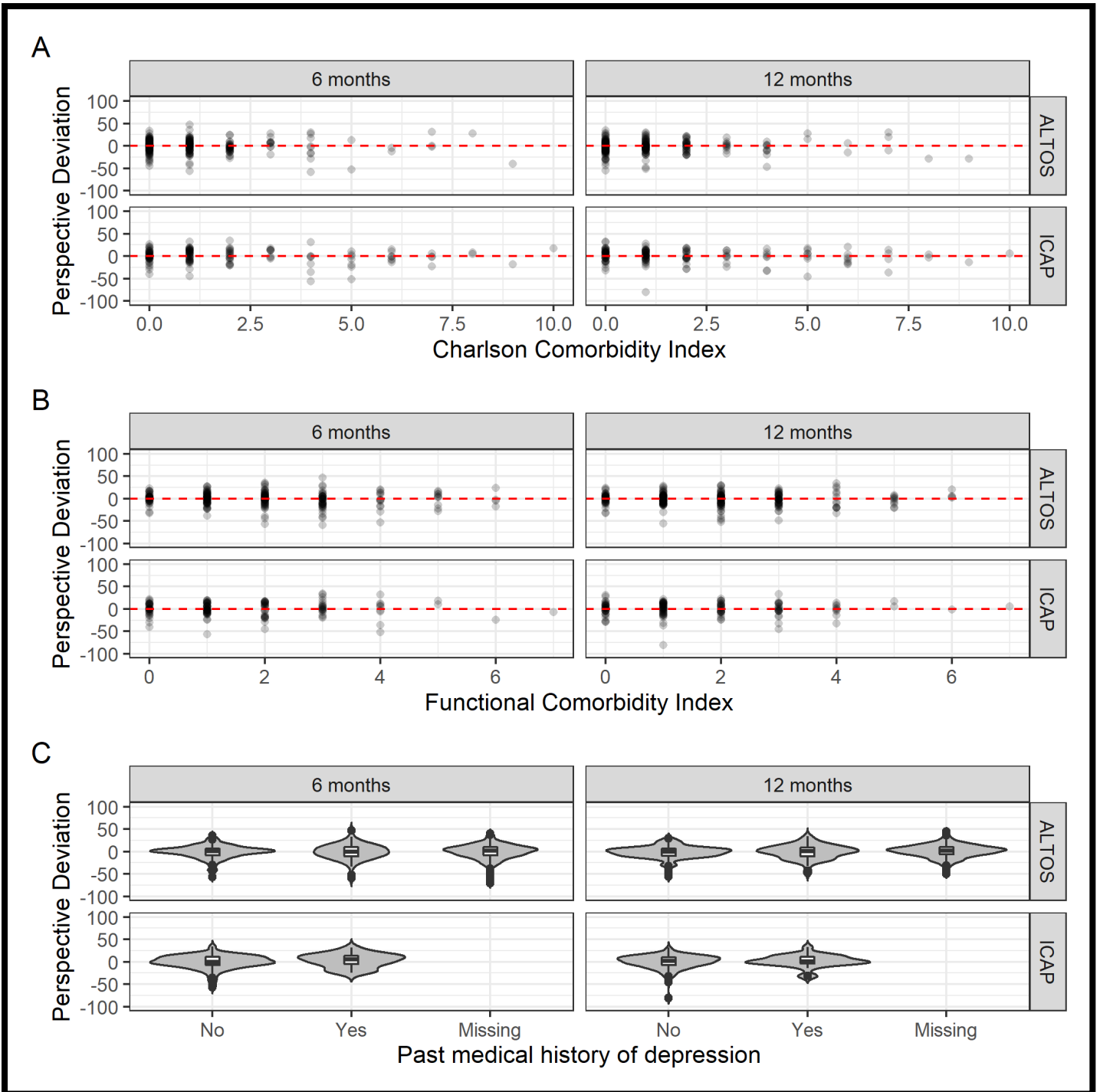
**e-Figure 4: Perspective deviation and continuous demographics** Scatterplots of perspective deviation and (A) age, (B) years of formal education, and (C) median income of patient's home zip code in US dollars. Plots are stratified by study and months since enrollment. The dashed red line indicates a perspective deviation of 0 observed when a survivor's perception of their health matched the expected perception of health given their responses to questions from the SF-36v2 and EQ-5D-3L about physical functioning, social functioning, mental health, bodily pain, role limitations due to physical health or emotional problems, and vitality. **Abbreviations:** ALTOS = ARDSNET Long Term Outcomes Study; ICAP = The Improving Care of Acute Lung Injury Patients study

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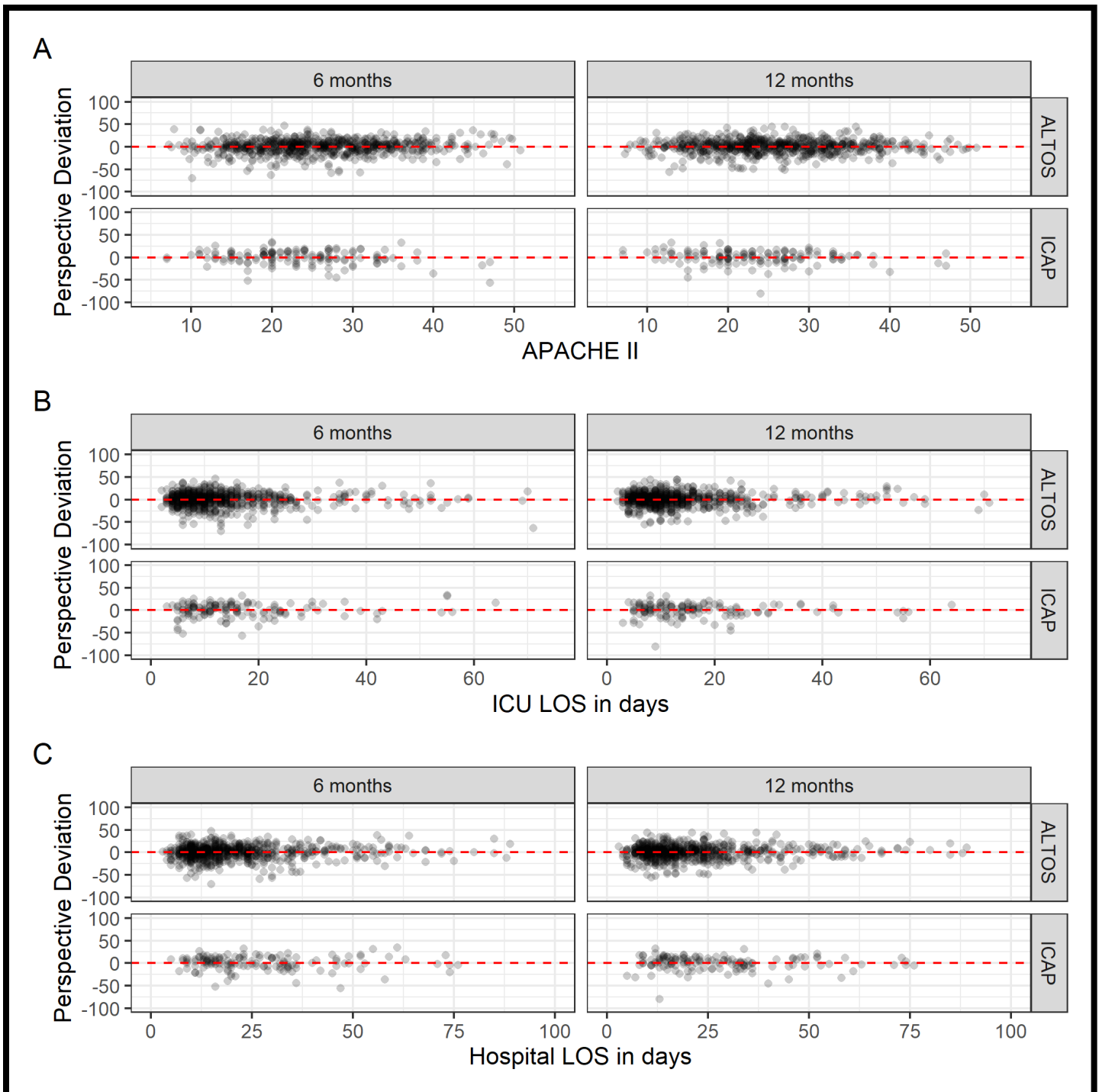




**e-Figure 5: Perspective deviation and categorical demographics** Violin plots of perspective deviation and **(A)** gender, and **(B)** race. Plots are stratified by study and months since enrollment. **Abbreviations:** ALTOS = ARDSNET Long Term Outcomes Study; ICAP = Improving Care of Acute Lung Injury Patients study

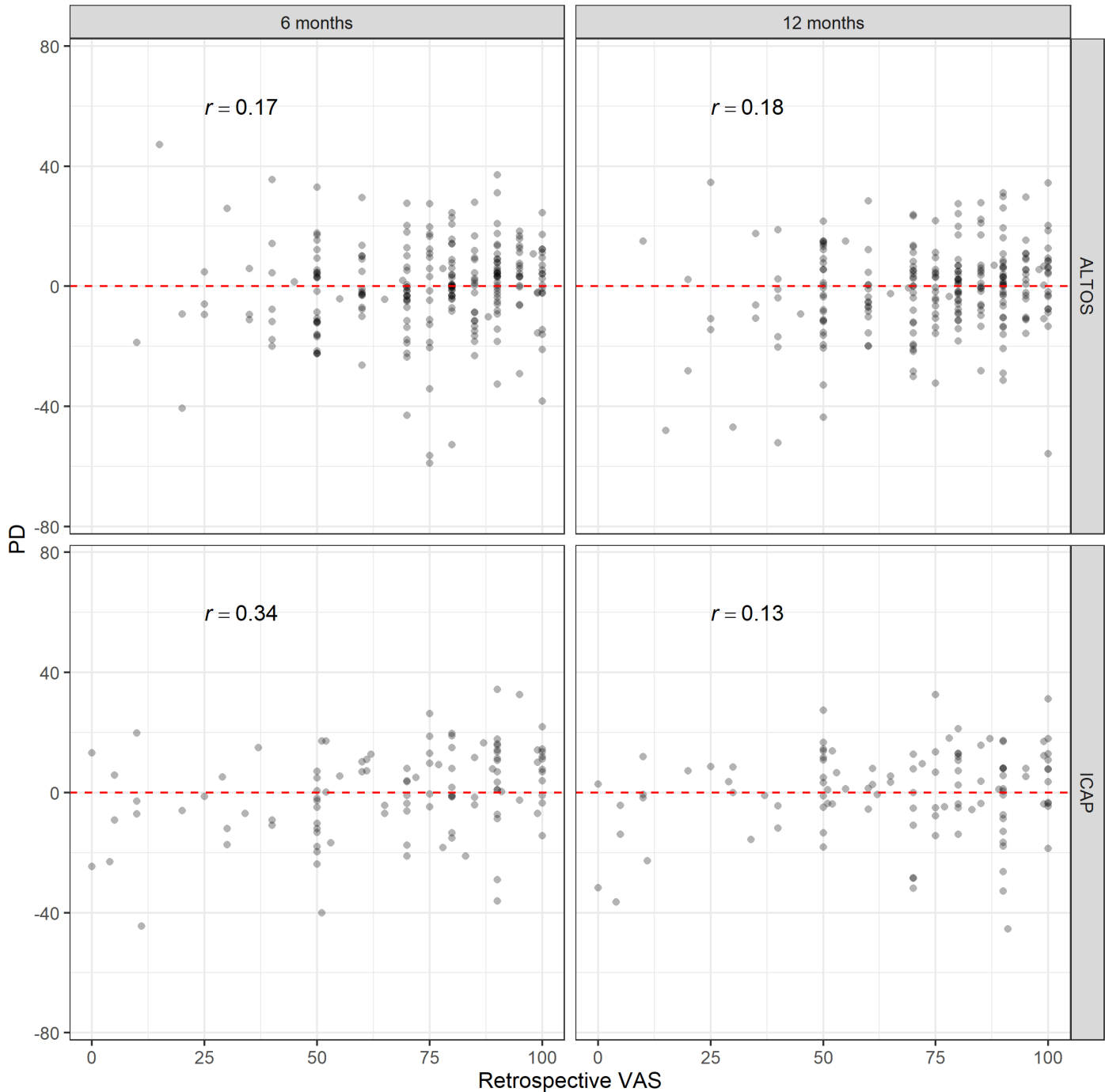


**e-Figure 6: Perspective deviation and pre-ARDS comorbidity** Scatterplots of perspective deviation and **(A)** Charlson score, and **(B)** Functional Comorbidity Index score. Violin plot of perspective deviation and **(C)** past medical history of depression. Plots are stratified by study and months since enrollment. The dashed red line indicates a perspective deviation of 0 observed when a survivor’s perception of their health matched the expected perception of health given their responses to questions from the SF-36v2 and EQ-5D-3L about physical functioning, social functioning, mental health, bodily pain, role limitations due to physical health or emotional problems, and vitality. **Abbreviations:** ALTOS, ARDSNet Long Term Outcomes Study; ARDS, Acute Respiratory Distress Syndrome; ICAP, Improving Care of Acute Lung Injury Patients



**e-Figure 7: Perspective deviation and severity of illness** Scatterplots of perspective deviation and **(A)** APACHE II score, **(B)** ICU length of stay in days, and **(C)** Hospital length of stay in days. Plots are stratified by study and months since enrollment. The dashed red line indicates a perspective deviation of 0 observed when a survivor’s perception of their health matched the expected perception of health given their responses to questions from the SF-36v2 and EQ-5D-3L about physical functioning, social functioning, mental health, bodily pain, role limitations due to physical health or emotional problems, and vitality, energy, and fatigue. **Abbreviations:** ALITOS, ARDSNet Long Term Outcomes Study; APACHE, Acute Physiology and Chronic Health Evaluation; ICAP, Improving Care of Acute Lung Injury Patients; ICU, Intensive Care Unit; LOS, Length of Stay

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**e-Figure 8: Perspective deviation and retrospective VAS score** Plots are stratified by study and months since enrollment. Spearman’s correlation coefficients reported. The dashed red line indicates a perspective deviation of 0 observed when a survivor’s perception of their health matched the expected perception of health given their responses to questions from the SF-36v2 and EQ-5D-3L about physical functioning, social functioning, mental health, bodily pain, role limitations due to physical health or emotional problems, and vitality, energy, and fatigue.

**Abbreviations:** ALTOS, ARDSNet Long Term Outcomes Study; ICAP, Improving Care of Acute Lung Injury Patients