SUPPLEMENTAL INFORMATION

DIGITAL PHYSIOLOGICAL BIOMARKERS PREDICT SYMPTOM CHANGE IN COMPLEX CHRONIC ILLNESS

SI 1. FULL MLM HIERARCHICAL REGRESSION TABLES

SI Table 1.

			Crash Step 1		
Predictors	*Odds Ratios*	*std. Beta*	*CI*	*standardized CI*	*p*
(Intercept)	52.43	99.89	6.65 – 413.58	13.57 – 735.45	**<0.001**
Observation Date	1.00	1.00	1.00 – 1.00	1.00 – 1.00	**<0.001**
Number of Obs	1.00	0.94	1.00 – 1.00	0.87 – 1.01	0.084
Age	1.00	1.03	1.00 – 1.01	0.96 – 1.12	0.378
Gender (M)	1.41	1.16	1.18 – 1.68	1.08 – 1.25	**<0.001**
Sensor Modality	2.30	1.01	0.79 – 6.72	1.00 – 1.01	0.129
Random Effects					
σ^2	3.29				
$\tau_{00\ user\_id\_pk}$	4.36				
ICC	0.57				
$N_{\ user\_id\_pk}$	3295				
Observations	325656				
Marginal R^2 / Conditional R^2	0.003 / 0.571				

			Crash Step 2		
Predictors	*Odds Ratios*	*std. Beta*	*CI*	*standardized CI*	*p*
(Intercept)	39.80	96.27	4.60 – 344.22	11.62 – 797.86	**0.001**
Observation Date	1.00	1.00	1.00 – 1.00	1.00 – 1.00	**<0.001**
Number of Obs	1.00	0.94	1.00 – 1.00	0.89 – 0.99	**0.021**
Age	1.00	1.02	1.00 – 1.01	0.97 – 1.08	0.416
Gender (M)	1.28	1.11	1.13 – 1.46	1.05 – 1.18	**<0.001**
Sensor Modality	2.34	1.01	0.71 – 7.66	1.00 – 1.02	0.161
Crash Prior Day	6.44	2.24	6.30 – 6.59	2.22 – 2.26	**<0.001**

Random Effects

σ^2	3.29
$\tau_{00\ user\_id\_pk}$	2.16
ICC	0.40
$N_{\ user\_id\_pk}$	3295
Observations	325656
Marginal R^2 / Conditional R^2	0.110 / 0.463

SI Table 2.

			Fatigue Step 1		
Predictors	*Estimates*	*std. Beta*	*CI*	*standardized CI*	*p*
(Intercept)	2.04	0.51	1.68 – 2.40	0.10 – 0.91	**<0.001**
Observation Date	-0.00	-0.00	-0.00 – -0.00	-0.00 – -0.00	**0.017**
Number of Obs	-0.00	-0.01	-0.00 – 0.00	-0.03 – 0.01	0.543
Age	0.00	0.02	-0.00 – 0.00	-0.01 – 0.04	0.176
Gender (M)	0.13	0.07	0.09 – 0.18	0.05 – 0.09	**<0.001**
Sensor Modality	-0.00	-0.00	-0.27 – 0.26	-0.00 – 0.00	0.982
Random Effects					
σ^2	0.36				
$\tau_{00\ user\_id\_pk}$	0.31				
ICC	0.46				
$N_{\ user\_id\_pk}$	3767				
Observations	459609				
Marginal R^2 / Conditional R^2	0.005 / 0.463				

			Fatigue Step 2		
Predictors	*Estimates*	*std. Beta*	*CI*	*standardized CI*	*p*
(Intercept)	1.39	0.34	1.06 – 1.73	-0.05 – 0.72	**<0.001**
Observation Date	-0.00	-0.00	-0.00 – 0.00	-0.00 – 0.00	0.098
Number of Obs	-0.00	-0.00	-0.00 – 0.00	-0.02 – 0.01	0.601
Age	0.00	0.01	-0.00 – 0.00	-0.00 – 0.03	0.150

Gender (M)	0.09	0.05	0.06 – 0.12	0.03 – 0.06	**<0.001**
Sensor Modality	0.03	0.00	-0.22 – 0.28	-0.00 – 0.00	0.827
Fatigue Prior Day	0.31	0.31	0.31 – 0.31	0.31 – 0.31	**<0.001**

Random Effects

σ^2	0.33
$\tau_{00\ user\_id\_pk}$	0.15
ICC	0.31
$N_{user\_id\_pk}$	3767
Observations	459609
Marginal R^2 / Conditional R^2	0.127 / 0.395

SI Table 3

			Brain Fog Step 1		
Predictors	*Estimates*	*std. Beta*	*CI*	*standardized CI*	*p*
(Intercept)	2.95	1.88	2.56 – 3.34	1.50 – 2.26	**<0.001**
Observation Date	-0.00	-0.00	-0.00 – -0.00	-0.00 – -0.00	**<0.001**
Number of Obs	-0.00	-0.02	-0.00 – 0.00	-0.04 – 0.01	0.201
Age	-0.00	-0.01	-0.00 – 0.00	-0.03 – 0.02	0.633
Gender (M)	0.11	0.05	0.06 – 0.17	0.03 – 0.08	**<0.001**
Sensor Modality	-0.03	-0.00	-0.28 – 0.23	-0.00 – 0.00	0.844

Random Effects

σ^2	0.34
$\tau_{00\ user\_id\_pk}$	0.50
ICC	0.59
$N_{user\_id\_pk}$	3379
Observations	402858
Marginal R^2 / Conditional R^2	0.003 / 0.594

			Brain Fog Step 2		
Predictors	*Estimates*	*std. Beta*	*CI*	*standardized CI*	*p*
(Intercept)	1.76	1.15	1.43 – 2.10	0.80 – 1.49	**<0.001**

Observation Date	-0.00	-0.00	-0.00 – -0.00	-0.00 – -0.00	**<0.001**
Number of Obs	-0.00	-0.01	-0.00 – 0.00	-0.02 – 0.01	0.246
Age	-0.00	-0.00	-0.00 – 0.00	-0.02 – 0.01	0.642
Gender (M)	0.07	0.03	0.04 – 0.10	0.02 – 0.05	**<0.001**
Sensor Modality	0.05	0.00	-0.18 – 0.28	-0.00 – 0.00	0.682
Brain Fog Prior Day	0.41	0.41	0.41 – 0.42	0.41 – 0.42	**<0.001**

Random Effects

σ^2	0.29
$\tau_{00\ user\_id\_pk}$	0.17
ICC	0.37
$N_{\ user\_id\_pk}$	3379
Observations	402858
Marginal R^2 / Conditional R^2	0.249 / 0.528

SI 2. GLMER MLM REGRESSION TABLES

Supplementary Table 4. GLMER predicting dichotomized Fatigue

	Fatigue Dichotomized				
Predictors	*Odds Ratios*	*std. Beta*	*CI*	*standardized CI*	*p*
(Intercept)	1.16	22.67	0.15 – 8.86	4.73 – 108.63	0.885
HR (WP)	1.01	1.06	1.01 – 1.01	1.05 – 1.07	**<0.001**
HRV (WP)	0.99	0.94	0.99 – 0.99	0.93 – 0.95	**<0.001**
BreathRate (WP)	1.00	1.00	1.00 – 1.00	0.99 – 1.01	0.514
7 Day HR CoV (WP)	3.12	1.04	2.35 – 4.15	1.03 – 1.05	**<0.001**
7 Day HRV CoV (WP)	1.84	1.03	1.47 – 2.30	1.02 – 1.04	**<0.001**

7 Day BreathRate CoV (WP)	1.10	1.01	0.98 – 1.24	1.00 – 1.02	0.117
HR (BP)	1.02	1.18	1.01 – 1.03	1.09 – 1.28	**<0.001**
HRV (BP)	0.99	0.94	0.98 – 1.00	0.86 – 1.01	0.104
BreathRate (BP)	1.06	1.08	1.01 – 1.11	1.01 – 1.15	**0.029**
HR CoV (BP)	320.64	1.17	25.71 – 3998.21	1.09 – 1.26	**<0.001**
HRV CoV (BP)	30.57	1.14	3.64 – 256.54	1.05 – 1.24	**0.002**
BreathRate CoV (BP)	1.27	1.01	0.31 – 5.19	0.94 – 1.09	0.738
Observation Date	1.00	1.00	1.00 – 1.00	1.00 – 1.00	**<0.001**
max_obs	1.00	1.16	1.00 – 1.00	1.09 – 1.23	**<0.001**
Age	1.00	1.06	1.00 – 1.01	0.98 – 1.14	0.119
Gender (F)	1.46	1.46	1.21 – 1.76	1.21 – 1.76	**<0.001**
Gender (NB)	1.62	1.62	1.20 – 2.21	1.20 – 2.21	**0.002**
Fatigue_Dicho_1d_lag1	3.22	3.22	3.17 – 3.27	3.17 – 3.27	**<0.001**
Source Device	1.27	1.00	0.37 – 4.38	0.99 – 1.01	0.710

Random Effects

σ^2	3.29
$\tau_{00\ user\_id\_pk}$	3.21
ICC	0.49
$N_{\ user\_id\_pk}$	3624
Observations	470523
Marginal R^2 / Conditional R^2	0.078 / 0.534

Supplementary Table 5. GLMER predicting dichotomized Brain Fog

	Brain Fog Dichotomized				
Predictors	*Odds Ratios*	*std. Beta*	*CI*	*standardized CI*	*p*
(Intercept)	0.14	1.92	0.01 – 1.46	0.32 – 11.55	0.101

HR (WP)	1.01	1.04	1.00 – 1.01	1.03 – 1.05	**<0.001**
HRV (WP)	1.00	0.97	0.99 – 1.00	0.96 – 0.98	**<0.001**
BreathRate (WP)	1.00	1.00	1.00 – 1.00	0.99 – 1.01	0.476
7 Day HR CoV (WP)	1.89	1.02	1.39 – 2.57	1.01 – 1.03	**<0.001**
7 Day HRV CoV (WP)	1.44	1.02	1.13 – 1.85	1.01 – 1.03	**0.003**
7 Day BreathRate CoV (WP)	1.00	1.00	0.87 – 1.14	0.99 – 1.01	0.968
HR (BP)	1.02	1.16	1.01 – 1.03	1.06 – 1.26	**0.002**
HRV (BP)	0.99	0.93	0.97 – 1.00	0.85 – 1.01	0.096
BreathRate (BP)	1.08	1.11	1.02 – 1.14	1.03 – 1.20	**0.007**
HR CoV (BP)	16180.11	1.31	918.16 – 285131.88	1.21 – 1.41	**<0.001**
HRV CoV (BP)	7.47	1.08	0.65 – 85.37	0.98 – 1.19	0.106
BreathRate CoV (BP)	1.61	1.02	0.32 – 8.09	0.94 – 1.11	0.563
Observation Date	1.00	1.00	1.00 – 1.00	1.00 – 1.00	**0.026**
max_obs	1.00	1.04	1.00 – 1.00	0.97 – 1.11	0.276
Age	1.00	0.96	0.99 – 1.00	0.89 – 1.05	0.405
Gender (F)	1.22	1.22	0.98 – 1.52	0.98 – 1.52	0.072
Gender (NB)	1.78	1.78	1.25 – 2.52	1.25 – 2.52	**0.001**
BrainFog_Dicho_1d_lag1	5.18	5.18	5.08 – 5.28	5.08 – 5.28	**<0.001**
Source Device	2.07	1.01	0.70 – 6.12	1.00 – 1.01	0.187

Random Effects

σ^2	3.29
$\tau_{00\ user\_id\_pk}$	3.92
ICC	0.54
$N_{\ user\_id\_pk}$	3241
Observations	412180
Marginal R^2 / Conditional R^2	0.117 / 0.597

SI 3. Autoregressive MLM predicting First Instance of Crash

Supplementary Table 6. Autoregressive MLM predicting First Instance of Crash

	Crash 1st				
Predictors	*Odds Ratios*	*std. Beta*	*CI*	*standardized CI*	*p*
(Intercept)	1963778.35	216190.27	37136.66 – 103844168.66	15328.29 – 3049148.53	**<0.001**
HR (WP)	1.01	1.08	1.01 – 1.02	1.06 – 1.09	**<0.001**
HRV (WP)	0.99	0.94	0.99 – 0.99	0.92 – 0.95	**<0.001**
BreathRate (WP)	1.00	1.00	1.00 – 1.00	0.99 – 1.01	0.891
7 Day HR CoV (WP)	1.44	1.01	0.93 – 2.21	1.00 – 1.03	0.099
7 Day HRV CoV (WP)	1.53	1.02	1.08 – 2.18	1.00 – 1.03	**0.018**
7 Day BreathRate CoV (WP)	0.98	1.00	0.81 – 1.19	0.99 – 1.01	0.876
HR (BP)	1.00	0.98	0.99 – 1.00	0.92 – 1.04	0.441
HRV (BP)	0.98	0.91	0.98 – 0.99	0.86 – 0.97	**0.002**
BreathRate (BP)	1.02	1.03	0.99 – 1.06	0.98 – 1.09	0.208
HR CoV (BP)	58.48	1.12	8.82 – 387.59	1.06 – 1.18	**<0.001**
HRV CoV (BP)	8.39	1.08	1.64 – 42.81	1.02 – 1.15	**0.011**
BreathRate CoV (BP)	1.24	1.01	0.42 – 3.64	0.96 – 1.07	0.699

Observation Date	1.00	1.00	1.00 – 1.00	1.00 – 1.00	**<0.001**
Number of Obs	1.00	0.85	1.00 – 1.00	0.81 – 0.89	**<0.001**
Age	1.00	0.96	0.99 – 1.00	0.91 – 1.02	0.185
Gender (F)	1.16	1.16	1.01 – 1.34	1.01 – 1.34	**0.036**
Gender (NB)	1.27	1.27	1.00 – 1.60	1.00 – 1.60	**0.047**
Source Device	0.45	0.99	0.11 – 1.79	0.99 – 1.00	0.257

Random Effects

σ^2	3.29
$\tau_{00\ user\_id\_pk}$	1.22
ICC	0.27
$N_{\ user\_id\_pk}$	2992
Observations	294537
Marginal R^2 / Conditional R^2	0.017 / 0.283

Supplementary Table 7. Autoregressive MLM predicting First Instance of Fatigue

	Fatigue 1st				
Predictors	*Odds Ratios*	*std. Beta*	*CI*	*standardized CI*	*p*
(Intercept)	14680.35	25174.85	1759.73 – 122468.93	3314.83 – 191193.22	**<0.001**
HR (WP)	1.01	1.06	1.01 – 1.01	1.05 – 1.07	**<0.001**
HRV (WP)	0.99	0.94	0.99 – 0.99	0.93 – 0.95	**<0.001**
BreathRate (WP)	1.00	1.00	1.00 – 1.00	0.99 – 1.01	0.778
7 Day HR CoV (WP)	1.39	1.01	0.96 – 2.03	1.00 – 1.02	0.082

7 Day HRV CoV (WP)	1.43	1.01	1.07 – 1.92	1.00 – 1.03	**0.017**
7 Day BreathRate CoV (WP)	1.03	1.00	0.88 – 1.21	0.99 – 1.01	0.674
HR (BP)	1.00	1.03	1.00 – 1.01	1.00 – 1.07	0.055
HRV (BP)	1.00	0.98	0.99 – 1.00	0.95 – 1.02	0.342
BreathRate (BP)	1.03	1.04	1.01 – 1.05	1.01 – 1.07	**0.007**
HR CoV (BP)	5.47	1.04	1.81 – 16.50	1.02 – 1.07	**0.003**
HRV CoV (BP)	7.05	1.08	2.77 – 17.94	1.04 – 1.11	**<0.001**
BreathRate CoV (BP)	0.70	0.98	0.38 – 1.30	0.95 – 1.01	0.260
Observation Date	1.00	1.00	1.00 – 1.00	1.00 – 1.00	**<0.001**
Number of Obs	1.00	0.96	1.00 – 1.00	0.93 – 0.98	**0.002**
Age	1.00	0.97	1.00 – 1.00	0.94 – 1.00	0.076
Gender (F)	1.20	1.20	1.11 – 1.30	1.11 – 1.30	**<0.001**
Gender (NB)	1.29	1.29	1.14 – 1.48	1.14 – 1.48	**<0.001**
Source Device	1.78	1.00	0.42 – 7.47	0.99 – 1.01	0.433

Random Effects

σ^2	3.29
$\tau_{00\ user\_id\_pk}$	0.32
ICC	0.09
$N_{user\_id\_pk}$	3044
Observations	195500
Marginal R^2 / Conditional R^2	0.010 / 0.099

Supplementary Table 8. Autoregressive MLM predicting First Instance of Brain Fog

	Brain Fog 1st				
Predictors	*Odds Ratios*	*std. Beta*	*CI*	*standardized CI*	*p*
(Intercept)	930711.08	1699338.92	69822.39 – 12406093.56	156494.53 – 18452739.63	**<0.001**
HR (WP)	1.01	1.04	1.00 – 1.01	1.03 – 1.05	**<0.001**
HRV (WP)	0.99	0.97	0.99 – 1.00	0.96 – 0.98	**<0.001**
BreathRate (WP)	1.00	1.00	1.00 – 1.00	0.99 – 1.01	0.865
7 Day HR CoV (WP)	1.49	1.01	1.00 – 2.23	1.00 – 1.03	0.051
7 Day HRV CoV (WP)	1.40	1.01	1.02 – 1.93	1.00 – 1.03	**0.040**
7 Day BreathRate CoV (WP)	1.12	1.01	0.94 – 1.33	1.00 – 1.02	0.218
HR (BP)	1.01	1.06	1.00 – 1.01	1.00 – 1.12	**0.046**
HRV (BP)	0.99	0.95	0.98 – 1.00	0.90 – 1.01	0.104
BreathRate (BP)	1.05	1.07	1.01 – 1.09	1.02 – 1.13	**0.007**
HR CoV (BP)	69.48	1.12	10.59 – 455.98	1.06 – 1.17	**<0.001**
HRV CoV (BP)	6.90	1.08	1.41 – 33.75	1.01 – 1.14	**0.017**
BreathRate CoV (BP)	0.85	0.99	0.29 – 2.43	0.94 – 1.05	0.756
Observation Date	1.00	1.00	1.00 – 1.00	1.00 – 1.00	**<0.001**
Number of Obs	1.00	0.89	1.00 – 1.00	0.85 – 0.93	**<0.001**
Age	0.99	0.92	0.99 – 1.00	0.87 – 0.97	**0.002**

Gender (F)	1.23	1.23	1.07 – 1.42	1.07 – 1.42	**0.004**
Gender (NB)	1.54	1.54	1.22 – 1.93	1.22 – 1.93	**<0.001**
Source Device	3.14	1.01	1.08 – 9.14	1.00 – 1.02	**0.035**

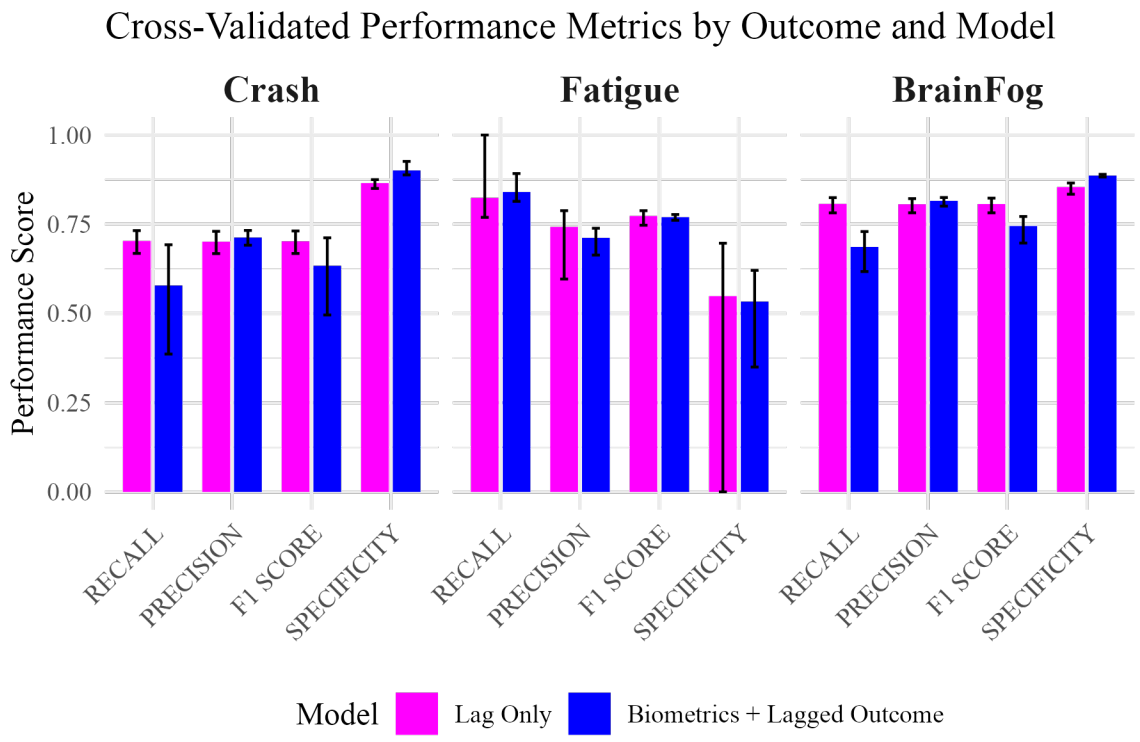
Random Effects

σ^2	3.29
$\tau_{00\ user\_id\_pk}$	1.30
ICC	0.28
$N_{\ user\_id\_pk}$	2985
Observations	273194
Marginal R^2 / Conditional R^2	0.018 / 0.296

SI 4. Predictive model detection performance

Supplementary Table 9. Detection Performance Scores in Primary Predictive Models

		Recall	Precision	F1 Score	Specificity
Lag Only	*Crash*	0.70	0.70	0.70	0.87
	Fatigue	0.82	0.74	0.77	0.55
	Brain Fog	0.81	0.81	0.81	0.85
Biometrics + Day Prior Outcome	*Crash*	0.58	0.71	0.63	0.90
	Fatigue	0.84	0.71	0.77	0.53
	Brain Fog	0.69	0.82	0.75	0.89



Supplementary Figure 1. Detection Performance Scores
Detection metrics for primary prediction models. Each panel corresponds to a detection metrics for one of three symptom outcomes: Crash, Fatigue, and Brain Fog. Within each panel, five classification metrics are shown along the x-axis: Precision, Recall, F1 Score, Specificity, and False Positive Rate (FPR). Performance is plotted for two model types: models using only lag-only features (colored magenta) and models that also include biometrics + lagged outcomes (colored blue). Bars represent mean classification scores, with vertical error bars showing the minimum and maximum values across cross-validation folds .

SI 5. Predictive model metrics (with random effects)

Supplementary Table 10. Mean ROC-AUC, Recall, Precision, F1 for Crash, Fatigue, and Brain Fog Using Lag Only and Lag + Biometric (with random effects)

		ROC-AUC	Recall	Precision	F1 Score	Specificity
Lag Outcome Only	*Crash*	0.87	0.60	0.74	0.66	0.90
	Fatigue	0.88	0.84	0.75	0.79	0.60
	Brain Fog	0.91	0.78	0.82	0.80	0.87
	Crash	0.88	0.59	0.75	0.66	0.91
	Fatigue	0.88	0.83	0.75	0.79	0.63

Biometrics + Lag Outcome	*Brain Fog*	0.91	0.78	0.83	0.80	0.88

SI 6. Biometric only predictive model metrics (with and without random effects)

Supplementary Table 11. Mean ROC-AUC for Crash, Fatigue, and Brain Fog Using Biometrics Only

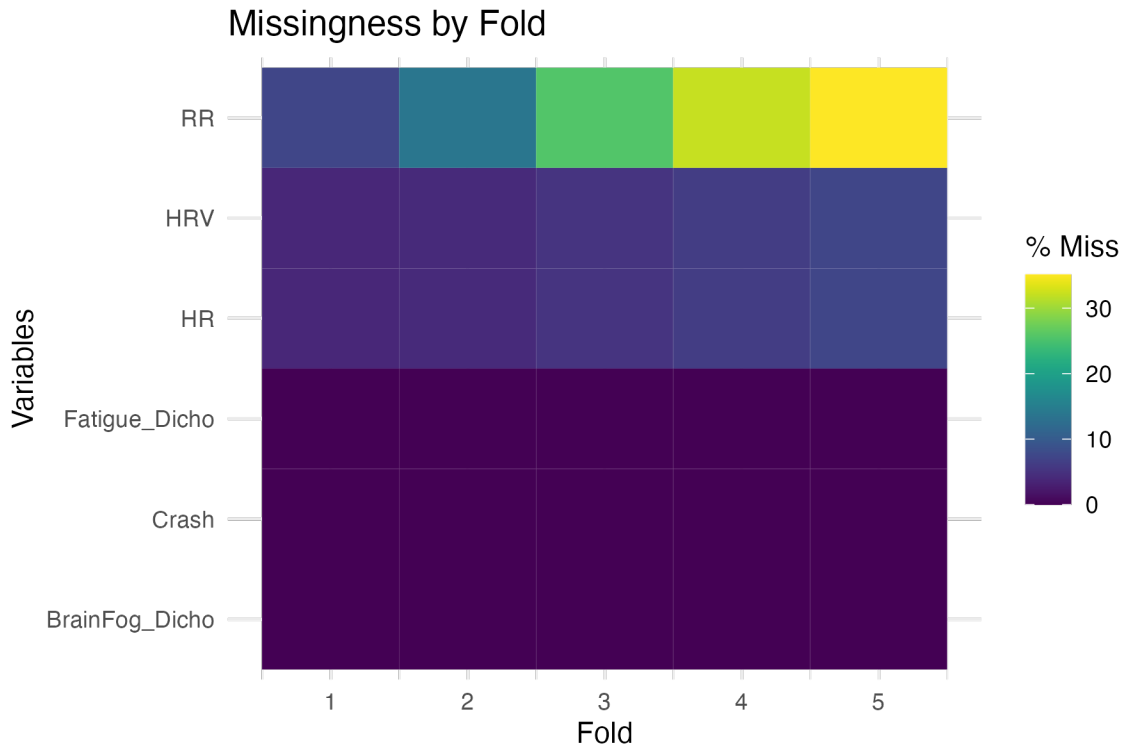
		ROC-AUC	
	Outcome	**Stratified CV (no-Random Effects)**	**Stratified CV (Random Effects)**
Biometrics Only	*Crash*	0.58	0.78
	Fatigue	0.57	0.77
	Brain Fog	0.59	0.88

Supplementary Table 12. Mean Recall, Precision, F1 for Crash, Fatigue, and Brain Fog Using Biometrics Only

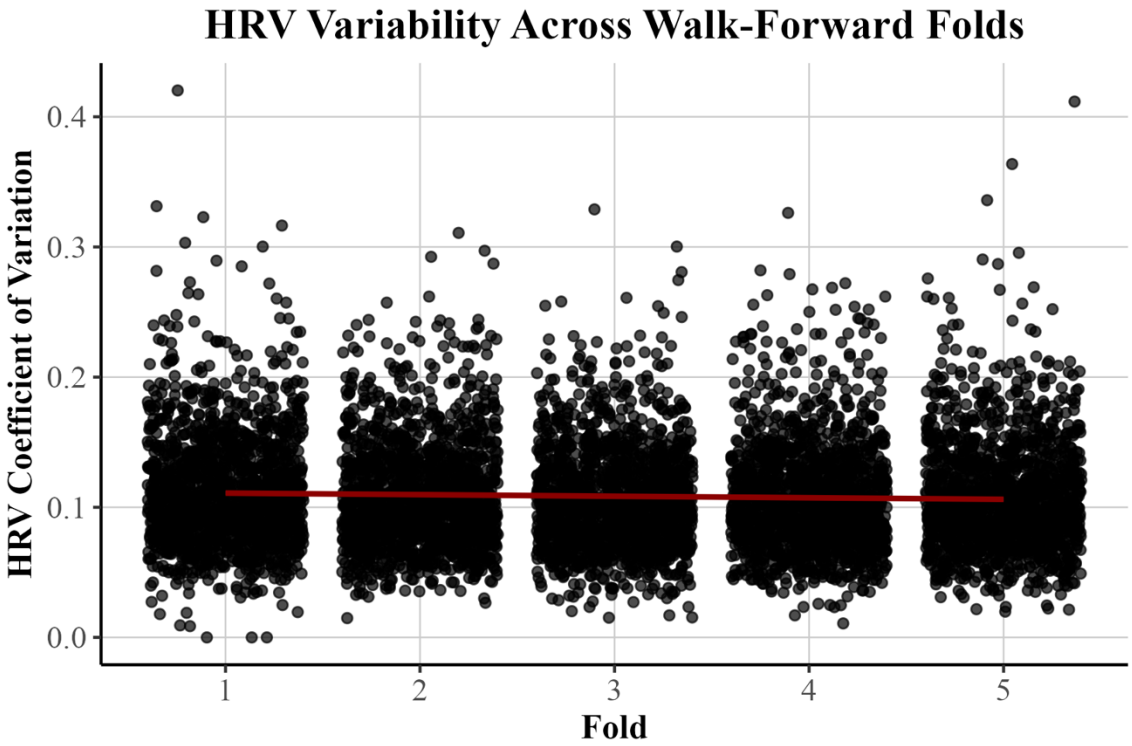
		Recall	
	Outcome	**Stratified CV (no-Random Effects)**	**Stratified CV (Random Effects)**
Biometrics Only	*Crash*	0.02	0.46
	Fatigue	0.99	0.82
	Brain Fog	0.17	0.72
		Precision	
	Outcome	**Stratified CV (no-Random Effects)**	**Stratified CV (Random Effects)**
Biometrics Only	*Crash*	0.45	0.71
	Fatigue	0.58	0.72
	Brain Fog	0.56	0.79
		F1 Score	
	Outcome	**Stratified CV (no-Random Effects)**	**Stratified CV (Random Effects)**
Biometrics Only	*Crash*	0.05	0.56
	Fatigue	0.73	0.77

	Brain Fog	0.25	0.76
		Specificity	
	Outcome	**Stratified CV (no-Random Effects)**	**Stratified CV (Random Effects)**
Biometrics Only	*Crash*	0.99	0.92
	Fatigue	0.01	0.57
	Brain Fog	0.90	0.86

SI 7. Missingness Visualizations



Supplementary Figure 2.
Missingness heatmap across five cross-validation folds. Respiration rate (RR) shows the highest level of missingness, reaching up to 30% in the final fold. In contrast, heart rate variability (HRV), heart rate (HR), and symptom outcome variables (Crash, Fatigue, Brain Fog) exhibit relatively low levels of missing data across all folds.



Supplementary Figure 3.
Change in HRV variability and overtime, across each walk-forward fold. Scatterplot showing HRV coefficient of variation (CoV) as a function of fold number. The null trend suggests that HRV variability is not demonstrating systematic change over time.