

Supplementary Information

Factors Associated with Reduction in Quality of Life After SARS-CoV-2 Infection

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Supplementary Table S1

Independent variables used in the recursive feature elimination and how they were measured.

Variables	Measures
Fatigue	FACIT-Fatigue Scale
Personal stress	PSS total score
Cognitive functioning	MoCA total score
Subjective cognitive decline	Yes, No
Subjective word finding disorder	Yes, No
Sex	Male, Female
Age	Years
BMI	Weight, Height
Employment (At follow-up: Loss of employment)	Employed, Not employed (Yes, No)
Partner	Yes, No
Vaccinated	Yes, No
More than 12 years education	Yes, No
Treatment during initial SARS-CoV-2 infection	Yes, No
Treatment at home	Yes, No
Stationary treatment	Yes, No
Treatment in intensive care unit	Yes, No
Treatment with ventilation	Yes, No
Initial infection symptoms	Number of symptoms during initial SARS-CoV-2 infection
Time since infection	Days between initial SARS-CoV-2 infection and assessment
Pre-diagnosed diseases	
Any neurological/psychiatric disease	Yes, No
COPD	Yes, No
Sleep apnea	Yes, No
Tumor disease	Yes, No
Depression	Yes, No
Anxiety	Yes, No
Migraine	Yes, No
Remaining symptoms	Number of symptoms remaining from initial SARS-CoV-2 infection
Smelling disturbance	Yes, No
Impaired sense of taste	Yes, No
Stomach pain	Yes, No
Confusion	Yes, No
Diarrhea	Yes, No
Vomiting	Yes, No
Nausea	Yes, No
Vertigo	Yes, No
Coughing	Yes, No
Hoarseness	Yes, No
Sore throat	Yes, No
Running nose	Yes, No
Chills	Yes, No
Muscle pain	Yes, No
Joint pain	Yes, No
Shortness of breath	Yes, No
Wheezing	Yes, No
Chest pain	Yes, No
Rash	Yes, No
Fever	Yes, No
Headache	Yes, No
Hair loss	Yes, No

Note. Highlighted variables were also selected for the follow-up Analyses. BMI, Body-Mass-Index; EQ-5D-5L, European Quality of Life 5 Dimensions 5 Level Version; FACIT-Fatigue Scale, Functional Assessment of Chronic Fatigue Illness – Fatigue Subscore; MoCA, Montreal Cognitive Assessment; PSS, Perceived Stress Scale.

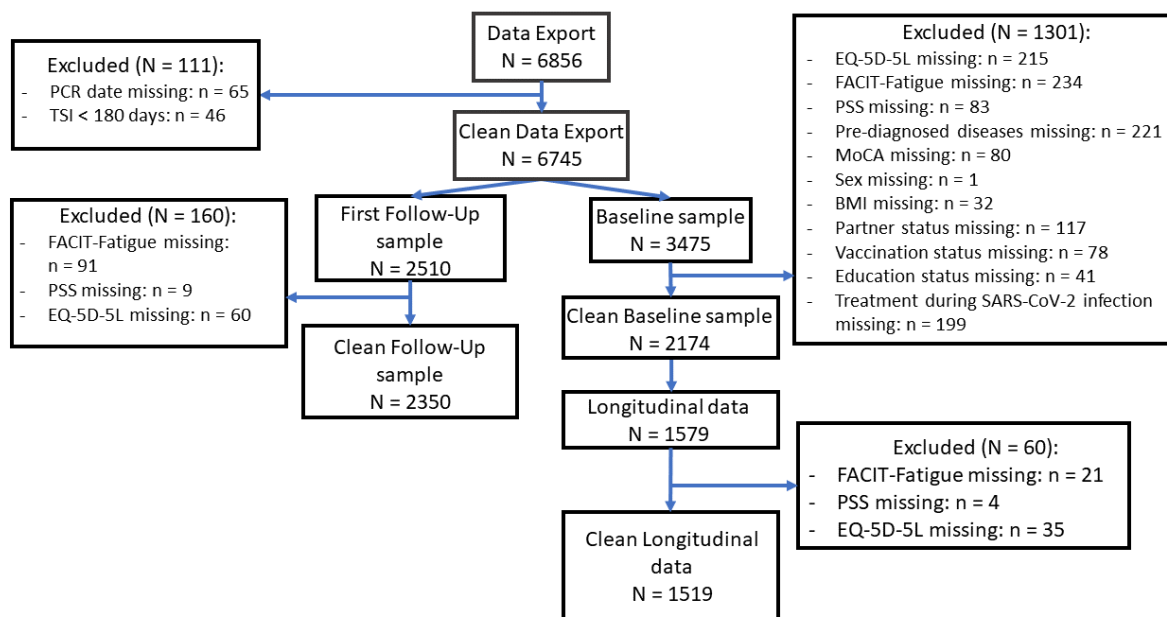
Supplementary Table S2

Sociodemographic and clinical characteristics of the COVIDOM study sample at baseline.

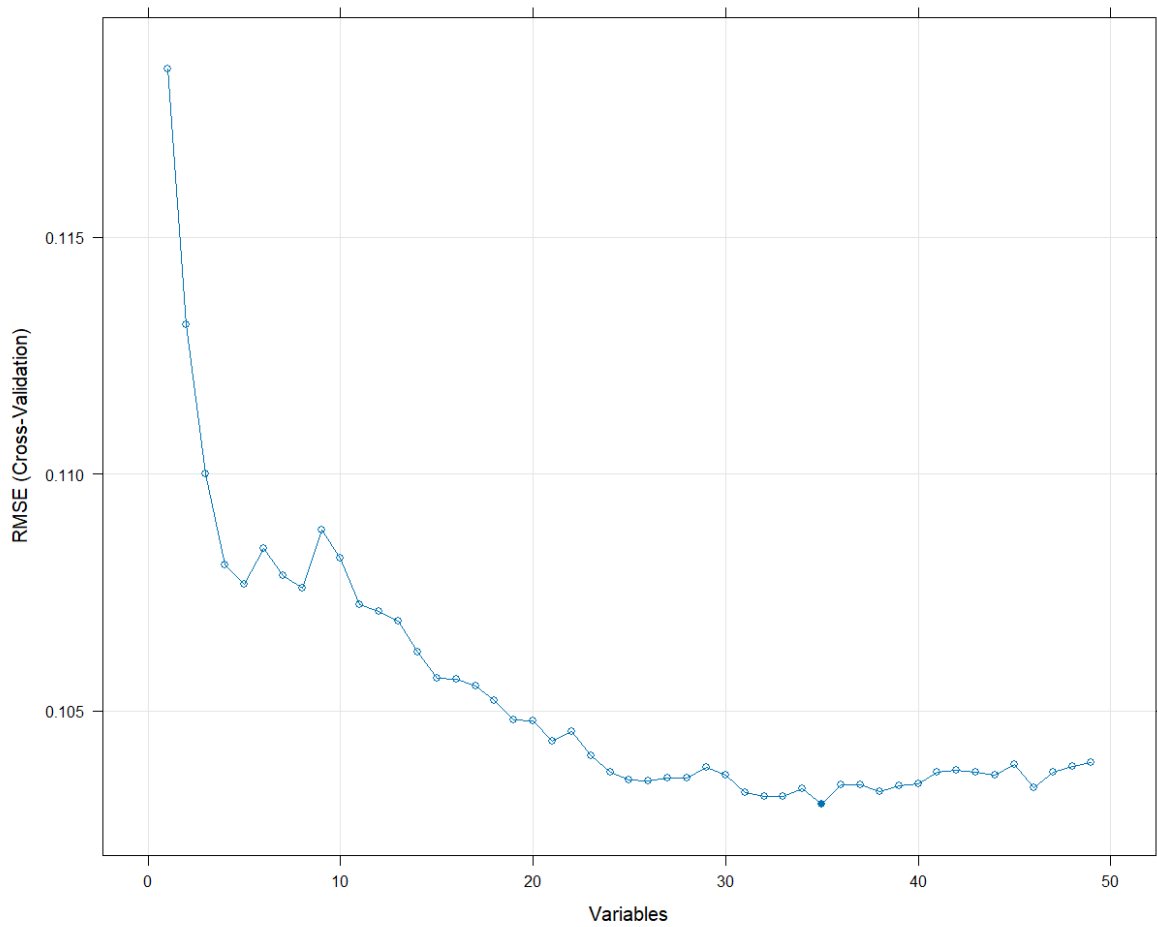
Characteristics [N]	Baseline = 3475	Follow-Up = 2510		
sex	Missing = 2			
Female [N (%)]	1944 (56)		1422 (57)	
Male [N (%)]	1529 (44)		1088 (43)	
Age [years]				
18-34 [N (%)]	1078 (31)		712 (28)	
35-49 [N (%)]	952 (27)		652 (26)	
50-64 [N (%)]	1091 (31)		851 (34)	
65-88 [N (%)]	354 (10)		295 (12)	
Unemployment				
Yes [N (%)]	628 (18)		-	
BMI	Missing = 39			
Underweight [N (%)]	44 (1)		-	
Normal weight [N (%)]	1392 (40)		-	
Overweight [N (%)]	1164 (33)		-	
Obese [N (%)]	836 (24)		-	
Time between initial SARS-CoV-2 infection and baseline				
6 – 9 months [N (%)]	1618 (47)		-	
9 – 12 months [N (%)]	1334 (38)		-	
≥12 months [N (%)]	523 (15)		-	
Number of initial infection symptoms		Missing = 30		
Asymptomatic [N (%)]	306 (9)		202 (8)	
1 – 5 [N (%)]	528 (15)		396 (16)	
6 – 8 [N (%)]	701 (20)		493 (20)	
9 – 11 [N (%)]	783 (23)		560 (22)	
12 – 21 [N (%)]	1157 (33)		829 (33)	
Number of remaining symptoms				
Asymptomatic [N (%)]	1912 (55)		1433 (57)	
1 – 5 [N (%)]	1353 (39)		974 (39)	
6 – 8 [N (%)]	155 (4)		74 (3)	
9 – 11 [N (%)]	43 (1)		24 (1)	
12 – 21 [N (%)]	12 (< 1)		5 (< 1)	
Clinically relevant fatigue (FACIT-Fatigue Scale)	Missing = 266		Missing = 91	
Yes	689 (20)		444 (18)	
Pre-diagnosed COVID-19 comorbidity		Missings		Missings
Any neurological/psychiatric disorder	841 (24)	11	602	110
Depression	387 (11)	113	290	101
Migraine	309 (10)	92	220	103
Anxiety	108 (3)	94	71	83
Apnea	146 (4)	70	113	101

COPD	53 (1)	92	38	73
Tumor	48 (1)	58	30	40
EQ-5D-5L “mobility”	Missing = 176	Missing = 62		
No problems	2544 (73)	1961 (78)		
Slight problems	459 (13)	293 (12)		
Moderate problems	220 (6)	150 (6)		
Major problems	73 (2)	44 (2)		
Extreme problems	3 (< 1)	0 (0)		
EQ-5D-5L “self-care”	Missing = 172	Missing = 62		
No problems	3168 (91)	2348 (94)		
Slight problems	91 (3)	67 (3)		
Moderate problems	29 (< 1)	23 (1)		
Major problems	10 (< 1)	9 (< 1)		
Extreme problems	5 (< 1)	1 (< 1)		
EQ-5D-5L “usual activities”	Missing = 177	Missing = 66		
No problems	2036 (59)	1647 (66)		
Slight problems	756 (22)	522 (21)		
Moderate problems	338 (10)	176 (7)		
Major problems	150 (4)	89 (4)		
Extreme problems	18 (< 1)	10 (< 1)		
EQ-5D-5L “pain/discomfort”	Missing = 170	Missing = 63		
No problems	1478 (43)	1306 (52)		
Slight problems	1073 (31)	684 (27)		
Moderate problems	553 (16)	339 (14)		
Major problems	186 (5)	108 (4)		
Extreme problems	15 (< 1)	10 (< 1)		
EQ-5D-5L “anxiety/depression”	Missing = 178	Missing = 63		
No problems	2041 (59)	1614 (64)		
Slight problems	802 (23)	556 (22)		
Moderate problems	294 (8)	179 (7)		
Major problems	132 (4)	80 (3)		
Extreme problems	28 (< 1)	18 (< 1)		

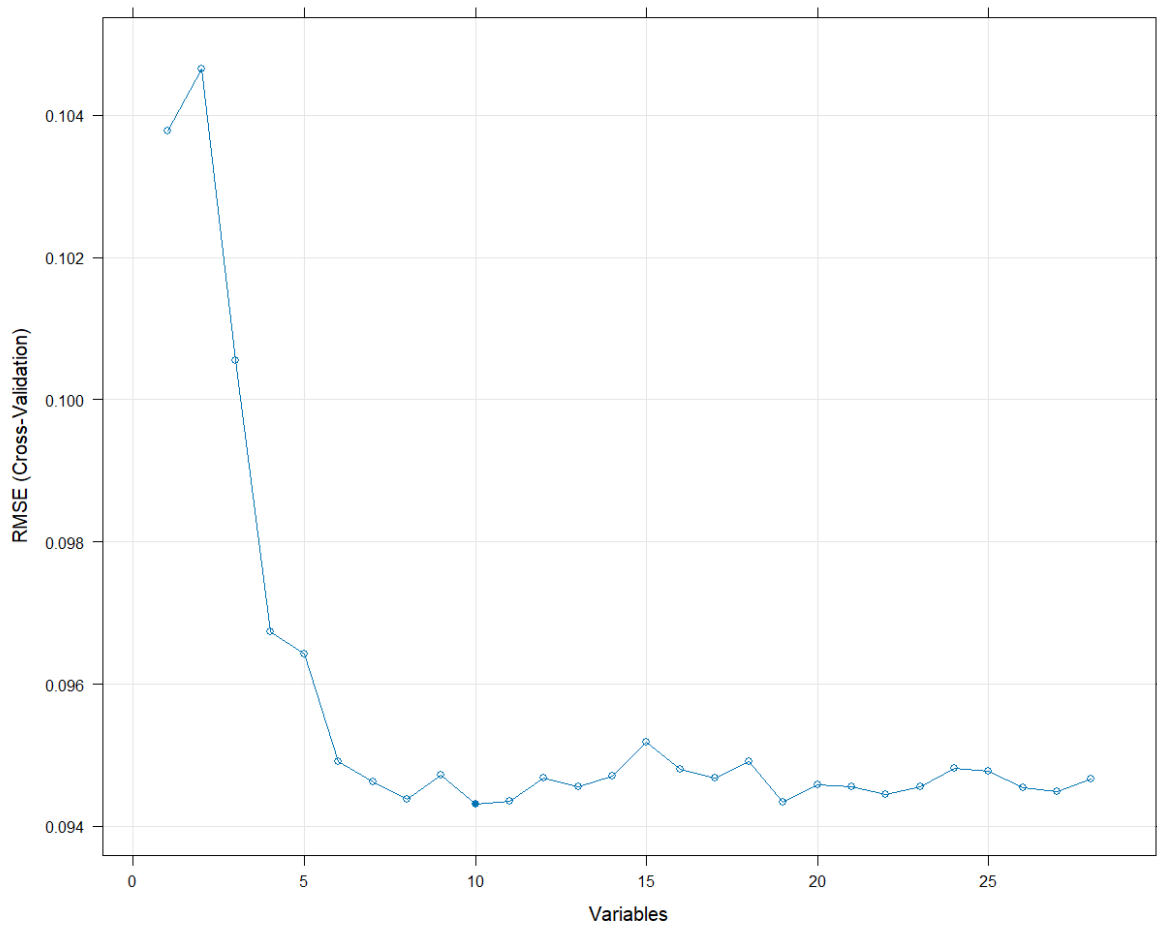
Note. BMI, Body-Mass-Index; COPD, chronic obstructive pulmonary disease; EQ-5D-5L, European Quality of Life 5 Dimensions 5 Level Version; FACIT-Fatigue Scale, Functional Assessment of Chronic Fatigue Illness – Fatigue Subscore



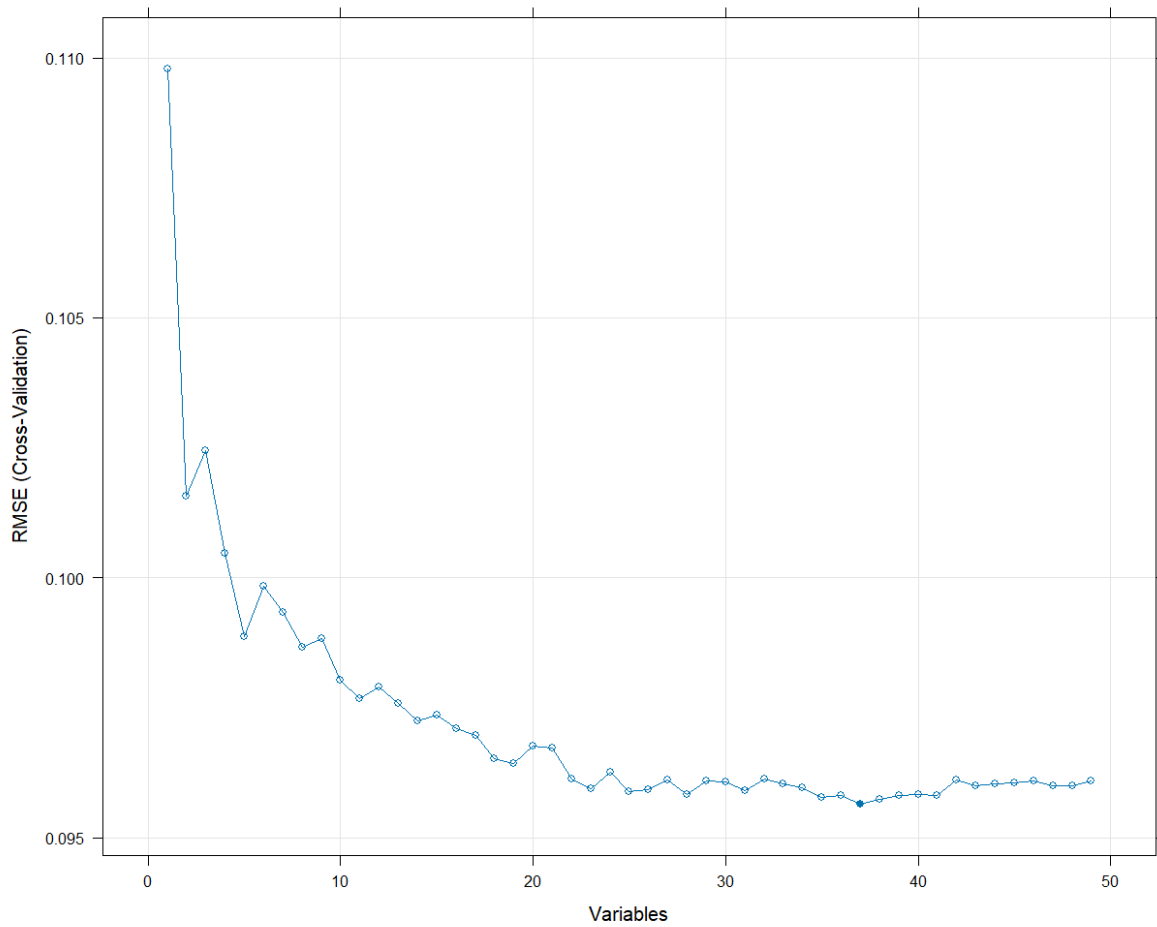
Supplementary Fig. S3 Steps and sequence of data cleaning for the COVIDOM study samples. BMI, Body-Mass-Index; EQ-5D-5L, European Quality of Life 5 Dimensions 5 Level Version; FACIT-Fatigue Scale, Functional Assessment of Chronic Fatigue Illness – Fatigue Subscore; MoCA, Montreal Cognitive Assessment; PSS, Perceived Stress Scale; TSI, Time since infection



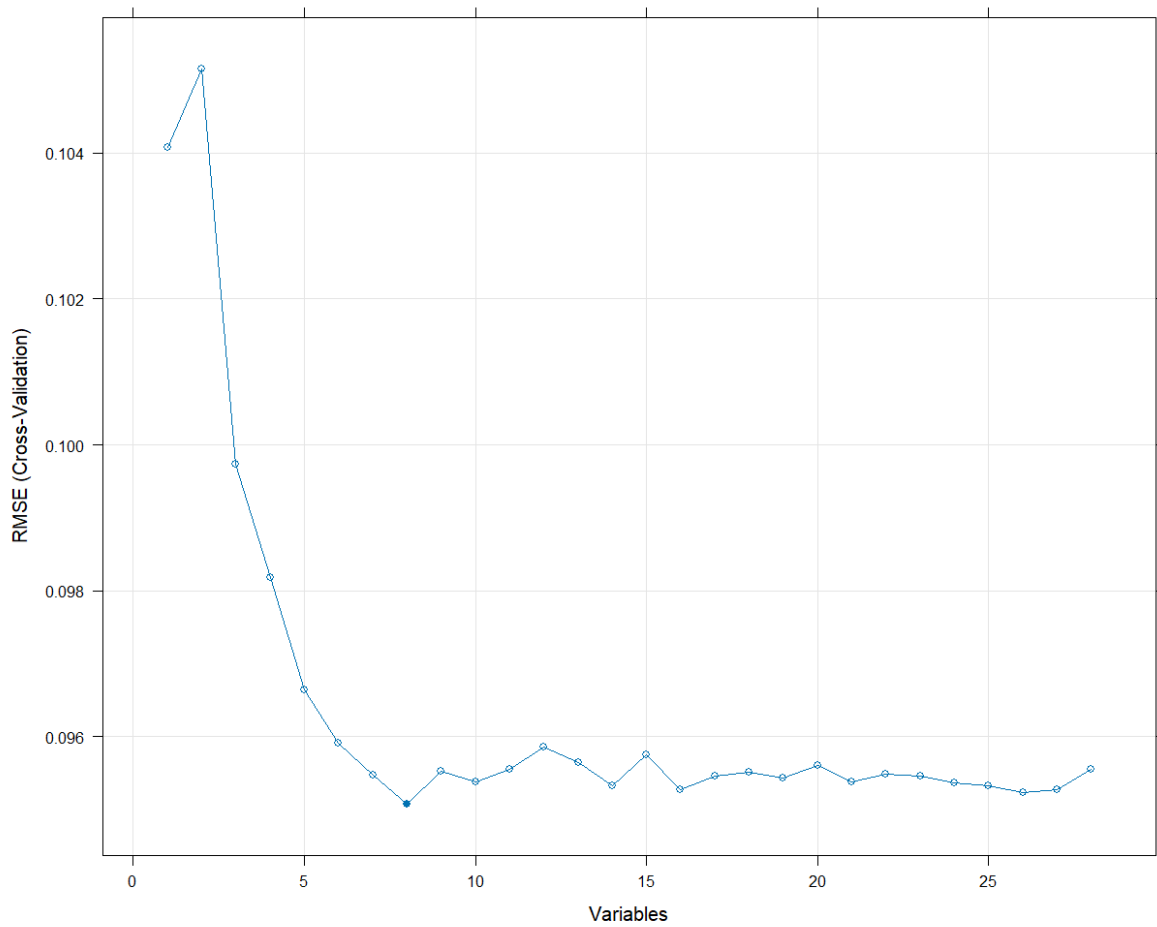
Supplementary Fig. S4 Root mean square errors (RMSE) of the models calculated by recursive feature elimination using the European Quality of Life 5 Dimensions 5 Level Version (EQ-5D-5L) index at baseline as the dependent variable. It shows the model fit in dependence of the number of selected features. The dark-blue point is the number of features with the lowest RMSE. A 35-variable model was calculated as the model with the lowest RMSE of 0.1 to explain the EQ-5D-5L index. We chose a 5-variable model as the final model because the RMSE with 5 variables is only 0.005 less than the RMSE with 35 variables, while using significantly fewer variables



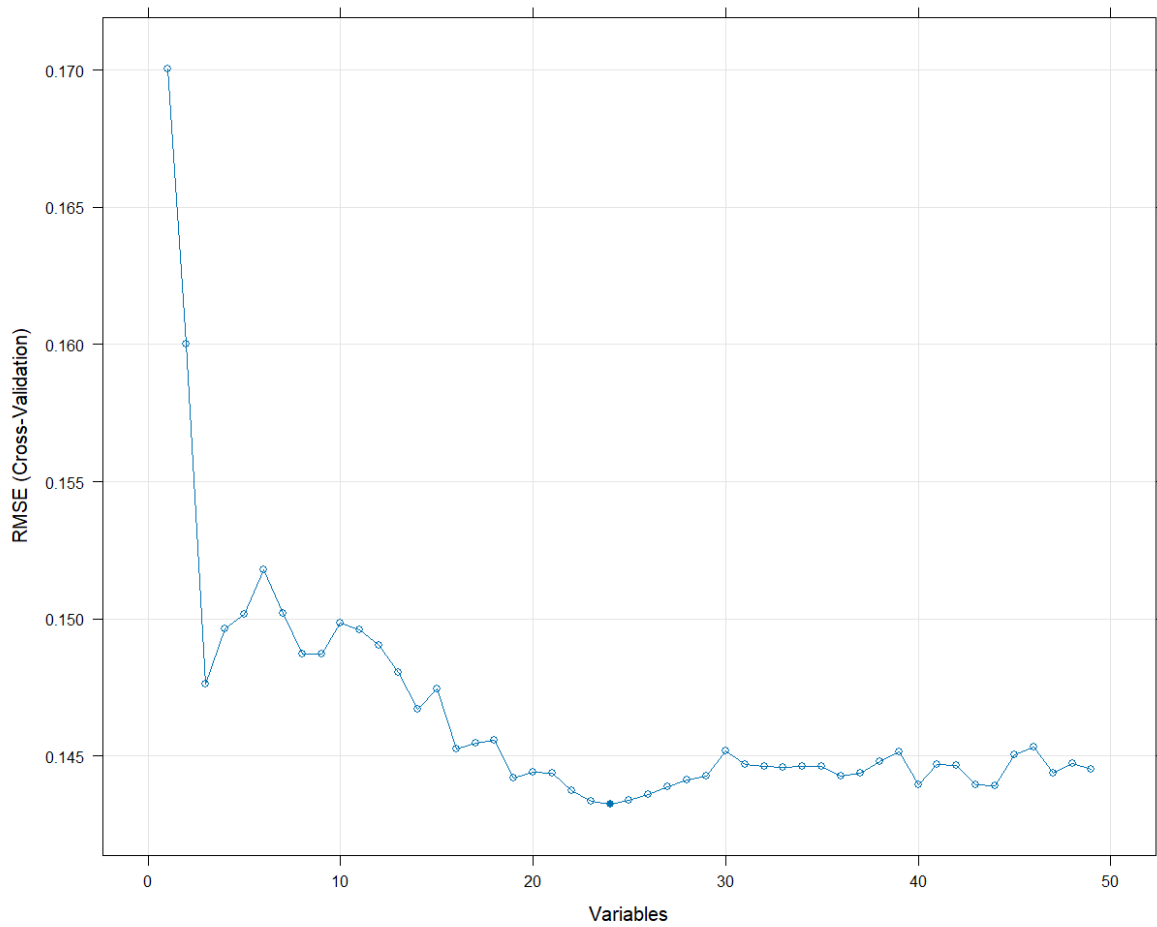
Supplementary Fig. S5 Root mean square errors (RMSE) of the models calculated by recursive feature elimination using the European Quality of Life 5 Dimensions 5 Level Version (EQ-5D-5L) index at follow-up as the dependent variable. It shows the model fit in dependence of the number of selected features. The dark-blue point is the number of features with the lowest RMSE. A 10-variable model as the model with the lowest RMSE of 0.09 to explain the EQ-5D-5L index. We chose a 6-variable model as the final model because the RMSE with 6 variables was also 0.09, while using significantly fewer variables



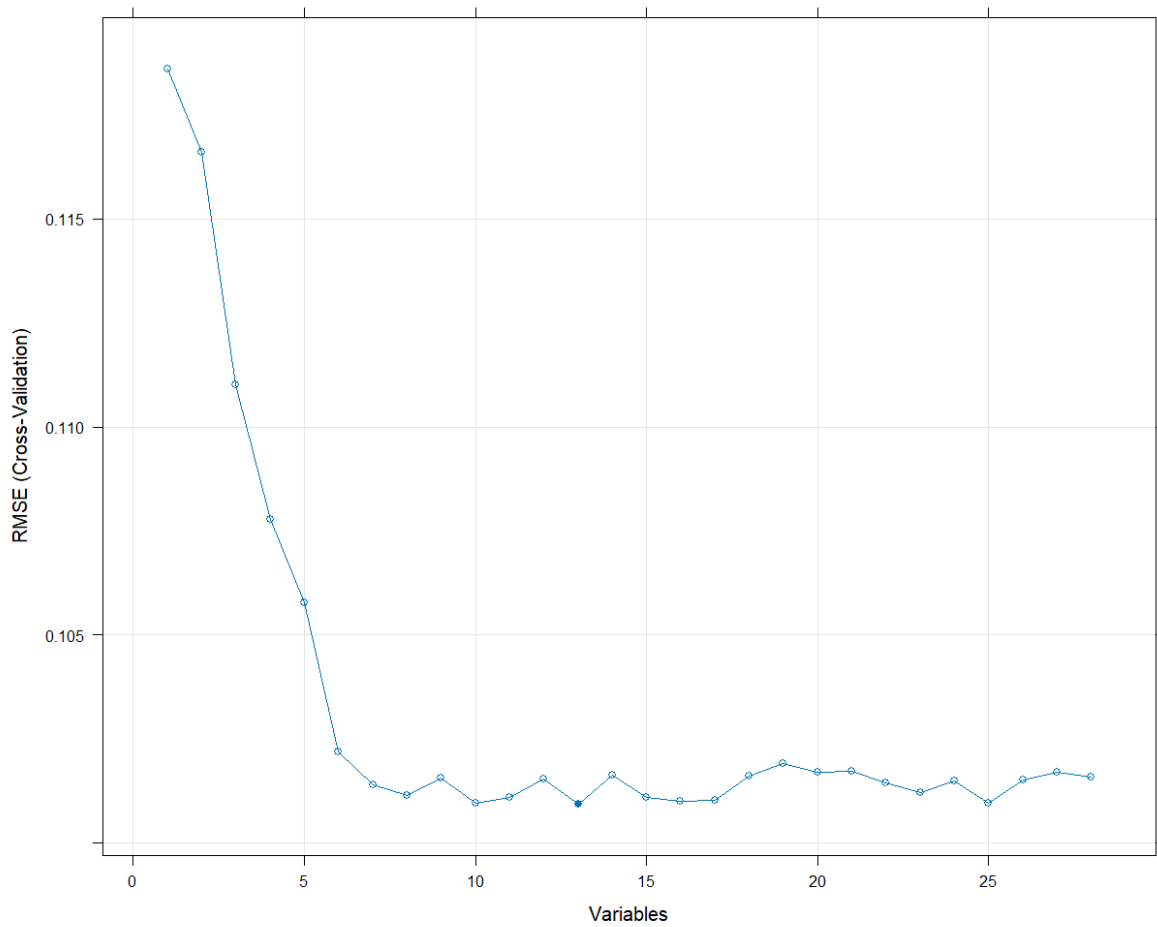
Supplementary Fig. S6 Root mean square errors (RMSE) of the models calculated by recursive feature elimination using the European Quality of Life 5 Dimensions 5 Level Version (EQ-5D-5L) index at baseline as the dependent variable for participants without a pre-diagnosed anxiety or depression. It shows the model fit in dependence of the number of selected features. The dark-blue point is the number of features with the lowest RMSE. A 37-variable model as the model with the lowest RMSE of 0.1 to explain the EQ-5D-5L index. We chose a 5-variable model as the final model because the RMSE with 6 variables was still 0.1, while using significantly fewer variables



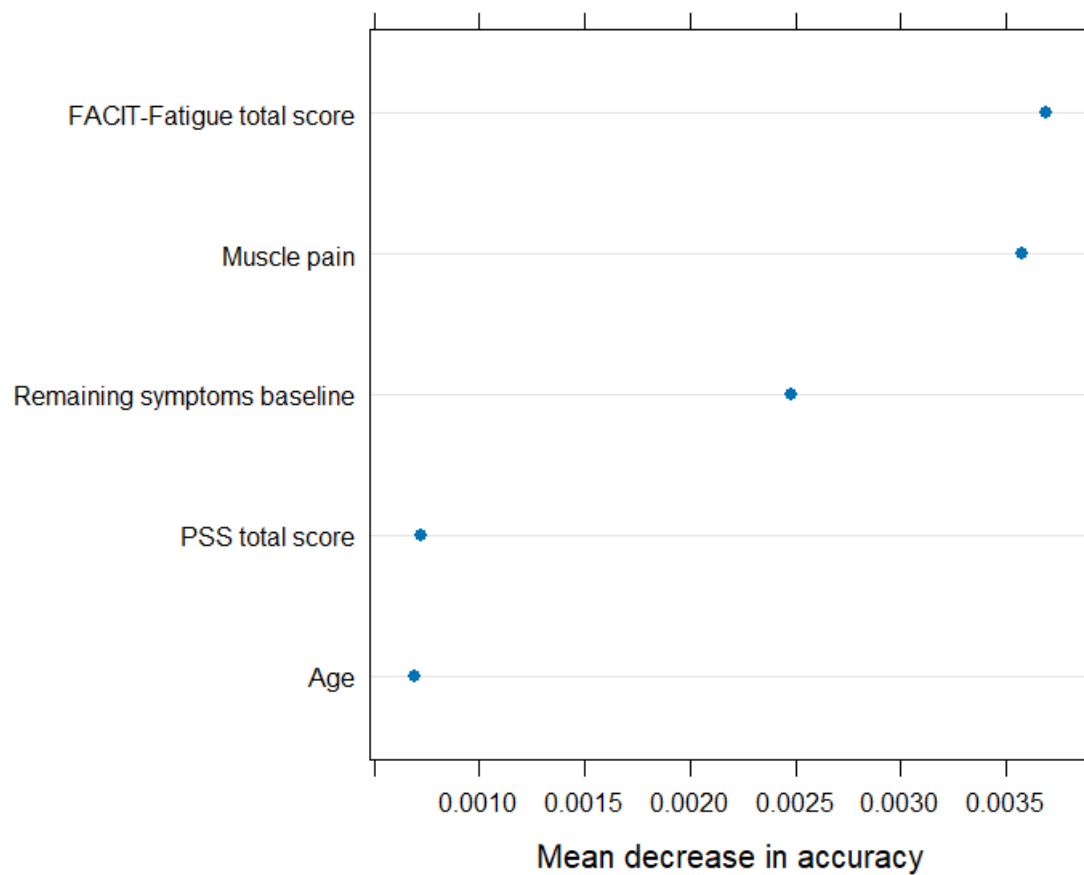
Supplementary Fig. S7 Root mean square errors (RMSE) of the models calculated by recursive feature elimination using the European Quality of Life 5 Dimensions 5 Level Version (EQ-5D-5L) index at follow-up as the dependent variable for participants without a pre-diagnosed anxiety or depression. It shows the model fit in dependence of the number of selected features. The dark-blue point is the number of features with the lowest RMSE. An 8-variable model as the model with the lowest RMSE of 0.10 to explain the EQ-5D-5L index. We chose a 6-variable model as the final model because the RMSE with 6 variables was only 0.001 less than the RMSE with 8 variables, while using significantly fewer variables



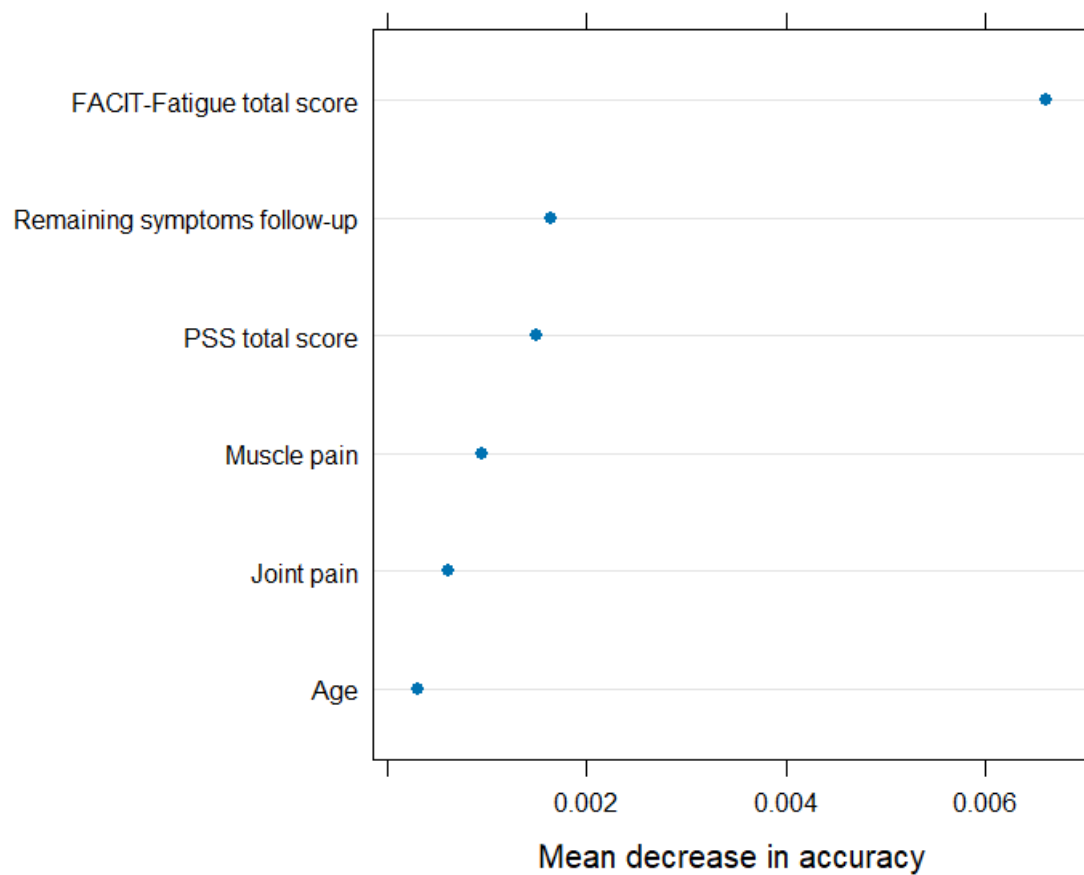
Supplementary Fig. S8 Root mean square errors (RMSE) of the models calculated by recursive feature elimination using the European Quality of Life 5 Dimensions 5 Level Version (EQ-5D-5L) index at baseline as the dependent variable for participants with a pre-diagnosed anxiety or depression. It shows the model fit in dependence of the number of selected features. The dark-blue point is the number of features with the lowest RMSE. A 24-variable model as the model with the lowest RMSE of 0.14 to explain the EQ-5D-5L index. We chose a 3-variable model as the final model because the RMSE with 3 variables was only 0.004 lower than the RMSE with 24 variables, while using significantly fewer variables



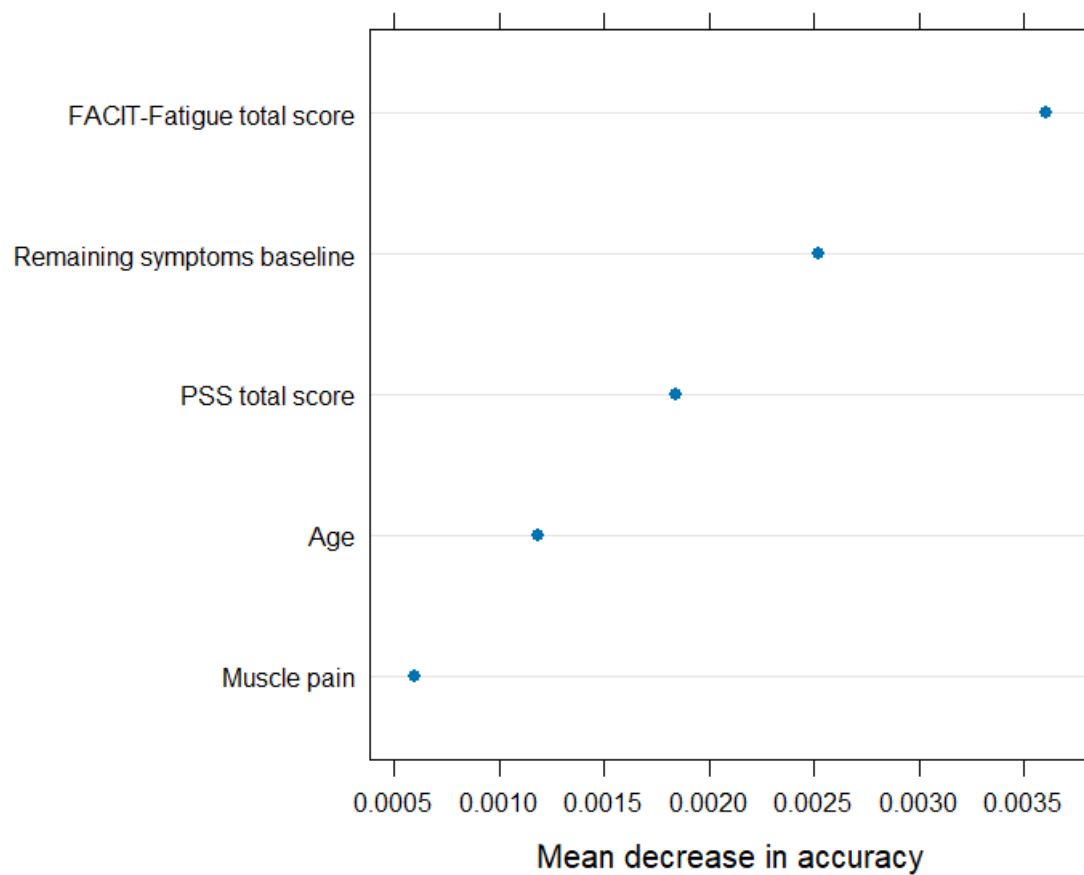
Supplementary Fig. S9 Root mean square errors (RMSE) of the models calculated by recursive feature elimination using the European Quality of Life 5 Dimensions 5 Level Version (EQ-5D-5L) index at follow-up as the dependent variable for participants with pre-diagnosed anxiety or depression. It shows the model fit in dependence of the number of selected features. The dark-blue point is the number of features with the lowest RMSE. A 13-variable model as the model with the lowest RMSE of 0.10 to explain the EQ-5D-5L index. We chose a 6-variable model as the final model because the RMSE with 6 variables was still 0.10, while using significantly fewer variables



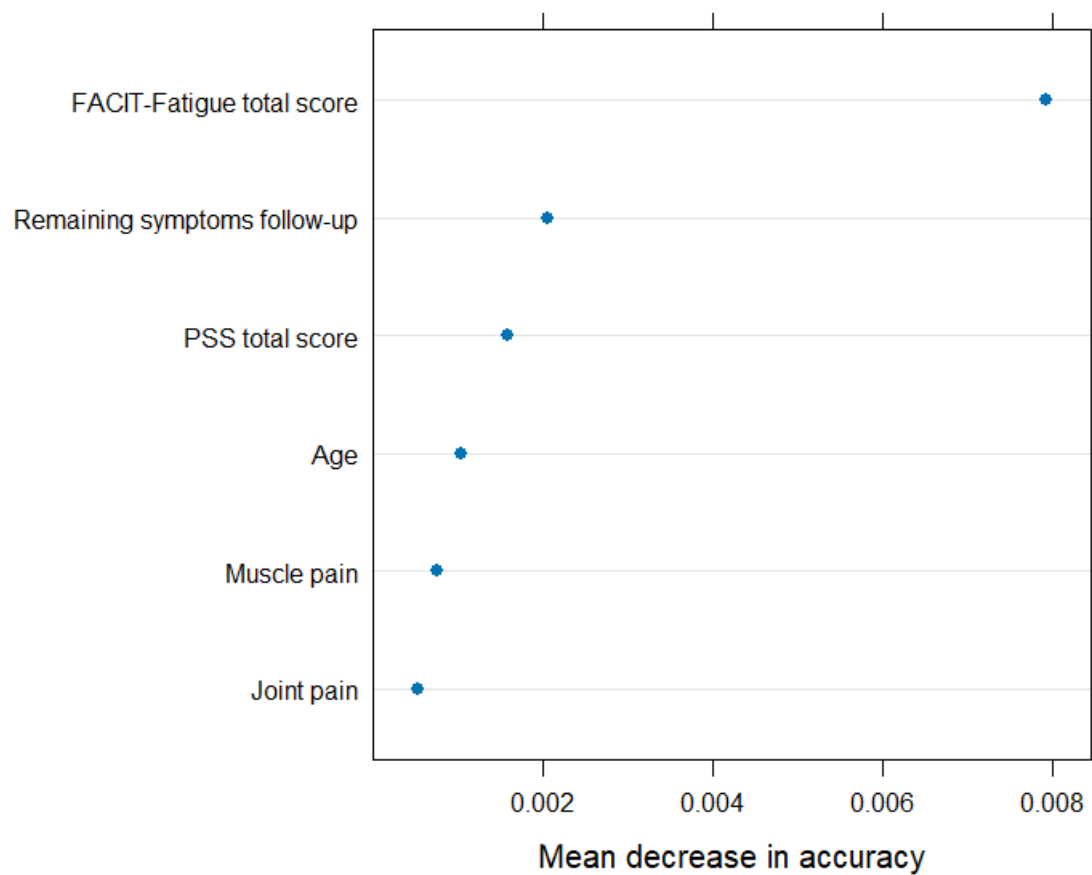
Supplementary Fig. S10 Mean decrease in accuracy of the selected variables at baseline after a random forest regression on the training set with the European Quality of Life 5 Dimensions 5 Level Version index as the dependent variable. FACIT-Fatigue Scale, Functional Assessment of Chronic Fatigue Illness – Fatigue Subscore; PSS, Perceived Stress Scale



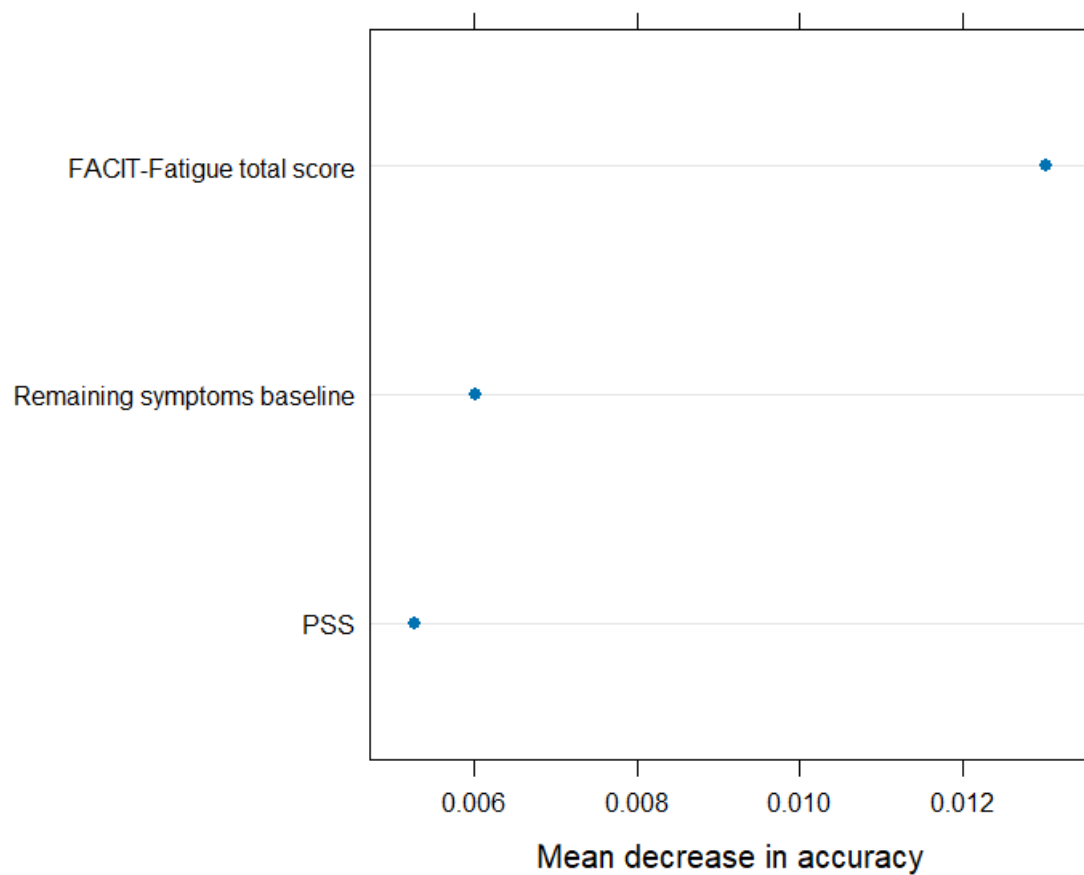
Supplementary Fig. S11 Mean decrease in accuracy of the selected variables at follow-up after a random forest regression on the training set with the European Quality of Life 5 Dimensions 5 Level Version index as the dependent variable. FACIT-Fatigue Scale, Functional Assessment of Chronic Fatigue Illness – Fatigue Subscore; PSS, Perceived Stress Scale



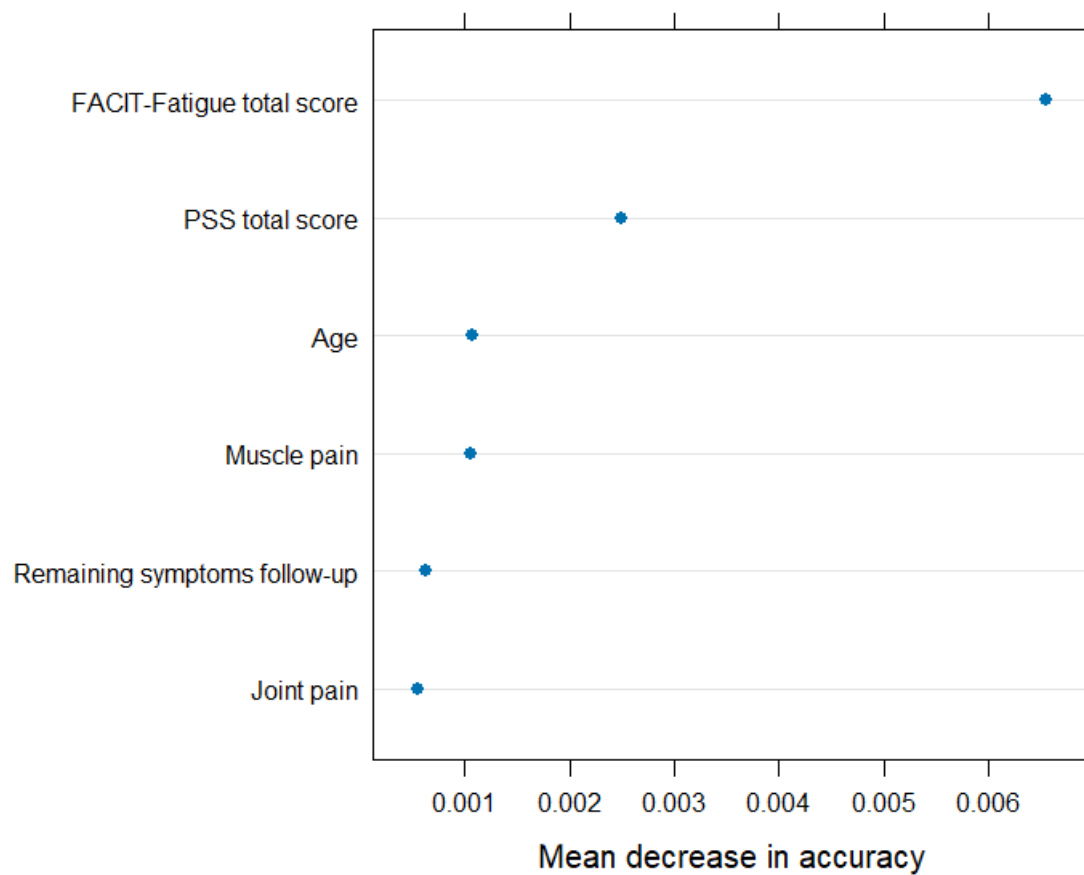
Supplementary Fig. S12 Mean decrease in accuracy of the selected variables at baseline after a random forest regression on the training set with the European Quality of Life 5 Dimensions 5 Level Version index as the dependent variable for participants without a pre-diagnosed anxiety or depression. FACIT-Fatigue Scale, Functional Assessment of Chronic Fatigue Illness – Fatigue Subscore; PSS, Perceived Stress Scale



Supplementary Fig. S13 Mean decrease in accuracy of the selected variables at follow-up after a random forest regression on the training set with the European Quality of Life 5 Dimensions 5 Level Version index as the dependent variable for participants without a pre-diagnosed anxiety or depression. FACIT-Fatigue Scale, Functional Assessment of Chronic Fatigue Illness – Fatigue Subscore; PSS, Perceived Stress Scale



Supplementary Fig. S14 Mean decrease in accuracy of the selected variables at baseline after a random forest regression on the training set with the European Quality of Life 5 Dimensions 5 Level Version index as the dependent variable for participants with a pre-diagnosed anxiety or depression. FACIT-Fatigue Scale, Functional Assessment of Chronic Fatigue Illness – Fatigue Subscore; PSS, Perceived Stress Scale



Supplementary Fig. S15 Mean decrease in accuracy of the selected variables at follow-up after a random forest regression on the training set with the European Quality of Life 5 Dimensions 5 Level Version index as the dependent variable for participants with pre-diagnosed anxiety or depression. FACIT-Fatigue Scale, Functional Assessment of Chronic Fatigue Illness – Fatigue Subscore; PSS, Perceived Stress Scale

Supplementary Table S16

Order of selected variables after recursive feature elimination for each final random forest regression model at baseline and follow-up.

EQ-5D-5L	During Baseline			During Follow-Up		
	Relevant independent variables	R^2 [%]	RMSE	Relevant independent variables	R^2 [%]	RMSE
Index	1. FACIT-Fatigue Scale 2. Muscle pain 3. Remaining symptoms 4. PSS 5. Age	39.22	0.11	1. FACIT-Fatigue Scale 2. Remaining symptoms 3. PSS 4. Muscle pain 5. Joint pain 6. Age	54.07	0.10
Index – participants without a pre-diagnosed neurological/psychiatric disorder	1. FACIT-Fatigue Scale 2. Remaining symptoms baseline 3. PSS 4. Age 5. Muscle pain	34.54	0.09	1. FACIT-Fatigue Scale 2. Remaining symptoms follow-up 3. PSS 4. Age 5. Muscle pain 6. Joint pain	43.26	0.09
Index – participants with at least one pre-diagnosed neurological/psychiatric disorder	1. FACIT-Fatigue Scale 2. Remaining symptoms baseline 3. PSS	30.22	0.15	1. FACIT-Fatigue Scale 2. PSS 3. Age 4. Muscle pain 5. Remaining symptoms 6. Joint pain	53.25	0.11

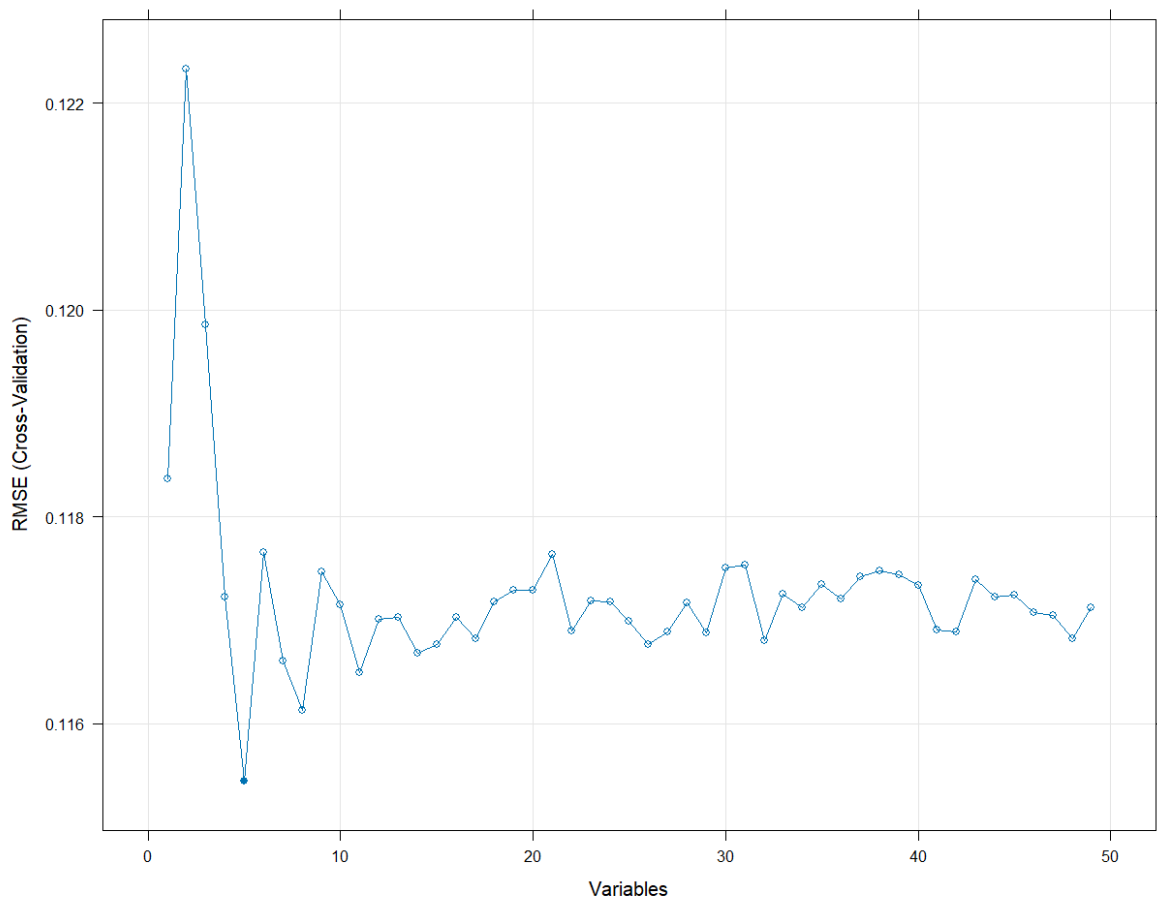
Note. EQ-5D-5L, European Quality of Life 5 Dimensions 5 Level Version; FACIT-Fatigue Scale, Functional Assessment of Chronic Fatigue Illness – Fatigue Subscore; PSS, Perceived Stress Scale

Supplementary Table S17

Coefficient of determination (R^2) and root mean square error (RMSE) for each dimension of the EQ-5D-5L at baseline and follow-up

EQ-5D-5L	During Baseline		During Follow-Up	
	R^2 [%]	RMSE	R^2 [%]	RMSE
Mobility	28.58	0.61	23.43	0.59
Self-Care	3.68	0.31	13.60	0.29
Usual activities	47.12	0.62	51.04	0.55
Pain/discomfort	37.76	0.72	39.56	0.70
Anxiety/depression	29.37	0.71	43.00	0.62

Note. Calculated using random forest regression models with FACIT-Fatigue Scale, age, PSS, number of symptoms remaining from initial SARS-CoV-2 infection, and muscle pain as independent variables. EQ-5D-5L, European Quality of Life 5 Dimensions 5 Level Version; FACIT-Fatigue Scale, Functional Assessment of Chronic Fatigue Illness – Fatigue Subscore; PSS, Perceived Stress Scale



Supplementary Fig. S18 Root mean square errors (RMSE) of the models calculated by recursive feature elimination predicting the European Quality of Life 5 Dimensions 5 Level Version EQ-5D-5L index at follow-up using baseline variables. It shows the model fit in dependence of the number of selected features. The dark-blue point is the number of features with the lowest RMSE. A 5-variable model was calculated as the model with the lowest RMSE of 0.12 to explain the EQ-5D-5L index.