

Table S1 Sensitivity analysis of longitudinal associations between dynamic trajectories of eCRF and depression risk using **GLM and Xgboost**

Covariates	sequences of treatment	OR	OR_Std	OR_Pvalue	OR_95CI_lower	OR_95CI_upper
male,age,married	(1,0,0)	0.561	0.200	0.003778106	0.379	0.829
	(1,1,0)	0.534	0.181	0.000518602	0.374	0.761
	(1,1,1)	0.364	0.143	1.73684E-12	0.275	0.482
male,age,married, bmi,smoker	(1,0,0)	0.914	0.291	0.758680528	0.517	1.618
	(1,1,0)	0.563	0.292	0.048971871	0.318	0.997
	(1,1,1)	0.468	0.165	4.39493E-06	0.339	0.647
age,bmi,chol, hba1c,sbp	(1,0,0)	0.889	0.215	0.657632656	0.596	1.387
	(1,1,0)	0.473	0.240	0.001784611	0.296	0.757
	(1,1,1)	0.348	0.143	2.04698E-13	0.263	0.461
male,age,bmi, chol,hba1c,sbp	(1,0,0)	0.925	0.266	0.768224564	0.549	1.558
	(1,1,0)	0.511	0.284	0.017951901	0.293	0.891
	(1,1,1)	0.346	0.165	1.28237E-10	0.250	0.478
male,age,married, bmi,active,smoker	(1,0,0)	1.092	0.265	0.737175443	0.650	1.836
	(1,1,0)	0.590	0.301	0.079342041	0.327	1.064
	(1,1,1)	0.541	0.159	0.000115135	0.396	0.739
male,age,married, bmi,smoker, chol,hba1c,sbp	(1,0,0)	0.841	0.285	0.541420174	0.481	1.468
	(1,1,0)	0.574	0.292	0.047003692	0.324	1.017
	(1,1,1)	0.406	0.151	2.32897E-09	0.302	0.546
male,age,married, chol,hba1c,sbp	(1,0,0)	0.661	0.191	0.030151531	0.455	0.961
	(1,1,0)	0.545	0.189	0.001360191	0.376	0.790
	(1,1,1)	0.396	0.133	2.3934E-12	0.305	0.513

Table S2 Sensitivity analysis of longitudinal associations between dynamic trajectories of eCRF and depression risk using **Xgboost**

Covariates	sequences of treatment	OR	OR_Std	OR_Pvalue	OR_95CI_lower	OR_95CI_upper
male,age,married	(1,0,0)	0.633	0.209	0.028618098	0.420	0.953
	(1,1,0)	0.591	0.178	0.003125317	0.417	0.838
	(1,1,1)	0.438	0.136	1.25824E-09	0.336	0.572
male,age,married, chol,hba1c,sbp	(1,0,0)	0.820	0.252	0.43247783	0.500	1.345
	(1,1,0)	0.543	0.257	0.017758812	0.328	0.900
	(1,1,1)	0.450	0.139	8.65132E-09	0.342	0.590
age,bmi,chol, hba1c,sbp	(1,0,0)	0.689	0.040	2.00227E-20	0.636	0.745
	(1,1,0)	0.450	0.039	2.61268E-92	0.417	0.486
	(1,1,1)	0.326	0.047	6.7525E-125	0.297	0.357
male,age,bmi, chol,hba1c,sbp	(1,0,0)	0.774	0.030	6.61359E-18	0.730	0.820
	(1,1,0)	0.501	0.029	3.4548E-124	0.473	0.530
	(1,1,1)	0.367	0.035	6.0986E-181	0.343	0.393
male,age,married,	(1,0,0)	0.815	0.056	0.000264372	0.730	0.910

bmi,active,smoker	(1,1,0)	0.555	0.043	1.04705E-43	0.510	0.603
	(1,1,1)	0.537	0.044	4.80184E-45	0.492	0.586
male,age,married,	(1,0,0)	0.710	0.037	1.73192E-20	0.661	0.764
bmi,smoker,	(1,1,0)	0.513	0.034	1.25962E-83	0.479	0.549
chol,hba1c,sbp	(1,1,1)	0.428	0.039	1.7458E-104	0.396	0.462
male,age,married, bmi,smoker	(1,0,0)	0.348	0.056	0.290828046	0.350	1.369
	(1,1,0)	0.307	0.043	0.009015988	0.245	0.819
	(1,1,1)	0.158	0.044	1.01478E-10	0.265	0.492

Table S3 Sensitivity analysis of longitudinal associations between dynamic trajectories of eCRF and depression risk using **RandomForest**

Covariates	sequences of treatment	OR	OR_Std	OR_Pvalue	OR_95CI_lower	OR_95CI_upper
male,age,married	(1,0,0)	0.984	1.091	0.988319463	0.116	8.352
	(1,1,0)	0.420	0.591	0.142565076	0.132	1.339
	(1,1,1)	0.225	0.436	0.000618223	0.096	0.528
male,age,married, chol,hba1c,sbp	(1,0,0)	0.616	0.035	2.65683E-43	0.575	0.660
	(1,1,0)	0.753	0.036	5.05199E-15	0.701	0.809
	(1,1,1)	0.211	0.048	1.0252E-230	0.192	0.232
male,age,married, bmi,smoker	(1,0,0)	0.741	0.326	0.357681017	0.391	1.404
	(1,1,0)	0.840	0.270	0.518873904	0.494	1.427
	(1,1,1)	0.163	0.233	6.126E-15	0.103	0.257
age,bmi,chol, hba1c,sbp	(1,0,0)	0.557	0.028	2.28446E-99	0.528	0.588
	(1,1,0)	0.651	0.030	9.00549E-46	0.614	0.691
	(1,1,1)	0.171	0.035	0	0.160	0.183
male,age,married, bmi,rhr,active,sm oker	(1,0,0)	0.565	0.344	0.096640164	0.288	1.108
	(1,1,0)	0.453	0.281	0.004871244	0.261	0.786
	(1,1,1)	0.213	0.164	4.3736E-21	0.154	0.293

Table S4 Sensitivity analysis comparing complete case and imputed data: ORs estimated via SuperLearner-GLM

Covariates	Missing Data Method	OR	OR_Std	OR_Pvalue	OR_95CI_lower	OR_95CI_upper
male,age,married	Complete Case Analysis	0.572	0.333	0.093594512	0.297	1.099
	Multiple Imputation	0.354	0.163	1.84459E-10	0.257	0.487
male,age,married, chol,hba1c,sbp	Complete Case Analysis	0.775	0.344	0.459175109	0.395	1.522
	Multiple Imputation	0.374	0.160	7.11801E-10	0.274	0.511
male,age,married, bmi,smoker	Complete Case Analysis	0.304	0.393	0.002470858	0.141	0.657
	Multiple Imputation	0.444	0.186	1.32609E-05	0.308	0.640
age,bmi,chol, hba1c,sbp	Complete Case Analysis	0.268	0.192	6.90624E-12	0.184	0.391
	Multiple Imputation	0.373	0.104	2.51641E-21	0.304	0.458
male,age,bmi, chol,hba1c,sbp	Complete Case Analysis	0.268	0.180	2.98267E-13	0.188	0.382
	Multiple Imputation	0.311	0.111	6.49975E-26	0.250	0.386
male,age,married, bmi,active,smoker	Complete Case Analysis	0.401	0.159	1.00969E-08	0.294	0.548
	Multiple Imputation	0.526	0.111	6.17934E-09	0.424	0.653

male,age,married, bmi,smoker, chol,hba1c,sbp	Complete Case Analysis	0.340	0.175	7.51843E-10	0.241	0.480
	Multiple Imputation	0.385	0.111	8.17926E-18	0.310	0.479

Table S5 Sensitivity analysis comparing complete case and imputed data: ORs estimated via
SuperLearner-**RandomForest**

Covariates	Missing Data Method	OR	OR_Std	OR_Pvalue	OR_95CI_lower	OR_95CI_upper
male,age,married	Complete Case Analysis	0.631	1.440	0.749248489	0.038	1.613
	Multiple Imputation	0.225	0.436	0.000618223	0.096	0.528
male,age,married, chol,hba1c,sbp	Complete Case Analysis	0.478	0.392	0.059921318	0.222	1.031
	Multiple Imputation	0.163	0.233	6.126E-15	0.103	0.257
age,bmi,chol, hba1c,sbp	Complete Case Analysis	0.366	0.095	2.43609E-26	0.304	0.440
	Multiple Imputation	0.171	0.035	0	0.160	0.183
male,age,bmi, chol,hba1c,sbp	Complete Case Analysis	0.461	0.070	2.10565E-28	0.402	0.529
	Multiple Imputation	0.367	0.035	6.0986E-181	0.343	0.393
male,age,married, bmi,rhr,active, smoker	Complete Case Analysis	0.312	0.304	0.000129952	0.172	0.567
	Multiple Imputation	0.213	0.164	4.3736E-21	0.154	0.293

Table S6 Sensitivity analysis comparing complete case and imputed data: ORs estimated
viaSuperLearner-**XGBoost**

Covariates	Missing Data Method	OR	OR_Std	OR_Pvalue	OR_95CI_lower	OR_95CI_upper
male,age,married	Complete Case Analysis	0.673	0.278	0.154630412	0.390	1.161
	Multiple Imputation	0.438	0.136	1.25824E-09	0.336	0.572
male,age,married, chol,hba1c,sbp	Complete Case Analysis	0.715	0.265	0.205254929	0.425	1.202
	Multiple Imputation	0.450	0.139	8.65132E-09	0.342	0.590
male,age,married, bmi,smoker	Complete Case Analysis	0.397	0.362	0.010881467	0.195	0.808
	Multiple Imputation	0.361	0.158	1.01478E-10	0.265	0.492
age,bmi,chol, hba1c,sbp	Complete Case Analysis	0.377	0.088	2.75427E-28	0.317	0.448
	Multiple Imputation	0.326	0.047	6.7525E-125	0.297	0.357
male,age,bmi, chol,hba1c,sbp	Complete Case Analysis	0.461	0.070	2.10565E-28	0.402	0.529
	Multiple Imputation	0.367	0.035	6.0986E-181	0.343	0.393
male,age,married, bmi,active,smoker	Complete Case Analysis	0.489	0.083	4.47826E-18	0.416	0.575
	Multiple Imputation	0.537	0.044	4.80184E-45	0.492	0.586
male,age,married, bmi,smoker, chol,hba1c,sbp	Complete Case Analysis	0.394	0.074	2.33007E-36	0.341	0.455
	Multiple Imputation	0.428	0.039	1.7458E-104	0.396	0.462

Table S7 Sensitivity analysis comparing complete case and imputed data: ORs estimated via
SuperLearner-**XGBoost and GLM**

Covariates	Missing Data Method	OR	OR_Std	OR_Pvalue	OR_95CI_lower	OR_95CI_upper
male,age,married	Complete Case Analysis	0.564	0.313	0.06692486	0.305	1.041

	Multiple Imputation	0.364	0.143	1.73684E-12	0.275	0.482
male,age,married,	Complete Case Analysis	0.753	0.329	0.389025537	0.395	1.436
chol,hb1c,sbp	Multiple Imputation	0.396	0.132	2.3934E-12	0.305	0.513
male,age,married,	Complete Case Analysis	0.340	0.364	0.003066875	0.167	0.694
bmi,smoker	Multiple Imputation	0.468	0.165	4.39493E-06	0.339	0.647
age,bmi,chol,	Complete Case Analysis	0.282	0.284	8.52864E-06	0.162	0.493
hb1c,sbp	Multiple Imputation	0.348	0.144	2.04698E-13	0.263	0.461
male,age,bmi,	Complete Case Analysis	0.287	0.420	0.002964469	0.126	0.654
chol,hb1c,sbp	Multiple Imputation	0.346	0.165	1.28237E-10	0.250	0.478
male,age,married,	Complete Case Analysis	0.436	0.473	0.079223987	0.172	1.102
bmi,active,smoker	Multiple Imputation	0.541	0.159	0.000115135	0.396	0.739
male,age,married,	Complete Case Analysis	0.340	0.395	0.006352033	0.157	0.738
bmi,smoker,						
chol,hb1c,sbp	Multiple Imputation	0.406	0.151	2.32897E-09	0.302	0.546

Table S8 Subgroup analysis

Group	N	OR (95% CI)	P-value	P for Interaction
Sex				
Male	3204	0.45 (0.29-0.70)	< 0.001	0.420
Female	3904	0.46 (0.31-0.68)	< 0.001	
Age (Years)				
Age < 70	4607	0.46 (0.30-0.71)	< 0.001	0.655
Age ≥ 70	2501	0.67 (0.39-1.14)	0.138	
Smoking Status				
Never Smoker	2626	0.35 (0.20-0.61)	< 0.001	0.773
Current/EX Smoker	4482	0.42 (0.28-0.63)	< 0.001	

Table 9 Odds Ratios (95% CI) for Depression Risk According to Longitudinal e-CRF Trajectories.

Trajectory	N (%)	Model 1	Model 2	Model 3
Stable Low	2112	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Moderate/Fluctuating	1574	0.45 (0.39-0.52)***	0.56 (0.47-0.66)***	0.52 (0.42-0.63)***
Stable High	2020	0.24 (0.21-0.28)***	0.36 (0.29-0.45)***	0.31 (0.23-0.40)***
Increasing	50	0.37 (0.17-0.73)**	0.48 (0.22-0.96)	0.47 (0.21-0.94)*
Decreasing	1352	0.43 (0.37-0.50)***	0.53 (0.44-0.63)***	0.49 (0.40-0.60)***

Notes: OR, odds ratio; CI, confidence interval; e-CRF, estimated cardiorespiratory fitness.

Model 1: Crude model without adjustment.

Model 2: Adjusted for age and sex.

Model 3: Further adjusted for marital status, body mass index (BMI), and smoking status.

*p < 0.05, **p < 0.01, ***p < 0.001.