Supplementary material

Statistical analyses

We performed the statistical analyses in four stages utilizing STATA 16.1(33). We investigated how MI, AF or stroke were associated with mental health trajectories over time relative to the first MI, AF or stroke event. Time was represented by date of birth, attendance date, and date of the event. The timeline was the difference between attendance date and date of MI, AF or stroke event.

Stage 1 Descriptive characteristics. Calculations of means, standard deviations and percentages of the variables stratified by severity of self-reported anxiety and depression symptoms at baseline were conducted, in addition to the frequency of observations for each diagnosis of MI, AF or stroke for each period. It is shown in Table 1.

Stage 2 Development of sample characteristics over time relative to CVD diagnosis. We used cross-tabulation to describe the number of participants with significant mental health symptoms in different periods relative to the CVD event. Participants were grouped relative to the first MI, AF and stroke diagnosis at >10, 10-5, 4.9-1, and <1 year before the event and 1 and >1 year after the event. It is shown in Table 2. We utilized a nonparametric series estimation, i.e. cubic B-spline estimation, to model the mean of symptom levels. The intention is to prevent the problems that result from inappropriate linearity assumptions. Another way to look at splines is a technique to make smooth curves out of irregular data points (34). We fitted separate models with mental health scores as the dependent variable before and after the event with three knots. The result is shown in Figure 2, calculated from the predictions of the already fitted models.

Stage 3 Mixed-effects model. We wanted to assess how health, lifestyle and social factors related to a mental health outcome. We fitted two-level ML logistic models for ordered responses (35) with mental health scores as the dependent variable (HSCL-10/CONOR-MHI) and with test scores (i) nested within participants (j).

We fitted separate models for each CVD diagnosis before and after the event, a total of six models with an independent covariance structure. We encountered no estimation problems (e.g. improper variance estimates). Age was, as expected, related to hypertension (R=0.45), hyperlipidaemia (R=0.29) and diabetes (R=0.54). Being married was related to living in a shared household (R=.47). Intra-class correlation estimates were calculated based on inter-rater reliability using one-way random effects. The average intra-class correlation was 0.79 (95% CI: 0.78, 0.81).

The sample included all validated CVD events. The observations were marked as before or after the event. We fitted separate models for each condition, MI, AF and stroke, to estimate the effect of having increased symptom levels on the ordinal response variable (no symptoms/sub-threshold/significant symptoms) for all independent variables. Significant symptoms are assumed to correspond to “higher” outcomes (i.e. odds ratio above 1.0). It made it possible to consider a model that included the time scales and sex, comorbid diseases, physiological measurements (BMI, serum cholesterol, HbA1c and systolic blood pressure), education, leisure-time physical activity, alcohol intake and smoking habit independent variables. It is presented in Table 3. We checked covariance for all independent variables, and the highest correlation was between age and diabetes (0.537). K_S represents the cut-off for the mental health categories.

$$logit\{Pr\ (Mental\ health_{ij} > s|time\ \ _{ij})\}$$
$$= \beta_1 sex_{ij} + \beta_2 age_{ij} + \beta_3 BMI\ group_{ij} + HII_{ij} + \beta_5 hypertension_{ij} + \beta_6 lipid_{ij}$$
$$+ \beta_7 diabetes_j\ + \beta_8 smoking_j\ + \beta_9 alcohol_{ij} + \beta_{11} physical\ activity_{ij}$$
$$+ \beta_{12} married_{ij} + \beta_{13} living\ alone_{ij} + \beta_{14} education_{ij} - K_s$$

Stage 4 Fixed-effects model. We wanted to assess the relationship between mental health trajectories and CVD onset. We included all validated CVD events and marked them as before or after the event. We estimated how MI, AF and stroke influenced mental health trajectories relative to the time of the event and fitted independent models for each of the diagnoses. The multilevel statistical modelling utilizes the continuous overlap of individual trajectories to span the time range of interest based on an average timespan of 14 years. Participants need at least two measurements to be included in either model. The data were organized as panel data and fixed-effects estimation nests the repeated measures (i) at the individual level (j). In the analysis, each participant thus became his/her control. Therefore, the estimate focused on the within-subject changes as the status of MI changes. The statistical models for AF and stroke were applied similarly. For MI, time was included as the time difference between attendance date (measured in days) and first MI event, making it possible to consider a model that includes time scale as the covariate. We fitted separate models for each CVD diagnosis before and after the event. We did this to improve the model's fit, given that changes in mental health symptoms increased before the event and tended to remain high or decline after the event. This two-stage trend can be seen in Table 2 and Figure 2, showing descriptive statistics and plots for the mental health symptom trajectories. This piecewise approach was chosen instead of a single model to offer a more straightforward interpretation of the development relative to the time of the CVD event. When used as a continuous variable, time squared was fitted adjusting for non-linear development.

The final model was for MI: $\text{Mental health}_{ij} = \beta_1 \text{time}_{ij} + \beta_2 \text{time}_{ij}^2 + \beta_0 + \zeta_{1j} + \varepsilon_{ij}$

The final model was for AF and STROKE: $\text{Mental health}_{ij} = \beta_1 \text{time}_{ij} + \beta_0 + \zeta_{1j} + \varepsilon_{ij}$

The random intercept (ζ_{1j}) and the occasion-specific error (ε_{ij}) allow the responses ($Mental\ health_{ij}$) to deviate from the polynomial function. Adding time to the slope in the random part ($\zeta_{2\ time\ ij}$) did not significantly improve the model. The odds ratios, shown in Table 4, were estimated from a chosen set of time points from -10 to 10 in two-year intervals.

Mental health trajectories relative to the time of diagnosis

Supplementary Table 1: Linear regression coefficients for the association between time in years relative to diagnosis and standardized mental health symptom score ten years before and after the cardiovascular event. The Tromsø Study.

		Myocardial infarction		
	Before		After	
Time in years relative to diagnosis	0.024*	(0.003,0.046)	-0.028***	(-0.043,-0.013)
Time squared	0.001*	(0.000,0.002)	0.001*	(0.000,0.001)
Constant	0.025	(-0.066,0.115)	0.145***	(0.064,0.225)
		Atrial fibrillation		
	Before		After	
Time in years relative to diagnosis	0.005	(-0.000,0.010)	-0.004	(-0.013,0.005)
Constant	-0.003	(-0.053,0.047)	0.052	(-0.019,0.123)
		Stroke		
	Before		After	
Time in years relative to diagnosis	0.025*	(0.003, 0.048)	-0.015**	(-0.026,-0.005)
Constant	0.142*	(0.023, 0.262)	0.218***	(0.119,0.317)

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

95% confidence intervals in brackets

Supplementary Table 2: Standardized mental health symptoms score for the time before and after atrial fibrillation and stroke for women in the Tromsø Study.

	Women
Mental health change	
Years before Atrial fibrillation	n=730
-10	0.127 (0.089, 0.165)
-8	0.155 (0.115, 0.195)
-6	0.183 (0.134, 0.232)
-4	0.211 (0.150, 0.273)
-2	0.239 (0.163, 0.315)
0	0.268 (0.176, 0.359)
Years after Atrial fibrillation	n=371
0	0.344 (0.207, 0.482)
2	0.336 (0.233, 0.440)
4	0.328 (0.253, 0.404)
6	0.320 (0.258, 0.383)
8	0.312 (0.240, 0.385)
10	0.304 (0.205, 0.403)

Note: Estimates with 95% confidence intervals in brackets for the years before and after the cardiovascular event.

Mental health or just a heart disease

The study was stratified in specific cardiovascular outcomes that are not easily differentiated from mental health symptoms. A patient with cardiovascular disease may have fatigue as the dominant symptom. In the HSCL-10, there are questions like: “Have you felt that everything is a struggle?”; or faintness or dizziness. These symptoms may be related to organic heart disease and can significantly impact mental health scores.

We examined our data to see the variance of symptoms between heart patients (myocardial infarction, atrial fibrillation or stroke) and those with no CVD. Symptoms like dizziness could be connected to anxiety and heart disease (Supplementary Table 1). However, fear, feeling depressed, feeling useless, and self-blame are not. We also observe that the heart patients in our study reported more fear but less self-blame and depression. Although the symptoms mentioned above do not explain the HSCL-10 score, the analysis is not conclusive.

Supplementary Table 3: Odds ratios from random-effects models examining differences between individuals with and without CVD on symptoms of anxiety and depression. The Tromsø Study.

	Myocardial infarction	Atrial fibrillation	Stroke
Have you experienced sudden fear without apparent reason during the last week?	1.88***	1.75**	1.36
	(1.30, 2.70)	(1.20, 2.54)	(0.88, 2.12)
Have you felt afraid or anxious during the last week?	0.87	1.07	0.84
	(0.63, 1.21)	(0.77, 1.48)	(0.57, 1.23)
Have you experienced faintness or dizziness during the last week?	1.72***	2.12***	2.20***
	(1.46, 2.03)	(1.78, 2.53)	(1.79, 2.71)
Have you felt tense or upset during the last week?	0.57***	0.55***	0.51***
	(0.46, 0.71)	(0.44, 0.69)	(0.39, 0.67)
Have you easily blamed yourself during the last week?	0.58***	0.74**	0.51***
	(0.46, 0.72)	(0.59, 0.92)	(0.39, 0.67)
Have you had sleeping problems during the last week?	1.03	1.11	0.89
	(0.91, 1.18)	(0.96, 1.27)	(0.76, 1.06)
Have you felt depressed or sad during the last week?	0.73*	0.70**	0.74
	(0.57, 0.94)	(0.54, 0.91)	(0.55, 1.00)
Have you felt useless, worthless during the last week?	1.32*	1.12	1.61**
	(1.02, 1.70)	(0.86, 1.46)	(1.18, 2.19)
Have you felt that everything is a struggle during the last week?	1.02	0.81	0.85
	(0.84, 1.24)	(0.65, 1.00)	(0.66, 1.09)
Have you felt hopelessness with regard to the future during the last week?	0.99	1.18	0.98
	(0.77, 1.28)	(0.91, 1.53)	(0.72, 1.33)

Exponentiated coefficients; 95% confidence intervals in brackets

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