

Psychological Distress, Heart-Related Quality of Life, and Follow-up Participation in Outpatient Cardiac Rehabilitation: A Retrospective Longitudinal Cohort Study

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Research Article

Keywords: cardiac rehabilitation, health-related quality of life, HeartQoL, psychological distress, follow-up participation, programme dropout

Posted Date: October 18th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-11149865/v1>

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Additional Declarations: No competing interests reported.

Abstract

Background

To examine associations of baseline depression and anxiety with HeartQoL levels and change, questionnaire follow-up participation, and documented early programme dropout during outpatient cardiac rehabilitation (CR). Sex differences were evaluated as a secondary question.

Methods

HeartQoL data from 453 adults entering a nine-week outpatient CR programme at a Swiss centre (1 July 2022–31 December 2024) were analysed using random-intercept linear mixed-effects models with patient-level CR2 inference. Follow-up participation and documented early dropout were examined in a linked cohort of 453 participants using age- and sex-adjusted logistic regression, bootstrap analysis, and multiple imputation.

Results

Mean age was 62.6 years, 104 (23.0%) were female, and 249 (55.0%) had valid Global HeartQoL follow-up. HeartQoL increased in Global ($B = 0.308$), Physical ($B = 0.344$), and Emotional domains ($B = 0.208$; all $p < .001$). Higher PHQ-9 scores were associated with lower HeartQoL across domains, while higher GAD-7 scores were associated with lower Global and Emotional HeartQoL. No distress-by-time interaction reached statistical significance; the Emotional HeartQoL Time $\times$ GAD-7 estimate was borderline ($B = 0.032$, 95% CI $[-0.001, 0.066]$, $p = .060$) and remained so in the expanded sensitivity analysis ($p = .053$). In the linked cohort, 204/453 (45.0%) had no nine-week HeartQoL item. Higher baseline distress was associated with missing follow-up (OR = 1.44 per SD, 95% CI $[1.15, 1.80]$, $p = .001$), but not clearly with documented early programme dropout (OR = 1.26, 95% CI $[0.98, 1.61]$, $p = .068$). Of 76 documented dropouts, 60 lacked follow-up and 16 provided it.

Conclusions

Baseline psychological distress was associated with poorer HeartQoL and lower questionnaire follow-up participation, but did not clearly predict documented early programme dropout. The borderline anxiety-related estimate for Emotional HeartQoL change was exploratory and requires confirmation. Programme dropout and questionnaire nonresponse should be recorded and analysed as distinct outcomes.

Background

Cardiovascular disease (CVD) causes more than three million deaths annually in ESC member countries and remains Europe's leading cause of mortality [1]. In Switzerland, 116,389 people were hospitalised for CVD in 2024 (58.8% men and 41.2% women), and CVD-related hospitalisations have risen by approximately 20% since 2002 [2]. Although mortality from coronary heart disease and stroke declined across most sex and age groups between 1995 and 2018, plateaus emerged in selected groups [3].

Health-related quality of life (HRQoL) is a multidimensional, patient-centred outcome with prognostic relevance [4]. It cannot be inferred reliably from left ventricular ejection fraction, B-type natriuretic peptide, or angiographic disease severity [5–7]. Impaired HRQoL predicts cardiovascular morbidity, mortality, and rehospitalisation [8–10].

Women with coronary disease often report lower HRQoL and greater psychological burden than men [11, 12]. However, sex-specific responses to CR vary by diagnosis, treatment pathway, outcome domain, and study. Comparable improvements have been reported after CABG, whereas women after PCI showed less favourable anxiety and mental-HRQoL trajectories in one study [13]. A 2022 review found heterogeneous sex differences and frequent similarity in outcome gains despite poorer status among women at entry [14]. Diagnosis-specific differences in enrolment and outcomes among women have also been reported [15].

Exercise-based CR improves HRQoL and functional capacity in coronary disease and heart failure [16, 17]. Swiss studies found physical HRQoL gains in both sexes [18]. A Swiss phase II cohort published online in 2022 likewise reported significant improvement in women and men across HRQoL domains, with women entering CR at lower levels [19]. Better baseline exercise capacity predicts higher long-term physical HRQoL [20, 21].

Psychological distress is common in CR: depression affects approximately 18–40% of patients after myocardial infarction [22], and anxiety, depressive, or stress symptoms occur in many CR participants [23]. CR generally improves physical HRQoL and anxiety, although effects on depression are less consistent [24].

Baseline depression and anxiety are associated with lower CR adherence and dropout [25, 26] and may adversely affect exercise performance [27]. They may also influence change in selected HRQoL domains [28]. In REACH-HF, patients with heart failure and elevated depressive symptoms obtained larger HeartQoL benefits from home-based CR, whereas anxiety-related effects varied by outcome [29].

Few real-world outpatient CR studies have jointly examined depression, anxiety, multidomain HeartQoL trajectories, questionnaire follow-up, and documented programme dropout. This distinction is clinically and methodologically important because an absent patient-reported outcome is often treated as evidence of programme discontinuation, although the two events may not coincide. We therefore examined whether baseline depressive and anxiety symptoms were associated with HeartQoL levels and nine-week change, and whether baseline psychological distress predicted questionnaire follow-up nonavailability or documented early programme dropout. Sex differences in HeartQoL trajectories and distress associations were retained as secondary, exploratory questions.

Methods

Study Design and Setting

This retrospective longitudinal cohort study analysed routinely collected clinical data from the outpatient CR programme at a regional centre hospital in Eastern Switzerland. Eligible programme entries occurred between 1 July 2022 and 31 December 2024. The study was conducted in accordance with Swiss research legislation. The study was approved by the Ethics Committee of Eastern Switzerland (Ethikkommission Ostschweiz, EKOS), St. Gallen, Switzerland (BASEC No. 2025 – 01098). All patients had provided written institutional general consent for the secondary use of routinely collected health-related data.

Participants

All adult patients (age ≥ 18 years) with sufficient German language proficiency enrolled in the outpatient CR programme and holding a valid general consent were included. Patients without general consent or with insufficient German language proficiency were excluded, as psychometric screening is not conducted under these conditions in routine clinical practice. Entries before 1 July 2022 were outside the study period. The PsyEq export contained 457 project-65 records through 31 December 2024. Two test records were removed, leaving 455 source records for both analyses. One entry before the study start of 1 July 2022 and one record with a purported nine-week HeartQoL assessment dated on programme-entry day and no baseline HeartQoL assessment were excluded from each analysis. The final common cohort comprised 453 participants. The longitudinal analysis required a valid Global HeartQoL score, whereas the linked analysis counted any nine-week HeartQoL item. Figure 1 shows the common source count, exclusions, and follow-up definitions. Sex was obtained from the routinely collected administrative patient record and was coded as female or male; information on gender identity was not available.

Reporting followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations.

Programme Description

The multidisciplinary outpatient CR programme included standardised ergometry and psychometric assessment at programme entry. The total duration of rehabilitation varied according to attendance and completion of the prescribed sessions. A standardised psychometric follow-up assessment was scheduled nine weeks after programme entry using the same instrument battery. Discharge ergometry was not systematically available for analysis, as a substantial proportion of patients completed exit ergometry with external cardiologists, precluding uniform data capture.

Outcome Measures

HRQoL was assessed at programme entry and at the scheduled nine-week follow-up using the 14-item HeartQoL questionnaire. The Physical subscale comprises 10 items, the Emotional subscale four items, and the Global scale all 14 items. Scores range from 0 to 3, with higher scores indicating better HRQoL [30, 31]. Baseline PHQ-9 (depression; 0–27) [32] and GAD-7 (anxiety; 0–21) [33] were analysed continuously. Baseline exercise capacity, LVEF, myocardial infarction subtype, heart failure, and five cardiovascular risk factors were obtained from routine records. Four contradictory STEMI/NSTEMI records were treated as missing for subtype.

Statistical Analysis

Descriptive statistics are reported as means and standard deviations or frequencies and percentages. Cardiac characteristics and cardiovascular risk factors were summarised for the cohort and by sex using variable-specific denominators; these sex comparisons were descriptive. Baseline characteristics were compared between patients with and without a valid Global HeartQoL follow-up using Welch tests with Cohen d or chi-square tests with Cramer V .

Primary longitudinal analyses used random-intercept LMMs and all available outcome observations. Model 1 included time; Model 2 added sex, centred age, and Time $\times$ Sex; Model 3 added centred baseline PHQ-9 and GAD-7 and their interactions with time. Separate exploratory models tested Time $\times$ Sex $\times$ PHQ-9 and Time $\times$ Sex $\times$ GAD-7.

A linked analysis examined questionnaire nonavailability and documented early programme dropout in the broader PsyEq cohort of 453 participants. Follow-up was considered unavailable when no nine-week HeartQoL item had been completed. A separate list of withdrawals during programme weeks 1–8 was linked to PsyEq by date of birth; programme-entry year was used only to resolve duplicate birth dates. All uniquely linked participants were classified as documented early dropout irrespective of questionnaire availability; records without a unique PsyEq match were excluded. A baseline distress composite was calculated as the mean of standardised PHQ-9 and GAD-7 scores and rescaled to one standard deviation. Logistic models used HC3 standard errors and adjusted for age and sex. Entry year was included only in a sensitivity model. The complete-case estimate was supplemented by 2,000 bootstrap samples and multiple imputation with 20 datasets for missing PHQ-9 or GAD-7 values.

Fixed-effect inference used patient-level cluster-robust CR2 standard errors with coefficient-specific Satterthwaite degrees of freedom following Bell-McCaffrey small-sample methods [34]. Results are unstandardised coefficients (B), robust standard errors, 95% confidence intervals, and two-sided p values. Statistical significance was set at .05. Nested comparisons between Models 1–3 used maximum-likelihood likelihood-ratio tests restricted to identical domain-specific analytic samples; models with different fixed effects were not compared using restricted maximum likelihood. Interaction analyses were exploratory, and no adjustment for multiple testing was applied. Primary analyses were conducted in R 4.3.1 [35].

Primary models used complete observed baseline covariates. A sensitivity analysis used 20 chained-equation imputations with posterior sampling for missing baseline covariates; HeartQoL outcomes were not imputed. The expanded sensitivity model included time, sex, age, STEMI, NSTEMI, heart failure, LVEF, exercise capacity, a five-factor cardiovascular risk count, PHQ-9, GAD-7, and Time $\times$ Sex, Time $\times$ PHQ-9, and Time $\times$ GAD-7. CR2 covariance estimates were calculated within each imputation and pooled using Rubin rules with Barnard-Rubin degrees of freedom. This analysis included 448 patients, 691 observed outcome records, and all 249 follow-ups. Imputation reduced loss caused by missing baseline covariates but did not resolve potentially informative outcome nonresponse. The missing-at-random assumption remains untestable.

Use of Generative Artificial Intelligence

ChatGPT (OpenAI, San Francisco, CA, USA; accessed August–September 2026) was used to support English-language editing, manuscript organisation, presentation of statistical results, and the generation and checking of code for secondary sensitivity analyses. It was not used to generate primary data or to make final analytical or interpretive decisions. All AI-assisted output was critically reviewed, verified against the source data and statistical results, and revised by the authors, who take full responsibility for the final manuscript.

Results

Sample Characteristics and Follow-up Availability

Table 1 summarises cardiac characteristics by sex. STEMI was recorded in 149 (32.9%) and NSTEMI in 137 (30.2%) participants; heart failure was present in 147/420 (35.0%). Hypercholesterolaemia (358/415, 86.3%), hypertension (238/414, 57.5%), and smoking (233/413, 56.4%) were common. Smoking was descriptively more frequent among men, whereas hypertension and diabetes were more frequent among women. Table 2 compares the 249 participants with and 204 without Global HeartQoL follow-up. Baseline PHQ-9 and GAD-7 scores were higher when follow-up was unavailable; age, sex, HeartQoL, LVEF, and exercise capacity did not differ significantly.

Table 1
Baseline Cardiac Characteristics and Cardiovascular Risk Factors by Sex

Variable	Total	Men	Women
STEMI	149/453 (32.9%)	119/349 (34.1%)	30/104 (28.8%)
NSTEMI	137/453 (30.2%)	105/349 (30.1%)	32/104 (30.8%)
Coronary heart disease	374/422 (88.6%)	295/324 (91.0%)	79/98 (80.6%)
Heart failure	147/420 (35.0%)	108/324 (33.3%)	39/96 (40.6%)
Any cardiac intervention	398/420 (94.8%)	306/322 (95.0%)	92/98 (93.9%)
Angiography with stent	318/386 (82.4%)	252/302 (83.4%)	66/84 (78.6%)
Positive family history	141/416 (33.9%)	113/321 (35.2%)	28/95 (29.5%)
Arterial hypertension	238/414 (57.5%)	179/320 (55.9%)	59/94 (62.8%)
Hypercholesterolaemia	358/415 (86.3%)	279/320 (87.2%)	79/95 (83.2%)
Smoking	233/413 (56.4%)	191/320 (59.7%)	42/93 (45.2%)
Diabetes mellitus	136/410 (33.2%)	100/318 (31.4%)	36/92 (39.1%)
LVEF, %, mean (SD)	52.2 (11.3); n = 411	51.6 (11.4); n = 316	54.1 (10.9); n = 95
Exercise capacity, W, mean (SD)	120.6 (42.9); n = 410	131.5 (41.2); n = 318	83.1 (22.8); n = 92
Note. Values are n/N (%) unless otherwise stated. Denominators vary because of missing routine clinical data. STEMI and NSTEMI required a concordant incident indicator and exactly one subtype flag; four contradictory records were treated as missing. Diagnoses and risk factors are not mutually exclusive. Sex comparisons are descriptive. LVEF = left ventricular ejection fraction; NSTEMI = non-ST-elevation myocardial infarction; STEMI = ST-elevation myocardial infarction.			

Table 2
Baseline Characteristics by Availability of a Valid Nine-Week Global HeartQoL Score in the Primary Longitudinal Cohort

Variable	Total n (%) or M (SD)	Follow-up available n (%) or M (SD)	Follow-up unavailable n (%) or M (SD)	p	Effect size
Sex				.278	V = 0.05
Female	104 (23.0%)	62 (24.9%)	42 (20.6%)		
Male	349 (77.0%)	187 (75.1%)	162 (79.4%)		
Age	62.6 (11.3)	63.4 (10.8)	61.6 (11.8)	.090	d = -0.16
PHQ-9	4.4 (4.6)	3.7 (3.9)	5.2 (5.2)	< .001	d = 0.33
GAD-7	4.0 (4.1)	3.4 (3.6)	4.8 (4.6)	< .001	d = 0.34
HeartQoL Global	2.20 (0.61)	2.25 (0.57)	2.14 (0.65)	.061	d = -0.18
HeartQoL Physical	2.14 (0.68)	2.19 (0.66)	2.08 (0.71)	.098	d = -0.16
HeartQoL Emotional	2.35 (0.67)	2.40 (0.65)	2.29 (0.70)	.073	d = -0.17
LVEF, %	52.2 (11.3)	52.2 (11.0)	52.1 (11.7)	.938	d = -0.01
Exercise capacity, W	120.6 (42.9)	123.6 (44.5)	116.7 (40.4)	.101	d = -0.16
Note. Both analyses used the same 453 participants after exclusion of one pre-study entry and one invalid same-day assessment from 455 source records. Total N = 453; follow-up available n = 249; unavailable n = 204. Follow-up availability in this table was defined by a valid nine-week Global HeartQoL score in the primary longitudinal cohort. This endpoint differs from the any-item follow-up definition used in the linked 453-participant analysis. Questionnaire availability does not indicate completion or discontinuation of the rehabilitation programme. Continuous variables were compared using Welch tests; effect sizes are Cohen d. Sex was compared using a chi-square test; effect size is Cramer V. Positive d values indicate higher values among participants without follow-up. LVEF = left ventricular ejection fraction; PHQ-9 = Patient Health Questionnaire-9; GAD-7 = Generalized Anxiety Disorder-7.					

Follow-up Participation and Documented Programme Dropout

After exclusion of the same-day assessment, the linked PsyEq cohort comprised 453 participants: 249 (55.0%) completed at least one nine-week HeartQoL item and 204 (45.0%) did not. The external dropout list contained 130 records, of which 80 records were linked to PsyEq and represented 77 unique PsyEq codes. After resolving duplicate entries, 76 PsyEq participants had a documented early dropout; 60 lacked follow-up and 16 nevertheless had follow-up data. Documented early dropout therefore accounted for 60/204 (29.4%) of missing follow-ups, whereas 144/204 (70.6%) had no linked early-dropout record. The 16 participants with follow-up remained in the documented dropout group because programme discontinuation and questionnaire completion are distinct outcomes. The 50 dropout-list records without a unique PsyEq match were excluded from participant-level classification and regression analyses, irrespective of list year.

Among participants with complete PHQ-9 and GAD-7 data (n = 441), each one-standard-deviation increase in the distress composite was associated with higher odds of missing follow-up (OR = 1.44, 95% CI [1.15, 1.80], p =

.001). The association was supported by the bootstrap interval (95% CI [1.17, 1.84]) and multiple imputation in all 453 participants (OR = 1.39, 95% CI [1.12, 1.71], $p = .002$). Distress was not clearly associated with documented early dropout (OR = 1.26, 95% CI [0.98, 1.61], $p = .068$). After excluding participants with documented early dropout, distress remained associated with missing follow-up (OR = 1.39, 95% CI [1.08, 1.78], $p = .009$). Adjustment for entry year produced a similar estimate (OR = 1.43, 95% CI [1.13, 1.82], $p = .003$).

Linear Mixed-Effects Models

Across the three HeartQoL outcomes, the time-only models (Model 1) showed significant increases in HeartQoL from baseline to the 9-week follow-up. Model 2 additionally included sex, age, and the Time $\times$ Sex interaction. At baseline and mean age, female sex was associated with lower Global ($B = -0.229$, $p = .001$), Physical ($B = -0.206$, $p = .010$), and Emotional HeartQoL ($B = -0.288$, $p < .001$). Compared with Model 1, Model 2 significantly improved model fit for Global HeartQoL, $\chi^2(3) = 20.4$, $p < .001$, Physical HeartQoL, $\chi^2(3) = 12.9$, $p = .005$, and Emotional HeartQoL, $\chi^2(3) = 31.9$, $p < .001$.

Model 3 added baseline PHQ-9 and GAD-7 scores and their interactions with time and further improved model fit compared with Model 2 (Global: $\chi^2(4) = 267.0$; Physical: $\chi^2(4) = 159.0$; Emotional: $\chi^2(4) = 427.0$; all $p < .001$).

Fixed-effect estimates from Model 3 are presented in Table 3. HeartQoL increased in the Global ($B = 0.308$), Physical ($B = 0.344$), and Emotional domains ($B = 0.208$; all $p < .001$). Higher baseline PHQ-9 scores were associated with lower HeartQoL across all domains. Higher baseline GAD-7 scores were associated with lower Global and Emotional, but not Physical, HeartQoL. Female sex remained associated with lower Emotional HeartQoL ($B = -0.130$, $p = .024$), but not with Global or Physical HeartQoL after distress adjustment.

Table 3
Primary Linear Mixed-Effects Models Predicting Global, Physical, and Emotional HeartQoL

Predictor	Global B (robust SE)	95% CI	p	Physical B (robust SE)	95% CI	p	Emotional B (robust SE)	95% CI	p
Intercept	2.215 (0.026)	[2.165, 2.266]	< .001	2.153 (0.032)	[2.089, 2.216]	< .001	2.374 (0.023)	[2.329, 2.420]	< .001
Time (9-week vs. baseline)	0.308 (0.034)	[0.240, 0.375]	< .001	0.344 (0.037)	[0.270, 0.418]	< .001	0.208 (0.038)	[0.132, 0.284]	< .001
Sex (female vs. male)	-0.109 (0.056)	[-0.219, 0.001]	.053	-0.102 (0.069)	[-0.238, 0.034]	.139	-0.130 (0.057)	[-0.242, -0.018]	.024
Age (centred)	-0.002 (0.002)	[-0.005, 0.002]	.399	-0.003 (0.002)	[-0.007, 0.002]	.230	0.002 (0.002)	[-0.002, 0.005]	.336
Depression (PHQ-9, centred)	-0.056 (0.008)	[-0.072, -0.039]	< .001	-0.065 (0.010)	[-0.086, -0.044]	< .001	-0.033 (0.010)	[-0.052, -0.014]	< .001
Anxiety (GAD-7, centred)	-0.039 (0.010)	[-0.058, -0.020]	< .001	-0.017 (0.012)	[-0.042, 0.007]	.159	-0.092 (0.011)	[-0.113, -0.070]	< .001
Time × Sex	-0.070 (0.073)	[-0.214, 0.074]	.339	-0.092 (0.081)	[-0.253, 0.069]	.260	0.001 (0.087)	[-0.171, 0.173]	.991
Time × Depression	0.003 (0.011)	[-0.019, 0.024]	.791	0.007 (0.011)	[-0.016, 0.029]	.561	-0.002 (0.015)	[-0.033, 0.028]	.883
Time × Anxiety	0.022 (0.013)	[-0.004, 0.049]	.099	0.016 (0.013)	[-0.011, 0.043]	.238	0.032 (0.017)	[-0.001, 0.066]	.060
Note. B = unstandardised regression coefficient; SE = standard error; CI = confidence interval. Inference uses patient-level CR2 standard errors and Satterthwaite small-sample corrections. Model 3 included time, sex, centred age, centred PHQ-9 and GAD-7, and Time × Sex, Time × PHQ-9, and Time × GAD-7, with a patient-specific random intercept. Male sex and baseline were reference categories. Bold values denote p < .05.									

Table 4
Associations of Baseline Psychological Distress with Follow-up Nonresponse and Documented Early Programme Dropout

Outcome or analysis	Predictor	N	Events	OR	95% CI	p
No follow-up	Distress composite, per 1 SD	441	198	1.44	1.15–1.80	.001
No follow-up	PHQ-9, per 5 points	441	198	1.44	1.13–1.84	.003
No follow-up	GAD-7, per 5 points	443	199	1.52	1.18–1.97	.001
Documented early dropout	Distress composite, per 1 SD	441	74	1.26	0.98–1.61	.068
No follow-up after excluding documented dropout	Distress composite, per 1 SD	367	140	1.39	1.08–1.78	.009
No follow-up, entry-year sensitivity	Distress composite, per 1 SD	441	198	1.43	1.13–1.82	.003
No follow-up, multiple imputation	Distress composite, per 1 SD	453	204	1.39	1.12–1.71	.002
Note. Odds ratios are adjusted for age and sex unless otherwise specified. The entry-year sensitivity additionally included programme-entry year. The multiple-imputation model used 20 datasets and included all 453 participants. The primary distress estimate was also supported by a 2,000-sample bootstrap interval (OR 95% CI 1.17–1.84). OR = odds ratio; CI = confidence interval; PHQ-9 = Patient Health Questionnaire-9; GAD-7 = Generalized Anxiety Disorder-7. Bold p values denote $p < .05$.						

No Time $\times$ Sex or Time $\times$ PHQ-9 interaction was significant. Time $\times$ GAD-7 was also non-significant for Global and Physical HeartQoL. For Emotional HeartQoL, the estimate was positive but did not meet the significance threshold ($B = 0.032$, 95% CI $[-0.001, 0.066]$, $p = .060$).

CR2 Sensitivity Analysis Retaining All Follow-ups

The expanded CR2 sensitivity models retained all 249 follow-up assessments after imputation of baseline covariates. HeartQoL increased across domains, and Time $\times$ Sex and Time $\times$ PHQ-9 remained non-significant. The Emotional HeartQoL Time $\times$ GAD-7 estimate remained borderline but non-significant ($B = 0.033$, 95% CI $[-0.0005, 0.066]$, $p = .053$); corresponding Global and Physical interactions were non-significant. Exercise capacity was associated with higher Global and Physical HeartQoL, whereas cardiovascular risk-factor count was not. Full results are reported in Additional file 1.

Supplementary Time $\times$ Sex $\times$ Distress Interaction Analyses

Exploratory Models 3a and 3b examined whether the association between baseline psychological distress and HeartQoL change over time differed by sex. In Model 3a, none of the Time $\times$ Sex $\times$ PHQ-9 interactions was statistically significant for Global ($B = 0.008$, 95% CI $[-0.030, 0.045]$, $p = .679$), Physical ($B = 0.011$, 95% CI $[-0.033, 0.055]$, $p = .613$), or Emotional HeartQoL ($B = -0.003$, 95% CI $[-0.058, 0.052]$, $p = .921$). Likewise, in Model 3b, none of the Time $\times$ Sex $\times$ GAD-7 interactions was significant for Global ($B = 0.007$, 95% CI $[-0.034, 0.049]$, $p = .717$), Physical ($B = 0.005$, 95% CI $[-0.041, 0.051]$, $p = .812$), or Emotional HeartQoL ($B = 0.005$, 95% CI $[-0.048, 0.058]$, $p = .854$). Thus, the associations between baseline depressive or anxiety symptoms and

HeartQoL change over time did not differ significantly between women and men. Full coefficient estimates are provided in Additional file 1.

Discussion

The central finding was that baseline psychological distress related to both patient-reported health status and subsequent questionnaire participation, but not clearly to documented programme withdrawal. Higher depression and anxiety scores were associated with poorer HeartQoL levels, while higher composite distress increased the odds of missing nine-week follow-up. HeartQoL nevertheless increased across all domains among participants who contributed data, and no robust distress-by-time interaction was detected. The only near-threshold interaction was the positive Emotional HeartQoL Time $\times$ GAD-7 estimate, which remained borderline but non-significant in the primary and expanded sensitivity models. Programme dropout and questionnaire nonresponse overlapped only partly and should not be treated as interchangeable outcomes.

Psychological Distress, Follow-up Participation, and Programme Dropout

The linked analysis refined the interpretation of missing follow-up. Greater baseline distress was associated with missing questionnaire follow-up, and this association persisted after multiple imputation, adjustment for entry year, and exclusion of documented early dropouts. By contrast, the association between distress and documented early programme dropout did not reach statistical significance. These results suggest that the observed distress signal relates more consistently to questionnaire non-response or other forms of follow-up loss than to confirmed early withdrawal from the rehabilitation programme.

The estimated increases of 0.308 points in Global and 0.344 points in Physical HeartQoL were approximately one-half of the baseline standard deviation and may therefore be of potentially meaningful magnitude [12]. The smaller Emotional HeartQoL increase of 0.208 points was below this distribution-based benchmark. However, a universally accepted anchor-based minimal clinically important difference for HeartQoL has not been established, and group-level mean changes do not indicate that every patient experienced a clinically important improvement.

Sex differences may reflect illness perceptions, health literacy, symptoms, and coping [38]. Adding PHQ-9 and GAD-7 attenuated female-sex coefficients, indicating statistical overlap but not mediation. Shared construct content and possible overadjustment must be considered; Model 3 estimates conditional associations, not causal explanations.

Psychological Distress and HeartQoL

Baseline anxiety was associated with lower Global and Emotional HeartQoL levels. The positive Time $\times$ GAD-7 estimate for Emotional HeartQoL was borderline in the primary model ($p = .060$) and in the expanded CR2 sensitivity analysis retaining all follow-ups ($p = .053$). Its confidence interval included zero, corresponding interactions for Global and Physical HeartQoL were non-significant, and no Time $\times$ Sex $\times$ GAD-7 interaction was detected. The directionally consistent estimate may justify prospective study, but it is not robust evidence that baseline anxiety predicts a different emotional recovery trajectory [28, 29, 38].

Higher depressive symptoms were associated with lower HeartQoL levels across all domains. Nevertheless, depression did not predict the magnitude of HeartQoL change in the primary LMMs, and no Time × Sex × PHQ-9 interaction was significant in the supplementary longitudinal models. This distinction between an association with HeartQoL level and moderation of longitudinal change is important: poorer HeartQoL among patients with greater baseline distress does not imply a detectably different rehabilitation trajectory. A 2024 meta-analysis found that CR improves the physical component of HRQoL and reduces anxiety, whereas effects on depression were less consistent [24]. Although non-significant interactions are not proof of equivalence, the present findings provide no evidence that distress-related differences in HeartQoL trajectories are confined to one sex. Because baseline depression, anxiety, and HeartQoL were assessed concurrently, the observed associations between baseline distress and HeartQoL level cannot establish temporal or causal direction. Although psychological distress was also assessed at follow-up, changes in distress were not modelled as time-varying predictors of HeartQoL. Studies with multiple intermediate assessments are needed to examine reciprocal longitudinal pathways and formally test mediation.

Exercise Capacity and HeartQoL

Higher baseline exercise capacity was independently associated with higher physical and global HeartQoL, consistent with the established evidence base [18, 20]. However, the Time x Exercise Capacity interactions were not significant. Baseline exercise capacity therefore reflected physical and global HeartQoL levels but did not predict HeartQoL improvement. Because discharge ergometry was not uniformly available, this study could not determine whether change in exercise capacity tracked or mediated change in HeartQoL. Such analyses require repeated, consistently captured functional measurements.

HeartQoL Trajectories and Sex

Women had lower age-adjusted baseline HeartQoL in all domains. After adjustment for depression and anxiety, only the Emotional-domain difference remained significant. Change did not differ detectably by sex. This agrees with the 2022 review by Smith et al., which described heterogeneous sex differences but broadly similar benefits in many CR cohorts [14], and with the Swiss phase II study published online in 2022 in which both sexes improved across HRQoL domains [19]. Recent reviews and guidance continue to emphasise barriers and heterogeneous outcomes among women [36, 37]. These findings do not establish equivalence because fewer women contributed follow-up data.

Only 60 of the 204 participants without any nine-week HeartQoL item had a linked early-dropout record; 144 had no documented early dropout. Conversely, 16 participants with a linked early dropout nevertheless provided follow-up data. Programme discontinuation and questionnaire availability are therefore related but non-equivalent outcomes. Several mechanisms could contribute to questionnaire non-response, including reduced motivation, avoidance, illness-related fear, competing health demands, and difficulties engaging with assessment procedures. Depression has been associated with dropout in home-based CR [26], but the present analysis does not establish that distress caused programme withdrawal.

The 50 records in the external dropout list without a unique PsyEq match could not be assigned participant-level baseline PHQ-9 or GAD-7 values and were therefore excluded from the classified dropout group and regression analyses, irrespective of list year. Their absence from PsyEq may reflect missing registration or baseline assessment, but the available data do not permit a more specific interpretation. Prospective studies should

distinguish questionnaire non-response, temporary interruption, medically indicated discontinuation, and programme dropout, and should record reasons and timing systematically.

Clinical Implications

Baseline PHQ-9 and GAD-7 scores identified clinically relevant psychological burden associated with poorer HeartQoL and lower follow-up questionnaire participation. Brief screening at programme entry may therefore support clinical assessment, psychocardiological referral when indicated, and proactive follow-up contact. Screening alone does not identify the reason for nonresponse and should not be used as a programme-dropout prediction rule. Exercise testing and HRQoL assessment remain important for individualised exercise prescription and patient-centred outcome monitoring [4, 16, 17]. Women-focused and mobile-health approaches may support selected outcomes [42, 43], while current guidance emphasises psychosocial management, flexible delivery, and individualised strategies [36, 37, 39, 44–46].

Limitations

Several limitations merit consideration. The retrospective, uncontrolled, single-centre design precludes attribution of observed change to CR and limits generalisability beyond comparable German-speaking outpatient settings. Eligibility depended on sufficient German proficiency and valid general consent, which may have introduced selection. In the primary 453-person longitudinal cohort, Global HeartQoL follow-up was unavailable for 45.0%; in the broader 453-person linkage cohort, 204 participants had no completed nine-week HeartQoL item. Linkage identified documented early dropout for only 60 of these 204 participants, but the external dropout list may be incomplete and 50 listed records could not be uniquely linked to PsyEq and were excluded irrespective of year. The smaller number of women, particularly the 62 women with valid Global HeartQoL follow-up, limited precision for interaction estimates and precludes claims of equivalence.

The primary LMMs and multiple-imputation sensitivity analysis rely on missing-at-random assumptions conditional on included variables. These assumptions are untestable, and imputation of baseline covariates does not resolve potentially informative outcome nonresponse. With only baseline and one scheduled follow-up, the models estimate average change between two occasions and cannot characterise nonlinear trajectories or the timing of change. CR2 inference reduces sensitivity to some covariance misspecification but does not correct informative attrition or a misspecified mean structure. The Emotional HeartQoL Time $\times$ GAD-7 result was close to .05 across specifications, arose among several unadjusted exploratory interaction tests, and should not be interpreted as confirmatory evidence.

The clinically heterogeneous cohort may obscure diagnosis-specific trajectories. Routine cardiac variables had missing data and did not capture disease severity, treatment control, socioeconomic circumstances, or cumulative exposure. Baseline PHQ-9, GAD-7, and HeartQoL were measured concurrently, limiting temporal interpretation and raising the possibility of shared construct variance. Discharge exercise capacity was not captured uniformly, preventing analysis of whether functional improvement accompanied HeartQoL change. Future multicentre studies should document programme status and reasons for nonresponse, repeat psychological and functional measurements, and prespecify missing-outcome sensitivity and multiplicity strategies.

Conclusions

In this real-world outpatient CR cohort, higher baseline depression and anxiety were associated with poorer HeartQoL levels, while HeartQoL increased across Global, Physical, and Emotional domains among participants contributing longitudinal data. Distress measures did not robustly predict different HeartQoL trajectories. The positive Time $\times$ GAD-7 estimate for Emotional HeartQoL was borderline across primary and sensitivity specifications and should be treated as exploratory rather than as evidence of an anxiety-related recovery effect. The uncontrolled design prevents causal attribution of improvement to CR.

Higher baseline psychological distress was associated with missing questionnaire follow-up but not clearly with documented early programme dropout. Of 76 documented dropouts, 16 still provided follow-up data, confirming that programme discontinuation and questionnaire nonresponse are related but distinct outcomes. Routine psychological screening may help identify patients requiring clinical assessment and proactive contact, whereas prospective studies should record the timing and reasons for nonresponse and programme withdrawal separately. Sex differences remain relevant secondary findings, but no detectable sex-specific difference in HeartQoL change or distress-related trajectory was observed.

Declarations

Ethics approval and consent to participate

The Ethics Committee of Eastern Switzerland (Ethikkommission Ostschweiz, St. Gallen, Switzerland) approved the study (BASEC No. 2025-01098). All included patients had provided written institutional general consent for the secondary use of routinely collected health-related data.

Consent for publication

Not applicable.

Availability of data and materials

The individual-level data underlying this article cannot be shared publicly because they contain sensitive health information and are subject to Swiss data-protection, ethics, and institutional requirements. Requests for access to de-identified data may be directed to the corresponding author and will require approval by the responsible institution and ethics committee.

Competing interests

The authors declare that they have no competing interests.

Funding

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Authors' contributions

Stefan Brokatzky: Conceptualization, Methodology, Formal analysis, Investigation, Ethics application, Project administration, Writing - original draft, Writing - review and editing. Rahel Sila: Conceptualization, Methodology, Formal analysis, Validation, Ethics application, Writing - review and editing. Lena Jellestad: Psychocardiological conceptualization, Validation, Writing - review and editing. Marc Buser: Cardiology methodology, Selection and interpretation of clinical variables, Rehabilitation expertise, Writing - review and editing. Nikolas German: Software implementation, Data curation, Staff training, Resources, Writing - review and editing. Hans Rickli: Supervision, Validation, Writing - review and editing. Dagmar Astrid Schmid: Conceptualization, Methodology, Project administration, Supervision, Critical revision, Writing - review and editing. All authors read and approved the final manuscript.

Acknowledgements

Not applicable.

Patient and public involvement

There was no formal patient or public involvement in the prioritisation, design, conduct, analysis, interpretation, or dissemination of this study.

References

1. Timmis A, Townsend N, Gale CP, et al. European Society of Cardiology: cardiovascular disease statistics 2023. *Eur Heart J*. 2023;44:3992-4126. doi:10.1093/eurheartj/ehad583
2. Bundesamt für Statistik. Gesundheitsstatistik 2025. Neuchâtel: Bundesamt für Statistik; 2025.
3. Sorrentino L, Chiolerio A, Carmeli C. Cardiovascular mortality trends in Switzerland 1995-2018. *Eur J Public Health*. 2022;32:891-893. doi:10.1093/eurpub/ckac164
4. Rumsfeld JS, Alexander KP, Goff DC Jr, et al. Cardiovascular health: the importance of measuring patient-reported health status. *Circulation*. 2013;127:2233-2249. doi:10.1161/CIR.0b013e3182949a2e
5. Rumsfeld JS. Health status and clinical practice: when will they meet? *Circulation*. 2002;106:5-7.
6. Rector TS, Anand IS, Cohn JN. Relationships between clinical assessments and patients' perceptions of the effects of heart failure on their quality of life. *J Card Fail*. 2006;12:87-92. doi:10.1016/j.cardfail.2005.10.002
7. Nelson CL, Herndon JE, Mark DB, et al. Relation of clinical and angiographic factors to functional capacity as measured by the Duke Activity Status Index. *Am J Cardiol*. 1991;68:973-975. doi:10.1016/0002-9149(91)90423-I
8. Dixon T, Lim LLY, Heller RF. Quality of life: an index for identifying high-risk cardiac patients. *J Clin Epidemiol*. 2001;54:952-960. doi:10.1016/S0895-4356(01)00368-7
9. Hofer S, Benzer W, Oldridge N. Change in health-related quality of life in patients with coronary heart disease predicts 4-year mortality. *Int J Cardiol*. 2014;174:7-12.

10. Hansen TB, Thygesen LC, Zwisler AD, et al. Self-reported health-related quality of life predicts 5-year mortality and hospital readmissions in patients with ischaemic heart disease. *Eur J Prev Cardiol.* 2015;22:882-889. doi:10.1177/2047487314535682
11. Vynckier P, Van Wilder L, Kotseva K, et al. Sex differences in health-related quality of life and psychological distress in coronary patients: EUROASPIRE V. *Int J Cardiol.* 2023;371:36-44. doi:10.1016/j.ijcard.2022.09.009
12. De Smedt D, Clays E, Höfer S, et al. The use of HeartQoL in patients with coronary heart disease: association with risk factors and European reference values. *Eur J Prev Cardiol.* 2016;23:1174-1186. doi:10.1177/2047487316631400
13. Terada T, Vidal-Almela S, Tulloch HE, Pipe AL, Reed JL. Cardiac rehabilitation following percutaneous coronary intervention is associated with superior psychological health and quality of life in males but not in females. *J Cardiopulm Rehabil Prev.* 2021;41:345-350. doi:10.1097/HCR.0000000000000597
14. Smith JR, Thomas RJ, Bonikowske AR, Hammer SM, Olson TP. Sex differences in cardiac rehabilitation outcomes. *Circ Res.* 2022;130:552-565. doi:10.1161/CIRCRESAHA.121.319894
15. Baig M, Imran HM, Gaw A, Stabile L, Wu WC. Cardiac rehabilitation in women: comparison of enrollment, adherence and outcomes between heart failure and coronary artery disease. *Heart Lung.* 2021;50:223-229. doi:10.1016/j.hrtlng.2020.12.004
16. Dibben GO, Faulkner J, Oldridge N, et al. Exercise-based cardiac rehabilitation for coronary heart disease: a meta-analysis. *Eur Heart J.* 2023;44:452-469. doi:10.1093/eurheartj/ehac747
17. Molloy CD, Long L, Mordi IR, et al. Exercise-based cardiac rehabilitation for adults with heart failure: a meta-analysis. *Eur J Heart Fail.* 2023;25:2263-2273. doi:10.1002/ehf.3046
18. Lanini LLS, Euler S, Zuccarella-Hackl C, et al. Differential associations of sex and age with changes in health-related quality of life during outpatient cardiac rehabilitation. *J Patient Rep Outcomes.* 2024;8:11. doi:10.1186/s41687-024-00688-x
19. Jellestad L, Auschra B, Zuccarella-Hackl C, et al. Sex and age as predictors of health-related quality-of-life change in phase II cardiac rehabilitation. *Eur J Prev Cardiol.* 2023;30:128-136. doi:10.1093/eurjpc/zwac199
20. Auschra B, Euler S, Zehnder Y, et al. Long-term follow-up of HRQoL up to six years after outpatient phase-II cardiac rehabilitation. *Healthcare (Basel).* 2024;12:357. doi:10.3390/healthcare12030357
21. Fuentes Artilles R, Euler S, Auschra B, et al. Predictors of gain in exercise capacity through cardiac rehabilitation: sex and age matter. *Heart Lung.* 2023;62:200-206. doi:10.1016/j.hrtlng.2023.08.003
22. Bertolín-Boronat C, Marcos-Garcés V, Merenciano-González H, et al. Depression, anxiety, and quality of life in a cardiac rehabilitation program without dedicated mental health resources post-myocardial infarction. *J Cardiovasc Dev Dis.* 2025;12:92. doi:10.3390/jcdd12030092
23. Rao A, Zecchin R, Newton PJ, et al. Prevalence and impact of depression and anxiety in cardiac rehabilitation. *Eur J Prev Cardiol.* 2020;27:478-489. doi:10.1177/2047487319871716
24. Moreira J, Bravo J, Aguiar P, Delgado B, Raimundo A, Boto P. Physical and mental components of quality of life after a cardiac rehabilitation intervention: a systematic review and meta-analysis. *J Clin Med.* 2024;13:5576. doi:10.3390/jcm13185576
25. McGrady A, McGinnis R, Badenhop D, Bentle M, Rajput M. Effects of depression and anxiety on adherence to cardiac rehabilitation. *J Cardiopulm Rehabil Prev.* 2009;29:358-364.

doi:10.1097/HCR.0b013e3181be7a8f

26. Browne J, Medbury E, Ursillo J, Wu WC. Depression increases the risk of dropout from home-based cardiac rehabilitation. *J Cardiopulm Rehabil Prev.* 2025;45:227-229. doi:10.1097/HCR.0000000000000946
27. Ricci M, Pozzi G, Caraglia N, Chieffo DPR, Polese D, Galiuto L. Psychological distress affects performance during exercise-based cardiac rehabilitation. *Life (Basel).* 2024;14:236. doi:10.3390/life14020236
28. García-Sánchez E, Santamaría-Peláez M, González-Bernal JJ, et al. Impact of cardiac rehabilitation on anxiety, depression, and health-related quality of life in cardiovascular patients. *Egypt Heart J.* 2025;77:64. doi:10.1186/s43044-025-00658-8
29. Lambert J, Dibben G, van Beurden SB, et al. Impact of home-based cardiac rehabilitation in people with heart failure with elevated depressive and anxiety symptoms. *Eur J Cardiovasc Nurs.* 2026;25:186-192. doi:10.1093/eurjcn/zvaf196
30. Oldridge N, Hofer S, McGee H, et al. The HeartQoL: part I. Development of a new core health-related quality-of-life questionnaire for patients with ischemic heart disease. *Eur J Prev Cardiol.* 2014;21:90-97. doi:10.1177/2047487312450544
31. Oldridge N, Hofer S, McGee H, et al. The HeartQoL: part II. Validation of a new core health-related quality-of-life questionnaire for patients with ischemic heart disease. *Eur J Prev Cardiol.* 2014;21:98-106. doi:10.1177/2047487312450545
32. Kroenke K, Spitzer RL, Williams JBW. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med.* 2001;16:606-613.
33. Williams N. The GAD-7 questionnaire. *Occup Med (Lond).* 2014;64:224.
34. Pustejovsky JE, Tipton E. Small-sample methods for cluster-robust variance estimation and hypothesis testing in fixed effects models. *J Bus Econ Stat.* 2018;36:672-683. doi:10.1080/07350015.2016.1247004
35. R Core Team. R: A language and environment for statistical computing. Vienna: R Foundation for Statistical Computing; 2023. <https://www.R-project.org/>.
36. Coutinho T, Khadanga S, Adedinsewo D, et al. Cardiac rehabilitation in women: a scientific statement from the American Heart Association. *Circulation.* 2025;152:e376-e390. doi:10.1161/CIR.0000000000001379
37. McFeely AE, Bittner V. Sex- and gender-based differences in outcomes of cardiac rehabilitation following acute myocardial infarction. *Curr Atheroscler Rep.* 2025;27:109. doi:10.1007/s11883-025-01360-5
38. Jennings CS, Astin F, Prescott E, et al. Illness perceptions and health literacy are strongly associated with health-related quality of life, anxiety, and depression in patients with coronary heart disease: results from EUROASPIRE V. *Eur J Cardiovasc Nurs.* 2023;22:719-729. doi:10.1093/eurjcn/zvac105
39. McDonagh STJ, Dalal HM, Moore S, et al. Home-based versus centre-based cardiac rehabilitation. *Cochrane Database Syst Rev.* 2023;10:CD007130. doi:10.1002/14651858.CD007130.pub5
40. Tokarewicz J, Jankowiak B, Klimaszewska K, et al. Acceptance of illness and health-related quality of life in patients after myocardial infarction: narrative review. *J Clin Med.* 2025;14:729. doi:10.3390/jcm14030729
41. Deb R, Morgan N. The role of social support and sex on completion of cardiac rehabilitation. *J Am Coll Cardiol.* 2020;75(Suppl 1):abstract.
42. Osumi A, Kanejima Y, Kitamura M, Ishihara K, Izawa KP. Effects of cardiac rehabilitation on female patients with heart disease: a systematic review and meta-analysis. *Maturitas.* 2025;199:108653.

43. Dodson JA, Adhikari S, Schoenthaler A, et al. Rehabilitation at home using mobile health for older adults hospitalised for ischemic heart disease: the RESILIENT randomised clinical trial. JAMA Netw Open. 2025;8:e2453499.
44. Suebkinorn O, Ramos JS, Grace SL, Gebremichael LG. Effectiveness of alternative exercises in cardiac rehabilitation for program completion and outcomes in women with or at high risk of cardiovascular disease: a systematic review and meta-analysis. JBI Evid Synth. 2025;23:1041-1076. doi:10.11124/JBIES-24-00457
45. Brown TM, Pack QR, Aberegg E, et al. Core components of cardiac rehabilitation programs: 2024 update. Circulation. 2024;150:e328-e347. doi:10.1161/CIR.0000000000001289
46. Latir A, Hafiz E, Suhaimi A. Barriers to participation and adherence in cardiac rehabilitation programs: a scoping review of recent evidence from industrialized and developing countries. Rev Cardiovasc Med. 2026;27:45898.

Figures

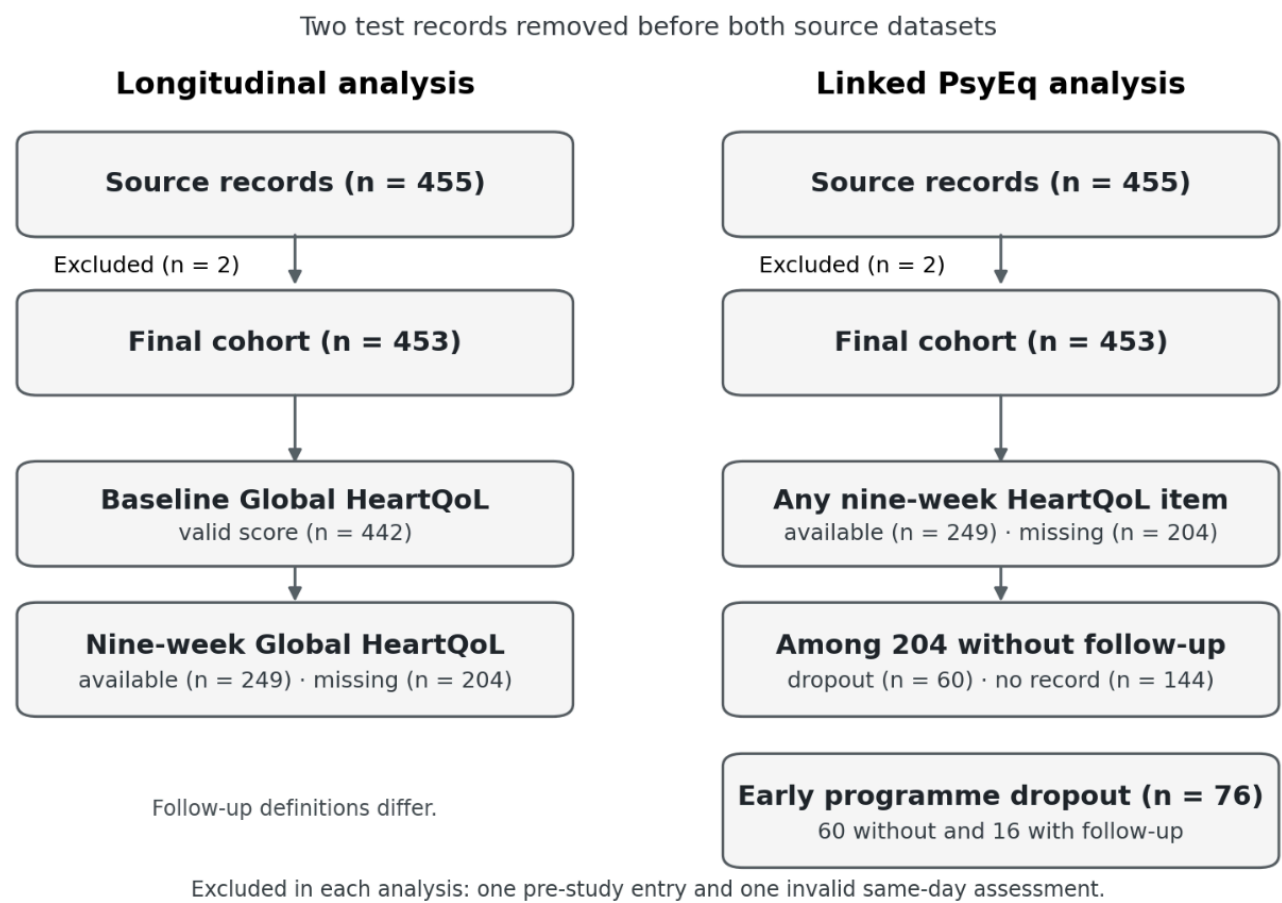


Figure 1

Study cohort and nine-week follow-up classification

Reporting followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations.

Supplementary Files

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