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Disease-Related Anxiety, Clinical Health Outcomes, and Health-Related Quality of Life in Patients with Cardiovascular Disease: A Systematic Review and Meta-Analysis

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Abstract

Cardiovascular Disease (CVD) constitutes the single leading cause of death and disability worldwide. Although mortality rates have been declining in recent decades, CVD still represents a severe threat to patients' health and health-related quality of life (HRQoL). Patients who develop comorbid disease-related anxiety are at increased risk for worse disease progression and impaired HRQoL. The purpose of this paper was to review the current scientific evidence and to perform a meta-analysis on the relationship between disease-related anxiety and clinical health outcomes in patients with CVD. Due to an insufficient number of studies, our analysis focused on the relationship between cardiac anxiety and HRQoL. The literature was searched for eligible articles published by September 2021 on eight online databases. Data extraction revealed 12 observational studies eligible for inclusion in the systematic review. Of those, 4 articles (including 985 patients) fulfilled the criteria to be included in the meta-analyses, which examined the association between cardiac anxiety and both physical and mental HRQoL, respectively. Under the random-effects model, we found a significant and negative correlation between cardiac anxiety and physical HRQoL ($r = -0.53$; 95% CI $[-0.57, -0.48]$; $p < .001$). Additionally, we found a significant and negative correlation of small-to-moderate strength between cardiac anxiety and mental HRQoL ($r = -0.43$; 95% CI $[-0.50, -0.35]$; $p < .001$). These results implicate that, on average, patients with CVD experience lower levels of both physical and mental HRQoL with increasing levels of cardiac anxiety. Our findings further suggest that routine screenings should be implemented in clinical practice to identify and potentially treat at-risk patients. Future research on the cause-and-effect of these relationships is warranted.

Keywords: cardiovascular disease, disease-specific anxiety, cardiac anxiety, kinesiophobia, fear of movement, cardiac rehabilitation

Layman's Abstract

Heart disease is a very common and serious health condition that causes death and disability worldwide. Some heart disease patients develop heart-focused fear, which causes them to worry excessively about their heart and health. Moreover, they often avoid activities that may cause them to experience negative heart-related symptoms (e.g., a fast heartbeat), such as physical activities and exercise. This, however, can lead to more heart damage and health-related problems, such as lower health-related quality of life (HRQoL). The goal of this paper was to summarize the available studies by other researchers on the relationship between heart-focused fear and HRQoL in patients with heart disease. We searched for articles that were published by September 2021 on eight online databases. In total, we identified 12 articles that fitted our research question. Of those, 4 studies (including 985 patients) fulfilled the criteria to be included in a statistical analysis. Our results showed that, on average, patients who experience greater heart-focused fear, seem to experience lower levels of HRQoL. These findings demonstrate that heart-focused fear can play an important role in the well-being of patients with heart disease. We propose that early routine check-ups should be carried out in patients with heart disease to identify and potentially treat at-risk patients before their symptoms worsen. More research on the direct and indirect relationships of heart-focused fear, HRQoL, and heart disease is needed.

Keywords: cardiovascular disease, disease-specific anxiety, cardiac anxiety, kinesiophobia, cardiac rehabilitation

Disease-Related Anxiety, Clinical Health Outcomes, and Health-Related Quality of Life in Patients with Cardiovascular Disease: A Systematic Review and Meta-Analysis

Cardiovascular disease (CVD), a group of diseases that affect the heart or blood vessels, constitutes the single leading cause of premature death and disability worldwide (WHO, 2021). In 2019 alone, an estimated 18.6 million deaths were attributed to the repercussions of CVD (Roth et al., 2020). Due to significant advances in the treatment of CVD, age-standardized mortality rates have been declining in many high-income countries in recent decades (e.g., Sanchis-Gomar et al, 2016). However, CVD prevalence and CVD-associated disease burden continue to increase globally (Roth et al., 2020). Cardiac rehabilitation has traditionally focused on the physical recovery of cardiac health and the prevention of secondary events (Clark et al., 2005; Mampuya, 2012). In recent decades, the improvement of health-related quality of life (HRQoL) has emerged as an additional major goal of cardiac rehabilitation after medical treatment (Krumholz et al., 2005; Shephard & Franklin, 2001). HRQoL constitutes a measure of an individual's physical and mental health and well-being (Karimi & Brazier, 2016) and is considerably determined by the way patients perceive and adjust to their illness (Petrie & Weinman, 2006). Thus, HRQoL extends beyond physical recovery and reflects the impact of CVD and its symptomatology on the patient's physical, mental, emotional, and social functioning (De Smedt et al., 2012). Importantly, impaired HRQoL is independently associated with worse cardiac disease progression (Tackmann & Dettmer, 2018) and cardiac rehabilitation outcomes (Tušek-Bunc & Petek, 2016), underlining its importance as an indicator of disease severity cardiac rehabilitation effectiveness (Morys et al., 2016).

Current international guidelines for cardiac rehabilitation, such as the American Heart Association (AHA) or the European Society of Cardiology (ESC), conclusively endorse physical activity and exercise as an integral cornerstone to comprehensive cardiac care (e.g., Corrà et al., 2012; Balady et al., 2011; Pelliccia et al., 2005, 2021; Price et al., 2016). A recent Cochrane review and meta-analysis comprising 63 randomized controlled trials concluded that exercise-based cardiac rehabilitation in coronary heart disease patients was associated with reductions in cardiovascular mortality and hospital readmissions as well as significant improvements in HRQoL (Anderson et al., 2016). Despite its evident benefits, non-adherence to cardiac rehabilitation and exercise recommendations is common, especially in individuals with comorbid psychopathologies (Harris et al., 2019; McGrady et al., 2009).

While the impact of psychological influences on the pathogenesis and management of CVD has previously been underemphasized in clinical practice (Flint et al., 2019), contemporary research suggests that psychological comorbidities in CVD patients can represent significant barriers to successful rehabilitation (Keessen, 2020). Although most patients manage to rebalance and adjust to CVD, a subgroup of patients experiences profound psychological adjustment difficulties, including anxiety and depression, in response to their chronic disease (Wilder Schaaf et al., 2013). Convergent evidence indicates that more than one in three hospitalized patients suffer from severe comorbid

anxiety following a major cardiac event and/or intervention (Murphy et al., 2019). Moreover, initial symptoms can persist well beyond hospitalization and physical recovery (Ópic et al., 2016) and may manifest and advance into full-scale comorbid psychopathologies (Cohen et al., 2015; Richardson et al., 2012). These symptoms carry important clinical implications as they are associated with increased cardiac morbidity and mortality (Abed et al., 2014) as well as significant reductions in HRQoL (Hoekstra et al., 2013; Tušek-Bunc & Petek, 2016).

The disruptive and life-threatening nature of CVD causes some survivors to develop disease-specific anxiety. Although having received less empirical attention compared to CVD-associated depression in cardiac patients, recent research has identified comorbid disease-related anxiety as an additional important and highly prevalent psychological construct that may influence the disease progression of CVD (Celano et al., 2016). Compared to general (i.e., non-specific) anxiety, disease-specific anxiety in cardiac patients relates more closely to the specific symptomatology of CVD that distinguishes CVD patients from individuals without heart disease. A distinct subtype of disease-specific anxiety constitutes heart-focused, or cardiac, anxiety. Cardiac anxiety was first defined by Georg Eifert (1992) as a fear of cardiac-specific stimuli and sensations due to their perceived harmful consequences. It comprises (a) fear and worries about heart sensations, (b) excessive heart-focused attention and symptom monitoring, and (c) cardioprotective avoidance behavior to prevent or reduce cardiac symptoms (Eifert et al., 2000b). The presence of cardiac anxiety has since been demonstrated in patients with various types of cardiovascular disease, including individuals with myocardial infarction (Van Beek et al., 2012), heart failure (Sager et al., 2020), atherosclerosis (Marker et al., 2008), and cardiac arrhythmias (Hamang et al., 2011). In the clinical context, cardiac anxiety is associated with prolonged recovery (Fischer et al., 2012), adverse physical and psychological health outcomes (Köllner et al., 2007), and poor HRQoL (Bunz et al., 2015; Wedegärtner et al., 2020).

Acute cardiac anxiety can be triggered by episodes of chest pain or subjective alterations in heart functioning and activity (e.g., palpitations). Although these often-benign cardiopulmonary sensations are not necessarily related to underlying cardiac pathologies, they are frequently interpreted as an indication of an imminent (recurring) cardiac crisis (Eifert et al., 2000b). The Fear Avoidance model offers an empirical framework to understand the development and manifestation of cardiac anxiety in patients with CVD. Originally introduced as a model to explain avoidance behavior in chronic pain patients by Vlaeyen (1995, 2016), it describes how the experience of certain stimuli (i.e., pain) can lead to one of two potential cascades of events, based on the cognitive appraisal of stimuli-related fear (Vlaeyen & Linton, 2000). More specifically, experiencing pain can be perceived as either threatening or benign. If perceived as harmful, an individual might engage in maladaptive avoidant behaviors, such as catastrophizing, becoming hypervigilant, and avoiding movement altogether. Over time, the repeated patterns of avoidance tendencies may develop into an automatic response to the pain experience, thereby manifesting the experienced fear. By extension, the anxious preoccupation of CVD patients with potential organic dysfunction can in, and of itself, cause and

exacerbate physical sensations, which, in turn, reinforces the manifestation of cardiac anxiety. As a result, cardiac-anxious patients typically avoid behaviors that might elicit aversive cardiac symptoms, including physical activity and exercise (Eifert et al., 1996; Hohls et al., 2020). Repeated reinforcement of anxiety-related movement avoidance can eventually lead to the development of kinesiophobia (Åsenlöf & Söderlund, 2010; Leeuw et al., 2007).

Patients suffering from kinesiophobia experience “an excessive, irrational, and debilitating fear of movement and activity, resulting from a feeling of vulnerability to painful injury and re-injury” (Kori et al., 1990). In the cardiology domain, kinesiophobia has been linked to worse cardiac rehabilitation outcomes, including poor quality of life (Bäck et al., 2013; Van Ittersum et al., 2003). Like cardiac anxiety patients, patients with kinesiophobia often avoid physical activity and exercise due to fear of overexertion and pain (Keessen, 2020; Vlaeyen et al., 1995). In a prospective study by Åhlund et al. (2013), higher levels of kinesiophobia predicted poor cardiac rehabilitation attendance and lower levels of both physical activity and HRQoL.

While the initial avoidance of exercise and overexertion may constitute an adaptive reaction to acute injury, long-term exercise-related avoidance is associated with a range of adverse health consequences. In post-myocardial infarction patients, for instance, cardiac anxiety and anxiety-related avoidance of exercise predicted the occurrence of a new major adverse cardiac event (MACE), independent of disease severity (Van Beek et al., 2016). Importantly, early-stage avoidance tendencies may develop into maladaptive physical inactivity and sedentary behavior, which both represent major independent risk factors for secondary cardiac events (Lavie et al., 2019). The exercise-related avoidance tendencies commonly seen in both cardiac anxiety and kinesiophobia may substantially interfere with the implementation of cardiac risk-reducing behaviors, such as physical activity. Cardiac anxiety and kinesiophobia may thus represent significant barriers to successful cardiac rehabilitation and secondary prevention. Reducing cardiac anxiety and kinesiophobia in this patient group could therefore constitute a crucial aspect in the promotion and maintenance of cardiac rehabilitation adherence and, ultimately, in the facilitation of cardiac health and improved HRQoL.

Although the concept of disease-related anxiety is relatively well established in the literature, to our knowledge, no systematic review or meta-analysis assessing the strengths of the relationships between cardiac anxiety and kinesiophobia and clinical cardiac outcomes in CVD patients exists. This paper initially set out to perform a systematic review and meta-analysis of the relationship between cardiac anxiety and kinesiophobia in patients with CVD and clinical cardiac health outcomes. We hypothesized that higher levels of experienced cardiac anxiety and kinesiophobia in CVD patients would be related to adverse cardiac health, indexed as higher mortality rates, increased disease morbidity, and reductions in HRQoL. While all available publications discussing these outcomes were included in the systematic review, a preliminary literature search revealed only a sparse number of publications with the potential to be meaningfully included in the meta-analysis. Given the limited statistical data, HRQoL became the primary outcome of the meta-analysis.

Methods

Eligibility Criteria

The eligibility assessment was conducted using the program “Rayyan QCRI” by Ouzzani et al. (2016). Studies were eligible for inclusion if they (1) provided a full-length manuscript of quantitative research published in either English, German, or Dutch; (2) included a study population consisting of adult (i.e., age 18 years or older) non-congenital CVD patients; and (3) assessed at least one predictor of interest (i.e., cardiac-related anxiety and kinesiophobia, respectively) and at least one of the cardiac outcomes. Relevant outcome variables included (1) total and cardiac mortality, (2) patient longevity, (3) patient morbidity, (4) non-fatal recurrent cardiac events, (5) rates of hospital (re)admissions, (6) duration of hospitalization, (7) disease advancement, (8) functional outcome, and, finally, (9) health-related quality of life. Studies were excluded if predictor and outcome variables were measured at different time points. Systematic reviews, meta-analyses, case reports, and nonempirical studies were not considered for inclusion. Studies that did not meet the inclusion criteria were excluded and reasons for exclusion were registered in Rayyan QCRI.

Search Strategy

The search strategy was performed following guidelines outlined in the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P; Page et al., 2021). A comprehensive search string was designed with the guidance of a librarian. It comprised four keyword clusters: (1) cardiovascular disease, (2) cardiac rehabilitation (including secondary prevention, aftercare, and rehab), (3) disease-specific fear (including heart-related fear/anxiety, cardiac fear/anxiety, health anxiety, fear of movement/exercise, kinesiophobia, fear-avoidance/fear-avoidance beliefs), and (4) clinical cardiac outcomes (total and cardiac mortality, patient longevity, patient morbidity, non-fatal recurrent cardiac events, rates of hospital (re)admissions, duration of hospitalization, disease advancement, pain severity, functional outcome, and health-related quality of life). The literature was searched for eligible articles published by September 2021 on eight online databases, including PubMed, MEDLINE (OVID), PsychINFO, Embase, Web of Science, Cochrane Library, and Academic Search Premier. Medical Subject Headings (MeSh) were customized across databases. Additionally, reference lists of key articles, reviews, and meta-analyses were reviewed to identify additional articles eligible for inclusion (i.e., snowballing). Moreover, the primary authors of 13 studies were contacted by the thesis supervisor (TR) and were asked to provide additional data. Reminders were sent after four weeks of no response. Unfortunately, no authors were able and willing to share their data. Duplicates were removed and the selected articles were saved and entered in the bibliographical software manager Zotero. The full search string is included in Appendix A.

Two stages of study selection were conducted by two independent reviewers (CD and RC). First, titles and abstracts were screened contingent on pre-determined inclusion and exclusion criteria. Second, full-text evaluations of the eligible articles were carried out. Cases of conflict or doubt were

discussed and resolved through consensus between the two reviewers and, if necessary, the thesis supervisor (TR).

Data Extraction and Quality Assessment

Data from eligible studies were extracted and registered in an electronic spreadsheet using a standardized data extraction template. Besides publication title, author, and year, relevant extracted data included sample demographics, predictor and outcome variables, method and time of assessment, and reported results. Each selected study was individually assessed for study quality and validity utilizing the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for analytical cross-sectional studies (Moola et al., 2017; see Appendix B) The checklist is comprised of eight items containing (1) a clear definition of inclusion criteria, (2) subjects and setting description, (3) exposure measurement, (4) condition measurement, (5) identification of confounding factors and (6) strategies to deal with them, (7) outcome measurement, and (8) appropriate statistical analysis. Each item column is answered with either Yes, No, Unclear, or Not applicable. Finally, an overall study appraisal is given, indicated as either Include, Exclude, or Seek further information.

Statistical Analysis

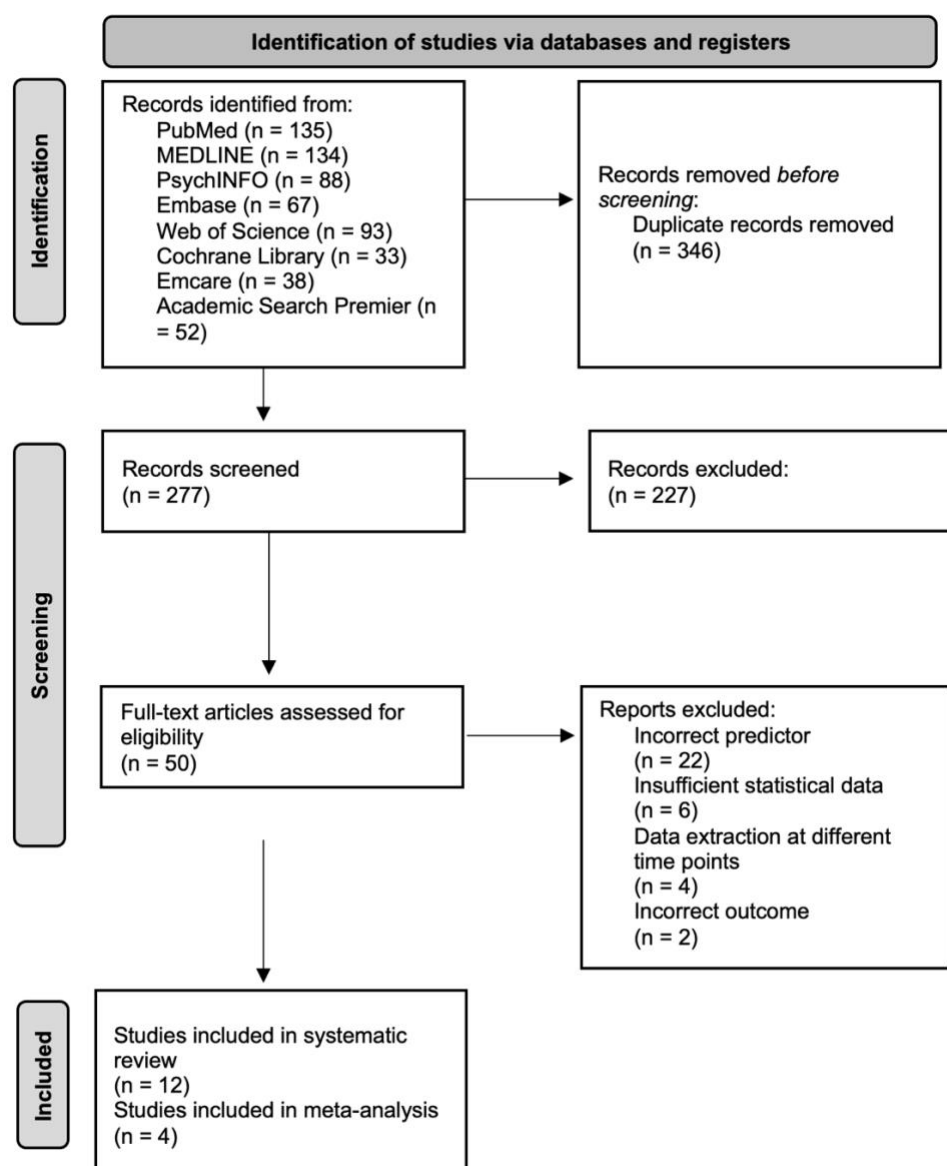
The meta-analysis was conducted using the software Comprehensive Meta-Analysis Version 3 (CMA-V3; <http://www.meta-analysis.com>). For articles reporting suitable statistics, two meta-analyses were conducted assessing the relationship between cardiac anxiety and the (1) physical and (2) mental dimensions of HRQoL, respectively. Yielded correlation coefficients were converted into their corresponding Fisher-Z scale and later re-converted into correlation coefficients for presentation. A random-effects model was applied. Following the central premise that each study assesses a unique effect, employing this model allowed for the relative weight of individual studies to be more equally distributed. Due to an insufficient number of eligible articles, a meta-analysis on the relationship between kinesiophobia and clinical health outcomes could not be performed. To retain Instead, the articles that were identified by the systematic literature search were qualitatively summarized in Table 2. Heterogeneity was assessed using Cochran's Q test and the I^2 , T , and T^2 -statistics. The Q-statistic is calculated as the weighted sum of squared differences between individual study effects and the pooled effect across studies. Following a Chi-square (X^2) distribution with k-1 degrees of freedom, the Q-statistic represents a probability that, when significant, reflects variation within subjects rather than across studies and therefore suggests statistical heterogeneity. While I^2 reflects the percentage of the total variability in results that is due to true effects rather than sampling error, T and T^2 represent estimates of the standard deviation of underlying effects across studies and the between-study variance, respectively. Further, the prediction interval was computed using CMA's extension program "Prediction Intervals" (CMA-V3; <https://www.meta-analysis.com/pages/prediction.php>) to estimate the distribution of true effect sizes. Potential causes of heterogeneity of effect sizes were assessed by performing subgroup analyses (Cochrane's Q-test of heterogeneity). Forest plots were created to evaluate the presence of publication bias.

Results

The literature search initially identified 277 unique citations. After the title and abstract screening, 50 studies were selected for subsequent full-text retrieval. Of those, 38 articles were excluded for not meeting inclusion criteria. Reasons for exclusion were incorrect predictor (22 studies), insufficient statistical data (6 studies), varying time points of data collection (4 studies), and incorrect outcome (2 studies). Finally, a total of 12 articles were included in the current qualitative review, of which 4 studies fulfilled the criteria to be included in the meta-analysis. The agreement rate between investigators was 98.2%. A PRISMA flowchart depicting study selection is presented in Figure 1. Quality assessment was carried out using the JBI Critical Appraisal Checklist (Moola et al., 2017) and revealed some quality issues in terms of reporting and controlling for covariates in ten studies. To retain as much data as possible, we allowed all studies to be included in the analysis. A detailed table can be found in Appendix B.

Figure 1

PRISMA 2020 flow diagram for a schematic depiction of the search strategy



Cardiac Anxiety

Study Characteristics

Data extraction revealed eight studies examining cardiac anxiety and its associations with different clinical health outcomes. In total, the systematic review included 1448 cardiac anxiety patients, primarily comprising patients with cardiac arrhythmias (with and without device implantation, $n = 687$), myocardial infarction ($n = 383$), chronic heart failure ($n = 227$), and coronary artery disease ($n = 161$). The mean age of all included participants was 55.38 years of age and ranged from 56.1 years to 63.29 years of age across studies. Publication dates ranged from the year 2006 until the year 2020. In all included studies, the assessment of cardiac anxiety was performed using the Cardiac Anxiety Questionnaire (CAQ; Eifert, 2000a). The CAQ is an 18-item self-report measure that assesses overall cardiac anxiety and three component scores, reflecting (1) heart-related worry and fear, (2) attention, (3) and avoidance behavior. Each item is rated on a five-point Likert-scale, ranging from zero (never) to four (always). Higher scores represent higher cardiac anxiety symptomatology. The selected studies provided the following somatic health outcomes: HRQoL (Bunz et al., 2015; Einsle et al., 2009; Hoyer et al., 2008; Kovacs et al., 2006; Wedegärtner et al., 2020), disease severity (Bunz et al., 2015; Van Beek et al., 2012; Van Beek et al., 2016), cardiac risk factors (Wedegärtner et al., 2020), functional status (Bunz et al., 2015; Wedegärtner et al., 2020), adverse health outcomes (Van Beek et al., 2016), health status and generic health-related quality of life (QoL; Van Beek et al., 2012), cardiopulmonary complaints (Van den Broek et al., 2009), and physical activity (Wedegärtner et al., 2020). Some of the outcome variables (e.g., disease severity) were operationalized by combining multiple cardiac variables, including heart rate, blood pressure, troponin and CKmax levels, and left-ventricular ejection fraction (LVEF). Further characteristics (including study setting and used measurement tools) of the selected studies for the current review are presented in Table 1.

Meta-Analysis

Given the high variability of reported outcome data, not all studies could be included in a meaningful meta-analysis. Given that four studies examined the relationship between cardiac anxiety and HRQoL, we decided to focus on HRQoL as the primary outcome measure. HRQoL was assessed using the Short-Form Health Survey (SF-12; $n = 3$) and the Minnesota Living with Heart Failure Questionnaire (MLHFQ; $n = 1$). Both scales represent self-report measures that provide an overall HRQoL score as well as a physical and mental subscale score. While higher scores on the SF-12 reflect better physical and mental health status, respectively, the opposite is true for the MLHFQ. Here, lower scores indicate better HRQoL.

Due to variations in reported data and use of (sub)scales, data extraction revealed two studies that provided data of overall HRQoL (Bunz et al., 2015; Wedegärtner et al., 2020) and four studies that provided data of physical and mental HRQoL, respectively (Bunz et al., 2015; Einsle et al., 2009; Hoyer et al., 2008; Kovacs et al., 2006). Two separate meta-analyses were conducted using the physical and mental health dimensions of HRQoL as outcomes, respectively. This resulted in a total

of eight estimates with the correlation coefficient (r) representing the effect size index. To allow for generalization to comparable studies, the random effects model was employed for both analyses. A total of 958 patients were included in the meta-analysis with the number of participants varying from 71 to 687 across the included studies.

Physical Health-Related Quality of Life

Figure 2 illustrates the results of the analysis examining the relationship between cardiac anxiety and the physical dimension of HRQoL. Under the random-effects model, assuming that each study is estimating a unique effect, we found a significant and negative moderate correlation between cardiac anxiety and physical HRQoL ($r = -0.53$; 95% CI $[-0.57, -0.48]$; $p < .001$). The assigned relative weight ranged from 6.68% (Kovacs et al., 2006) to 60.38% (Einsle et al., 2009). Given the considerable difference in attributed weight between the studies, a secondary analysis was carried out omitting the study by Einsle et al. (2009) to rule out skewness in data. The results remained significant ($r = -0.52$; 95% CI $[-0.61, -0.42]$; $p < .001$). The heterogeneity of our data was tested by the Q -statistic, which showed to be nonsignificant ($Q(3) = 3.41$, $p = .332$), indicating little observed dispersion. The I^2 -statistic ($I^2 = 3.59$) demonstrated that about 4% of the observed dispersion reflected the variance in true effects rather than sampling error. The variance of true effects (T^2) was 0.00 and the standard deviation of true effects (T) was 0.01. The prediction interval (PI) was -0.63 to -0.41, suggesting that in 95% of all populations, the true effect size would fall in this range. Therefore, the strength of the relationship between cardiac anxiety and physical HRQoL in people with cardiac disease is expected to range between small to moderate across populations. The visual inspection of the funnel plots revealed a symmetrical distribution of effect sizes, suggesting no indication of publication bias (Figure 3). Additionally, we performed a classic Fail-Safe N (FSN) test, which indicated that 95 undetected zero-effect-size studies would be necessary to change the significant result of our meta-analysis to a nonsignificant result.

Mental Health-Related Quality of Life

Figure 2 also illustrates the results of the analysis examining cardiac anxiety and the mental dimension of HRQoL. The summary estimate of the correlation indicated a significant and negative correlation between cardiac anxiety and mental HRQoL ($r = -0.43$; 95% CI $[-0.50, -0.35]$; $p < .001$). The assigned relative weight ranged from 12.81% (Kovacs et al., 2006) to 42.12% (Einsle et al., 2009). To rule out data skewness, a secondary analysis omitting the study by Einsle et al. (2009) was performed. The results remained significant ($r = -0.45$; 95% CI $[-0.56, -0.33]$; $p < .001$). The heterogeneity was tested by the Q -statistic, which showed to be nonsignificant ($Q(3) = 5.58$, $p = .134$), indicating little observed dispersion. The I^2 -statistic ($I^2 = 46.27$) indicated that about 46% of the observed dispersion reflected the variance in true effects rather than sampling error. The variance of true effects (T^2) was 0.004 and the standard deviation of true effects (T) was 0.07. The prediction interval (PI) was -0.67 to -0.11. The visual inspection of the funnel plots revealed a symmetrical

distribution of effect sizes, suggesting no indication of publication bias (Fig. 6). An additional Fail-Safe N test indicated strong robustness of our results (FSN = 189).

Figure 2

Forrest plots of Pearson's correlation coefficients between cardiac anxiety and both physical and mental HRQoL – random effect model

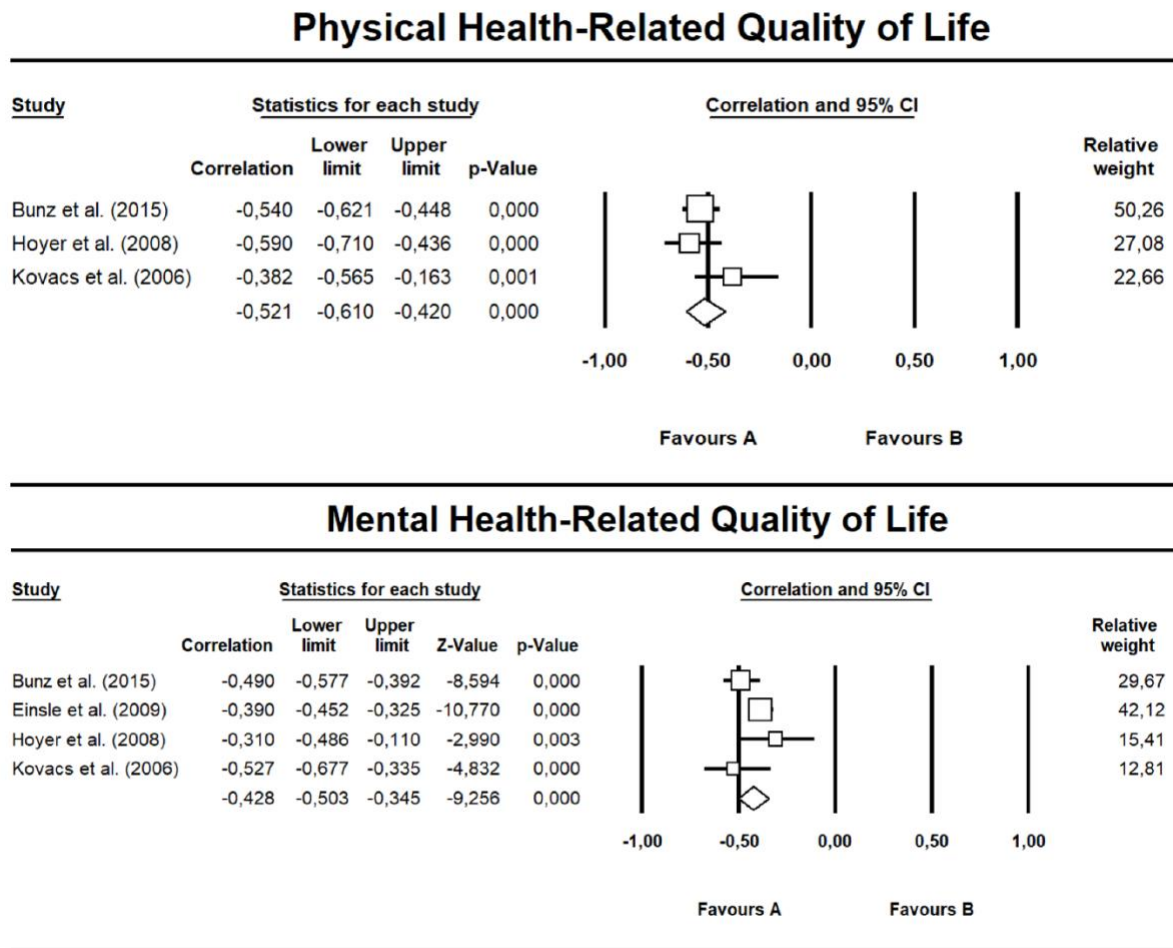


Table 1*Characteristics of studies evaluating cardiac anxiety (using the CAQ) and different clinical health outcomes*

Author (year)	Study design	Study setting and location	CVD type (n)	Mean age (SD)	Outcome Type	Outcome Measure	Main results
Bunz et al. (2015)	Cross-sectional design	Saarland University Medical Center, Homburg, Germany	Chronic heart failure before ICD implantation (110)	60.5 (14.9)	HRQoL	MLHFQ	Significant positive correlations between cardiac anxiety and HRQoL ($r = 0.58, p < 0.001$), physical functioning (HRQoL-phys; $r = 0.54, p > 0.001$), and psychological distress (HRQoL-psych; $r = 0.49, p > 0.001$).
					Functional status	(NYHA classification)	Non-significant associations between cardiac anxiety and functional status.
					Disease severity	Ejection fraction Heart rate Blood pressure Former occurrence of myocardial infarction	Significant negative correlations between cardiac anxiety and a history of myocardial infarction ($r = -0.29, p = 0.002$) and systolic blood pressure ($r = -0.20, p = 0.044$). Non-significant associations between cardiac anxiety and ejection fraction, functional status, diastolic blood pressure, and heart rate.
Einsle et al. (2009)	Cross-sectional design	University Hospital Dresden, Germany	Clinically relevant cardiac arrhythmias (687)	68.3 (11.2)	HRQoL	SF-12	Significant negative correlations between cardiac anxiety and physical HRQoL ($r = -0.39, p < 0.01$) and psychological HRQoL ($r = -0.35, p < 0.01$).
Hoyer et al. (2008)	Multigroup cohort design	University Hospital Dresden, Germany	Coronary artery disease (90)	66.9 (8.51)	HRQoL	SF-12	Significant negative correlations between cardiac anxiety and physical HRQoL ($r = -0.59, p < 0.01$) and psychological HRQoL ($r = -0.31, p < 0.01$).
Kovacs et al. (2006)	Cross-sectional design	Toronto, Canada	Coronary artery disease (71)	56.1 (11.6)	HRQoL	SF-12	Significant negative correlations between cardiac anxiety and physical HRQoL ($r = -0.382, p < 0.001$) and psychological HRQoL ($r = -0.527, p < 0.001$).
Van Beek et al. (2012)	Prospective cohort design	Radboud University Nijmegen Medical Center, the Netherlands	Myocardial infarction (STEMI and NSTEMI) (194)	61.8 (11.5)	HRQoL	EQ-5D	High levels of cardiac anxiety had significantly lower HRQoL scores compared to intermediate ($P = 0.0479$, low ($P = 0.004$), and high-low ($P = 0.006$) groups.
					Disease severity	Occurrence of STEMI/NSTEMI,	Negative correlations between CAQ and STEMI/NSTEMI ($r = -0.18, p = 0.004$), troponin levels ($r = -0.13, p = 0.06$), and CKmax level ($r = -0.13, p = 0.06$).

						troponin levels, and CKmax level	
Van Beek et al. (2016)	Prospective cohort design	Radboud University Nijmegen Medical Center, the Netherlands	Myocardial infarction (189)	62.35 (11.3)	Adverse health outcomes	Occurrence of a MACE	Cardiac anxiety was significantly associated with a higher risk of a MACE, independent of age and gender, LVEF, and cardiac history (HR = 1.59, 95% CI [1.04-2.43]).
Wedegärtner et al. (2020)	Cross-sectional design	Saarland University Medical Center, Homburg, Germany	Stable heart failure (107)	67.1 (9.04)	HRQoL	KCCQ	Significant negative correlations between cardiac anxiety and HRQoL ($r = -0.575$, $p = 0.01$), indicating worse HRQoL with increasing levels of cardiac anxiety.
					Physical activity		Significant negative correlations between cardiac anxiety and physical activity ($r = -0.196$, $p = 0.01$)
					Functional status	(NYHA classification)	Significant positive correlations between cardiac anxiety and functional status ($r = 0.191$, $p = 0.05$)
					Cardiac risk factors	Alcohol consumption, eGFR, AF, hyperlipidemia, NT-proBNP, LVEF, obesity, and number of risk factors	Significant negative correlations between cardiac anxiety and alcohol consumption ($r = -0.194$, $p = 0.01$) and eGFR ($r = -0.296$, $p = 0.01$). Significant positive correlations between cardiac anxiety and AF ($r =$ 0.225 , $p = 0.05$), hyperlipidemia ($r = 0.224$, $p = 0.05$), NT-proBNP ($r =$ 0.207 , $p = 0.05$). Non-significant correlations between cardiac anxiety and LVEF, obesity, and number of risk factors

Note. AF: Arterial fibrillation, CAQ: Cardiac Anxiety Questionnaire, CK max: Maximum amount of creatine kinase, eGFR: Estimated Glomerular Filtration Rate in ml/min per 1.73m², EQ-5D: European Quality of Life Five Dimension, HCS: Health Complaints Scale, HRQoL: Health-related quality of life, ICD: implantable cardioverter defibrillator, KCCQ: Kansas City Cardiomyopathy Questionnaire, LVEF: Left ventricular ejection fraction, NSTEMI: Non-ST-elevation myocardial infarction, NT-proBNP: N-Terminal pro-Brain Natriuretic Peptide in pg/ml, NYHA: New York Heart Association Functional Classification, MACE: major adverse cardiac event, MLHFQ: Minnesota living with Heart Failure Questionnaire, SF-12: 12-Item Short-Form Health Survey, STEMI: ST-elevation myocardial infarction, HCS: Health Complaint Scale, KCCQ: Kansas City Cardiomyopathy Questionnaire.

Figure 3

Funnel plot of the effect estimates of the included studies (cardiac anxiety and physical HRQoL)

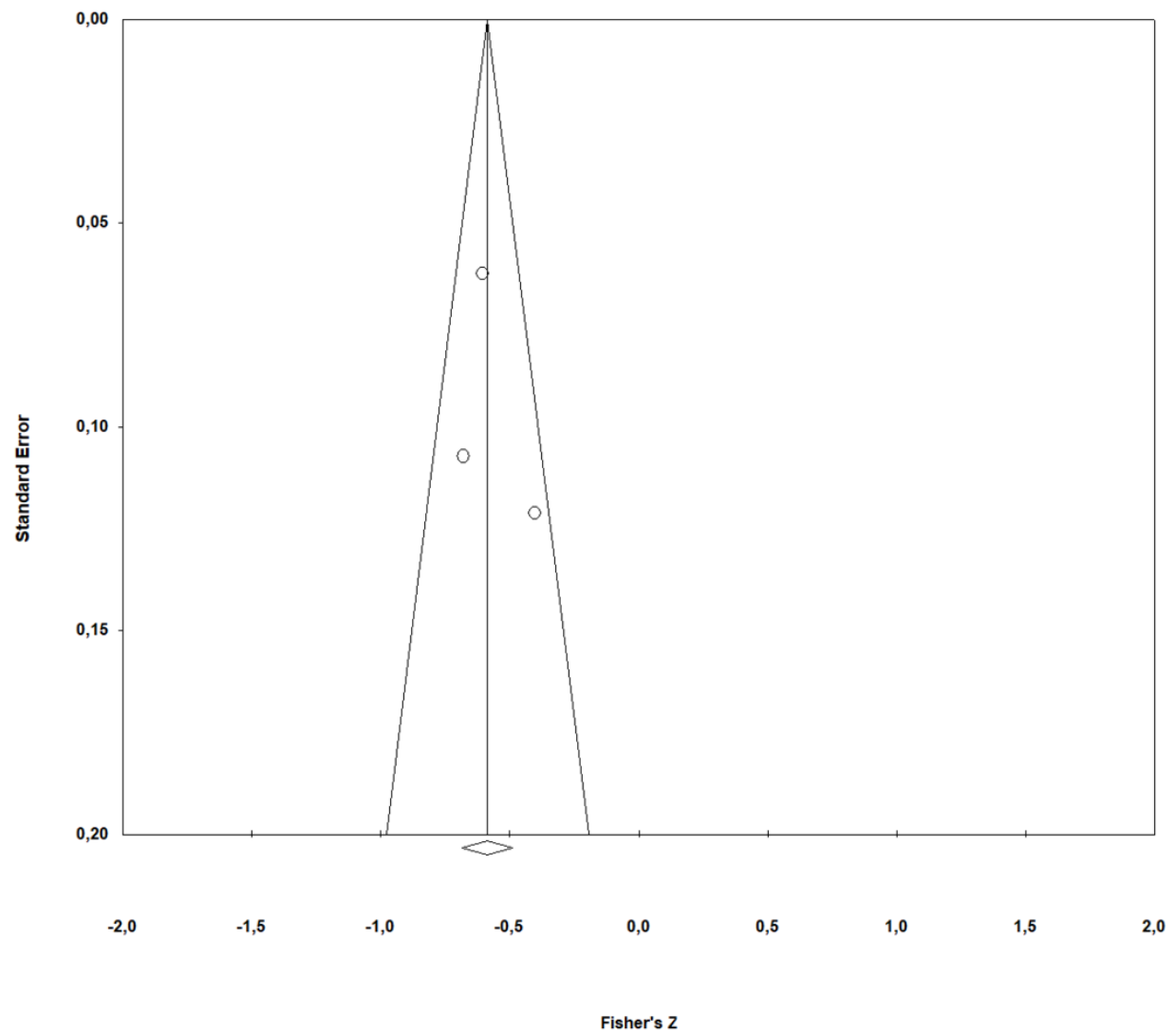
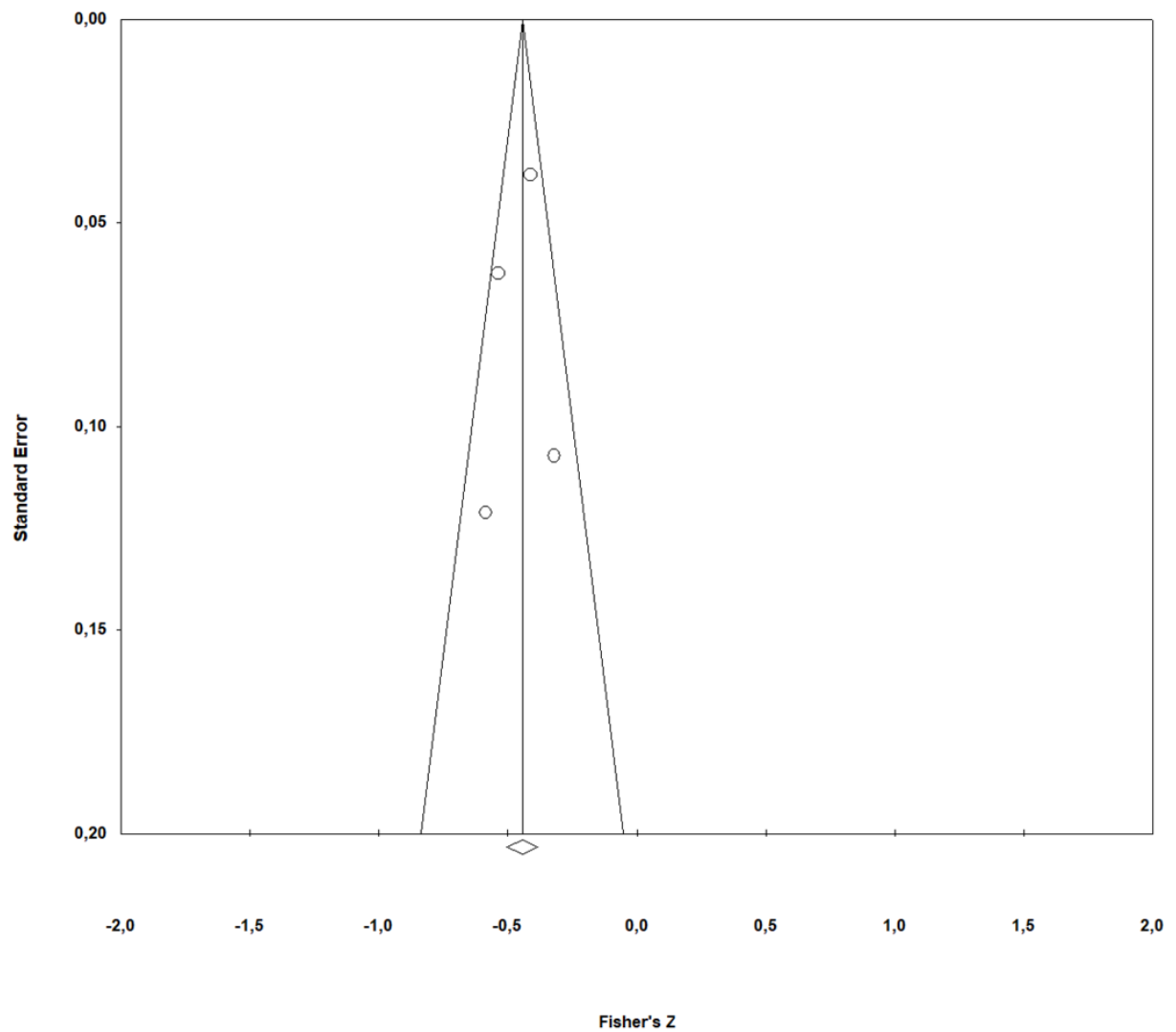


Figure 4

Funnel plot of the effect estimates of the included studies (cardiac anxiety and mental HRQoL)



Kinesiophobia

Study Characteristics

Data extraction revealed five studies that assessed the relationship between kinesiophobia and clinical health outcomes. In total, the studies assessed 634 kinesiophobia patients, comprising patients with coronary artery disease (n = 549), pulmonary arterial hypertension (n = 43), and heart failure (n = 42). Notably, the two studies by Bäck et al. (2013, 2016) comprise the same patients. The patients' mean age equaled 62.17 years of age and ranged from 55.36 years to 67.39 years of age across studies. Publication dates ranged from the year 2003 until the year 2020. Further characteristics of the selected studies are presented in Table 2.

Across all studies, kinesiophobia was measured using an adaptation of the Tampa Scale of Kinesiophobia (TSK), the TSK Heart (Bäck et al., 2012). While the original scale was initially designed for patients suffering from chronic pain (Vlaeyen et al., 1995), the TSK Heart provides a means of assessing kinesiophobia in cardiac patients. It measures four constructs, of which two constructs relate to beliefs and mental imaginings (i.e., perceived danger for heart problem and fear of injury) and two relate to irrational perceptions and beliefs about rehabilitation (i.e., avoidance of exercise and dysfunctional self). The TSK Heart comprises 17 items that are self-rated on a four-point Likert scale, ranging from “strongly disagree” to “strongly agree”. The sum score varies between 17 and 68, with higher values indicating higher levels of experienced kinesiophobia.

Study outcomes included physical activity (Dąbek et al., 2020), complications/interventions at the hospital (Bäck et al., 2013), previous medical history (Bäck et al., 2013), disease duration (Bäck et al., 2013), cardiac rehabilitation attendance (Bäck et al., 2016) as well as generic QoL (Acar et al., 2016) and HRQoL (Van Ittersum et al., 2003). Due to the very heterogenous outcome data, a meta-analysis on the relationship between kinesiophobia and clinical health outcomes could not be performed.

Table 2

Characteristics of studies evaluating kinesiophobia and fear of exercise (using the TSK- Heart) and different clinical health outcomes

Author (year)	Study design	Study setting and location	CVD type (n)	Mean age (SD)	Type Outcome	Outcome Measure	Main results
Acar (2016)	Cross-sectional	Izmir, Turkey	Pulmonary arterial hypertension (43) Heart failure (42)	55.36 (14.92)	Generic QoL	NHP	Moderate positive correlation between kinesiophobia and QoL ($r = 0.374, p < 0.01$), indicating lower levels of QoL with increasing levels of kinesiophobia.
					Physical activity	IPAQ, 6MWT	Non-significant correlations between kinesiophobia and measures of physical activity.
Bäck (2013)	Cross-sectional	Sahlgranska University Hospital, Gothenburg, Sweden	Coronary artery disease (332)	65 (9.1)	Previous medical history	All information retrieved from patient files. Further information about assessment not available	Significant negative correlations between kinesiophobia and (1) a previous history of myocardial infarction ($r = -0.12, p < 0.05$), CABG, ($r = -0.12, p < 0.05$), diabetes ($r = -0.15, p < 0.01$), and hypertension ($r = -0.12, p < 0.05$). Non-significant correlations between kinesiophobia and previous history of angina pectoris, PGI, and heart failure.
					Complications/interventions at hospital		Significant negative correlations between kinesiophobia and complications/interventions in hospital involving heart failure ($r = -0.14, p < 0.05$) and atrial fibrillation ($r = -0.13, p < 0.05$). Non-significant correlations between kinesiophobia and complications/interventions in hospital involving PGI and CABG.
					Disease duration		Non-significant correlations between kinesiophobia and disease duration.
Bäck (2016)	Cross-sectional	Sahlgranska University Hospital, Gothenburg, Sweden	Coronary artery disease (332)	65 (9.1)	Exercise-based CR attendance		Kinesiophobia reduced attendance at exercise-based CR ($p = 0.001$), while attendance at exercise-based CR was predicted by a recent CABG ($p < 0.001$), and a diagnosis of STEMI ($p = 0.004$).
Dąbek (2020)	Cross-sectional	Cardiology Hospital department, Katowice, Poland	Coronary artery disease (217)	67.39 (8.2)	Physical activity		Significant negative correlation between kinesiophobia and physical activity ($r = -0.558, p < 0.000$).
Van Ittersum (2003)	Cross-sectional	University Hospital, Groningen, the Netherlands	Cardiac arrhythmias with an implanted ICD (83)	58.1 (13.1)	HRQoL		Significant positive correlations coefficients of linear regression analysis between fear of exercise and HRQoL measured by the QoLMI-DV ($r = 0.557, p < 0.05$) and the Rand-36 ($r = 0.572, p < 0.05$). The authors concluded that higher levels of kinesiophobia were associated with significantly worse HRQoL in their patient population compared to healthy subjects.

Note. CABG: Coronary artery bypass grafting, CR: Cardiac rehabilitation, HRQoL: Health-related quality of life, IPAQ: International Physical Activity Questionnaire, NHP: Nottingham Health Profile, PGI: Percutaneous coronary intervention, QoL: Quality of life, QoLMI-DV: Quality of Life After Myocardial Infarction Dutch language version, Rand-36: Research and Development 36-Item Short Form Survey, STEMI: ST-elevation myocardial infarction.

Discussion

The present study set out to perform a systematic review and meta-analysis on the relationships between different forms of disease-specific anxiety and clinical health outcomes among patients with CVD. Due to limited available data, the primary analysis of this paper focused on the association between cardiac anxiety and the physical and mental subdimensions of HRQoL. In line with predictions, our results provide evidence of a moderate and significant negative correlation between cardiac anxiety and physical HRQoL among patients with CVD. In addition, we found a significant negative correlation between cardiac anxiety and mental HRQoL of small-to-moderate strength. Taken together, our results suggest that, on average, CVD patients who display higher levels of self-reported cardiac anxiety tend to experience lower levels of both physical and mental HRQoL.

Although both clinical and empirical definitions operationalize physical and mental HRQoL as distinct constructs (Karimi & Brazier, 2016), the literature offers little discussion on whether or how physical and mental HRQoL relate differently in patients with CVD. Our results suggest that cardiac patients perceive their physical HRQoL as slightly worse than their mental HRQoL. These findings are supported by a recent prospective study by Schluep et al. (2022) who found that cardiac arrest patients reported lower physical HRQoL scores compared to mental HRQoL scores at both 3 months and 12 months follow-up. It seems plausible to hypothesize that the anxious preoccupation with the physical CVD symptomatology may pose a more prominent perceived threat to a patient's physical rather than mental HRQoL, while further research is needed to support the latter.

To our knowledge, this was the first meta-analysis on the relationship between cardiac anxiety and HRQoL. Despite its clinical importance, literature on disease-specific anxiety and HRQoL in patients with CVD remains scarce. However, our results reflect contemporary research on the negative associations between disease-specific anxiety and HRQoL in other clinical populations. For example, the association between disease-related anxiety and HRQoL has been demonstrated in patients with irritable bowel syndrome (Jerndal et al, 2010), COPD (Reijnders et al., 2018), and different types of cancer (e.g., Erim et al., 2020, Rogers et al., 2017).

Disease-related fears are, by definition, specific to the experienced disease-induced physical and psychological symptoms. In contrast, general HRQoL, as measured in the examined studies, relates to a far broader, non-disease-specific framework. Accordingly, our findings suggest that the impact of specific cardiac anxiety on HRQoL can generalize beyond cardiac-specific contexts. For example, cardiac anxiety may extend to and adversely affect non-CVD-specific areas of a patient's everyday life that are affected by impaired HRQoL. In addition, cardiac anxiety may restrict the extent to which a patient is capable of performing activities of daily living, which has been shown to predict impaired HRQoL (Andersen et al., 2004). A patient who fears the experience of cardiac-specific stimuli (i.e., heart palpitations) may avoid or give up certain activities to prevent the occurrence of these symptoms. The subsequent confrontation with CVD-induced restrictions of daily activities, including hobbies, may result in health dissatisfaction and, in turn, in impaired HRQoL (Geri et al.,

2017). Moreover, cardiac anxiety may transfer to other detrimental fears such as impaired functional capacity and independence or loss of a normal social life, which are known to diminish HRQoL (e.g., Geri et al., 2017; Heo et al., 2009; Schluep et al., 2022).

The Fear Avoidance Model offers one possible explanation for the impaired HRQoL in patients with cardiac anxiety. As mentioned above, patients with cardiac anxiety tend to avoid behaviors that might trigger adverse cardiac symptoms (i.e., heart palpitations), including physical activity and exercise. The Fear Avoidance Model suggests that repeated avoidance of symptom-eliciting activities can lead to progressive sedentary behavior and, subsequently, to physical deconditioning (Vlaeyen & Linton, 2000). The experienced disease-related fear may thus serve as a reinforcer of the manifestation of disease-related fear-avoidance beliefs and tendencies. This reinforcement process may not only represent a barrier to achieving cardiac health but may further pose a direct detrimental threat to the cardiovascular system. As such, low activity levels and sedentary behavior could result from disease-specific fear and HRQoL, which, in turn could then lead to further health deterioration. Future research is necessary to assess the direct and indirect effects of cardiac anxiety and HRQoL on CVD progression.

While it is tempting to assume a causal role of disease-specific anxiety and impaired HRQoL on worse disease progression, the correlational nature of our data does not allow for causal inferences. At present, our data merely suggest that the presence of cardiac anxiety and reduced HRQoL represent separate important factors regarding CVD health outcomes. However, the specific underlying psychopathological mechanisms that underpin their association remain unknown and further research is warranted to empirically investigate their interrelationships and dynamics. Nevertheless, our findings remain important to secondary prevention approaches in which disease-specific anxiety and impaired HRQoL in CVD patients can represent important risk factors (Shepherd & While, 2012). Research has broadly demonstrated adverse associations between impaired HRQoL and clinical health outcomes in CVD patients. For example, previous investigators found links between low HRQoL and decreased treatment compliance (Celano et al., 2022; Komorovsky et al., 2008), increased rate of hospital readmissions (Rodríguez-Artalejo et al., 2005), as well as increased risks of post-event complications and mortality (Heidenreich et al., 2006; Rodríguez-Artalejo et al., 2005). Although previous studies have consistently linked general anxiety to adverse cardiac outcomes (e.g., Abed et al., 2014; Roest et al., 2010), research investigating cardiac anxiety and its direct association with adverse outcomes in CVD patients is limited. However, our systematic review provides some insights into the topic. Cardiac anxiety has been linked to increased disease severity (Van Beek et al. 2012), occurrences of major adverse health outcomes (Van Beek et al., 2016), reduced physical activity (Wedegärtner et al., 2020), and cardiac risk factors (Wedegärtner et al., 2020).

Despite its significant implications, disease-specific anxiety is still widely under-recognized in standard clinical practice (Flint et al., 2019; Grace et al., 2004). Routine screenings using disease-specific screening tools should be carried out by general practitioners to identify the presence of

disease-specific anxiety as early as possible. Early identification of symptoms is of importance as it allows clinicians to intervene and treat initial anxiousness before it may manifest and cause potential detrimental health effects. Compared to specialized physicians such as cardiologists, general practitioners are often in closer and more frequent contact with their patients and their everyday life. Thus, they may be more receptive to alterations in their patients' mood and behavior and, in turn, may prompt appropriate risk stratification and management (Michaels & Goldschlager, 2000)

Additionally, patient subgroups that display clinically relevant levels of cardiac anxiety should be offered disease-specific treatment. In accordance with the previously described vicious cycle of fear avoidance, research on chronic pain points towards the use of cognitive-behavioral intervention-based rehabilitation programs to reduce disease-specific fear and subsequent avoidance tendencies (Baez et al., 2018). However, disease-specific treatment in CVD patient populations is understudied. It is therefore of crucial importance to stimulate research that investigates treatment approaches that aim to reduce cardiac anxiety and increase HRQoL to facilitate treatment response.

Several limitations of the present study should be acknowledged. First, the relatively small number of studies that were included in the meta-analyses should be considered. While there is no academic consensus on the minimal required number of studies to appropriately conduct a meta-analysis, a small sample size tends to undermine the reliability of findings. Our findings should therefore be interpreted with caution. We hope that with accumulating research in this field, future analyses may achieve to include additional studies, resulting in robust meta-analytic evidence. Additionally, a comprehensive study of qualitative research could provide additional insights that were neglected by quantitative studies. A second important limitation constitutes the quality assessment of the included studies. Although the Joanna Briggs Institute (JBI) Critical Appraisal Checklist (Moola et al., 2017) is commonly used to evaluate study quality in cross-sectional work, the evaluation of inclusion versus exclusion appraisal is solely dependent on the subjective interpretations of the researcher. In this paper, issues regarding the reporting and assessing of potential confounding variables (see Appendix B) were disregarded to retain and include as much data as possible in the meta-analysis. It remains questionable to which extent this approach limited the integrity of our findings.

In conclusion, our study demonstrated significant negative associations between cardiac anxiety, and both physical and mental HRQoL, respectively. Given the adverse relationship between cardiac anxiety and impaired HRQoL with cardiac health outcomes, future research on the multifaceted interplay between these constructs is warranted. Understanding the underlying mechanisms of the development and maintenance of cardiac anxiety and HRQoL in CVD patients is crucial in designing targeted patient interventions that lead to successful disease management and recovery. Moreover, raising awareness of the psychological and physical implications that cardiac anxiety and low HRQoL can have in CVD patients and their disease outcomes, may prompt

professionals to integrate routine screenings and treatment into clinical practice to alleviate disease burden.

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Appendix A

Table A1

Search Terms of Systematic Literature Review by Data Base

Data Base	Search String
PubMed	(("Cardiovascular Diseases"[majr:noexp] OR "Heart Diseases"[majr] OR "Cardiovascular Diseases"[ti] OR "Cardiovascular disease"[ti] OR "coronary heart disease"[ti] OR "coronary heart diseases"[ti] OR "coronary disease"[ti] OR "coronary diseases"[ti] OR "coronary artery disease"[ti] OR "coronary artery diseases"[ti] OR "myocardial infarction"[ti] OR "myocardial infarctions"[ti] OR "myocardial infarct"[ti] OR "myocardial infarcts"[ti] OR "cardiac care"[ti] OR "angina"[ti] OR "Chest Pain"[majr] OR "Chest Pain"[ti] OR "heart failure"[ti] OR "coronary artery bypass graft"[ti] OR "percutaneous coronary intervention"[ti] OR "heart disease"[ti] OR "heart diseases"[ti] OR "cardiac disease"[ti] OR "cardiac diseases"[ti] OR "cardiovascular abnormalities"[ti] OR "cardiovascular abnormality"[ti] OR "cardiac abnormalities"[ti] OR "cardiac abnormality"[ti] OR "cardiac arrest"[ti] OR "long QT syndrome"[ti] OR "hypertrophic cardiomyopathy"[ti] OR "hypertrophic cardiomyopathies"[ti] OR "Defibrillators, Implantable"[majr] OR "implantable cardioverter-defibrillator"[ti] OR "implantable cardioverter-defibrillator"[ti] OR "arrhythmia"[ti] OR "arrhythmias"[ti] AND ("cardiac anxieties"[tiab] OR "cardiac anxiety"[tiab] OR "cardiac fear"[tiab] OR "cardiac fears"[tiab] OR "disease related anxieties"[tiab] OR "disease related anxiety"[tiab] OR "disease related fear"[tiab] OR "disease related fears"[tiab] OR "disease specific anxieties"[tiab] OR "disease specific anxiety"[tiab] OR "disease specific fear"[tiab] OR "disease specific fears"[tiab] OR "fear of exercise"[tiab] OR "fear of exercises"[tiab] OR "fear of movement"[tiab] OR "fear of movements"[tiab] OR "fear avoidance"[tiab] OR "fear avoidance belief"[tiab] OR "fear avoidance beliefs"[tiab] OR "fear avoiding"[tiab] OR "fear avoiding"[tiab] OR "health anxieties"[tiab] OR "health anxiety"[tiab] OR "heart focused anxieties"[tiab] OR "heart focused anxiety"[tiab] OR "kinesiophobia"[tiab] OR "kinesiophobias"[tiab] OR ("Fear"[majr] OR "fear"[ti] OR "fears"[ti] OR "Anxiety"[majr] OR "Anxiety Disorders"[majr] OR "anxiety"[ti] OR ("Stress, Psychological"[majr] AND ("fear"[tw] OR "fears"[tw] OR "anxiety"[tw] OR "anxieties"[tw]))) AND ("Cardiovascular Diseases/psychology"[majr:noexp] OR "Heart Diseases/psychology"[majr:noexp])) AND ("Cardiac outcome"[tiab] OR "Cardiac outcomes"[tiab] OR "cardiology outcomes"[tiab] OR "Patient Reported Outcome Measures"[majr] OR "Patient Reported Outcome Measures"[tiab] OR "Patient Reported Outcome Measure"[tiab] OR "Patient Reported Outcome"[tiab] OR "Patient Reported Outcomes"[tiab] OR "PROMs"[tiab] OR "PROM"[tiab] OR "cardiac event"[tiab] OR "cardiac events"[tiab] OR "recurrent chest pain"[tiab] OR "recurrent myocardial infarction"[tiab] OR "recurrent congestive heart failure"[tiab] OR "recurrent ischemia"[tiab] OR "recurrent ischaemia"[tiab] OR "recurrent heart attack"[tiab] OR "recurrent heart failure"[tiab] OR "Recurrence"[majr] OR "Recurrence"[tiab] OR "Atherosclerosis"[majr] OR "atherosclerosis"[tiab] OR "Hypertension"[majr] OR "hypertension"[tiab] OR "pain intensity"[tiab] OR "pain severity"[tiab] OR "Patient Admission"[majr] OR "hospital admission"[tiab] OR "hospital admission"[tiab] OR "Hospitalization"[majr] OR "hospitalization"[tiab] OR "hospitalisation"[tiab] OR "disease severity"[tiab] OR "Severity of Illness Index"[majr] OR "Severity of Illness"[tiab] OR "Severity of Disease"[tiab] OR "illness severity"[tiab] OR "Disease Progression"[majr] OR "Disease Progression"[tiab] OR "Disease Progress"[tiab] OR "disease advancement"[tiab] OR "Morbidity"[majr] OR "Morbidity"[tiab] OR "patient morbidity"[tiab] OR "Mortality"[majr] OR "mortality"[Subheading] OR "mortality"[tiab] OR "Longevity"[majr] OR "longevity"[tiab] OR "functional outcome"[tiab] OR "functional outcome"[tiab] OR "functional measure"[tiab] OR "functional measure"[tiab] OR "functional capacity"[tiab] OR "Recovery of Function"[majr] OR "recovery of function"[tiab] OR "Treatment Outcome"[majr] OR "Health Status"[majr] OR "Health"[majr:NoExp] OR "physical health"[tiab] OR "cardiac health"[tiab] OR "Quality of Life"[majr] OR "health-related quality of life"[tiab] OR "HRQOL"[tiab] OR "quality of life"[tiab] OR "qol"[tiab]) AND (english[la] OR german[la] OR dutch[la]))
MEDLINE via OVID	((*"Cardiovascular Diseases"/ OR exp *"Heart Diseases"/ OR "Cardiovascular Diseases".ti OR "Cardiovascular disease".ti OR "coronary heart disease".ti OR "coronary heart diseases".ti OR "coronary disease".ti OR "coronary diseases".ti OR "coronary artery disease".ti OR "coronary artery diseases".ti OR "myocardial infarction".ti OR "myocardial infarctions".ti OR "myocardial infarct".ti OR "myocardial infarcts".ti OR "cardiac care".ti OR "angina".ti OR exp *"Chest Pain"/ OR "Chest Pain".ti OR "heart failure".ti OR "coronary artery bypass graft".ti OR "percutaneous coronary intervention".ti OR "heart disease".ti OR "heart diseases".ti OR "cardiac disease".ti OR "cardiac diseases".ti OR "cardiovascular abnormalities".ti OR "cardiovascular abnormality".ti OR "cardiac abnormalities".ti OR "cardiac abnormality".ti OR "cardiac arrest".ti OR "long QT syndrome".ti OR "hypertrophic cardiomyopathy".ti OR "hypertrophic cardiomyopathies".ti OR exp *"Defibrillators, Implantable"/ OR "implantable cardioverter-defibrillator".ti OR "implantable cardioverter-defibrillator".ti OR "arrhythmia".ti OR "arrhythmias".ti) AND ("cardiac anxieties".ti,ab OR "cardiac anxiety".ti,ab OR "cardiac fear".ti,ab OR "cardiac fears".ti,ab OR "disease related anxieties".ti,ab OR "disease related anxiety".ti,ab OR "disease related fear".ti,ab OR "disease related fears".ti,ab OR "disease specific

anxieties".ti,ab OR "disease specific anxiety".ti,ab OR "disease specific fear".ti,ab OR "disease specific fears".ti,ab OR "fear of exercise".ti,ab OR "fear of exercises".ti,ab OR "fear of movement".ti,ab OR "fear of movements".ti,ab OR "fear avoidance".ti,ab OR "fear avoidance belief".ti,ab OR "fear avoidance beliefs".ti,ab OR "fear avoiding".ti,ab OR "health anxieties".ti,ab OR "health anxiety".ti,ab OR "heart focused anxieties".ti,ab OR "heart focused anxiety".ti,ab OR "kinesiophobia".ti,ab OR "kinesiophobias".ti,ab OR ((exp *"Fear"/ OR "fear".ti OR "fears".ti OR exp *"Anxiety"/ OR exp *"Anxiety Disorders"/ OR "anxiety".ti OR (exp *"Stress, Psychological"/ AND ("fear".mp OR "fears".mp OR "anxiety".mp OR "anxieties".mp))) AND (*"Cardiovascular Diseases"/px OR *"Heart Diseases"/px))) AND ("Cardiac outcome".ti,ab OR "Cardiac outcomes".ti,ab OR "cardiology outcomes".ti,ab OR exp *"Patient Reported Outcome Measures"/ OR "Patient Reported Outcome Measures".ti,ab OR "Patient Reported Outcome Measure".ti,ab OR "Patient Reported Outcome".ti,ab OR "Patient Reported Outcomes".ti,ab OR "PROMs".ti,ab OR "PROM".ti,ab OR "cardiac event".ti,ab OR "cardiac events".ti,ab OR "recurrent chest pain".ti,ab OR "recurrent myocardial infarction".ti,ab OR "recurrent congestive heart failure".ti,ab OR "recurrent ischemia".ti,ab OR "recurrent ischaemia".ti,ab OR "recurrent heart attack".ti,ab OR "recurrent heart failure".ti,ab OR exp *"Recurrence"/ OR "Recurrence".ti,ab OR exp *"Atherosclerosis"/ OR "atherosclerosis".ti,ab OR exp *"Hypertension"/ OR "hypertension".ti,ab OR "pain intensity".ti,ab OR "pain severity".ti,ab OR exp *"Patient Admission"/ OR "hospital admission".ti,ab OR "hospital admission*".ti,ab OR exp *"Hospitalization"/ OR "hospitalization".ti,ab OR "hospitalisation".ti,ab OR "disease severity".ti,ab OR exp *"Severity of Illness Index"/ OR "Severity of Illness".ti,ab OR "Severity of Disease".ti,ab OR "illness severity".ti,ab OR exp *"Disease Progression"/ OR "Disease Progression".ti,ab OR "Disease Progress".ti,ab OR "disease advancement".ti,ab OR exp *"Morbidity"/ OR "Morbidity".ti,ab OR "patient morbidity".ti,ab OR exp *"Mortality"/ OR "mortality".fs OR "mortality".ti,ab OR exp *"Longevity"/ OR "longevity".ti,ab OR "functional outcome".ti,ab OR "functional outcome*".ti,ab OR "functional measure".ti,ab OR "functional measure*".ti,ab OR "functional capacity".ti,ab OR exp *"Recovery of Function"/ OR "recovery of function".ti,ab OR exp *"Treatment Outcome"/ OR exp *"Health Status"/ OR "Health"/ OR "physical health".ti,ab OR "cardiac health".ti,ab OR exp *"Quality of Life"/ OR "health-related quality of life".ti,ab OR "HRQOL".ti,ab OR "quality of life".ti,ab OR "qol".ti,ab) AND (english.la OR german.la OR dutch.la))

PsycINFO (TX("Cardiovascular Disease" OR "Heart Disease" OR "Cardiovascular Diseases" OR "Cardiovascular disease" OR "coronary heart disease" OR "coronary heart diseases" OR "coronary disease" OR "coronary diseases" OR "coronary artery disease" OR "coronary artery diseases" OR "myocardial infarction" OR "myocardial infarctions" OR "myocardial infarct" OR "myocardial infarcts" OR "cardiac care" OR "angina" OR "Thorax Pain" OR "Chest Pain" OR "heart failure" OR "coronary artery bypass graft" OR "percutaneous coronary intervention" OR "heart disease" OR "heart diseases" OR "cardiac disease" OR "cardiac diseases" OR "cardiovascular abnormalities" OR "cardiovascular abnormality" OR "cardiac abnormalities" OR "cardiac abnormality" OR "cardiac arrest" OR "long QT syndrome" OR "hypertrophic cardiomyopathy" OR "hypertrophic cardiomyopathies" OR "cardiac implantable electronic device" OR "implantable cardioverter-defibrillator" OR "implantable cardioverter-defibrillator" OR "arrhythmia" OR "arrhythmias") AND TX("cardiac anxiety" OR "cardiac anxieties" OR "cardiac anxiety" OR "cardiac fear" OR "cardiac fears" OR "disease related anxieties" OR "disease related anxiety" OR "disease related fear" OR "disease related fears" OR "disease specific anxieties" OR "disease specific anxiety" OR "disease specific fear" OR "disease specific fears" OR "fear of exercise" OR "fear of exercises" OR "fear of movement" OR "fear of movements" OR "fear avoidance" OR "fear avoidance belief" OR "fear avoidance beliefs" OR "fear avoiding" OR "health anxieties" OR "health anxiety" OR "heart focused anxieties" OR "heart focused anxiety" OR "kinesiophobia" OR "kinesiophobias") AND TX("Cardiac outcome" OR "Cardiac outcomes" OR "cardiology outcomes" OR "Patient Reported Outcome Measures" OR "Patient Reported Outcome Measures" OR "Patient Reported Outcome Measure" OR "Patient Reported Outcome" OR "Patient Reported Outcomes" OR "PROMs" OR "PROM" OR "cardiac event" OR "cardiac events" OR "recurrent chest pain" OR "recurrent myocardial infarction" OR "recurrent congestive heart failure" OR "recurrent ischemia" OR "recurrent ischaemia" OR "recurrent heart attack" OR "recurrent heart failure" OR "Recurrence" OR "Recurrence" OR "Atherosclerosis" OR "atherosclerosis" OR "Hypertension" OR "hypertension" OR "pain intensity" OR "pain severity" OR "Patient Admission" OR "hospital admission" OR "hospital admission*" OR "Hospitalization" OR "hospitalization" OR "hospitalisation" OR "disease severity" OR "Severity of Illness Index" OR "Severity of Illness" OR "Severity of Disease" OR "illness severity" OR "Disease Progression" OR "Disease Progression" OR "Disease Progress" OR "disease advancement" OR "Morbidity" OR "Morbidity" OR "patient morbidity" OR "Mortality" OR "mortality".fs OR "mortality" OR "Longevity" OR "longevity" OR "functional outcome" OR "functional outcome*" OR "functional measure" OR "functional measure*" OR "functional capacity" OR "Recovery of Function" OR "recovery of function" OR

"Treatment Outcome" OR "Health Status" OR "Health" OR "physical health" OR "cardiac health" OR "Quality of Life" OR "health-related quality of life" OR "HRQOL" OR "quality of life" OR "qol"))
AND (english.la OR german.la OR dutch.la))

Embase ((("Cardiovascular Disease"/ OR exp *"Heart Disease"/ OR "Cardiovascular Diseases".ti OR "Cardiovascular disease".ti OR "coronary heart disease".ti OR "coronary heart diseases".ti OR "coronary disease".ti OR "coronary diseases".ti OR "coronary artery disease".ti OR "coronary artery diseases".ti OR "myocardial infarction".ti OR "myocardial infarctions".ti OR "myocardial infarct".ti OR "myocardial infarcts".ti OR "cardiac care".ti OR "angina".ti OR exp *"Thorax Pain"/ OR "Chest Pain".ti OR "heart failure".ti OR "coronary artery bypass graft".ti OR "percutaneous coronary intervention".ti OR "heart disease".ti OR "heart diseases".ti OR "cardiac disease".ti OR "cardiac diseases".ti OR "cardiovascular abnormalities".ti OR "cardiovascular abnormality".ti OR "cardiac abnormalities".ti OR "cardiac abnormality".ti OR "cardiac arrest".ti OR "long QT syndrome".ti OR "hypertrophic cardiomyopathy".ti OR "hypertrophic cardiomyopathies".ti OR exp *"cardiac implantable electronic device"/ OR "implantable cardioverter-defibrillator".ti OR "implantable cardioverter-defibrillator".ti OR "arrhythmia".ti OR "arrhythmias".ti) AND ("cardiac anxiety"/ OR "cardiac anxieties".ti,ab OR "cardiac anxiety".ti,ab OR "cardiac fear".ti,ab OR "cardiac fears".ti,ab OR "disease related anxieties".ti,ab OR "disease related anxiety".ti,ab OR "disease related fear".ti,ab OR "disease related fears".ti,ab OR "disease specific anxieties".ti,ab OR "disease specific anxiety".ti,ab OR "disease specific fear".ti,ab OR "disease specific fears".ti,ab OR "fear of exercise".ti,ab OR "fear of exercises".ti,ab OR "fear of movement".ti,ab OR "fear of movements".ti,ab OR "fear avoidance".ti,ab OR "fear avoidance belief".ti,ab OR "fear avoidance beliefs".ti,ab OR "fear avoiding".ti,ab OR "health anxieties".ti,ab OR "health anxiety".ti,ab OR "heart focused anxieties".ti,ab OR "heart focused anxiety".ti,ab OR "kinesiophobia".ti,ab OR "kinesiophobias".ti,ab) AND ("Cardiac outcome".ti,ab OR "Cardiac outcomes".ti,ab OR "cardiology outcomes".ti,ab OR exp *"Patient-Reported Outcome"/ OR "Patient Reported Outcome Measures".ti,ab OR "Patient Reported Outcome Measure".ti,ab OR "Patient Reported Outcome".ti,ab OR "Patient Reported Outcomes".ti,ab OR "PROMs".ti,ab OR "PROM".ti,ab OR "cardiac event".ti,ab OR "cardiac events".ti,ab OR "recurrent chest pain".ti,ab OR "recurrent myocardial infarction".ti,ab OR "recurrent congestive heart failure".ti,ab OR "recurrent ischemia".ti,ab OR "recurrent ischaemia".ti,ab OR "recurrent heart attack".ti,ab OR "recurrent heart failure".ti,ab OR exp *"Recurrence"/ OR "Recurrence".ti,ab OR exp *"Atherosclerosis"/ OR "atherosclerosis".ti,ab OR exp *"Hypertension"/ OR "hypertension".ti,ab OR "pain intensity".ti,ab OR "pain severity".ti,ab OR exp *"Hospital Admission"/ OR "hospital admission".ti,ab OR "hospital admission*".ti,ab OR exp *"Hospitalization"/ OR "hospitalization".ti,ab OR "hospitalisation".ti,ab OR exp *"disease severity"/ OR "disease severity".ti,ab OR exp *"Severity of Illness Index"/ OR "Severity of Illness".ti,ab OR "Severity of Disease".ti,ab OR "illness severity".ti,ab OR exp *"Disease exacerbation"/ OR "Disease Progression".ti,ab OR "Disease Progress".ti,ab OR "disease advancement".ti,ab OR exp *"Morbidity"/ OR "Morbidity".ti,ab OR "patient morbidity".ti,ab OR exp *"Mortality"/ OR "mortality".fs OR "mortality".ti,ab OR exp *"Longevity"/ OR "longevity".ti,ab OR "functional outcome".ti,ab OR "functional outcome*".ti,ab OR "functional measure".ti,ab OR "functional measure*".ti,ab OR "functional capacity".ti,ab OR exp *"Convalescence"/ OR "recovery of function".ti,ab OR exp *"Treatment Outcome"/ OR exp *"Health Status"/ OR "Health"/ OR "physical health".ti,ab OR "cardiac health".ti,ab OR exp *"Quality of Life"/ OR "health-related quality of life".ti,ab OR "HRQOL".ti,ab OR "quality of life".ti,ab OR "qol".ti,ab) AND (english.la OR german.la OR dutch.la)) NOT (conference review or conference abstract).pt

Web of Science (TI=("Cardiovascular Disease" OR "Heart Disease" OR "Cardiovascular Diseases" OR "Cardiovascular disease" OR "coronary heart disease" OR "coronary heart diseases" OR "coronary disease" OR "coronary diseases" OR "coronary artery disease" OR "coronary artery diseases" OR "myocardial infarction" OR "myocardial infarctions" OR "myocardial infarct" OR "myocardial infarcts" OR "cardiac care" OR "angina" OR "Thorax Pain" OR "Chest Pain" OR "heart failure" OR "coronary artery bypass graft" OR "percutaneous coronary intervention" OR "heart disease" OR "heart diseases" OR "cardiac disease" OR "cardiac diseases" OR "cardiovascular abnormalities" OR "cardiovascular abnormality" OR "cardiac abnormalities" OR "cardiac abnormality" OR "cardiac arrest" OR "long QT syndrome" OR "hypertrophic cardiomyopathy" OR "hypertrophic cardiomyopathies" OR "cardiac implantable electronic device" OR "implantable cardioverter-defibrillator" OR "implantable cardioverter-defibrillator" OR "arrhythmia" OR "arrhythmias") AND TS=("cardiac anxiety" OR "cardiac anxieties" OR "cardiac anxiety" OR "cardiac fear" OR "cardiac fears" OR "disease related anxieties" OR "disease related anxiety" OR "disease related fear" OR "disease related fears" OR "disease specific anxieties" OR "disease specific anxiety" OR "disease specific fear" OR "disease specific fears" OR "fear of exercise" OR "fear of exercises" OR "fear of movement" OR "fear of movements" OR "fear avoidance" OR "fear avoidance belief" OR "fear avoidance beliefs" OR "fear avoiding" OR

"health anxieties" OR "health anxiety" OR "heart focused anxieties" OR "heart focused anxiety" OR "kinesiophobia" OR "kinesiophobias") AND TS=("Cardiac outcome" OR "Cardiac outcomes" OR "cardiology outcomes" OR "Patient-Reported Outcome" OR "Patient Reported Outcome Measures" OR "Patient Reported Outcome Measure" OR "Patient Reported Outcome" OR "Patient Reported Outcomes" OR "PROMs" OR "PROM" OR "cardiac event" OR "cardiac events" OR "recurrent chest pain" OR "recurrent myocardial infarction" OR "recurrent congestive heart failure" OR "recurrent ischemia" OR "recurrent ischaemia" OR "recurrent heart attack" OR "recurrent heart failure" OR "Recurrence" OR "Recurrence" OR "Atherosclerosis" OR "atherosclerosis" OR "Hypertension" OR "hypertension" OR "pain intensity" OR "pain severity" OR "Hospital Admission" OR "hospital admission" OR "hospital admission*" OR "Hospitalization" OR "hospitalization" OR "hospitalisation" OR "disease severity" OR "disease severity" OR "Severity of Illness Index" OR "Severity of Illness" OR "Severity of Disease" OR "illness severity" OR "Disease exacerbation" OR "Disease Progression" OR "Disease Progress" OR "disease advancement" OR "Morbidity" OR "Morbidity" OR "patient morbidity" OR "Mortality" OR "mortality" OR "Longevity" OR "longevity" OR "functional outcome" OR "functional outcome*" OR "functional measure" OR "functional measure*" OR "functional capacity" OR "Convalescence" OR "recovery of function" OR "Treatment Outcome" OR "Health Status" OR "Health" OR "physical health" OR "cardiac health" OR "Quality of Life" OR "health-related quality of life" OR "HRQOL" OR "quality of life" OR "qol") AND LA=(english OR german OR dutch)) NOT DT=(meeting abstract)

Cochrane ((("Cardiovascular Disease" OR "Heart Disease" OR "Cardiovascular Diseases" OR "Cardiovascular disease" OR "coronary heart disease" OR "coronary heart diseases" OR "coronary disease" OR "coronary diseases" OR "coronary artery disease" OR "coronary artery diseases" OR "myocardial infarction" OR "myocardial infarctions" OR "myocardial infarct" OR "myocardial infarcts" OR "cardiac care" OR "angina" OR "Thorax Pain" OR "Chest Pain" OR "heart failure" OR "coronary artery bypass graft" OR "percutaneous coronary intervention" OR "heart disease" OR "heart diseases" OR "cardiac disease" OR "cardiac diseases" OR "cardiovascular abnormalities" OR "cardiovascular abnormality" OR "cardiac abnormalities" OR "cardiac abnormality" OR "cardiac arrest" OR "long QT syndrome" OR "hypertrophic cardiomyopathy" OR "hypertrophic cardiomyopathies" OR "cardiac implantable electronic device" OR "implantable cardioverter defibrillator" OR "implantable cardioverter defibrillator" OR "arrhythmia" OR "arrhythmias") AND ("cardiac anxiety" OR "cardiac anxieties" OR "cardiac anxiety" OR "cardiac fear" OR "cardiac fears" OR "disease related anxieties" OR "disease related anxiety" OR "disease related fear" OR "disease related fears" OR "disease specific anxieties" OR "disease specific anxiety" OR "disease specific fear" OR "disease specific fears" OR "fear of exercise" OR "fear of exercises" OR "fear of movement" OR "fear of movements" OR "fear avoidance" OR "fear avoidance belief" OR "fear avoidance beliefs" OR "fear avoiding" OR "health anxieties" OR "health anxiety" OR "heart focused anxieties" OR "heart focused anxiety" OR "kinesiophobia" OR "kinesiophobias") AND ("Cardiac outcome" OR "Cardiac outcomes" OR "cardiology outcomes" OR "Patient Reported Outcome" OR "Patient Reported Outcome Measures" OR "Patient Reported Outcome Measure" OR "Patient Reported Outcome" OR "Patient Reported Outcomes" OR "PROMs" OR "PROM" OR "cardiac event" OR "cardiac events" OR "recurrent chest pain" OR "recurrent myocardial infarction" OR "recurrent congestive heart failure" OR "recurrent ischemia" OR "recurrent ischaemia" OR "recurrent heart attack" OR "recurrent heart failure" OR "Recurrence" OR "Recurrence" OR "Atherosclerosis" OR "atherosclerosis" OR "Hypertension" OR "hypertension" OR "pain intensity" OR "pain severity" OR "Hospital Admission" OR "hospital admission" OR "hospital admission*" OR "Hospitalization" OR "hospitalization" OR "hospitalisation" OR "disease severity" OR "disease severity" OR "Severity of Illness Index" OR "Severity of Illness" OR "Severity of Disease" OR "illness severity" OR "Disease exacerbation" OR "Disease Progression" OR "Disease Progress" OR "disease advancement" OR "Morbidity" OR "Morbidity" OR "patient morbidity" OR "Mortality" OR "mortality" OR "Longevity" OR "longevity" OR "functional outcome" OR "functional outcome*" OR "functional measure" OR "functional measure*" OR "functional capacity" OR "Convalescence" OR "recovery of function" OR "Treatment Outcome" OR "Health Status" OR "Health" OR "physical health" OR "cardiac health" OR "Quality of Life" OR "health related quality of life" OR "HRQOL" OR "quality of life" OR "qol")):ti,ab,kw NOT (conference abstract OR meeting abstract):pt

Emcare ((*("Cardiovascular Disease"/ OR exp *("Heart Disease"/ OR "Cardiovascular Diseases".ti OR "Cardiovascular disease".ti OR "coronary heart disease".ti OR "coronary heart diseases".ti OR "coronary disease".ti OR "coronary diseases".ti OR "coronary artery disease".ti OR "coronary artery diseases".ti OR "myocardial infarction".ti OR "myocardial infarctions".ti OR "myocardial infarct".ti OR "myocardial infarcts".ti OR "cardiac care".ti OR "angina".ti OR exp *("Thorax Pain"/ OR "Chest Pain".ti OR "heart failure".ti OR

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Academic (TI("Cardiovascular Disease" OR "Heart Disease" OR "Cardiovascular Diseases" OR "Cardiovascular disease" OR "coronary heart disease" OR "coronary heart diseases" OR "coronary disease" OR "coronary diseases" OR "coronary artery disease" OR "coronary artery diseases" OR "myocardial infarction" OR "myocardial infarctions" OR "myocardial infarct" OR "myocardial infarcts" OR "cardiac care" OR "angina" OR "Thorax Pain" OR "Chest Pain" OR "heart failure" OR "coronary artery bypass graft" OR "percutaneous coronary intervention" OR "heart disease" OR "heart diseases" OR "cardiac disease" OR "cardiac diseases" OR "cardiovascular abnormalities" OR "cardiovascular abnormality" OR "cardiac abnormalities" OR "cardiac abnormality" OR "cardiac arrest" OR "long QT syndrome" OR "hypertrophic cardiomyopathy" OR "hypertrophic cardiomyopathies" OR "cardiac implantable electronic device" OR "implantable cardioverter-defibrillator" OR "implantable cardioverter-defibrillator" OR "arrhythmia" OR "arrhythmias") AND TI("cardiac anxiety" OR "cardiac anxieties" OR "cardiac anxiety" OR "cardiac fear" OR "cardiac fears" OR "disease related anxieties" OR "disease related anxiety" OR "disease related fear" OR "disease related fears" OR "disease specific anxieties" OR "disease specific anxiety" OR "disease specific fear" OR "disease specific fears" OR "fear of exercise" OR "fear of exercises" OR "fear of movement" OR "fear of movements" OR "fear avoidance" OR "fear avoidance belief" OR "fear avoidance beliefs" OR "fear avoiding" OR "health anxieties" OR "health anxiety" OR "heart focused anxieties" OR "heart focused anxiety" OR "kinesiophobia" OR "kinesiophobias") AND TX("Cardiac outcome" OR "Cardiac outcomes" OR "cardiology outcomes" OR "Patient Reported Outcome" OR "Patient Reported Outcome Measures" OR "Patient Reported Outcome Measure" OR "Patient Reported Outcome" OR "Patient Reported Outcomes" OR "PROMs" OR "PROM" OR "cardiac event" OR "cardiac events" OR "recurrent chest pain" OR "recurrent myocardial infarction" OR "recurrent congestive heart failure" OR "recurrent ischemia" OR "recurrent ischaemia" OR "recurrent heart attack" OR "recurrent heart failure" OR "Recurrence" OR "Recurrence" OR "Atherosclerosis" OR "atherosclerosis" OR "Hypertension" OR "hypertension" OR "pain intensity" OR "pain severity" OR "Hospital Admission" OR "hospital admission" OR "hospital admission*" OR "Hospitalization" OR "hospitalization" OR "hospitalisation" OR "disease severity" OR "disease severity" OR "Severity of Illness Index" OR "Severity of Illness" OR "Severity of Disease" OR "illness severity" OR "Disease exacerbation" OR "Disease Progression" OR "Disease Progress"

OR "disease advancement" OR "Morbidity" OR "Morbidity" OR "patient morbidity" OR "Mortality" OR "mortality" OR "Longevity" OR "longevity" OR "functional outcome" OR "functional outcome*" OR "functional measure" OR "functional measure*" OR "functional capacity" OR "Convalescence" OR "recovery of function" OR "Treatment Outcome" OR "Health Status" OR "Health" OR "physical health" OR "cardiac health" OR "Quality of Life" OR "health related quality of life" OR "HRQOL" OR "quality of life" OR "qol")) OR (TI("Cardiovascular Disease" OR "Heart Disease" OR "Cardiovascular Diseases" OR "Cardiovascular disease" OR "coronary heart disease" OR "coronary heart diseases" OR "coronary disease" OR "coronary diseases" OR "coronary artery disease" OR "coronary artery diseases" OR "myocardial infarction" OR "myocardial infarctions" OR "myocardial infarct" OR "myocardial infarcts" OR "cardiac care" OR "angina" OR "Thorax Pain" OR "Chest Pain" OR "heart failure" OR "coronary artery bypass graft" OR 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avoidance beliefs" OR "fear avoiding" OR "health anxieties" OR "health anxiety" OR "heart focused anxieties" OR "heart focused anxiety" OR "kinesiophobia" OR "kinesiophobias") AND TX("Cardiac outcome" OR "Cardiac outcomes" OR "cardiology outcomes" OR "Patient Reported Outcome" OR "Patient Reported Outcome Measures" OR "Patient Reported Outcome Measure" OR "Patient Reported Outcome" OR "Patient Reported Outcomes" OR "PROMs" OR "PROM" OR "cardiac event" OR "cardiac events" OR "recurrent chest pain" OR "recurrent myocardial infarction" OR "recurrent congestive heart failure" OR "recurrent ischemia" OR "recurrent ischaemia" OR "recurrent heart attack" OR "recurrent heart failure" OR "Recurrence" OR "Recurrence" OR "Atherosclerosis" OR "atherosclerosis" OR "Hypertension" OR "hypertension" OR "pain intensity" OR "pain severity" OR "Hospital Admission" OR "hospital admission" OR "hospital admission*" OR "Hospitalization" OR "hospitalization" OR "hospitalisation" OR "disease severity" OR "disease severity" OR "Severity of Illness Index" OR "Severity of Illness" OR "Severity of Disease" OR "illness severity" OR "Disease exacerbation" OR "Disease Progression" OR "Disease Progress" OR "disease advancement" OR "Morbidity" OR "Morbidity" OR "patient morbidity" OR "Mortality" OR "mortality" OR "Longevity" OR "longevity" OR "functional outcome" OR "functional outcome*" OR "functional measure" OR "functional measure*" OR "functional capacity" OR "Convalescence" OR "recovery of function" OR "Treatment Outcome" OR "Health Status" OR "Health" OR "physical health" OR "cardiac health" OR "Quality of Life" OR "health related quality of life" OR "HRQOL" OR "quality of life" OR "qol")) OR (TI("Cardiovascular Disease" OR "Heart Disease" OR "Cardiovascular Diseases" OR "Cardiovascular disease" OR "coronary heart disease" OR "coronary heart diseases" OR "coronary disease" OR "coronary diseases" OR "coronary artery disease" OR "coronary artery diseases" OR "myocardial infarction" OR "myocardial infarctions" OR "myocardial infarct" OR "myocardial infarcts" OR "cardiac care" OR "angina" OR "Thorax Pain" OR "Chest Pain" OR "heart failure" OR "coronary artery bypass graft" OR "percutaneous coronary intervention" OR "heart disease" OR "heart diseases" OR "cardiac disease" OR "cardiac diseases" OR "cardiovascular abnormalities" OR "cardiovascular abnormality" OR "cardiac abnormalities" OR "cardiac abnormality" OR "cardiac arrest" OR "long QT syndrome" OR "hypertrophic cardiomyopathy" OR "hypertrophic cardiomyopathies" OR "cardiac implantable electronic device" OR "implantable cardioverter-defibrillator" OR "implantable cardioverter-defibrillator" OR "arrhythmia" OR "arrhythmias") AND AB("cardiac anxiety" OR "cardiac anxieties" OR "cardiac anxiety" OR "cardiac fear" OR "cardiac fears" OR "disease related anxieties" OR "disease related anxiety" OR "disease related fear" OR "disease related fears" OR "disease specific anxieties" OR "disease specific anxiety" OR "disease 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OR "disease severity" OR "disease severity" OR "Severity of Illness Index" OR "Severity of Illness" OR "Severity of Disease" OR "illness severity" OR "Disease exacerbation" OR "Disease Progression" OR "Disease Progress" OR "disease advancement" OR "Morbidity" OR "Morbidity" OR "patient morbidity" OR "Mortality" OR "mortality" OR "Longevity" OR "longevity" OR "functional outcome" OR "functional outcome*" OR "functional measure" OR "functional measure*" OR "functional capacity" OR "Convalescence" OR "recovery of function" OR "Treatment Outcome" OR "Health Status" OR "Health" OR "physical health" OR "cardiac health" OR "Quality of Life" OR "health related quality of life" OR "HRQOL" OR "quality of life" OR "qol")) OR (KW("Cardiovascular Disease" OR "Heart Disease" OR "Cardiovascular Diseases" OR "Cardiovascular disease" OR "coronary heart disease" OR "coronary heart diseases" OR "coronary disease" OR "coronary diseases" OR "coronary artery disease" OR "coronary artery diseases" OR 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"hypertension" OR "pain intensity" OR "pain severity" OR "Hospital Admission" OR "hospital admission" OR "hospital admission*" OR "Hospitalization" OR "hospitalization" OR "hospitalisation" OR "disease severity" OR "disease severity" OR "Severity of Illness Index" OR "Severity of Illness" OR "Severity of Disease" OR "illness severity" OR "Disease exacerbation" OR "Disease Progression" OR "Disease Progress" OR "disease advancement" OR "Morbidity" OR "Morbidity" OR "patient morbidity" OR "Mortality" OR "mortality" OR "Longevity" OR "longevity" OR "functional outcome" OR "functional outcome*" OR "functional measure" OR "functional measure*" OR "functional capacity" OR "Convalescence" OR "recovery of function" OR "Treatment Outcome" OR "Health Status" OR "Health" OR "physical health" OR "cardiac health" OR "Quality of Life" OR "health related quality of life" OR "HRQOL" OR "quality of life" OR "qol")) OR (AB("Cardiovascular Disease" OR "Heart Disease" OR "Cardiovascular Diseases" OR "Cardiovascular disease" OR "coronary heart disease" OR "coronary heart diseases" OR "coronary disease" OR "coronary diseases" OR "coronary artery disease" OR "coronary artery diseases" OR "myocardial infarction" OR "myocardial infarctions" OR "myocardial infarct" OR "myocardial infarcts" OR "cardiac care" OR "angina" OR "Thorax Pain" OR "Chest Pain" OR "heart failure" OR "coronary artery bypass graft" OR "percutaneous coronary intervention" OR "heart disease" OR "heart diseases" OR "cardiac disease" OR "cardiac diseases" OR "cardiovascular abnormalities" OR "cardiovascular abnormality" OR "cardiac abnormalities" OR "cardiac abnormality" OR "cardiac arrest" OR "long QT syndrome" OR "hypertrophic cardiomyopathy" OR "hypertrophic cardiomyopathies" OR "cardiac implantable electronic device" OR "implantable cardioverter-defibrillator" OR "implantable cardioverter-defibrillator" OR "arrhythmia" OR "arrhythmias") AND KW("cardiac anxiety" OR "cardiac anxieties" OR "cardiac anxiety" OR "cardiac fear" OR "cardiac fears" OR "disease related anxieties" OR "disease related anxiety" OR "disease related fear" OR "disease related fears" OR "disease specific anxieties" OR "disease specific anxiety" OR "disease specific fear" OR "disease specific fears" OR "fear of exercise" OR "fear of exercises" OR "fear of movement" OR "fear of movements" OR "fear avoidance" OR "fear avoidance belief" OR "fear avoidance beliefs" OR "fear avoiding" OR "health anxieties" OR "health anxiety" OR "heart focused anxieties" OR "heart focused anxiety" OR "kinesiophobia" OR "kinesiophobias") AND TX("Cardiac outcome" OR "Cardiac outcomes" OR "cardiology outcomes" OR "Patient Reported Outcome" OR "Patient Reported Outcome Measures" OR "Patient Reported Outcome Measure" OR "Patient Reported Outcome" OR "Patient Reported Outcomes" OR "PROMs" OR "PROM" OR "cardiac event" OR "cardiac events" OR "recurrent chest pain" OR "recurrent myocardial infarction" OR "recurrent congestive heart failure" OR "recurrent ischemia" OR "recurrent ischaemia" OR "recurrent heart attack" OR "recurrent heart failure" OR "Recurrence" OR "Recurrence" OR

"Atherosclerosis" OR "atherosclerosis" OR "Hypertension" OR "hypertension" OR "pain intensity" OR "pain severity" OR "Hospital Admission" OR "hospital admission" OR "hospital admission*" OR "Hospitalization" OR "hospitalization" OR "hospitalisation" OR "disease severity" OR "disease severity" OR "Severity of Illness Index" OR "Severity of Illness" OR "Severity of Disease" OR "illness severity" OR "Disease exacerbation" OR "Disease Progression" OR "Disease Progress" OR "disease advancement" OR "Morbidity" OR "Morbidity" OR "patient morbidity" OR "Mortality" OR "mortality" OR "Longevity" OR "longevity" OR "functional outcome" OR "functional outcome*" OR "functional measure" OR "functional measure*" OR "functional capacity" OR "Convalescence" OR "recovery of function" OR "Treatment Outcome" OR "Health Status" OR "Health" OR "physical health" OR "cardiac health" OR "Quality of Life" OR "health related quality of life" OR "HRQOL" OR "quality of life" OR "qol"))

Appendix B

Table B1

Quality assessment using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist (Moola et al., 2017)

Study	Were the criteria for inclusion in the sample clearly defined?	Were the study subjects and the setting described in detail?	Was the exposure measured in a valid and reliable way?	Were objective, standard criteria used for measurement of the condition?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the outcomes measured in a valid and reliable way?	Was appropriate statistical analysis used?	Overall appraisal
Acar et al., 2016	Yes Inclusion criteria: - Being followed regularly for pulmonary arterial hypertension or heart failure - Sound performance in speech production and fluency in reading - Diagnosed at least 3 months earlier - Age between 18 and 85 years - Volunteering to participate Exclusion criteria: - Neuromusculoskeletal problems induced during physical activity or exercise	Yes Pulmonary arterial hypertension and heart failure patients regularly attending the cardiology clinic were enrolled in the study between September 2013 and December 2013. Demographics: age, sex, height, weight, and BMI	Yes Kinesiophobia – TSK Heart Turkish Version	Unclear Clinical characteristics including clinical disease type and medication information were recorded, however, the paper does not specify how.	No X	No X	Yes Physical endurance – 6MWT Physical activity level – IPAQ Generic quality of life – NHP	Yes The study performed translation, back translation, and cross-cultural adaptation of the TSK Heart. Cronbach's alpha and exploratory factor analysis were used to assess questionnaire's reliability. To assess convergent validity, Pearson's correlations of the outcomes were performed with the TSK Heart Turkish Version	Include
Bäck et al., 2013	Yes Inclusion criteria: - Principal diagnosis of CAD Exclusion criteria: - Death during hospital period - Serious disease interfering with study participation - Inability to understand Swedish language - Time-lapse >10 months after hospital discharge	Yes CAD patients were recruited between 2007 and 2009 at Sahlgrenska University Hospital about six months after hospital discharge Demographics: sex, age, and current smoking.	Yes Kinesiophobia – TSK Heart Swedish Version	Unclear Medical variables like previous history (myocardial infarction, angina pectoris, PCI, CABG, heart failure, diabetes, hypertension), type of CAD (STEMI, non-STEMI, unstable/stable angina), complications/interventions in hospital (PCI, CABG, heart failure, atrial fibrillation), and duration of CAD were all assessed. However, method of this data collection is not specified.	No X	Unclear Confounders are not directly specified; however, current smoking was included into the binary logistic regression as a covariate.	Yes Body functions: waist-hip ratio, muscle endurance (unilateral isotonic heel-lift, unilateral isotonic shoulder flexion, bilateral shoulder abduction), Physical activity – pedometer, IPAQ, activity diary HRQoL – RAND SF-36	Unclear Difference between groups of high vs. low kinesiophobia were tested with a student's t-test and Pearson's chi-square test. To analyze the between-group difference in a single model, a binary logistic regression was performed with the variables dichotomized.	Include

Bäck et al., 2016	Yes Inclusion criteria: - Principal diagnosis of CAD Exclusion criteria: - Inability to understand Swedish - Time-lapse of >10 months after hospital discharge (*patients with diabetes were included, but excluded from taking the oral glucose tolerance test)	Yes Patients with a primary diagnosis of CAD recruited between 2007 and 2009 at Sahlgrenska university Hospital, enrolled within a median of 6 months after hospital discharge, at the end of conventional EBCR. Demographics: gender and age	Yes Kinesiophobia – TSK Heart Swedish version HqoL – RAND SF-36	Yes Diagnosis of CAD was confirmed by coronary angiography prior to or at the time of hospitalization. Data on clinical variables were collected: blood sampling, blood pressure, detailed history of smoking, history of disease (angina pectoris, heart failure, percutaneous coronary intervention, coronary artery bypass grafting, diabetes, hypertension), current type of CAD registered at the cardiac ICU, complications/interventions at the hospital, current medication, BMI, muscle endurance, blood glucose.	No X	No X	Yes Physical activity – IPAQ Daily steps – Pedometer CR attendance – collected by physiotherapist in interviews and from medical records HRQoL- The Short Form-26 Oral glucose tolerance test Serum lipids (enzymatic photometric method using venous blood) 24hr blood pressure and heart rate	Yes Between-group differences were assessed with Student's t-test and Pearson's x ² test. To analyze the influences on attendance at exercise-based CR by different types of predictors, an exploratory path model analysis was carried out. Probit regression was used to evaluate direct and indirect effects of the path model using modification indices.	Include
Bunz et al., 2015	Yes Inclusion criteria: - Patients suffering from heart failure eligible for ICD implantation for causes of primary or secondary prevention Exclusion criteria: - If symptoms of progressing dementia, drug abuse or forms of endogenous or exogenous psychosis applied - If time interval between admittance to the hospital and the implantation was too short for inclusion - If the patients had been previously informed about the necessity of an ICD	Yes HF patients eligible for ICD implantation were recruited between July 2010 and May 2014 at the Saarland University Medical Center. Demographics: age, gender, education, and relationship status.	Yes Cardiac anxiety – CAQ	Yes Participants underwent a physical examination to assess relevant clinical parameters and to eliminate the risk of cardiac decompensation. Laboratory values (haemoglobin, potassium, creatinine and NT-proBNP) were measured, functional status according to NYHA class, BMI and blood pressure were	Yes Potential confounders: MI and systolic blood pressure	Yes Correlations between HFA and all clinical parameters were performed and those that were correlated significantly were entered into the multiple regression analysis.	Yes HRQoL – MLHFQ Ejection Fraction – Echocardiography Systolic and diastolic blood pressure Myocardial infarction	Yes Group differences were assessed via parametric and non-parametric measures of mean differences (t test, Mann-Whitney U test, Kruskal-Wallis test, x ² test). Bivariate (Pearson's and Spearman's) correlations were performed to assess associations between variables. Stepwise linear multiple regression was performed to identify predictors of HFA.	Include

	before they were admitted to hospital for implantation and before they were approached for participation - If the patients did not consent to participate			determined. Heart rate and basic rhythm were obtained through an ECG. EF was measured via echocardiography.			classification - NYHA		
Dąbek et al., 2020	Yes Inclusion criteria: - Voluntary participation - Sufficient mental fitness (contact w/ patient, lack of cognitive disorders) - To understand questions and statements in the questionnaire - Professional inactivity caused by retirement or pension (to exclude the area of “forced” physical activity through professional work) No specific exclusion criteria reported	Unclear CVD patients hospitalized in the Department of Cardiology in Katowice, southern Poland, during a period of 6 months in 2017. It is not specified during which exact months recruitment took place. Demographics: gender, age, morphological parameters (height and weight), size of residence, way of living, education, time from diagnosis of CVD and its type, and chronic non-cardiac comorbidities	Yes Kinesiophobia – TSK Heart Polish Version	No X	No X	No X	Yes Physical activity - IPAQ	Yes Relationships between variables were calculated using Pearson’s correlation coefficients.	Include
Einsle et al., 2009	Yes Inclusion criteria: - Implantation of pacemaker or ICD device or being treated with anti-arrhythmic medication Exclusion criteria: - none	Yes Patients with clinically relevant arrhythmias between November 2002 until February 2004 at the cardiology department of the University hospital in Dresden, Germany Demographics: age, gender, medication use	Yes Cardiac anxiety – CAQ (incl. all subscales)	Unclear X	No X	No X	Yes HRQoL – SF-12 (PCS, MCS)	Yes Correlational analyses were conducted ANOVA and ANCOVA for variance and covariance analyses	Include
Hoyer et al., 2008	Yes Inclusion criteria: - Consecutive cardiology patients before (and after) elective cardiac surgery Exclusion criteria: - patients aged <18 - Emergency cases - Illiterate patients or if unable to converse in German	Yes Consecutive cardiology patients of the Dresden Heart Center who were undergoing cardiac surgery including coronary bypass, valve replacement, and combined surgery.	Yes Cardiac anxiety - CAQ	Yes As for clinical variables, the type of surgery was drawn from medical records.	No X	No X	Yes HRQoL – RAND SF-12	Yes Pearson Product–Moment Correlations were computed to assess relations between CAQ scales and global measures of anxiety, depression, and quality of life.	Include

		Demographics: age, sex, education, and marital and professional status.							
Kovacs et al., 2006	No X	Yes	Yes	Unclear	No	No	Yes	Yes	Include
		English speaking adults, physician-referred, to a full day cardiac risk-reduction education program participated.	Cardiac anxiety – CAQ	Medical history and cardiac medications were both assessed; however, it is not specified how they were obtained.	X	X	HRQoL- RAND SF-12 PCS	Correlation analysis was carried out to examine the associations between cardiac anxiety and quality of life.	
		Demographics: ethnicity, marital status, household status, education, occupation, and income.							
Van Beek et al., 2012	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Include
	Inclusion criteria: - Final diagnosis of Myocardial Infarction (both STEMI and non-STEMI)	Patients admitted into the department of cardiology between November 2006 and December 2007 were recruited and screened for eligibility by a senior cardiologist within two days of admission.	Cardiac anxiety - CAQ	The diagnosis of a MI was based on clinical history and a rise and fall of troponin I. Cardiac disease status was also assessed along with a somatic history of other related diseases (hypertension, hypercholesterolemia, diabetes, peripheral atherosclerotic disease, stroke, CAD, CR assignment). All were properly defined, collected by a cardiologist in training and checked by a consultant cardiologist.	Potential confounders were socio-demographic and cardiac variables.	Classes were compared regarding relevant sociodemographic, cardiac, and psychiatric variables at baseline and quality of life endpoint, by performing ANOVA for continuous variables or X ² -tests for categorical variables.	QoL - EQ-5D	A latent class growth analysis was performed to find the model fit which was most optimal to check whether the different symptom clusters result in similar trajectories or whether they are subscale specific. Classes were compared regarding relevant socio-demographic, cardiac and psychiatric variables at baseline and QoL at endpoint through an ANOVA or x ² test.	
	Exclusion criteria: - age above 85 years - discharge out of hospital within two days of admission - inability to fill in questionnaires (due to insufficient knowledge of Dutch, cognitive impairment, too ill to participate)	Socio-demographics: age, sex, relationship status, education level, and employment status.							
Van Beek et al., 2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
	Inclusion criteria: - Diagnosis of STEMI or NSTEMI confirmed by the presence of a rise and fall of troponin I (>0.20 µg/L).	Patients with myocardial infarction consecutively admitted to hospital between November 2006 and December 2007 to the Department of Cardiology at Radboud University Medical	Cardiac anxiety - CAQ	Clinical data regarding severity of the disease (LVEF, history of MI) and relevant cardiac risk factors (smoking, hypertension, hypercholesterolemia, diabetes, history of	Potential confounders were identified as sociodemographic and	In the basic model, data was adjusted for age and gender. A priori adjustment for history of MI and LVEF as	Disease severity	Linear and logistic regression for multiple imputations was performed. Differences between groups were assessed using Student's t test or Mann-Whitney U-test. Associations between variables were evaluated	
	Exclusion criteria: - Age above 85 years						Adverse outcomes – (major adverse outcomes (MACE), defined by all-cause		

Wedegärtner et al., 2020	X	Out- and inpatients with stable heart failure and reduced left ventricular ejection fraction of the Department of Internal Medicine III of the Saarland University Medical Center were recruited between 2014 and 2019.	Cardiac anxiety - CAQ	Medical records and physical examination yielded information on presence of CHD, atrial fibrillation, prior MI, reanimation, implantation of a pacemaker or ICD, NYHA classification, LVEF, hyperlipidemia, diabetes, obesity, family history of CVD, number of CV risk factors. Lab results obtained included eGFR and NT-proBNP.	Potential confounders: alcohol consumption, physical activity, atrial fibrillation, NYHA class, hyperlipidemia, NT-proBNP	Demographic and clinical variables were tested in the correlation analysis with CAQ. Significant correlations were then entered into the stepwise regression analysis.	HRQoL – KCCQ	First, significant correlations between CAQ scores and predictor variables were tested by Pearson correlation. Next, a stepwise regression analyses were used to predict CAQ scores with predictors that showed significant correlations to determine the effect of each predictor on the outcome while controlling for the influence of the remaining predictors.
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Note: 6MWT: 6-Minute Walk Test, ANCOVA: Analysis of Covariance, ANOVA: Analysis of Variance, BMI: Body mass index, CABG: coronary artery bypass grafting, CAD: Coronary artery disease, CAQ: Cardiac Anxiety Questionnaire, CHD: Coronary heart disease, CR: cardiac rehabilitation, CK max: maximum amount of creatin kinase, CVD: Cardiovascular disease, ECG: Electrocardiogram, EF: Ejection fraction, eGFR: estimated Glomerular Filtration Rate in ml/min per 1.73m², EQ-5D: European Quality of Life Five Dimension, HCS: Health Complaints Scale, HFA: Heart focused anxiety, hr: hour, HRQoL: Health-related quality of life, ICD: implantable cardioverter defibrillator, ICU: Intensive Care Unit, IPAQ: International Physical Activity Questionnaire, KCCQ: Kansas City Cardiomyopathy Questionnaire, LVEF: left ventricular ejection fraction, NHP: Nottingham Health Profile, NSTEMI: Non-ST-elevation myocardial infarction, NT-proBNP: N-Terminal pro-Brain Natriuretic Peptide in pg/ml, NYHA: New York Heart Association Functional Classification, MACE: major adverse cardiac event, MCS: Mental component score, MI: Myocardial infarction, MLHFQ: Minnesota living with Heart Failure Questionnaire, PCS: Physical component score, PGI: percutaneous coronary intervention, RAND SF-12: Research and Development 12-Item Short Form Health Survey, RAND SF-36: Research and Development 36-Item Short Form Survey, STEMI: ST-elevation myocardial infarction, TSK: Tampa Scale of Kinesiophobia, QoL: Quality of life, QoLMI-DLV: Quality of Life After Myocardial Infarction Dutch language version