

# Exercise type and settings, quality of life, and mental health in coronary artery disease: a network meta-analysis

Angel Toval <sup>1,†</sup>, Esmée A. Bakker <sup>1,2,\*†</sup>, Joao Bruno Granada-Maia<sup>1</sup>, Sergio Núñez de Arenas-Arroyo <sup>3</sup>, Patricio Solis-Urra <sup>1,4,5</sup>, Thijs M.H. Eijvogels <sup>6</sup>, Irene Esteban-Cornejo <sup>1,7,8</sup>, Vicente Martínez-Vizcaíno <sup>3,9</sup>, and Francisco B. Ortega <sup>1,7,10,\*</sup>

<sup>1</sup>Department of Physical Education and Sports, Faculty of Sport Sciences, Sport and Health University Research Institute (iMUDS), University of Granada, Carretera de Alfacar, S/N 18071, Granada, Spain; <sup>2</sup>Department of Primary and Community Care, Radboud university medical center, P.O.Box 9101, 6500 HB Nijmegen, The Netherlands; <sup>3</sup>Health and Social Research Center, Universidad de Castilla-La Mancha, Cuenca, Spain; <sup>4</sup>AdventHealth Research Institute, Neuroscience Institute, Orlando, FL, USA; <sup>5</sup>Faculty of Education and Social Sciences, Universidad Andres Bello, Viña del Mar 2531015, Chile; <sup>6</sup>Department of Medical BioSciences, Exercise Physiology Research Group, Radboud university medical center, Nijmegen, The Netherlands; <sup>7</sup>CIBER de Fisiopatología de la Obesidad y Nutrición (CIBEROBN), Instituto de Salud Carlos III, Av. de Monforte de Lemos, 5, 28029 Madrid, Spain; <sup>8</sup>Instituto de Investigación Biosanitaria ibs, Granada, Spain; <sup>9</sup>Universidad Autónoma de Chile, Facultad de Ciencias de la Salud, Talca, Chile; and <sup>10</sup>Faculty of Sport and Health Sciences, University of Jyväskylä, PO Box 35, FI-40014 University of Jyväskylä, Jyväskylä, Finland

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## Abstract

### Background and Aims

Individuals with coronary artery disease have poorer mental health, health-related quality of life (HR-QoL), and cognition compared with (age-matched) controls. Exercise training may attenuate these effects. The aim is to systematically review and meta-analyse the effects of different exercise types and settings on brain structure/function, cognition, HR-QoL, mental health (e.g. depression, anxiety), and sleep in patients with coronary artery disease.

### Methods

A systematic search was conducted and a network meta-analysis compared (i) exercise types, high-intensity interval training (HIIT), HIIT + resistance (HIIT + R), moderate-intensity training (MIT), MIT + R and stretching-toning-balance training, and (ii) exercise settings, in-person and home-based.

### Results

A total of 42 randomized controlled trials with a parallel group design were identified, of which 36 were included in the meta-analysis. Few studies included cognition ( $n = 2$ ), sleep ( $n = 2$ ), and none brain structure/function ( $n = 0$ ). Most studies examined HR-QoL ( $n = 30$ ), depression ( $n = 15$ ), and anxiety ( $n = 9$ ), in which outcomes were meta-analysed. HIIT + R, HIIT, and MIT were associated with improved HR-QoL vs. no exercise (i.e. usual care) [standardized mean difference, SMD: 1.53 (95% confidence interval 0.83; 2.24), 0.44 (0.15; 0.73), and 0.44 (0.20; 0.67), respectively]. In-person exercise was associated with larger and significant improvements [HR-QoL SMD: 0.51 (0.28; 0.74), depressive SMD: -0.55 (-1.03; -0.07), and anxiety symptoms SMD: -1.16 (-2.05; -0.26)] compared with no exercise, whereas home-based programmes were not significantly associated with improvements in these outcomes. Findings were robust in secondary (i.e. intervention duration and volume) and sensitivity analyses excluding high risk of bias studies.

### Conclusions

Exercise training, especially in-person sessions, was associated with improved HR-QoL, depression and anxiety, independently of exercise type. However, this study raises concern about the effectiveness of home-based programmes in improving these outcomes.

Study protocol was registered in PROSPERO (ID: CRD42023402569).

\* Corresponding author. Tel: +34 958246651, Email: [ortegaf@ugr.es](mailto:ortegaf@ugr.es) (F.B.O.); Email: [Esmee.Bakker@radboudumc.nl](mailto:Esmee.Bakker@radboudumc.nl) (E.A.B.)

† Shared first authorship.

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## Structured Graphical Abstract

### Key Question

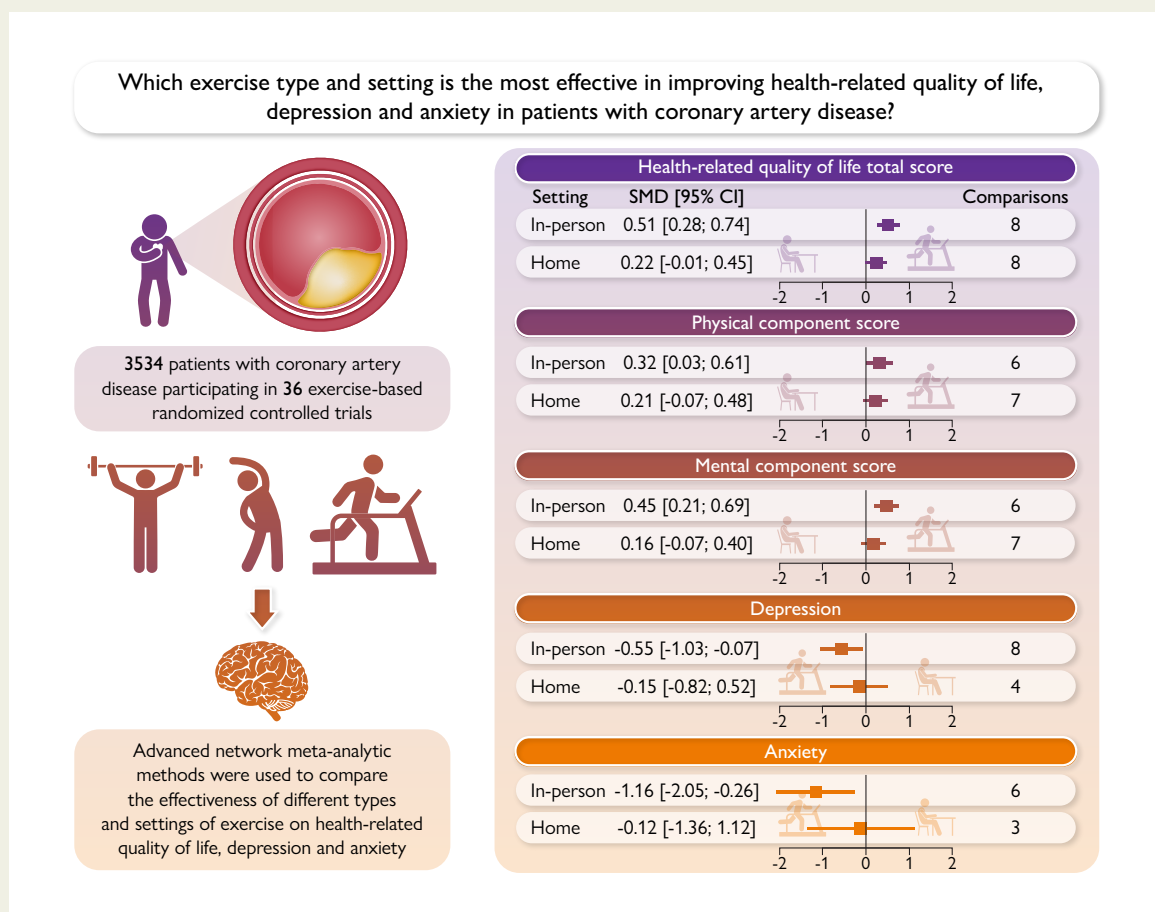
Which exercise type and setting is most effective in improving brain-related outcomes in patients with coronary artery disease (CAD)?

### Key Finding

- In this network meta-analysis, most studied outcomes were health-related quality of life (HR-QoL), depression, and anxiety, while brain structure/function, cognition, and sleep were investigated in very few studies.
- No differences were observed between types of exercise.
- In-person exercise, but not home-based, was associated with improved HR-QoL, depression, and anxiety.

### Take Home Message

Prescribing exercise, especially through in-person programs, is associated with improvements in HR-QoL, less depressive symptoms and reduced anxiety in patients with CAD, while previously used home-based exercise interventions need to be optimized to obtain brain-related benefits.



Summary of methods and key findings from the meta-analysis. The right-hand graphs display results from top to bottom for health-related quality of life: total score, physical component, and mental component, followed by depression and anxiety estimates across different exercise training settings compared with no exercise, based on network meta-analysis. The comparisons are the number of studies included in the analysis. For quality of life, positive differences indicate an improvement, whereas for depression and anxiety, negative differences indicate a reduction in symptoms. CI, confidence interval; SMD, standardized mean difference.

### Keywords

Exercise • Mental health • Cognition • Brain • Cardiovascular disease • Ischaemic disease • Coronary heart disease

## Introduction

Coronary artery disease (CAD) is the most prevalent type of cardiovascular disease (CVD) and one of the leading causes of mortality,

and economic burden worldwide.<sup>1-4</sup> Recently, several studies have revealed that the incidence of cognitive impairment in patients with CAD is markedly higher compared with age-matched healthy controls.<sup>5-9</sup> Likewise, the prevalence of depression and anxiety in cardiac

patients is four times higher (15%–20%) than in the general population (5%), resulting not only in an increased morbidity and mortality but also in a decreased health-related quality of life (HR-QoL).<sup>10–14</sup>

Brain health is a broad concept referring to the optimal functioning of behavioural and biological brain measures and the subjective experiences arising from brain function. This means that brain health includes outcomes related to neurobiological markers (e.g. structural brain morphology, brain function) and its behavioural manifestations, such as cognitive function, HR-QoL, mental health disorders (e.g. depression, anxiety), and sleep.<sup>15,16</sup> Thus, it is necessary to identify effective and sustainable initiatives, which can attenuate the accelerated brain health deterioration in the CAD patient population.<sup>5–14</sup>

Mounting evidence supports that exercise training has important systemic and multi-organ health benefits in patients with CAD<sup>15,17–23</sup> and is recommended in clinical guidelines of the American Heart Association<sup>24</sup> and the European Society of Cardiology.<sup>25</sup> Importantly, literature showed that exercise might also mitigate cognitive and mental health impairments observed in this population. However, the effect of different types and settings of exercise on distinct domains of brain health remains unclear. The ambiguity is partly due to the diversity (e.g. type, duration) and settings (e.g. in-person, home-based) of exercise interventions, heterogeneity in the instruments to assess different brain-related outcomes, and the predominant use of multi-component interventions.<sup>19,26–28</sup> Advances in meta-analytic methods, such as network meta-analysis techniques, allow for better synthesis of existing evidence, including direct and indirect comparisons among different types and settings of exercise.

Therefore, the present systematic review and meta-analysis examines the impact of different exercise types and settings on a broad set of brain-related outcomes. More specifically, the study aims to (i) systematically identify and synthesize current literature examining the effects of physical exercise on brain-related outcomes in individuals with CAD and (ii) quantify and compare the effect of different types and settings of exercise on the most studied outcomes in CAD patients using a network meta-analysis.

## Methods

### Protocol and registration

This systematic review and network meta-analysis has been designed and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020 statement),<sup>29</sup> the extended PRISMA statement for Network Meta-Analyses,<sup>30</sup> the Cochrane Handbook for Systematic Reviews of Interventions,<sup>31</sup> and the National Institute for Health and Care Excellence (2021) guidelines.<sup>32</sup> The protocol was previously registered in the international database of systematic reviews PROSPERO (ID: CRD42023402569, in March 2023).

### Search strategy and information sources

Selection of eligible studies and search strategy was structured following the PICOS (Population/Patient, Intervention, Comparison/Control, Outcome and Study design) framework strategy.<sup>31</sup> Detailed description of the search strategy can be found in [Supplementary data online, File S1](#). The systematic search has been conducted in different electronic databases, from inception to 12 June 2023, including Web of Science, MEDLINE (via PubMed), Scopus, EMBASE, Central Register of Controlled Trials, SPORTDiscus, and PsycINFO. In addition, we also included the Google Scholar search engine. Due to the limitation of characters allowed in Google Scholar, the search strategy was adapted, and the first 200 results sorted by relevance were extracted as previously recommended.<sup>33</sup> The search strategy was developed among several researchers (A.T., E.A.B., J.B.G.-M., F.B.O., P.S.-U., and

I.E.-C.) and optimized for different search engines using the Polyglot Search Translator tool from SR-Accelerator website (<https://sr-accelerator.com/>).<sup>34</sup>

### Eligibility criteria

Studies were included if they (i) assessed effects of physical activity or exercise programmes on brain structure/function, cognition, HR-QoL, mental health, and sleep in patients with CAD aged 18 years or older, (ii) were intervention studies involving any type of physical exercise, and (iii) included at least two conditions/intervention groups (i.e. exercise vs. control or exercise vs. exercise), since we were interested in comparisons. Studies were excluded when (i) they had a quasi-experimental design without comparison group/condition, (ii) they were animal studies, (iii) they included patients with other CVDs, unless the study population contained >85% of patients with CAD, (iv) they consisted of grey literature (e.g. letters to the editor, congress abstracts, unpublished studies), (v) they were not published in English, Spanish, Dutch, or Portuguese, and (vi) study arms were excluded when they combined exercise with other therapies (e.g. pharmacologic treatment, diet, psychological, or educational therapy) unless the intervention groups only differed on the exercise component.

### Study selection process

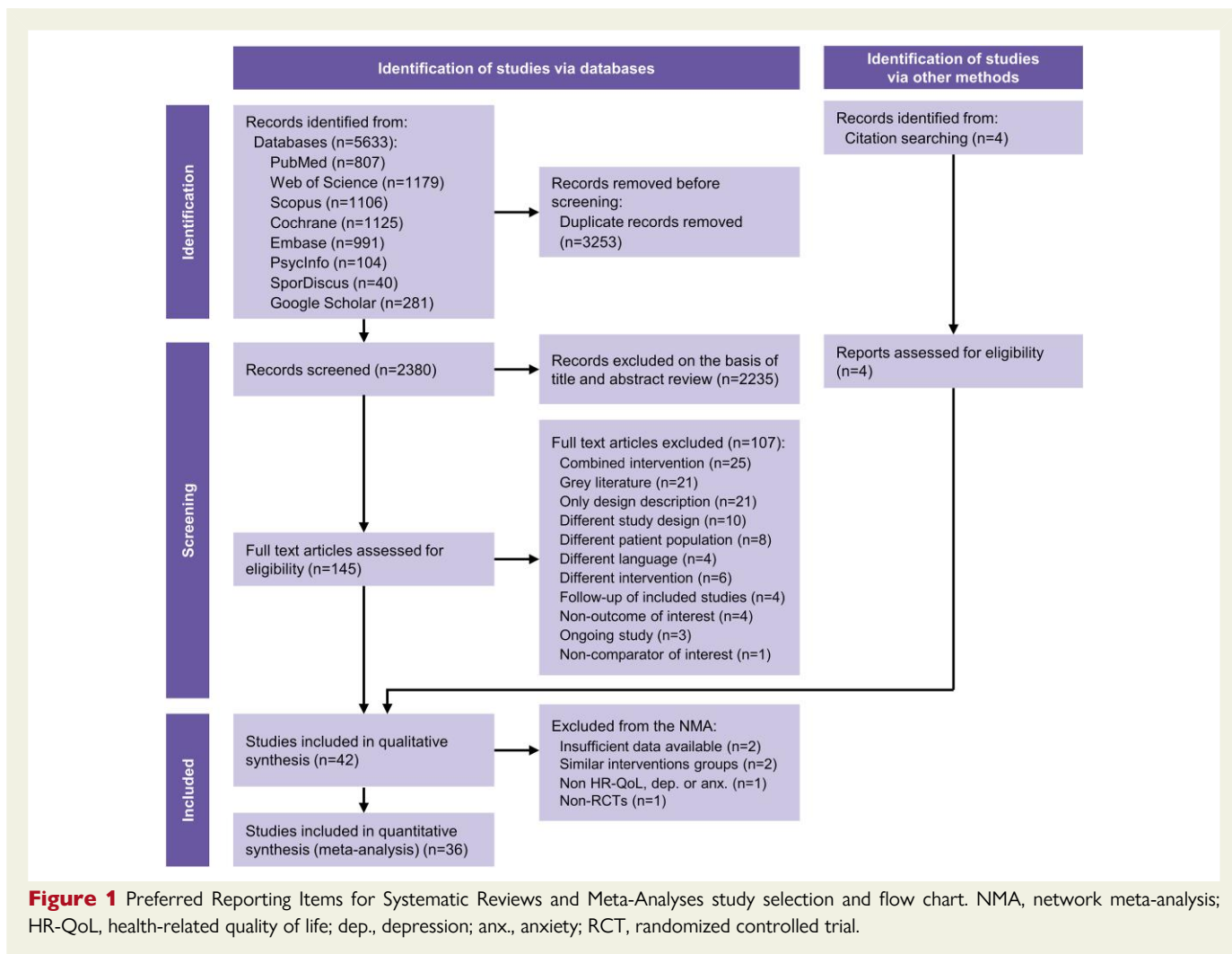
The study identification, screening, and inclusion of eligible studies were carried out by three reviewers (A.T., E.A.B., and J.B.G.-M.) independently and followed the PRISMA flow chart ([Figure 1](#)). After a comprehensive search of multiple databases, duplicate publications were removed. Next, the titles and abstracts were screened, and then the full texts were screened against inclusion/exclusion criteria. When necessary, an additional reviewer (F.B.O.) resolved discrepancies between reviewers prior to reaching a consensus. Covidence software was used to manage records throughout the study selection/screening process.<sup>35</sup> For the quantitative synthesis (network meta-analysis), we only included the studies assessing HR-QoL, depression, and/or anxiety due to the low number of studies assessing other brain-related outcomes.

### Data extraction and processing

Data from included records were extracted by two researchers independently (A.T. and E.A.B.) using a standardized, pre-specified, and piloted form. Based on the PICOS strategy, we extracted information on the population and study characteristics, intervention, comparison, and outcomes. More details are provided in [Supplementary data online, File S2](#) (extended methods).

### Categories of different types of exercise

Many studies have shown the differential physiological adaptations derived from different types of exercise, such as aerobic training, resistance training, and the combination of aerobic and resistance training.<sup>36,37</sup> Furthermore, studies suggested differential effects on physiological outcomes as response to high-intensity interval training (HIIT) and moderate-intensity training (MIT)<sup>38,39</sup> justifying that HIIT and MIT could be considered as two different types of exercise.<sup>40</sup> We categorized the studies into five exercise types based on available literature and the designs of the network plots: HIIT, MIT, HIIT with resistance training (HIIT + R), MIT with resistance training (MIT + R), and stretching-toning-balance training (STBT; [Table 1](#)). The following information on the exercise interventions was extracted from each study: exercise type, setting (i.e. in-person or home-based), duration of the intervention, frequency (sessions/week), duration of the sessions, and exercise intensity (i.e. moderate or high). Due to the large heterogeneity of reporting exercise intensity (e.g. % of maximum heart rate, % of maximum oxygen uptake, rate of perceived exertion) and the number of repetitions during resistance exercise, we decided not to extract or analyse this information.



## Data processing

Change-from-baseline values (to post-intervention) were used as main outcome. We calculated missing standard deviations (SDs) based on the standard error, 95% confidence intervals (CIs), or inter-quartile range.<sup>31</sup> As most studies did not report change-from-baseline values, we estimated the change-from-baseline with corresponding SDs using the pre- and post-intervention values with an imputed correlation of 0.66.<sup>31</sup> This imputed correlation was based on the weighted average correlation from some of the included studies reporting change-from-baseline values for the study outcomes ( $n = 7$ ). For the sensitivity analyses, we used a more conservative correlation of 0.50.<sup>32</sup> When the change-from-baseline and the pre- and post-intervention values were not reported, we contacted the study authors to request this information ( $n = 4$ ).<sup>41–44</sup> For studies including only a visual presentation ( $n = 1$ ),<sup>45</sup> we used a graphical software programme (WebPlotDigitizer, version 4.6, <https://automeris.io/WebPlotDigitizer>)<sup>46,47</sup> and averaged the results of both reviewers (A.T. and E.A.B.). More detailed information about the data processing and calculating the overall and mental component score (MCS) and physical component score (PCS) of HR-QoL are described in the extended methods (see [Supplementary data online, File S2](#)).

## Risk of bias

Risk of bias was assessed for randomized controlled trials (RCTs) using the Cochrane risk-of-bias tool (RoB 2) for randomized trials.<sup>48</sup> Two reviewers

(A.T. and E.A.B.) individually assessed the risk of bias, and disagreements were solved between the two reviewers or by consulting the third reviewer (F.B.O.) if necessary. To evaluate the certainty of the evidence, we used the Confidence in Network Meta-Analysis.<sup>49,50</sup>

## Statistical analyses

Our network meta-analysis compared the effect of different (i) exercise types, i.e. HIIT, HIIT + R, MIT, MIT + R, and STBT, and (ii) exercise settings i.e. in-person and home-based, on the most studied outcomes (i.e. HR-QoL, depression, and anxiety). Of the 37 studies focused on these outcomes, all but one were RCTs. Therefore, we excluded the single non-RCT<sup>51</sup> from the analyses to obtain more robust and homogeneous estimates based only on the best study design, i.e. RCTs. We created network geometry graphs to examine the shape of the network of HR-QoL, PCS, MCS, depression, and anxiety. We excluded outcomes from the network meta-analysis when a star-shaped network occurred (i.e. one intervention is compared with all others but direct comparisons between these others are absent). Next, we conducted a random-effects network meta-analysis of which specific details are provided in the extended methods (see [Supplementary data online, File S2](#)). The results were presented using league tables and forest plots of the network estimates using no exercise as reference category. The main network meta-analysis assumptions (i.e. transitivity and consistency) were checked (see [Supplementary data online, File S2](#)). We assessed statistical heterogeneity in each pairwise and network meta-analysis comparison using  $t^2$  and  $I^2$  statistics. The  $I^2$  statistic was

**Table 1** Characteristics of the exercise types included in the network meta-analysis

|          |   |
|----------|---|
| MIT      | Aerobic moderate continuous training refers to exercise interventions that increase heart rate and energy expenditure with a constant but moderate intensity. It includes activities such as walking, jogging and cycling, outdoor or indoor                        |
| HIIT     | Aerobic high-intensity interval training refers to exercise interventions that consist of short and repeated bouts performed at high intensity (i.e. close to maximal intensities), interspersed by periods of lower intensity exercise or rest for recovery        |
| MIT + R  | Aerobic moderate continuous training combined with resistance training. Resistance exercise refers to exercise interventions that aim to increase muscular strength and power, including exercises performed with dumbbells, Thera-bands, or pneumatic machines     |
| HIIT + R | Aerobic high-intensity interval training combined with resistance training. Resistance exercise refers to exercise interventions that aim to increase muscular strength and power, including exercises performed with dumbbells, Thera-bands, or pneumatic machines |
| STBT     | Stretching-toning-balance training. Refers to physical exercises that include Tai-Chi, yoga, qigong, among others, excluding interventions focused on or combined with mind exercises   |

interpreted as not important (0%–30%), moderate (30%–50%), substantial (50%–75%), or considerable (75%–100%), and the corresponding *P*-values were also considered. Ranking probabilities for different exercise interventions were estimated using *P*-scores. *P*-scores were measured on a scale from 0 (worst) to 1 (best). Finally, we created funnel plots to explore potential presence of publication bias. We did not perform statistical testing for publication bias, because there were <10 studies available per direct comparison.<sup>52</sup>

Based on the results of the main analysis (i.e. no clear differences between exercise intensity such as HIIT vs. MIT), we examined the effect of in-person vs. home-based exercise vs. no exercise by creating a new network. Since the difference between HIIT and MIT was absent but the difference between exercise settings (i.e. in-person vs. home-based) was clearly present, we decide to create the following groups for the additional analyses on duration and total volume: in-person exercise >12 weeks, in-person exercise ≤12 weeks, home-based exercise >12 weeks, and home-based exercise ≤12 weeks and in-person exercise >24 h (total volume is hours trained during the intervention), in-person exercise ≤24 h, home-based exercise >24 h, and home-based exercise ≤24 h. Study characteristics of [Table 2](#) were used to create cut-off values for duration (i.e. 12 weeks) and total volume (i.e. 24 h). Sensitivity analyses were performed using a conservative correlation (0.5) and excluding studies with a high risk of bias. The analyses were performed with R (version 4.2.3) using the packages ‘netleague’ and ‘netmeta’. Statistical significance (two sided) was set at *P* < .05.

## Results

### Synthesis of studies found in the systematic search

Our systematic search identified 2380 studies, of which 145 underwent full-text review. Additionally, four studies were identified from manual

citation searching. A total of 42 studies<sup>28,41–45,51,53–87</sup> were included in the qualitative synthesis and 36 studies<sup>28,42,43,45,53–76,78–84</sup> were included in the quantitative synthesis (meta-analysis) as summarized in [Figure 1](#). From the 42 studies included in the qualitative synthesis, the most assessed outcome was HR-QoL (36 studies, 86%; *n* = 3476 subjects), followed by depression (17 studies, 40%; *n* = 2032) and anxiety (9 studies, 21%; *n* = 946). Two studies evaluated cognitive function, two studies examined sleep, and none of the studies evaluated neurobiological markers, such as structure and function using neuroimaging techniques or any other methods.

### Characteristics of studies included in the network meta-analysis

The 36 studies included in the meta-analysis were RCTs with parallel group design using the outcomes HR-QoL (*n* = 30), depression (*n* = 15), and anxiety (*n* = 9). Overall, 3534 participants with CAD were randomly assigned to exercise (*n* = 2707) or no exercise (*n* = 827). In all studies, the ‘no exercise’-intervention arm consisted of usual care. The mean age was 62 (SD 9.3) years, and the mean percentage of women was 23%. Most interventions were performed when patients were eligible for cardiac rehabilitation (CR) or within 2–6 months after the cardiovascular event (23 studies, 64% of the total included). The most common exercise was MIT (26 studies, 72%, *n* = 1479), followed by HIIT (15 studies, 42%, *n* = 621), MIT + R (7 studies, 19%, *n* = 473), STBT (2 studies, 6%, *n* = 89), and HIIT + R (1 study, 3%, *n* = 45). In-person exercise was performed in 28 studies (78%, *n* = 2065), while home-based interventions were performed in 14 studies (39%, *n* = 642; [Table 2](#)).

We found no clear evidence of violations of the transitivity assumption in the studies characteristics ([Table 2](#)) suggesting that the included participants had similar characteristics (i.e. effect modifiers) across comparisons. In terms of risk of bias, most studies were rated with some concerns (18 studies; 50% of the included studies), followed by a low risk (10 studies, 28%) and a high risk (8 studies, 22%, see [Supplementary data online, Figures S1 and S2](#)).

### Structure of network

[Figure 2](#) shows the networks of eligible comparisons for HR-QoL, depression, and anxiety of the main analyses regarding exercise types. The network graphs of HR-QoL were well connected, but for depression and anxiety, we found a star network that prevented us from running analyses including indirect comparisons. [Supplementary data online, Figure S3](#) presents the networks for the analyses regarding exercise setting (i.e. in-person vs. home-based vs. no exercise), in which all networks were well connected. For the secondary analyses focused on intervention duration and total exercise volume, the network plots were well connected for all HR-QoL outcomes, but not for the depression and anxiety (i.e. star shaped).

### Different types of exercise and health-related quality of life

Based on the network meta-analysis, in-person HIIT + R was associated with the largest, statistically significant improvement for the total score of HR-QoL [standardized mean difference (SMD) 1.53, 95% CI 0.83; 2.24, [Figure 3](#) and [Table 3](#)] compared with no exercise, followed by in-person HIIT (SMD 0.44, 95% CI 0.15; 0.73) and in-person MIT (SMD 0.44, 95% CI 0.20; 0.67). However, in-person HIIT + R was

**Table 2** Characteristics of the studies included in the network meta-analysis

| Study                             | Sample size (% women) | Age, years | Intervention type  | Duration of exercise interventions | Time after event <sup>a</sup> | HR-QoL  | Instruments   |
|-----------------------------------|-----------------------|------------|--|------------------------------------|-------------------------------|---|---|
| Avila et al. <sup>53</sup>        | 84 (11%)              | 61 ± 8     | (i) Home MIT, (ii) in-person MIT + R, (iii) nEX                              | 12 weeks                           | 3                             | 36-Item Short Form Survey (SF-36)   | Depression<br>Anxiety   |
| Belardinelli et al. <sup>54</sup> | 118 (16%)             | 57 ± 10    | (i) In-person MIT, (ii) nEX  | 26 weeks                           | 4                             | Duke Activity Status Index (DASI), Medical Outcomes Study (MOS)   | Depression  |
| Blumenthal et al. <sup>55</sup>   | 134 (31%)             | 63 ± 10    | (i) In-person MIT, (ii) SM <sup>b</sup> , (iii) nEX                          | 16 weeks                           | 2, 3                          |   | Beck's Depression Inventory II (BDI-II)<br>The State-Trait Anxiety Inventory (STAI-State) |
| Blumenthal, et al. <sup>56</sup>  | 101 (32%)             | 64 ± NR    | (i) In-person MIT, (ii) MED <sup>b</sup> , (iii) nEX                         | 16 weeks                           | 4                             |   | Hamilton Depression Rating Scale (HAM-D)  |
| Blumenthal et al. <sup>57</sup>   | 128 (29%)             | 65 ± 10    | (i) In-person MIT, (ii) MED <sup>b</sup> , (iii) nEX                         | 12 weeks                           | 4                             |   | BDI-II, Hospital Anxiety and Depression Scale (HADS-D)                                    |
| Brouwers et al. <sup>42</sup>     | 300 (11%)             | 61 ± 10    | (i) Home MIT + R, (ii) in-person MIT + R                                     | 13 weeks                           | 2                             | European Quality of Life 5 Dimensions 5 Level Version (EQ-5D-5L), European Quality of Life Visual Analogue Scale (EQ-VAS) | HADS-A, STAI-State  |
| Conrads et al. <sup>58</sup>      | 174 (20%)             | 58 ± 9     | (i) In-person HIIT, (ii) in-person MIT                                       | 12 weeks                           | 2                             | 12-Item Short Form Survey (SF-12)   | Depression  |
| Currie et al. <sup>59</sup>       | 19 (7%)               | 65 ± 8     | (i) In-person MIT, (ii) in-person HIIT                                       | 12 weeks                           | 2                             | SF-36   | Depression  |
| Deka et al. <sup>60</sup>         | 90 (24%)              | 69 ± 5     | (i) In-person HIIT + R, (ii) nEX   | 8 weeks                            | 4                             | SF-36   | Depression  |
| Deng et al. <sup>61</sup>         | 70 (14%)              | 81 ± 4     | (i) In-person MIT, (ii) nEX  | 12 weeks                           | 1                             | SF-12   | Zung Self-Rating Depression Scale (SDS)<br>Self-Rating Anxiety Scale (SAS)                |
| Dor-Haim et al. <sup>62</sup>     | 29 (0%)               | R 47–69    | (i) In-person MIT, (ii) in-person MIT + R                                    | 12 weeks                           | 2                             | SF-12   | Depression  |
| Fang et al. <sup>63</sup>         | 67 (37%)              | 61 ± 10    | (i) Home MIT, (ii) nEX   | 6 weeks                            | 2                             | SF-36   | Cardiac Depression Scale (CDS)<br>Patient Health Questionnaire (PHQ-9)                    |
| Ghisi et al. <sup>64</sup>        | 115 (29%)             | 60 ± 9     | (i) In-person MIT + R + Edu <sup>b</sup> , (ii) in-person MIT + R, (iii) nEX | 26 weeks                           | 2                             |   | Depression  |
| Giggins et al. <sup>65</sup>      | 17 (18%)              | 70 ± 8     | (i) Home MIT + R, (ii) in-person MIT + R                                     | 8 weeks                            | 2                             | SF-12   | Depression  |

Continued

**Table 2 Continued**

| Study                                   | Sample size (% women) | Age, years                            | Intervention type  | Duration of exercise interventions | Time after event <sup>a</sup> | Instruments   |   |            |
|---|-----------------------|---------------------------------------|--|------------------------------------|-------------------------------|---|---|------------|
|   |                       |                                       |  |                                    |                               | HR-QoL  | Depression  | Anxiety    |
| Jauguizar et al. <sup>66</sup>          | 72 (15%)              | 58 ± 11                               | (i) In-person HIIT, (ii) in-person MIT                       | 8 weeks                            | 2                             | SF-36, MacNew Heart Disease health-related quality of life (MacNew) |   |            |
| Jiang et al. <sup>67</sup>              | 120 (60%)             | 62 ± 10                               | (i) In-person STBT, (ii) nEX                                 | 13 weeks                           | 1                             | SF-36   | HAM-D, SDS  | HAM-A, SAS |
| Johnson et al. <sup>68</sup>            | 154 (100%)            | (i) 64 (IQR 14)<br>(ii) 62 (IQR 12)   | (i) Home MIT, (ii) nEX                                       | 12 weeks                           | 3                             | MacNew  |   |            |
| Kristiansen et al. <sup>69</sup>        | 142 (17%)             | 67 ± 9                                | (i) In-person HIIT, (ii) nEX                                 | 12 weeks                           | 3                             | SF-36   |   |            |
| Lee et al. <sup>70</sup>                | 31 (100%)             | 68 ± 9                                | (i) Home HIIT, (ii) home MIT                                 | 24 weeks                           | 2                             |   | Center for Epidemiologic Studies Depression Scale (CES-D) |            |
| Maddison et al. <sup>43</sup>           | 171 (19%)             | 60 ± 9                                | (i) Home MIT, (ii) nEX                                       | 24 weeks                           | 2, 3                          | SF-36, EQ-5D-5L   |   |            |
| Maddison et al. <sup>71</sup>           | 140 (14%)             | 61 ± 13                               | (i) Home MIT, (ii) in-person MIT                             | 12 weeks                           | 2                             | EQ-5D   |   |            |
| Madsen et al. <sup>72</sup>             | 49 (27%)              | (i) 64 (R 47–78)<br>(ii) 59 (R 42–71) | (i) Home HIIT, (ii) nEX                                      | 52 weeks                           | 3                             | MacNew  |   |            |
| McGregor et al. <sup>73</sup>           | 382 (7%)              | 59 ± 10                               | (i) In-person HIIT, (ii) in-person MIT                       | 8 weeks                            | 2                             | EQ-5D-5L, EQ-VAS  |   |            |
| Moholdt et al. <sup>74</sup>            | 26 (20%)              | 63 ± 8                                | (i) In-person MIT + R, (ii) home HIIT                        | (i) 4 weeks, (ii) 26 weeks         | 2                             | MacNew  |   |            |
| Okur et al. <sup>75</sup>               | 20 (10%)              | 61 ± 5                                | (i) In-person MIT, (ii) in-person HIIT, (iii) in-person HIIT | 5 weeks                            | 2                             | SF-36, MacNew   |   |            |
| Reed et al. <sup>76</sup>               | 130 (15%)             | 61 ± 7                                | (i) In-person HIIT, (ii) in-person MIT, (iii) in-person MIT  | 12 weeks                           | 2                             | SF-36, HeartHR-QoL  | BDHI  |            |
| Salmirago-Blotcher et al. <sup>77</sup> | 29 (27%)              | 68 ± 10                               | (i) In-person STBT, (ii) in-person STBT                      | (i) 12 weeks, (ii) 24 weeks        | 2                             | SF-8  |   |            |
| Schönfelder et al. <sup>78</sup>        | 60 (26%)              | 61 ± 12                               | (i) In-person MIT, (ii) in-person HIIT, (iii) in-person MIT  | 6 weeks                            | 2                             | MacNew  | HADS-D  | HADS-A     |
| Snoek et al. <sup>79</sup>              | 118 (18%)             | 60 ± 10                               | (i) Home MIT, (ii) nEX                                       | 26 weeks                           | 2                             | Dutch version of the Quality of Life after Myocardial Infarction    | HADS-D  | HADS-A     |
| Takroni et al. <sup>80</sup>            | 79 (19%)              | 55 ± 7                                | (i) In-person MIT, (ii) home MIT, (iii) nEX                  | 8 weeks                            | 3                             | SF-36   | HADS-D  | HADS-A     |
| Taylor et al. <sup>81</sup>             | 93 (16%)              | 65 ± 8                                | (i) In-person HIIT, (ii) in-person MIT                       | 52 weeks                           | 2                             | MacNew  |   |            |
| Terrada et al. <sup>82</sup>            | 130 (15%)             | 61 ± 7                                | (i) In-person HIIT, (ii) in-person MIT, (iii) in-person MIT  | 12 weeks                           | 2                             | SF-36, HeartHR-QoL  | BDHI  |            |

Continued

Table 2 Continued

| Study                           | Sample size<br>(% women) | Age, years | Intervention type                              | Duration of<br>exercise<br>interventions | Time<br>after<br>event <sup>a</sup> | HR-QoL | Depression  | Anxiety                |
|---------------------------------|--------------------------|------------|--|--|-------------------------------------|--------|---|------------------------|
| Vieira et al. <sup>83</sup>     | 33 (NR)                  | 58 ± 9     | (i) Home MIT + R, (ii) home MIT + R, (iii) nEX | 26 weeks                                 | 3                                   | MacNew | The Depression, Anxiety and Stress Scale - 21 Items (DASS-21) | DASS-21                |
| Villafaina et al. <sup>84</sup> | 21 (0%)                  | 56 ± 6     | (i) In-person HIIT, (ii) in-person MIT         | 12 weeks                                 | 3                                   | SF-12  |   |                        |
| Yakut et al. <sup>28</sup>      | 21 (14%)                 | 59 ± 5     | (i) Home HIIT, (ii) home MIT                   | 12 weeks                                 | 2,3                                 | MacNew |   |                        |
| Yu et al. <sup>45</sup>         | 204 (24%)                | 64 ± 11    | (i) In-person MIT, (ii) nEX                    | 8 weeks                                  | 2                                   | SF-36  | Symptoms Questionnaire  | Symptoms Questionnaire |

Data are presented as mean ± SD, mean [range (R)], or median (QR), as appropriate.

NR, not reported; RCT, randomized controlled trial; nEX, non-exercise; MIT, moderate-intensity training; HIIT, high-intensity interval training; STBT, stretching-toning-balance training; SM, stress management programme; MED, medication treatment; ses, sessions; HR-QoL, health-related quality of life; Dep, depression; Anx, anxiety.

<sup>a</sup>Time after event: (i) eligible for cardiac rehabilitation and within 1 month after event, (ii) eligible for cardiac rehabilitation or within 2–6 months after event, (iii) after cardiac rehabilitation or 6 months after the event, and (iv) not reported.

<sup>b</sup>Intervention arm was excluded from the network meta-analysis because it included a pharmacological or psychological treatment or additionally included education besides exercise.

solely based on one study, whereas in-person HIIT and MIT were based on multiple comparisons. No differences were found in HR-QoL changes between HIIT and MIT, either in-person (SMD 0.00, 95% CI -0.20; 0.21) or home-based (SMD -0.09, 95% CI -0.50; 0.32, Table 3).

In-person HIIT (SMD 0.41; 95% CI 0.05–0.77) and in-person MIT (SMD 0.36; 95% CI 0.05; 0.67) were significantly associated with improvements in the PCS compared with no exercise (Figure 3 and Table 3). In-person STBT (SMD 1.19; 95% CI 0.58; 1.79), in-person MIT (SMD 0.37; 95% CI 0.11; 0.64), and in-person HIIT (SMD 0.37; 95% CI 0.07; 0.67) were significantly associated with improvements in the MCS (Figure 3 and Table 3). In-person STBT was solely based on one comparison (that was rated as high risk of bias, see Supplementary data online, Figure S2), whereas in-person HIIT and MIT were based on multiple comparisons and are therefore more robust estimates. No differences were found between HIIT and MIT in the improvement of the PCS and MCS, either in-person and home-based (Table 3).

All pairwise comparisons for the different HR-QoL outcomes are shown in Supplementary data online, Figures S4–S6. We found no global inconsistency using the random-effects model for the overall score of HR-QoL, PCS, and MCS, but local inconsistency was presented for some comparisons (see Supplementary data online, Figures S7–S9). The funnel plots included both positive and negative mean differences (see Supplementary data online, Figure S10).

## Different types of exercise and depressive and anxiety symptoms

Only pairwise comparisons (i.e. conventional meta-analysis and not network meta-analysis) were performed for depression and anxiety due to star-shaped networks (see Supplementary data online, Figures S11 and S12). No statistically significant improvements for depression and anxiety were found for different types of exercise.

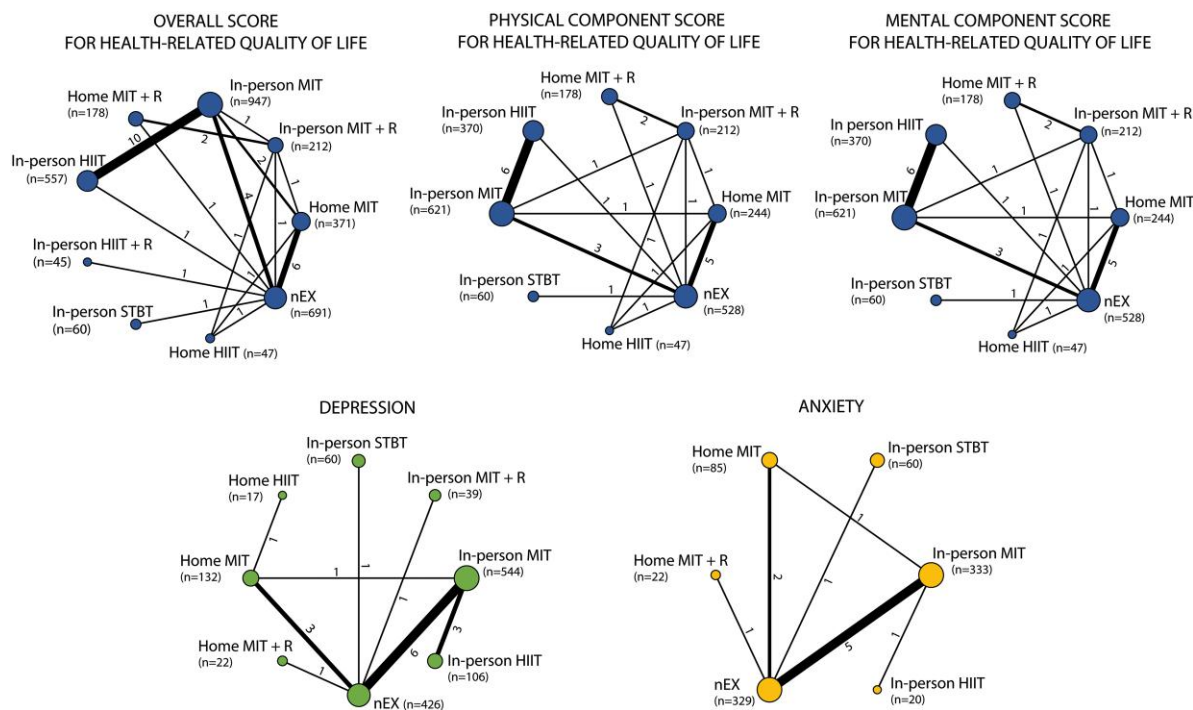
## In-person vs. home-based exercise

In-person exercise was associated with significant improvements of HR-QoL, depression, and anxiety compared with no exercise (Figure 4, Table 4, and Structured Graphical Abstract). A smaller and non-significant effect of home exercise on all outcomes was found. All pairwise comparisons are shown in Supplementary data online, Figures S13–S17. There was no evidence for global or local inconsistency (see Supplementary data online, Figures S18–S22).

## Additional analyses

Secondary analyses examining the effect of the intervention duration and total exercise volume of the intervention on HR-QoL showed similar effect estimates between longer vs. shorter intervention duration and between larger vs. smaller total training volumes, in which all were in favour of in-person exercise. Except for the PCS when comparing in-person exercise >12 weeks, in-person >24 h, and in-person ≤24 h with no exercise, no significant effects were found (see Supplementary data online, Tables S3 and S4). Sensitivity analyses using a conservative correlation (0.5) and excluding studies with a high risk of bias resulted in similar effect estimates compared with our main analyses (see Supplementary data online, Tables S1 and S2).





**Figure 2** Network of eligible comparisons for different brain-related outcomes. The width of the lines is proportional to the number of trials comparing each pair of treatments. The size of the nodes is proportional to the number of participants. The outcomes were assessed as follows: (i) overall score of health-related quality of life in  $n = 30$ , (ii) PCS of health-related quality of life in  $n = 25$ , (iii) MCS of health-related quality of life in  $n = 25$ , (iv) depression in  $n = 15$ , and (v) anxiety in  $n = 9$  studies. HIIT, high-intensity interval training; HIIT + R, high-intensity interval training plus resistance training; MIT, moderate-intensity training; MIT + R, moderate-intensity training plus resistance training; STBT, stretching-toning-balance training; nEX, no exercise

## Discussion

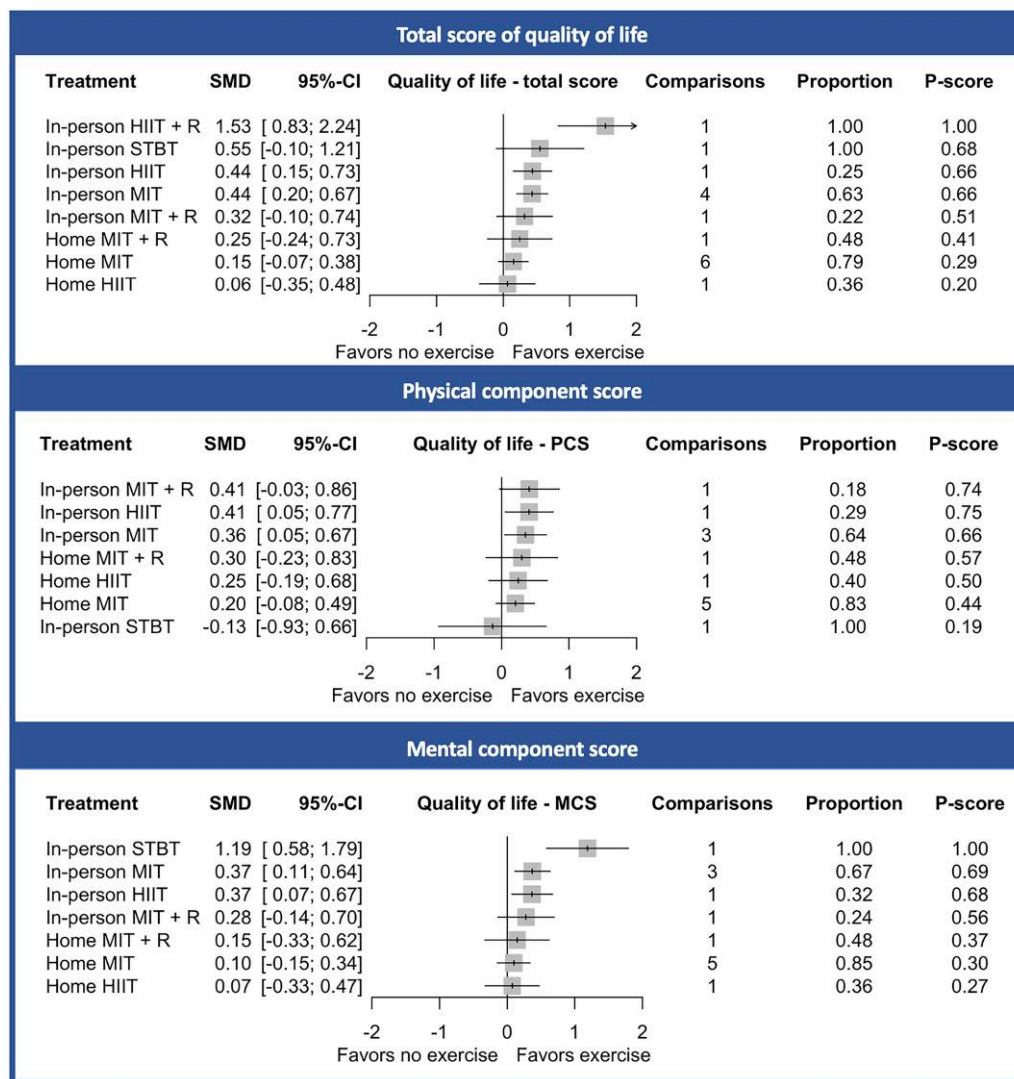
This systematic review and network meta-analysis showed that most research assessing the effects of exercise on brain-related outcomes in CAD patients focused on HR-QoL, depression and anxiety, while there was a lack of studies assessing other dimensions of brain-related outcomes, such as brain structure/function, cognition or sleep. The network meta-analysis revealed that in-person exercise training was associated with improved HR-QoL and reduced depressive and anxiety symptoms, while the same type of exercise delivered at home had markedly and consistently smaller effect estimates for improving these outcomes. Furthermore, HIIT seems to be equally effective as MIT in improving these outcomes. Likewise, the intervention duration or volume of exercise training did not impact the outcomes. Overall, these findings suggest that exercise training, especially in-person programmes, could improve the HR-QoL, attenuate depressive symptoms, and reduce anxiety in patients with CAD. These findings were robust and persisted in our secondary and sensitivity analyses (i.e. excluding studies with high risk of bias).

### Effects of exercise on HR-QoL

HR-QoL is reduced in patients with CAD, especially after diagnosing CAD.<sup>88,89</sup> The present meta-analysis indicates that in-person exercise training is associated with improved HR-QoL outcomes (i.e. overall, PCS, and MCS), independent of the type of exercise. This

beneficial impact of exercise on HR-QoL is consistent with previous meta-analyses including other diseased populations, such as patients with heart failure,<sup>90</sup> stroke,<sup>91</sup> cancer,<sup>92</sup> or Parkinson disease.<sup>93</sup>

We found that HIIT had a similar effect estimate as MIT for improving HR-QoL. This aligns with results of previous meta-analyses,<sup>94,95</sup> except for one previous study in which HIIT exhibited greater improvement in PCS compared with MIT.<sup>95</sup> Several types of exercise had only one comparison (e.g. HIIT + R and STBT), and no strong conclusions can be therefore drawn for these intervention types. Particularly interesting is the lack of studies evaluating the effects of resistance exercise alone, which might impact brain-related outcomes of CAD patients,<sup>96,97</sup> and therefore needs more research in the future. Recent studies are developing exercise programmes combining both aerobic and resistance training, which aligns with the recommendations of the World Health Organization.<sup>36</sup> Our network meta-analysis suggested that HIIT + R could be effective in improving HR-QoL and that MIT + R showed a tendency towards positive effects, although these were not statistically significant. One advantage of our network meta-analysis approach is the incorporation of indirect comparisons, enabling for the inclusion of more studies. However, these results should be interpreted with some caution as there is a large heterogeneity in the findings. This heterogeneity could be attributed to differences in the studies, such as characteristics of the exercise intervention (e.g. intensity continuum, diversity on the exercises included, such as different types of activities or equipment, outdoor or indoor) or CAD patient population (e.g. severity of disease, time after diagnosis, baseline mental status or medication use),



**Figure 3** Health-related quality of life estimates for total, physical, and mental component scores for different types of exercise compared with no exercise (usual care) using the network meta-analysis. The comparisons are the number of studies included in the analyses. The proportion represents the amount of direct evidence that was used to determine the effect estimates. P-scores were scaled from 0 (worst) to 1 (best). SMD, standardized mean difference; 95% CI, 95% confidence interval; HIIT, high-intensity interval training; HIIT + R, high-intensity interval training plus resistance training; MIT, moderate-intensity training; MIT + R, moderate-intensity training plus resistance training; STBT, stretching-toning-balance training; PCS, physical component score; MCS, mental component score

which have been pointed to exert distinct impacts on the HR-QoL of patients with CAD.<sup>88</sup> Our network meta-analysis is an important step in comparing different types of exercise, but future studies are needed to unravel the moderating effects of different factors (i.e. characteristics of exercise interventions and patient population) to move towards a more ‘personalized medicine’ approach to exercise prescription in CAD patients.

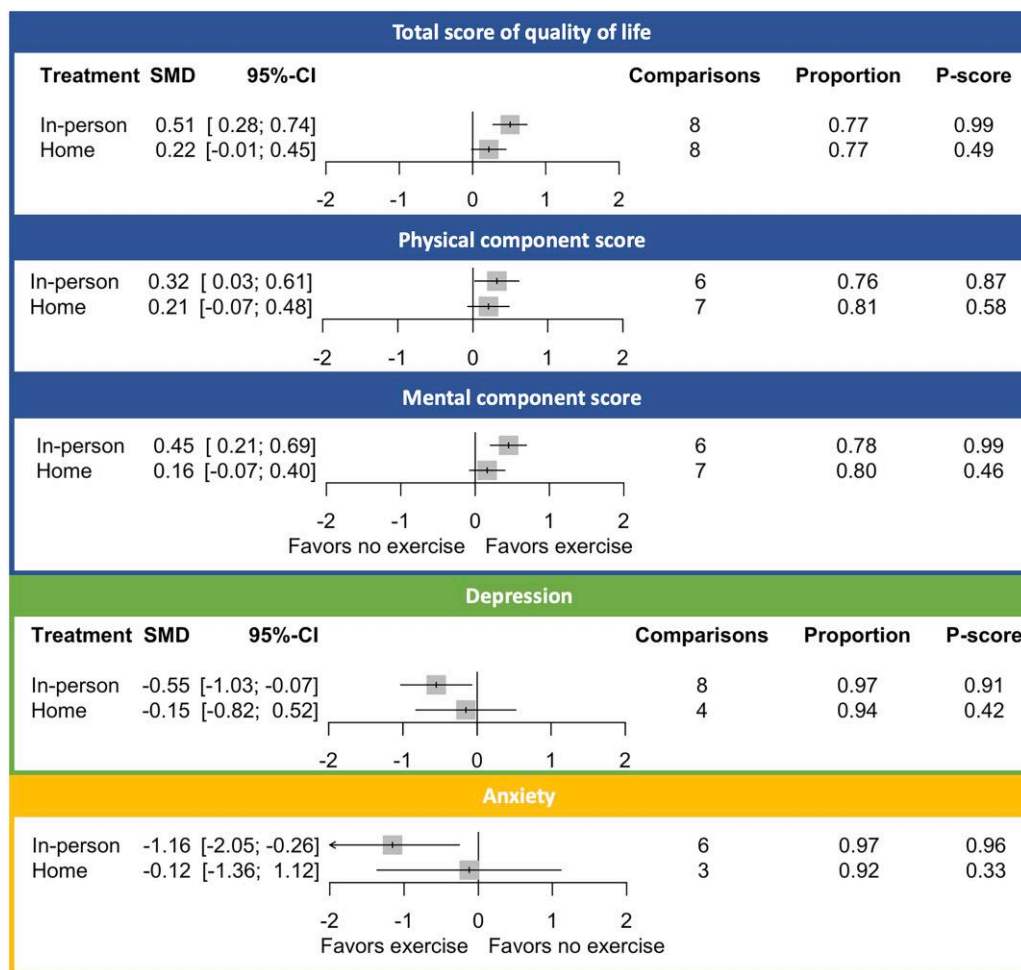
A major contribution of our study to the existing literature is the differential effect sizes of in-person vs. home-based exercise. These differences could be attributed to several factors, such as differences in adherence, better monitoring and live feedback-to-patients of face-to-face sessions, and/or social interaction. However, these factors are poorly and heterogeneously reported in the included studies. Interestingly, our results are contradictory to a previous systematic

review<sup>98</sup> in CVD patients. In this review, the authors concluded that both home- and centre-based CR provided similar improvements in HR-QoL. Potential explanations for the conflicting outcomes may relate to differences in the target population (all CVDs vs. only CAD in our study), interventions (CR vs. exercise in our study), number of included studies (17 vs. 30 in our study), and methodological approach (they did not run any meta-analysis *per se* on this outcome but used vote counting vs. network meta-analysis in our study). In addition, the authors decided that pooling data were too complex due to large variations in HR-QoL instruments. Nevertheless, we included standardized changes-from-baseline and ranked instruments to pool data and perform the network meta-analysis. Our network meta-analysis further allowed multiple comparisons using both direct and indirect effects, which resulted in a clear differential effect between exercise

**Table 3** League table with pooled standardized mean difference for different exercise types and health-related quality of life; total, physical, and mental component score

| Health-related quality of life—total score              |                             | 0.04 (−0.18; 0.25)  | 0.21 (−0.36; 0.78)       |
|---|-----------------------------|---------------------|--------------------------|
| <b>In-person HIIT</b>                                   |                             |                     |                          |
| <b>−1.09 (−1.86; −0.33)</b>                             | <b>In-person HIIT + R</b>   |                     | <b>1.53 (0.83; 2.24)</b> |
| 0.00 (−0.20; 0.21)                                      | <b>1.10 (0.35; 1.84)</b>    | 0.31 (−0.09; 0.71)  | <b>0.60 (0.31; 0.90)</b> |
| 0.12 (−0.35; 0.59)                                      | <b>1.21 (0.39; 2.03)</b>    | −0.09 (−0.88; 0.70) | −0.03 (−0.92; 0.85)      |
| −0.11 (−0.83; 0.61)                                     | <b>0.98 (0.01; 1.95)</b>    |                     | 0.55 (−0.10; 1.21)       |
| 0.38 (−0.11; 0.87)                                      | <b>1.47 (0.65; 2.29)</b>    | <b>Home HIIT</b>    | −0.18 (−0.88; 0.51)      |
| 0.29 (−0.04; 0.62)                                      | <b>1.38 (0.64; 2.12)</b>    | −0.09 (−0.50; 0.32) | 0.16 (−0.09; 0.41)       |
| 0.19 (−0.35; 0.74)                                      | <b>1.29 (0.43; 2.15)</b>    | −0.19 (−0.77; 0.40) | <b>Home MIT + R</b>      |
| <b>0.44 (0.15; 0.73)</b>                                | <b>1.53 (0.83; 2.24)</b>    | 0.06 (−0.35; 0.48)  | 0.22 (−0.49; 0.92)       |
|   |                             | 0.15 (−0.07; 0.38)  | <b>nEX</b>               |
|   |                             | 0.25 (−0.24; 0.73)  |                          |
| Health-related quality of life—physical component score |                             | 0.47 (−0.19; 1.13)  |                          |
| <b>In-person HIIT</b>                                   |                             |                     |                          |
| 0.06 (−0.18; 0.29)                                      | <b>In-person MIT</b>        | 0.34 (−0.31; 0.98)  | <b>0.43 (0.04; 0.82)</b> |
| 0.00 (−0.51; 0.51)                                      | −0.06 (−0.53; 0.42)         | 0.37 (−0.55; 1.30)  | −0.03 (−1.08; 1.01)      |
| 0.54 (−0.33; 1.42)                                      | 0.49 (−0.37; 1.35)          | 0.07 (−0.68; 0.82)  | −0.13 (−0.93; 0.66)      |
| 0.17 (−0.37; 0.70)                                      | 0.11 (−0.39; 0.61)          |                     | 0.00 (−0.69; 0.69)       |
| 0.21 (−0.22; 0.63)                                      | 0.15 (−0.23; 0.53)          | <b>Home HIIT</b>    | 0.28 (−0.03; 0.60)       |
| 0.11 (−0.50; 0.72)                                      | 0.05 (−0.52; 0.63)          | 0.18 (−0.45; 0.80)  | 0.14 (−0.63; 0.90)       |
| <b>0.41 (0.05; 0.77)</b>                                | <b>0.36 (0.05; 0.67)</b>    | −0.10 (−0.67; 0.47) | <b>Home MIT + R</b>      |
|   |                             | 0.20 (−0.08; 0.49)  | 0.30 (−0.23; 0.83)       |
|   |                             | 0.25 (−0.19; 0.68)  | <b>nEX</b>               |
| Health-related quality of life—mental component score   |                             | 0.00 (−0.54; 0.54)  |                          |
| <b>In-person HIIT</b>                                   |                             |                     |                          |
| −0.00 (−0.21; 0.20)                                     | <b>In-person MIT</b>        | 0.48 (−0.06; 1.02)  | <b>0.57 (0.25; 0.89)</b> |
| 0.09 (−0.39; 0.58)                                      | 0.10 (−0.36; 0.55)          | 0.34 (−0.48; 1.16)  | 0.17 (−0.69; 1.03)       |
| <b>−0.82 (−1.49; −0.14)</b>                             | <b>−0.81 (−1.47; −0.16)</b> | −0.16 (−0.92; 0.59) | <b>1.19 (0.58; 1.79)</b> |
| 0.29 (−0.19; 0.78)                                      | 0.30 (−0.16; 0.76)          |                     | −0.25 (−0.92; 0.42)      |
| 0.27 (−0.09; 0.64)                                      | 0.28 (−0.05; 0.60)          | <b>Home HIIT</b>    | 0.16 (−0.11; 0.43)       |
| 0.22 (−0.32; 0.77)                                      | 0.23 (−0.29; 0.75)          | 0.00 (−0.53; 0.53)  | 0.12 (−0.56; 0.81)       |
| <b>0.37 (0.07; 0.67)</b>                                | <b>0.37 (0.11; 0.64)</b>    | −0.02 (−0.41; 0.37) | <b>Home MIT + R</b>      |
|   |                             | −0.05 (−0.56; 0.46) | 0.15 (−0.33; 0.62)       |
|   |                             | 0.07 (−0.33; 0.47)  | <b>nEX</b>               |

Upper right triangle presents the pooled mean differences from direct comparisons and the lower left triangle pooled mean differences from the network meta-analysis. Columns are relative to the rows. Statistically significant differences are highlighted in bold values. Positive differences indicate an improvement in quality of life.  
 HIIT, high-intensity interval training; HIIT + R, high-intensity interval training plus resistance training; MIT, moderate-intensity training; MIT + R, moderate-intensity training plus resistance training; STBT, stretching-toning-balance training.



**Figure 4** Health-related quality of life estimates for total, physical, and mental component scores for different settings of exercise training compared with no exercise using the network meta-analysis. The comparisons are the number of studies included in the analysis. The proportion refers to the amount of direct evidence that was used to determine the effect estimates. *P*-scores were scaled from 0 (worst) to 1 (best). For quality of life, positive differences indicate an improvement, whereas for depression and anxiety, negative differences indicate a reduction in symptoms. SMD, standardized mean difference; 95% CI, 95% confidence interval

settings, i.e. two times larger effect in total HR-QoL and three times larger effect in MCS when comparing in-person vs. home-based.

## Effects of exercise on depressive and anxiety symptoms

In-person exercise interventions were associated with a positive effect on reducing depressive and anxiety symptoms among CAD patients, while home-based interventions did not yield significant improvements in both outcomes. Interestingly, the examination of various exercise types, yielded no statistically significant effects, and the same happened when classifying interventions based on their duration and total volume. Consistent with previous literature, our work holds the promise in ameliorating anxiety and depression symptoms in CAD patients with exercise.<sup>99–101</sup> Most previous studies addressing depressive and anxiety symptoms on CAD have focused on multi-component CR programmes, and therefore, interpreting and comparing these findings becomes challenging since not all changes can be solely attributed to exercise.<sup>98,100</sup> Furthermore, baseline levels of anxiety and depression may also impact the effects of exercise<sup>100</sup> in which exercise might

provide even bigger benefits in patients with more depressive and anxiety symptoms.

## Clinical implications

To enhance participation in CR programmes, home-based exercise interventions are becoming increasingly popular, and a previous systematic review had suggested that they can be equally effective as in-person exercise-based programmes.<sup>98</sup> However, in the present updated and comprehensive systematic review, using data harmonization and advanced network meta-analysis techniques, we observed a clear differential effect, suggesting that in-person programmes are markedly superior in improving HR-QoL, depression, and anxiety in CAD patients. These findings have important clinical implications. While home-based interventions may be a promising (and probably necessary) strategy to encourage participation in exercise programmes, the present network meta-analysis suggests that the current literature raises concerns regarding its effectiveness in improving HR-QoL, depression, and anxiety and therefore opens venues for discussion on

**Table 4** League table with pooled standardized mean difference for different settings of exercise training and health-related quality of life, depression, and anxiety

| Health-related quality of life—total score              |                     |                             |
|---|---------------------|-----------------------------|
| <b>In-person</b>  | 0.17 (–0.15; 0.49)  | <b>0.60 (0.33; 0.87)</b>    |
| <b>0.29 (0.04; 0.55)</b>                                | <b>Home</b>         | 0.13 (–0.14; 0.39)          |
| <b>0.51 (0.28; 0.74)</b>                                | 0.22 (–0.01; 0.45)  | <b>nEX</b>                  |
| Health-related quality of life—physical component score |                     |                             |
| <b>In-person</b>  | 0.16 (–0.22; 0.54)  | 0.32 (–0.01; 0.66)          |
| 0.11 (–0.20; 0.42)                                      | <b>Home</b>         | 0.22 (–0.08; 0.52)          |
| <b>0.32 (0.03; 0.61)</b>                                | 0.21 (–0.07; 0.48)  | <b>nEX</b>                  |
| Health-related quality of life—mental component score   |                     |                             |
| <b>In-person</b>  | 0.21 (–0.11; 0.54)  | <b>0.53 (0.25; 0.81)</b>    |
| <b>0.29 (0.02; 0.55)</b>                                | <b>Home</b>         | 0.10 (–0.16; 0.37)          |
| <b>0.45 (0.21; 0.69)</b>                                | 0.16 (–0.07; 0.40)  | <b>nEX</b>                  |
| Depression  |                     |                             |
| <b>In-person</b>  | –0.38 (–1.81; 1.04) | <b>–0.55 (–1.03; –0.07)</b> |
| –0.40 (–1.18; 0.38)                                     | <b>Home</b>         | –0.15 (–0.84; 0.55)         |
| <b>–0.55 (–1.03; –0.07)</b>                             | –0.15 (–0.82; 0.52) | <b>nEX</b>                  |
| Anxiety   |                     |                             |
| <b>In-person</b>  | –0.58 (–2.79; 1.64) | <b>–1.18 (–2.09; –0.27)</b> |
| –1.03 (–2.45; 0.39)                                     | <b>Home</b>         | –0.02 (–1.31; 1.27)         |
| <b>–1.16 (–2.05; –0.26)</b>                             | –0.12 (–1.36; 1.12) | <b>nEX</b>                  |

Upper right triangle presents the pooled mean differences from direct comparisons and the lower left triangle pooled mean differences from the network meta-analysis. Columns are relative to the rows. Statistically significant differences are highlighted in bold values. For quality of life, positive differences indicate an improvement, whereas for depression and anxiety, negative differences indicate a reduction in symptoms.

which features of home-based programmes could be optimized to become more effective.

## Strengths and limitations

The main strengths of our study are that we analysed the effects of different types, settings, duration, and volume (and indirectly intensity) of exercise on several brain-related dimensions and that we used a network meta-analysis approach enabling for both direct and indirect effect estimates. Furthermore, the search and selection process has been rigorously carried out, according to the most up-to-date guidelines and including many electronic databases to guarantee adequate and efficient coverage. Our network meta-analysis is based only on RCTs, which is the best study design available to investigate cause-effects.

Our study also has some limitations that must be addressed. First, the selection process has been restricted to studies examining the isolated effects of exercise, and we excluded grey literature, which might have impacted our results. Second, nearly half of the studies were rated with some concerns for the risk of bias and another 22% as high risk of bias. However, the sensitivity analyses excluding studies with a high risk of bias revealed similar effect estimates. To increase the quality of evidence, studies need to improve their reporting about the randomization process, study deviations, and (pre-) selected outcomes.<sup>102</sup> Third, several types of exercise had only one comparison (e.g. HIIT + R and STBT), and no major conclusions can therefore be drawn

about the effectiveness of these types of exercise. Future network meta-analyses including more studies should confirm our results for different types of exercise. Furthermore, some potential local inconsistencies were found, which could not be explained by the study characteristics. However, additional comparisons improving both direct and indirect evidence and under-reported factors, such as adherence, compliance and intensity, are important to improve the current study and need further investigation. Finally, we had significant heterogeneity in the analyses, which might be explained by variability in several key factors such as differences in characteristics of the patients and exercise interventions, as these factors could lead to different physiological adaptations. Furthermore, the included studies used a wide variety of instruments to assess brain-related outcomes. The use of different instruments forced us to include standardized changes-from-baseline, which could also introduce heterogeneity. Nevertheless, we standardized the change-from-baseline using pooled pre-SDs of studies using the same instruments.

## Conclusions

Our systematic review has identified that most of the current research on exercise brain-related outcomes in CAD patients is focused on HR-QoL, depression, and anxiety and highlights the need of studies assessing other dimensions of brain, such as brain structure/function,

cognition, and sleep. Second, our network meta-analysis provided robust evidence supporting that in-person exercise interventions were associated with improved HR-QoL (including both the PCS and MCS) as well as reduced depressive and anxiety symptoms and should therefore be encouraged by health care providers. Furthermore, our study supports that the effectiveness of exercise reduces considerably when delivered by home-based interventions. Third, HIIT seems to be equally effective as MIT in improving these outcomes, suggesting that intensity might not impact these outcomes, yet needs further study. Future research should thoroughly investigate whether specific types or novel approaches in home-based interventions could prove more effective in enhancing brain-related outcomes than those utilized until the moment.

## Acknowledgements

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## Supplementary data

Supplementary data are available at *European Heart Journal* online.

## Declarations

### Disclosure of Interest

All authors declare no disclosure of interest for this contribution.

### Data Availability

No data were generated. All extracted data and data processing scripts are available upon request to the corresponding authors.

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### Ethical Approval

Ethical approval was not required.

### Pre-registered Clinical Trial Number

Study protocol was registered in PROSPERO (ID: CRD42023402569).

## References

1. WHO. Cardiovascular Diseases (CVDs). World Health Organization, Geneva, Switzerland. 2021. [https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-\(cvds\)](https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)).
2. Tsao CW, Aday AWW, Almarzooq ZI, Anderson CA, Arora P, Avery CL, et al. Heart disease and stroke statistics—2023 update: a report from the American Heart Association. *Circulation* 2023;**147**:e93–621. <https://doi.org/10.1161/CIR.0000000000001123>
3. Timmis A, Vardas P, Townsend N, Torbica A, Katus H, De Smedt D, et al. European Society of Cardiology: cardiovascular disease statistics 2021. *Eur Heart J* 2022;**43**:716–99. <https://doi.org/10.1093/eurheartj/ehab892>
4. Malakar AK, Choudhury D, Halder B, Paul P, Uddin A, Chakraborty S. A review on coronary artery disease, its risk factors, and therapeutics. *J Cell Physiol* 2019;**234**:16812–23. <https://doi.org/10.1002/jcp.28350>
5. Schievink SH, van Bostel MP, Deckers K, van Oostenbrugge RJ, Verhey FR, Köhler S. Cognitive changes in prevalent and incident cardiovascular disease: a 12-year follow-up in the Maastricht Aging Study (MAAS). *Eur Heart J* 2022;**43**:e2–9. <https://doi.org/10.1093/eurheartj/ehx365>
6. Roger VL. The heart–brain connection: from evidence to action. *Eur Heart J* 2017;**38**:3229–31. <https://doi.org/10.1093/eurheartj/ehx387>
7. Singh-Manoux A, Sabia S, Lajnef M, Ferrie JE, Nabi H, Britton AR, et al. History of coronary heart disease and cognitive performance in midlife: the Whitehall II study. *Eur Heart J* 2008;**29**:2100–7. <https://doi.org/10.1093/eurheartj/ehn298>
8. Xie W, Zheng F, Yan L, Zhong B. Cognitive decline before and after incident coronary events. *J Am Coll Cardiol* 2019;**73**:3041–50. <https://doi.org/10.1016/j.jacc.2019.04.019>
9. Saeed A, Lopez O, Cohen A, Reis SE. Cardiovascular disease and Alzheimer's disease: the heart–brain axis. *J Am Heart Assoc* 2023;**12**:e030780. <https://doi.org/10.1161/JAHA.123.030780>
10. Jha MK, Qamar A, Vaduganathan M, Charney DS, Murrrough JW. Screening and management of depression in patients with cardiovascular disease: JACC state-of-the-art review. *J Am Coll Cardiol* 2019;**73**:1827–45. <https://doi.org/10.1016/j.jacc.2019.01.041>
11. Farquhar JM, Stonerock GL, Blumenthal JA. Treatment of anxiety in patients with coronary heart disease: a systematic review. *Psychosomatics* 2018;**59**:318–32. <https://doi.org/10.1016/j.psym.2018.03.008>
12. Tušek-Bunc K, Petek D. Comorbidities and characteristics of coronary heart disease patients: their impact on health-related quality of life. *Health Qual Life Outcomes* 2016;**14**:159. <https://doi.org/10.1186/s12955-016-0560-1>
13. Muhammad I, He HG, Kowitlawakul Y, Wang W. Narrative review of health-related quality of life and its predictors among patients with coronary heart disease. *Int J Nurs Pract* 2016;**22**:4–14. <https://doi.org/10.1111/ijn.12356>
14. Carney RM, Freedland KE. Depression and coronary heart disease. *Nat Rev Cardiol* 2017;**14**:145–55. <https://doi.org/10.1038/nrcardio.2016.181>
15. 2018 Physical Activity Guidelines Advisory Committee. *2018 Physical Activity Guidelines Advisory Committee Scientific Report*. Washington, DC: U.S. Department of Health and Human Services, 2018.
16. Erickson KI, Hillman C, Stillman CM, Ballard RM, Bloodgood B, Conroy DE, et al. Physical activity, cognition, and brain outcomes: a review of the 2018 physical activity guidelines. *Medicine (Baltimore)* 2019;**51**:1242–51. <https://doi.org/10.1249/MSS.0000000000001936>
17. Pareja-Galeano H, Garatachea N, Lucia A. Exercise as a poly pill for chronic diseases. *Prog Mol Biol Transl Sci* 2015;**135**:497–526. <https://doi.org/10.1016/bs.pmbts.2015.07.019>
18. Fiuzza-Luces C, Santos-Lozano A, Joyner M, Carrera-Bastos P, Picazo O, Zugaza JL, et al. Exercise benefits in cardiovascular disease: beyond attenuation of traditional risk factors. *Nat Rev Cardiol* 2018;**15**:731–43. <https://doi.org/10.1038/s41569-018-0065-1>
19. Anderson L, Oldridge N, Thompson DR, Zwisler A-D, Rees K, Martin N, et al. Exercise-based cardiac rehabilitation for coronary heart disease: Cochrane systematic review and meta-analysis. *J Am Coll Cardiol* 2016;**67**:1–12. <https://doi.org/10.1016/j.jacc.2015.10.044>
20. Goldhammer E, Tanchilevitch A, Maor I, Beniamini Y, Rosenschein U, Sagiv M. Exercise training modulates cytokines activity in coronary heart disease patients. *Int J Cardiol* 2005;**100**:93–9. <https://doi.org/10.1016/j.ijcard.2004.08.073>
21. Niessner A, Richter B, Penka M, Steiner S, Strasser B, Ziegler S, et al. Endurance training reduces circulating inflammatory markers in persons at risk of coronary events: impact on plaque stabilization? *Atherosclerosis* 2006;**186**:160–5. <https://doi.org/10.1016/j.atherosclerosis.2005.06.047>
22. Lavie CJ, Milani RV. Cardiac rehabilitation and exercise training in secondary coronary heart disease prevention. *Prog Cardiovasc Dis* 2011;**53**:397–403. <https://doi.org/10.1016/j.pcad.2011.02.008>
23. Muscella A, Stefano E, Marsigliante S. The effects of exercise training on lipid metabolism and coronary heart disease. *Am J Physiol Heart Circ Physiol* 2020;**319**:H76–88. <https://doi.org/10.1152/ajpheart.00708.2019>
24. Virani SS, Newby LK, Arnold SV, Bittner V, Brewer LC, Demeter SH, et al. 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA guideline for the management of patients with chronic coronary disease: a report of the American Heart Association/American College of Cardiology joint committee on clinical practice guidelines. *Circulation* 2023;**148**:e9–119. <https://doi.org/10.1161/CIR.0000000000001168>
25. Byrne RA, Rossello X, Coughlan J, Barbato E, Berry C, Chieffo A, et al. 2023 ESC guidelines for the management of acute coronary syndromes: developed by the task force on the management of acute coronary syndromes of the European Society of Cardiology (ESC). *Eur Heart J* 2023;**44**:3720–826. <https://doi.org/10.1093/eurheartj/ehad191>

26. Anderson L, Taylor RS. Cardiac rehabilitation for people with heart disease: an overview of Cochrane systematic reviews. *Cochrane Database Syst Rev* 2014;**2014**: CD011273. <https://doi.org/10.1002/14651858.CD011273.pub2>
27. Francis T, Kabboul N, Rac V, Mitsakakis N, Pechlivanglou P, Bielecki J, et al. The effect of cardiac rehabilitation on health-related quality of life in patients with coronary artery disease: a meta-analysis. *Can J Cardiol* 2019;**35**:352–64. <https://doi.org/10.1016/j.cjca.2018.11.013>
28. Yakut H, Dursun H, Felekoğlu E, Başkurt AA, Alpaydın AO, Özalevi S. Effect of home-based high-intensity interval training versus moderate-intensity continuous training in patients with myocardial infarction: a randomized controlled trial. *Ir J Med Sci* 2022;**191**:2539–48. <https://doi.org/10.1007/s11845-021-02867-x>
29. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;**372**:n71. <https://doi.org/10.1136/bmj.n71>
30. Hutton B, Salanti G, Caldwell DM, Chaimani A, Schmid CH, Cameron C, et al. The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations. *Ann Intern Med* 2015;**162**:777–84. <https://doi.org/10.7326/M14-2385>
31. Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al. *Cochrane Handbook for Systematic Reviews of Interventions*. 2nd edn. Chichester, UK: John Wiley & Sons, 2019.
32. Daly C, Dias S, Welton NJ, Anwer S, Ades AE. *NICE Guidelines Technical Support Unit. Meta-Analysis. Guideline Methodology Documents*. London, UK: National Institute for Health and Care Excellence, 2021.
33. Bramer WM, Rethlefsen ML, Kleijnen J, Franco OH. Optimal database combinations for literature searches in systematic reviews: a prospective exploratory study. *Syst Rev* 2017;**6**:245. <https://doi.org/10.1186/s13643-017-0644-y>
34. Clark JM, Sanders S, Carter M, Honeyman D, Cleo G, Auld Y, et al. Improving the translation of search strategies using the Polyglot Search Translator: a randomized controlled trial. *Med Libr Assoc* 2020;**10**:195–207. <https://doi.org/10.5195/jmla.2020.834>
35. Covidence systematic review software. *Veritas Health Innovation*. Melbourne, Australia. [www.covidence.org](http://www.covidence.org). (4 December 2024, date last accessed).
36. Bull FC, Al-Ansari SS, Biddle S, Borodulin K, Buman MP, Cardon G, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. *Br J Sports Med* 2020;**54**:1451–62. <https://doi.org/10.1136/bjsports-2020-102955>
37. Pelliccia A, Sharma S, Gati S, Back M, Borjesson M, Caselli S, et al. 2020 ESC guidelines on sports cardiology and exercise in patients with cardiovascular disease. *Eur Heart J* 2021;**42**:17–96. <https://doi.org/10.1093/eurheartj/ehaa605>
38. Ramos JS, Dalleck LC, Tjonna AE, Beetham KS, Coombes JS. The impact of high-intensity interval training versus moderate-intensity continuous training on vascular function: a systematic review and meta-analysis. *Sports Med* 2015;**45**:679–92. <https://doi.org/10.1007/s40279-015-0321-z>
39. Weston KS, Wisloff U, Coombes JS. High-intensity interval training in patients with lifestyle-induced cardiometabolic disease: a systematic review and meta-analysis. *Br J Sports Med* 2014;**48**:1227–34. <https://doi.org/10.1136/bjsports-2013-092576>
40. Martinez-Vizcaino V, Amaro-Gahete FJ, Fernandez-Rodriguez R, Garrido-Miguel M, Caverro-Redondo I, Pozuelo-Carrascosa DP. Effectiveness of fixed-dose combination therapy (Polypill) versus exercise to improve the blood-lipid profile: a network meta-analysis. *Sports Med* 2022;**52**:1161–73. <https://doi.org/10.1007/s40279-021-01607-6>
41. Arthur HM, Gunn E, Thorpe KE, Ginis KM, Mataseje L, McCartney N, et al. Effect of aerobic vs combined aerobic-strength training on 1-year, post-cardiac rehabilitation outcomes in women after a cardiac event. *J Rehabil Med* 2007;**39**:730–5. <https://doi.org/10.2340/16501977-0122>
42. Brouwers RWM, van der Poort EKJ, Kemps HMC, van den Akker-van Marle ME, Kraal JJ. Cost-effectiveness of cardiac telerehabilitation with relapse prevention for the treatment of patients with coronary artery disease in The Netherlands. *JAMA Netw Open* 2021;**4**:e2136652. <https://doi.org/10.1001/jamanetworkopen.2021.36652>
43. Maddison R, Pfaeffli L, Whittaker R, Stewart R, Kerr A, Jiang Y, et al. A mobile phone intervention increases physical activity in people with cardiovascular disease: results from the HEART randomized controlled trial. *Eur J Prev Cardiol* 2015;**22**:701–9. <https://doi.org/10.1177/2047487314535076>
44. Peixoto TC, Begot I, Bolzan DW, Machado L, Reis MS, Papa V, et al. Early exercise-based rehabilitation improves health-related quality of life and functional capacity after acute myocardial infarction: a randomized controlled trial. *Can J Cardiol* 2015;**31**: 308–13. <https://doi.org/10.1016/j.cjca.2014.11.014>
45. Yu C-M, Lau C-P, Chau J, McGehee S, Kong S-L, Cheung BM-Y, et al. A short course of cardiac rehabilitation program is highly cost effective in improving long-term quality of life in patients with recent myocardial infarction or percutaneous coronary intervention. *Arch Phys Med* 2004;**85**:1915–22. <https://doi.org/10.1016/j.apmr.2004.05.010>
46. Rohatgi A. *WebPlotDigitizer (Version 4.4)* [software]. Austin, Texas: Automeris, 2020. <https://automeris.io/WebPlotDigitizer>. (4 December 2024, date last accessed).
47. Drevon D, Fursa SR, Malcolm AL. Intercoder reliability and validity of WebPlotDigitizer in extracting graphed data. *Behav Modif* 2017;**41**:323–39. <https://doi.org/10.1177/0145445516673998>
48. Sterne JA, Savovic J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. Rob 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;**366**:i4898. <https://doi.org/10.1136/bmj.i4898>
49. Nikolakopoulou A, Higgins JP, Papakonstantinou T, Chaimani A, Del Giovane C, Egger M, et al. CINeMA: an approach for assessing confidence in the results of a network meta-analysis. *PLoS Med* 2020;**17**:e1003082. <https://doi.org/10.1371/journal.pmed.1003082>
50. Papakonstantinou T, Nikolakopoulou A, Higgins JP, Egger M, Salanti G. Cinema: software for semiautomated assessment of the confidence in the results of network meta-analysis. *Campbell Syst Rev* 2020;**16**:e1080. <https://doi.org/10.1002/cl2.1080>
51. Hu Y, Li L, Wang T, Liu Y, Zhan X, Han S, et al. Comparison of cardiac rehabilitation (exercise + education), exercise only, and usual care for patients with coronary artery disease: a non-randomized retrospective analysis. *Pharmacol Res Perspect* 2021;**9**: e00711. <https://doi.org/10.1002/prp2.711>
52. Peters JL, Sutton AJ, Jones DR, Abrams KR, Rushton L. Contour-enhanced meta-analysis funnel plots help distinguish publication bias from other causes of asymmetry. *J Clin Epidemiol* 2008;**61**:991–6. <https://doi.org/10.1016/j.jclinepi.2007.11.010>
53. Avila A, Claes J, Goetschalckx K, Buys R, Azzawi M, Vanhees L, et al. Home-based rehabilitation with telemonitoring guidance for patients with coronary artery disease (short-term results of the TRICH study): randomized controlled trial. *J Med Internet Res* 2018;**20**:e225. <https://doi.org/10.2196/jmir.9943>
54. Belardinelli R, Paolini I, Cianci G, Piva R, Georgiou D, Purcaro A. Exercise training intervention after coronary angioplasty: the ETICA trial. *Am Coll Cardiol* 2001;**37**:1891–900. [https://doi.org/10.1016/S0735-1097\(01\)01236-0](https://doi.org/10.1016/S0735-1097(01)01236-0)
55. Blumenthal JA, Sherwood A, Babyak MA, Watkins LL, Waugh R, Georgiades A, et al. Effects of exercise and stress management training on markers of cardiovascular risk in patients with ischemic heart disease: a randomized controlled trial. *JAMA* 2005;**293**: 1626–34. <https://doi.org/10.1001/jama.293.13.1626>
56. Blumenthal JA, Sherwood A, Babyak MA, Watkins LL, Smith PJ, Hoffman BM, et al. Exercise and pharmacological treatment of depressive symptoms in patients with coronary heart disease: results from the UPBEAT (understanding the prognostic benefits of exercise and antidepressant therapy) study. *J Am Coll Cardiol* 2012;**60**:1053–63. <https://doi.org/10.1016/j.jacc.2012.04.040>
57. Blumenthal JA, Smith PJ, Jiang W, Hinderliter A, Watkins LL, Hoffman BM, et al. Effect of exercise, escitalopram, or placebo on anxiety in patients with coronary heart disease: the understanding the benefits of exercise and escitalopram in anxious patients with coronary heart disease (UNWIND) randomized clinical trial. *JAMA psychiatry* 2021;**78**:1270–8. <https://doi.org/10.1001/jamapsychiatry.2021.2236>
58. Conraads VM, Pattyn N, De Maeyer C, Beckers PJ, Coeckelberghs E, Cornelissen VA, et al. Aerobic interval training and continuous training equally improve aerobic exercise capacity in patients with coronary artery disease: the SAINTEX-CAD study. *Int J Cardiol* 2015;**179**:203–10. <https://doi.org/10.1016/j.ijcard.2014.10.155>
59. Currie KD, Bailey KJ, Jung ME, McKelvie RS, MacDonald JM. Effects of resistance training combined with moderate-intensity endurance or low-volume high-intensity interval exercise on cardiovascular risk factors in patients with coronary artery disease. *J Sci Med Sport* 2015;**18**:637–42. <https://doi.org/10.1016/j.jsams.2014.09.013>
60. Deka P, Pathak D, Klompstra L, Sempere-Rubio N, Querol-Giner F, Marques-Sule E. High-intensity interval and resistance training improve health outcomes in older adults with coronary disease. *J Am Med Dir Assoc* 2022;**23**:60–5. <https://doi.org/10.1016/j.jamda.2021.05.034>
61. Deng B, Shou X, Ren A, Liu X, Wang Q, Wang B, et al. Effect of aerobic training on exercise capacity and quality of life in patients older than 75 years with acute coronary syndrome undergoing percutaneous coronary intervention. *Physiother Theory Pract* 2022;**38**:1135–44. <https://doi.org/10.1080/09593985.2020.1825580>
62. Dor-Haim H, Barak S, Horowitz M, Yaakobi E, Katzburg S, Swissa M, et al. Improvement in cardiac dysfunction with a novel circuit training method combining simultaneous aerobic-resistance exercises. A randomized trial. *PLoS One* 2018;**13**: e0188551. <https://doi.org/10.1371/journal.pone.0188551>
63. Fang J, Huang B, Xu D, Li J, Au WW. Innovative application of a home-based and remote sensing cardiac rehabilitation protocol in Chinese patients after percutaneous coronary intervention. *Telemed J E Health* 2019;**25**:288–93. <https://doi.org/10.1089/tmj.2018.0064>
64. Ghisi GLM, Chaves GSS, Ribeiro AL, Oh P, Britto RR, Grace SL. Comprehensive cardiac rehabilitation effectiveness in a middle-income setting: a RANDOMIZED CONTROLLED TRIAL. *J Cardiopulm Rehabil Prev* 2020;**40**:399–406. <https://doi.org/10.1097/HCR.0000000000000512>
65. Giggins OM, Doyle J, Smith S, Vavasour G, Moran O, Gavin S, et al. Remotely delivered cardiac rehabilitation exercise for coronary heart disease: nonrandomized feasibility study. *JMIR cardio* 2023;**7**:e40283. <https://doi.org/10.2196/40283>
66. Jaureguizar KV, Vicente-Campos D, Bautista LR, de la Peña CH, Gómez MJ, Rueda MJ, et al. Effect of high-intensity interval versus continuous exercise training on functional capacity and quality of life in patients with coronary artery disease: a randomized clinical trial. *J Cardiopulm Rehabil Prev* 2016;**36**:96–105. <https://doi.org/10.1097/HCR.0000000000000156>
67. Jiang J, Chi Q, Wang Y, Jin X, Yu S. Five-animal frolics exercise improves anxiety and depression outcomes in patients with coronary heart disease: a single-blind

- randomized controlled trial. *Evid Based Complement Alternat Med* 2020;**2020**:6937158. <https://doi.org/10.1155/2020/6937158>
68. Johnson NA, Lim LL, Bowe SJ. Multicenter randomized controlled trial of a home walking intervention after outpatient cardiac rehabilitation on health-related quality of life in women. *Eur J Cardiovasc Prev Rehabil* 2009;**16**:633–7. <https://doi.org/10.1097/HJR.0b013e32832e8eba>
  69. Kristiansen J, Sjørødson T, Grove EL, Rasmussen J, Kristensen SD, Hvas AM, et al. Feasibility and impact of whole-body high-intensity interval training in patients with stable coronary artery disease: a randomised controlled trial. *Sci Rep* 2022;**12**:17295. <https://doi.org/10.1038/s41598-022-21655-w>
  70. Lee LS, Tsai M-C, Brooks D, Oh PI. Randomised controlled trial in women with coronary artery disease investigating the effects of aerobic interval training versus moderate intensity continuous exercise in cardiac rehabilitation: CAT versus MICE study. *BMJ Open Sport Exerc Med* 2019;**5**:e000589. <https://doi.org/10.1136/bmjsem-2019-000589>
  71. Maddison R, Rawstorn JC, Stewart RA, Benatar J, Whittaker R, Rolleston A, et al. Effects and costs of real-time cardiac telerehabilitation: randomised controlled non-inferiority trial. *Heart* 2019;**105**:122–9. <https://doi.org/10.1136/heartjnl-2018-313189>
  72. Madssen E, Arbo I, Granøien I, Walderhaug L, Moholdt T. Peak oxygen uptake after cardiac rehabilitation: a randomized controlled trial of a 12-month maintenance program versus usual care. *PLoS One* 2014;**9**:e107924. <https://doi.org/10.1371/journal.pone.0107924>
  73. McGregor G, Powell R, Begg B, Birkett ST, Nichols S, Ennis S, et al. High-intensity interval training in cardiac rehabilitation (HIIT or MISS UK): a multi-centre randomised controlled trial. *Eur J Prev Cardiol* 2023;**30**:745–55. <https://doi.org/10.1093/eurjpc/zwad039>
  74. Moholdt T, Bekken Vold M, Grimsmo J, Slørdahl SA, Wisløff U. Home-based aerobic interval training improves peak oxygen uptake equal to residential cardiac rehabilitation: a randomized, controlled trial. *PLoS One* 2012;**7**:e41199. <https://doi.org/10.1371/journal.pone.0041199>
  75. Okur I, Aksoy CC, Yaman F, Sen T. Which high-intensity interval training program is more effective in patients with coronary artery disease? *Int J Rehabil Res* 2021;**45**:168–75. <https://doi.org/10.1097/MRR.0000000000000524>
  76. Reed JL, Terada T, Cotie LM, Tulloch HE, Leenen FH, Mistura M, et al. The effects of high-intensity interval training, Nordic walking and moderate-to-vigorous intensity continuous training on functional capacity, depression and quality of life in patients with coronary artery disease enrolled in cardiac rehabilitation: a randomized controlled trial (CRX study). *Prog Cardiovasc Dis* 2022;**70**:73–83. <https://doi.org/10.1016/j.pcad.2021.07.002>
  77. Salmoirago-Blotcher E, Wayne PM, Dunsiger S, Krol J, Breault C, Bock BC, et al. Tai chi is a promising exercise option for patients with coronary heart disease declining cardiac rehabilitation. *Am Heart Assoc* 2017;**6**:e006603. <https://doi.org/10.1161/JAHA.117.006603>
  78. Schönfelder M, Oberreiter H, Egger A, Tschentscher M, Droese S, Niebauer J. Effect of different endurance training protocols during cardiac rehabilitation on quality of life. *Am J Med* 2021;**134**:805–11. <https://doi.org/10.1016/j.amjmed.2020.10.048>
  79. Snoek JA, Meindersma EP, Prins LF, Van't Hof AVW, de Boer MJ, Hopman MT, et al. The sustained effects of extending cardiac rehabilitation with a six-month telemonitoring and telecoaching programme on fitness, quality of life, cardiovascular risk factors and care utilisation in CAD patients: the TeleCaRe study. *J Telemed Telecare* 2021;**27**:473–83. <https://doi.org/10.1177/1357633X19885793>
  80. Takroni MA, Thow M, Ellis B, Seenan C. Home-based versus outpatient-based cardiac rehabilitation post-coronary artery bypass graft surgery: a randomized controlled trial. *J Cardiovasc Nurs* 2022;**37**:274–80. <https://doi.org/10.1097/JCN.0000000000000763>
  81. Taylor JL, Holland DJ, Keating SE, Leveritt MD, Gomersall SR, Rowlands AV, et al. Short-term and long-term feasibility, safety, and efficacy of high-intensity interval training in cardiac rehabilitation: the FITR heart study randomized clinical trial. *JAMA Cardiol* 2020;**5**:1382–9. <https://doi.org/10.1001/jamacardio.2020.3511>
  82. Terada T, Cotie LM, Tulloch H, Mistura M, Vidal-Almela S, O'Neill CD, et al. Sustained effects of different exercise modalities on physical and mental health in patients with coronary artery disease: a randomized clinical trial. *J Cardiol* 2022;**38**:1235–43. <https://doi.org/10.1016/j.jcica.2022.03.017>
  83. Vieira Á, Melo C, Machado J, Gabriel J. Virtual reality exercise on a home-based phase III cardiac rehabilitation program, effect on executive function, quality of life and depression, anxiety and stress: a randomized controlled trial. *Disabil Rehabil Assist Technol* 2018;**13**:112–23. <https://doi.org/10.1080/17483107.2017.1297858>
  84. Villafaina S, Gimenez-Guervos Perez MJ, Fuentes-García JP. Comparative effects of high-intensity interval training vs moderate-intensity continuous training in phase III of a tennis-based cardiac rehabilitation program: a pilot randomized controlled trial. *Sustainability* 2020;**12**:4134. <https://doi.org/10.3390/su12104134>
  85. Garcia-Bravo S, Cano-de-la-Cuerda R, Dominguez-Paniagua J, Campuzano-Ruiz R, Barrenada-Copete E, Jesus Lopez-Navas M, et al. Effects of virtual reality on cardiac rehabilitation programs for ischemic heart disease: a randomized pilot clinical trial. *Int J Environ Res Public Health* 2020;**17**:8472. <https://doi.org/10.3390/ijerph17228472>
  86. Nagyova I, Jendrichovsky M, Kucinsky R, Lachytova M, Rus V. Effects of nordic walking on cardiovascular performance and quality of life in coronary artery disease. *Eur J Phys Rehabil Med* 2020;**56**:616–24. <https://doi.org/10.23736/S1973-9087.20.06120-1>
  87. Webb-Peploe KM, Chua TP, Harrington D, Henein MY, Gibson DG, Coats AJ. Different response of patients with idiopathic and ischaemic dilated cardiomyopathy to exercise training. *Int J Cardiol* 2000;**74**:215–24. [https://doi.org/10.1016/S0167-5273\(00\)00293-X](https://doi.org/10.1016/S0167-5273(00)00293-X)
  88. Sajobi TT, Wang M, Awosoga O, Santana M, Southern D, Liang Z, et al. Trajectories of health-related quality of life in coronary artery disease. *Circ Cardiovasc Qual Outcomes* 2018;**11**:e003661. <https://doi.org/10.1161/CIRCOUTCOMES.117.003661>
  89. Graham MM, Norris CM, Galbraith PD, Knudston ML, Ghali WA. Quality of life after coronary revascularization in the elderly. *Eur Heart J* 2006;**27**:1690–8. <https://doi.org/10.1093/eurheartj/ehl038>
  90. Taylor RS, Walker S, Smart NA, Piepoli MF, Warren FC, Ciani O, et al. Impact of exercise rehabilitation on exercise capacity and quality-of-life in heart failure: individual participant meta-analysis. *J Am Coll Cardiol* 2019;**73**:1430–43. <https://doi.org/10.1016/j.jacc.2018.12.072>
  91. Chen M-D, Rimmer JH. Effects of exercise on quality of life in stroke survivors: a meta-analysis. *Stroke* 2011;**42**:832–7. <https://doi.org/10.1161/STROKEAHA.110.607747>
  92. Buffart LM, Kalter J, Sweegers MG, Courneya KS, Newton RU, Aaronson NK, et al. Effects and moderators of exercise on quality of life and physical function in patients with cancer: an individual patient data meta-analysis of 34 RCTs. *Cancer Treat Rev* 2017;**52**:91–104. <https://doi.org/10.1016/j.ctrv.2016.11.010>
  93. Chen K, Tan Y, Lu Y, Wu J, Liu X, Zhao Y. Effect of exercise on quality of life in Parkinson's disease: a systematic review and meta-analysis. *Parkinsons Dis* 2020;**2020**:3257623. <https://doi.org/10.1155/2020/3257623>
  94. Gomes-Neto M, Duraes AR, Reis HFCD, Neves VR, Martinez BP, Carvalho VO. High-intensity interval training versus moderate-intensity continuous training on exercise capacity and quality of life in patients with coronary artery disease: a systematic review and meta-analysis. *Eur J Prev Cardiol* 2017;**24**:1696–707. <https://doi.org/10.1177/2047487317728370>
  95. Yu H, Zhao X, Wu X, Yang J, Wang J, Hou L. High-intensity interval training versus moderate-intensity continuous training on patient quality of life in cardiovascular disease: a systematic review and meta-analysis. *Sci Rep* 2023;**13**:13915. <https://doi.org/10.1038/s41598-023-40589-5>
  96. Kirkman DL, Lee DC, Carbone S. Resistance exercise for cardiac rehabilitation. *Prog Cardiovasc Dis* 2022;**70**:66–72. <https://doi.org/10.1016/j.pcad.2022.01.004>
  97. Jewiss D, Ostman C, Smart NA. The effect of resistance training on clinical outcomes in heart failure: a systematic review and meta-analysis. *Int J Cardiol* 2016;**221**:674–81. <https://doi.org/10.1016/j.ijcard.2016.07.046>
  98. McDonagh ST, Dalal H, Moore S, Clark CE, Dean SG, Jolly K, et al. Home-based versus centre-based cardiac rehabilitation. *Cochrane Database Syst Rev* 2023;**10**:CD007130. <https://doi.org/10.1002/14651858.CD007130.pub5>
  99. Touns M, Carmody T, Greer T, Rethorst C, Grannemann B, Trivedi MH. Exercise is an effective treatment for positive valence symptoms in major depression. *J Affect Disord* 2017;**209**:188–94. <https://doi.org/10.1016/j.jad.2016.08.058>
  100. Wang L, Sun Y, Zhan J, Wu Z, Zhang P, Wen X, et al. Effects of exercise therapy on anxiety and depression in patients with coronary heart disease: a meta-analysis of a randomized controlled study. *Front Cardiovasc Med* 2021;**8**:730155. <https://doi.org/10.3389/fcvm.2021.730155>
  101. Peterson JC, Charlson ME, Wells MT, Altemus M. Depression, coronary artery disease, and physical activity: how much exercise is enough? *Clin Ther* 2014;**36**:1518–30. <https://doi.org/10.1016/j.clinthera.2014.10.003>
  102. Cuschieri S. The CONSORT statement. *Saudi J Anaesth* 2019;**13**:S27–30. [https://doi.org/10.4103/sja.SJA\\_559\\_18](https://doi.org/10.4103/sja.SJA_559_18)