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Efficacy of psychological interventions on psychological outcomes in coronary artery disease: systematic review and meta-analysis

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Abstract

Background. The benefits of cognitive-behavioral treatment (CBT) and positive psychology therapy (PPT) in patients with cardiovascular disease are still not well defined. We assessed the efficacy of CBT and PPT on psychological outcomes in coronary artery disease (CAD) patients.

Methods. Randomized controlled trials evaluating CBT or PPT in CAD patients published until May 2018 were systematically analyzed. Primary outcomes were depression, stress, anxiety, anger, happiness, and vital satisfaction. Random effects meta-analyses using the inverse variance method were performed. Effects were expressed as standardized mean difference (SMD) or mean differences (MD) with their 95% confidence intervals (CIs); risk of bias was assessed with the Cochrane tool.

Results. Nineteen trials were included ($n = 1956$); sixteen evaluated CBT ($n = 1732$), and three PPT ($n = 224$). Compared with control groups, depressive symptoms (13 trials; SMD −0.80; 95% CI −1.33 to −0.26), and anxiety (11 trials; SMD −1.26; 95% CI −2.11 to −0.41) improved after the PI, and depression (6 trials; SMD −2.08; 95% CI −3.22 to −0.94), anxiety (5 trials; SMD −1.33; 95% CI −2.38 to −0.29), and stress (3 trials; SMD −3.72; 95% CI −5.91 to −1.52) improved at the end of follow-up. Vital satisfaction was significantly increased at follow-up (MD 1.30, 0.27, 2.33). Non-significant effects on secondary outcomes were found. Subgroup analyses were consistent with overall analyses.

Conclusion. CBT and PPT improve several psychological outcomes in CAD patients. Depression and anxiety improved immediately after the intervention while stress and vital satisfaction improve in the mid-term. Future research should assess the individual role of CBT and PPT in CAD populations.

Introduction

The optimal care for patients with acute or chronic coronary artery disease (CAD) needs a multi-disciplinary approach to reduce morbidity and mortality, improve symptoms and quality of life. There is reasonable evidence for the beneficial effect of a variety of interventions, including medical therapies, coronary revascularization, cardiac rehabilitation programs or lifestyle changes, such as quit smoking, healthy diet and physical activity (Fihn et al., 2014; Knuuti et al., 2020).

A comprehensive approach to improving the care for these patients should consider the psychological impact of the disease, including behavioral and several psychological factors, such as depression, anxiety, stress or anger, which have been empirically linked to increases in cardiovascular risk (Chida & Steptoe, 2009; Nicholson, Kuper, & Hemingway, 2006; Roest, Martens, de Jonge, & Denollet, 2010; Rozanski, 2014) and lower quality of life (Appels et al., 2006). Several psychological interventions (PIs) have been tested in this context and positive results have been described in narrative reviews (Linden, 2000, 2013) and meta-analyses (Dickens et al., 2013; Linden, Phillips, & Leclerc, 2007; Richards et al., 2018; Rutledge, Redwine, Linke, & Mills, 2013).

However, the routine use of PIs in cardiac rehabilitation programs remains controversial because, while these are recommended (Knuuti et al., 2020) and implemented in high-income countries (Abreu et al., 2019; Supervia et al., 2019), this is not the case everywhere (Moghei, Oh, Chessex, & Grace, 2019; Poffley et al., 2017). Controversies, such as which specific treatment components should be included, the type and duration of interventions, professional involved,

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duration of follow-up, and specific endpoints, may contribute to the limited inclusion of PIs in cardiac rehabilitation programs (Linden, 2013), and may explain in part why PIs have shown beneficial effects in CAD patients but with modest effects (Dickens et al., 2013; Linden, 2000, 2013; Linden et al., 2007; Richards et al., 2018; Rutledge et al., 2013). This may also be due to the use of different definitions or types of PIs. Although cognitive-behavioral treatment (CBT)-based PIs have been suggested as the most effective for CAD patients (Linden, 2013), with two exceptions (Dickens et al., 2013; Linden et al., 2007), a number of meta-analyses included broader categories of PIs, such as those based on not well-established paradigms, mixed PIs, and psychopharmacological treatments (Richards et al., 2018; Rutledge et al., 2013). Finally, only negative psychological outcomes were assessed (Dickens et al., 2013; Linden, 2000, 2013; Linden et al., 2007; Richards et al., 2018; Rutledge et al., 2013).

Cardiovascular positive health (Labarthe et al., 2016), a new concept based on the positive psychology paradigm (Seligman, Steen, Park, & Peterson, 2005) has emerged recently. It focuses on positive psychological factors, mainly dispositional optimism, happiness, positive emotions, sense of purpose or vital satisfaction, as potentially having a role in reducing cardiovascular risk (Boehm & Kubzansky, 2012; DuBois et al., 2015; Labarthe et al., 2016). Positive effects have been reported for some PIs based on the positive psychology therapy (PPT) paradigm in cardiac rehabilitation patients (Bolier et al., 2013; Huffman et al., 2016) but only in small trials, not considered in prior meta-analyses (Dickens et al., 2013; Linden, 2000, 2013; Linden et al., 2007; Richards et al., 2018; Rutledge et al., 2013).

The aim of this systematic review and meta-analysis was to evaluate the evidence supporting the efficacy of PIs on improving negative psychological outcomes (depression, anxiety, stress, and anger) as well as positive outcomes (happiness and vital satisfaction), specifically in patients with CAD, including only studies testing the efficacy of empirically supported psychological techniques based on CBT and/or PPT.

Methods

This systematic review was conducted in accordance with the Cochrane Handbook for systematic reviews of interventions (Higgins & Green, 2011) and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards (Moher, Liberati, Tetzlaff, & Altman, 2009).

Study search and selection criteria

We searched PubMed, PsycInfo, Scopus, The Web of Science, and Cochrane Library for randomized controlled trials (RCTs) evaluating PIs in patients with CAD or ischemic heart disease (IHD). The keywords used were *CAD*, *IHD*, *acute coronary syndrome, psychological treatment, PI, cognitive-behavioral therapy, and positive psychology intervention*. The search strategy for all databases is available in the online Supplementary material. No language limitations were imposed. In addition, we also searched reference lists of papers. The searches were done twice: First on May 2017 and an update in May 2018. We excluded case reports, editorials, meta-analyses, narrative reviews, and proceeding studies. Studies were eligible for inclusion if they met the following criteria: RCTs in humans including patients with CAD or IHD; the PIs and psychological techniques used in these therapies were based on CBT or PPT; and at least one of the psychological endpoints considered in this meta-analysis was reported. Exclusion criteria were: studies in which patient assignation to treatment conditions were not randomized or where there was no control group; PIs based on any treatment approach different to CBT or PPT; studies not describing the specific techniques used in their PIs; and when the treatment strategy only included physical exercise and educational or counseling programs. Selected studies were saved and screened using Mendeley (Reference Management Software & Researcher Network). Titles and abstracts of the citations identified from the searches were examined by three reviewers independently (IM, RJ, and LC) and disagreements were resolved by discussion.

Types of interventions

Two different types of PIs were considered: CBT and PPT paradigm. Both were PIs done in cardiac rehabilitation programs delivered by health professionals, including only adults diagnosed with CAD or IHD. We defined CBT as empirically supported PI based on the idea that learning principles and cognitions play a key role in human behavior and affective experience (Blagys & Hilsenroth, 2002), with an aim to reduce psychological distress and promoting an adaptive behavior in daily living by developing skills to manage physiological arousal and negative emotions, modifying dysfunctional beliefs and/or coping; CBT involves techniques such as relaxation training, emotion regulation, cognitive restructuring, problem-solving therapy, and/or relapse prevention (Blagys & Hilsenroth, 2002). PPT was defined as PIs focused on intervening on positive psychological dimensions and traits, such as positive emotions, vital satisfaction, dispositional optimism, happiness, or purposes of life and their link to well-being, and therefore aimed at developing individual strengths and not just correcting weaknesses through specific empirically supported positive techniques, such as gratitude training, three good things in life, developing you at your best or identifying and using signature strengths among others (Lee Duckworth, Steen, & Seligman, 2005; Seligman et al., 2005). PIs based on other psychological paradigms (e.g. psychodynamic, social learning theory, etc.) were excluded. Control groups were defined as those receiving usual cardiac rehabilitation, which could only include specific educational and/or physical activity training programs and medical treatment.

Psychological outcomes

Primary outcomes were depression, anxiety, stress, anger, vital satisfaction, and happiness. Secondary outcomes included negative affect, positive affect, hostility, daily activities, quality of life, and dispositional hope. These psychological outcomes were assessed by psychological self-report questionnaires designed specifically to quantify these psychological factors with adequate psychometric criteria. Outcomes were measured at the end of intervention (post-treatment) and/or at the end of the pre-specified follow-up time when this was longer than the intervention.

Data extraction

Three reviewers carried out data extraction independently and recorded on a Microsoft Excel® spreadsheet. Extracted data included year of publication, reference, patient population, study design, total patients, number of groups, type, techniques and description of PIs, intervention duration, timing of intervention after coronary event, follow-up time, and primary and secondary outcomes (as reported by authors) per intervention arm. After

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data extraction, two investigators (AVH and HBa) checked for the accuracy of extractions.

Risk of bias assessment

We used the Cochrane Collaboration's risk of the bias assessment tool (Higgins & Green, 2011). The risk of bias was evaluated with the following items: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other bias. Four reviewers (IM, RJ, LC, and HBa) evaluated risk of bias independently and labeled each study of having low, high, or unclear risk of bias. Trials with high risk of bias in any of the items of randomization or blinding were rated as having high risk of bias. Any disagreement was resolved by a senior investigator (AVH).

Statistical analysis

For studies reporting medians (m) and interquartile ranges (IQR), means were estimated by $x = (a + 2m + b)/4$, where m is the median and a and b are P25 and P75, respectively (Higgins & Green, 2011). SDs were estimated using SD= IQR/1.35. When median and ranges were provided, the mean was estimated by $x = (a + 2m + b)/4$ using the values of the median (m), the smallest and largest value (a and b, respectively); SD was estimated by SD= range/4 if the sample size was <70 and SD= range/6 if the sample size was >70 (Higgins & Green, 2011).

In our analyses, both CBT and PPT were combined as one PI arm. We used random effects meta-analyses and the inverse variance method. The DerSimonian and Laird method was used to calculate the tau estimator of heterogeneity. Effects of PIs *v.* controls on primary and secondary psychological outcomes were expressed as mean difference (MD) or standardized mean difference (SMD) and its 95% confidence interval (95% CI). SMDs were used as we anticipated different scales to measure primary and secondary outcomes across studies. To interpret SMD we used the guidelines of Cohen (Cohen, 1988): 0.2 was a small, 0.5 moderate, and 0.8 large difference. The analyses of outcomes were adjusted for baseline characteristics.

The degree of statistical heterogeneity was quantified with the inconsistency (I^2) metric (Higgins, Thompson, Deeks, & Altman, 2003). A low, moderate, and high degree of heterogeneity was defined as I^2 proportion of <30, 30–60, and >60%, respectively. We performed a number of pre-specified subgroup analyses per outcome: type of PI (CBT *v.* PPT), type intervention provider (psychologist *v.* unknown), post-treatment assessment (<10–12 weeks *v.* >10–12 weeks) and follow-up assessment time (<6 months *v.* >6 months), session type (group *v.* individual), type of CAD patient (acute coronary syndrome –ACS– *v.* any CAD, i.e. both acute and chronic CAD), and risk of bias (high *v.* low/unclear). Small study effects were evaluated with the funnel plot, and tested with the Egger's test of funnel plot asymmetry (Higgins & Green, 2011). Statistical analyses were conducted using Review Manager (RevMan 5.3; Cochrane Collaboration).

Results

Selection of studies

We identified 2556 publications. After removing duplicates and screening titles and abstracts, 395 articles were selected for full text evaluation (Fig. 1). Forty-four trials potentially had relevant information, and finally 19 trials ($n = 1956$) were found to have outcomes of interest. These 19 trials were reported in 20 studies (Table 1) (Bishop et al., 2005; Blumenthal et al., 2005; Dao et al., 2011; del Pino, Gaos, Dorta, & Garcia, 2005; Fernandes, McIntyre, Coelho, Prata, & Maciel, 2017; Freedland et al., 2009; Karlsson et al., 2007; Lv et al., 2016; Merswolken, Siebenhuener, Orth-Gomér, Zimmermann-Viehoff, & Deter, 2011; Michalsen et al., 2005; Mohammadi et al., 2018; Murphy et al., 2013; Nikrahan et al., 2016; Nyklíček, Dijksman, Lenders, Fonteijn, & Koolen, 2014; O'Neil et al., 2014; 2015; Rakowska, 2015; Sanjuan et al., 2016; Sebregts, Falger, Appels, Kester, & Bär, 2005; Trzcieniecka-Green & Steptoe, 1996). The results of one trial were reported separately in two publications (O'Neil et al., 2014, 2015).

Characteristics of included studies

Table 1 summarizes the main characteristics of included studies. Studies were published between 1996 and 2018. Mean patient's age was generally older than 50 years old. Most of the studies had small populations, <100 patients per arm in most cases. Trials included patients after an ACS event or were chronic CAD patients or had a combination of acute and chronic CAD patients. No studies included only chronic CAD patients. CBT interventions were heterogeneous across trials, mostly multicomponent and in person with the only exception of the trials by O'Neil *et al.* (2014, 2015) where the PIs were performed by telephone. Three trials evaluated PPTs (Mohammadi et al., 2018; Nikrahan et al., 2016; Sanjuan et al., 2016) and there was also heterogeneity of this type of intervention among studies. Interventions lasted between 1 week (Fernandes et al., 2017) and 12 months (Karlsson et al., 2007). Depression, anxiety, and stress were the outcomes more frequently reported, both after the intervention and at the end of follow-up. The time intervals defining post-treatment (at the end of the intervention) and end of follow-up showed high variability across RCTs, with post-treatment time ranging from 2–3 days (Fernandes et al., 2017) to 1 year (Karlsson et al., 2007; Michalsen et al., 2005), and follow-up assessment ranging from 3–4 weeks (Dao et al., 2011) to 2.5 years (Rakowska, 2015).

Risk of bias assessment

Sixteen trials had high risk of bias due to the lack of blinding of patients or personnel, or due to the use of wrong randomization methods (online Supplementary material Fig. S1). Only three RCTs (Michalsen et al., 2005; Mohammadi et al., 2018; Trzcieniecka-Green & Steptoe, 1996) had an overall low risk of bias. About 55% of trials had incomplete outcome data, and about 20% had selective reporting of outcomes.

Effect of psychological interventions on primary outcomes

Meta-analyses assessing depression showed that, compared with controls, PIs significantly decrease depressive symptoms not only immediately after the intervention (13 trials, $n = 1543$; SMD −0.80, 95% CI −1.33 to −0.26, $p = 0.003$) but also at the end of follow-up (6 trials, $n = 719$; SMD −2.08, 95% CI −3.22 to −0.94, $p = 0.0004$) (Figs 2*a* and 3*a*). Similarly, anxiety significantly decreased both immediately after the PIs and at the end of follow-up (11 trials, $n = 1230$; SMD −1.26, 95% CI −2.11 to

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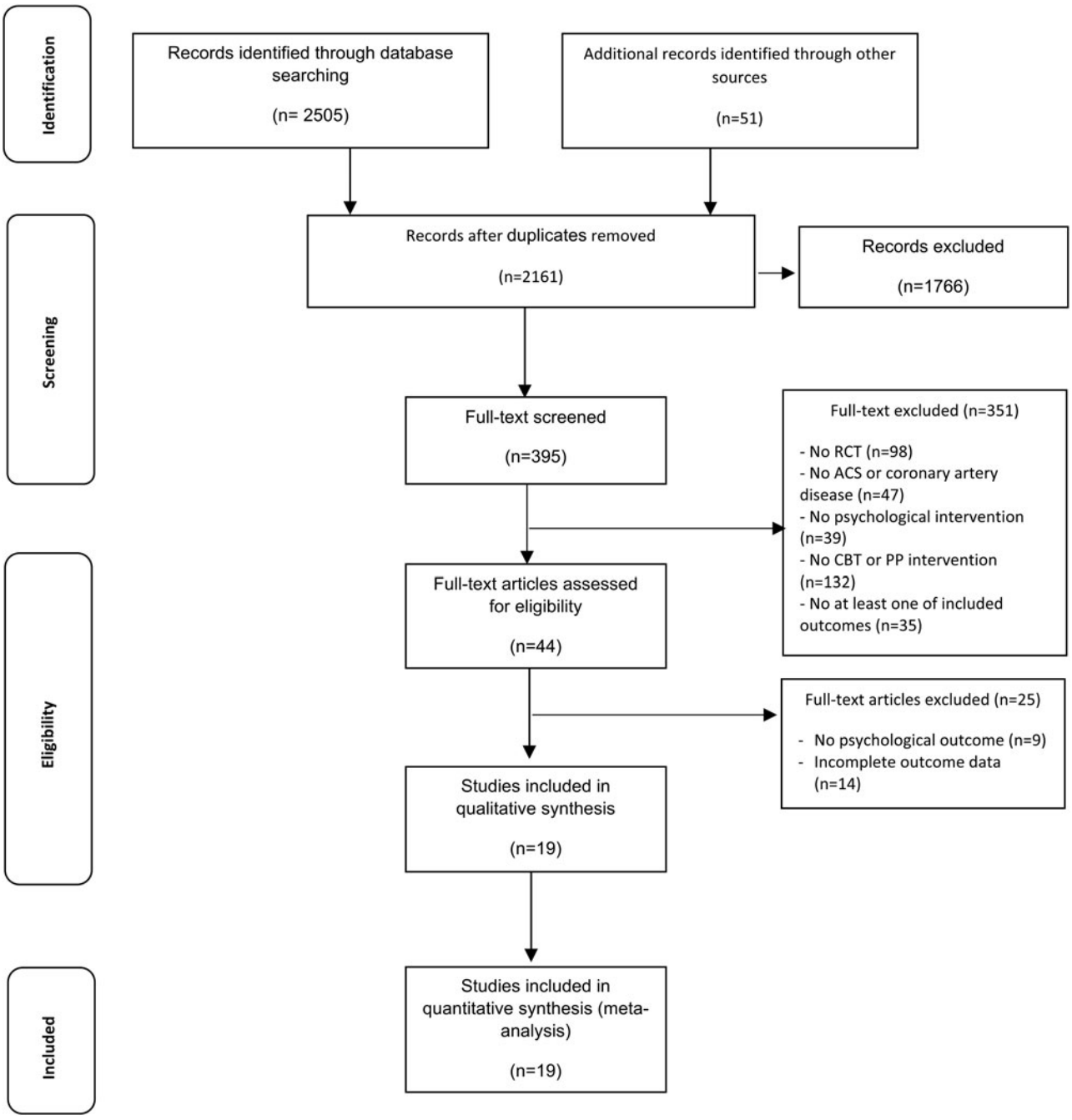

Fig. 1. Flowchart of study selection.

−0.41, $p = 0.004$; and 5 trials, $n = 445$; SMD −1.33, 95% CI −2.38 to −0.29, $p = 0.01$) (Figs 2*b* and 3*b*). However, although PIs did not decrease stress after the intervention (5 trials, $n = 461$; SMD −1.61, 95% CI −4.04 to 0.83, $p = 0.2$) (Fig. 2*c*), there was a significant reduction in stress levels at the end of follow-up (3 trials, $n = 256$; SMD −3.72, 95% CI −5.91 to −1.52, $p = 0.0009$) (Fig. 3*c*). No reduction in anger after PIs was found (3 trials, $n = 743$; SMD −0.07, 95% CI −0.29 to 0.14, $p = 0.5$) (Fig. 2*d*).

In relation to positive outcomes, although increases in vital satisfaction were not significant immediately after the two PIs ($n = 116$; MD 1.23 points, 95% CI −1.80 to 4.26, $p = 0.4$), the improvement was significant at the end of follow-up (MD 1.30 points, 95% CI 0.27–2.33, $p = 0.01$) (Figs 2*e* and 3*d*). On the contrary, meta-analyses of the same two trials showed no effect on happiness after treatment or follow-up (MD 0.97 points, 95% CI −10.79 to 12.73, $p = 0.9$; MD 7.35 points, 95% CI −5.59 to 20.29, $p = 0.3$, respectively) (Figs 2*f* and 3*e*).

Effect of psychological interventions on secondary outcomes

PIs did not reduce negative affect or increased positive affect immediately after the intervention (2 trials, $n = 169$; SMD −0.34, 95% CI −0.71 to 0.03, $p = 0.07$; and SMD 0.24, 95% CI −0.13 to 0.61, $p = 0.2$, respectively) (online Supplementary material Figs S2A and S2B). In three trials ($n = 314$), PIs significantly decreased hostility after the intervention (SMD −0.32, 95% CI

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Table 1. Study and patient characteristics of included RCTs

Author, year	Number of patients	Patient population. Diagnosis at entry	Age, mean (s.d.)	Description of interventions	Intervention duration	Outcomes	Evaluation at the end of treatment	Evaluation at the end of follow-up
Trzcieniecka-Green and Steptoe (1996)	Experimental group: *N* = 50, Control group: *N* = 50	ACS (+bypass)	Experimental group: 59.4 (7.7), Control group: 61 (6.7)	CBT. Psychologist: Yes. Multicomponent. Group sessions. In person. Description: Experimental group included psychoeducation, behavioral techniques for life style modification.	10 weeks	Depression; Anxiety; Daily activities; Physical Well-being	12 weeks	6 months
Bishop et al. (2005)	Experimental group: *N* = 29, Control group: *N* = 29	Others (CABG). Unspecified if acute or programmed	Only men. Experimental group: 54.7 (1.4), Control group: 53.3 (7.3)	CBT. Psychologist: Unknown. Multicomponent. Group sessions. In person. Description: Experimental group included behavioral techniques for life style modification, cognitive techniques.	6 weeks	Depression; Stress; Anxiety; Anger	6 weeks	3 months
Blumenthal et al. (2005)	Exercise group: *N* = 44, Stress management: *N* = 44, Control group: *N* = 42	IHD diagnosis (+ event or intervention)	Experimental group: 63 (9), Control group: 62 (10.5)	CBT. Psychologist: Unknown. Multicomponent. Group sessions. In person. Description: Experimental group included psychoeducation, behavioral techniques for life style modification and cognitive techniques.	Unknown	Depression; Anxiety; Hostility; Physical Well-being	16 weeks	No
del Pino et al. (2005)	Experimental group: *N* = 33, Educational group: *N* = 33, Control group: *N* = 32	CHD	Only men Experimental group: 49.65 (8.22), Control group: 58.09 (5.45)	CBT. Psychologist: Yes. Multicomponent. Group sessions. In person. Description: Experimental group included psychoeducation, relaxation techniques, behavioral techniques for life style modification, cognitive techniques.	9 months	Depression; Anger; Type A personality	9 months	12 and 24 months
Michalsen et al. (2005)	Experimental group: *N* = 48, Control group: *N* = 53	CAD (in medical treatment, excluded ACS)	Experimental group: 59.8 (7), Control group: 59.8 (8.6)	CBT. Psychologist: Unknown. Multicomponent. Group sessions. In person. Description: Experimental group included psychoeducation, relaxation techniques, relapse prevention, mindfulness.	12 months	Depression; Stress; Anxiety; Quality of life; Anger	12 months	No
Sebregts et al. (2005)	Experimental group: *N* = 94, Control group: *N* = 90	ACS (MI) or CABG. Unspecified if acute or programmed	Experimental group: 55.6 (8), Control group: 55.2 (9.7)	CBT. Psychologist: Yes. Multicomponent. Group sessions.	8 weeks	Depression; Hostility	8 weeks	9 months

				In person. Description: Experimental group included psychoeducation, relaxation techniques, behavioral techniques for life style modification, relapse prevention.				
Karlsson et al. (2007)	Experimental group: $N = 111$, Control group: $N = 113$	CAD (included ACS and intervention but not ACS)	Experimental group: 63.8 (7.2), Control group: 63.3 (7.3)	CBT. Psychologist: Unknown. Unicomponent. Group sessions. In person. Description: Experimental group included stress management program, 5-day stay at the patient hotel, behavioral techniques for life style modification.	12 months	Depression; Stress; Anxiety; Anger; Quality of life	12 months	No
Freedland et al. (2009)	Experimental group: CBT: $N = 41$, SSM: $N = 42$, Control group: $N = 40$	CABG surgery	Experimental group: 59 (10), Control group: 61 (9)	CBT. Psychologist: Yes. Multicomponent. Group sessions. In person. Description: Experimental group CBT group included psychoeducation, relaxation techniques, behavioral techniques for life style modification, relapse prevention.	12 weeks	Depression; Stress; Anxiety	3 months	6 and 9 months
Dao et al. (2011)	Experimental group: $N = 50$, Control group: $N = 50$	CAD (+CABG and also depression or anxiety diagnosis)	Experimental group: 62.8 (11.8), Control group: 64.2 (11.9)	CBT. Psychologist: Yes. Multicomponent. Group sessions. In person. Description: Experimental group: managing anxiety and depression using education and skills.	1–2 weeks	Stress; Depression; Anxiety; Quality of life; Hopeless; Vitally; Mindfulness; Positive and negative affect; Adherence to psychological treatment	At least 5 days after surgery	3–4 weeks
Merswolken et al. (2011)	Experimental group: $N = 25$, Control group: $N = 27$	ACS (+CHD diagnosis)	Experimental group: 62.5 (8.3), Control group: 59.8 (7.5)	CBT. Psychologist: Yes. Multicomponent. Group sessions. In person. Description: Experimental group included psychoeducation, relaxation, behavioral techniques for life style modification (stress management), cognitive restructuring and social components.	6 months	Depression; Anxiety	6 months	No
Turner, Hambridge, Baker, Bowman, and McElduff (2013)	Experimental group: $N = 25$ and Control group: $N = 32$	ACS (other possible diagnosis)	Experimental group: 61 (11), Control group: 62 (9)	CBT. Psychologist: Yes. Multicomponent. Group sessions. In person. Description: Experimental group included psychoeducation, behavioral techniques for life style modification, cognitive techniques, motivational techniques, relapse prevention.	6 weeks	Depression; Anxiety; Adherence to psychological treatment	No	2, 6, and 12 months

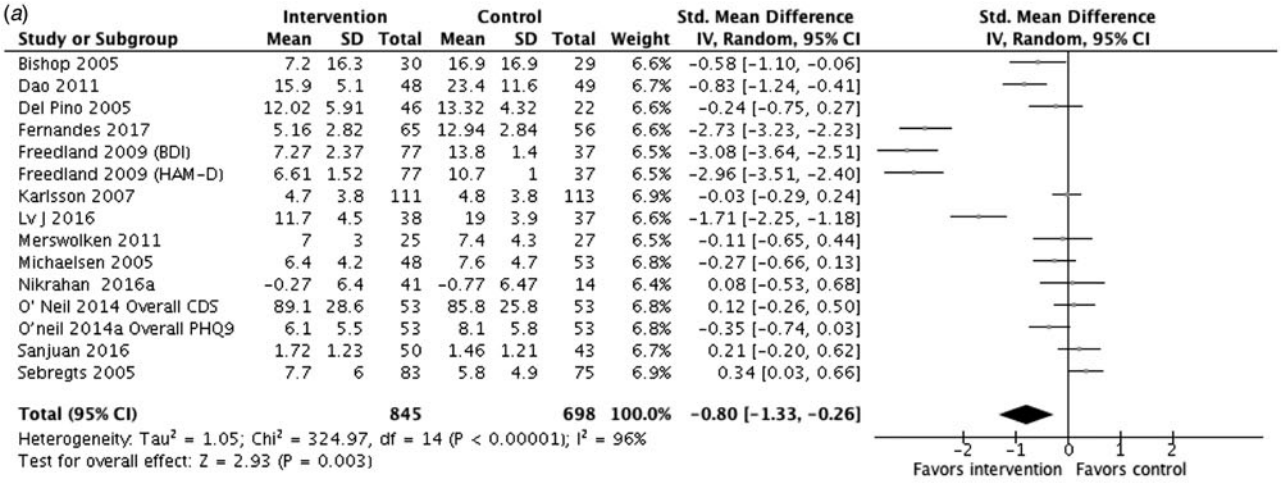
(*Continued*)

Table 1. (*Continued.*)

Author, year	Number of patients	Patient population. Diagnosis at entry	Age, mean (s.d.)	Description of interventions	Intervention duration	Outcomes	Evaluation at the end of treatment	Evaluation at the end of follow-up
Nyklíček et al. (2014)	Experimental group: *N* = 55 Control group: *N* = 52	Others: PCI – unspecified if acute or programmed	Experimental group: 55.4 (7.3), Control group: 56.3 (7.3)	CBT. Psychologist: Yes. Unicomponent. Group sessions. In person. Description: Experimental groupincluded mindfulness-based stress reduction (MBSR). Control group: self-help intervention bases on a booklet about group training written by the same psychologist.	4 weeks	Stress; Drug use; Positive and negative affect	4 weeks	No
O'Neil et al. (2014)	Experimental group: *N* = 61, Control group: *N* = 60	ACS: MI or unstable angina with clinical significant depressive symptomatology during hospitalization	Unknown	CBT. Psychologist: Yes. Multicomponent. Individual. Telephone-based. Description: Experimental group included relaxation techniques, behavioral techniques for life style modification, cognitive restructuring, motivational interviewing.	6 months	Depression; Quality of life	6 months	No
O'Neil et al. (2015)	The same as ÓNeil et al. (2014)	The same as ÓNeil et al. (2014)	The same as ÓNeil et al. (2014)	The same as ÓNeil et al. (2014)	The same as ÓNeil et al. (2014)	Depression; Stress; Quality of life	No	12 months
Rakowska (2015)	Experimental group: *N* = 41, Control group: *N* = 40	ACS (infarction)	Experimental group: 53.56 (4.58), Control group: 53.40 (4.27)	CBT. Psychologist: Yes. Multicomponent. Individual. In person. Description: Experimental group included problem solving, relapse prevention.	10 weeks	Stress; Quality of life	10 weeks	1 year and 2.5 years
Sanjuan et al. (2016)	Experimental group: *N* = 57, Control Group *N* = 51	ACS (+CHD diagnosis)	Experimental group: 54.3 (9.5) Control group: 54.5 (8.7)	PPT. Psychologist: Yes. Multicomponent. Group sessions. In person. Description: Experimental group included psychoeducation, relaxation, performance of acts of kindness, awareness of acts of gratitude, prioritizing positive thoughts and feelings.	8 weeks	Depression; Hostility; Positive and negative affect	8 weeks	No
Lv et al. (2016)	Experimental group: *N* = 38, Control group: *N* = 37	CHD + PCI, no events.	Experimental group: 52.4 (6.3), Control group: 52 (6.2)	CBT. Psychologist: Yes Multicomponent. Individual. In person. Description: Experimental group inlcuded psychoeducation, behavioral techniques for life style modification (identify and confirm treatment goals, develop plans for daily activities and track feedbacks, manage emotional and behavioral activation), cognitive restructuring.	8 weeks	Depression; Anxiety; Quality of life	8 weeks	No

Nikrahan et al. (2016)	Seligman group: *N* = 13, Lyubomirsky group: *N* = 13, Fordyce group: *N* = 15, Control group: *N* = 14	Group 1: CAD (+ CABG or PCI)	Seligman group: 55,8 (5,3), Lyubomirsky group: 59.2 (11.5), Fordyce group: 54.7 (10.1), Control group: 56.9 (6.7)	PPT. Psychologist: Yes. Multicomponent. In group In person. Description: Experimental group: (1) Lyubomirsky group: mindfulness, gratitude expression, forgiveness, commitment to goals; (2) Seligman group: positive emotions, optimism and happiness, strength, values and virtues, meaning of life, prioritizing positive thoughts and feelings; (3) Fordyce group: optimism, behavioral and social activation (increasing activity and social relationship, productivity and organizations), focusing on present, prioritizing positive thoughts and feelings.	6 weeks	Depression; Vital Satisfaction; Dispositional hope; Happiness	7 weeks	15 weeks
Fernandes et al. (2017)	Experimental group: *N* = 65, Control group: *N* = 56	ACS	Experimental group: 61.77 (12.11), Control group: 66.11 (12.11)	CBT. Psychologist: Yes. Multicomponent. Group sessions. In person. Description: Experimental group included psychoeducation, behavioral techniques for life style modification (promotion of psychosocial adjustment in post-ACS rehabilitation), cognitive techniques, relapse prevention.	1 week	Depression; Anxiety	2–3 days (hospital discharge)	1 and 2 months
Mohammadi et al. (2018)	Experimental group: *N* = 31, Control group: *N* = 30	Group 2: ACS (and clear diagnosis CHD)	Experimental group: 52.7 (5.0), Control group: 52.4 (5.9)	PPT. Psychologist: Yes. Multicomponent. Group sessions. In person. Description: Experimental group included optimism and happiness, posttraumatic growth	8 weeks	Depression; Anxiety; Dispositional Optimism; Vital satisfaction; Dispositional Hope; Happiness; Positive and negative affect	8 weeks	16 weeks

(*a*)



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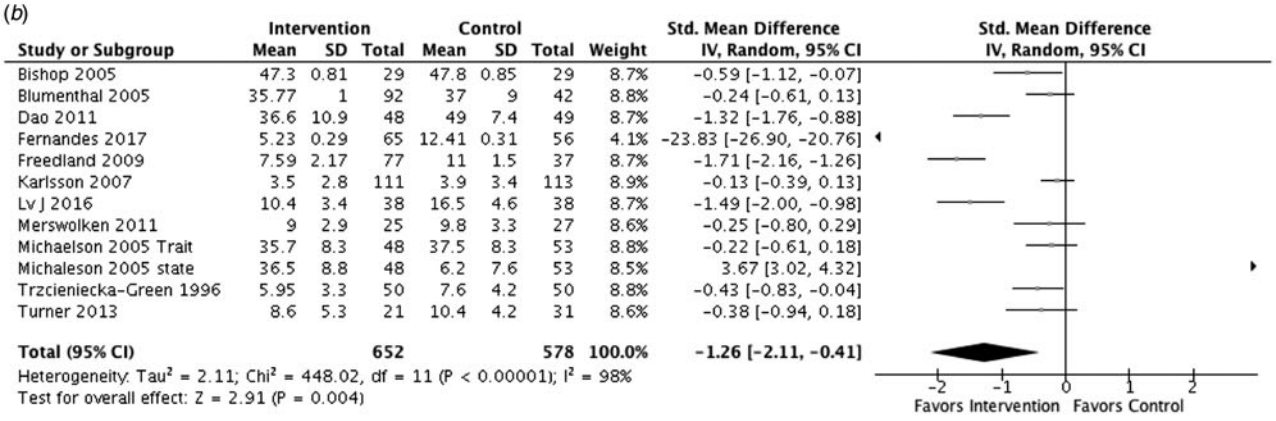

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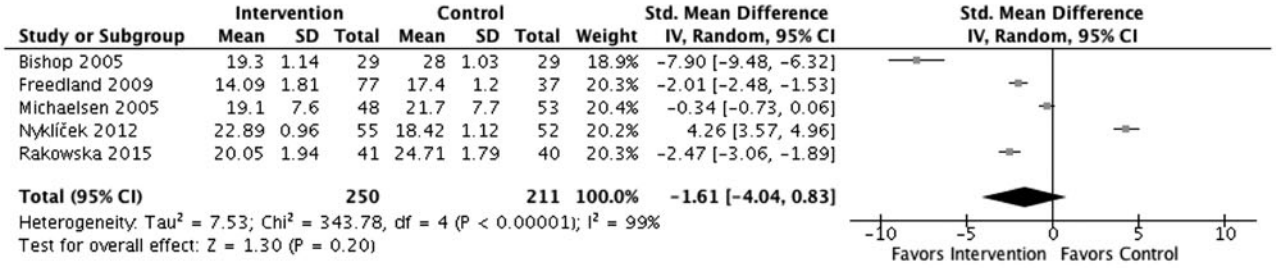

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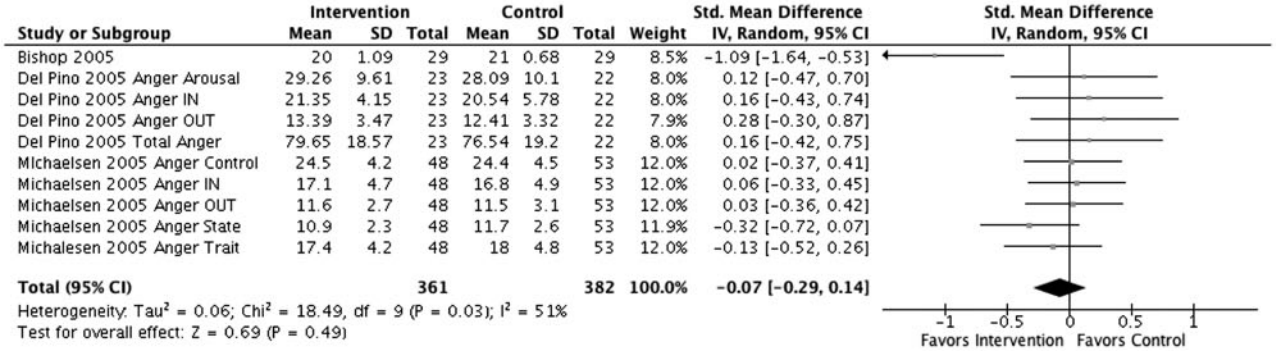

Fig. 2. Efficacy of PIs on psychological outcomes immediately after the intervention. Forest-plot showing the efficacy of PIs compared with control groups on pre-defined psychological outcomes immediately after the intervention: (*a*) Effect on depression. (*b*) Effect on anxiety. (*c*) Effect on stress. (*d*) Effect on anger. (*e*) Effect on vital satisfaction. (*f*) Effect on happiness.

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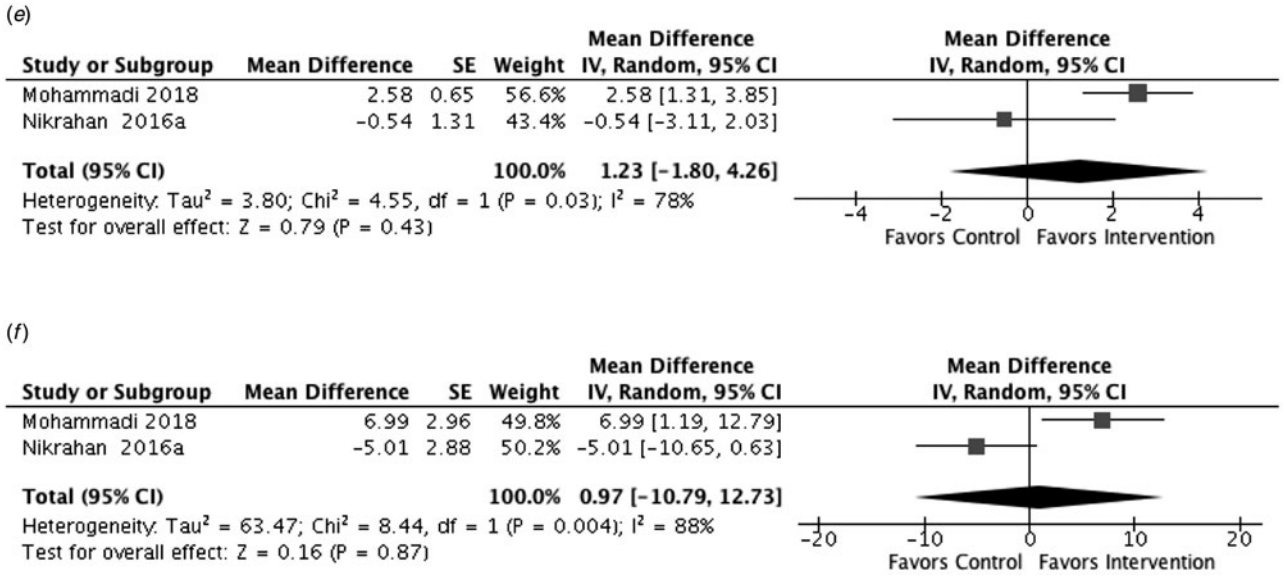

Fig. 2. Continued.

−0.60 to −0.03, $p = 0.03$, online Supplementary material Fig. S2C), and in four trials ($n = 374$), PIs significantly improved quality of life after the intervention (SMD 0.50, 95% CI 0.07–0.93, $p = 0.02$, online Supplementary material Fig. S2D). PIs did not improve daily activities (online Supplementary material Fig. S3A) or quality of life at the end of follow-up (online Supplementary material Fig. S3B), or dispositional hope at any time (online Supplementary material Figs S2E and S3C). For most outcomes, heterogeneity of effects was high.

Subgroup analyses

The effects of PIs on main outcomes were similar across most of the pre-specified subgroups. In particular, for depression, anxiety, and stress, both after treatment and at the end of follow-up (online Supplementary material Figs S4–S9). However, the improvement of anxiety after treatment was higher in ACS patients (5 trials, $n = 549$; SMD −3.29, 95% CI −4.96 to −1.611; $p = 0.0001$) compared with chronic or mixed CAD patients (7 trials, $n = 681$; SMD −0.29, 95% CI −1.34 to 0.76; $p = 0.59$; $\chi^2 = 8.85$, $p = 0.003$, online Supplementary material Fig. S6A), and in trials at high risk of bias (9 trials, $n = 928$; SMD −1.98, 95% CI −2.92 to −1.04; $p = 0.0001$) *v.* at low or unclear risk of bias (3 trials, $n = 302$; SMD 0.99, 95% CI −1.10 to 3.08, $p = 0.35$; $\chi^2 = 6.44$, $p = 0.01$, online Supplementary material Fig. S6B). Subgroups analysis by post-treatment and follow-up assessment time showed a larger reduction in anxiety at the end of treatment for treatment durations <10 weeks (6 trials, $n = 404$; SMD −4.24, 95% CI −6.24 to −2.23; $p = 0.0001$) than those with a duration ⩾10 weeks (7 trials, $n = 826$; SMD 0.08, 95% CI −0.77 to 0.92; $p = 0.004$; $\chi^2 = 15.11$, $p = 0.0001$, online Supplementary material Fig. S6C). Also, larger reduction in depression was found when follow-ups were developed in the first 6 months after the intervention (4 trials, $n = 330$; SMD −3.76, 95% CI −6.43 to −1.10; $p = 0.006$) *v.* >6 months (3 trials, $n = 389$; SMD −0.45, 95% CI −1.05 to 0.15; $p = 0.14$; $\chi^2 = 5.67$, $p = 0.02$, online Supplementary material Fig. S5C). While CBT significantly reduced depression at post-treatment (13 trials, $n = 302$; SMD −0.94, 95% CI −1.53 to −0.35; $p = 0.02$), PPT showed a neutral effect (2 trials, $n = 148$; SMD 0.17, 95% CI −0.17 to 0.51; $p = 0.003$; $\chi^2 = 10.14$, $p = 0.001$, online Supplementary material Fig. S4C). The improvement in depression after therapy was higher when PIs were provided by psychologists (11 trials, $n = 1047$; SMD −1.07, 95% CI −1.78 to −0.37, $p = 0.003$) in comparison with PIs provided by undisclosed professionals (4 trials, $n = 496$; SMD −0.01, 95% CI −0.36 to 0.33; $p = 0.94$; $\chi^2 = 7.07$, $p = 0.008$, online Supplementary material Fig. S4A). Finally, no differences according to session type (group *v.* individual) were found at any moment (online Supplementary material Figs S4E, S6D, S8C, and S9).

Discussion

Our study showed that different types of PIs can improve a number of psychological outcomes relevant to the patient´s global health and wellbeing in patients with CAD in the short- and in the mid-term. In particular, depression and anxiety improved immediately after PIs, and depression, anxiety, stress, and vital satisfaction scores significantly improved at the end of follow-up after these interventions.

Despite the relatively low number of patients and the heterogeneity of interventions, our findings show that PIs based on CBT and/or PPT are helpful in improving the patient´s psychological health, that is, improving their health in a broader way. The aims of medical therapy for CAD are improving prognosis, reducing symptoms, and improving quality of life (Knuuti et al., 2020). All established interventions – i.e. medical therapy, coronary revascularization, cardiac rehabilitation – have been tested for the improvement of clinical or biological outcomes (mortality, non-fatal clinical outcomes, symptoms, such angina presentation or functional capacity) (Ponikowski et al., 2016). However, although fostering quality of life is a central target in cardiac rehabilitation interventions as it might have a positive effect on

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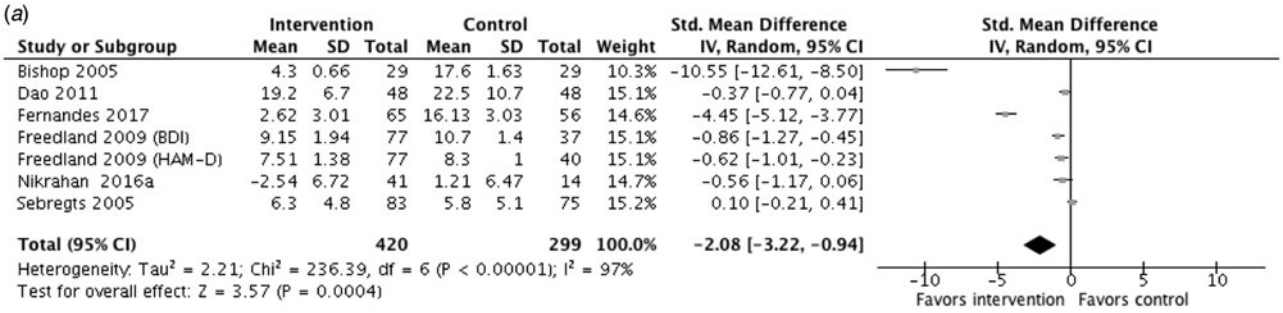

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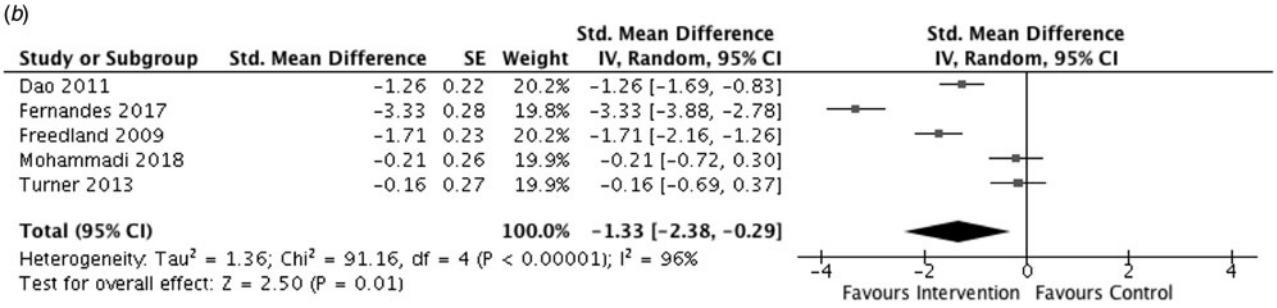

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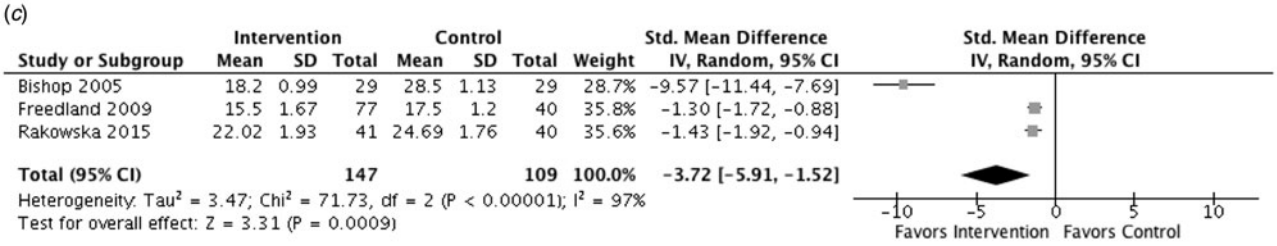

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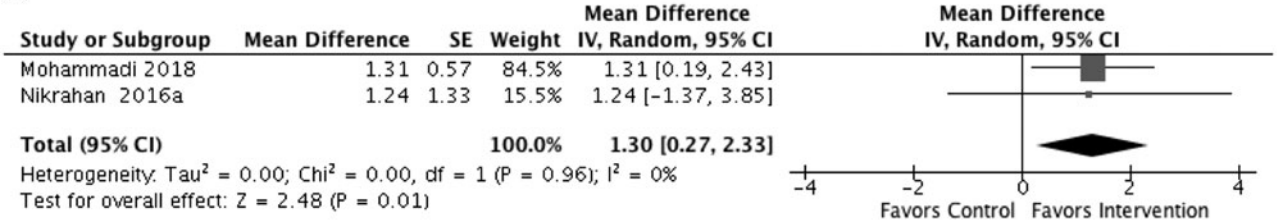

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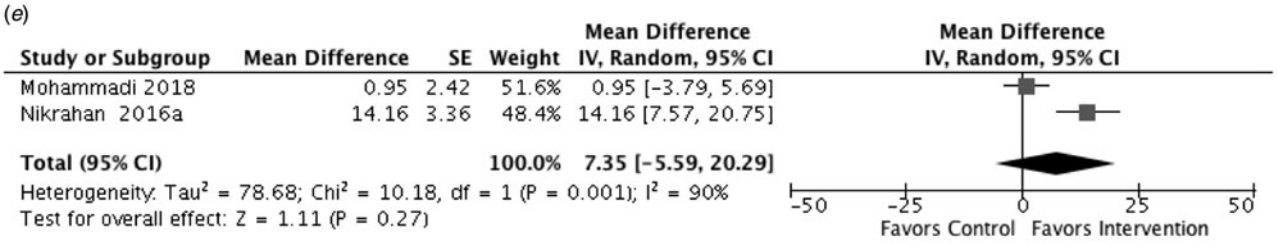

Fig. 3. Effect of PIs at the end of follow-up. Forest-plot showing the efficacy of PIs compared with control groups at the end of follow-up on the predefined psychological outcomes: (*a*) Effect on depression (average follow-up, 4.5 months). (*b*) Effect on anxiety (average follow-up, 5.6 months). (*c*) Effect on stress (average follow-up, 13 months). (*d*) Effect on vital satisfaction (average follow-up, 3.8 months). (*e*) Effect on happiness (average follow-up, 3.8 months).

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perceived wellbeing as well as on promoting treatment adherence, only a few interventions have evaluated their impact on quality of life (Riccioni et al., 2013; Stenvall et al., 2017; Weintraub et al., 2008; Zhang et al., 2018). Therefore, improving psychological outcomes is a key step for a comprehensive management of CAD from the patient´s perspective.

According to our data, PIs seemed to have positive and important effects on improving depression, anxiety, and stress not only immediately after the intervention, but also at the end of follow-up. Others meta-analyses (Dickens et al., 2013; Linden, 2000, 2013; Linden et al., 2007; Richards et al., 2018; Rutledge et al., 2013) had previously shown significant effects, although of a smaller magnitude. Indeed, our results are especially relevant because the effects on the three primary psychological outcomes (depression, anxiety, and stress) are not only significant but large after the intervention but the benefits increase at the end of follow-up, showing that PIs have long-lasting and robust beneficial effects, which are not explained by the mere course of time, when patients become more functional in their daily living and the cardiac event turns into something of the past. The implications of these results may be clinically relevant since depressive symptoms, anxiety or stress are considered risk factors for recurrent cardiac events or increased mortality risk (Arnold, Smolderen, Buchanan, Li, & Spertus, 2012; Carney & Freedland, 2017; Ossola, Gerra, De Panfilis, Tonna, & Marchesi, 2018; Tully et al., 2015). In addition, cardiac patients with depression or anxiety may be particularly compromised in their recovery (Nicholson et al., 2006; Roest et al., 2010; Rozanski, 2014).

Regarding positive psychological outcomes, this meta-analysis may be supporting the recently defined positive behavioral cardiology paradigm (Labarthe et al., 2016), as happiness and vital satisfaction showed large improvements after de intervention and at the end of follow-up, although only vital satisfaction was statistically significant at the end follow-up. The low statistical power probably explains the lack of significant effects. Nevertheless, these results should encourage psychologists and cardiologists to dedicate more energy and resources to the investigation of the effect of PPTs on psychological and clinical outcomes in CAD patients.

As noted above, compared to other narrative reviews (Linden, 2000, 2013) and meta-analyses (Dickens et al., 2013; Linden et al., 2007; Richards et al., 2018; Rutledge et al., 2013), our results show a larger magnitude of effects of PIs for improving psychological outcomes, which may be explained by the selection of only RCTs in which PIs were clearly based on empirically-based therapies, that is, the CBT paradigm (Linden, 2013), only done by Linden et al. (2007) and Dickens et al. (2013). The inclusion of the positive behavioral cardiology paradigm (Labarthe et al., 2016) as a well-established therapy paradigm specifically designed to improve positive psychological dimensions (Bolier et al., 2013; Huffman et al., 2016; Lee Duckworth et al., 2005; Seligman et al., 2005) is also new. Our meta-analysis, focusing specifically on the efficacy of PIs in improving psychological outcomes, both negative and positive, in CAD patients, clearly differentiates from previous studies focusing on quantifying the benefits of PIs on morbidity and mortality outcomes (Dickens et al., 2013; Linden et al., 2007; Richards et al., 2018; Rutledge et al., 2013), or their differential effects depending on distress reduction (Linden et al., 2007) or depression reduction (Rutledge et al., 2013). Only Richards et al. (2018) and Dickens et al. (2013) analyze their effects on some psychological outcomes. As PIs are specifically targeted to improve psychological outcomes, finding larger effects is no surprise, although this would not explain the differences found with the last Cochrane systematic review (Richards et al., 2018), where smaller but significant benefits on depression, anxiety, and stress reduction were reported. This difference may be explained by the inclusion of all kinds of PIs, while our meta-analysis selected only RCTs based on empirically supported PIs.

Although CBT- and PPT-based PIs are specifically designed to improve negative and positive psychological outcomes, respectively, the magnitude effect of PIs might be greater in CAD patients, in whom improving psychological health and wellbeing by reducing stress and negative emotions and fostering positive psychological factors could be an important target as these are linked, respectively, to a higher (Chida & Steptoe, 2009; Nicholson et al., 2006; Roest et al., 2010; Rozanski, 2014) and lower (Boehm & Kubzansky, 2012; DuBois et al., 2015; Labarthe et al., 2016) CV risk, as well as to a better quality of life (Appels et al., 2006). Therefore, CBT- and PPT-based PIs may have a positive impact on all-cause and CV morbidity and mortality, as changes in negative (Hamer & Malan, 2010; Lovallo & Gerin, 2003; Rozanski, 2014; Schwartz et al., 2003; Steptoe & Kivimäki, 2013; Wirtz & von Känel, 2017) and positive psychological factors (Labarthe et al., 2016; Rozanski, Bavishi, Kubzansky, & Cohen, 2019; Steptoe, Wardle & Marmot, 2005) may contribute modifying some clinical and CV parameters, according to Linden (2013). Although the mechanisms by which changes on psychological factors may improve clinical outcomes remain unclear, it is likely that these may have a direct effect by improving CV risk factors and, indirectly, by facilitating enjoying healthier lifestyles, social and psychological functioning (Labarthe et al., 2016; Rozanski, 2014; Rozanski et al., 2019; Steptoe & Kivimäki, 2013; Steptoe, Wardle, & Marmot, 2005; Wirtz & von Känel, 2017; Lovallo & Gerin, 2003; Schwartz et al., 2003; Hamer & Malan, 2010), and improving adherence.

Compared with PPT, CBT seems to improve depression after the intervention, which could be explained by the fact that CBT is a treatment package specifically designed to modify negative psychological factors (Blagys & Hilsenroth, 2002), such as depression, whereas PPTs are specifically aimed at improving positive psychological dimensions (Lee Duckworth et al., 2005; Seligman et al., 2005). Therefore, PPT may not be able to improve depression by itself. Unfortunately, the information is scarce and analyses could only be done for depression. Future research is needed to clarify the differential effect of CBT and PPT on CAD patients.

Furthermore, not only its role but the way PIs should be given and by whom are relevant questions. Although weak, our results show some evidence suggesting that PIs developed by well-trained health psychologists may have stronger effects. This seems to be particularly true in the effect on post-treatment depression benefits, a prevalent complication after myocardial infarction (Pino, Zuo, Borba, Henderson, & Kalesan, 2018; Smolderen et al., 2015, 2017), what is logical as they are professionals specifically trained for it. Unfortunately, and despite its relevance, this information was lacking in a majority of the studies reviewed, which may explain the weakness of the association found. The role of the incorporation of trained health psychologists to cardiovascular care teams to improve both psychological and clinical outcomes for CAD and other high-risk patients needs further attention and prospective and rigorous evaluation.

Acute CAD patients seem to have greater benefits in anxiety reduction after PIs. This is logical as ACS is associated with

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acute increases in the levels of anxiety and stress after the acute phase (Xu et al., 2017). However, the benefit was observed only immediately after the intervention with no persistence at the end of follow-up. Whether this is due to the described spontaneous time-dependent improvement of these psychological situations after ACS (Xu et al., 2015) or the lack of durability of the effects of PIs needs further study.

Finally, PIs in which the follow-up assessment occurred <6 months after the intervention showed significant benefits in depression compared with those with longer follow-ups. Reductions in anxiety were also larger when the intervention duration was <10 weeks, which is consistent with the findings by Linden (2013), where the beneficial effects of PIs fade away with time. This points out the importance of maintenance of the benefits as one important target for PIs.

Our meta-analysis is the first one to analyze the effects of PIs on positive psychology outcomes, including only empirically-supported PIs for CAD patients (Linden, 2013), an inclusion criterion only in a minority of prior studies (Dickens et al., 2013; Linden et al., 2007). Our meta-analysis is also new on its exclusive focus on psychological outcomes in CAD patients while the majority of prior publications mainly focused on morbidity and mortality or on the differential effects on these outcomes depending on distress reduction (Linden et al., 2007) or depression reduction (Rutledge et al., 2013). Only Richards et al. (2018) specifically evaluated the effects of PIs on stress, anxiety, and depression, and Dickens et al. (2013) on depression, but they did not study positive psychological outcomes.

A number of limitations should be acknowledged. First, the number of studies and the absolute number of patients enrolled is small. Second, PIs included a large variety of interventions with important differences in types, methods, professionals involved and duration as well as differences in outcomes and methods to measure the results. This information is not only diverse but is often lacking. Therefore, conclusions apply to a heterogeneous group in which differences in results may be explained by a variety of reasons. Third, our study confirms the important risk of bias to which these studies are subjected due to the impossibility of blinding patients or researchers to the intervention. This limitation can only be partially overcome by the analysis of results blinded to the intervention received by each group, a technique that should be mandatory in this kind of studies. And fourth, this meta-analysis does not address the efficacy of PIs on clinical outcomes, which will be the aim of a future analysis.

Conclusion

This systematic review and meta-analysis shows that PIs are effective in improving depression and anxiety immediately after the intervention, and may have a positive impact at the end of follow-up improving also stress and the level of vital satisfaction. However, much more research is needed in the field, with higher methodological standards in the trials, including detailed information of the type of intervention, professionals involved, timing and duration. Our results suggest that there is a role of clinical and health psychology for improving the care of patients with CAD and this option should be considered in cardiology departments.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0033291720000598

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