



Review article

Psychosocial treatment on psychological symptoms, adherence, and physiological function on transplanted patients: A systematic review and metanalysis

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A B S T R A C T

Objective: Transplantation represents an important source of hope for the candidates and produces an intense emotional effect. Psychosocial interventions can be helpful in all transplantation stages to better manage this extraordinarily stressful situation. Aim of the work is to verify the effects of the psychosocial interventions on recipients on psychological symptoms, medical adherence and transplanted solid organ functioning.

Methods: This work adhered to PRISMA, STROBE, Cochrane and New Castle Ottawa bias scales and it is registered in PROSPERO. Inserting “Transplant” and “Psychological intervention” as key words in PubMed, Psycinfo, Cochrane database resulted 977 studies from 2001 to 2021. A systematic review and metanalyses were processed on nineteen randomized controlled trials and observative prospective cohort studies. The difference between pre- and post- psychosocial intervention assessment on the psychological variables, medical adherence, and organ functioning outcome was processed.

Results: Main findings showed that the psychosocial interventions were effective on depression (0.62; CI: 0.32–0.92) and anxiety on kidney recipients (0.49; CI: 0.17–0.81), and on anxiety on heart recipients, mainly when administrated after the surgery (0.68; CI: 0.30–1.06). Moreover, the findings showed a lack of studies on the effectiveness of the psychosocial intervention on organ functioning.

Conclusion: The work highlighted the effectiveness of the psychosocial interventions on psychological outcome, particularly after the surgery and the need to address the research on the evaluation of the effectiveness of the psychosocial interventions on the organ functioning. The findings suggest to integrate the transplantation procedures with psychosocial interventions considering the different needs of recipients in relation to the specific transplanted organ.

1. Introduction

Transplantation is an invasive surgery that involves the replacement of a non-functional organ with a functional one [1], and it represents an important source of hope for many patients [2]. The transplant surgery commonly produces an intense emotional effect, with worries, alteration of the body image, pain, fear of possible organ rejection, and manifestations of psychological symptoms, such as anxiety and affective disorders [3]. These emotional and psychological manifestations are similar

in patients receiving solid organ transplants, but there is a growing literature showing that the anxiety disorders appear to be particularly associated with lung and heart transplant [4–6]. Moreover, several studies reported that stress, negative emotions, poor coping resources and dysfunctional lifestyle occurring in the different phases of the transplant process can have a significant impact on the recovery and rehabilitation of the transplanted patients, resulting in negative health outcomes posttransplant [7,8].

Previous research suggested that, after the organ transplant, patients

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usually go through an improvement in physical and social functioning, returning to daily activities, but they do not experience a consistent positive change in psychological outcomes [9].

Psychosocial interventions to the transplanted recipients could be important in order to achieve the reduction of psychosocial distress, and the improvement of personal functioning and the general perception of health [9,10]. Psychosocial interventions, that comprise interventions focused on psychological or social support, can be helpful in all transplantation stages enabling patients to better manage this extraordinarily stressful situation, as well as to promote and improve a good adherence in dialysis [11,12], to the medical cares, and to the adequate lifestyle indications [13,14]. Moreover, applying psychosocial interventions in all stages of the transplantation process (pre- and -post transplant) could allow to identify possible risk factors, and to prevent negative outcome of the surgery [3]. During the transplant process, receiving psychosocial support could be an important protective factor also for the patients awaiting the organ transplant who are handling with a stressful situation of the future uncertainty, that could increase anxious and depressive symptoms [15,16]. This symptomatology could be a predictor of post-transplant negative outcomes, increasing the possibility of rejection episodes and mortality [17,18].

Through a psychosocial intervention, not only the symptoms could improve, but also the patient's adherence to the therapeutic and medical indications [3]. The medical adherence, definable as the extent to which a person's behavior coincides with medical or therapeutic advice, is pivotal to prevent organ rejection in every type of solid organ transplant [9]. There are few studies focused on the medical adherence and the organ functioning after transplantation, however it has been found that psychological symptoms and insecure attachment style can be risk factors for the aforementioned outcomes, resulting in an increased risk of organ rejection [12,19].

Although the relevance of psychosocial interventions in solid organ transplantation is well recognized [9], evidence of their efficacy to improve medical adherence and organ functioning after transplantation are scarce.

The aim of the work is to verify the effects of the psychosocial interventions on transplanted patients. We want to test the effects of psychosocial interventions on psychological symptoms, medical adherence and on transplanted solid organ functioning.

2. Method

This study adhered to the preferred reporting items for systematic review and meta-analysis PRISMA guidelines (Appendix A of the Supplementary data) and it was registered with PROSPERO international prospective register of systematic review and meta-analysis (id. CRD42020211247-27-10-2020).

2.1. Search strategy

A literature search was conducted using PubMed, Psycinfo and Cochrane database. In accordance with the PICO framework (patient problem or population; intervention; comparison or control and outcome) the search strategies combined keywords such as: "Transplant" and "Psychological intervention". The literature search covered a period of publication from 2001 to 2021. The emerging records were analyzed for title, abstract and full text. Moreover, the reference lists of all selected articles and relevant systematic reviews were manually screened to identify any further references for possible inclusion.

2.2. Inclusion criteria

Only original research articles were considered for the inclusion in the systematic review and the meta-analysis, no limitations were set for study design, randomized controlled trial (RCT) and observational prospective cohort (OPC), and ethnicity. The inclusion criteria for the

studies were: 1) to include patients underwent a solid organ transplant or being in the waiting list for the solid organ transplantation surgery; 2) to provide at least one psychological, organ functioning, or adherence outcome assessed pre- and post- psychosocial interventions applied at any phases of the transplantation process (pre- and post- surgery). The psychosocial interventions comprise any psychological treatments, psychoeducational program, and social supports.

2.3. Exclusion criteria

The studies that did not include transplantation of solid organs, studies without psychosocial intervention, and studies not written in English language were excluded. Reading the full texts, the studies that did not report a baseline of the psychosocial intervention, and that were conducted on populations under 18 years were excluded.

2.4. Study selection

Following the search and exclusion of duplicates, two reviewers (authors DS and CC) independently screened the eligibility of the articles first on the title and the abstract, and on the full text according to the inclusion criteria. Disagreements were resolved by reviewer PA. According to the best practices for conducting a systematic review [20], the review team included at least one person with methodological expertise in conducting systematic reviews (PA and CL) and at least two experts on the topic under review (DS, CC, and GRP).

2.5. Data extraction and synthesis

Authors SD and CC independently extracted the following data from the included studies: first author and year of publication, Country, aim of the study, research design, kind of psychosocial intervention (Table 1). For each study, the samples or arms (groups of participants underwent or not to the psychosocial intervention) were differentiated in experimental samples, active control samples (participants underwent a psychosocial intervention as confrontation with another intervention), and control samples. For each sample the number and the age of participants were extracted (Table 1). Moreover, for each sample, the trials (sample or arm with a pre and post evaluation on a specific outcome) were identified (Table 1). Moreover, for each study, the assessment pre- and post- psychosocial intervention without comparison with control samples, the assessment pre- and post- psychosocial intervention and comparison with control samples, and follow-up points were reported (Table 1).

Moreover, further information was extracted (Table 2): study inserted in the meta-analysis, phase of the application of the psychosocial intervention (before or after the transplantation), length of the psychosocial intervention, who carried out the psychosocial intervention, time elapsed between application of the psychosocial intervention and organ transplant, assessment of the pre- and post- psychosocial intervention before the surgery transplant, assessment of the pre- and post- psychosocial intervention after the surgery transplant, pre-transplant psychosocial intervention with post-transplant assessment.

The two reviewers discussed any discrepancies and, if necessary, consulted a third team member (author CL) to reach a final decision.

2.6. Data analysis

For the systematic review, a qualitative analysis was processed through a distribution of the frequencies (Appendix A of the Supplementary data) and of the percentages of the trials with significant (improvement or worsening) and not significant changes (post- vs pre- psychosocial intervention) per different kind of treatments and solid organ. The qualitative analyses were performed considering the number of studies, the number of samples, and the number of trials. The samples considered were the experimental and the active control ones.

Table 1
Characteristics of the included studies.

Author, years	Country	Study aim	Study design	Type of psychological intervention	Assessment pre-post psychosocial intervention without comparison with control sample	Assessment pre-post psychosocial intervention and comparison with a control sample	Follow-up	Number of participants for the experimental sample, active control sample, and control sample, and (number of trials)	Age (mean and standard deviation)	Psychological outcome	Adherence outcome	Organ functioning outcome	Measure of psychological outcome	Measure of adherence	Kind of solid organ transplantation
Bailey et al., 2017 [21]	USA	To test the effectiveness of a telephone-delivered self-management intervention designed to teach patients and their caregiver cognitive behavioral coping skills and symptom management strategies	RCT	Experimental: Self-management telephone intervention Active control: telephone-delivered liver disease education		X (active control)	10 and 12 weeks	Experimental: 33 (2) Active control: 41 (2)	Experimental: 56.4 ± 9.9 Active control: 55.6 ± 10.0	Depression, Anxiety			CES-D, POMS anxiety subscale		Patients awaiting liver transplant
Baines et al., 2004 [22]	UK	To compare the effects of individual therapy vs. group therapy on depression.	RCT	Experimental: Individual systemic integrative psychotherapy Active control: group systemic integrative psychotherapy		X (1 active control, 1 control)	3–6–9–12 months	Experimental: 45 (1) Active control: 37 (1) Control: 37 (1)	Experimental: 36.2 ± 8.9 Active control: 39.1 ± 11.1 Control: 36.6 ± 11.9	Depression			BDI		Kidney transplant
Cukor et al., 2017 [23]	USA	To compare the adherence promotion program vs. standard care on medication adherence outcome	RCT	Experimental: Cognitive behavioral therapy and Motivational Interviewing		X		Experimental: 15 (1) Control: 18 (1)	Experimental: 55.6 ± 10.7 Control: 49.1 ± 12.3		X			Phone Pill Counts	Kidney transplant
Febrero et al., 2018 [24]	ES	To analyze preliminary results of the influence of group psychotherapy on the quality of life of patients on the LT waiting list	RCT	Experimental: Psychotherapy on emotions and feelings	X		6 months	Experimental: 7 (1)	From 49 to 63	QOL			NHP		Patients awaiting liver transplant
Febrero et al., 2019 [25]	ES	To analyze preliminary results of the influence of group psychotherapy on the quality of life of patients on the LT waiting list	RCT	Experimental: Psychotherapy on emotions and feelings		X	6 months	Experimental: 7 (1) Control: 5 (1)	From 49 to 63	Depression			BDI		Patients awaiting liver transplant
Gross et al., 2017 [26]	USA	To test the effectiveness of telephone-adapted	RCT	Experimental: Telephone-based (MBSR)		X (active control)	6 months	Experimental: 24 (4)	Experimental: 52.6 ± 12.6	Depression, Anxiety, QOL (physical)			CES-D STAI SF-12		Patients awaiting kidney transplant

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Table 1 (continued)

Author, years	Country	Study aim	Study design	Type of psychological intervention	Assessment pre-post psychosocial intervention without comparison with control sample	Assessment pre-post psychosocial intervention and comparison with a control sample	Follow-up	Number of participants for the experimental sample, active control sample, and control sample, and (number of trials)	Age (mean and standard deviation)	Psychological outcome	Adherence outcome	Organ functioning outcome	Measure of psychological outcome	Measure of adherence	Kind of solid organ transplantation
Gross et al., 2010 [27]	USA	MBSR on kidney transplant candidates To assess the effectiveness of MBSR in reducing symptoms of anxiety, depression on transplanted patients	RCT	Active control: Telephone-based support group Experimental: Telephone-based (MBSR) Active control: Health Education (active control)		X (active control)	8 weeks 6 months and 1 year	Active control: 27 (4) Experimental: 61 (3) Active control: 54 (3)	Active control: 54.6 ± 11.7 Experimental: 55.0 ± 11.3 Active control: 52.0 ± 10.4	and mental components) Depression, Anxiety, QOL			CES-D STAI SF-12 SF-36		Solid organs
Hedayati et al., 2017 [28]	IR	To test the effectiveness of the expressive emotion therapy on kidney transplanted patients	RCT	Experimental: Expressive emotion therapy		X	4 and 12 weeks	Experimental: 34 (2) Control: 30 (2)	Experimental: 39.3 ± 12.9 Control: 40.8 ± 14.4	Depression, Anxiety			GHQ-28		Kidney transplant
Hogan et al., 2015 [29]	USA	To develop a coping based medical music therapy protocol that combines coping-infused dialogue (CID) with patient-preferred live music (PPLM) and measure the effects of the resulting CID-PPLM protocol on mood (positive and negative affect) and pain in hospitalized transplanted patients.	RCT	Experimental: combines coping-infused dialogue (CID) with patient-preferred live music (PPLM) and measure the effects of the resulting protocol on mood (CID-PPLM)		X		Experimental: 12 (2) Control: 13 (2)	Experimental: 51.9 ± 7.3 Control: 50.4 ± 10.7	Depression (positive mood and negative mood)			GMS		Solid organ (kidney, liver, pancreas, multiple organs)
Rodrigue et al., 2005 [30]	USA	To evaluate the effectiveness of telephone-based QOLT in enhancing QoL reducing mood disturbance, and improving social intimacy among wait listed lung transplanted patients	RCT	Experimental: telephone-based QOLT Active control: telephone-based supportive therapy		X (active control)	1 and 3 months	Experimental: 17 (1) Active control: 17 (1)	Experimental: 48.4 ± 10.0 Active control: 49.0 ± 11.3	QOL			QOLI		Patients awaiting lung transplant
Rodrigue et al., 2011 [10]	USA	To test the effectiveness of telephone-based	RCT	Experimental: telephone-based QOLT		X (1 control, 1 active control)	12 weeks	Experimental: 20 (3) Active control:	Experimental: 53.2 ± 11.1 Active control:	Depression, Anxiety, QOL			POMS HSCL QOLI		Patients awaiting kidney transplant

(continued on next page)

Table 1 (continued)

Author, years	Country	Study aim	Study design	Type of psychological intervention	Assessment pre-post psychosocial intervention without comparison with control sample	Assessment pre-post psychosocial intervention and comparison with a control sample	Follow-up	Number of participants for the experimental sample, active control sample, and control sample, and (number of trials)	Age (mean and standard deviation)	Psychological outcome	Adherence outcome	Organ functioning outcome	Measure of psychological outcome	Measure of adherence	Kind of solid organ transplantation
		QOLT in enhancing QoL reducing mood disturbance, and improving social intimacy in adults approved for kidney transplant		Active control: telephone-based supportive therapy Control: Standard care				19 (3) Control: 17 (3)	48.6 ± 11.9 Control: 52.7 ± 12.7						
Baines et al., 2002 [31]	UK	Use psychotherapy principles to understand and intervene in emotional issue in recipients of cadaver kidney transplants	OPC	Experimental: Individual short-term psychotherapy	X		3–6–9-12 months	Experimental: 49 (1)	Experimental: 36.2 ± 8.9	Depression			BDI		Kidney transplant
Craig et al., 2017 [32]	CAN	To evaluate the use of the coping skills group therapy intervention to reduce anxiety, depression, and to increase QoL and healthy coping skills on patients destined for kidney transplantation	OPC	Experimental: Coping skills group therapy	X		1 month	Experimental: 20 (3)	Experimental: 46.4 (Awaiting kidney transplant) Experimental: 48.8 (Awaiting liver transplant); Experimental Total: 47.9	Depression, Anxiety Coping			HAM-D HAM-A Brief COPE		Patients awaiting kidney transplant
Dew et al., 2004 [33]	USA	To assess the effectiveness of an internet-based psychosocial intervention in improving mental health, QoL and medical compliance	OPC	Experimental: Internet-based psychosocial intervention		X	4 and 6 months	Experimental: 20 (4) Control: 34 (4)	Experimental: 45.8 Control: 57.5	Depression, anxiety, QOL	X		SCL-90 SF-36	5 specific compliance areas: 1) missed medications 2) missed clinic appointments 3) missed blood work 4) physical exercise 5) failed to follow diet	Heart transplant
Jutagir et al., 2018 [34]	UK	This stage IA psychotherapy development project (liver SMART program) developed and tested the feasibility, acceptability,	OPC	Experimental: Liver SMART program adapted the Stress Management and Relaxation Training for women with breast	X			Experimental: 17 (2)	Experimental: 55.07 ± 7.24	Depression Anxiety			BDI II BAI		Liver transplants

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Table 1 (continued)

Author, years	Country	Study aim	Study design	Type of psychological intervention	Assessment pre-post psychosocial intervention without comparison with control sample	Assessment pre-post psychosocial intervention and comparison with a control sample	Follow-up	Number of participants for the experimental sample, active control sample, and control sample, and (number of trials)	Age (mean and standard deviation)	Psychological outcome	Adherence outcome	Organ functioning outcome	Measure of psychological outcome	Measure of adherence	Kind of solid organ transplantation
Madson, et al., 2010 [35]	USA	To assess the impact of music therapy on anxiety, relaxation, pain and nausea levels on adult patients transplant	OPC	Experimental: Music Therapy	X			Experimental: 58 (1)	From 18 to 70 years old	Anxiety			Not validated questionnaire		Solid organs
Ordin, 2016 [36]	TUR	To examine the effect of support group intervention on the physical, psychosocial and social adaptation of liver transplant recipients	OPC	Experimental: Not specified therapy		X	3 months	Experimental: 35 (1) Control: 38 (1)	Experimental: 52.4 ± 10.4 Control: 50.2 ± 11.5	QOL			SF-36		Liver transplant
Stonnington et al., 2016 [37]	USA	To evaluate the feasibility, interest, acceptance, and stress-related outcomes with participation in a 6-week mindfulness-based resilience training class for transplant solid organ patients, and to test whether patients would be accepting of and benefit from an intervention direct at a mix of these patients	OPC	Experimental: Mindfulness based resilience training (MBRT)	X		6 week and 3 months	Experimental: 26 (4)	Experimental: 58.1 ± 9.3 (pretransplant) Experimental: 53.3 ± 14.8 (posttransplant)	Depression, Anxiety, QOL (physical and mental components)			PHQ-9 GAD-7 SF-36		Solid organ (kidney, liver and pancreas transplants)
Triffaux et al., 2001 [38]	BE	To analyze the evolution of psychological scores in heart transplanted patients who	OPC	Experimental: Not specified therapy	X		6 months	Experimental: 15 (2)	Experimental: 53.3 ± 9.6	Depression, anxiety			BDI STAI		Heart transplant

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3.3. Characteristics of the included studies in the systematic review

The systematic review included 19 studies, 11 RCT with 35 trials and 8 OPC with 18 trials. The number of samples and participants of each study was reported in Table 1. Gender and age were specified in all the RCT studies and in 7 OPC studies; the 11 RCT studies included 336 females and 363 males, the 7 OPC studies included 109 females and 179 males. The range of age of the RCT studies and the OPC studies was 36–70 years.

The 53 trials included in the systematic review were differentiated in trials with significant pre vs. post comparison (improvement or worsening) or non significant in Table 3. The more representative outcomes were the psychological variables (51/53 trials): the depression was considered in 20/51 trials coming from 14/19 studies, the anxiety was considered in 15/51 trials coming from 11/19 studies, the quality-of-life was considered in 15/51 trials coming from 8/19 studies, and the coping was considered in 1/51 trial coming from 1/19 studies. The adherence outcome was considered in 2/53 trials coming from 2/19 studies. There were not studies, samples, or trials related to the functionality of the transplanted organ. Total number of trials for each specific organ were: 23 for kidney, 6 for heart, 9 for liver, 2 for lung, 6 for solid organs and 7 for not specified organ.

The psychosocial interventions were categorized in four treatment categories: dynamic psychological therapies (short term psychotherapy, individual systemic integrative therapy, group systemic integrative therapies, short psychotherapy expressive emotionality, psychotherapy on emotions and feelings); cognitive behavioral therapies (CBT) (coping skills group, classic CBT, health education, liver disease education); supportive therapies (quality-of-life therapy, classic supportive therapy, telephone adapted mindfulness stress reduction, telephone-based support group, music therapy, self-management phone intervention, internet-based intervention, combines coping-infused dialogue, mindfulness resilience training liver SMART program adapted the Stress management and relaxation training for women with breast cancer program) and other not specified therapies by the articles. The psychosocial interventions were conducted by several professionals: by psychologists in 9 studies, by nurses in 1 study, by peer facilitators in 1 study, by music therapists in 2 studies, by social workers in 4 studies, by psychiatrists in 1 study, by therapists trained in mindfulness programs in 2 studies, by therapists specialized in CBT in 1 study, by therapists specialized in integrative systemic therapies in 1 study, and by practitioners authorized to provide psychosocial intervention in 1 study.

The dynamic therapies were performed in: 4 RCT studies with 130 participants (93 of the experimental sample and 37 of the active control one) for 6 trials; and 1 OPC study with 49 participants of the experimental sample for 1 trial. The CBT were performed in: 3 RCT studies with 102 participants (48 of the experimental sample and 54 of the active control one) for 6 trials; and 1 OPC study with 20 participants of the experimental sample for 3 trials. The supportive therapies were performed in: 6 RCT with 238 participants (134 of the experimental sample and 104 of the active control one) for 23 trials; and 4 OPC studies with 121 participants of the experimental sample for 11 trials. The studies that performed not specified therapies were 2 OPC with 50 participants of the experimental sample for 3 trials.

3.4. Psychological outcome in the systematic review

3.4.1. Depression, anxiety, quality-of-life and coping

The measures applied were Beck Depression Inventory (BDI) in 5 studies, Hamilton Depression Rating Scale (HAM-D) in 1 study, Center of Epidemiologic Studies-Depression Scale (CES-D) in 3 studies, Global Mood Scale (GMS) in 1 study, Beck Anxiety Inventory (BAI) in 1 study, Generalized anxiety disorder (GAD) in 1 study, Hamilton Anxiety Rating Scale (HAM-A) in 1 study, State-Trait Anxiety Inventory (STAI) in 3 studies, Profile of Mood States (POMS) in 2 studies, Hopkins Symptom Checklist-25 (HSCL) in 1 study, General Health Questionnaire (GHQ) in

2 studies, Symptom-Checklist-90 (SCL-90) in 2 studies, Quality of Life Inventory (QOLI) in 2 studies, 12 Item Short Form Health Survey (SF-12) in two studies, 36 Item Short Form Health Survey (SF-36) in 4 studies, Nottingham Health Profile (NHP) in 1 study, Patient Health Questionnaire (PHQ) in 1 study, and the Coping Orientation to the problem Experienced (COPE) in 1 study. On the 51 trials 32 showed a significant improvement: 15/20 trials on depression outcome (75%), 9/15 trials on anxiety (60%), 7/15 trials on quality-of-life (47%), 1/1 trial on coping (100%) (Table 3).

Dynamic therapies produced improvements on the depression outcome in 4/4 trials of kidney transplanted patients; on 1/1 of trial of liver transplanted patients; and on the anxiety outcome in 1/1 trial of kidney transplanted patients. Moreover, the dynamic therapies did not produce significant effects on quality-of-life in 1/1 trial of liver transplanted patients.

Cognitive behavioral therapies produced improvements on the depression outcome in 1/1 trial of kidney transplanted patients, and in 1/1 trial of not specified transplanted patients; on the anxiety outcome in 1/1 trial of kidney transplanted patients; on quality-of-life outcome in 1/1 trial of not specified transplanted patients; and on the coping outcome in 1/1 trial of kidney transplanted patients. Moreover, cognitive behavioral therapies produced not significant effects on the depression outcome in 1/1 trial of liver transplanted patients; and on anxiety outcome in 1/1 trial of liver transplanted patients, and in 1/1 trial of not specified transplanted patients.

Supportive therapies produced improvements on depression outcome in 2/4 trials of kidney transplanted patients, in 1/1 trial of heart transplanted patients, in 1/1 trial of not specified transplanted patients and in 3/3 trials of solid organs transplanted patients; on anxiety outcome in 2/4 trials of kidney transplanted patients, in 1/1 trial of heart transplanted patients, in 1/1 trial of solid organ transplanted patients, and 2/2 trials of not specified transplanted patients; on quality-of-life outcome in 1/6 trial of kidney transplanted patients, in 1/1 trial of heart transplanted patients, in 1/2 trial of lung transplanted patients, in 1/2 trial of solid organ transplanted patients and in 1/1 trial of not specified transplanted patients. Moreover, supportive therapies produced not significant effects on depression outcome in 2/4 trials of kidney transplanted patients, and in 2/2 trials of liver transplanted patients; on anxiety outcome in 2/4 trials of kidney transplanted patients, and in 2/2 trials of liver transplanted patients; and on quality-of-life outcome in 5/6 trials of kidney transplanted patients, in 1/2 trial of lung transplanted patients, and in 1/2 trial of solid organ in transplanted patients.

Not specified treatments produced improvements on depression outcome in 1/1 trial of heart transplanted patients; on anxiety outcome in 1/1 trial of heart transplanted patients; and on quality-of-life outcome in 1/1 trial of liver transplanted patients.

There were not trials that showed a worsening on any outcome.

3.5. Adherence outcome in the systematic review

Only two studies measured the adherence outcome. The first study (RCT) [23] assessed the adherence through phone pill counts method, the second study (OPC) [33] through a not specified interview addressing five elements of patients' adherence to medical regimen (missed medications, missed clinic appointments, missed blood work, physical exercise, and failed to follow diet). 1/2 trial showed a significant improvement (50%) (Table 3).

Cognitive behavioral therapies produced an improvement on adherence outcome in 1/1 trial of kidney transplanted patients, and supportive therapies did not produce a significant effect in 1/1 trial of heart transplanted patients (Table 3).

3.6. Organ functioning in the systematic review

At today there are not studies and trials that considered the organ

Table 2
Studies included in the systematic review differentiated for study design and time features of the psychosocial intervention.

Author, years	Study design	Study inserted in the meta-analysis	Phase of application of the psychological intervention	Length of the psychological intervention and -who carries out it	Months between psychological intervention and transplant	Psychological intervention assessment performed before the transplant	Psychological intervention assessment performed after the transplant	Pre-transplant psychological intervention with post-transplant assessment
Bailey et al., 2017 [21]	RCT		Before liver transplant	6 weekly session (30 min each) -nurse or social worker	Not reported	X		
Baines et al., 2004 [22]	RCT	X	After kidney transplant	12 weekly sessions -therapist trained in systemic integrative psychotherapy	3 months		X	
Cukor et al., 2017 [23]	RCT		After kidney transplant	2 sessions (2 h each) held within 1 or 2 weeks of each other -psychologist	Not reported		X	
Febrero et al., 2018 [24]	RCT		Before lung transplant	12 sessions biweekly (150 min) -psychologist and social worker trained in psychotherapy	Not reported	X		
Febrero et al., 2019 [25]	RCT		Before liver transplant	12 sessions biweekly (150 min) -psychologist and social worker trained in psychotherapy	Not reported	X		
Gross et al., 2017 [26]	RCT	X	Before kidney transplant	8 weekly session (2.5 h each) and a day-long retreat -mindfulness teacher for the experimental sample and experienced group facilitator for the active control sample	Not reported	X		X
Gross et al., 2010 [27]	RCT		After kidney, heart, lung, liver and kidney/pancreas transplants	8 weekly session (2.5 h each) and a day-long retreat -mindfulness teacher for the experimental sample and trained peer leaders supervised by a psychologist for the active control sample	Not reported		X	
Hedayati et al., 2017 [28]	RCT	X	After kidney transplant	Daily sessions held in a week (15 min per day) -expressive writing	Not reported		X	
Hogan et al., 2015 [29]	RCT		After solid organ transplant	Single session (30 min) -music therapist	No		X	
Rodrigue et al., 2005 [30]	RCT		Before lung transplant	8–12 weekly sessions -psychologist	Not reported	X		
Rodrigue et al., 2011 [10]	RCT	X	Before kidney transplant	8 weekly sessions held for 2 months -psychologist and social worker	Not reported	X		
Baines et al., 2002 [31]	OPC		After kidney transplant	12 weekly sessions -therapist trained in systemic integrative psychotherapy	3 months		X	
Craig et al., 2017 [32]	OPC	X	Before kidney or Liver transplants	8 weekly sessions (2 h each) -practitioner authorized to provide psychosocial intervention	Not reported	X		
Dew et al., 2004 [33]	OPC	X	After heart transplant	Weekly sessions for at least 4 months -psychologist	6–36 months		X	
Jutagir et al., 2018 [34]	OPC		Before liver transplant	8 weekly sessions lasting 60 min -therapist specialized in cognitive behavioral therapy and behavioral medicine	3 months	X		
Madson et al., 2010 [35]	OPC	X	After kidney, liver, heart, lung and pancreas transplants	One single session of 15–35 min -music therapist	Not reported		X	
Ordin & Karayurt, 2016 [36]	OPC		After liver transplant	15 monthly sessions (2 h each) -not specified with a supportive group	Not reported		X	
	OPC	X				X	X	

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Table 2 (continued)

Author, years	Study design	Study inserted in the metaanalysis	Phase of application of the psychological intervention	Length of the psychological intervention and -who carries out it	Months between psychological intervention and transplant	Psychological intervention assessment performed before the transplant	Psychological intervention assessment performed after the transplant	Pre-transplant psychological intervention with post-transplant assessment
Stonnington et al., 2016 [37]			Before and after solid organ transplant	Three rounds over a 1 year 15–20 ss per group -psychologist specialized in mindfulness	≥ 6 months ≤ 6 months			
Triffaux et al., 2001 [38]	OPC	X	Before and after heart transplant	Weekly sessions during hospitalization and monthly sessions after discharge -psychologist and psychiatrist	Not reported		X	

OPC: observational prospective cohort studies; RCT: randomized controlled trial.

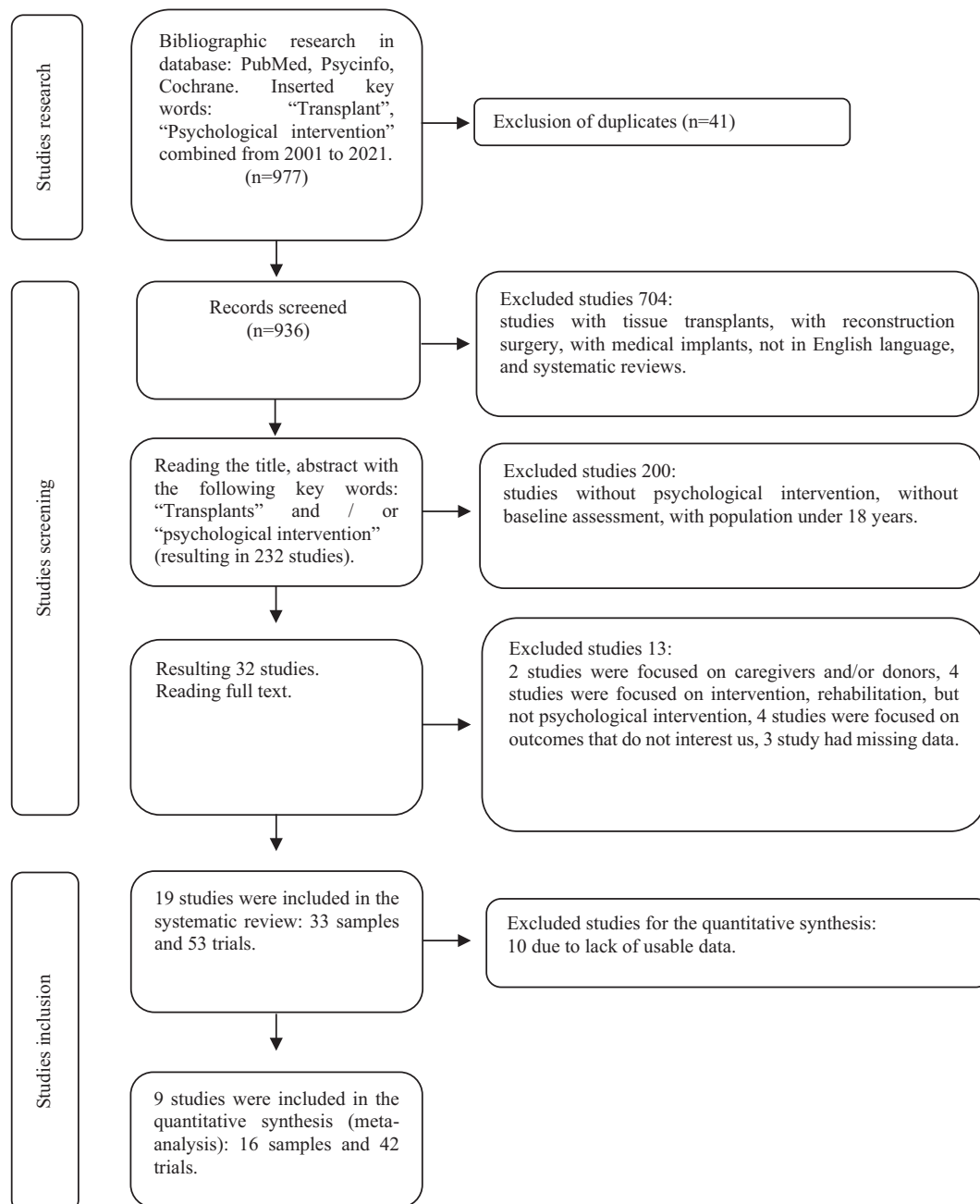


Fig. 1. Flow chart of the research, screening, and inclusion of the studies.

Table 3

Distribution of 53 trials coming from 25 samples (19 experimental (a) and 6 active control(b)) of the 19 studies included in the systematic review: 4 categories of treatments (dynamic therapies, cognitive behavioral therapies, supportive therapies, and not specified therapies) *per* 2 effects post- vs. pre-psychosocial intervention (improvement or not significant) of psychological (depression, anxiety, quality-of-life, and coping) and adherence outcomes.

Psychosocial interventions (25 samples with 53 trials)	Organ	Outcome									
		Depression (20 trials)		Anxiety (15 trials)		Quality-of-life (15 trials)		Coping (1 trial)		Adherence (2 trials)	
		Improvement (15 trials)	Not significant (5 trials)	Improvement (9 trials)	Not significant (6 trials)	Improvement (7 trials)	Not significant (8 trials)	Improvement (1 trial)	Not significant (0 trials)	Improvement (1 trial)	Not significant (1 trial)
Dynamic Therapies (7 trials)	Kidney (5 trials)	4/4 (Baines, 2002; Baines, 2004 (a); Baines, 2004 (b); Hedayati, 2017)		1/1 (Hedayati, 2017)							
	Liver (2 trials)	1/1 (Febrero, 2019)				1/1 (Febrero, 2018)					
Cognitive Behavioral Therapies (9 trials)	Kidney (4 trials)	1/1 (Craig, 2017)		1/1 (Craig, 2017)				1/1 (Craig, 2017)		1/1 (Cukor, 2017)	
	Liver (2 trials)	1/1 (Bailey, 2017 (a))		1/1 (Bailey, 2017 (a))							
Supportive Therapies (34 trials)	Not specified organs (3 trials)	1/1 (Gross, 2010 (b))		1/1 (Gross, 2010 (b))		1/1 (Gross, 2010 (b))					
	Kidney (14 trials)	2/4 (Rodrigue, 2011 (a); Rodrigue, 2011 (b))		2/4 (Gross, 2017 (a); Gross, 2017 (b))		2/4 (Rodrigue, 2011 (a); Rodrigue, 2011 (b))		1/6 (Rodrigue, 2011 (a))		5/6 (Rodrigue, 2011 (b); Gross, 2017 (a) (mental health); Gross, 2017 (a) (physical health); Gross, 2017 (b) (mental health); Gross, 2017 (b) (physical health)	
	Heart (4 trials)	1/1 (Dew, 2004)		1/1 (Dew, 2004)		1/1 (Dew, 2004)				1/1 (Dew, 2004)	
	Liver (4 trials)	2/2 (Bailey, 2017 (b); Juitagir, 2018)		2/2 (Bailey, 2017 (b); Juitagir, 2018)							
	Lung (2 trials)					1/2 (Rodrigue, 2005 (a))		1/2 (Rodrigue, 2005 (b))			
	All solid organ (6 trials)	3/3 (Hogan, 2015 (positive mood); Hogan, 2015 (negative mood); Stonnington, 2016)		1/1 (Stonnington, 2016)		1/2 (Stonnington, 2016) (mental health)		1/2 (Stonnington, 2016) (physical health)			
	Not specified (4 trials)	1/1 (Gross, 2010 (a))		2/2 (Gross, 2010 (a); Madson, 2010)		1/1 (Gross, 2010 (a))					
Not Specified Therapies (3 trials)	Heart (2 trials)	1/1 (Triffaux, 2001)		1/1 (Triffaux, 2001)							
	Liver (1 trial)					1/1 (Ordin, 2016)					

functioning as outcome.

3.7. Characteristics of the included studies in the metanalysis

The metanalysis included 9 studies, 4 RCT studies and 5 OPC studies, with 16 samples (9 experimental samples, 3 active control samples, and 4 control samples) for 42 trials. The 4 RCT studies included 10 samples (4 experimental samples, 3 active control samples, and 3 control samples) for 24 trials. The 5 OPC studies included 6 samples (5 experimental and 1 control sample) for 18 trials.

The range of age of RCT studies was 18–71 years, the range of age of the OPC studies was 18–70 years.

As regard to the therapies, 2 RCT and 0 OPC studies applied dynamic therapies, 1 OPC study applied CBT therapy, 2 RCT and 3 OPC studies applied supportive therapies, and 1 OPC study applied not specified treatments.

3.8. Psychological outcome in the metanalysis

3.8.1. Depression, anxiety, and quality-of-life

In the metanalysis the only outcome was the psychological one for depression, anxiety and quality-of-life, in this case there was a lack of data on coping. The scales applied were all those listed in the systematic review except for the Coping Orientation to the problem Experienced (COPE) and, obviously of the unspecified interview with five elements of patient adherence to the medical regimen (missed medications, missed clinical appointments, missed blood tests, exercise, disregard of diet, general difficulty with regimen).

Metanalyses and subgroup analyses were performed.

3.8.1.1. Kidney. The forest plot in Fig. 2 showed the effects of all kinds of psychosocial interventions between the psychosocial intervention samples (experimental and active control) and the control sample administered in pre- and post-transplant phases on depression in kidney transplanted patients. The plot included 3 RCT studies with 155 patients in the psychological intervention samples (99 of the experimental sample and 56 of the active control sample) and 138 participants in the control sample. The psychosocial interventions produced not significant effect on kidney transplanted patients (Total 95% CI 0.65 [−0.73, 2.03]; $I^2 = 96%$; $Z = 0.93$ ($p = 0.35$)).

The forest plot in Fig. 3 showed the effects of all kinds of psychosocial interventions between the psychosocial intervention samples (experimental and active control) and the control sample administered in pre- and post-transplant phases on anxiety in kidney transplanted patients. The plot included 2 RCT studies with 73 participants of the psychological treatment samples (54 of the experimental sample and 19 of the control active sample) and 64 participants of the control sample. The psychosocial interventions produced not significant effect on kidney transplanted patients (Total 95% CI −0.21 [−0.71, 0.29]; $I^2 = 51%$; $Z = 0.83$ ($p = 0.41$)).

The forest plot in Fig. 4 showed the findings of all the pre- vs post-psychosocial interventions on depression in samples (experimental and active control) of kidney transplanted patients, with interventions administered in pre- and post-transplant phases. The plot included 4 RCT with 221 participants at pre-psychosocial interventions (133 of the experimental sample and 88 of the control active sample) and 206 participants at post-psychosocial interventions (123 of the experimental sample and 83 of the control active sample). The psychosocial interventions produced significant effect on the depressed kidney transplanted patients (Total 95% CI 0.62 [0.32, 0.92]; $I^2 = 56%$; Test for overall effect: $Z = 4.02$ ($p < 0.0001$)).

The forest plot in Fig. 5 showed the findings of the pre- vs post-supportive psychosocial interventions on depression in samples (experimental and active control) of kidney transplanted patients, with interventions administered at pre-transplant phase. The plot included 2

RCT studies with 97 participants at pre-psychosocial interventions (49 of the experimental sample and 48 of the active control sample) and 90 participants at post-psychosocial interventions (44 of the experimental sample and 46 of the active control sample). The supportive intervention showed a significant effect on kidney transplanted patients (Total 95% CI 0.52 [0.09, 0.96]; $I^2 = 54%$ Test for overall effect: $Z = 2.35$ ($p = 0.02$)).

The forest plot in Fig. 6 showed the findings of the pre- vs post-dynamic psychological interventions on depression in samples (experimental and active control) of kidney transplanted patients, with interventions administered at post-transplant phase. The plot included 2 RCT studies with 124 participants at pre-psychosocial intervention (84 of the experimental sample and 40 of the active control one) and 116 participants at post-psychosocial intervention (79 of the experimental sample and 37 of the active control sample). The dynamic interventions showed a significant effect on kidney transplanted patients (Total 95% CI 0.73 [0.28, 1.18]; $I^2 = 66%$ Test for overall effect: $Z = 3.15$ ($p = 0.002$)).

The forest plot in Fig. 7 showed the findings of all the pre- vs post-psychosocial interventions on anxiety in samples (experimental and active control) of kidney transplanted patients, with interventions administered at pre- and post-transplant phases. The plot included 3 RCT studies, with 132 participants at pre-psychosocial intervention (84 of the experimental sample and 48 of the active control sample) and 124 participants at post-psychosocial intervention (78 of the experimental sample and 46 of the active control sample). The psychosocial interventions produced a significant effect on kidney transplanted patients (Total 95% CI 0.49 [0.17, 0.81]; $I^2 = 39%$ Test for overall effect: $Z = 2.97$ ($p = 0.003$)).

The forest plot in Fig. 8 showed the findings of the pre- vs post-supportive psychosocial interventions on anxiety in samples (experimental and active control sample) of kidney transplanted patients, with interventions administered at pre-transplant phase. The plot included 2 RCT studies with 97 participants at pre-psychosocial intervention (49 of the experimental sample and 48 of the active control sample) and 90 participants at post-psychosocial intervention (44 of the experimental sample and 46 of the active control sample). The supportive interventions showed a significant effect on kidney transplanted patients (Total 95% CI 0.52 [0.08, 0.95]; $I^2 = 54%$ Test for overall effect: $Z = 2.31$ ($p = 0.02$)).

The forest plot in Fig. 9 the findings of the pre- vs post-supportive psychosocial interventions on quality-of-life in samples (experimental and active control) of kidney transplanted patients, with interventions administered in pre-transplant phase. The plot included 2 RCT studies with 152 participants at pre-psychosocial intervention (76 of the experimental sample and 76 of the active control sample) and 139 participants at post-psychosocial intervention (66 of the experimental sample and 73 of the active control sample). The psychosocial interventions produced not significant effects on kidney transplanted patients (Total 95% CI −0.16 [−0.39, 0.07]; $I^2 = 0%$ Test for overall effect: $Z = 1.38$ ($p = 0.17$)).

3.8.1.2. Heart. The forest plot in Fig. 10 showed the findings of the pre- vs post-supportive psychosocial interventions on anxiety in samples (experimental and active control) of heart transplanted patients, with interventions administered in post-transplant phase. The plot included 2 OPC studies with 68 participants at pre-psychosocial intervention (46 of the experimental sample and 22 of the active control sample) and 50 participants at post-psychosocial intervention (35 of the experimental and 15 of the active control sample). The psychosocial interventions produced significant effect on heart transplanted patients (Total 95% CI 0.68 [0.30, 1.06]; $I^2 = 0%$ Test for overall effect: $Z = 3.53$ ($p = 0.0004$)).

3.8.1.3. Mixed solid organs. The forest plot in Fig. 11 showed the effects of the pre- vs post-supportive psychosocial interventions on anxiety in

experimental samples of mixed solid organs transplanted patients, with interventions administered in pre- and post-transplant phases. The plot included 3 OPC studies with 130 participants at pre-psychosocial intervention and 104 participants at post-psychosocial intervention. The psychosocial interventions produced significant effect on mixed solid organs transplanted patients (Total 95% CI 1.86 [0.15, 3.57]; $I^2 = 96\%$; $Z = 2.14$ ($p = 0.03$)).

3.9. Bias analysis, publication bias and GRADE assessment

The overall quality of the RCT studies was assessed through Cochrane bias scales: 1/11 study met all the quality criteria; 10/11 studies reported an adequate random sequence generation (1/11 did not), describing with sufficient details the method used to generate the allocation sequence; 3/11 studies had adequate allocation concealment (2/11 did not, 6/11 unclear), reporting how the intervention allocations could not be predicted before or during the enrollment of participants; 4/11 studies presented low risk of bias due to selective outcome reporting (1/11 high risk of bias, 6/11 unclear); 6/11 studies did not present performance bias, blinding participants and personnel from the knowledge of which intervention a participant received (5/11 unclear); 2/11 studies presented an adequate blinding of outcome assessment (3/11 did not, 6/11 unclear), describing the methods used to blind the outcome assessor from the knowledge of which intervention a participant received; and 8/11 studies reported low risk for incomplete outcome data (3/11 high risk) (Appendix A of the Supplementary data).

The overall quality of the OPC studies was assessed through Newcastle Ottawa Quality assessment scales: 1/8 study met all the quality criteria; 4/8 studies reported an adequate representativeness of the exposed cohort, describing with sufficient details the derivation from a specific population of the participants undergoing to psychosocial intervention (4/8 did not); 5/8 studies presented an adequate selection of the non-exposed cohort, because the participants of the control sample were drawn from the same population of the experimental sample (3/8 unclear); 7/8 studies presented an adequate ascertainment of the exposure, because the medical condition of the participants were assessed through objective data and self-report measures (1/8 did not); 6/8 studies presented an adequate demonstration that the outcome was not present at start of the study (2/8 did not); 7/8 studies presented an adequate comparability of cohorts on the basis of the design or analysis, because the study design allow to perform between or within groups comparisons (1/8 did not); 4/8 studies reported low risk of bias for detection of results measure, because the outcome was assessed through clinical evaluation and not only through self-report measures (3/8 high risk, 1/8 unclear); 4/8 studies reported an adequate follow-up completeness, reporting few drop-out during the follow-up points of assessment (4/8 did not) (Appendix A of the Supplementary data).

Moreover, STROBE checklist highlighted that some studies did not provide an exhaustive method and did not expose the bias risk (Appendix A of the Supplementary data). Moreover, with refer to the publication bias, the visual inspection of the funnel plots (supplementary material Figures from 1 s to 10s) was suggestive of publication bias for all the included outcomes. Lastly, GRADE for both RCTs and OPC studies ranged from low to very low. (Appendix A of the Supplementary data).

4. Discussion

The present study is the first attempt to investigate the effectiveness of psychological interventions on different outcomes related to the transplantation of the solid organs (kidney, heart, liver and lung).

The main finding of the present work highlighted that the psychosocial intervention showed a moderate effectiveness on transplanted patients. This result should be considered taking into account the specific kind of intervention administered. Indeed, from the systematic review emerged that the more applied psychological intervention was the supportive therapy, with a moderate effectiveness on all the

considered outcomes. Moreover, the meta-analyses showed that the supportive therapies produce an improvement of depressive and anxious symptoms overall in kidney recipients. These findings suggest that for the transplanted patients offering psychosocial support could be a solution to lead a better psychological health [13]. The systematic review highlighted that CBTs had a low application, and, as for the supportive therapies, the detected effect was moderate. Despite the dynamic therapies were applied only in five studies, they seemed to be the more effective showing significant improvements on depressive and anxiety symptoms. This result was confirmed from the meta-analysis, in which the dynamic therapies produced a significant effect, reducing depressive symptoms in kidney recipients. This kind of intervention was focused on redefine the patient's need of return to normality, working on deep feelings of uncertainty and fear of loss, integrating the experience of transplant in their own history of life [22,32].

Interestingly, the results of the present study highlighted that the effectiveness of psychosocial interventions seems to be related to the phase of application of the psychosocial intervention during the transplantation process. Specifically, as regard to the anxious symptoms, while for the kidney recipients, the efficacious psychosocial intervention was generally administered in the pre-transplant phase, for the heart recipients the effective intervention was generally administered in the post-transplant phase. This result suggests different psychological needs of these patients that seem to require a specific psychosocial care. In particular, for the heart recipients a psychological treatment administered in the post-transplant period seems to help in decreasing the anxious symptomatology probably because these patients, only after this high-risk transplant [43], could be able to focalize their thoughts and feelings on the future perspectives and on the perceived social support availability [33]. Differently, for the kidney recipients a psychosocial intervention seems to allow a focalization on thoughts and feelings about the life of the patients also before the surgery intervention. Moreover, considering that the chronic rejection is a present risk over the years, it seems to affect negatively the post-transplant psychological wellbeing. A pre-kidney transplant psychological intervention could be effective to prepare the patient in the redefinition of new life style [3,44].

In light of these previous considerations, a psychosocial intervention orientated to the recovery of anxious symptomatology should be focalized on the immediate control of the worry for transplantation for the heart recipients, while for the kidney recipients should be focalized on the future medical adherence, planning psychological counseling and health education to reduce non-adherence behaviors. [45].

Differently, the meta-analyses on the RCT studies showed that the efficacy of the psychosocial interventions on depression seems to be not associated to the time-points of the administration of the psychosocial intervention (pre- or post-transplant).

Moreover, on the quality-of-life outcome in the kidney recipients, the results of the meta-analysis on the RCT studies showed not significant effects of the supportive interventions administered in the pre-transplant phase [10,26,30] and this result is also confirmed by the systematic review. This finding could be explained considering the pervasive psychological effects of an unrealistic expectation related to the transplantation experience and its consequences: the quality of life could be negatively affected by a lack of a real perception of the long-term functioning of the new kidney [46].

Regarding the outcome considered in the present work, the systematic review highlighted that in the 19 included studies the psychological outcomes, as depression, anxiety, quality-of-life and coping, were the more investigated compared to the medical adherence and organ functioning. The most examined psychological variables were the depression and anxiety. Only one study dealt with the coping outcome. The medical adherence outcome was considered only in two studies, and not studies dealt with the organ functioning. The lack of studies with the evaluation of the effects of the psychological intervention on the medical adherence after the transplantation surgery and on the physiological variables

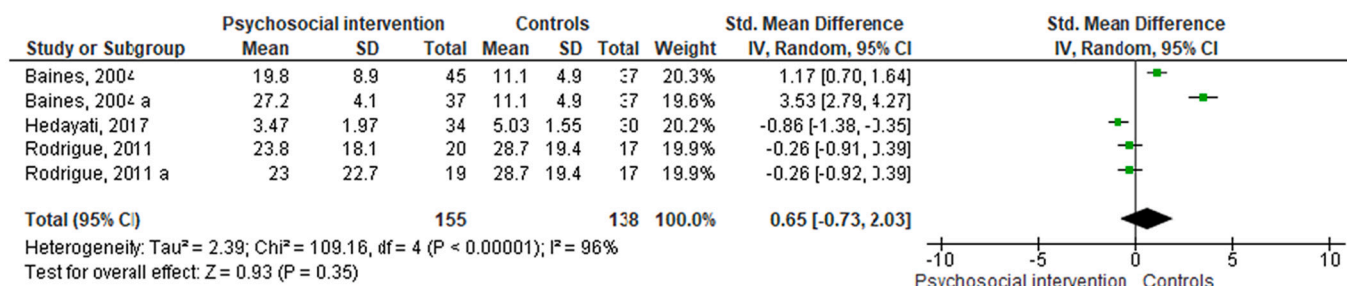


Fig. 2. Randomized controlled trials: effects of the comparison of all the psychosocial intervention samples and control samples on depression in samples of kidney transplanted patients.

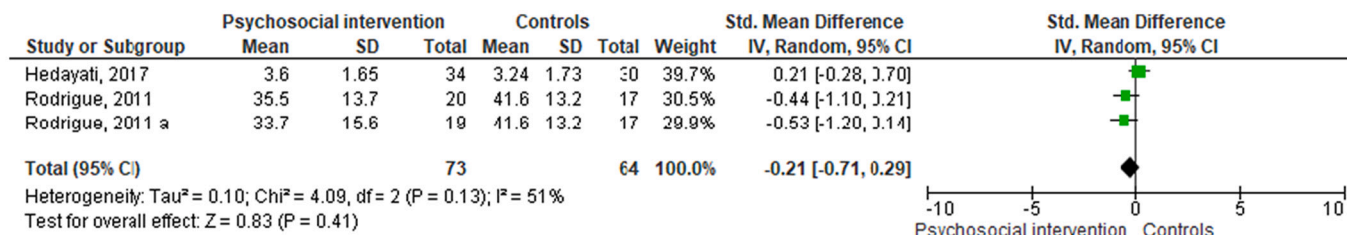


Fig. 3. Randomized controlled trials: effects of the comparison of all the psychosocial intervention samples and control samples on anxiety in samples of kidney transplanted patients.

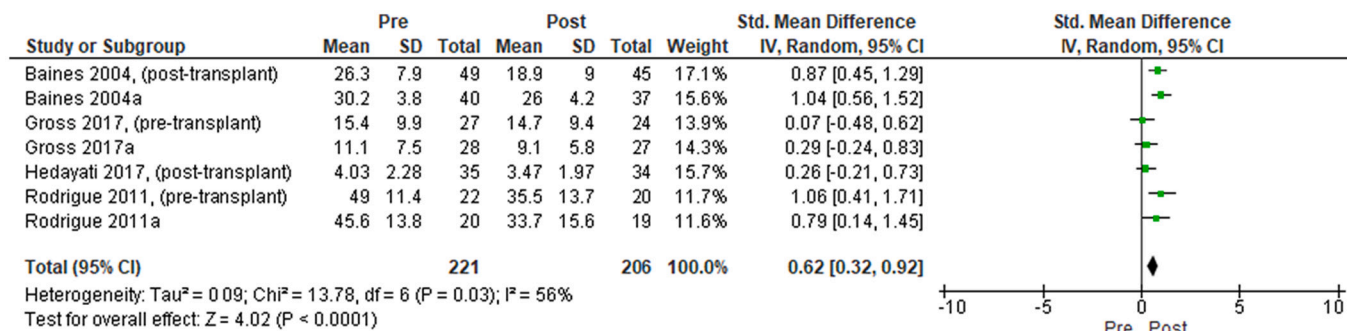


Fig. 4. Randomized Controlled Trials: effects of all the psychosocial interventions on depression in samples of kidney transplanted patients. Note. Pre-transplant = psychological intervention and assessment performed before transplantation; post-transplant = psychological intervention and assessment performed after transplantation.

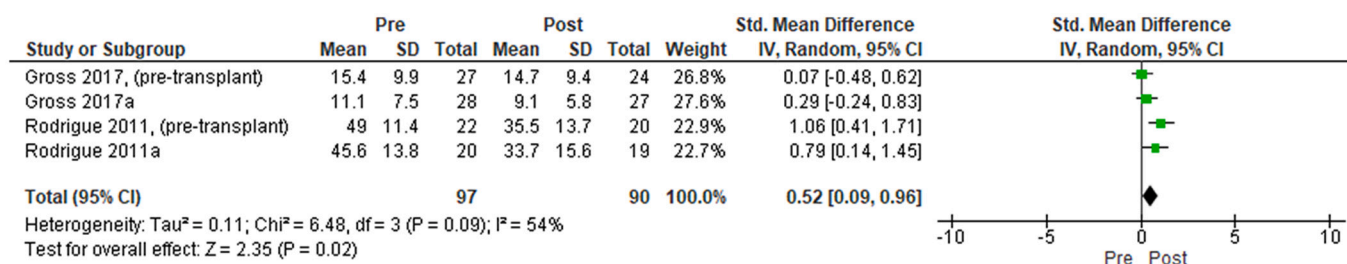


Fig. 5. Randomized Controlled Trials: effects of the supportive psychosocial interventions on depression in samples of transplanted kidney patients. Note. Pre-transplant = psychological intervention and assessment performed before transplantation.

related to the organ functioning and its acceptance, it highlights the need to plan future studies considering these secondary but relevant outcome.

The present work presents many limitations. Across the 11 studies included in the present work as RCT, only one study totally adhered to the criteria of the bias scales as Cochrane bias risk [40], across the 8 OPC studies only one totally adhered to the criteria of the bias risk of

Newcastle Ottawa Quality [41], and none fully adhered to the Strobe checklist [42]. Moreover, the size of the samples considered in the systematic review and meta-analyses was relatively not homogeneous with a consequent increase of the heterogeneity index. Lastly, in the present study, the certainty of the evidence for outcomes included in the meta-analyses ranged from low to very low due to inconsistency, indirectness, imprecision and suggestive publication bias. Further prospective,

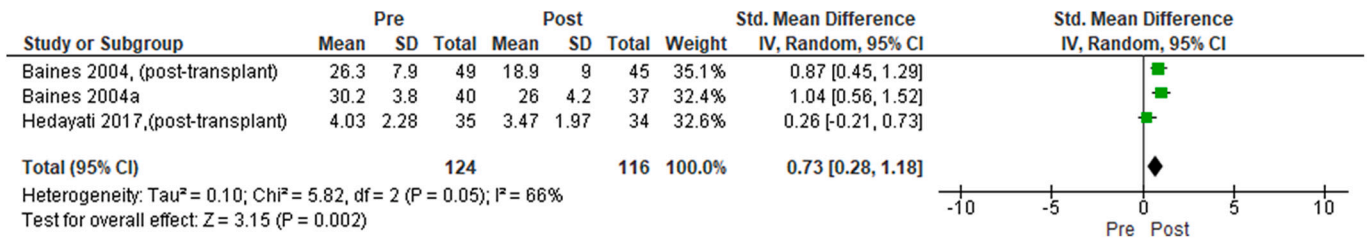


Fig. 6. Randomized Controlled Trials: effects of the dynamic psychological interventions on depression in samples of transplanted kidney patients. Note. Post- transplant = psychological intervention and assessment performed after transplantation.

multicentric, and adequately powered RCTs are required to strengthen the evidence on the effectiveness of psychosocial intervention, considering the importance of using standardized measure for the assessment of the main outcomes and wider samples adequately balanced.

Despite these limitations, this work could provide useful indications for clinical activity, highlighting the efficacious intervention practices related to specific organs. In particular, although in kidney recipients the effectiveness of psychosocial interventions is verified for depression and anxiety outcomes, the metaanalyses showed that the interventions seem to have more efficacy in reducing depressive symptoms compared to the anxious ones. Interestingly, the efficacy of psychosocial intervention on depression and anxiety in kidney recipients appears to be not significant when the intervention samples were compared with the control sample. This finding is likely attributable to the high heterogeneity of data between the only three studies that were suitable to be included in the metaanalysis. Moreover, the interpretation of this not significant finding should take into account the study of Baines et al. [22], included in the metaanalysis, in which at the baseline reported a significantly lower depression scores in the control group compared to the experimental group. Moreover, despite the systematic review showed that there was only one study on the coping [32] and only one study on the medical adherence [23] in kidney recipients, the CBTs therapies showed a good effectiveness on both the outcomes.

As regard to the heart transplantation, it was possible to compute quantitative data only on the OPC studies. The metaanalysis showed that the supportive intervention, applied in the post-transplant period, was effective on the anxiety [33,38]. This finding was confirmed also by the systematic review. Moreover, from the systematic review, significant effects emerged for the application of the supportive interventions on depression and the quality-of-life outcomes but not for adherence [33]. The administration of the CBTs did not show significant effect on anxiety and depression in hearth recipients.

For the liver transplantation, it was not possible to compute quantitative analyses. From the systematic review resulted that the psychosocial interventions did not show significant effects in the majority of the trials on the depression, in half of the trials on quality-of-life, and in all the trials on anxiety. There were not studies focused on the coping strategies and medical adherence outcomes in liver recipients. A

possible explanation of this not significant results may be ascribable to the fact that in 4/9 trials the intervention was delivered by telephone [21], suggesting that while telephone-delivered interventions have been successful in other patient population [47] in transplanted patients may be more effective face-to-face interventions. In particular, previous studies reported benefits in patients on the liver transplant waiting list of the social and family support [48] and group therapy [49] applied before the transplantation.

For the lung transplantation, it was not possible to compute quantitative analyses. From the systematic review resulted that the psychosocial interventions showed significant effects on the quality-of-life outcome in half of the trials. Interestingly, the systematic review highlighted that there were not studies focused on anxiety and depression in lung transplanted patients, despite the current literature reported that anxiety disorders are prominent in those patients [50]. Future studies are needed to focus on the effectiveness of the psychosocial interventions on anxiety and depression in patient underwent lung transplantation.

These findings suggest to take into account the specific emotional burden of recipients related to different transplanted organs in order to plan psychosocial interventions with specific goals that consider their different needs.

Moreover, the need to implement more focused intervention programs that can complement the work of the therapists should be considered in order to favor psychological state, adherence and acceptance of the organ. In this regard, previous studies highlighted the importance to plan peer-interventions in order to provide psychological support and to improve disease self-management during the transplant process [51,52]. Moreover, video-educational programs, which outline all stages of the transplant process, seem to help the transplanted patients to improve confidence, quality of life and medication adherence, promoting self-efficacy [53].

As previously noted, it was relevant that in 19 studies, the organ functioning has been never considered as an outcome. It seems important to plan future studies considering the effect of the psychosocial treatment also on the adherence to the medical care and on the biological outcome in order to increase an integrative and holistic insight in taking care of the patients and to plan intervention oriented to increase

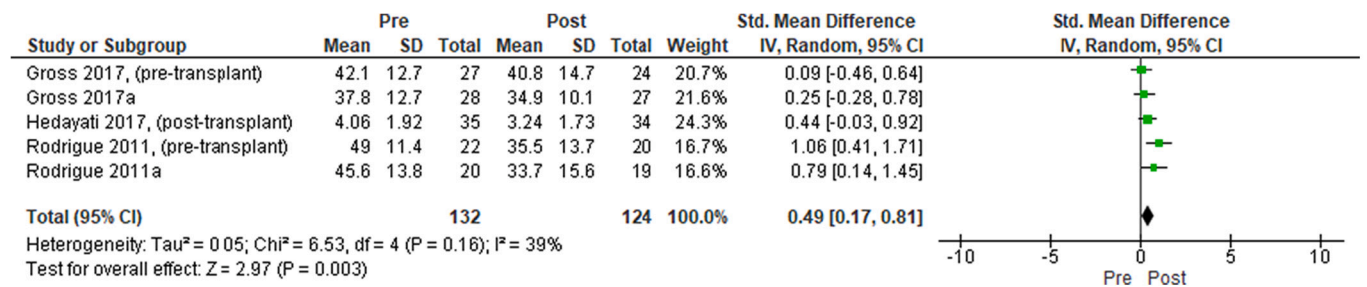


Fig. 7. Randomized Controlled Trials: effects of all psychosocial interventions on anxiety in samples of kidney transplanted patients. Note. Pre-transplant = psychological intervention and assessment performed before transplantation; post-transplant = psychological intervention and assessment performed after transplantation.

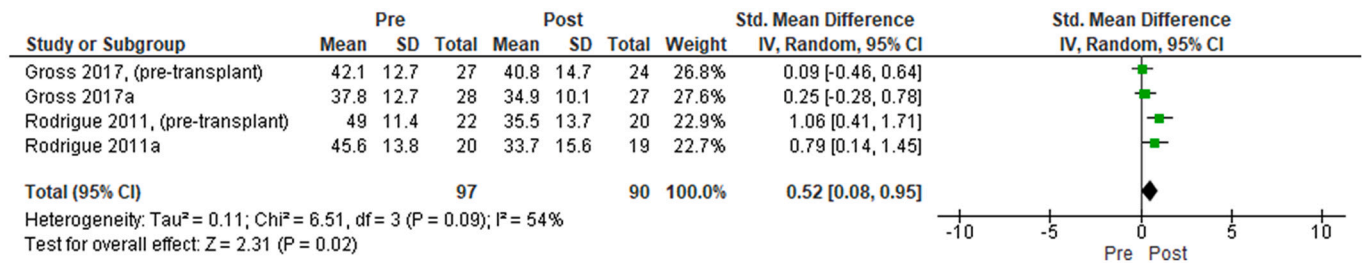


Fig. 8. Randomized Controlled Trials: effects of the supportive psychosocial interventions on anxiety in samples of transplanted kidney patients. Note. Pre- transplant = Psychological intervention and assessment performed before transplantation.

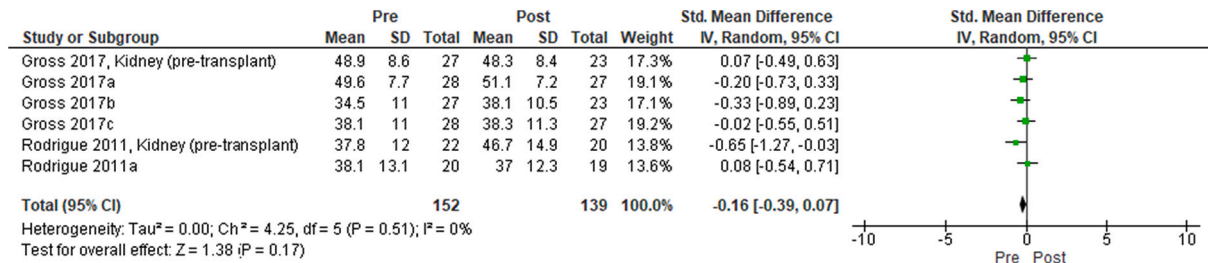


Fig. 9. Randomized Controlled Trials: effects of the supportive psychosocial interventions on quality-of-life in samples of kidney transplanted patients. Note. Pre- transplant = psychological intervention and assessment performed before transplantation.

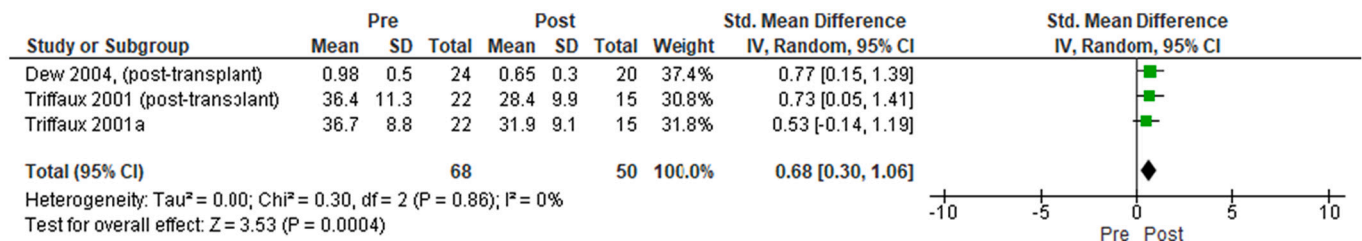


Fig. 10. Observational prospective cohort studies: effects of the supportive psychosocial intervention on anxiety in samples of heart transplanted patients. Note. Post- transplant = psychological intervention and assessment performed after transplantation.

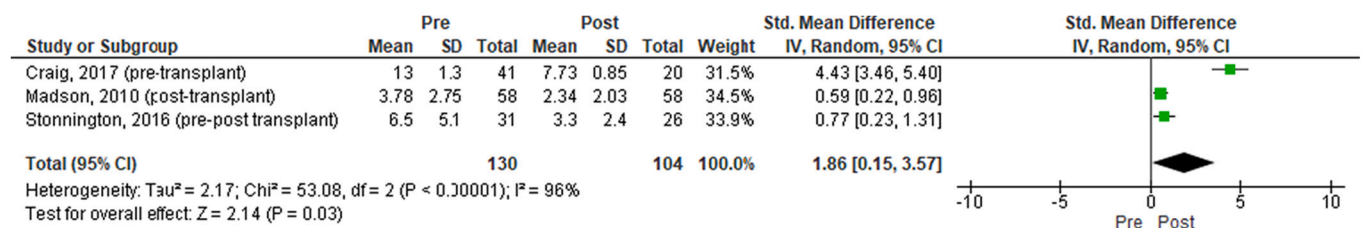


Fig. 11. Observational prospective cohort studies: effects of supportive psychosocial intervention on anxiety in mixed organs samples (kidney, liver, heart, lung, pancreas) of transplanted patients.

Note. Pre- transplant = psychological intervention and assessment performed before transplantation; post- transplant = psychological intervention and assessment performed after transplantation.

acceptance of the organ, to reduce mortality and health costs [19].

Authorship

All authors materially participated in the research and writing of the manuscript. All authors approved the final version of the manuscript.

Specifically, Carlo Lai supervised and coordinated the work. We list the contributor roles below conceptualization and investigation of the work, Daniela Sambucini; visualization and writing (original draft and review/editing), Paola Aceto; data curation formal analysis and writing original draft, Daniela Sambucini and Giorgia Zingaretti; visualization

and the writing original draft, Gaia Romana Pellicano; visualization, Chiara Ciacchella; methodology, Chiara Ciacchella and Daniela Sambucini; investigations: Laura Pierro; resources and the administration of the project, Chiara Ciacchella, Gaia Romana Pellicano, Daniela Sambucini; supervision and administration of the project, Carlo Lai.

Declaration of Competing Interest

Conflicts of interest to declare: none. The authors declare that there are no potential competing interests which include employment, consulting, share ownership, fees, paid expert testimony, patents

applications/registrations and grants or other funding.

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Appendix. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jpsychores.2022.110717>.

References

- ISS, Il trapianto e la donazione, Retrieved from Centro Nazionale trapianti: <http://www.trapianti.salute.gov.it>, 2018.
- L. Prihodova, I. Nagyova, J. Rosenberg, R. Roland, J. van Dijk, J.W. Groothoff, Impact of personality and psychological distress on health-related quality of life in kidney transplant recipients, *Transpl. Int.* 23 (2009) 484–492.
- C. De Pasquale, M.L. Pistorio, M. Veroux, L. Indelicato, G. Biffa, N. Bennardi, P. Veroux, Psychological and psychopathological aspects of kidney transplantation: a systematic review, *Front. Psychol.* 11 (2020) 106.
- R. Bricman, Distress and alexithymia in lung recipients—psychosocial strains and associations with chronic allograft dysfunction, *Swiss Med. Wkly.* 140 (2526) (2010).
- M.A. Dew, A.F. DiMartini, Psychological disorders and distress after adult cardiothoracic transplantation, *J. Cardiovasc. Nurs.* 20 (5S) (2005) S51–S66.
- L. Myaskovsky, M.A. Dew, M.L. McNulty, G.E. Switzer, A.F. DiMartini, R. L. Kormos, K.R. McCurry, Trajectories of change in quality of life in 12-month survivors of lung or heart transplant, *Am. J. Transplant.* 6 (8) (2006) 1939–1947.
- K.H. Schulz, S. Kroencke, Psychosocial challenges before and after organ transplantation, *Transpl. Res. Risk Manage.* 7 (2015) 45–58.
- F.B. Trevizan, Y.L. Silva, C.M. Roque, Quality of life, depression, anxiety and coping strategies after heart transplantation, *Braz. J. Cardiovasc. Surg.* 32 (3) (2017) 162–170.
- J.P. Rainer, C.H. Thompson, H. Lambros, Psychological and psychosocial aspects of the solid organ transplant experience—a practice review, *Psychother. Theory Res. Pract. Train.* 47 (3) (2010) 403.
- J. Rodrigue, D. Mandelbrot, M. Pavlakis, A psychological intervention to improve quality of life and reduce, *Nephrol. Dialy. Transplant.* 26 (2) (2011) 709–715.
- R. Calia, C. Lai, P. Aceto, M. Luciani, C. Saraceni, A.W. Avolio, S. Agnes, Psychological risk factors for graft rejection among liver transplant recipients, *Transplant. Proc.* 43 (2011) 1123–1127.
- R. Calia, C. Lai, P. Aceto, M. Luciani, C. Saraceni, F. Citterio, Preoperative psychological factors predicting graft rejection in patients undergoing kidney transplant: a pilot study, *Transplant. Proc.* 43 (2011) 1006–1009.
- J.S. Gonzalez, M.L. Tanenbaum, P.V. Commissariat, Psychosocial factors in medication adherence and diabetes self-management: implications for research and practice, *Am. Psychol.* 71 (7) (2016) 539.
- K.M. Murali, J. Mullan, S. Roodenrys, H.C. Hassan, K. Lambert, M. Lonergan, Strategies to improve dietary, fluid, dialysis or medication adherence in patients with end stage kidney disease on dialysis: a systematic review and meta-analysis of randomized intervention trials, *PLoS One* 14 (1) (2019), e0211479.
- A. López-Navas, A. Ríos, A. Riquelme, L. Martínez-Alarcón, J.A. Pons, M. Miras, P. Parrilla, Psychological characteristics of patients on the liver transplantation waiting list with depressive symptoms, *Transplant. Proc.* 43 (1) (2011, January) 158–160 (Elsevier).
- A. Lopez-Navas, A. Rios, F.J. Moya-Faz, B. Febrero, M.I. Jimenez-Morales, F. J. Orteso, P. Parrilla, Emotional-type psychopathologic symptoms among patients with terminal chronic alcohol-induced liver cirrhosis, *Transplant. Proc.* 44 (6) (2012, July) 1510–1512 (Elsevier).
- P.J. Smith, J.A. Blumenthal, E.P. Trulock, K.E. Freedland, R.M. Carney, R.D. Davis, S.M. Palmer, Psychosocial predictors of mortality following lung transplantation, *Am. J. Transplant.* 16 (1) (2016) 271–277.
- C. Stille, A. Di Martini, M. De Vera, W. Flynn, J. King, S. Sereika, G. Rathnamala, Individual and environmental correlates and predictors of early adherence and outcomes after liver transplantation, *Prog. Transplant.* 20 (1) (2010) 58–66.
- R. Calia, C. Lai, P. Aceto, M. Luciani, G. Camardese, S. Lai, F. Citterio, Attachment style predict compliance, quality of life and renal function in adult patients after kidney transplant: preliminary results, *Ren. Fail.* 37 (4) (2015) 678–680.
- V. Smith, D. Devane, C.M. Begley, M. Clarke, Methodology in conducting a systematic review of systematic reviews of healthcare interventions, *BMC Med. Res. Methodol.* 11 (1) (2011) 1–6.
- D.E. Bailey Jr., C.C. Hendrix, K.E. Steinhauser, K.M. Stechuchak, L.S. Porter, J. Hudson, J.A. Tulsy, Randomized trial of an uncertainty self-management telephone intervention for patients awaiting liver transplant, *Patient Educ. Couns.* 100 (3) (2017) 509–517.
- L. Baines, J. Joseph, R. Jindal, Prospective randomized study of individual and group psychotherapy versus controls in recipients of renal transplants, *Kidney Int.* 65 (2004) 1937–1942.
- D. Cukor, N. Ver Halen, M. Pencille, F. Tedla, M. Salifu, A pilot randomized controlled trial to promote immunosuppressant adherence in adult kidney transplant recipients, *Nephron* 135 (1) (2017) 6–14.
- B. Febrero, P. Ramirez, L. Martínez-Alarcón, C. Abete, M. Galera, A. Ríos, R. Robles-Martínez, P.M. Ramírez-Pino, J. Almela, G. Ramis, J.A. Pons, P. Parrilla, Quality of life and group psychological intervention in patients with cirrhosis on liver transplant waiting list, *Transplant. Proc.* 50 (9) (2018) 2626–2629.
- B. Febrero, P. Ramirez, L. Martínez-Alarcón, C. Abete, M. Galera, A. Ríos, R. Robles-Martínez, P.M. Ramírez-Pino, J. Almela, G. Ramis, J.A. Pons, P. Parrilla, Group psychotherapy could improve depression in cirrhotic patients on the liver transplant waiting list, *Transplant. Proc.* 51 (1) (2019) 28–32.
- C.R. Gross, M. Reilly-Spong, T. Park, R. Zhao, O.V. Gurvich, H.N. Ibrahim, Telephone-adapted mindfulness-based stress reduction (tMBSR) for patients awaiting kidney transplantation, *Contemp. Clin. Trials* 57 (2017) 37–43.
- C.R. Gross, M.J. Kreitzer, W. Thomas, M. Reilly-Spong, M. Cramer-Bornemann, J. A. Nyman, H.N. Ibrahim, Mindfulness-based stress reduction for solid organ transplant recipients: a randomized controlled trial, *Altern. Ther. Health Med.* 16 (5) (2010) 30.
- A. Hedayati, A. Noorbala, S. Khatami, The impact of expressive emotion brief psychotherapy on psychological health of kidney transplant recipients, *Iran Red Crescent Med J* 19 (3) (2016).
- T.J. Hogan, M.J. Silverman, Coping-infused dialogue through patient-preferred live music: a medical music therapy protocol and randomized pilot study for hospitalized organ transplanted patients, *J. Music. Ther.* 52 (3) (2015) 420–436.
- J. Rodrigue, M. Baz, M. Widows, S. Ehlers, A randomized evaluation of quality-of-life therapy with patients awaiting lung transplantation, *Am. J. Transplant.* 5 (2005) 2425–2432.
- L. Baines, J. Joseph, R. Jindal, Emotional issues after kidney transplantation: a prospective psychotherapeutic study, *Clin. Transpl.* 16 (2002) 455–460.
- J.A. Craig, D. Miner, T. Remtulla, J. Miller, L.W. Zanussi, Piloting a coping skills group intervention to reduce depression and anxiety symptoms in patients awaiting kidney or liver transplant, *Health Soc. Work* 42 (1) (2017) e44–e52.
- M. Dew, J. Goycoolea, R. Harris, A. Lee, R. Zomak, J. Dunbar-Jacob, R. Kormos, An internet-based intervention to improve psychosocial outcomes in heart transplant recipients and family caregivers: development and evaluation, *J. Heart Lung Transplant.* 23 (2004) 745–758.
- D.R. Jutagir, R.M. Saracino, A. Cunningham, K.A. Foran-Tuller, M.A. Driscoll, W. H. Sledge, D.C. Fehon, The feasibility of a group stress management liver SMART intervention for patients with end-stage liver disease: a pilot study, *Palliat. Support. Care* 17 (1) (2019) 35–41.
- A. Madson, M. Silverman, The effect of music therapy on relaxation, anxiety, pain perception, and nausea in adult solid organ transplanted patients, *J. Music. Ther.* 47 (3) (2010) 220–232.
- Y. Ordin, O. Karayurt, Effects of a support group intervention on physical, psychological, and social adaptation of liver transplant recipients, *Exp. Clin. Transplant.* 3 (2016) 329–337.
- C.M. Stonington, B. Darby, A. Santucci, P. Mulligan, P. Pathuis, A. Cuc, A. Sood, A resilience intervention involving mindfulness training for transplanted patients and their caregivers, *Clin. Transpl.* 30 (11) (2016) 1466–1472.
- J. Triffaux, J. Waunthy, J. Bertrand, R. Limet, A. Albert, M. Anseau, Psychological evaluation and assessment in patients undergoing orthotopic heart transplantation, *Eur. Psychol.* 16 (3) (2001) 180–185.
- Review Manager (RevMan) [Computer program]. Version 5.4, The Cochrane Collaboration, 2020.
- J. Higgins, D. Altaman, P. Gotsche, P. Juni, D. Moher, A. Oxman, J. Sterne, The Cochrane Collaboration's Tool for Assessing Risk of Bias in Randomised Trials, Retrieved from BMJ, 2011, <https://doi.org/10.1136/bmj.d5928>.
- G. Wells, B. Shea, D. O'Connell, J. Peterson, V. Welch, M. Losos, P. Tugwell, The Newcastle-Ottawa (NOS) Scale for Assessing the Quality of Non-randomized Studies in Meta-analyses, Retrieved from oxford, http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp, 2014.
- E. Von Elm, D. Altman, M. Egger, S. Pocock, P. Gotsche, J. Vandenbroucke, STROBE statement, *Terapia Evid. Based* 1 (1) (2008) 1–8.
- M. Yacoub, Heart transplants, reflections, & expectations: sir Magdi Yacoub reviews the history of heart transplantation and discusses expectations, *Eur. Heart J.* 38 (46) (2017) 3420–3422.
- M. Hassanein, J.J. Augustine, Chronic kidney transplant rejection, in: *StatPearls*, StatPearls Publishing, 2021.
- H.H. Tola, D. Shojaeizadeh, A. Tol, G. Garmaroudi, M.S. Yekaninejad, A. Kebede, E. Klinkenberg, Psychological and educational intervention to improve tuberculosis treatment adherence in Ethiopia based on health belief model: a cluster randomized control trial, *PLoS One* 11 (5) (2016), e0155147.
- M. Gruttadauria, C. Dunn, J. Lin, J.R. Kaminetsky, K. Applebaum, D. Portal, S. Greenstein, Patients' expectations for longevity of kidney transplant, *Prog. Transplant.* 29 (1) (2019) 48–53.
- B.B. Germino, M.H. Mishel, J. Crandell, L. Porter, D. Blyler, C. Jenerette, K.M. Gil, Outcomes of an uncertainty management intervention in younger African American and Caucasian breast cancer survivors, *Oncol. Nurs. Forum* 40 (1) (2013) 82–92.

- [48] A. López-Navas, A. Ríos, A. Riquelme, L. Martínez-Alarcón, J.A. Pons, M. Miras, A. Sanmartín, B. Febrero, P. Ramírez, P. Parrilla, Psychological care: social and family support for patients awaiting a liver transplant, *Transplant. Proc.* 43 (3) (2011) 701–704.
- [49] P. Ramírez, B. Febrero, L. Martínez-Alarcón, C. Abete, M. Galera, P. Cascales, P. Parrilla, Benefits of group psychotherapy in cirrhotic patients on the liver transplant waiting list, *Transplant. Proc.* 47 (8) (2015, October) 2382–2384 (Elsevier).
- [50] M.A. Dew, A.F. DiMartini, A.J.D. Dabbs, K.R. Fox, L. Myaskovsky, D.M. Posluszny, Y. Toyoda, Onset and risk factors for anxiety and depression during the first 2 years after lung transplantation, *Gen. Hosp. Psychiatry* 34 (2) (2012) 127–138.
- [51] L. Wright, J.J. Pennington, S. Abbey, E. Young, J. Haines, H. Ross, Evaluation of a mentorship program for heart transplant patients, *J. Heart Lung Transpl.: Off. Publ. Intern. Soc. Heart Transplant.* 20 (9) (2001) 1030–1033.
- [52] S.J. Anthony, K. Young, E. Ghent, A. Gold, K. Martin, M. Solomon, J. Stinson, Exploring the potential for online peer support mentorship: perspectives of pediatric solid organ transplant patients, *Pediatr. Transplant.* 25 (5) (2021), e13900.
- [53] H. Mansell, N. Rosaasen, P. West-Thielke, J. Wichart, C. Daley, R. Mainra, A. Shoker, J. Liu, D. Blackburn, Randomised controlled trial of a video intervention and behaviour contract to improve medication adherence after renal transplantation: the VECTOR study protocol, *BMJ Open* 9 (3) (2019), e025495.