

Review Article

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Corresponding author:

Eleni Petkari;

Email: eleni.petkari@unir.net

Which psychological interventions improve quality of life in patients with schizophrenia-spectrum disorders? A meta-analysis of randomized controlled trials

Eleni Petkari¹ , Elena Nikolaou² , Sandra Oberleiter³ , Stefan Priebe⁴ 
and Jakob Pietschnig³ 

¹Faculty of Health Sciences, Universidad Internacional de La Rioja (UNIR), Logroño, Spain; ²Licensed Clinical Psychologist, Independent Practice, Nicosia, Cyprus; ³Department of Developmental and Educational Psychology, Faculty of Psychology, University of Vienna, Vienna, Austria and ⁴Unit for Social and Community Psychiatry, WHO Collaborating Centre for Mental Health Services Development, Queen Mary University of London, London, UK

Abstract

Quality of life (QoL) is a major patient reported outcome used to measure the psychological treatments success in people with schizophrenia-spectrum disorders. To date, the specific impact of different interventions on QoL remains undefined. A meta-analysis of Randomized Controlled Trials (RCTs) was carried out for this purpose. We searched Proquest, PUBMED/MEDLINE, PsycINFO, WOS, Scopus, the Cochrane Library for RCTs published until January 2023. We used multilevel meta-analysis to examine differences between intervention effectiveness of experimental and control conditions whilst accounting for data dependencies. By means of subgroup analyses, we investigated influences of intervention types (i.e. psychoeducation *v.* CBT *v.* cognitive *v.* combination of several types *v.* other, such as psychodynamic, systemic, etc.) and continuous moderators were examined with precision-weighted meta-regressions. The generalizability of results across moderators, their combinations, and analytical approaches was investigated with multiverse meta-analyses. We examined data of 60 independent studies, reporting intervention effects for objective and subjective QoL ($k = 19$ and 70 effect sizes based on $N = 1024$ and 6254 participants, respectively). Overall, psychological interventions seemed to be more effective for objective than for subjective QoL. However, specific intervention results were differentiated, suggesting largest effects of psychoeducation on objective and combined interventions on subjective QoL. Our findings suggest that QoL is a valid outcome criterion for testing intervention effectiveness, as it is sensitive to change. Additionally, psychological interventions can improve patients' QoL, though the effects are small. Further testing of less widely used interventions and a shift toward the multidimensional nature of QoL is still necessary.

Introduction

Most psychological interventions that are currently used to treat patients with schizophrenia-spectrum disorders, such as psychoeducation, cognitive behavioral therapy (CBT), and cognitive interventions show only moderate beneficial effects on psychotic symptoms (Lincoln & Pedersen, 2019). This is evidenced through both low effect sizes of each of them and small differences between them with trivial clinical significance (Turner, van der Gaag, Karyotaki, & Cuijpers, 2014). Other outcomes that are closely related to the patients' everyday life, such as quality of life (QoL), may therefore represent a suitable candidate for evaluating treatment success (Awad & Voruganti, 2012). Nowadays, QoL is understood as a multidimensional construct which encompasses different indicators. Objective QoL refers to observable indicators such as finance, housing, or number of friends (Katschnig, 2006) whilst subjective QoL refers to an individual's appraisal of several life domains such as relationship quality, accommodation, or safety (Lehman, 1988). The person's subjective perception that is specifically related to their health status and its consequences is defined as health-related QoL (Patrick & Chiang, 2000).

So far, one prior meta-analysis aimed at assessing the intervention effectiveness for schizophrenia-spectrum disorders on QoL (Valiente, Espinosa, Trucharte, Nieto, & Martinez-Prado, 2019). However, the evidential value of this prior meta-analytical account is limited due to (i) an insufficient identification of eligible studies as a result of a suboptimal search strategy (i.e. limited databases, broadly defined search terms), as well as (ii) the unobserved heterogeneity that likely emerged from mixing both predicting (in terms of differences in intervention type and composition, as well as of inclusion of several different mental

diagnoses) and outcome variables (in terms of subjective *v.* objective QoL assessments). The latter point yields well-known effect-distorting mechanisms that are rooted in the apples-and-oranges problem [see Petkari, 2023, for a detailed review].

To be able to yield meaningful findings in terms of intervention effectiveness, the following points need to be taken into consideration. First, to guide clinical practice the effect sizes of standalone psychological interventions should be calculated separately (Mueser, Deavers, Penn, & Cassisi, 2013), without admixture with multicomponent care programs (i.e. medication, case management, assertive community treatment, vocational services), or peer-led interventions. Second, QoL differs between people with schizophrenia and other mental disorders (Ådnanes et al., 2019; Berghöfer, Martin, Hense, Weinmann, & Roll, 2020; Petkari & Priebe, 2023) suggesting differences in treatment effectiveness. Third, the effects on objective and subjective QoL indicators should be calculated separately, because in patients with schizophrenia they seem to be at best moderately associated with each other (Hayhurst, Massie, Dunn, Lewis, & Drake, 2014; Renwick et al., 2017) and the two QoL indicators show different relationships with other factors. For example, negative symptoms (Eack & Newhill, 2007) and functioning (Nevarez-Flores et al., 2019) show small associations with subjective QoL but large associations with objective QoL, whereas service satisfaction (Petkari & Pietschnig, 2015) shows moderate associations with subjective but no associations with objective QoL.

Therefore, the aims of the present meta-analysis are (i) to examine the effects of the psychological interventions on different QoL indicators (objective and subjective) in patients with schizophrenia-spectrum disorders; (ii) to determine which interventions are more effective (psychoeducation *v.* CBT *v.* cognitive *v.* combination of several types *v.* other psychological interventions such as psychodynamic, systemic, etc.); and (iii) to identify moderating variables of intervention effectiveness (i.e. duration of intervention; modality: group *v.* individual *v.* both; illness length; service context: outpatients *v.* inpatients *v.* both; and treatment of comparison group: TAU *v.* other psychological intervention *v.* non therapeutic intervention).

Methods

This meta-analysis was registered at PROSPERO (CRD4202233 5055) and was prepared according to the PRISMA guidelines (Page et al., 2021).

Literature search

The following databases were searched for documents until January 2023: Proquest, PUBMED/MEDLINE, PsycINFO, Web of Science, Scopus, and the Cochrane Library. Moreover, we hand-searched references of relevant articles and previous meta-analyses. Hits were not restricted in terms of language or publication period. The search included a combination of keywords related to the population, intervention types, design of studies and outcomes, and was based on Abstract, Title, and Keywords (wherever available). The specific search string was: ('Psychosis' OR 'Psychoses' OR 'Psychotic' OR 'severe mental illness' OR 'schizophrenia') AND ('Quality of Life' OR 'QoL') AND ('intervention' OR 'therapy' OR 'training') AND ('Randomised' OR 'Randomized' OR 'RCT').

Inclusion criteria

To be eligible for inclusion, primary studies needed to have (i) used an RCT design, (ii) studied adult patients suffering from schizophrenia-spectrum disorders (i.e. schizophrenia, schizoaffective, schizophreniform, delusional, as established by known diagnostic classification criteria (i.e. DSM, ICD) or clinical records; studies including participants with other diagnoses such as bipolar, depression, or other severe mental illnesses, and patients with substance abuse difficulties were excluded), (iii) included patients attending inpatient or outpatient clinical settings, (iv) examined the effectiveness of psychological interventions (i.e. theory-driven, delivered by a trained clinician) targeting QoL (or assessing it as an outcome), (v) included a control group of patients receiving treatment as usual (TAU: i.e. rehabilitation services, being on the waiting list for the treatment under study; receiving any other psychological intervention, or receiving non-therapeutic interventions matched for the study purposes such as computer games or befriending; we excluded multicomponent rehabilitation programs from which the intervention's unique effect could not be isolated, interventions targeting physical/body health [i.e. exercise, weight control, yoga/tai chi], vocational rehabilitation interventions, and interventions not including a therapist [i.e. virtual/mobile applications]), (vi) used a standardized instrument for QoL assessment (i.e. objective, subjective/health-related), (vii) reported sufficient statistical parameters to allow a calculation of effect sizes or provided them upon request from the corresponding authors, and (viii) not reported duplicates of data that had already been published elsewhere.

Screening and data extraction

One researcher (EP) performed the database searches, merged results, and removed duplicates. Two researchers (EN, EP) independently screened the search output based on Titles and Abstracts twice and then accessed the potentially eligible article full texts. The following information was coded from primary studies: study details: title, author, publication year, location; study design: duration, measured outcomes, follow-up period; participant demographics: age, sex, education; setting: outpatients *v.* inpatients *v.* both; sample size for treatment and control arms; diagnoses (% of patients with schizophrenia); mean illness length; medication (in Chlorpromazine-CPZ equivalents/day); intervention characteristics: duration, type, modality (group *v.* individual *v.* both interventions); control group intervention/condition: TAU *v.* other intervention *v.* other non-therapeutic intervention; outcomes: QoL indicator and measure; statistical parameters: means, standard deviations, sample sizes for QoL.

The interventions were grouped as follows, based on their content as described in the primary studies:

- (1) Psychoeducation: interventions focusing on psychoeducation/information provision for the patients only, or together with family members
- (2) Cognitive: interventions including cognitive training, remediation, metacognitive techniques
- (3) CBT: interventions based on cognitive behavioral components
- (4) Combination: interventions based on components of several approaches (i.e. combining psychoeducation with CBT; cognitive and problem-solving, etc.)
- (5) Other: interventions not fitting the previous categories, including third-generation interventions (i.e. mindfulness,

mentalizations), art therapy, solution-focused, etc. Discrepancies were resolved through discussion with a third independent researcher (SP). Eight corresponding authors were contacted and two provided missing information for eligible primary studies. A PRISMA flow-chart of study inclusion is available from online Supplementary Fig S1.

Outcomes and quality assessment

We calculated RCT-based changes in QoL indicators between treatment and control groups using the Hedges g metric (i.e. representing small sample-corrected standardized mean differences) as outcome variables. In cases where more than one effect size could be calculated (i.e. due to availability of multiple QoL indicators, treatment groups, or control groups), we included all effect sizes in our analyses and accounted for the resulting data dependencies by using a multilevel approach.

For our two-level multiverse analyses we (i) averaged effect sizes wherever several QoL subscale values were reported, (ii) preferred comparisons with more complex interventions (i.e. combining psychoeducation with CBT) wherever multiple treatment groups were reported, and (iii) preferred comparisons with control groups that had received treatment as usual in cases where multiple control groups were reported.

In all eligible primary studies, QoL was measured through standardized instruments for objective (i.e. QLS), subjective (i.e. MANSAs; LQOLP) and health-related (i.e. WHO-QoL) indicators. Subjective and health-related indicators were analyzed within a common category, given the subjective self-reported nature of the instruments.

Study quality was assessed twice by two independent researchers (EN, EP) using the Effective Public Health Practice Project Quality Assessment Tool (EPHPP; Thomas, Ciliska, Dobbins, & Micucci, 2004). Studies were rated based on study design, blinding, confounders, instruments psychometric characteristics, and withdrawals/dropouts (see online Supplementary Table S1 for details).

Statistical analyses

We ran all our analyses separately for effect sizes based on objective and subjective (including health-related) QoL. First, we synthesized effect sizes by means of a three-level model to account for within-studies effect size dependencies. To this end, we weighted effect sizes by standard errors (smaller standard errors indicating higher precision and therefore larger weights of studies) using maximum likelihood estimation in random-effects models.

Second, we calculated subgroup effects according to different interventions in the treatment groups (i.e. intervention type: psychoeducation *v.* CBT *v.* cognitive *v.* combination of several types *v.* other psychological interventions such as psychodynamic, systemic, etc.). Because of comparatively low within-subgroup effect size numbers, nominal statistical significance testing of between-subgroup effect differences was deemed unpractical to evaluate effect differences due to low power, but we provide 95% confidence intervals to allow readers to evaluate the amount of overlap.

Third, we ran a series of eight single precision-weighted mixed-effects multilevel meta-regressions (predictors: mean age; schooling years; percentage of women within sample; illness duration; mean medication [CPZ] intake; percentage of patients with schizophrenia within sample; patient service: inpatients *v.*

outpatients *v.* mixed; intervention modality: individual *v.* group *v.* both) for each outcome variable. We used single regressions instead of multiple models because of the expectable study attrition due to missing values for individual predictors. Categorical variables were dummy-coded prior to data analysis. In supplemental analyses, we investigated influences of differences between treatment and control groups in perceived symptoms and functioning on both QoL types.

We interpreted effect sizes according to the well-established thresholds of Cohen (2013), assuming absolute g s = 0.2, 0.5, and 0.8 to represent the lower thresholds of small, moderate, and large effects, respectively. All analyses were performed in the open source software environment R 4.2.0 (R Core Team, 2022) by means of the packages *metafor* (Viechtbauer, 2010) and *robustmeta* (Fisher, Tipton, & Zhipeng, 2017).

Dissemination bias

To investigate potentially confounding influences of dissemination bias, we visually inspected funnel plots and used four formal detection methods, namely: Trim and fill analysis, Egger's regression with sandwich estimators, MLMA-based Egger's regression, and a three-parameter selection model (see online Supplementary file S2 for a detailed description).

Multiverse analyses

It has been shown that different (reasonable) ways to specify study inclusion criteria and how to synthesize the resulting effect sizes may yield substantially differing summary effects and consequently effect interpretations (e.g. Pietschnig, Gerdemann, Zeiler, & Voracek, 2022). On the one hand, different researchers might disagree on an appropriate way to select primary studies that should be synthesized in a meta-analysis (e.g. preferring certain sample characteristics over others). On the other hand, they might disagree on the appropriate analysis approach (e.g. fixed-effect *v.* random-effects calculation).

In other words, different researchers may adopt differing approaches to conceptualize studies and analyze their data (this is typically referred to as researcher degrees of freedom e.g. Wicherts et al., 2016). Either approach may be equally reasonable, but may yield different results and therefore implications. Assessing the multiverse of different (un)reasonable ways to set up and analyze our data by means of specification curve and combinatorial meta-analysis can therefore inform us about (i) the generalizability of a given phenomenon and (ii) its robustness against the use of differing analytical approaches. In our multiverse analyses, we used two-level instead of multilevel modeling.

Specification Curve. In many meta-analyses, choosing a certain inclusion or analytical approach over another may seem equally reasonable to a given researcher. However, isolated specific (reasonable) data syntheses in conjunction with specific analyses may yield non-salient effects (see, for instance, the highly publicized but apparently flukish finding of larger destructive effects of hurricanes with girl *v.* boy names in the USA; Jung, Shavitt, Viswanathan, & Hilbe, 2014; see Simonsohn, Simmons, & Nelson, 2015; Voracek, Kossmeier, & Tran, 2019 for an overview).

Thus, contrasting evidence of primary and even meta-analytical studies may obscure salient effects that may be masked by their differentiation according to certain study or sample characteristics. In other words, it makes a difference which data are analyzed and how, but there is mostly no equivocal way to determine a single ideal specification. Instead, often there are many

ways to reasonably specify study designs and analytical approaches.

Therefore, calculating summary effects according to all possible combinations of reasonable selection and calculation criteria may provide an indication about the generality or specificity of a given effect. In other words, if summary effect sizes are similar in size, regardless of the respective specification, the true effect can be considered to generalize across moderators. But if effect estimates vary substantially across selection criteria or their combinations, this is indicative of effect differentiation.

Combinatorial Meta-Analysis. It can be argued that considering effects of reasonable specifications only may be insufficient to detect influences of moderators (e.g. because relevant moderators have not been identified yet). One way to identify influences of unobserved heterogeneity has been suggested in terms of combinatorial meta-analyses which is typically illustrated by means of GOSH plots (graphical display of study heterogeneity; Olkin, Dahabreh, & Trikalinos, 2012).

In this approach, all possible combinations of effect sizes are considered to represent a possible (albeit potentially unreasonable) way to estimate a summary effect. These summary effects are then related to the resulting between-studies heterogeneity of the corresponding summary effect calculation. When effects are stable, summary effect estimates should not show systematic associations with heterogeneity indices. Because the number of possible summary effect estimates ($2^k - 1$) typically exceeds the computational power of most computers nowadays (e.g. for subjective QoL, there would be $2^{45} \approx 35$ trillion possibilities to calculate two-level model-based summary effects), we sampled 100 000 combinations at random, following standard procedure (e.g. Pietschnig et al., 2022).

Results

Final sample

In all, we identified sixty independent studies that met our inclusion criteria, comprising $k = 89$ study effects ($k_s = 70$ and 19 for subjective and objective QoL; $N_s = 6254$ and 1024, respectively). More than half of the studies were from Europe ($k = 37$), nine studies were from Asia, five from USA/Canada, four from Australia, three from South America and two from Africa. The majority of the samples comprised only patients with schizophrenia (mean % of schizophrenia diagnosis within samples = 86.38%), with the rest comprising patients with schizophrenia-spectrum disorders (i.e. including schizoaffective, schizophreniform and delusional), that were predominantly male (63.90%), had on average 11.86 school years, and a mean age of 39.02 years. Mean illness duration was 13.94 years (s.d. = 5.22) and administered medication averaged at 536.14 (s.d. = 264.68) CPZ equivalents/day. Characteristics of the included studies are detailed in Table 1.

Study quality

In terms of the quality ratings by means of the EPHPP Quality Assessment Tool (Thomas et al., 2004), 32 studies were of strong, 21 of moderate, and 7 studies of weak quality (see online Supplementary Table S1). Global study quality ratings did not significantly predict effect sizes of neither subjective nor objective QoL ($p_s = 0.373$ and 0.783 , respectively), thus indicating no systematic influences of study quality on effect sizes.

Interventions and comparators

There were 15 studies with interventions targeting objective QoL. Six of them used cognitive interventions; four of them used CBT, three used a combination of interventions such as the Illness Management and Recovery (IMR), and two used psychoeducation. The interventions were compared with: other non-therapeutic conditions in seven studies (i.e. computer games, non-specific counseling); TAU in five studies; and other interventions in three studies.

For subjective QoL, there were 45 studies focusing on different interventions, with 11 of them using CBT; 12 of them using other intervention types such as systemic, psychodynamic (art therapy), mindfulness, or family therapy; eight using cognitive interventions; eight using interventions combining different elements such as the IMR or the Integrated Psychological Therapy (IPT); and five using psychoeducation. Most of the studies compared the interventions to TAU ($k = 31$), seven compared them to other interventions, and seven to other non-therapeutic conditions such as befriending or newspaper reading (see Table 1 for details).

Quality of life outcomes

Most of the studies examining interventions focusing on objective QoL included this as a primary outcome (12 out of 15 studies), whereas for subjective QoL this was true for less than half of the studies (26 out of 45), with the rest considering QoL a secondary outcome. All studies assessing objective QoL used the Quality of Life Scale (QLS) ($k = 15$). Subjective (including health-related) QoL was assessed through a variety of instruments, with the most commonly used being the WHO-QoL ($k = 13$) and the Manchester Short Assessment of Quality of Life (MANSA) ($k = 10$) (see Table 1).

Intervention effectiveness on QoL

Our results indicated substantial larger intervention effects of most treatments on objective QoL compared to subjective QoL. Overall, non-trivial and significant, albeit small positive effects of treatments compared to controls were observed for objective QoL (overall $g = 0.330$; $p = 0.026$), whilst overall treatment effects on subjective QoL were non-significant and merely trivial (overall $g = 0.184$; $p = 0.118$; Table 2).

This general pattern of results held up for almost all intervention-based multilevel subgroup analyses. For objective QoL, psychoeducation appeared to have the most beneficial intervention effects, yielding a significant large effect ($g = 0.909$, $p = 0.048$). CBT-based interventions showed a modest-to-strong ($g = 0.653$) and cognitive interventions a small, but non-trivial, positive effect ($g = 0.241$), although both summary effects were nominally non-significant. A combination of therapeutic interventions did not yield any meaningful influences either (top half of Table 2).

The only meaningful treatment effect for subjective QoL was observed for a combination of treatments ($g = 0.314$, $p = 0.036$). None of the other examined interventions yielded summary effects that exceeded triviality or significance thresholds (excepting cognitive interventions, which yielded a significant, but trivial effect; bottom half of Table 2).

Regression analyses

In our meta-regressions, we investigated potential influences of eight predictors on effect sizes. Neither objective nor subjective

Table 1. Characteristics of included studies^a

Number	Authors	Country of study, sample, % Female (n mean age (s.d.))	Diagnosis/Diagnostic Tool Patient type (in/out) Psychosis duration (years M; s.d.)	Primary Intervention type	Intervention Group: description	Control Group: description	Intervention Duration and type (group/individual)	Medication CPZ mg/day (M; s.d.)	Type of outcome and Instruments for QoL, symptoms, functioning	Assessment time-points	Main conclusions
1	Aloi et al. (2018)	Italy IPT N = 24 F% = 40 Age M = 50.5 (10.0) TAU N = 22 F% = 19 Age M = 52.14 (9.7)	Schizophrenia DSM-5 Inpatients IPT: 22.9 (3.5) TAU: 23.4 (2.3)	Combination	IPT Integrated Psychological Therapy Composed of five subprograms: cognitive differentiation, social perception, verbal communication; One role-playing; one problem solving Plus TAU	TAU not defined	Twice a week, 45 min each session for 36 weeks Group	IPT: 632.4 (437.9) TAU: 674.2 (489.4)	Primary Health related: WHO QoL Symptoms: PANSS Functioning: GAF	Pre post	Results revealed significant differences in favor of the IPT group in QoL
2	Andreou et al. (2017)	Germany MCT + N = 46 F% = 54 Age M = 36.91 (12.5) CogPack N = 46 F% = 34.7 Age M = 35.59 (13.1)	Schizophreniaspectrum DSM-IV Both inpatients and outpatients	Cognitive	MCT + History taking, intervention rationale, development of a personal illness model; cognitive biases, social interaction, mood and stress coping Plus TAU	Cognitive Training (Cog Pack) computerized; targets cognitive dysfunctions: memory, reasoning, selective attention, psychomotor speed. Plus TAU	Twice a week approx. 45-60 min, six weeks Individual	MCT + : 344.56 (424.0) CogPack: 305.49 (393.5)	Secondary Health related: WHO QoL-BREF Symptoms: PANSS	Pre post Follow-up 6 months	Only a transient effect on QoL environment factor at T1; no other significant effects on quality of life
3	Atkinson et al. (1996)	UK Psychoeducation N = 57 F% = N/A Age N/A Waiting list N = 73 F% = N/A Age M = N/A	Schizophrenia DSM-III-R outpatients	Psychoeducation	Psychoeducation information and problem-solving sessions	Waiting List	Weekly, 1.5 h 20 weeks Group	N/A	Primary Objective: QLS Symptoms: BPRS Functioning: GAS; SFS	Pre post Follow up three months	There were significant QoL improvements in post and follow-up for psychoeducation attendees
4	Bambini et al. (2022)	Italy PragmaCom N = 15 F% = 46.6 Age M = 40.87 (10.49) Active Control N = 15 F% = 26.6 Age M = 44.00 (8.94)	Schizophrenia DSM-5 outpatients PragmaCom 17.93 (9.45) Newspaper 19.40 (11.22)	Cognitive	PragmaCom focuses on comprehension and understanding of figurative language; production and quantity and relevance of the information provided in speech	Newspaper discussion group Reading newspaper articles about recent local and political issues, summary of the most important information and opinion expression	Weekly, 40 min, 13 weeks Group	PragmaCom: 408.94 (213.12) Newspaper: 481.71 (154.21)	Secondary Objective: QLS Symptoms: PANSS	Pre post Follow up three months	Small QoL gains for the intervention group at post intervention, large QoL gains at follow-up
5	Baumgartner et al. (2022)	Tanzania Psychoeducation N = 33 F% = 39.4 Age M = 33.64 (7.52) Standard Care N = 33 F% = 27.3% Age M = 32.45 (7.94)	Schizophrenia Schizoaffective ICD-10 Outpatients	Psychoeducation	Family psychoeducation information about biological, psychological and social aspects of mental illness; the nature, effects and side effects of psychiatric treatments; recovery and relapse prevention; mental illnesses management; problem solving coping skills, personal care Plus Standard Care	Standard Care not defined	Weekly, 1.5-2 h, for 12 weeks Group	N/A	Primary Health related WHOQoL	Pre post 4 months follow up	Higher QoL for the intervention group

(Continued)

Table 1. (Continued.)

Number	Authors	Country of study, sample, % Female (n) mean age (s.d.)	Diagnosis/Diagnostic Tool Patient type (in/out) Psychosis duration (years M; s.d.)	Primary Intervention type	Intervention Group: description	Control Group: description	Intervention Duration and type (group/individual)	Medication CPZ mg/day (M; s.d.)	Type of outcome and Instruments for QoL, symptoms, functioning	Assessment time-points	Main conclusions
6	Bechdolf et al. (2010)	Germany CBT N = 40 F% = 55 Age M = 32.2 (9.9) Psychoeducation N = 48 F% = 54.2 Age M = 31.4 (10.6)	Schizophrenia spectrum ICD-10 Inpatients CBT 4.7 (5.4) Psychoeducation 4.16 (4.89)	CBT	CBT (i) sharing information about voices and delusions, models of psychosis; (ii) improving self-esteem; (iii) formulation of key problems; (iv) reducing severity and occurrence of key problems; and (v) relapse prevention/keeping well Plus TAU	Psychoeducation symptoms and models of psychosis, medication effects and side-effects, maintenance medication, relapse early symptoms and prevention. Plus TAU	Twice a week, between 60–90 min eight weeks Group	CBT 431.7 (201.0) PE 375.0 (349.5)	Secondary Subjective: MSQoL Symptoms: PANSS	Pre Post Six months follow up	QoL improved in both groups. No significant differences between CBT and PE were found at post-treatment, or at 6-month follow up.
7	Böge et al. (2017)	Germany MBGT N = 21 F% = 47.6 Age M = 37.71 (12.82) TAU N = 19 F% = 31.5 Age M = 42.74 (14.11)	Schizophrenia spectrum DSM-5; ICD-10 Both inpatients and outpatients MBGT: 11.33 (9.1) TAU: 12.71 (1.22)	Other	Mindfulness-based group therapy (MBGT) understanding of four core aspects of mindfulness (breath, senses, detachment, and body awareness) Plus TAU	TAU Multiprofessional program: psychological interventions, occupational therapy, physiotherapy, and physical exercises, psychopharmacological treatment.	Three therapy sessions per week (1 60 min, 2 30 min), four weeks Group	MBGT: 375 (475.0) TAU: 975.0 (1425.0)	Primary Health related: WHOQoL-bref Symptoms: PANSS Functioning: PSP	Pre post three months follow-up	QoL showed significant improvements in the MBGT group
8	Briki et al. (2014)	France Metacognitive N = 25 F% = 36 Age M = 41.1 (8.1) ST N = 25 F% = 32 Age M = 41.1 (12.4)	Schizophrenia spectrum DSM-IV Both in and outpatients MCT: 14.6 (8.4) ST: 17.8 (10.9)	Cognitive	MCT cognitive bias exploration Plus TAU	Standard Treatment (ST) Experience sharing, verbal interaction promotion Included some elements of psychoeducation Plus TAU	Twice a week 1 h, 8 weeks (16 sessions) Group	MCT: 1519 (1635) ST: 1359 (1516)	Primary Objective: QLS Symptoms: PANSS	Pre post	There was a trend of QoL improvement
9	Bryce et al. (2018)	Australia CR N = 29 F% = 34 Age M = 40.34 (9.62) CG N = 27 F% = 26 Age M = 41.78 (9.35)	Schizophrenia Schizoaffective DSM-IV Outpatients CR 13.55 (7.69) CG 14.73 (8.43)	Cognitive	Cognitive Remediation (CR) With COGPAC. Cognitive tasks, performance feedback, discussions about relevant task-specific strategies, encouragement to practice	Computer Games (CG): commercially available games (e.g. arcade and puzzle games)	Twice weekly 1hour sessions, 20 weeks Group	CR: 738.45 (510.54) CG 666.35: (454.63)	Secondary Subjective: EUROHIS-QOL Symptoms: PANSS	Pre post three months follow-up	No differences in QoL following intervention
10	Bucci et al. (2013)	Italy NIT N = 25 F% = 16 Age M = 39.48 (9.49) SSIT N = 33 F% = 21 Age M = 37.27 (8.18)	Schizophrenia Schizoaffective Clinical records Outpatients NIT: 19.36 (7.57) SSIT: 15.39 (8.68)	Cognitive	Neurocognitive Individualized Training (NIT) Used the REHACOM Cognitive tasks, positive and/or corrective feedback and strategy coaching or compensatory skills training	Social Skills Individualized Training (SSIT) Training individual social and emotional perception and expressiveness, conversation skills	Two sessions per week 1 h, six months Individual	N/A	Primary Objective: QLS Symptoms: PANSS	Pre post Six months follow-up	In the NIT group improvement of interpersonal relationships and in the SSIT group improvement of instrumental role

(Continued)

Table 1. (Continued.)

Number	Authors	Country of study, sample, % Female (n) mean age (s.d.)	Diagnosis/Diagnostic Tool Patient type (in/out) Psychosis duration (years M; s.d.)	Primary Intervention type	Intervention Group: description	Control Group: description	Intervention Duration and type (group/individual)	Medication CPZ mg/day (M; s.d.)	Type of outcome and Instruments for QoL, symptoms, functioning	Assessment time-points	Main conclusions
11	Cavallaro et al. (2009)	Italy CR N = 50 F% = N/A Age M = 33.2(9.5) PBO N = 36 F% = N/A Age M = 34.2 (6.8)	Schizophrenia Outpatients DSM-IV CR 8.28 (6.7) PBO 8.08 (5.1)	Cognitive	Cognitive Remediation (CR) COGPACK Cognitive tasks, feedback Plus TAU (Schizophrenia Rehabilitation Treatment-SRT) medication management, psychiatric evaluation, rehabilitation, Communication, Social Skills Training, Problem Solving, psychoeducation	Computer aided activity (PBO) computer-aided nondomain-specific activity Plus TAU (SRT)	Three sessions a week, 1 h, 12 weeks. Individual	N/A	Primary Objective: QLS Symptoms: PANSS	Pre post	Significant improvements for the SRT + CR group in QoL
12	Chen et al. (2021)	China MCT N = 58 F% = 58.6 Age M = 55.28 (9.51) CBR N = 62 F% = 61.2 Age M = 52.90 (12.14)	Schizophrenia outpatients DSM-IV MCT: 22.69 (12.02) CBR: 23.35 (12.70)	Cognitive	Metacognitive Training (MCT): cognitive and social biases training Plus TAU Community-Based Rehabilitation (CBR): medication training, relapse identification, physical management, life, social and occupational skills	TAU (CBR)	Weekly, 60 min, 8 weeks Group f	N/A	Primary Health-related: Schizophrenia Quality of Life Scale (SQLS) Symptoms: PANSS	Pre post	The QoL of patients in the MCT group improved at post-treatment
13	Contreras et al. (2018)	Australia VPT + CR N = 13 F% = 60 Age M = 34.10 (12.9) CR N = 12 F% = 30 Age M = 39.2 (5.37)	Schizophrenia Clinical Records Outpatients	Cognitive	Visual Processing Therapy (VPT) six modules targeting key aspects of visual discrimination (2 tasks) or perceptual organization (4 tasks). + COGPACK	Cognitive Remediation with COGPACK four different sets of domain-specific exercises, plus social encouraging interaction and use of new performance strategies	Twice a week, for 80 min each time 10 weeks Group	N/A	Primary Health-related: Quality of Life Scale (EUROHIS-QoL) Symptoms: PANSS	Pre post	Significant QoL improvements in both groups, no differences between them
14	Crawford et al. (2012)	UK Art therapy N = 140 F% = 36 Age M = 41(11) Activity group N = 140 F% = 36 Age M = 42 (12) TAU N = 137 F% = 28 Age M = 40 (12.0)	Schizophrenia ICD-10; DSM-5 outpatients	Other	Art Therapy potential to explore relationships between group members. Use of art materials to express feelings freely and spontaneously. Plus TAU secondary-care mental health services, care co-ordination, pharmacotherapy and the option of referral to other services	Activity group themed discussion, board games, watching and discussing DVDs, visits to local cafés, visits to places of interest. Plus TAU	Weekly, 90 min for 12 months Group	N/A	Primary Health related QoL: EQ-5D Symptoms: PANSS Functioning: GAF	Pre post 24 months	No QoL improvements in the art group therapy compared to the activity or TAU group

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Table 1. (Continued.)

Number	Authors	Country of study, sample, % Female (n) mean age (s.d.)	Diagnosis/Diagnostic Tool Patient type (in/out) Psychosis duration (years M; s.d.)	Primary Intervention type	Intervention Group: description	Control Group: description	Intervention Duration and type (group/individual)	Medication CPZ mg/day (M; s.d.)	Type of outcome and Instruments for QoL, symptoms, functioning	Assessment time-points	Main conclusions
15	D'Amato et al. (2011)	France CR N = 39 F% = 25.6 Age M = 33.4 (6.09) TAU N = 38 F% = 23.6 Age M = 32.2 (6.0)	Schizophrenia DSM-IV CR:8.7 (6.6) TAU: 8.1 (4.5)	Cognitive	Cognitive Remediation (CR) RehaCom Training: attention/concentration, working memory, logic, and executive functions Plus TAU	TAU	Twice a week, 2-h sessions, 7 weeks Individual	CR:337 (215) TAU :441 (230)	Secondary Health-related: SQLS Symptoms: PANSS	Pre post	QoL showed trends toward improvement in both groups
16	Dellazizzo et al. (2021)	Canada VRT N = 37 F% = 21.6 Age M = 43.6 (12.0) CBT N = 37 F% = 24.3 Age M = 42.5 (12.7)	Schizophrenia/Schizoaffective Clinical records outpatients VRT 18.0 (10.6) CBT 14.6 (10.2)	Other	Virtual Reality Therapy Avatar creation and immersion, hallucinatory experience confrontation, self-esteem, final consolidation Plus TAU	CBT History of voices and goal setting, assessing and learning about cognitive model of hallucinations, metacognition, attributions, common beliefs Plus TAU	Weekly, 1 h, 9 weeks Individual	N/A	Secondary Subjective Quality of Q-LES-Q-SF Symptoms: PANSS	Pre post 3 months	VRT significantly ameliorated quality of life. A trend of group x time interaction for QoL
17	Fardig et al. (2011)	Sweden IMR N = 21 F% = 38 Age M = 40.38 (6.76) TAU N = 20 F% = 55 Age M = 40.45 (6.64)	Schizophrenia/Schizoaffective DSM-IV outpatients	Combination	Illness management recovery (IMR): recovery strategies, facts about schizophrenia, stress-vulnerability model and treatment strategies, building social support, effective use of medication, relapse reduction, coping with stress, persistent symptoms, meet needs	TAU Case management, medication, psychotherapy, access to recreational and therapeutic activities	Weekly, 1 h, 40 weeks Group	N/A	Primary Subjective: MANSA Symptoms: Psychosis Evaluation Tool for Common Use by Caregivers (PECC)	Pre post 21 months	No QoL differences for any of the time points
18	Freeman et al. (2015)	UK CBT N = 24 F% = 33 Age M = 39.6 (11.6) TAU N = 26 F% = 31 Age M = 42.2 (13.5)	Schizophrenia/spectrum Clinical records outpatients	CBT	CBT assessment of the triggering and maintenance of sleep difficulties, goal setting stimulus control and improvement of daytime activity levels	TAU Antipsychotic medication, meetings with the psychiatrist, nurse, gp, day-care center	Eight sessions over 12 weeks with flexible duration Individual	CBT 363.7 (266.5) TAU 495.8 (358.1)	Secondary Health related: EQ-5D Symptoms: PANSS	Pre post 24 weeks	Participants in the CBT group improved QoL levels in 24 weeks compared to TAU
19	Freeman et al. (2021)	UK Feeling Safe N = 64 F% = 47 Age M = 41.29 (12.3) Befriending N = 66 F% = 33 Age M = 41.3 (12)	Schizophrenia/spectrum Clinical records outpatients	CBT based	Feeling Safe improving sleep, reducing worry, increasing self-confidence, reducing the impact of voices, improving reasoning processes, and feeling safe Plus TAU	Befriending simulate how a good friend would respond, involving: a general focus on non-threatening topics, non-confrontation, empathy, and supportiveness Plus TAU	Weekly 20 sessions Individual	FS 449.9 (392.7) BF 514.1 (412.9)	Secondary Health related: EQ-5D Symptoms: PSYRATS	Pre post 12 months	Significant improvements in QoL with the Feeling Safe Program compared with befriending

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20	Garety et al. (2021)	UK Slowmo N = 181 F% = 27.1 Age M = 43.1 (11.7) TAU N = 180 F% = 33.3 Age M = 42.2 (11.6)	Schizophreniaspectrum ICD-10 outpatients	CBT	SlowMo blended digital psychological intervention for paranoia aims to build awareness of a tendency to JTC and develop increased belief flexibility	TAU antipsychotic therapy, outpatient psychiatric appointments	8 sessions, 60–90 min, 12 weeks Individual	SlowMo 452.96 (399.45) TAU 519.97 (419.80)	Secondary Subjective QoL: MANSA Symptoms: PSYRATS; SAPS	Pre post 24 weeks	QoL significant benefits for the SlowMo participant in comparison to TAU
21	Garrido et al. (2013)	Spain Cognitive Remediation N = 38 F% = 29 Age M = 33.37 (8.32) Watching Videos N = 29 F% = 24 Age M = 33.21 (6.89)	Schizophrenia outpatients DSM-IV CR: 11.84 (8.23) WV: 10.68 (6.66)	Cognitive	Cognitive Remediation computerized program, neurocognitive exercises on attention, working memory, executive function. The therapist facilitated efficient problem-solving strategies	Watching videos nature, science and culture documentaries	48 sessions of therapy or 1 h six months. Individual	CR 307.64 (228.60) WV 326.99 (275.07)	Secondary Objective QLS Symptoms PANSS	Pre Post	An advantage was observed for cognitive remediation in QoL
22	Halperin et al. (2000)	Australia CBT N = 8 F% = N/A Age M = N/A Wait List control N = 8 F% = N/A Age M = N/A	Schizophrenia Clinical records outpatients	CBT	CBT exposure situations, cognitive restructuring, and homework assignments Plus TAU	Wait list control	weekly for 8 weeks in 2-h sessions Group	N/A	Primary Subjective Q-LES-Q	Pre post six weeks	Significant improvement of QoL that was maintained in follow-up
23	Halverson et al. (2021)	USA I-CAT N = 19 F% = 47 Age M = 23.6 (4.3) TAU N = 19 F% = 47 Age M = 24.9 (3.86)	Schizophrenia spectrum DSM-IV Outpatients I-CAT 1.7 (1.5) TAU 1.8 (2.0)	Combination	Integrated-Coping Awareness Therapy (I-CAT) integration of positive psychology to increase positive emotions and behavioral flexibility; mindfulness to increase capacity for stress and build resilience. Plus TAU	TAU Medication management, family therapy, supported employment, peer support	Weekly, up to 24 sessions Individual	N/A	Primary Objective: QLS Symptoms: PANSS Social Functioning: FESFS	Pre post three months follow-up	No significant differences in QoL between groups
24	Hasan and Musleh (2017)	Jordan Empowerment N = 56 F% = 35.7 Age M = 37.6 (5.6) TAU N = 56 F% = 41.1 Age M = 36.9 (6.3)	Schizophrenia Schizoaffective DSM-5 outpatients Empowerment 7.7 (4.3) TAU 8.2 (4.5)	Other	Empowerment Six topics : comprehending recovery from an illness, doing and undoing: efforts made for recovery and the route to the best recovery Plus TAU	TAU medication and laboratory examinations	Weekly, 20–30 min, 6 sessions Group	N/A	Secondary Subjective SQoL: Schizophrenia–Quality of Life-18 Symptoms: PANSS	Pre post Three months	The empowerment intervention was superior In improving QoL
25	Hayes et al. (1995)	Australia Social Skills Training N = 32 F% = N/A Age M = N/A Discussion group N = 31 F% = N/A Age M = N/A	Schizophrenia DSM-III-R outpatients	CBT	Social Skills training CBT based Emphasized interpersonal skills, social problem solving, positive time use skills, generalization enhancement techniques. Plus TAU	Discussion group Focused on the topics of interpersonal relations and purposeful use of time Plus TAU	Biweekly, 75 min 18 weeks Group	N/A	Primary Objective QLS Symptoms: BPRS Functioning: GAS	Pre post follow-up	Both groups improved in QoL, no significant differences between them

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Number	Authors	Country of study, sample, % Female (n) mean age (s.d.)	Diagnosis/Diagnostic Tool Patient type (in/out) Psychosis duration (years M; s.d.)	Primary Intervention type	Intervention Group: description	Control Group: description	Intervention Duration and type (group/ individual)	Medication CPZ mg/day (M; s.d.)	Type of outcome and Instruments for QoL, symptoms, functioning	Assessment time-points	Main conclusions
26	Kurtz et al. (2015)	USA CR N = 26 F% = 73 Age M = 36.1 (12.8) Computer skills N = 30 F% = 73 Age M = 37.1 (12.1)	Schizophrenia Schizoaffective DSM-IV Outpatients CR 12.8 (11.8) CS 12.4 (10.7)	Cognitive	Cognitive Remediation computer-assisted cognitive exercises to improve attention, memory, executive-function, language processing through repeated drill-and-practice Plus Social Skills training Conversation, assertiveness, friendship skills	Computer skills Computerized tutorials, computer literacy specific skills Plus Social Skills training	Three days per week, 50 min, 23 weeks Individual	N/A	Primary Objective: QLS-B Symptoms: PANSS	Pre post	QoL did not differ between the groups
27	Lee et al. (2012)	Korea CBSST N = 8 F% = 62.5 Age M = 36.38 (11.56) TAU N = 12 F% = 58.3 Age M = 29.67 (8.9)	Schizophrenia DSM-IV Inpatients CBSST: 15.38 (9.67) TAU: 23 (10.1)	CBT	CBSST – Cognitive Behavioral Social Skills Training Mistakes in thinking Communication skills Expressing feelings and making positive requests Identify problem behaviors and feelings Plus TAU	TAU not defined	Twice a week, 45 min. 12 sessions. Group	N/A	Primary Health related: WHO QoL-BREF Positive Symptoms: SAPS Negative Symptoms: SANS Functioning: ILSS	Pre post	QoL increase in the CBSST group compared with TAU
28	Lee et al. (2010)	Korea SOPs: N = 23 F% = 47.8 Age M = 43.81 (5.07) CG N = 23 F% = 47.8 Age M = 44.75 (3.19)	Schizophrenia DSM-IV Inpatients SOPs: 18.44 (4.3) CG: 16.44 (2.89)	CBT	SOPs – (Self-Stigma Overcome program): CBT techniques for sense of security, sense of purpose, and sense of competence	Control Group Not defined	Once a week, 15 sessions, 15 weeks. Group	SOPs: 311.35 (175.37) CG: 313.23 (178.33)	Primary Health related: WHO QoL – BREF Symptoms: PANSS	Pre post	There were no significant improvements on QoL for the CBT group
29	Li et al. (2018)	China CbCI: N = 199 F% = 50.8 Age M = 40.21 (7.57) TAU N = 185 F% = 46.5 Age M = 39.7 (7.83)	Schizophrenia ICD-10 Outpatients CbCI: 14.11 (7.49) TAU: 15 (8.45)	Combination	Community-based comprehensive intervention (CbCI): Strategies against stigma and discrimination (SASD) Psychoeducation, Social skills, Medication self-management, CBT Plus TAU	TAU Not defined	Monthly in the first six months, twice in the last three months. Group	N/A	Primary Health related SQLS Symptoms BPRS Functioning: GAF	Pre post	There were no significant differences on SQLS between the two groups
30	Montag et al. (2014)	Germany AT: N = 29 F% = 20.8 Age M = 38.8 (10.4) TAU N = 24 F% = 21 Age M = 39.6 (10.6)	Schizophrenia DSM-IV Inpatients AT: 12.1 (12.1) TAU: 15.2 (9.3)	Other	Psychodynamic Art Therapy: Non-directive supporting the art process and helping to understand the image. shared viewing and reflecting on the images.	TAU: supportive contact, pharmacotherapy, CBT, psychodynamic, occupational therapy, music therapy, cognitive and social skills training, excursions, relaxation, sports.	12 sessions, 90 min each for 6 weeks. Group	CPZ mg/day (M; s.d.) AT: 352.5 (264.1) TAU: 522 (298.4)	Secondary Subjective MSQoL Symptoms – negative: SANS Symptoms – positive: SAPS Functioning: GAF	Pre post Follow up 12 weeks	No effects of AT on QoL

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Table 1. (Continued.)

Number	Authors	Country of study, sample, % Female (n mean age (s.d.))	Diagnosis/Diagnostic Tool Patient type (in/out) Psychosis duration (years M; s.d.)	Primary Intervention type	Intervention Group: description	Control Group: description	Intervention Duration and type (group/ individual)	Medication CPZ mg/day (M; s.d.)	Type of outcome and Instruments for QoL, symptoms, functioning	Assessment time-points	Main conclusions
31	Moritz et al. (2014)	Germany MCT: N = 76 F% = 40.8 Age M = 36.82 (11.12) CogPack N = 74 F% = 33.8 Age M = 32.68 (9.54)	Schizophreniaspectrum DSM-IV inpatients and outpatients	Cognitive	MCT (metacognitive training): attributional style, JTC, changing beliefs TOM/social cognition memory/ overconfidence Plus antipsychotic medication	CogPack: neuropsychological training Plus antipsychotic medication	Twice a week, 45–60 min, four weeks Group	MCT: 72.37 (61.59) CogPack: 79.71 (63.20)	Primary Health related: WHO QoL – BREF Symptoms – positive, total: PANSS	Pre post Follow-up 3 years	No post-intervention differences, significant group differences at the 3-year follow-up
32	Morrison et al. (2018)	UK CBT N = 26 F% = 38 Age M = 23.19 (6.32) CBT plus Antipsychotics N = 25 F% = 44 Age M = 24.44 (6.86) Antipsychotics N = 24 F% = 46 Age M = 23.21 (4.97)	Schizophreniaspectrum ICD-10 outpatients	CBT	CBT Problem focused	Antipsychotics	Weekly, Six months Individual	N/A	Secondary Health related WHO-QoL Symptoms PANSS Functioning: PSP	Pre post one-year	There were QoL improvements, no differences between groups
33	Muhić et al. (2022)	Bosnia Herzegovina Multifamily groups (MFG): N = 36 F% = 67 Age M = 45 TAU N = 36 F% = 64 Age M = 43	Schizophrenia ICD-10 Outpatients	Other	Multifamily groups (MFG): bring together patients with schizophrenia, their family and friends, sharing of experiences, mutual support, Plus TAU	TAU not defined	Monthly, 2 h, 6 months Group	N/A	Primary Subjective: MANSAs Symptoms: BPRS	Pre post Follow up 12 months	The intervention significantly improved quality of life at 6 12 months compared with TAU
34	Ngoc et al. (2016)	Viet nam FSPP: N = 30 F% = 51.4 Age M = 24.87 (5.11) TAU N = 29 F% = 48.6 Age M = 23.69 (4.37)	Schizophrenia ICD-10 Inpatients FSPP: 1.58 (1.13) TAU: 1.99 (1.06)	Psychoeducation	FSPP (Family Schizophrenia Psychoeducation Program) Schizophrenia as a medical condition, family support, community reintegration Plus TAU (medication)	TAU (medication)	10 days, 3 sessions, 1.5 h each session. Individual	N/A	Primary Subjective: Q-LES-Q- SF	Pre post	QoL showed a significant treatment effect favoring the FSPP group.
35	O'Donnell et al. (2003)	Ireland Compliance therapy: N = 28 F% = 32.14 Age M = 32 (9) Control Group: N = 28 F% = 21.4 Age M = 32 (9)	Schizophrenia DSM-III-R Inpatients CT: 6 (7) CG: 4 (5)	CBT	Compliance therapy: Review of the patient's illness history and understanding of illness, maintenance medication, and stigma.	Non-specific counseling Discussion sessions with the patients with non-therapeutic content	Monthly, 30–60 min, six months Individual	CT: 835 (507) CG: 883 (715)	Secondary Objective: QLS Symptoms: PANSS Functioning: GAF	Pre post Follow-up 1 year	No differences between the intervention and control group post intervention

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Table 1. (Continued.)

Number	Authors	Country of study, sample,% Female (n) mean age (s.d.)	Diagnosis/Diagnostic Tool Patient type (in/out) Psychosis duration (years M; s.d.)	Primary Intervention type	Intervention Group: description	Control Group: description	Intervention Duration and type (group/ individual)	Medication CPZ mg/day (M; s.d.)	Type of outcome and Instruments for QoL, symptoms, functioning	Assessment time-points	Main conclusions
36	Omrani et al. (2012)	Iran CT: N = 38 F% = 31.57 Age M = 29.9 (9.27) SC: N = 38 F% = 31.57 Age M = 31.1 (10.35)	Schizophrenia spectrum DSM-IV Inpatients and outpatients	CBT	Compliance therapy (CT): evaluation, solving problems of medical therapy, identifying conflicts of treatment, attitudes and attentions to treatment, false beliefs and attitudes about the disease and its medications, describing discrimination between true beliefs and superstitions	Supportive counseling (SC) non – specific counseling, guidance and encouragement to develop the patient's own resources; does not specifically focus on any aspects of psychotherapy.	At first every two weeks and then monthly, 30–60 min, eight sessions, six months. Individual	N/A	Primary Objective: QLS Symptoms: PANNS Functioning: GAF	Pre post	Compliance therapy improved QoL in comparison to Control intervention
37	Penn et al. (2011)	USA GRID: N = 23 F% = 39.1 Age M = 23.48 (3.89) TAU: N = 23 F% = 39.1 Age M = 20.96 (2.14)	Schizophrenia spectrum DSM-IV outpatients GRID: 4.65 (9.71) TAU: 3.83 (7.88)	CBT	Graduated Recovery Intervention Program (GRID): CBT based engagement and wellness management; substance use; persistent symptoms; functional recovery. Plus TAU	TAU – OASIS program: Case management based on individual needs	Once a week for 36 weeks. Individual format.	N/A	Primary Objective QLS Symptoms PANNS Community Functioning: RFS	Pre post Follow up 3 months	Participants who received GRIP showed trend level improvement in quality of life.
38	Pitkänen et al. (2012)	Finland CB N = 100 CE N = 106 F% = N/A Age = N/A TAU: N = 105 F% = N/A Age M = N/A	Schizophrenia spectrum ICD-10 inpatients	Psychoeducation	2 interventions Computer-based patient education (CB) & Conventional education with standard leaflets (CE): CB systematic computer-based education program (Mieli. Net): information areas: illness, treatment, well-being, support and patients' rights. CE information in written leaflets and sessions corresponding to the information areas, as in the CB education group.	TAU: patient education according to usual ward procedures.	CB: Weekly, 40 min, 5 sessions. CE: Weekly, 30 min, 5 sessions. Individual	N/A	Primary Subjective: Q-LES-Q-SF Symptoms PANNS Functioning: SDS	Pre post Follow up 12 months	QoL improved in all education groups. There were no significant differences between groups
39	Pontes (2012)	Brasil Cognitive training N = 9 F% = 11 Age M = 37.1 (8.1) Newspaper group N = 8 F% = 25 Age M = 39.3 (6.4)	Schizophrenia DSM-IV-R Outpatients	Cognitive	Cognitive training Attention and memory exercises	Newspaper group	20 sessions 40–60 min weekly Group	N/A	Secondary Health-related WHOQoL PANSS	Pre post	No significant differences between the two groups

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Table 1. (Continued.)

Number	Authors	Country of study, sample, % Female (n) mean age (s.d.)	Diagnosis/Diagnostic Tool Patient type (in/out) Psychosis duration (years M; s.d.)	Primary Intervention type	Intervention Group: description	Control Group: description	Intervention Duration and type (group/individual)	Medication CPZ mg/day (M; s.d.)	Type of outcome and Instruments for QoL, symptoms, functioning	Assessment time-points	Main conclusions
40	Pot-Kolder et al. (2018)	Netherlands VR – CBT: N = 58 F % = 31 Age M = 36.5 (10) Waiting List – TAU: N = 58 F % = 28 Age M = 39.5 (10)	Schizophrenia spectrum DSM-IV outpatients VR – CBT: 13.3 (10.6) TAU: 14.9 (9.5)	CBT	Virtual-reality-based cognitive behavioral therapy (VR – CBT): Exposure to idiosyncratic social environmental cues that elicited fear, paranoid thoughts, and safety behaviors. Plus TAU	TAU – Waiting list: Antipsychotic medication, regular contact with a psychiatrist to control symptoms, regular contact with a psychiatric nurse to improve self-care, daytime activities, and social and community functioning.	Biweekly, 1 h, 40 min. 8 to 12 weeks Individual		Secondary Subjective: MANSAs Symptoms: Green et al., Paranoid Thoughts Scale Functioning: SOFAS	Pre post Follow up 6 months	Quality of life at the post-treatment or follow-up assessments did not differ significantly between groups.
41	Priebe et al. (2015)	UK DIALOG + N = 94 F % = 30 Age M = 41.5 (10.7) CG N = 85 F % = 33 Age M = 41.7 (9.3)	Schizophrenia spectrum ICD-10 outpatients	Other	DIALOG+ Informed by the principles of Solution-Focused Therapy: (1) understanding the patient's concerns and previous effective coping strategies; (2) identifying best-case scenarios and smallest steps for improvement; (3) exploring options available to the patient, including the patient's own resources, the clinician's and those of others in the patient's life, and finally, (4) address concerns	Control Group Patients provide QoL and treatment ratings	Monthly, six months Individual	N/A	Primary Subjective: MANSAs Functioning PANSS	Pre post 12 months	Patients in the intervention group had significantly better QoL in all time points
42	Priebe et al. (2007)	UK, Spain, the Netherlands, Sweden, Germany, Switzerland DIALOG: N = 256 F % = 32.5 Age M = 42.5 (11.3) TAU: N = 235 F % = 35.2 Age M = 41.8 (11.6)	Schizophrenia spectrum ICD-10 outpatients DIALOG: 16.6 (10.5) TAU: 15.2 (9.9)	Other	DIALOG: Discuss satisfaction with life and treatment domains (mental health, physical health, accommodation, job situation, leisure activities, friendships, relationship with family/partner, personal safety, practical help, psychological help, medication). Plus TAU	TAU not defined	Every 2 months, one year Individual	N/A CPZ	Primary Subjective: MANSAs Symptoms: PANNS	Pre post	Patients receiving the intervention had better QoL
43	Priebe et al. (2016)	UK BPT: N = 140 F % = 26 Age M = 41.1 (10.1) Pilates (CG): N = 135 F % = 26 Age M = 43.3 (11.1)	Schizophrenia ICD-10 outpatients BPT: 11 (7-18) Pilates: 10 (7-19)	Other	Body Psychotherapy Treatment (BPT): Mirroring tasks, body sculpturing using art materials, group tasks used to explore distinction between self and other.	Pilates – (CG): A fitness and physical health intervention	Biweekly, 90 min, 20 sessions 10 weeks Group		Secondary Subjective: MANSAs Symptoms PANNS	Pre post Follow up 6 months	Body psychotherapy did not improve QoL more than the CG

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Table 1. (Continued.)

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44	Rakitzi et al. (2016)	Greece IPT: N = 24 F% = 33 Age M = 31.3 (7.2) TAU: N = 24 F% = 33 Age M = 33.8 (6.7)	Schizophrenia DSM-IV Outpatients IPT: 5.4 (1.3) TAU: 5.9 (1.1)	Combination	Integrated Psychological Therapy (IPT): Cognitive Differentiation, Social Perception, Verbal Communication Plus TAU	TAU: medication, case management and individual supportive non specific therapy by a psychiatrist or psychologist.	Bi-weekly sessions, 60 min 10 weeks Group	IPT: 542.1 (391.1) TAU: 512.1 (355)	Secondary Health related: WHOQOL Symptoms: PANNS Functioning: GAF	Pre post Follow up 3 months	Significant effects favoring TAU were found in the QoL at follow-up.
45	Rami et al. (2018)	Egypt CA – BFPEP: N = 30 F% = 27 Age M = 33.1(9.3) TAU: N = 30 F% = 33 Age M = 35.2 (10.9)	Schizophrenia DSM-IV outpatients BFPEP: 8.3 (6.9) TAU: 9.4 (7.3)	Psychoeducation	Culturally Adapted Program Behavioral family psycho-educational program (CA – BFPEP): Psychoeducation about the signs, symptoms, etiology and relapse signs of schizophrenia, communication enhancement training, problem-solving skills training Plus Pharmacotherapy	TAU: Medical consultation and advice, family educational sessions on the management of the immediate family conflicts Focused on improving knowledge but not on changing attitudes or developing problem-solving skills.	Weekly in the first two months, twice/month in the second two months/ every three weeks for the last two months 14 sessions, 1 h, Individual	N/A	Primary Objective: QLS Symptoms: PANNS Functioning: SFQ	Pre post	The CA-BFPEP group demonstrated greater improvement of QoL compared to patients in the control group.
46	Richardson et al. (2007)	UK AT: N = 43 F% = 34.88 Age M = 39.6 (10.5) SPC: N = 47 F% = 34.04 Age M = 42.6 (11.5)	Schizophrenia Clinical records Inpatients AT: 12.6 SPC: 13.4	Other	Art Therapy (AT): Use of art material and associated imagery to understand patterns of behavior causing distress.	Standard Psychiatric Care (SPC): Regular contact with services, medication review, access to a variety of day treatment facilities	Weekly sessions 1, 5 h. Group	N/A	Primary Subjective: LQLP Symptoms: BPRS Functioning: SFS	Pre post follow up 6 months	Art therapy had non-significant impact on QoL
47	Röhrich et al. (2006)	UK BPT: N = 24 F% = 50 Age M = 38.8 (9.3) SC: N = 21 F% = 52.38 Age M = 37.7 (9.5)	Schizophrenia DSM-IV outpatients BPT: 12.1 (10.5) SC: 10.8 (7.3)	Other	Body-oriented psychotherapy (BPT): communication, cognitive and emotional awareness toward the body, activity and emotional responsiveness, exploration of self-potentials, body strength and capability, modify dysfunctional self-perception Plus TAU	Supportive Counseling (SC): Focused on individual difficulties and corresponding problem-solving strategies regarding the core negative symptoms. Plus TAU	Biweekly, 60–90 minutes each, 10 weeks. Group	BPT: 497.9 (289.1) SC: 440.5 (324.8)	Secondary Subjective: MANSA Symptoms: PANNS	Pre post follow up 4 months	QoL scores did not differ significantly between groups.
48	Ruiz-Iriondo et al. (2019)	Spain IPT + EMT: N = 42 F% = N/A Age M = N/A TAU: N = 35 F% = N/A Age M = N/A	Schizophrenia ICD-10 Outpatients	Combination	Integrated psychological therapy (IPT) plus emotional management training (EMT): IPT: Cognitive differentiation, social perception, verbal communication, social skills, Interpersonal problem solving.	TAU Medication, regular visits to the mental health center, social and leisure activities in a daycare center	Twice a week, 60–90 min, 8 months Group	N/A	Primary Subjective LQLP Symptoms: BPRS Functioning: SFS	Pre post	Patients in the experimental group improved in QoL compared to TAU

(Continued)

Table 1. (Continued.)

Number	Authors	Country of study, sample, % Female (n) mean age (s.d.)	Diagnosis/Diagnostic Tool Patient type (in/out) Psychosis duration (years M; s.d.)	Primary Intervention type	Intervention Group: description	Control Group: description	Intervention Duration and type (group/individual)	Medication CPZ mg/day (M; s.d.)	Type of outcome and instruments for QoL, symptoms, functioning	Assessment time-points	Main conclusions
					EMT: Reducing the influence of negative emotions, Analysis of negative emotions, coping with negative feelings, practicing adaptive emotional techniques, Learning activation control techniques Plus TAU						
49	Sachs et al. (2012)	Germany TAR: N = 20 F% = 44 Age M = 27.2 (7.17) TAU: N = 18 F% = 56 Age M = 31.72 (9.35)	Schizophrenia DSM-IV Inpatients and outpatients TAR: M = 24.31 (6.74) TAU: M = 24.33 (9.62)	Cognitive	Training of affect recognition (TAR): neuropsychological strategies, direct positive reinforcement, verbalization, and self-instruction.	TAU including occupational therapy (no other information available)	Biweekly, 6 weeks. Individual	N/A	Primary Health related: WHO QoL – BREF Symptoms: PANSS	Pre post	The TAR group improved significantly in the QoL domain of social relationships compared to the TAU group.
50	Salyers et al. (2014)	USA IMR: N = 59 F% = 23 Age N/A PS: N = 57 F% = 17 Age N/A	Schizophrenia spectrum DSM-IV Both inpatients and outpatients	Combination	Illness Management and Recovery (IMR): Incorporating psychoeducation, cognitive-behavioral approaches, relapse prevention, social skills training, and coping skills training. Plus TAU	Problem – Solving intervention (PS): Discuss current concerns and receive group support for solving problems, no use of structured problem-solving tasks. Plus TAU	Weekly, 9 months. Group	N/A	Primary Objective QLS Symptoms: PANNS	Pre post follow up 18 months	No significant QoL differences were found between IMR and problem-solving. Both groups improved significantly over time
51	Schrank et al. (2016)	UK PPT: N = 47 F% = 44.7 Age M = 43 (11) TAU: N = 47 F% = 36.2 Age M = 42 (11.5)	Schizophrenia spectrum Clinical records Both inpatients and outpatients PPT: M = 13 (11) TAU: M = 14 (11)	Other	Positive psychotherapy – (WELLFOCUS PPT): Increasing positive experiences; amplifying strengths; fostering positive relationships; and creating a more meaningful self-narrative. Plus TAU	TAU: Medication, social or psychological interventions.	Weekly 90 min, 11 weeks Group	N/A	Primary Subjective: MANSAs Symptoms: BPRS	Pre post	Significant improvement in the intervention group for QoL
52	Sibitz et al. (2006)	Austria Booster: N = 48 F% = 54.2 Age M = 35.5 (8.9) Non – booster: N = 55 F% = 54.5 Age M = 36.7 (9.7)	Schizophrenia spectrum ICD-10 outpatients Booster: M = 12.5 (8.7) Non – booster: M = 11(9)	Psychoeducation	Psychoeducational intervention with booster sessions concept of illness, symptoms and early warning signs, medication, stigma, well-being, friendships, everyday life management, create pleasant environments, 'Booster sessions' were conducted to systematically repeat and discuss topics from the intervention Plus TAU	Non – booster condition plus TAU: Psychoeducation same as intervention group but after 9 weeks no further group booster meetings, only routine clinical care.	Weekly, 75 min, 9 weeks. Booster sessions: 75 min each, 9 months. Group	N/A	Primary Health related: QLI Symptoms: PANSS	Pre post follow up 12 months	Positive effects for both groups in QoL, retained over the 12-month period in both conditions.

(Continued)

Table 1. (Continued.)

Number	Authors	Country of study, sample, % Female (n) mean age (s.d.)	Diagnosis/Diagnostic Tool Patient type (in/out) Psychosis duration (years M; s.d.)	Primary Intervention type	Intervention Group: description	Control Group: description	Intervention Duration and type (group/ individual)	Medication CPZ mg/day (M; s.d.)	Type of outcome and Instruments for QoL, symptoms, functioning	Assessment time-points	Main conclusions
53	Staring et al. (2010)	Netherlands TAT: N = 47 F% = N/A Age M = N/A TAU: N = 55 F% = N/A Age M = N/A	Schizophrenia spectrum DSM-IV outpatients	CBT	Treatment adherence therapy (TAT): Motivational interviewing, medication optimization, behavioral training.	TAU: Sessions with a Clinician when indicated. The content was around symptoms, social participation, work, daily activities and medication	Varied according to personal needs No more than 6 months. Individual	N/A	Secondary Health related EQ – 5D Symptoms PANSS	Pre post Follow up 6 months	No QoL improvement
54	Valencia et al. (2020)	Colombia Psychoeducation N = 90 F% = 28 Age M = N/A TAU N = 86 F% = 23 Age M = N/A	Schizophrenia ICD-10 Outpatients	Psychoeducation	Brief group psychoeducation on clinical manifestations, pharmacological treatment lifestyle, routine, physical care, risk of addiction, role of family members; duties and rights Plus TAU	TAU Psychiatrist consultation: drug prescription, clinical and psychosocial assessment; consultation leaflet	Five sessions Group	N/A	Secondary Health related: WHOQoL Symptoms SAPS; SANS	Pre post	No significant differences in QoL
55	Vass et al. (2021)	Hungary VR-TOMIS: N = 9 F% = 44.4 Age M = 38.6 (13.49) VR PASSIVE: N = 8 F% = 62.5 Age M = 48.8 (8.87)	Schizophrenia DSM-IV-TR outpatients VR-TOMIS: 20.8 (12.65) VR-Passive 21.5 (7.19)	CBT	Virtual reality (VR)-based targeted theory of mind (ToM) intervention (VR-ToMIS): Based on CBT Active VR included simulated social interactions with an avatar in immersive VR environments, followed by a task, where the patient had to visualize the inferred emotions of the avatar and then discuss simulation with psychotherapist	VR – Passive: In passive VR patients could freely explore the virtual Destinations but they could not contact any avatars and did not receive any interventions.	Weekly, 50 min per session, 9 weeks Individual	N/A	Primary Subjective: LQLP Symptoms PANNS	Pre post	No significant change in QoL scores
56	Wang et al. (2015)	China E: N = 14 F% = 50 Age M = 38.2 (15.9) PMR: N = 12 F% = 41.7 Age M = 39.2 (16.3) E & PMR N = 13 F% = 46.2 Age M = 38.7 (15.8) Control group: N = 13 F% = 28.6 Age M = 31.88 (9.43)	Schizophrenia DSM-IV outpatients E = 14.7 (14.2), PMR = 13.9 (13.6) E & PMR = 14.5 (13.8) Control: 15.2 (14.5)	Combination	3 intervention groups: (1) Education (E): Education sessions respectively covering five topics: illness, treatment, well-being, support, and patients' rights. (2) Progressive Muscle Relaxation (PMR): Group discussion of PMR experiences, self-practice of PMR, brochure describing relaxation. (3) Education plus PMR: Combination of the above	Control: Usual ward procedures	Education: Weekly, 30-min group PMR: Biweekly, 30-min group	E = 595.3 (397.6), PMR = 632.6 (421.2) E & PMR = 615.9 (415.8) Control: M = 604.7 (412.5)	Primary Subjective: LQLP Symptoms: SAPS Functioning: SDS	Pre post follow up 10 weeks	Education and PMR alone resulted in QoL improvement after the intervention and follow-up. Combined education and PMR showed better effects on improving QoL than did education or PMR alone

(Continued)

Table 1. (Continued.)

Number	Authors	Country of study, sample, % Female (n) mean age (s.d.)	Diagnosis/Diagnostic Tool Patient type (in/out) Psychosis duration (years M; s.d.)	Primary Intervention type	Intervention Group: description	Control Group: description	Intervention Duration and type (group/individual)	Medication CPZ mg/day (M; s.d.)	Type of outcome and Instruments for QoL, symptoms, functioning	Assessment time-points	Main conclusions
57	Weijers et al. (2021)	Netherlands MBTp: N = 42 F% = 45.2 Age M = 31.21 (7.8) TAU: N = 42 F% = 28.6 Age M = 31.88 (9.43)	Schizophrenia spectrum DSM-IV-TR outpatients MBTp: 5.45 (3.54) TAU: 5.17 (3.32)	Other	Mentalization-based treatment for psychotic disorders (MBTp): Focusing on affect, establishment of a secure treatment relationship, balancing the complexity of mentalization and stress, adopting a 'not-knowing' therapeutic stance, educate patients about mentalizing. Plus TAU	TAU: Usual procedures	Weekly, 1 h group session per week and a half-hour individual session once per 2 weeks, 18 months	N/A	Secondary Subjective: MANSAs Symptoms: PANSS Functioning: SFS	Pre post Follow up 6 months	No significant differences between groups in QoL
58	Wijnen et al. (2018)	Netherlands CBTsa: N = 49 F% = 24.5 Age M = 25.14 (4.47) TAU: N = 50 F% = 14 Age M = 25.72 (4.44)	Schizophrenia spectrum DSM-IV-TR Both inpatients and outpatients	CBT	Cognitive behavioral therapy for social activation (CBTsa): CBT based group and individual sessions. Included topics around peer support, social goals, obstacles to goals and dysfunctional cognitions, behavioral experiments. Plus TAU	TAU: Day or outpatient treatment. Medication, supportive therapy, psychoeducation, family support, physical health care, psycho-motor therapy and/or vocational therapy	(1) Biweekly, 60 min, 4 weeks, group (2) Weekly, 45 min, 6–8 weeks, Individual		Primary Health related: EQ-5D Symptoms – PANSS Functioning: GAF	Pre post and follow up 6 months	No QoL improvement for the intervention group compared to TAU
59	Yildiz et al. (2019)	Turkey PSST N = 10 F% = 30 Age M = 37.4 (10.7) MCT N = 10 F% = 40 Age M = 33.1 (4.6)	Schizophrenia spectrum DSM-IV outpatients PSST: 13.2 (8.4) MCT: 13.6 (6.1)	CBT	Psychosocial skills training (PSST): CBT social skills Training: communication, problem solving skills, attention and memory problems among others	Metacognitive Training (MCT): Psychoeducation, elimination of cognitive biases around delusional thinking	Weekly, 40–50 min 20 weeks Group	N/A	Primary Objective: QLS Symptoms: PANSS Functioning: GAF	Pre post	No significant differences between the groups in terms of effect size.
60	Zimmer et al. (2007)	Brazil IPT: N = 20 F% = 15 Age M = 36.05 (7.09) TAU: N = 36 F% = 30.5 Age M = 39.31 (8.85)	Schizophrenia spectrum ICD-10 outpatients IPT: 15.25 (8.18) TAU: 17.14 (8.47)	Combination	Integrated Psychological Therapy (IPT): Cognitive Differentiation; Social Perception; Verbal Communication; Social Skills Training; Interpersonal Problem-Solving. Plus TAU	TAU: Outpatient consultations, every two weeks with psychiatry residents	Weekly, 60-min sessions 3 months, Group	N/A	Primary Health related: WHO QoL – BREF Symptoms: BPRS Functioning: GAF;SOFAS	Pre post	IPT had a positive effect on the QoL psychological domain compared to TAU

^aReferences provided as online supplementary material (Supplementary File 1).

Table 2. Multilevel meta-analyses of (specific) intervention effectiveness on objective and subjective Quality of Life

	<i>k</i> (level 3)	<i>n</i>	<i>I</i> ²	Hedges <i>g</i>	<i>p</i>	<i>LCI</i>	<i>UCI</i>
Objective quality of life							
Overall	19 (15)	1024	46.67	0.330	0.026	0.039	0.622
CBT	4 (4)	212	25.90	0.653	0.196	-0.336	1.640
Cognitive	9 (6)	458	6.32	0.241	0.101	-0.040	0.450
Psychoeducation	2 (2)	164	5.48	0.909	0.048	0.010	1.808
Combination	4 (3)	190	<0.01	-0.073	0.612	-0.256	0.210
Other	0 (0)	-	-	-	-	-	-
Subjective quality of life							
Overall	70 (45)	6254	90.28	0.184	0.118	-0.470	0.415
CBT	21 (11)	923	<0.001	0.085	0.193	-0.043	0.214
Cognitive	19 (8)	1120	<0.001	0.124	0.036	0.008	0.240
Psychoeducation	9 (5)	1264	15.74	0.178	0.190	-0.088	0.443
Combination	13 (8)	892	19.79	0.314	0.036	0.021	0.606
Other	16 (12)	1976	88.73	0.169	0.671	-0.613	0.952

QoL effects appeared to be significantly affected by any of the predictors, excepting for more positive influences of group therapy interventions for subjective QoL (Table 3). However, this significant result should be interpreted with caution because it may be a consequence of familywise error accumulation (i.e. Bonferroni-corrected significance levels for within QoL-domain regressions is 0.006 *v.* an observed *p* value for group-treatment of 0.021; see Table 3).

Summary estimates of treatment dependent symptom and functioning differences can be seen in online Supplementary Table S2 (positive signs indicate more beneficial effects of treatment compared to control groups). We used primary study effect sizes to predict subjective and objective QoL-related between-groups effects in a further set of single precision-weighted multilevel meta-regressions. In these analyses, positive effects of predictors can be interpreted as indicative for positive effects of treatments on the predictor side leading to positive effects on the outcome side (in other words, if treatments alleviate symptoms or enhance functioning, they also lead to more favorable QoL outcomes).

We observed significant positive effects of predictors for symptoms and functioning for objective QoL effect sizes, thus indicating more beneficial effects in treatment compared to control groups for both effect size types (top half of online Supplementary Table S3). Interestingly, predictor patterns were differentiated in regard to subjective QoL. Whilst functioning (barely) and total symptoms showed positive signs, positive, negative, and general symptoms predicted subjective QoL significantly negative (bottom half of online Supplementary Table S3). This may mean that treatment-dependent symptom changes are not linked to treatment-related favorable subjective QoL outcomes, but may even have adverse effects.

Dissemination bias

Visual inspection of contour-enhanced confetti funnel plots did not indicate funnel plot asymmetry of neither objective nor subjective QoL analyses (online Supplementary Figs 2 and 3,

respectively). Our trim-and-fill analyses supported this interpretation, indicating no missing studies on the left-hand side of the summary effect estimate for either analysis.

Our three multilevel modeling-based approaches showed a consistent pattern of results within both analyses. Whilst no detection method indicated confounding influences of dissemination bias for objective QoL effects, all of them did so for subjective QoL.

On the one hand, for objective QoL neither Egger's regression test by means of sandwich estimators only, nor MLMA-based Egger's regression were indicative of bias (*ps* = 0.581 and 0.696, respectively). Furthermore, the three parameter selection approach showed no evidence for bias-related effect inflation ($\chi^2(1) = 1.788$; *p* = 0.181). On the other hand, for subjective QoL Egger's sandwich regression (*p* = 0.054), the MLMA-based Egger's regression (*p* = 0.024), as well as the selection approach ($\chi^2(1) = 20.537$; *p* < 0.001) yielded significant results, thus indicating an inflated summary effect.

Multiverse analysis

Specification curve

The descriptive specification curve indicated largely positive summary effects for objective QoL, with a median summary effect of *g* = 0.252 that ranged from *g* = -0.144 to 1.240 (25th and 75th percentiles indicated that 50% of values were between *g* = 0.055 and 0.415). All summary effects that reached nominal statistical significance had positive signs, thus indicating a rather robust beneficial therapeutic effect (Fig. 1). This may be interpreted as evidence for a robust, non-trivial, albeit small beneficial intervention effect on objective QoL compared to controls.

The largest positive intervention effects were observed when cognitive behavioral therapy or psychoeducation were used, although estimation precision was volatile. In terms of treatment type, our analyses showed that an exclusive use of group treatments yielded the least beneficial effects (or was even less favorable) compared to controls. For individual therapy and either therapy types, all summary effects were positive and predominantly significant.

Table 3. Single precision-weighted multilevel regression models for objective and subjective QoL

	<i>k</i> (level 3)	<i>b</i>	s.e.	<i>p</i>
Objective quality of life				
Mean age	16 (12)	−0.015	0.033	0.636
Mean years of schooling	11 (8)	−0.046	0.082	0.575
Percentage of women within sample	16 (12)	−0.007	0.015	0.617
Illness duration	15 (11)	−0.006	0.022	0.768
Medication mean (CZP)	5 (4)	≥0.001	<0.001	0.198
Percentage patients with schizophrenia	8 (8)	0.013	0.008	0.125
Outpatients ^a	19 (15)	0.184	0.652	0.778
In- and outpatients ^a		0.431	0.703	0.540
Group ^b	19 (15)	−0.451	0.290	0.119
Individual and group ^b		–	–	–
Subjective quality of life				
Mean age	62 (41)	−0.001	0.005	0.878
Mean years of schooling	28 (17)	−0.007	0.009	0.406
Percentage of women within sample	66 (42)	0.010	0.010	0.302
Illness duration	36 (26)	−0.002	0.037	0.955
Medication mean (CZP)	22 (14)	0.001	0.001	0.117
Percentage patients with schizophrenia	53 (36)	0.015	0.008	0.059
Outpatients ^a	69 (44)	−0.272	0.300	0.365
In- and outpatients ^a		0.258	0.408	0.527
Group ^b	70 (45)	0.543	0.235	0.021
Individual and group ^b		0.225	0.555	0.686

^aReferenced to inpatients.

^bReferenced to individual treatment.

For subjective QoL, effects were once again predominantly positive, albeit in general smaller and seemingly more likely to fail reaching nominal statistical significance. Effects ranged from $g = -1.523$ to 1.614 with a median summary effect of $g = 0.137$ (25th and 75th percentiles indicated that 50% of values were between $g = -0.001$ and 0.361). Most nominally significant summary effects had positive signs, although some specifications yielded negative signs (Fig. 2). These results show that evidence for a meaningful beneficial intervention effect on subjective QoL cannot be established. No clear pattern for drivers of influential moderator effects of factor levels was found, excepting an apparent tendency of lower treatment benefits when therapies were compared to other (non-therapeutic) control conditions.

Combinatorial meta-analysis

Random specifications of (unreasonable) combinations for objective QoL effects showed that summary effect estimations and between-studies heterogeneity seem to be systematically affected by the inclusion of certain studies (or study subsets). Visual inspection of GOSH-plots (online Supplementary Fig. S4) shows that larger effects are associated with larger between-studies variances. The median summary effect was somewhat larger than in specification curve analysis ($g = 0.380$; 25th and 75th percentiles = 0.239 and 0.513) with I^2 values indicating moderate-to-large between-studies heterogeneity (I^2 -squared median = 85.03 ; 25th and 75th percentiles = 61.30 and 89.54)

according to well-established heterogeneity thresholds (Higgins, Thompson, Deeks, & Altman, 2003).

A similar pattern was observed for subjective QoL. Once again, the GOSH-plot revealed systematic associations of summary effect estimates with between-studies variability (online Supplementary Fig. S5), although largest variabilities appeared to be associated with lower effect sizes. The median summary effect was once more trivial ($g = 0.185$; 25th and 75th percentiles = 0.096 and 0.278) and I^2 values indicated large between-studies heterogeneity (I^2 median = 92.48 ; 25th and 75th percentiles = 84.53 and 95.09).

In the light of these results, it cannot be ruled out that the presently observed pattern of effect size and between-studies heterogeneity differences for both objective as well as subjective QoL may be a consequence of unobserved systematic between-studies variance.

Discussion

Key findings

This meta-analysis aimed to contribute toward clarifying the effectiveness of different psychological interventions for improving QoL of patients with schizophrenia-spectrum disorders. The findings suggest that psychoeducation effectively improves objective QoL, and interventions that combine different therapeutic approaches (i.e. psychoeducation, CBT, problem solving, etc.) improve subjective QoL, although the effect is small. Group

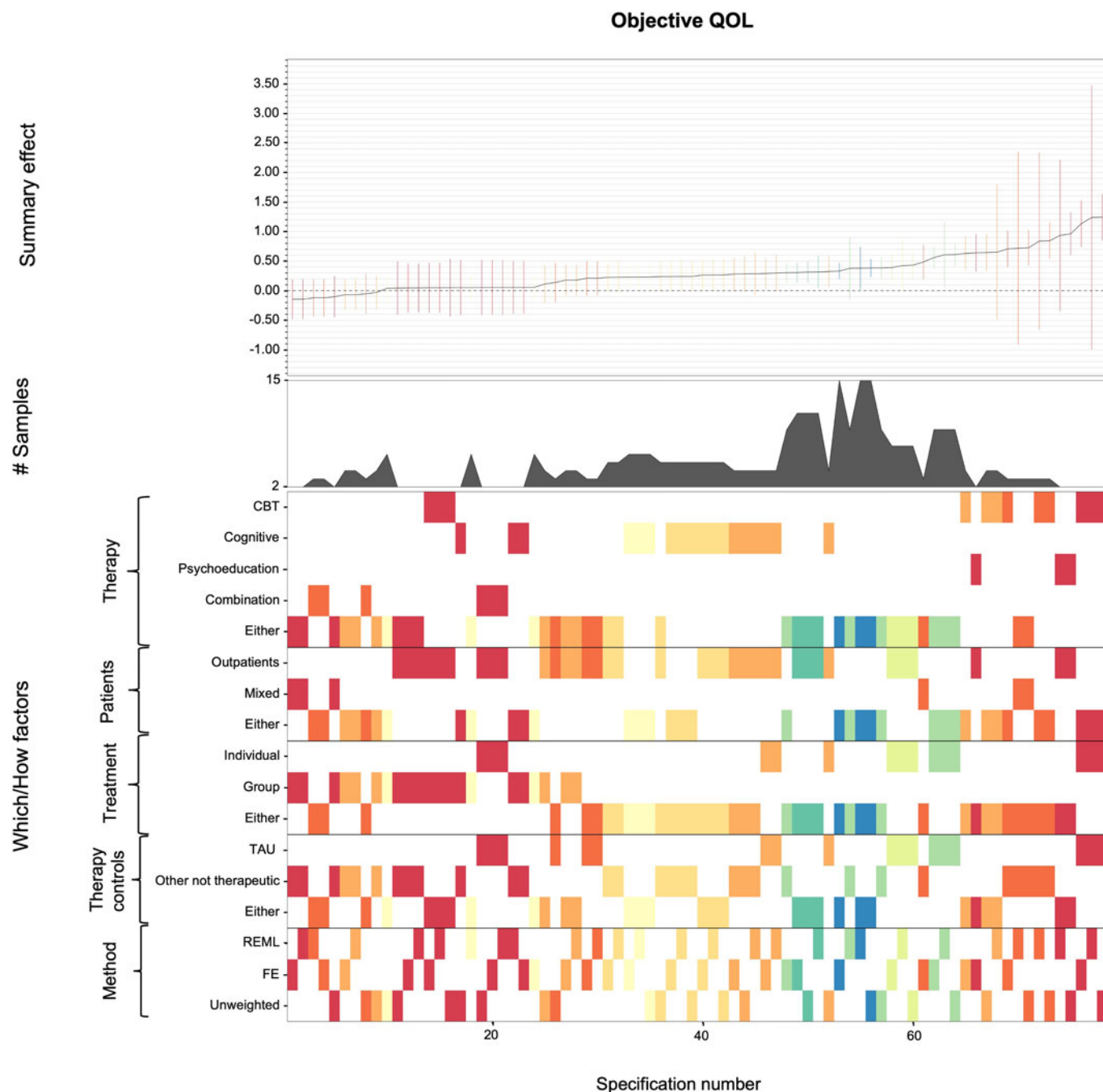


Figure 1. Descriptive meta-analytic specification curve of summary effects (Hedges g) for all reasonable specifications for objective QoL.

Note. The top panel shows summary effects with 95% confidence intervals in increasing order according to effect strength. This means that the leftmost effect represents the most negative effect that was observed according to any specification whilst the rightmost effect represents the most positive one. The y-axis provides effect strength in terms of Hedges g . The center panel indicates the number of samples within the data subset that a respective effect estimate is based on. The bottom panel indicates the combinations of specific characteristics in terms of selected data and which analytical approach was used to calculate the respective summary estimate. Warmer colors indicate lower precision (i.e. larger confidence intervals) of summary effect calculation. Confidence intervals that overlap with dashed reference line indicate non-significance of summary effect.

interventions seem to be more beneficial for improving subjective QoL, though this finding should be interpreted with caution. Importantly, the results suggest the existence of unobserved systematic between-studies variance for both subjective and objective QoL, thus indicating further systematic moderating influences that have not yet been identified. There were no indications for dissemination bias-related effect inflation for objective QoL, whilst some subjective QoL effects appeared to have been somewhat inflated.

Comparison with the existing literature

Our findings go beyond those of individual studies targeting QoL, providing a comprehensive systematic examination of therapy-dependent intervention effects. In this vein, our analytical approach allowed us a more fine-grained assessment of different intervention types and effectiveness on QoL compared to prior investigations (Correll *et al.*, 2018; Laws, Darlington, Kondel,

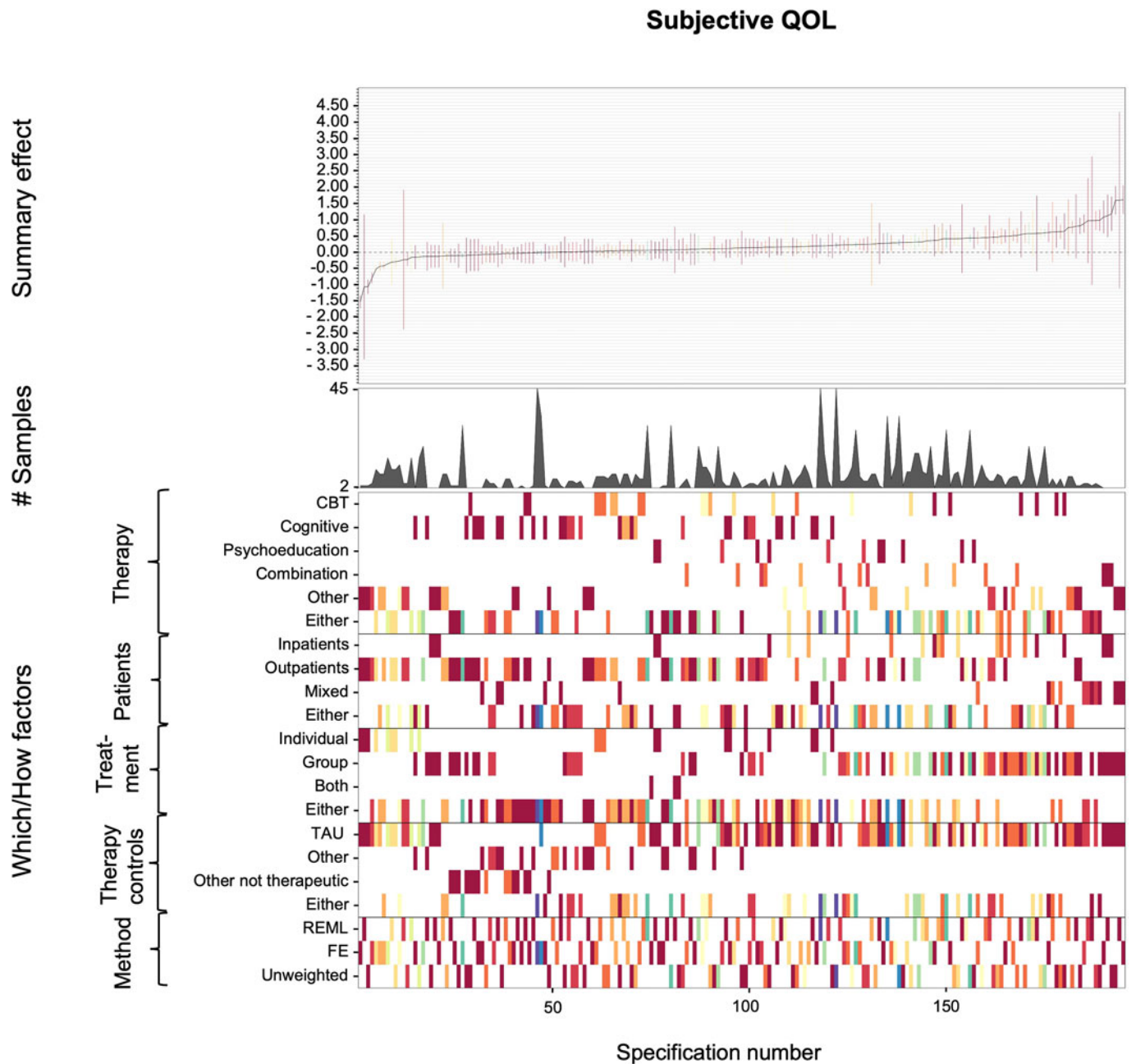


Figure 2. Descriptive meta-analytic specification curve of summary effects (Hedges *g*) for all reasonable specifications for subjective QoL. *Note.* The top panel shows summary effects with 95% confidence intervals in increasing order according to effect strength. This means that the leftmost effect represents the most negative effect that was observed according to any specification whilst the rightmost effect represents the most positive one. The y-axis provides effect strength in terms of Hedges *g*. The center panel indicates the number of samples within the data subset that a respective effect estimate is based on. The bottom panel indicates the combinations of specific characteristics in terms of selected data and which analytical approach was used to calculate the respective summary estimate. Warmer colors indicate lower precision (i.e. larger confidence intervals) of summary effect calculation. Confidence intervals that overlap with dashed reference line indicate non-significance of summary effect.

McKenna, & Jauhar, 2018; Valiente et al., 2019) as well as the first examination of their interactions. For instance, Laws et al. (2018) examined the effectiveness of CBT on the recovery of patients with schizophrenia, including nine studies that targeted QoL as one of the outcomes, revealing no benefit for QoL. However, this conclusion may be misleading, because similar to Valiente et al. (2019) (i) their meta-analytical results were based on studies including several different diagnoses (schizophrenia-spectrum and others) and (ii) no distinction was made in terms of objective and subjective QoL scores, thus leaving potential specific

CBT-dependent therapy effects in terms of diagnosis or QoL type unclear. Our findings show that there is no meaningful effect of CBT on subjective QoL whilst the observed evidence for an effect on objective QoL remains ambiguous (i.e. despite an observed moderate effect, the associated confidence interval overlapped considerably with the null, thus leaving a potential advantage of CBT over TAU in need of substantiation), thus indicating that CBT does not improve QoL of patients with schizophrenia beyond treatment as usual. This is important, because CBT is the most widely used intervention for schizophrenia patients

and recommended by the NICE guidelines as the gold standard (NICE, 2014).

Another prior meta-analysis (Correll *et al.*, 2018) examined the effectiveness of Early Intervention Services (EIS) on several outcomes of patients with first episode psychosis. They included four studies about subjective QoL and revealed a weak effect. Given that EIS typically adopt a multidisciplinary approach involving psychological treatments but also occupational therapy, assertive management treatment, carer support, etc., it is not possible in such primary studies (and resulting meta-analyses) to untangle effects of specific psychological treatments, which limits the validity of their reported treatment effects.

It is worth noting that the majority of the included studies focus on subjective QoL, whilst objective QoL is less often targeted by psychological interventions. This may be explained by the priority in inclusion of (subjective) QoL as a patient reported outcome, instead of its inclusion as an observer-rated outcome. However, our results of overall intervention effectiveness on objective QoL indicate that this outcome is very relevant as a criterion for testing interventions, though it has been suggested to more closely represent indicators related to standards of living, or 'quality of living', rather than QoL (Awad & Voruganti, 2012).

Our moderator analyses suggest that symptom-alleviating and functioning-improving interventions substantially ameliorate objective QoL. This idea is consistent with the well-established negative relationship of objective QoL with symptom severity (Eack & Newhill, 2007). This means that an overall improvement of the clinical condition can be expected to improve a given patient's life conditions. These findings are consistent with the previously observed strong relationship of overall functioning with objective QoL (Nevarez-Flores *et al.*, 2019). Of note, our results indicate that when positive, negative, and general symptoms improve, treatment group patients provide more negative evaluations of their life conditions than control group patients. This may be explained by the 'insight paradox' (Davis, Lysaker, Salyers, & Minor, 2020). That is, patients with increased disease awareness perceive their (subjective) QoL worse than those with poor insight. This phenomenon is exacerbated for people with decreased symptomatology. As the person gets better, they begin to have a better understanding of how their life is constrained by psychosis, and thus appraise their life conditions in a more negative way.

Moreover, our findings show that group interventions are more effective in improving subjective QoL compared to individual or combined format interventions. These findings are in line with prior evidence on social functioning (Orfanos, Banks, & Priebe, 2015) and may reflect well-established beneficial effects of group therapy for patients with psychosis (Kanas, 1996). Typically, this increased effectiveness is attributed to groups offering such patients an opportunity for experience sharing and relationship establishment with people that share similar concerns toward life. However, this finding should be interpreted with caution because the nominal statistical superiority of group interventions disappeared when correcting for statistical family-wise error accumulation.

Strengths and limitations

Our present approach allowed us to provide the first meta-analytical evidence of specific intervention effects on QoL in patients with schizophrenia-spectrum disorders based on the so far most comprehensive data and analyses of this topic.

Specifically, we were able to (i) disentangle differential treatment effects according to specific QoL outcomes, (ii) assess influences of different intervention types, (iii) examine moderating effects of sample-level characteristics as well as their interactions within moderators and design variables, (iv) investigate evidence for effect inflation due to dissemination bias, as well as (v) explore the impact of researcher degrees of freedom-dependent (un-)reasonable decisions in terms of data selection and ways to analyze them in multiverse analyses.

However, some limitations should be noted. First, we did not distinguish between self-reports of subjective and health-related QoL in our main analyses, thus potentially introducing statistical noise. However, supplementary separate analyses for both health-related and subjective QoL yielded virtually identical results (omitted for brevity). Second, we included studies assessing QoL based on the EQ-5D questionnaire, which in the past raised concerns regarding the extraction of conclusions on the individual QoL rates of patients with psychosis (Brazier, 2010). However, more recent evidence suggests that this instrument provides reliable QoL assessments to be used for group comparisons (Barton *et al.*, 2009; Pitkänen *et al.*, 2012). Therefore, we considered studies using EQ-5D to be eligible for answering our research question. Third, WHO-QoL subscale scores were averaged for our multiverse calculations. This was necessary to allow an examination of the impact of moderator interaction effects because multilevel modeling is currently unfeasible in this approach. Fourth although it is highly recommended to use disease-specific instruments when the aim is to detect treatment effects (Karow, Wittmann, Schöttle, Schäfer, & Lambert, 2014) this was only observed for objective QoL (i.e. using the QLS) whereas most studies targeting subjective QoL used a variety of generic assessments (i.e. not specifically designed for assessing QoL in patients with schizophrenia, such as the WHO-QoL; MANSA, Q-LES, etc.). Also, although all QoL instruments employed in the included studies have been widely used within this population, none of the instruments follow the Patient-Reported Outcomes Measurement Information System (PROMIS) (Cella *et al.*, 2010), which would allow for more accurate comparisons across studies. Fifth, only few studies reported outcomes of intention-to-treat analyses. Therefore, a completer-only bias may have contaminated our findings. Given the small number of studies that followed this approach, it was not possible to test for this bias using sensitivity analyses. This limitation illustrates that gold standard approaches of RCT-based reporting (see for instance CONSORT checklist item 16; Schulz, Altman, & Moher, 2010) is still insufficiently practiced. Sixth, the results of the presently meta-analytically summarized data should not be generalized beyond the context of Western countries, due to the majority of included studies having been conducted in WEIRD (Western, Educated, Industrialized, Rich, Democratic; Henrich, Heine, & Norenzayan, 2010) countries.

Implications for research and practice

In all, our findings suggest that the interventions' benefits vary based on outcome and intervention type. We purposefully excluded studies that included patients with diagnoses other than schizophrenia (i.e. bipolar disorder, depression). Though one may argue that interventions offered in the context of mental health services should adopt a transdiagnostic approach, focusing on the patients' reported difficulties instead of their symptoms, it has often been shown that QoL differs among diagnostic

populations (Ådnanes et al., 2019; Berghöfer et al., 2020; Petkari & Priebe, 2023) and this may impact the intervention effectiveness. Therefore, future studies should either target populations with refined diagnostic criteria, or at least compare the outcomes of different diagnostic subgroups receiving the same intervention. Even within the schizophrenia spectrum, our findings revealed a trend of diagnosis as moderator of the intervention effectiveness. That is, interventions may be more effective when targeting samples of schizophrenia patients only, compared to when targeting patients within the whole schizophrenia spectrum (schizoaffective, delusional, etc.). Therefore, to be able to extract refined conclusions about what works for whom, future studies need to provide more information on how interventions benefit patients with different diagnoses within diagnostic subgroups.

Also, although illness duration did not emerge as a meaningful moderator, QoL levels and determinants may differ between patients with early psychosis and chronic patients (Gardsjord et al., 2016). In our analysis, there were only four studies focusing on samples with early psychosis, two targeting objective QoL and two subjective QoL, therefore a comparison with more chronic samples was not possible. Given the importance of the first-five-years-from-onset period for determining functional outcomes (Crumlish et al., 2009), further RCTs that target QoL are needed to determine the best intervention to implement with these patients.

Moving beyond this in this meta-analysis we did not test the intervention effects on different QoL dimensions (i.e. environment, health, living conditions), as QoL scores were considered as a whole. The scores on QoL dimensions may be fluctuating (Berghöfer et al., 2020), with patients for instance reporting high appraisal of environment, but not of social relationships; therefore, there may be a differential effect of interventions depending on the QoL dimension under study. Future studies are encouraged to report scores on QoL dimensions to be able to detect potential intervention targets.

Furthermore, interventions based on a variety of different approaches (i.e. systemic, psychodynamic art-therapy, mindfulness, etc.) were considered together under the umbrella of 'other', because there were not enough studies for creating dedicated categories. Future studies are needed to disentangle their effects based on robust RCTs. For instance, third generation approaches seem to be promising for improving QoL, but the evidence is still scarce (Jansen, Gleeson, Bendall, Rice, & Alvarez-Jimenez, 2020).

According to our results, psychoeducation improves objective QoL, suggesting that receiving information on how to handle the disorder and its consequences may help the person to ameliorate their life conditions; however, this finding should be interpreted with caution, because it is based on two studies only. Combined interventions seem to work better for improving subjective QoL. Given the variability among the included multicomponent interventions, extracting results on what exactly works is quite challenging. What these interventions have in common though is that they are all manualized and multifaceted, targeting a series of elements within the same program, such as education on the disorder characteristics, problem solving, emotional and cognitive skills. Therefore, they may be an ideal candidate for improving the patient's life appraisal.

Conclusions

The findings suggest that QoL is a valid outcome criterion for assessing psychological interventions, as it is sensitive to change.

However, the effect is small and there is large variability depending on the QoL and intervention type, which call for the testing of new solutions. This testing should be conceived either in terms of more in-depth examinations of different intervention types (i.e. included in this meta-analysis under the umbrella of 'combined' and 'other') that may ameliorate QoL, or in terms of focusing on different QoL dimensions that may be more plausible to target through the available interventions.

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