Effect of Psychotherapy for Borderline Personality Disorder on Quality of Life: a meta-analysis

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Samenvatting

Achtergrond. Borderlinepersoonlijkheid stoornis (BPS) is een psychische aandoening waar rond de 0.5%-2.5% van de populatie onder lijdt. Het is al bewezen dat meerdere psychotherapieën effectief zijn voor de behandeling van deze stoornis. Echter is de impact van deze therapieën op de kwaliteit van leven (KVL) nog niet uitgebreid bestudeerd. Er zijn tot nu toe maar een aantal onderzoeken naar deze impact gedaan, en het huidige onderzoek heeft als doel om de bestaande onderzoeken samen te voegen en de gevonden effecten te bestuderen.

Methode. Er werd een meta-analyse uitgevoerd op 9 RCTs, waarin psychotherapie voor volwassenen met BPS werd vergeleken met ofwel de gebruikelijke behandeling (TAU) ofwel een actieve controlegroep. De data verzameling omvatte populatie, interventie, en methodologische kenmerken per conditie, en de Risk of Bias (RoB) van de individuele onderzoeken werd vastgesteld door middel van 4 domeinen van het Cochrane Collaboration Risk of Bias Tool. Uitkomsten werden samengevoegd door middel van een random-effects model. Gestandaardiseerde effectgroottes (Cohen's *d*) werden berekend voor voor KvL op de post-test, follow-up, en met verwijderde uitschieters. Publication bias en heterogeniteit werden ook in kaart gebracht.

Resultaten. Een klein tot matig effect voor KvL werd gevonden (d = 0.47, 95% CI 0.09-0.85, $p \le 0.01$). Wanneer rekening werd gehouden met uitschieters, bleef er een significant effect van 0.28 over (95% CI 0.11-0.45, $p \le 0.001$). De effectgrote bij follow-up was 0.23 (95% CI 0.02-0.43, $p \le 0.05$, $p \ge 0.001$). Publication bias speelde een kleine rol in de effectgrootten. *Conclusies.* Psychotherapieën gericht op BPS-patiënten leken een positief effect te hebben op hun kwaliteit van leven, al is het onduidelijk of dit kwam door de gerichte aandacht voor KvL in de therapieën of door het afnemen van de heftigheid van de symptomen. Het huidige onderzoek heeft laten zien dat kwaliteit van leven een belangrijk onderdeel is van de mentale en fysieke gezondheid van een patiënt, en dat behandeling hier een positieve uitwerking op lijkt te hebben.

Abstract

Background. Borderline personality disorder (BPD) is a debilitating condition affecting around 0.5%-2.5% of the population. Several psychotherapies have been proven to be effective. However, the impact of these psychotherapies on Quality of Life (QoL) has not been extensively studied. There are but a few studies available studying these effects, and this study will aim to pool together the studies conducted thus far and study the found effect *Method*. A meta-analysis was conducted on 9 randomised clinical trials comparing psychotherapy for adults diagnosed with BPD with either a Treatment as Usual (TAU) or active control group. Data extraction involved population, intervention and methodologist characteristics per condition, and the risk of bias of the individual studies was assessed using 4 domains of the Cochrane Collaboration Risk of Bias tool. Outcomes were pooled using a random-effects model. Standardized effect sizes (Cohen's *d*) were calculated for QoL at posttest, follow-up, and with outliers removed. Publication bias and heterogeneity were examined as well.

Results. A small to moderate effect size for QoL was found (d = 0.47, 95% CI 0.09-0.85, p \leq 0.01). When adjusted for outliers, a significant effect size of 0.28 (95% CI 0.11-0.45, p \leq 0.001) remained. The effect size at follow-up was 0.23 (95% CI 0.02-0.43, p \leq 0.05, p \geq 0.001). Publication bias played a small part in the effect sizes.

Conclusions. Psychotherapies aimed at Borderline patients appeared to have a positive effect on a borderline patient's Quality of Life, though it is unclear whether this is connected to the special attention therapies give to QoL or the decreased symptom severity. The current study showed that Quality of Life is an important part of a patient's mental and physical health, and treatment seems to positively affect this construct.

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Introduction

A lot of research has been conducted on the effects of psychotherapy on several (personality) disorders. However, in the last decade or so, there have been increasing interest in not just the absence of pathology, but also the presence of clients' strengths and mental health (Seligman & Csikszentmihalyi, 2000), otherwise known as the field of Positive Psychology. This field concerns itself with well-being, contentment, satisfaction, hope, optimism, flow and happiness, in the past, present and future. From this way of thinking, the term Quality of Life (QoL) has gained more and more traction within the psychological field. QoL encompasses all the aforementioned subjects of positive psychology, and several therapies have been erected around this concept. Mindfulness Based Stress Reduction (MSBR; Grossman, Niemann, Schmidt, & Walach, 2004), Mindfulness Based Cognitive Therapy (MBCT; Dimidjan, Kleiber, & Segal, 2009), Acceptance and Commitment Therapy (ACT; Hayes, Strosahl, & Wilson, 1999); all examples of therapies and trainings that are becoming increasingly validated and popular in the treatment of mental illness. QoL in general is fast becoming an "important component in the evaluation and management of disease" (Ishak et al., 2013, p. 139). Quality of Life has become an integral part of most therapies, a state of being to achieve while also attempting to battle mental illnesses. This construct is especially interesting when paired severe mental illnesses such as with Borderline Personality Disorder (BPD). Can a person achieve Quality of Life, when suffering from something so severe as BPD? The aim of the present work is to establish with a meta-analysis whether the current psychotherapeutic treatments for Borderline Personality Disorder have an effect on Quality of Life, therefore increasing (or decreasing) a patient's quality of life.

Borderline personality disorder is a debilitating mental disorder, and one of the most prevalent personality disorders (Ishak et al., 2013), with an estimation of 0.5%-2.5% of the general population suffering from it (Van Asselt et al., 2007). It is characterized by a pervasive pattern of instability in interpersonal relationships, identity, and affect. Furthermore, severe impulsiveness accompanies the disorder, starting from a young age and present in a multitude of contexts (Hengeveld, 2014, p. 456). Self-harm (75%) and suicide (8-10%, twice as high as in the general population) often characterize this disorder as well (Cristea et al., 2017). Not only that, functional impairment is extremely prevalent with this disorder, more so than with other personality disorders. This means that BPD patients often struggle to fulfil social roles. This manifests itself in deficiencies in work, school and interpersonal relationships (Wilks, Korslund, Harned, & Linehan, 2016). Interpersonal dysfunction in particular can persist even after the symptoms of BPD itself diminish (McMain et al., 2012). The impulsive behaviours, like self-harm or substance abuse, exhibited by BPD patients are thought to be a part of attempts to regulate emotions, with which these patients have severe difficulties (Wilks et al., 2016). These behaviours offer immediate relief from the emotional distress but are problematic for normal day-to-day functioning and have adverse long-term health effects. Several factors have been found to predispose an individual to BPD, including inheritable factors, childhood adversities and low Social Economic Status (SES) (Leppänen, Hakko, Sintonen, & Lindeman, 2015).

Quality of life (QoL) is a psychological construct that is usually defined as high wellbeing and happiness (Lustosa, Melo, Gonçalves, & Souto, 2018), or living a good, happy life, but this is a rather simplified definition. While not technically faulty, it is lacking several key points, mainly with regards to mental health. The World Health Organization created a definition that is still used today, and which includes several important key points. According to the WHO, QoL is the "individuals' perception of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards and concerns" (The WHOQOL Group, 1995). In short, QoL shows how positively an individual regards their life and the way they are living it. With this definition, it is quite possible to have a form of quality of life, to have a good life, while still dealing with mental illness. As long as patients learn to cope with the difficulties their mental illness can cause, they can still live a relatively qualitative life. Another relevant definition was posited by Costanza et al. (2008), in which they stated: "Quality of Life (QOL) is the extent to which objective human needs are fulfilled in relation to personal or group perceptions of subjective well-being. Human needs are basic needs for subsistence, reproduction, security, affection, etc." (p. 12). Not only does the subjective well-being matter (WHOQOL), but so does the fulfilment of basic human needs (Costanza). A severe impairment in either one is sure to cause psychological problems.

In recent years, the concepts Quality of Life and well-being have been often used to describe similar concepts. They have been used interchangeably, and well-being is even used to define Quality of Life (Pinto, Fumincelli, Mazzo, Caldeira, & Martins, 2017). This has led to some confusion as to the true meaning of these concepts. Here, too, Quality of Life has been defined with the help of well-being (Lustosa et al., 2018; Costanza et al., 2012). This is unsurprising, as reviews suggest that these two concepts overlap considerably. Pinto et al (2017) provided an overview of the similarities and differences of these two concepts. Well-being and Quality of Life overlap in their inclusion of happiness, interpersonal relationships, and in their multidimensionality (pertaining to the physical, social, mental, and environmental

aspects of life). They differ, however, in the fact that Quality of Life is also concerned with the *development* and *improvement* of life, with the personal *empowerment* and *independence* of the individual, with living a dignified life, and with achieving personal goals. Thus, while well-being is an important part of Quality of Life, QoL entails more than being happy or having positive relationships.

QoL in relation with BPD is complicated, because the severe symptoms often overshadow the patients' ability to fulfil their human needs, and even more their ability to positively perceive their position in life. For example, an unstable self-image and stressrelated dissociative symptoms are expected to interfere with a sense of wellbeing, and the self-rating of QoL (Ishak et al., 2013), and indeed the results from this literature review show that QoL is seriously impaired in patients with BPD. It is important to know whether the current psychotherapies for BPD have a positive impact on Quality of Life, as well as the symptoms. Every person has a right to have their basic human needs met, and thus therapies should also aim to increase QoL.

Since BPD is a chronic condition, it is difficult to treat, though several psychotherapies have been proven effective, amongst which are dialectical behaviour therapy (DBT) and cognitive behaviour therapy (CBT) (Cristea et al., 2017). DBT emphasizes the psychosocial aspects of a patient's problems, and mostly focuses on teaching emotion regulation skills, social skills, and other skills that people with BPD often lack (Grohol, 2018; Linehan, Bosch, Merkus & Damen, 2016). The therapy calls upon a patient's independence. Instead of the therapist offering patients all kinds of solutions, the therapy supplies patients with tools and skills training to come to solutions themselves. Furthermore, research has shown that clinical group-DBT improves the psychosocial functioning and lessens borderline specific symptoms at end of treatment and follow-up (Oostendorp & Chakhssi, 2017). The main goal or theme within DBT is that the patient learns to change their problematic patterns of behaviour, emotions, thought processes and interpersonal interactions (Linehan et al., 2016). DBT thereby addresses the patient's own strengths and resilience. The patient needs to work at themselves if they want to change. Resilience is an important construct in DBT. Resilience can mean 'positive adaptation, or the ability to maintain or regain mental health, despite experiencing adversity' (Herrman et al, 2011; p. 259).

'Regaining' is the key in DBT. Patients with BPD suffer severely from their symptoms, which often leads to the aforementioned (self-)destructive behaviours to cope with the stress. As described above, DBT aims to change these behaviours, so patients can cope with stress in constructive ways, and thereby *regain* (a part of) their mental health. While

DBT is mainly focused on working with Borderline Personality Disorder, CBT is used for a wider array of problems and disorders, including anxiety or addiction (Grohol, 2018). DBT aims to teach patients skills to cope. CBT, on the other hand, is aimed at changing attitudes and behaviours, and focusing on thoughts, images, beliefs and attitudes that relate to behaviours, and altering these processes to change the behaviour. The therapy addresses and challenges thinking errors and works to find alternative patterns of thought to replace these erroneous thoughts. Examples of thinking errors are personalisation and dichotomous thinking. When a person relates negative events to themselves, they are making the error of personalisation; they think something negative has to do with them, even when there is no basis for this attribution. With dichotomous thinking, people think in a very black and white manner; they often think they only have two options in situations, and these are often extreme (Herkov, 2016). CBT aims to address and correct these and other types of thinking errors, and thereby change a person's often unhealthy behaviour. Cristea et al. (2017) recently conducted a meta-analysis to study the effectiveness of psychotherapy for the BPD symptoms and found significant positive effects on these symptoms for these psychotherapies. This proved that psychotherapy can be effective for BPD. However, their meta-analysis focussed solely on the improvement of the clinical symptoms. The current meta-analysis will expand on their research by studying the efficacy of psychotherapy for BPD on Quality of Life.

In conclusion, the problems people suffering from BPD face are severe, and there has been evidence that psychotherapy is in fact effective as a therapy for BPD. However, it is not well-known if psychotherapy is also effective for increasing QoL in people with BPD, which can help in their treatment. Meta-analyses have the advantage of being able to estimate the true effect of interventions more precisely and accurately, because it combines several individual studies. Furthermore, it can help explore inconsistencies between studies, helping to better understand which processes can influence the effects (Cuijpers, 2016). Therefore, this meta-analysis will pool the small amount of studies concerning BPD and QoL together and study these effects. It will do so by building on the study by Cristea at al. (2017), and by attempting to answer the following research question: *What is the efficacy of psychotherapy for Borderline Personality Disorder (BPD) on Quality of Life (QoL) in adults with BPD?* There are but a few studies available studying these effects, and since quality of life is an important part of daily living, this study will aim to pool together the studies conducted thus far and study the found effect.

Methods

Search strategy

A systematic literature search was conducted (3 April 2018) in two electronic databases: PsycINFO and PubMed. The search string that was used was nearly identical to the one that Cristea (2017) utilised (see Appendix A). The current search included all studies up to April 2018.

Study selection

The screening of titles, abstracts and full-text articles was independently conducted by four researchers. Any disagreements were discussed and resolved.

The inclusion criteria were as follows: studies were included when they (1) used a psychotherapy, (2) had an adult (>18) sample, (3) had BPD patients as participants, (4) were an RCT study, (5) used a QoL measurement in pre- and posttest (e.g. the WHOQOL, the EQ-5D, etc.), and (6) were an original study with original data. Furthermore, an exclusion criterium was included. The studies should not have compared two different types of versions of the same psychotherapy. If for example, a study compared an older version of a therapy with a newer, updated version, the study was excluded. For full overview of study characteristics, see Table 1.

Data extraction

From the included studies, the following data were extracted: 1) population characteristics (age and gender), 2) intervention characteristics (therapy and control), such as type (e.g. CBT, DBT, or TAU, WL), duration (weeks/months/years), format (group/individual), and setting (in-/outpatient), 3) methodologist characteristics per condition, like design, sample sizes, measurement points (pre, post, and follow-up), and outcome measures, both BPD and QoL.

Quality assessment

Risk of Bias (RoB) was evaluated within 4 domains of the Cochrane Collaboration Risk of Bias tool (Higgins et al., 2011), which evaluates the potential risks of biases. Rated domains were (1) sequence generation, (2) allocation concealment, (3) blinding of outcome assessors, and (4) incomplete outcome data. Within the domain 'sequence generation', all studies were checked whether or not the participants were allocated randomly to the different conditions. Studies that applied coin tosses, random number tables, or any other valid method the researchers described were scored as low RoB. Studies that did not mention a sequence generation were scored as high RoB. If it was properly concealed which participant was allocated to which condition, so only the therapist would know, studies received low RoB. If concealment was not possible or not maintained, they received high RoB. When outcome assessors were sufficiently blinded to the conditions, studies received low RoB. When outcome assessors knew to which condition the participants were assigned, studies received high RoB. If studies conducted an Intent-to-Treat analysis on all the data, including the dropouts or missing data, and could give reasonable explanation for the missing data, they received low RoB. If ITT was not conducted, they received high ROB. A low RoB received a score of 0, and a high RoB a score of 1, which meant a study could score between 0 (no risk of bias) and 4 (high risk of bias).

Studies with high RoB may alter the results of the analysis in a significant way, which would make the result unreliable. In contrast, studies with low RoB have a low risk of contaminating the results. A meta-analysis with numerous high-risk studies may be less reliable than one with more low-risk studies.

Statistical analysis

The treatment effect was calculated by inputting the means and standard deviations into Comprehensive Meta-Analysis Software (CMA, version 3, Biostat). As in Cristea et al. (2017), the effect size was calculated as the difference between the intervention and control groups at post-test and at follow-up. However, in this study, there were no small samples to correct for (Hedges & Olkin, 2014), so instead of Hedges g, Cohen's $d(\delta = \frac{\mu^2 - \mu^1}{\sigma})$ was used as effect size outcome, where μ_i is the mean outcome of a group, and σ is the standard deviation. A small effect (d = .2) indicates that there is unlikely to be an effect that significantly impacts the area of study. A large effect size (d = .8) in turn indicates a large impact on the area of study – in this study, a large effect size would mean psychotherapy has a great impact on a patient's Quality of Life. A medium effect size (d = .5) would indicate a subtle impact; greater than if the effect was small, but obviously less indicative of a great impact (Fritz, Morris & Richler, 2012). The studies differed sufficiently to necessitate the use of the random effects model to account for heterogeneity among the studies; for example, the experimental condition varied widely across studies, as did the control condition. Furthermore, the same statistical analysis was conducted on the studies when the outliers were removed and using the follow-up results.

Heterogeneity of effect sizes was examined using the Q and I^2 statistics. The Q

statistic examines whether the effect sizes differ more significantly than chance would dictate (Chakhssi, Kraiss, Sommers-Spijkerman, & Bohlmeijer, 2018). A significant Q ($p \le 0.05$) indicates significant heterogeneity, which means that differences in effect sizes across studies cannot be explained by chance alone (Spijkerman, Pots, & Bohlmeijer, 2016). According to Gavaghan, Moore, and McQuay (2000), the Q test has very low power to detect true heterogeneity in meta-analyses with small sample size. However, they also stress that failure to detect heterogeneity cannot ascertain whether data is truly homogeneous (p. 421). The decision to include the statistic here despite this evidence, was based on the fact that Cristea's meta-analysis (2017), on which the current analysis is based, also used this statistic. Gavaghan et al. (2000) advised to treat the statistic with caution, if it needed to be used. To estimate the percentage of heterogeneity that was not due to random sample error alone, the I^2 statistic was calculated. A value of 0% indicated no heterogeneity, and indicators of low, moderate and high degrees are 25%, 50% and 75% respectively (Higgins & Thompson, 2002).

Publication bias was assessed in three ways. First, a funnel plot plotting the overall mean effect size against study size was created. A symmetric distribution of studies across the effect size indicates the absence of publication bias, but a higher concentration of studies on one side than the other indicates the presence of publication bias (Spijkerman et al., 2016). Second, a fail-safe *N* was calculated. A fail-safe *N* is a formal test of funnel plot asymmetry and indicates the required number of unpublished studies that have shown no significant effects, that would lower the overall effect size below significance. Findings were considered robust if the fail-safe $N \ge 5n + 10$, *n* being the number of comparisons (Rosenberg, 2005), using Rosenthal's method (1991). Finally, Duval and Tweedie's (2000) trim-and-fill procedure was applied. This procedure produces and adjusted effect size which accounts for the missing studies calculated by the fail-safe *N*.



Figure 1. Flowchart of the study selection process

Results

Selection of included studies

1041 possible studies were included for screening. First, duplicates were removed, which resulted in 989 studies to be screened based on their title. From this, 99 remained to be checked for suitability. Most articles that were excluded based on their abstracts, were excluded because they did not meet one or more of the criteria mentioned above. Furthermore, several were excluded because they were study protocols, not a RCT, or a follow-up study.

After exclusion by abstract, 52 articles remained to be screened by full-text. The same inclusion criteria were used to find suitable articles. The articles that were excluded, were almost all of them excluded because they did not use a QoL measurement. One was excluded because it turned out they did not use a BPD sample, and another because the full text was written in French. Lastly, a Dutch study was removed further along in the process because it was the same, but translated, study as one of the other included studies. In the end, nine suitable studies were included in this meta-analysis (see Figure 1).

Study Characteristics

The 9 trials included 397 participants in the treatment conditions, and 406 participants in the control conditions. Two trials had female-only samples, and this percentage ranged from 70 to 91% in the remaining studies (M=85.9%). The mean age ranged from 24.5 to 34.3, with a mean of 31.9 years.

Eight trials targeted Borderline Patients, while one targeted BPD as well as other personality disorders. The utilised psychotherapies were DBT (3 studies), Community Treatment By Expert (CTBE; 2 studies), CBT, Emotion Regulation Group Therapy (ERGT), Schema-Focussed Therapy (SFT), and Systems Training for Emotional Predictability and Problem Solving (STEPPS). The control conditions were mainly Treatment as Usual (7 studies, one of which had TAU+Waitlist), but the other three used active control groups, namely General Psychiatric Management (GPM), Rogerian Supportive Therapy (RST), and Transference Focussed Therapy (TFP). Treatment duration ranged from 14 weeks up to a year, with one study even extending treatment to three years, and the amount of sessions ranged from 14 to 156. Four trials used a group format for therapy in their experimental condition, four an individual therapy format, and the remaining used a mixture of both group and individual therapy. In the control condition, three trials used group therapy, four used individual therapy, and one used both. It was not clear what format the remaining study used. With regards to the setting, all trials made use of outpatient sample. Eight of the studies used a stand-alone design, while the last one compared Treatment as Usual (TAU) with CBT added on to the TAU. For every study, the results of the pre-tests, post-tests and follow-up were gathered. One study did not give pre-test results, and five studies did not gather follow-up information. With regards to therapy intensity, most studies held therapy sessions once a week, or once every other week. Some studies had both individual sessions as well as group sessions in a week, and one even had sessions twice a week. The intensity of only one control condition is known; one hour a week.

Several different tools to quantify QoL were used. Two studies applied the WHOQOL-bref, the shortened version of the WHOQOL questionnaire, which another study did use. Two other studies applied the EQ-5D, the EuroQol instrument to measure health-related quality of life. Other instruments included the Manchester Short Assessment of Quality of Life (MANSA), the Quality of Life Inventory (QOLI), and the Social Adjustment Scale (SAS).

Table 1. Study char	acteristic.	s of inclu	ded trials in the syster	natic review and meta-analys	is				
First Author (year)	% female	Mean age	BPD assessment	Psychotherapy (n); control (n)	Setting (duration in weeks)	QoL outcome	BPD outcome	Trial Quality	Country
Bos (2010)	86.3	32.3	SCID-II/PDQ-4	STEPPS (42); TAU (37)	Outpatient (18w)	WHOQOL-Bref	BPD-40	1	NL
Carter (2010)	100	24.5	CI / IPDE	DBT (38); TAU+WL (35)	Outpatient (24w)	WHOQOL-Bref		3	Australia
Cottraux (2009)	77.0	33.5	DIBR	CT (33); RST (32)	Outpatient (104w)	SAS		3	France
Davidson (2006)	84.0	31.9	SCID-II	CBT+TAU (54); TAU (52)	Outpatient (52w)	EQ-5D		3	UK
Giesen-Bloo (2006)	93.0	30.6	SCID-II/BPDSI-IV	SFT (45); TFP (43)	Outpatient (156w)	WHOQOL	BPDSI-IV	4	NL
Gratz (2014)	100	33.2	DIPD-IV	ERGT (31); TAU (30)	Outpatient (14w)	QOLI	BEST	2	USA
Leppänen (2016)	86.3	32.1	SCID-II	ST/DBT (24); TAU (47)	Outpatient (52w)	15D	BPDSI-IV	2	Finland
McMain (2009)	86.1	30.4	IPDE	DBT (90); GPM (90)	Outpatient (52w)	EQ-5D	ZAN-BPD	4	Canada
Priebe (2012)	87.5	32.2	SCID- II	DBT (40); TAU (40)	Outpatient (52w)	MANSA	ZAN-BPD	3	UK

Note. BEST = Borderline Evaluation of Severity over Time, BPD = Borderline personality disorder; BPD-40 = Borderline Personality Disorder checklist – 40, BPDSI-IV = Borderline personality disorder severity index-IV, CI = Clinical Interview DSM-IV, CT = Cognitive therapy, DBT = Dialectical behavior therapy, DIBR=Interview for Borderline Personality Disorder-Revised, DIPD-IV= Diagnostic Interview for DSM-IV Personality Disorders, ERGT= Emotion regulation group therapy, EQ-5D = EuroQol 5D, GPM= General psychiatric management, IPDE = International Personality Disorder Examination, MANSA = Manchester Short Assessment of Quality of Life, MINI = Mini International Neuropsychiatric Interview, NL = the Netherlands, PDQ-4 = Personality Diagnostic Questionnaire, QOLI= Quality of Life inventory, RST = Rogerian supportive therapy, SAS = Social Adjustment Scale of Marks, SCID-II = Structured Clinical Interview for DSM-IV axis II disorders, SFT = Schema Focused Therapy, ST/DBT = psychotherapy combining elements of schema therapy and dialectical behavior therapy; STEPPS = Systems Training for Emotional Predictability and Problem Solving, TAU = Treatment as usual, TFP = Transference Focused Therapy, UK = United Kingdom, USA = United States of America, 15D = 15D measuring Health Related Quality of Life, WHOQOL= World Health Organization Quality of Life Assessment-Bref, WL= Wait-list, ZAN-BPD= Zanarini Rating Scale for Borderline Personality Disorder.

Risk of bias

The quality assessment scores ranged from 0 to 3 (see Table 1). Most studies (n=6) had a low risk of bias, one of which had no RoB at all. Descriptions of the randomization process was the most poorly rated, with only 2 studies meeting this criterion. Both allocation concealment and incomplete outcome data was best rated, with 7 studies each meeting these criteria. Overall, the meta-analysis seems mostly free from bias. A high bias can lead to either over- or underestimation in the results of the meta-analysis.

Table 2. Methodologi	cal quality of s	stuales incluaea	in meta-analysis		
Study (year)	Random sequence generation	Allocation concealment	Blinding of outcome assessment	Incomplete outcome data	Total
Bos (2010)	unclear	unclear	unclear	yes	3 (high)
Carter (2010)	no	yes	no	no	3 (high)
Cottraux (2009)	unclear	unclear	no	yes	3 (high)
Davidson (2006)	unclear	yes	yes	yes	1 (low)
Giesen-Bloo (2006)	yes	yes	yes	yes	0 (no risk)
Gratz (2014)	unclear	yes	yes	yes	1 (low)
Leppänen (2016)	unclear	yes	unclear	yes	2 (low)
McMain (2009)	unclear	yes	yes	yes	1 (low)
Priebe (2012)	yes	yes	no	unclear	2 (low)

Table 2. Methodological quality of studies included in meta-analysis
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Figure 2. The standardized posttest effect sizes of comparisons between investigated psychotherapies and control conditions for QoL relevant outcomes for 9 trials.

Quality of Life

Nine comparisons were included in the meta-analysis of QoL. The mean effect size (Cohen's *d*) at post-test (see Figure 2) indicated a significant moderate effect on QoL. When adjusted for outliers, a significant effect size of 0.28 (95% CI 0.11-0.45, p≤0.001) remained. The effect size at follow-up was 0.23 (95% CI 0.02-0.43, p=0.03). Given the fact that the effect size after removal of outliers and at follow-up was still within significance, it can be concluded that the effect is reasonably robust. With regards of heterogeneity, the level of heterogeneity was high (I^2 =83.65), and the Q-test resulted in a significant level of heterogeneity (Q=48.92, p≤0.001). This suggests that the found effect size is possibly moderated by one or several differing variables between the studies. After adjusting for outliers, a low level of heterogeneity (Q=8.08, p>0.05). These results suggest that the effect size is not likely to be moderated by differing variables between the studies.

Publication Bias

In general, slight publication bias was found. Save for one outlier that fell slightly outside the funnel plot, the studies were reasonably well divided around the mean. Furthermore, the fail-safe *N* indicated that the current findings were unrobust; based on the current findings, 18 studies with a non-significant outcome would be required to generate a non-significant effect size. Based on Rosenthal's calculations ($N \ge 5n + 10$), the findings would have been robust when N \ge 55.

After adjusting for publication bias using the Trim and Fill method the mean effect size dropped to 0.23 (95% CI 0.08-0.37), suggesting that publication bias played a minor but significant part in the observed effect sizes.



Figure 3. Funnel plot of d. Publication bias will result in asymmetry of the funnel plot. Point a indicates publication bias, meaning one study may have influenced the results unfairly.

Discussion

In this study, we examined the efficacy of psychotherapy for BPD on a patient's overall QoL. Very little research has been done that focusses on this effect, which is rather odd, as QoL is seriously impaired in BPD patients (Ishak et al., 2013). Cristea et al. (2017) did show that psychotherapy appears to be significantly effective for treating BPD symptoms. The current study attempted to add to that, by studying the effect psychotherapy might have on a person's Quality of Life. The results showed that psychotherapies seem to have a positive effect on a patients' Quality of Life. This means that, after administering therapies like CBT or DBT, a patient's Quality of Life generally seems to have increased. Even after excluding outliers, and adjusting for publication bias, the effect on QoL did not disappear, though it did shrink. Based on the current findings, psychotherapy for BPD appears to have a significantly positive moderate effect on not only the borderline-specific symptoms, but on several domains of a patient's life as well, such as social and emotional functioning. These results are in line with previous work (Oostendorp & Chakhssi, 2017; Ishak et al., 2013) and are important because QoL is often found to be low in BPD patients (Ishak et al., 2013). Furthermore, it is broadly accepted that low QoL often predicts vulnerability for psychological problems in future (Lamers, Westerhof, Glas, & Bohlmeijer, 2015), and therefore can lead to relapses in previous, often destructive behaviour. This is in line with the two-continua model postulated by Keyes (2005), which states that mental health does not merely mean the absence of mental illness. Keyes showed that mental health and mental illness are not opposites on a single continuum, but rather that they are separate, but correlated, concepts. This means that a decrease in symptoms does not automatically mean an increase in mental health, including **QoL**-levels.

The results of the current study can be interpreted along these same lines; there is a significant positive effect on QoL, which indicates that these psychotherapies in some way have an effect of QoL. However, some caution is required when interpreting these results. The rise in QoL levels may have nothing to do with the psychotherapies themselves, but simply with the fact that the BPD symptoms have decreased at post-test. The relieve that the reduction of the severe symptoms brings is sure to increase a patient's QoL, no matter how small. It is clear that after treatment, the QoL is elevated, but it is as of yet unclear what processes contributed to that result. Future research could benefit from specific studies researching these processes in more detail.

These findings, in combination with Cristea's work (2017), do showcase the efficacy of psychotherapy for borderline personality disorder, however they are interpreted. These

findings are important, as they suggest that psychotherapy can not only alleviate the BPD symptoms (Cristea et al., 2017), but also improve the life of a patient in some way, despite being burdened by (mental) health issues.

There was one notable outlier amongst the studies. Giesen-Bloo et al. (2006)'s effect size was significantly more positive than the other studies. Furthermore, after removing this outlier from the analysis, evidence for heterogeneity nearly disappeared, suggesting that this study differed in very important ways from the other eight studies included. Indeed, upon closer inspection the difference was notable. For example, Giesen-Bloo et al. ran their study for three years, while the others had a maximum length of one year. Additionally, their sessions were held twice a week, whilst the others held their sessions only weekly or less. All this may have contributed to the strong effect size found in their study, and why it impacted the entire analysis in this way. The fact that their effect size was so strong may indicate a longer and more intensive treatment is beneficial for patients suffering from BPD, but further research is needed before such a conclusion can be made.

As mentioned before, there were three studies with a high Risk of Bias (Bos, Van Wel, Apello, & Verbraak, 2015; Carter, Wilcox, Lewin, Conrad, & Bendit, 2010; Cottraux et al., 2009). These studies may have biased the results slightly. However, as only three out of nine studies had this level of RoB, and that they all had one domain that still remained free of bias, it was decided not to further investigate the effects of the possible biases.

Of interest was also the physical and mental health components of Quality of Life. QoL is a subjective and difficult to measure concept, and it is possible that the different QoL measures assessed slightly different areas or parts of life (Kolovos, Kleijboer, & Cuijpers, 2016). The WHOQOL-bref, for example, does separate the different areas in life – assessing not only mental and physical health, but also social and environmental health/status. However, only one study (Carter et al., 2010) differentiated between these domains in life, and therefore it was not possible to study these effects more closely. A future study may be needed to examine whether the increase in QoL reported in this study is simply due to one of the components, or if both increased after treatment ended.

Limitations and future research

A limitation of this study was the small number of usable studies. It is difficult to make solid conclusions on the basis of merely nine studies. Even though several authors have suggested that all one needs for a viable meta-analysis is "two studies" (Valentine, Pigott, & Rothstein, 2010), it is well-known that a larger amount of studies can increase the power of a study

(Hedges & Pigott, 2001; p. 210). Another weakness was the small number of studies that included follow-up, with only three out of nine having done so. It is vital to know whether the effects showed at post-test remain visible at follow-up, to ensure Quality of Life remains improved on the long term.

The fail-safe method used in this study (where $N \ge 5n + 10$, *n* being the number of comparisons) has been shown to neither be a method of identifying publication bias nor is it a method of accounting for publication bias that does exist (Rosenberg, 2005, p. 467). Rosenberg showed that this method often overestimates the number of studies needed to reduce a meta-analysis to nonsignificance. New calculations devised by Rosenberg turned robust fail-safe numbers into unrobust ones. This method is mostly intuitive and cannot for certain point to the robustness of the effects of an analysis.

Another limitation was the fact that two studies had active control groups (Cottraux et al., 2009; McMain et al., 2012). While the other studies all used a Treatment as Usual or Treatment as Usual plus Waiting List, Cottraux (2009) used Rogerian Supportive Therapy, and McMain (2012) used General Psychiatric Management. This makes these studies more difficult to compare to the other seven studies, as the active control groups presumably show a completely different effect than TAU. For future research, it should be considered not including active control groups as comparisons.

Future research can benefit from more RCTs focussing on Quality of Life in relation to BPD. Furthermore, a more in-depth study is needed on the processes that influence Quality of Life. Is it the relief of symptoms that increases QoL? Does the psychotherapy specifically target this concept to increase it, separate from relieving symptoms? These questions deserve answers if we are to help Borderline patients to the best of our abilities. Several RCTs focussing on a single therapy, for example DBT, and with a focus on the different Quality of Life domains, might enable us to understand these processes better. Comparing DBT and CBT might also be an interesting approach, as DBT is specifically designed to treat BPD. CBT is a more global therapy, and it would be interesting to see if there are differences in effect on QoL. And lastly, Giesen-Bloo et al. (2006)'s approach of a lengthier treatment raised another important question: Are BPD patients more likely to benefit from a longer treatment? It is also a possibility for future research to examine this further, with experimental designs lasting longer than a year.

Conclusion

Psychotherapies aimed at Borderline patients appeared to have a positive effect on a borderline patient's Quality of Life, though it is unclear whether this is connected to the therapies themselves or the decreased symptom severity. The effect found was moderate and remained significant even after removal of outliers and at follow-up. Treatment intensity may have a positive influence as well, as Giesen-Bloo et al.'s (2006) study was high in intensity and had a larger than average effect size.

The current study showed that Quality of Life is an important part of a patient's mental and physical health, and treatment seems to positively affect this construct. Research into the relation between BPD and QoL has been scarce, and this meta-analysis gathered the first few studies to examine the effect. It can therefore be viewed as a starting point: further studies in this field should aim to solidify and replicate this claim, as well dive deeper into the physical and mental health components separately in an attempt to further understand how treatments may affect a BPD patient's Quality of Life.

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Appendix A

<u>Search strategy Cristea et al (2017)</u> Pubmed: "borderline personality" Filter: Clinical trials Date: November 6th 2015; Hits: 230

Current search strategy

PubMed

("Borderline Personality Disorder"[Mesh] OR "Borderline Personality Disorder") AND (randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti] NOT (animals[mh] NOT humans [mh]))

PsycINFO

(DE "Borderline Personality Disorder" OR "borderline personality") AND (SU.EXACT("Treatment Effectiveness Evaluation") OR SU.EXACT.EXPLODE ("Treatment Outcomes") OR SU.EXACT("Placebo") OR SU.EXACT("Followup Studies") OR placebo* OR random* OR "comparative stud*" OR clinical NEAR/3 trial* OR research NEAR/3 design OR evaluat* NEAR/3 stud* OR prospectiv* NEAR/3 stud* OR (singl* OR doubl* OR trebl* OR tripl*) NEAR/3 (blind* OR mask*)