Chapter 6

Psychological Treatment of Anxiety in Primary Care: A Meta-Analysis

Abstract

Background

Guidelines and mental health care models suggest the use of psychological treatment for anxiety disorders in primary care, but systematic estimates of the effect of their effects in primary care settings are lacking.

Objective

The objective of this study is to examine the effectiveness of psychological therapies in primary care for anxiety disorders.

Methods

The databases Cochrane (central register of controlled trials), EMBASE, Medline, PsycINFO and, Pubmed were searched in July 2010. Manuscripts describing psychological treatment for anxiety disorders/increased level of anxiety symptoms in primary care were included if the research design was a randomized controlled trial and if the psychological treatment was compared to a control group.

Results

In total, 1343 abstracts were identified. Of these, twelve manuscripts described a randomized controlled trial comparing psychological treatment for anxiety with a control group in primary care. The pooled standardized-effect size (twelve comparisons) for reduced symptoms of anxiety at post-intervention was $d = 0.57$ (95% confidence interval: 0.29-0.84; $P = 0.00$; the number needed to treat: 3.18). Heterogeneity was not significant among the studies ($I^2 = 58.55$, $Q: 26.54; P < 0.01$).

Conclusions

We found a moderate effect size for the psychological treatment of anxiety disorders in primary care. Several aspects of treatment are related to effect-size. More studies are needed to evaluate long-term effects given the chronicity and recurrent nature of anxiety.
Background

Anxiety disorders are common; the estimates for the 1-year and lifetime prevalence are 10.6% and 16.6%, respectively.\[1\] A large number of people experience anxiety disorders on a continuing or recurrent basis. A large number of patients is treated in primary care and only few are referred to specialized mental health care.\[2,3\] Of the patients who receive any type of care for their anxiety disorder, 31.9% receive care in primary care.\[2\] Panic disorder, social phobia, agoraphobia, and generalized anxiety disorder are encountered most frequently in primary care. The majority of patients prefer psychological treatment\[4\], but many general practitioners (GPs) tend to prescribe antidepressants or benzodiazepines and although these are effective\[5\], they also have adverse effects. For example, benzodiazepines can cause dependency and antidepressants can increase the risk of suicidal thinking in younger adults or can have potentially serious interactions with other medication or alcohol.

Recent guidelines are changing in favor of psychological treatment. The NICE clinical guideline for anxiety disorders covers the care of adults who have panic disorder (with or without agoraphobia) or generalized anxiety disorder.\[6\] The recommended psychological treatments include self-help or cognitive behavioral therapy (CBT) in individual or group setting. The American Psychological Association (APA) Guidelines also suggest CBT as the initial psychological treatment for panic disorder.\[7\]

Although evidence-based clinical guidelines are available for the treatment of anxiety disorders in primary care, initiation of, and adherence to effective treatment is usually poor.\[3,8-9\] Given this problem and the fact that anxiety disorders have a high burden of disease, there is a need for better managed and structured treatment in primary care. Recent studies of treating depression and anxiety in primary care have proposed several models of disease management\[10\], collaborative care\[11\] and stepped care.\[12\] These care models use evidence-based psychological treatments. Evidence-based treatments for anxiety, such as brief problem solving therapy (PST) or CBT, are effective for treating anxiety disorders\[13,14\] and are suitable for treating anxiety disorders in primary care. The use of online or computer-assisted CBT has also been proven efficacious for anxiety disorders.\[15\] For most general practitioners it is too time-consuming to provide treatment and most are not fully trained to treat psychiatric illness, but it is possible that such treatments can be performed effectively by other primary care workers, such as nurses or social workers. There is evidence that nurses can be trained to provide psychological treatments successfully. Nurses have, for example, used behavioral methods to treat phobic patients\[16\] and provide Problem-solving Therapy (PST) in primary care.\[13\] With psychological therapies, like CBT and PST and recent developments on Internet-delivered self-help, the treatment of anxiety disorders in primary care has potential, but psychological treatments for anxiety disorders have not been thoroughly studied in primary care settings.

So far, reviews of psychological treatments combine primary care and specialized mental health care studies\[14,17\], combine anxiety disorders with depression\[18,19\], focus on a specific type of intervention\[20,21\], or on treatment of a specific anxiety disorder in non-inpatient settings.\[22\] We will conduct a meta-analysis to examine the effectiveness of psychological therapies in primary care for anxiety disorders. In addition we examine several aspects of treatment (e.g., type of treatment or treatment provider) that can be related to effect-sizes.
Method

Search Strategy

Studies were identified by searching the databases Cochrane (central register of controlled trials), EMBASE, Medline, PsycINFO and Pubmed from 1963 to July 2010. We used a search string involving the MeSH term for anxiety disorders and combinations of 'anxiety disorder' ('anxiety disorder' or 'anxiety'), 'primary care' terms ('primary care' or 'general practice' or 'primary health care' or 'community care' or 'family practice' or 'community health services' or 'family physician' or 'family medicine') and the MeSH term for 'treatment' and combination of terms ('therapy' or 'treatment' or psychol* or 'behavior therapy' or 'behaviour therapy' or 'relaxation' or 'exposure' or 'feedback' or 'counseling' or 'psychotherapy' or 'cognitive analytic therapy' or 'debriefing') in order to maximize identification of relevant studies. Additional papers were identified from reference lists. We did not contact study authors for additional data, unpublished studies and studies in press.

Inclusion and Exclusion Criteria

For this meta-analysis we included published (a) RCTs (b) of psychological therapies (c) for adult patients (d) with an anxiety disorder based on DSM-criteria or an increased level of symptoms on a anxiety questionnaire (e) provided in general practice (f) compared with a control condition.

Psychological treatments were defined as interventions in which verbal communication between a therapist and a client was the core element, or in which a psychological treatment was written down in a book format or a computer program (guided self-help or bibliotherapy) that the client worked through more or less independently, but with some kind of personal support from a therapist (by telephone, email, or otherwise).[23] We included studies in which a DSM-diagnosis was used to establish the presence of anxiety disorders or increased levels on anxiety symptoms questionnaires.

Studies were excluded if they focused on children or adolescents (< 18 years of age). Studies were also excluded when the psychological treatment could not be discerned from a care program (for example: disease management, collaborative care, stepped care or combinational use of psychological treatment with pharmacotherapy), in which a standardized effect size could not be calculated, which focused on inpatients or on patients who were both anxious and depressed. No language restrictions were applied.

Data Extraction

Studies were coded on several domains to examine the effects of the most probable and useful modifiers. We coded (1) recruitment method (recruitment from referral or from screening) because a recent meta-analyses demonstrated that recruitment caused lower effect-sizes that other types of recruitment[23]; (2) type of therapy (cognitive behavior therapy (CBT) or other therapies) because CBT is effective for the treatment of anxiety and also suitable for primary care[24,25]; (3) number of treatment sessions (≤ 7 or ≥ 8 sessions), because a recent analysis demonstrated that brief therapies are effective for treating anxiety disorders in primary care[18]; (4) professional background of the therapist (clinical psychologist or other providers), because
recent studies demonstrated that the background of the therapist in relevant in treating depression in primary care, and, type of control group (care as usual or other control groups), because lower effect-sizes were found when psychological treatment was compared to care as usual. When psychological treatment was compared to pharmacotherapy, we only used the data of the psychological treatment and the pill-placebo groups. An overview of the studies can be found in Table 1.

Quality Assessment

To give an impression of the quality of the studies we assessed the quality using a number of basic criteria as suggested by the Cochrane Handbook. WS and RK separately assessed the quality using the six criteria according to the Cochrane Collaboration's tool for assessing risk of bias: adequate sequence generation; allocation concealment; blinding of assessors of outcomes; completeness of follow-up data; no selective outcome reporting; and no other problems that could put the study at risk of bias. Afterwards they discussed disagreements until a consensus was reached. Due to the (interpersonal) nature of psychological treatment, blinding of participants and personnel (treatment provider) is not possible in psychological treatment. However, we did check for blinding of the post-treatment assessor. We assessed whether incomplete data were adequately addressed, by checking whether outcome data were assessed using intention-to-treat analyses.

Analyses

Effect sizes (standardized mean difference $d$) were calculated by subtracting (at post-test) the average score of the psychological treatment group from the average score of the comparison group, and dividing the result by the pooled standard deviations (SDs) of the two groups. A $d$ of 0.5 thus indicates that the mean of the experimental group is half a standard deviation larger than the mean of the control group. Values of $d$ from 0.56 to 1.20 can be assumed to be large, 0.33 to 0.55 are moderate, and 0 to 0.32 are small. Only those instruments that explicitly measure symptoms of anxiety were used in the calculations of the effect sizes. If more than one measurement of anxiety symptoms was used, they were combined and the mean effect sizes were calculated, so that each study only contributed one effect size. When means and SDs were not reported, other statistics (for example: t-value, $P$-value, number of patients) were used to calculate the effect sizes.

The standardized mean difference is difficult to interpret from a clinical perspective and therefore the numbers-needed-to-treat (NNT) were also calculated, using the formulae provided by Kraemer and Kupfer. The NNT is defined as the number of patients one would need to treat with a psychological treatment to have one more successful outcome compared to the same number of patients in the control group.
<table>
<thead>
<tr>
<th>Disorder</th>
<th>Recruitment</th>
<th>Ψ treatment</th>
<th>No. of sessions</th>
<th>n</th>
<th>Treatment provider</th>
<th>Control</th>
<th>n</th>
<th>Instruments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social phobia</td>
<td>Screening</td>
<td>Exposure therapy</td>
<td>9*</td>
<td>92</td>
<td>Physician</td>
<td>PL</td>
<td>92</td>
<td>CGI-S-AA /FQ/SPS</td>
</tr>
<tr>
<td>GAD</td>
<td>Referral</td>
<td>CBT+relaxation/Anxiety management training</td>
<td>8</td>
<td>10</td>
<td>Therapist (Psychiatric nurse)</td>
<td>WL</td>
<td>10</td>
<td>CAQ/GHQ-A/Z-SAS</td>
</tr>
<tr>
<td>GAD</td>
<td>Referral</td>
<td>CBT</td>
<td>6</td>
<td>10</td>
<td>Psychologist</td>
<td>PL</td>
<td>11</td>
<td>HAM-A/K&amp;S</td>
</tr>
<tr>
<td>GAD</td>
<td>Referral</td>
<td>CBT</td>
<td>7</td>
<td>21</td>
<td>Clinical Psychologists</td>
<td>PL</td>
<td>19</td>
<td>Ratings GP - patient - psychologist</td>
</tr>
<tr>
<td>PD</td>
<td>Referral</td>
<td>CBT</td>
<td>9</td>
<td>30</td>
<td>Clinical Psychologists</td>
<td>PL</td>
<td>28</td>
<td>FQ/HAM-A/K&amp;S</td>
</tr>
<tr>
<td>PD</td>
<td>Referral</td>
<td>Group CBTa/Individual CBTb</td>
<td>8</td>
<td>20/31</td>
<td>Psychological Therapist</td>
<td>WL</td>
<td>19</td>
<td>ASA/HADS-A/K&amp;S</td>
</tr>
<tr>
<td>PD/phobic avoidance</td>
<td>Referral</td>
<td>Conventional treatment plus anxiety management booklet</td>
<td>3</td>
<td>27</td>
<td>GP</td>
<td>CAU</td>
<td>18</td>
<td>AS/A/HADS-A/K&amp;S</td>
</tr>
<tr>
<td>GAD</td>
<td>Screening/Referral</td>
<td>CBT-GAD/TC</td>
<td>8</td>
<td>5</td>
<td>Post doctoral- and residency-level clinicians</td>
<td>CAU</td>
<td>4</td>
<td>BAI/GADS</td>
</tr>
<tr>
<td>GAD</td>
<td>Referral</td>
<td>CBT</td>
<td>10</td>
<td>70</td>
<td>Master level therapists</td>
<td>CAU</td>
<td>64</td>
<td>GADSS/SIGH-A</td>
</tr>
<tr>
<td>PD/GAD</td>
<td>Referral</td>
<td>CBT</td>
<td>12</td>
<td>63</td>
<td>GP/therapist</td>
<td>CAU</td>
<td>26</td>
<td>STAI (state &amp; trait)</td>
</tr>
<tr>
<td>PD/GAD</td>
<td>Referral</td>
<td>CBT</td>
<td></td>
<td></td>
<td></td>
<td>CAU</td>
<td>16</td>
<td>HAM-A</td>
</tr>
</tbody>
</table>

* The exact number of sessions is unclear, but is estimated to be 9.

This manuscript reports two psychological treatments and is used as two comparisons

Abbreviations: ASA = Analogue Scales for Anxiety, BAI = Beck Anxiety Inventory, CAQ = Cognitive Anxiety Questionnaire, CAU = Care as Usual, CBT = Cognitive-Behavioral Therapy, CGI-ΑΑ = Clinical Global Impression – Anxiety Attacks, FQ = Fear Questionnaire, GADS = Generalized Anxiety Disorder severity, based on the GAD section of The Structured Clinical Interview for DSM, GADDS = Generalized Anxiety Disorder Severity Scale, GHQ-A = General Health Questionnaire – Anxiety, GP = General Practitioner, HADS-A = Hospital anxiety and depression scale (Anxiety), HAM-A = Hamilton Anxiety Scale, K&S = Kellner and Sheffield Symptom Rating Test, nos = not otherwise specified, PD = Panic Disorder, PL = Placebo, SIGH-A = Structured Interview Guide for the Hamilton Anxiety Scale, SP = Social Phobia Scale, STAI = Spielberger State-Trait Anxiety Inventory, WL = Waiting List, Z-SAS = Zung Self-rating Anxiety Scale, Ψ = psychological.
A computer program, Comprehensive Meta-analysis (CMA; version 2.2.021) was used to calculate pooled mean effect sizes, and the random effects model was used to conduct all analyses because considerable heterogeneity was expected. We calculated the Q statistic as an indicator of heterogeneity and the $I^2$ statistic as an indicator of heterogeneity in percentages. A value of 0% indicates no observed heterogeneity and larger values indicating larger heterogeneity (25% = low, 50% = moderate, 75% = high). We tested for publication bias by inspecting the funnel plot of the meta-analysis and by using Egger’s test. The analyses of funnel plots provide a test for the likely presence of bias in the meta-analysis. Egger’s linear regression method quantifies the bias captured by the funnel plot. Egger’s method uses the actual values of the effect sizes and their precision. To yield an estimate of the effect size after publication bias we used the Duval and Tweedie’s ‘trim and fill’ procedure. This procedure is based on the expectation that if no publication bias is present, the effect sizes will be dispersed equally on either side of the overall effect. The funnel plot is expected to be asymmetric when there is an indication for publication bias. The Duval and Tweedie procedure allows imputation of these missing studies. This method determines where the missing studies are likely to fall, adds them to the analysis and recomputed combined effect sizes.

Subgroup analyses were conducted in CMA using mixed-effects analyses that pooled studies within subgroups with the random effects model, but tested for significant differences between subgroups with the fixed effects model.

**Results**

**Description of Studies**

Searching the databases yielded 1343 manuscripts and after reading the titles, 191 manuscripts remained. Five manuscripts were retrieved from reference lists. After removing the duplicates there were 123 manuscripts left, of which we retrieved the full articles [Figure 1]. In total 111 studies were excluded: 30 were no randomized trials, 8 did not focus on anxiety, 34 did not contain a psychological treatment, 5 were not conducted in primary care, and 34 because of other reasons (e.g., outcome of cost-effectiveness, psychological treatment combined with pharmacotherapy, no control group, or evaluations of other research) [Figure 1].

Twelve manuscripts met all inclusion criteria, in which 13 psychological treatment conditions were compared to a control group. Two manuscripts described different outcomes for one study. One study described two psychological treatment conditions (group CBT and individual CBT) with a control group. We treated these two comparisons as two different studies. However, these comparisons are not independent because they are compared to the same control group. Therefore, we used half of the control group as a comparison for the group-CBT and the other half as a comparison for the individual-CBT. This results in a total of 12 comparisons, in which a total of 759 patients participated (424 in the psychological treatment conditions and 335 in the control conditions). Selected characteristics of the studies included are presented in [Table 1].
Five comparisons included patients with GAD, five comparisons included panic disorder; one included social phobia and two included both GAD and panic disorder. Nine comparisons had adults as their target group and three comparisons were focused on older adults. In nine comparisons CBT was used as psychological treatment and in the other comparisons other treatments were used (i.e., exposure therapy, individual sessions of modular psychotherapy or anxiety management booklet). The treatment was provided by psychologists in seven comparisons and by GPs or trained psychology students in the remaining comparisons. Patients were recruited via referral by the GP in 9 comparisons, through screening in one comparison while a combination of referral and screening was used in two comparisons.

**Quality Assessment**

The quality of studies was not optimal; only one manuscript met all quality criteria. Seven of the 12 manuscripts gave insufficient information whether the allocation sequence was generated...
adequately. Eight manuscripts gave insufficient information about whether the allocation was adequately concealed. Because blinding of participants and treatment provider is not possible in psychological treatment, we checked for blinding of the post-treatment assessor. In two studies the outcome was rated by the GP and psychologist who were both not blinded. In the remaining studies self-reports were used as post-assessment. We assessed whether incomplete data were adequately addressed, by checking whether outcome data were assessed using intention-to-treat analyses. This was the case in four of the 12 manuscripts. Clinical effectiveness may be overestimated if an intention to treat analysis is not done.[48] In one manuscript referral of patients with longstanding anxiety problems was particularly encouraged. The lack of quality in these studies might have caused bias (for example selective drop-out) and this might have led to higher effect-sizes than in reality.

Effects of Psychological Treatments

In the 12 comparisons a psychological treatment is compared to one of the following types of control group: waiting list (WL), care as usual (CAU) or placebo (PL) [Table 2]. The random effect model showed an overall effect size of $d = 0.57$ (95% confidence interval (CI) = 0.29 to 0.84), which is considered to be a medium effect [Table 3]. However, the fixed effect model showed that heterogeneity was significant and moderate to high ($I^2 = 55.55$). In our analysis we included one study[37] in which two psychological treatments were compared to a waiting list. Both comparisons were included in the same analysis. However, these comparisons are not independent and this might have resulted in an artificial reduction of heterogeneity. When we include only the comparison with the largest effect size, because this is considered to be the most conservative approach in estimating heterogeneity, the random effect model showed an overall effect size of $d = 0.61$ (95% CI = 0.31 to 0.90). This analysis indicates that heterogeneity increased, but was still moderate to high ($I^2 = 62.01$).
### Table 2. Effect-sizes of psychological treatment versus control group per study

<table>
<thead>
<tr>
<th>Study name</th>
<th>Std diff in means</th>
<th>Variance</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>Z-Value</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blomhoff, 2001</td>
<td>0.220</td>
<td>0.022</td>
<td>-0.070</td>
<td>0.509</td>
<td>1.485</td>
<td>0.137</td>
</tr>
<tr>
<td>Lindsay, 1987</td>
<td>1.234</td>
<td>0.239</td>
<td>0.277</td>
<td>2.191</td>
<td>2.526</td>
<td>0.012</td>
</tr>
<tr>
<td>Power, 1989</td>
<td>1.523</td>
<td>0.256</td>
<td>0.531</td>
<td>2.514</td>
<td>3.009</td>
<td>0.003</td>
</tr>
<tr>
<td>Power, 1990</td>
<td>1.503</td>
<td>0.210</td>
<td>0.605</td>
<td>2.401</td>
<td>3.280</td>
<td>0.001</td>
</tr>
<tr>
<td>Sharp, 1996, 1997</td>
<td>1.232</td>
<td>0.179</td>
<td>0.403</td>
<td>2.060</td>
<td>2.914</td>
<td>0.004</td>
</tr>
<tr>
<td>Sharp, 2004</td>
<td>0.268</td>
<td>0.105</td>
<td>-0.366</td>
<td>0.902</td>
<td>0.829</td>
<td>0.407</td>
</tr>
<tr>
<td>Sharp, 2004a</td>
<td>1.053</td>
<td>0.097</td>
<td>0.443</td>
<td>1.663</td>
<td>3.382</td>
<td>0.001</td>
</tr>
<tr>
<td>Sorby, 1991</td>
<td>0.129</td>
<td>0.096</td>
<td>-0.478</td>
<td>0.736</td>
<td>0.416</td>
<td>0.678</td>
</tr>
<tr>
<td>Stanley, 2003</td>
<td>0.574</td>
<td>0.470</td>
<td>-0.770</td>
<td>1.918</td>
<td>0.837</td>
<td>0.403</td>
</tr>
<tr>
<td>Stanley, 2009</td>
<td>0.227</td>
<td>0.030</td>
<td>-0.113</td>
<td>0.568</td>
<td>1.310</td>
<td>0.190</td>
</tr>
<tr>
<td>van Boeijen, 2005</td>
<td>0.301</td>
<td>0.055</td>
<td>-0.158</td>
<td>0.761</td>
<td>1.286</td>
<td>0.198</td>
</tr>
<tr>
<td>Wetherell, 2009</td>
<td>0.037</td>
<td>0.129</td>
<td>-0.667</td>
<td>0.742</td>
<td>0.104</td>
<td>0.918</td>
</tr>
</tbody>
</table>

![Control vs Therapy Graph](image-url)
Table 3. Results of meta-analysis

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>d</th>
<th>95% CI</th>
<th>P</th>
<th>Q</th>
<th>$I^2$</th>
<th>$P_a$</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>All studies</td>
<td>12</td>
<td>0.57</td>
<td>0.29-0.84</td>
<td>0.00</td>
<td>26.54</td>
<td>55.55</td>
<td>3.18</td>
<td></td>
</tr>
<tr>
<td>Lowest ES included (per study)</td>
<td>12</td>
<td>0.34</td>
<td>0.12-0.56</td>
<td>&lt;0.01</td>
<td>17.90</td>
<td>38.54</td>
<td>5.26</td>
<td></td>
</tr>
<tr>
<td>Highest ES included (per study)</td>
<td>12</td>
<td>0.80</td>
<td>0.46-1.13</td>
<td>0.00</td>
<td>38.08</td>
<td>71.11</td>
<td>2.34</td>
<td></td>
</tr>
<tr>
<td>HAM-A</td>
<td>5</td>
<td>1.11</td>
<td>0.43-1.79</td>
<td>&lt;0.01</td>
<td>17.78</td>
<td>72.94</td>
<td></td>
<td></td>
</tr>
<tr>
<td>K&amp;S</td>
<td>5</td>
<td>0.44</td>
<td>0.15-0.73</td>
<td>&lt;0.01</td>
<td>3.79</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAD</td>
<td>5</td>
<td>0.96</td>
<td>0.28-1.64</td>
<td>&lt;0.01</td>
<td>13.43</td>
<td>70.21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>7</td>
<td>0.41</td>
<td>0.12-0.70</td>
<td>&lt;0.01</td>
<td>11.60</td>
<td>48.28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of Treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CBT</td>
<td>9</td>
<td>0.78</td>
<td>0.41-1.15</td>
<td>0.00</td>
<td>20.47</td>
<td>60.91</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>3</td>
<td>0.18</td>
<td>-0.06-0.43</td>
<td>0.14</td>
<td>0.26</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of Control</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAU</td>
<td>5</td>
<td>0.22</td>
<td>-0.01-0.45</td>
<td>0.06</td>
<td>0.73</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>7</td>
<td>0.91</td>
<td>0.44-1.39</td>
<td>0.00</td>
<td>20.88</td>
<td>71.26</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment Provider</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical psychologist/therapist</td>
<td>7</td>
<td>0.92</td>
<td>0.50-1.34</td>
<td>0.00</td>
<td>14.09</td>
<td>57.41</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>5</td>
<td>0.21</td>
<td>0.01-0.40</td>
<td>0.04</td>
<td>0.59</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of sessionsb</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤7</td>
<td>6</td>
<td>0.49</td>
<td>0.08-0.89</td>
<td>0.02</td>
<td>13.51</td>
<td>62.98</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;7</td>
<td>6</td>
<td>0.69</td>
<td>0.28-1.12</td>
<td>&lt;0.01</td>
<td>12.48</td>
<td>59.94</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recruitment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Referral</td>
<td>9</td>
<td>0.71</td>
<td>0.36-1.07</td>
<td>0.000</td>
<td>22.33</td>
<td>64.18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screening (or both)</td>
<td>3</td>
<td>0.21</td>
<td>-0.06-0.47</td>
<td>0.121</td>
<td>0.52</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a The $P$-value indicates whether the difference between subgroups is significant.

b In one study the number of sessions was unclear. $d$ = standardized mean difference. CI = Confidence Interval. $I^2$ = indicator of heterogeneity in percentages. ES = effect size. NNT = Numbers-needed-to-treat. HAM-A = Hamilton Rating Scale for Anxiety. K&S = Kellner and Sheffield Symptom Rating Test, CBT = Cognitive behavior therapy. CAU = Care as usual.

Subgroup Analyses

An attempt was made to identify subgroups of studies that could explain differences in effect and heterogeneity. The comparisons of these modifiers are shown in Table 3. We found a significant difference ($P < 0.01$) between CBT ($d = 0.78; 95\% \text{ CI} = 0.41 \text{ to } 1.15$) and other treatments ($d = 0.18; 95\% \text{ CI} = -0.06 \text{ to } 0.43$). We also found significant effects for type of control group ($P = 0.01$) with a lower effect-size for care as usual ($d = 0.22; 95\% \text{ CI} = -0.01 \text{ to } 0.45$) compared to other controls (WL or PL) ($d = 0.91; 95\% \text{ CI} = 0.44 \text{ to } 1.39$). The difference between treatment providers was also significant ($P < 0.01$). If the treatment was given by a clinical psychologist, the effect-size was significant higher ($d = 0.92; 95\% \text{ CI} = 0.50 \text{ to } 1.34$) compared to other treatment providers (for example GP or trained master level student) ($d = 0.21; 95\% \text{ CI} = 0.01 \text{ to } 0.40$). The difference in effect-size between screening (or both screening and referral) ($d = 0.21; 95\% \text{ CI} = -0.06 \text{ to } 0.47$) and referral by GP ($P = 0.71; 95\% \text{ CI} = 0.36 \text{ to } 1.07$) in the recruitment phase was also significant ($P = 0.03$) in favor of referral by GP. In the subgroup-analyses we found no significant differences between the type of disorder ($P = 0.14$) or the number of
treatment sessions \((P = 0.50)\). For the number of sessions we also performed a meta-regression, but this shows no significant results (slope = -0.05; 95% CI = -0.12 to 0.02).

**Publication Bias**

Funnel plots showed significant asymmetry in the studies (Egger's test, two-tailed \(P = 0.02\)). The Duval and Tweedie’s Trim and Fill suggest that three studies were potentially missing and, if imputed, the overall effect size would drop to \(d = 0.37\) but would still be significant (95% CI = 0.08 to 0.67) [Figure 2].

**Longer-Term Follow-Up**

Three studies\[^{40,45,46}\] report data on a six month follow-up. Psychological treatment versus control on a six months follow-up results in an effect-size of \(d = 0.29\) (95% CI = 0.07 to 0.52; \(P = 0.01\)) and zero heterogeneity. When we compared the outcomes of the psychological treatment at post-test with the outcomes of the psychological treatment at six months follow-up, the effect-size is \(d = 0.13\) (95% CI = -0.18 to 0.41; \(P = 0.42\)). This low, not significant, effect-size \((d = 0.13)\) suggests that the effects of the treatment persist over time.

Two studies\[^{45,46}\] report data on a twelve month follow-up. When psychological treatment was compared with control after twelve months, the effect-size is \(d = 0.14\) (95% CI = -0.11 to 0.38; \(P = 0.27\)) and zero heterogeneity. When we compared the outcomes of psychological treatment at post-test with the twelve months follow-up, the effect-size is \(d = 0.05\) (95% CI = -0.19 to 0.28; \(P = 0.71\)) and zero heterogeneity.
Figure 2. Funnel Plot with imputed studies adjusting for publication bias
Discussion

Summary of Main Findings

The psychological treatment of anxiety disorders is effective in primary care patients, especially when patients receive cognitive behavioral therapy, provided by psychologists, compared to a placebo control and when patients were referred to treatment. Somewhat lower effect-sizes are found at 6-months follow up and the difference in effect between treatment group and control group disappears after 12 months between treatment group and control, however these findings are based on a few studies.

Strengths and Limitations

A strength of this study is that we included only manuscripts in which psychological treatment was actually provided in primary care. Another strength is that several aspects of treatment (e.g. treatment provider, number of sessions, type of treatment) were assessed as modifiers. Some of these aspects of treatment are strongly related with effect-size. Therefore they are important to take into account for future research or when psychological treatment or care models are implemented in primary care.

This study also has several limitations. First of all, the number of studies included is relatively low and might not be a fair representation of the actual treatment of anxiety in primary care. A second limitation is the differences between the studies regarding the types of anxiety disorder. For example, panic disorder and GAD have different characteristics and treatment of these disorders might lead to different outcomes. However, we chose to combine these studies, because treatment of these disorders in primary care is mostly short-term and aimed at anxiety symptom reduction. Furthermore, CBT has been proven effective and is advised in the guidelines for most anxiety disorders. A third limitations is the fact that there is considerable heterogeneity in most analyses, which suggests that the effect of therapies might be associated with, or confounded by, other characteristics than those examined in the subgroup-analysis. Another limitation is that care as usual (CAU) is poorly described in most studies, therefore the contrast with the effect of psychological treatment it is difficult to interpret, because it might contain a variety of treatments or maybe no treatment at all, this might have affected the outcomes of this meta-analysis. There are few studies that reported any data on follow-up measurements. We reported some calculations on the six and twelve month’s follow-up, we reported some conclusions but these have to be interpreted with some caution. Finally, the results show that there is a significant publication bias in studies on psychological treatment for anxiety in primary care, although the effect-size remains significant after imputation.

Comparison with Existing Literature

CBT is effective for treating patients with anxiety disorders in primary care. The effectiveness of CBT for patients with anxiety disorders in general has been well established.[24,25] Together with the recent development of effective CBT self-help courses or treatment via Internet for anxiety disorders,[49,50] this could be an opportunity for effective and evidence-based treatment of anxiety disorders in primary care. They can be used as (low-intensity) treatment for primary mental health care models like stepped care or collaborative care provided by a practice nurse.
or psychologist. The (short-term) psychological treatment of anxiety in primary care is important for reducing waiting lists for specialized mental health care, but also to meet the preferences of the patient. As mentioned it is possible that such treatments can be performed effectively by primary care workers, such as nurses or social workers.

As expected the analyzed modifiers showed results corresponding to prior research either conducted in other settings or focused on depression instead of anxiety. When psychological treatment is compared to CAU smaller effect sizes are found than when they are compared with other groups, like waiting lists or placebo. A meta-analysis on Internet-based and other computerized psychological treatments for adult depression also found that wait-list control had higher effect sizes than CAU or other control groups. This seems self-evident because offered therapy in CAU is often an active treatment instead of waiting lists or placebo.

A therapist or clinical psychologist as treatment provider is more effective than other treatment providers (for example: GP or trained students). A meta-analysis on paraprofessionals treating anxiety and depressive disorders found that interventions conducted by professional therapists were more effective than those conducted by paraprofessionals. The term paraprofessional referred to a broad category of mental health professionals who are not qualified as psychiatrists, psychologists, social workers, or nurses and who are below a master’s degree level of education. Cuijpers also found that therapist background was related to effect size, but in the opposite direction: studies in which health professionals delivered the intervention had smaller effect sizes than those in which the intervention was delivered by mixed or other therapists and those that did not report the background of the therapist. Cuijpers also found that interventions conducted by students had lower effect sizes than those conducted by psychologists and other health professionals. However, these studies were not conducted in primary care settings.

Treatment of patients recruited through screening seems less effective than when the patients treated are referred by their GP. This may be a rather crucial factor. Cuijpers performed a meta-analysis on psychological treatment for depression in primary care and found that studies in which patients were referred by their also had significantly higher effect sizes ($d = 0.43; \text{NNT} = 4.20$) than studies in which patients were recruited through systematic screening ($d = 0.13$, not significantly different from zero; $\text{NNT} = 13.51$). The difference may be caused by both related patient factors (severity of the anxiety and motivation for treatment) and GP related factors. However, outside of research projects such screening is applied in primary care.

We find a moderate effect size for the treatment of anxiety in primary care, follow-up analysis show a decrease of this effect in at six-months and the effect disappeared on 12 months. Given the chronicity of anxiety disorders the lack of enduring effects can be expected. Recently NESDA presented the results of a two-year course of depressive and anxiety disorders. These results present 2-year diagnostic and symptom trajectory outcome of depressive and anxiety disorders. The course of pure anxiety disorders was less favorable than for pure depression. Therefore, treatment of anxiety disorders in primary care is effective, but probably, given the disappeared effect on 12 months not sufficient for most patients. If psychological treatment for anxiety disorders is implemented in primary care, it is important to monitor the patient at certain moments during the year. This could be achieved when psychological treatment is part of a
stepped care or collaborative care model. More research is needed on the follow-up effect of psychological treatment of anxiety in primary care.

**Conclusions**

Despite limitations and publication bias, we found a moderate effect size for the psychological treatment of anxiety disorders in primary care. This effect still remained after imputation for the ‘missing’ studies. Psychological therapies show larger effect sizes when the treatment is CBT, when therapy is delivered by a (clinical) psychologist, when the patients are referred to the therapy by their GP and when it is compared to another control group then care as usual. Chronicity of anxiety disorders can lead to lack of enduring effects. Therefore it is advised to provide least intensive treatments to those with low chronicity risk and providing more intensive treatment for those with high chronicity risk. In primary care it is also important to monitor chronic patients after treatment in primary care.

Psychological treatment of anxiety disorders is effective but shows somewhat lower effect-sizes compared to psychological treatment in specialized mental health care. More studies are needed to evaluate long-term effects given the chronicity and recurrent nature of anxiety.
References


