SPECIAL THEME

Meta-analysis on the Effectiveness of Family-focused Intervention Among Patients with Depression and Anxiety

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Background: Depression and anxiety are the most common mental disorders seen and managed in primary care. Both mental disorders have been increasingly prevalent worldwide. Filipinos are known for being family-centered and the family has been consistently a good ally in healthcare. A family- focused intervention is believed to be a good adjunct in the reduction of symptom severity of depression and anxiety.
Objective: This study aims to systematically analyze the effectiveness of family-focused interventions among patients with depression and anxiety.
Methods: Studies were obtained from electronic search for literature (PubMed, Cochrane, HERDIN). Additional cross-referencing was done from the reference lists of included studies. Two independent reviewers assessed the methodological quality of included trials.
Results: Two studies met the selection criteria and were included for meta-analysis. There was a total of 224 participants who were all clinically diagnosed with depression and anxiety. Compared with the standard care for depression and anxiety, family-focused intervention was found to be more effective (SMD=–1.20, z=6.92, p=0.001, 95% CI=–1.54 to –0.86). There was also no substantial heterogeneity (I^2=13.80%) seen among the included studies (Q=1.16, p=0.281; τ^2=0.01).
Conclusion: Family-focused intervention was shown to be effective in reducing the symptom severity of depression and anxiety.
Recommendation: The authors recommend future researchers to use more studies, both published and unpublished, on the utilization of family-focused interventions in the management of depression and anxiety. Applicability of the results in the Asian region, especially in the Philippines, should be explored. This review also suggests the option to provide different family-focused intervention techniques as an adjunct in the management of depression and anxiety in primary care.

Keywords: family-focused intervention, depression, anxiety

Introduction

At present, two of the most common and prevalent mental disorders worldwide are depressive disorders and anxiety disorders. In fact, the people suffering from depression alone accounts for more than 4% of the total population globally. The number of people suffering from such mental disorders is continuously increasing worldwide and is found to be more prominent in lower-income countries.[1] There is also an increasing prevalence of mental disorders noted in the Philippines. In the 2011-2016 National Objectives for Health, the Department of Health reported that mental illness ranked third most prevalent form of disability in the Philippines.[2] Patients with depressive or anxiety disorders are often seen and continue their treatment in the primary care clinics.[3] The increasing prevalence of mental disorders gives a vital role to the primary care physician in the management of these disorders: screening, appropriate referrals and long-term holistic care.

Treatment Approaches to Depression and Anxiety

Treatment goals for depression include the following: to ensure the safety of the patient, to provide a complete diagnostic evaluation, and to make a treatment plan that covers both the immediate and long-term well-being of the patient. It is important to determine first whether the patient's condition warrants hospitalization or out-patient care. In the out-patient setting, pharmacotherapy and psychotherapy are usually combined. The drug of choice for depression usually belong to the second and third generation antidepressants. Selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) are most often used. Monoamine oxidase

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inhibitors (MAOIs) are believed to be effective for patients with atypical symptom features. Choices for psychotherapy include cognitive therapy, interpersonal therapy, behavior therapy, psychoanalytically oriented therapy, and family therapy. The treatment for anxiety also entails pharmacotherapy, psychotherapy, or a combination of both. Patients with anxiety seldom requires hospitalization and treatment is usually in an out-patient setting. The first-line drugs for anxiety are SSRIs and SNRIs. Other recommended second-line drugs are tricyclic antidepressants, MAOIs, benzodiazepines, other psychotropics, atypical antipsychotics and anticonvulsants. Psychotherapy options for anxiety include cognitive therapy, behavior therapy, interpersonal psychotherapy, virtual therapy, supportive psychotherapy, and insight-oriented psychotherapy. Psychotherapies are the first-line choice for certain types of anxiety such as specific phobias.[4]

Family-focused Intervention

In the Philippines, the family plays an important part in healthcare. Whenever someone gets sick in a Filipino household, it is customary that a family member actively provides care in different ways. A family member is often present during consultations or bedside taking the role of caregiver. Hence, this concept is given importance in Family Medicine training in the Philippines. The newly-developed Patient-centered, Family-focused and Community-oriented (PFC) matrix is a tool for biopsychosocial approach in primary care, which includes different strategies that also highlight the role of the family from the assessment to management plan. In its family-focused matrix, the management/ interventions often include the family wellness plan, health education and counselling of family members.[5]

Currently, there are few systematic reviews/meta-analyses that recognize the effectiveness of family interventions in the management of mental illnesses, specifically clinical depression and anxiety. This may be due to 1) the use of family intervention or family therapy is still growing in this field and 2) patients with depression and anxiety belong to the vulnerable population. Although still growing in number, some meta-analyses demonstrate already favorable outcomes in terms of the effectiveness of family interventions. A meta- analysis done on family intervention and perinatal depression shows that family intervention is effective in both prevention and treatment of perinatal depression.[6] Another meta-analysis done on family intervention and severe mental illness shows that cognitive behavioral family intervention is effective in the treatment of severe mental illness, such as schizophrenia and bipolar disorder.[7]

Relevance of the Review

This review puts into perspective the role of the Filipino family in the management of mental illness. Family-focused interventions may also be effective as adjuncts in the treatment of depression and anxiety. This will strengthen the thrust of the primary care physician in bringing the family as ally in healthcare and promote the development and utilization of more family-focused interventions for the management of depression and anxiety in the future.

This study aimed to systematically analyze the effectiveness of family-focused interventions among patients with depression and anxiety.

Methods

Protocol and Registration

This protocol was registered under the Research Committee of the Philippine Academy of Family Physicians (PAFP). It was also registered under the Department of Medical Education and Research (DMER) of the University of Santo Tomas Hospital. This was guided by the PRISMA for systematic reviews and meta-analyses.[8]

Eligibility Criteria

This systematic review utilized only published randomized controlled trials and excluded descriptive studies. Studies written in foreign languages were also used as long as English translations were available. Publication date was restricted to 2015 until 2020.

The participants in the study included patients clinically diagnosed with depression or anxiety using the DSM criteria and any of their family members. The patients with depression or anxiety may have other co-morbidities.

The studies considered for this review should have a family-focused intervention. This may involve psychoeducation in the form of lectures, trainings or workshops. The intervention may also be in the form of counseling or psychotherapy. The family-focused intervention should involve at least one family member who takes the role as caregiver of the patient diagnosed with depression and anxiety. These interventions may be given alone or as adjunct to the usual care or other interventions. Table 1 shows details of the intervention.

The control intervention given to patients with depression and anxiety comprised of usual care/standard treatment or wait-listed. The usual care can be in the form of pharmacotherapy or individual psychotherapy or a combination of both.

The primary outcome included in this review was the reduction of the severity of depressive or anxiety symptoms, which were measured using appropriate scales corresponding to the mental illness involved.

Information Sources

An electronic search was done on databases including PubMed, Cochrane Library and HERDIN. Publication dates of studies were restricted to the last 5 years 2015-2020).

Search Methods

Electronic search was done looking for comparison between family-focused intervention and usual care/standard care for reduction in the severity of depression and anxiety. Cross- referencing from the reference lists from retrieved articles was also performed. Boolean logic (AND/OR) was used to combine terms. Table 2 shows the search terms employed.

Study Selection

Selection of studies, guided by the set inclusion criteria, was performed independently by the two authors. Disagreements were

Table 1. Criteria for considering studies in this review

	Inclusion	Exclusion
Population	Patient clinically diagnosed with depression and anxiety (DSM criteria)	
Setting	Out-patient care	Hospital-based (in-patient)
Study design	Randomized controlled trial studies	Descriptive studies
Language	All studies written in any language, as long as English translations were available	
Publication timeframe	Studies published from 2015 until 2020	
Outcome	Reduction in severity of depression and anxiety	
Intervention	Family-focused intervention Types: Psychoeducation Counselling/psychotherapy Format: Face-to-face or web-based Delivery: Sessions – group or individual, involving any family member as caregiver Frequency:	Family member with cognitive impairment, paid caregivers
	Single or multiple sessions	
Control	Usual care Control intervention Wait-listed Types: Pharmacotherapy Psychotherapy	

Table 2. Database and keywords used in the search.

PubMed	Family focused intervention Depression OR anxiety Filters: Publication date 2015-2020, RCTs
Cochrane Library	Family focused intervention Depression OR anxiety Filters: Publication date 2015-2020, clinical trials Cochrane group: mental disorders
HERDIN	Family intervention Depression OR anxiety Filters: publication date 2015-2020, clinical trials

resolved with thorough discussion. The consultant co-investigator served as the arbiter if the disagreement between the authors were not resolved. Details of the selection of articles were presented in a PRISMA flow diagram.

Data Collection Process

A simple format was used for the data collection using the principles of PRISMA statement for reporting systematic review. Data extracted from the studies included: 1) study details (author, year of publication, country of publication), 2) participants (setting, characteristics and other pertinent data noted), 3) intervention, 4) control, and 5) outcome measures.

Risk of Bias in Individual Studies

Publication bias was assessed using both graphical and statistical approaches. Graphical approach for publication bias included contour-enhanced funnel plots, while statistical assessment of funnel plot asymmetry was performed using Begg's asymmetry test (Higgins, 2003).

Synthesis of Results

Statistical analyses were conducted using STATA MP Statistical Software, Version 13, College Station, TX: StataCorp LP. A p-value ≤ 0.05 was considered statistically significant. Since this study did not assume one effect size among all the studies, the overall effect of the meta-analysis was derived using a random-effects model (REM), which takes within-study and between-study variation into account. Cognizant that outcomes were measured as a continuous variable, standardized mean difference was used as the effect or summary measure. Statistical heterogeneity between studies were scrutinized using Q statistics test, I^2 statistics, and tau squared (τ^2) statistics.[9] I^2 values greater than 50% imply substantial heterogeneity.[9]

Results

Study Selection

There was a total of 55 articles retrieved from an electronic search using online databases such as PubMed, Cochrane and HERDIN. The online search focused on family intervention, depression and/

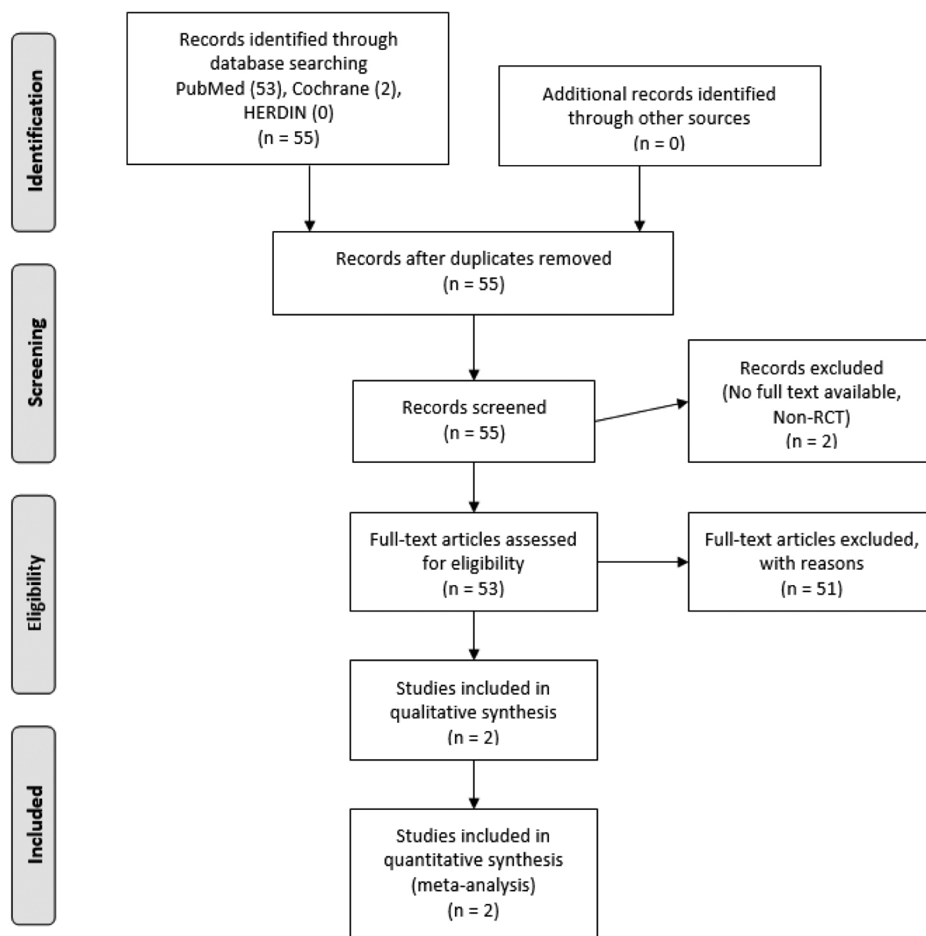

Figure 1. Prisma flow diagram of included studies

Table 3. Characteristics of the studies included in this review

Year published	Participants	Setting	Inclusion	Intervention	Control	Outcome
Gorenstein 2015	33 8-17 years Diagnosed with anxiety (OCD)	Out-patient Institute of Psychiatry, University of Sao Paulo Medical School (Sao Paulo, Brazil)	Randomized-controlled trial Anxiety clinically diagnosed using DSM IV criteria Family-focused intervention (inclusive of parent)	Group Cognitive-Behavioral Therapy (GCBT) 14 weekly, 2-hour sessions	Fluoxetine 10-60mg/day for 14 weeks	OCD (anxiety) symptom severity Yale-Brown Obsessive-Compulsive Scale (Y-BOCS)
Luby 2018	191 3-6 years Diagnosed with depression	Out-patient Washington University School of Medicine (St. Louis, Missouri, United States of America)	Randomized-controlled trial Depression clinically diagnosed using DSM V criteria Family-focused intervention (inclusive of parent)	Parent Child Interaction Therapy – Emotion Development (PCIT-ED) 18 weeks, 20 sessions (12 PCIT and 8 ED)	Waiting list control condition	Depression symptom severity Schedule for Affective Disorders and Schizophrenia – Early Childhood (K-SADS-EC)

or anxiety. After the articles were screened, only 2 articles were able to meet the inclusion criteria. These 2 studies were then assessed for eligibility. All studies met the requirements of having a participant clinically diagnosed with depression and anxiety thru The Diagnostic and Statistical Manual of Mental Disorders (DSM IV/V) and having a family intervention as one of the treatment interventions provided. Family intervention in each study was compared to a standard point of care or usual care for the treatment of depression and anxiety. All studies were randomized controlled trials.

Study Characteristics

All studies had a total of 224 participants, wherein 116 participants received family- focused intervention (experimental) while 108 participants received the standard or usual care for depression and anxiety (control). The participants belonged to the pediatric age group, whose ages ranged from 3 to 17 years old. The study of Gorenstein[10] had the higher mean age because the participants were 8 to 17 years old while with Luby's study[11] the age range was 3 to 6 years old. All the participants have been clinically diagnosed with depression and anxiety using the DSM criteria of mental disorders. All studies were done in an out-patient setting.

In the study of Gorenstein[10], the family-focused intervention used was the Group Cognitive-Behavioral Therapy (GCBT), which lasted for 14 weeks with 2-hour sessions weekly. GCBT included psychoeducation (with the parent/caregiver), exposure/response prevention techniques and relapse prevention. The control intervention used was fluoxetine, which was given 10-60mg/day for 14 weeks. The symptom severity of

anxiety (OCD) was measured by the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS). On the other hand, the study of Luby[11] used the Parent Child Interaction Therapy – Emotion Development (PCIT-ED) as the family-focused intervention, which lasted for 18 weeks, with a total of 20 sessions (12 PCIT and 8 ED). PCIT-ED involved psychotherapy and education techniques with the parent/caregiver to enhance the child's emotional competence and regulation. The control intervention utilized was a waiting list control condition. The symptom severity of depression was measured by the Schedule for Affective Disorders and Schizophrenia – Early Childhood (K-SADS-EC). (Table 3)

Synthesis of Results

Figure 2 illustrates the pooled estimate for the effect of family-focused intervention. A total of two studies were included, yielding a total of 116 patients in the intervention (family- focused intervention) and 108 patients in the control. Results showed that there is evidence that the family-focused intervention was more effective than the control (SMD=−1.20, z=6.92, p=0.001, 95% CI=−1.54 to −0.86). It is also interesting to note that there was no substantial heterogeneity (I^2=13.80%) among the included studies (Q=1.16, p=0.281; τ^2=0.01).

Risk of Bias Across Studies

The risk of bias and the quality of evidence analysis of the included studies are depicted in Figure 3. Among the included studies, all studies have low risk for random sequence, blinding of outcome assessor, incomplete data, and selective reporting. On the other hand, the risk attributed to allocation concealment and blinding of participants was 50% unclear.

The graphical analysis of publication bias using contour-enhanced funnel plots is illustrated in Figure 4. Graphical assessment of the funnel plot indicated right-sided funnel asymmetry, suggestive of publication bias. Statistical analysis using Begg's test further confirmed the probability of publication bias among the included studies (z=1.00, p=0.317).

Discussion

Summary of Evidence

There are 2 randomized controlled trials (RCT) included in this systematic review and all the RCTs included employed a type of family-focused intervention as one of the interventions for the management of depression and anxiety. All the RCTs showed that the family- focused intervention was more effective compared to the control. The pooled standardized mean difference showed a statistically significant reduction in symptom severity of depression and anxiety was seen in the family-focused intervention group compared to the standard care or control group.

Generally, all included studies posed low risk of bias. All studies have low risk for random sequence, blinding of outcome assessor, incomplete data, and selective reporting. However, the risk attributed to allocation concealment and blinding of participants was 50%

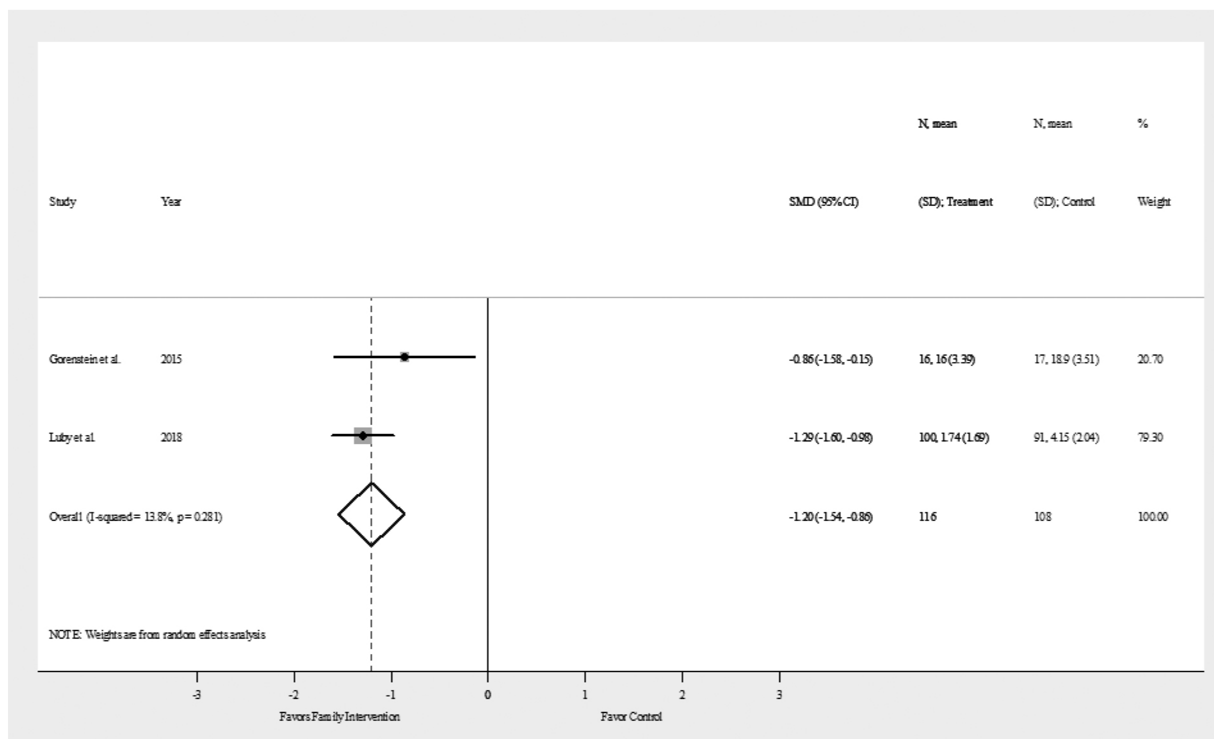

Figure 2. Pooled estimate for the effects of family-focused intervention

unclear. The study of Luby (2018) mentioned that it was a single blind randomized controlled trial while in the study of Gorenstein (2015), also a randomized controlled trial, but it was not clearly stated that there was blinding among the participants. Moreover, there was also poor report regarding the difficulty in blinding participants or the staff performing the study.

All the studies included had participants who were clinically diagnosed with depression or anxiety thru the DSM criteria of mental disorders. No study was included which involved participants observed to have symptoms of depression or anxiety but with no clinical diagnosis. The interventions used, though varying in composition of techniques employed, were all considered to be family-focused interventions. Strict implementation of the inclusion criteria made the result generalizable to patients with depression and anxiety. Although this may be specific to pediatric depression and anxiety since the participants in all included studies belonged to the pediatric age group. The result showed low heterogeneity (I^2=13.80%) among the included studies (Q=1.16, p=0.281; τ^2=0.01). All studies included were similar

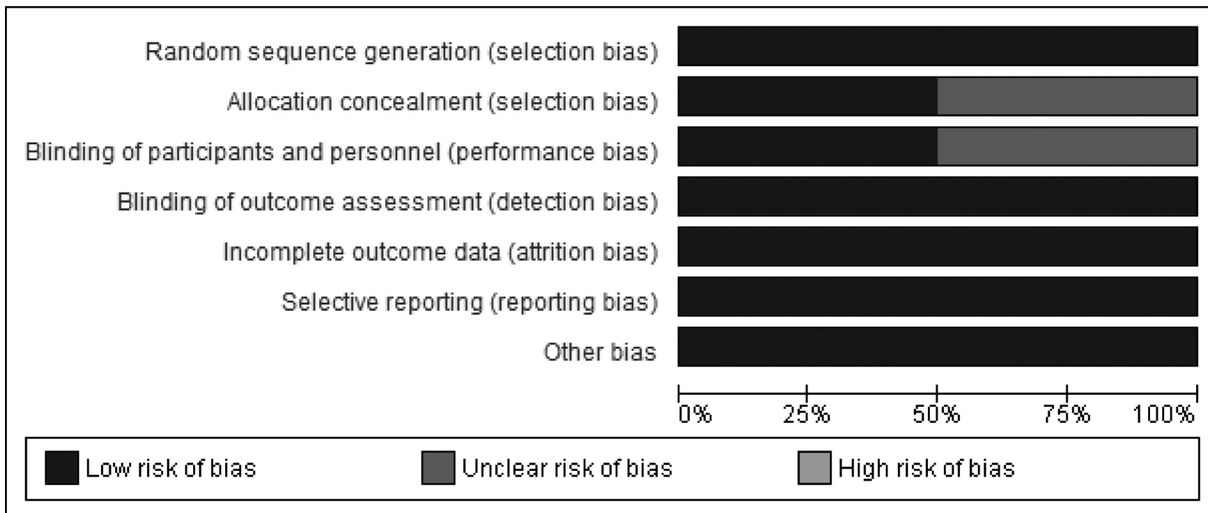

Figure 3. Risk of bias summary of studies included in this review

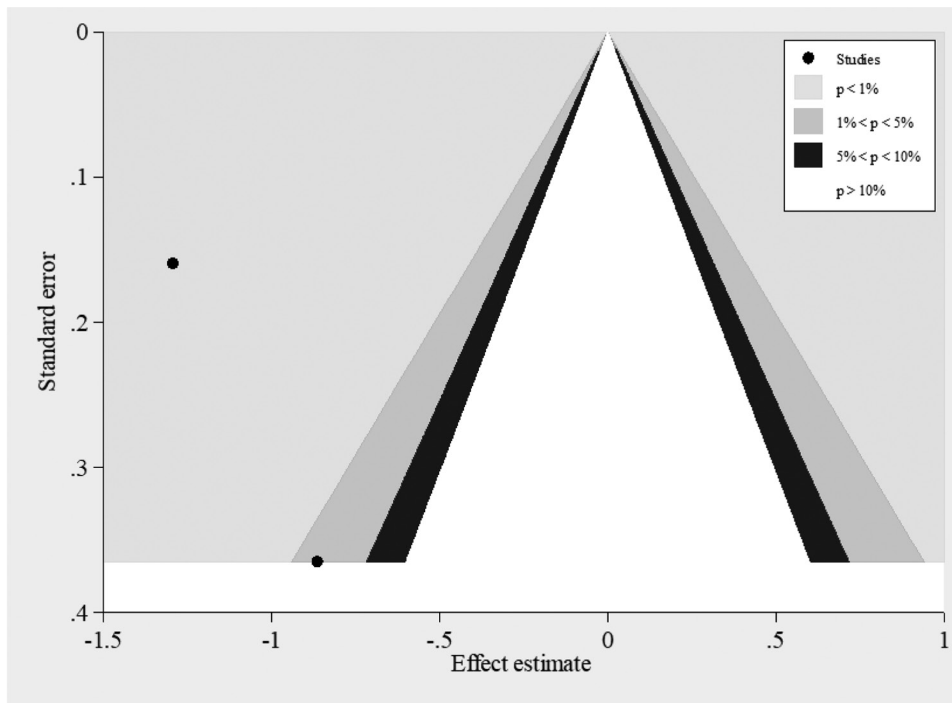

Figure 4. Funnel plot of studies included in this review

in their treatment intervention and showed benefit in the symptom reduction of depression and anxiety. The result showed right-sided funnel asymmetry and statistical analysis using Begg's test point to the probability of publication bias among the included studies (z=1.00, p=0.317). This study showed high quality of evidence that family-focused intervention can reduce symptom severity among patients with depression and anxiety (SMD=–1.20, z=6.92, p=0.001, 95% CI=–1.54 to – 0.86).

Potential Bias in the Review Procedure

This meta-analysis has several limitations. The available studies were relatively small, including the participants subjected to the interventions. This may be due to the involvement of participants with depression and anxiety, who belonged to the vulnerable population. The participants also belonged to the pediatric age group and no adult population was represented. The review was limited to published studies within the last 5 years and the studies were all conducted in America. This review has observed a low dropout rate; hence attrition bias was minimized. Randomization was done in all included studies, but concealment was difficult due to the nature of the interventions. One study did not conceal the intervention. Although the funnel plot showed no bias, due to the small number of studies, the generalization can be affected. Moreover, the funnel plot suggested the presence of publication bias. The statistical analysis using Begg's test confirmed the probability of publication bias among the included studies.

The reviewers' varying preferences and opinions could be a source of bias during the review of studies. Implementation of a strict inclusion criteria was observed during the review of the studies. A third party was made available to intercede should there be instances of disagreement among the reviewers.

Limitations

Although the studies were replicable, family-focused interventions need to be studied further due to the different techniques of the family-focused intervention utilized in the studies included. There can be many possible combinations of techniques that can be used in the family-focused intervention sessions, such as psychotherapy, psychoeducation, skills-training and many more. Also, one or more family members can be involved in a family-focused intervention. Some techniques of the family-focused intervention may not be available in primary care. Certain techniques may require at least a trained master's level therapist. Primary care providers should be trained first before performing such techniques. This may be a possible difficulty in replicating the studies.

Conclusion and Recommendation

Based on the results presented, family-focused intervention was shown to be effective in reducing the symptom severity of depression and anxiety.

The authors recommend future researchers to use more studies, both published and unpublished, on the utilization of family-focused interventions in the management of depression and anxiety. Applicability of the results in the Asian region, especially in the Philippines, should be explored. This review also suggests the option to provide different family-focused intervention techniques as an adjunct in the management of depression and anxiety in primary care.

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