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A Systematic Review and Meta-analysis of the Effects of Psychological Interventions on Patients with Pediatric Chronic Illnesses

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Abstract

Background: Children with chronic physical illnesses exhibit internalizing disorders such as anxiety and depression at higher rates than healthy children. Therefore, the need for and importance of effective psychological support for such children is high though such support is not yet widely established.

Methods: This study utilized databases such as Web of Science, PubMed, PsycINFO, MEDLINE, CENTRAL, and CINAHL to define psychological interventions for internalizing disorders in children with chronic physical illnesses. We conducted a search for terms that had already been defined. The review included all studies (randomized and nonrandomized designs) that investigated interventions aimed primarily at treating common psychiatric symptoms in children with chronic physical illnesses. For each article, two reviewers independently assessed the identified abstracts' validity and extracted and analyzed the relevant data.

Results: Thirty studies met the meta-analysis inclusion criteria. The analyzed diseases included diverse chronic conditions such as asthma and childhood cancer. Furthermore, the analysis showed that various intervention techniques, such as cognitive-behavioral therapy and art therapy, were being used for treating psychiatric symptoms in children with chronic physical illnesses. The post-intervention scores for internalizing disorders showed that the intervention group experienced significant positive effects compared to the control group; however, no significant results were obtained for follow-up data or quality of life.

Conclusions: Preliminary evidence attests that psychological approaches are effective for treating internalizing disorders such as depression and anxiety in children with chronic physical illness. However, the current evidence is weak, and randomized controlled trials with adequate power are necessary for establishing psychological treatments' effectiveness for this vulnerable population.

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Background

Chronic pediatric diseases are illnesses that occur during childhood and have long-term impacts on both physical and psychological health. Due to the painful symptoms and repetitive tests and procedures, children with chronic diseases (hereafter referred to as "patients") often face restrictions in their activities and daily lives compared to their peers. These patients have a higher risk of internalizing disorders such as anxiety and depression than healthy children [1]. Pao and Bosk [2] indicated that early prolonged hospitalization can lead children to develop separation anxiety regarding home and caregivers, the potential for obsessive handwashing behavior due to hygiene practices to prevent infections, and the occurrence of social anxiety symptoms resulting from long-term school absenteeism. In general, moderate-to-severe anxiety symptoms can affect symptom management, treatment adherence, and patients' ability to cope with the illness.[2] Therefore, experts must determine whether the relevant anxiety stems directly from a physical illness or is a secondary response. Appropriate identification and treatment of anxiety disorders can reduce both psychological and physical symptoms [2].

One large-scale survey on the health-related quality of life (QOL) of children with chronic diseases (e.g., asthma, eczema, and migraine) compared to those without such diseases revealed that children with chronic diseases had lower self-esteem. In particular, children with migraines scored lower in mental health than those without migraines [3]. Thus, from a holistic perspective, comprehensive support is necessary for these patients.

Psychological interventions have been administered to such patients. Specifically, psychoeducation [4], mindfulness interventions [5], cognitive-behavioral therapy [6], and art therapy [7] have been implemented, demonstrating their effectiveness for reducing internalizing disorders such as depression and anxiety and improving QOL. Furthermore, Bennett et al. [8] reviewed psychotherapy's effectiveness for treating psychiatric symptoms in children with chronic diseases, suggesting that interventions using cognitive-behavioral therapy can effectively treat depression and anxiety.

However, their meta-analysis eventually resulted in the extraction of only knowledge related to cognitive-behavioral therapy, leaving the effects of other therapeutic approaches unknown. Additionally, the analysis focused solely on internalizing problems. However, given the characteristics of chronic diseases and the perspective of living with illnesses and their symptoms, it is also important to consider QOL. Research on psychological support for children with chronic illnesses

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has increased rapidly in recent years. Although not exact, a search on PubMed for studies published since 2000 using the terms "psychological interventions" AND "pediatric chronic illnesses" showed an average of 11 studies published per year from 2000 to 2015, with a peak of 24 studies being published in 2015. However, from 2016 to 2020, the average number of studies increased to 38 per year, with 47 studies being published in 2020.

Thus, this current systematic review aimed to update the findings of Bennett et al. [8] and organize evidence regarding psychological interventions' effectiveness for treating internalizing disorders and improving quality of life (QOL) in children with chronic illnesses up to 2020. If the sample size is sufficient, a network meta-analysis will be conducted to verify effectiveness. Unlike standard meta-analysis, which is limited to pairwise comparisons, network meta-analysis allows comparisons among three or more interventions [9], providing insights into the effectiveness of intervention methods that are directly compared less frequently.

Materials and Methods

Systematic reviews were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement on reporting guidelines for systematic reviews [10]. The review plan was registered with PROSPERO (registration number: CRD42021255661).

Selection criteria

The inclusion criteria were selected based on the following eligibility and exclusion criteria. The eligibility criteria were (a) participants aged between 3 and 19 years, (b) study of chronic illness (e.g., cancer, heart disease, asthma, chronic pain), (c) involving psychological intervention, (d) inclusion of a control group, (e) involving measurement of internalizing disorders (depression and anxiety), and (f) publication in a peer-reviewed journal in English. Exclusion criteria were (a) a diagnosis of a psychiatric disorder; (b) intervention or disease management program combined with pharmacotherapy; (c) review article, survey study, protocol only, or case study; and (d) the subjects were only caregivers or foster parents.

Article search

Articles were electronically searched using Web of Science, EBSCO (PsycINFO, PsycARTICLES, MEDLINE, CINAHL), PubMed, Cochrane Database of Systematic Reviews, and CENTRAL (search date: August 18, 2020). The search criteria included any of the words "depress," "affect," "mood," "anxiety," "internal," or "phobi"; any of the words "child," "Adolec "youth," or "pediatric"; any of the words "intervention" or "prevent"; and any of the words "illness," "disease," or "disability." In total, 47,086 papers were identified. Of these, 18,376 were deleted due to duplication, resulting in a total of 28,710.

Study selection

Two authors independently evaluated each paper based on the extraction criteria. They read the titles and abstracts, and if they could not make a judgment, they read the full text. If their evaluations did not match, these were resolved through discussion. After applying the extraction criteria, 28,609 papers were excluded based on their titles and abstracts, and 170 papers underwent full-text review. Consequently, 121 papers were excluded, and 49 were extracted. Of these, 30 that contained the necessary information for calculating effect sizes were included in the meta-analysis (Figure 1).

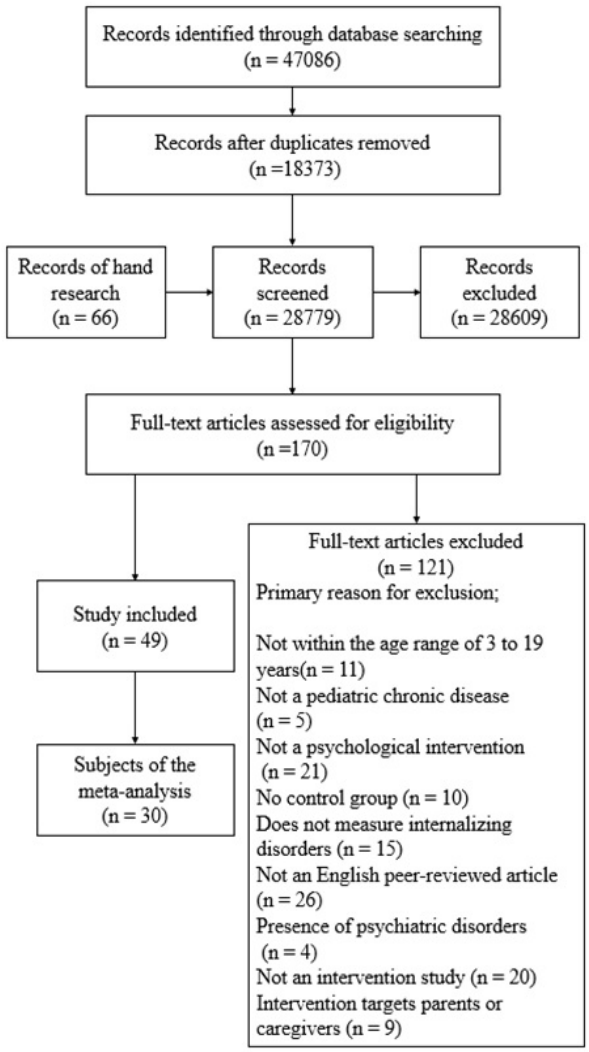

Figure 1: Flowchart of Study Selection.

Data extraction

The information extracted from each study included participants' age, sex, disease name, intervention contents for both the intervention and the control groups, types of outcome measures, timing of measurement (post and follow-up), and measurement results.

Analysis methods

The meta-analysis examined studies included in systematic reviews that reported data on post-intervention mean values, standard deviations (*SD*), and sample sizes for internalizing disorders; furthermore, QOL indicators were selected. The meta-analysis estimated the standardized mean difference (Cohen's *d*) between the intervention and control groups using a random effects model. The criteria for judging the magnitude of the effect size were based on Cohen's [11] standards: 0.2 (small effect), 0.5 (medium effect), and 0.8 (large effect). Additionally, 95% confidence intervals for the *d* values, *Q* statistic as a measure of heterogeneity among studies, and I^2 as an indicator of the degree of heterogeneity in the effect sizes were used.

Results and Discussion

The characteristics of the selected studies are presented in Table 1. The chronic pediatric diseases included in the studies were asthma (6 studies), type 1 diabetes (5 studies), pediatric cancer (3 studies), chronic pain (3 studies), and various other chronic pediatric diseases (29 studies). Furthermore, three studies targeted general chronic diseases. While psychological interventions for various chronic pediatric diseases were indicated, the number of relevant studies varied by disease type. The intervention contents for the intervention groups were categorized into six types: (1) cognitive and behavioral approaches (e.g., cognitive therapy and behavior therapy) (14 studies); (2) mindfulness, acceptance, and commitment therapy (7 studies); (3) educational approaches such as psychoeducation (4 studies); (4) spiritual interventions (3 studies); (5) combined approaches incorporating two to four of the mentioned methods (14 studies); (6) art therapy (2 studies); and (7) other (5 studies).

Psychological interventions for chronic pediatric diseases predominantly utilized cognitive-behavioral approaches; however, many interventions combined multiple intervention methods. The control groups included waiting-list control groups (17 studies), non-intervention control groups (2 studies), attention control groups (20 studies), and treatment-as-usual control groups (10 studies).

For outcome measures, indicators for measuring internalizing disorders included the Children's Depression Inventory evaluated by children and adolescents (CDI), State-Trait Anxiety Inventory for Children (STAI-C), and Hospital Anxiety and Depression Scale (HADS). Indicators for measuring QOL included the Pediatric Quality of Life Inventory (PedsQL) and the Cerebral Palsy Quality of Life Questionnaire (CP QOL). Due to the insufficient sample size, it was not possible to conduct a network meta-analysis. Therefore, a meta-analysis was conducted for subsequent analyses (Table 1) (Supplementary File).

Results of the meta-Analysis

At the post-intervention stage, of the 30 studies included in the meta-analysis, 58 post-intervention data points were analyzed. The scores for internalizing disorders (depression and anxiety) were significantly lower in the intervention group compared to the control group (d = -0.49, SE = 0.23, p = 0.03, 95% CI [-0.94, -0.03]) (Table 1). The heterogeneity indicator, I^2 = 95.63%, showed significant homogeneity (Q (31) = 289.78, p < .0001). Therefore, considering the large variability among the studies included in the meta-analysis is important (Figure 2).

At the post-intervention stage, the intervention group showed significantly lower scores for internalizing disorders such as depression and anxiety than the control group, indicating the psychological interventions' effectiveness for treating these patients. However, inter-study variability must be considered; effect sizes ranged from small to large, suggesting differences in the magnitude of the effects across studies. Most of the interventions included cognitive-behavioral approaches such as third-generation cognitive-behavioral therapy, which is considered an effective intervention method for patients. Although this study could not examine the effectiveness of each intervention type due to the limited number of studies, future research could contribute toward proposing more effective intervention methods by evaluating each intervention type's effectiveness. Additionally, it is unclear whether interventions are generally effective for all chronic diseases, or whether specific interventions are appropriate for specific diseases. By conducting controlled studies that account for the disease type and severity, more refined interventions can be developed.

Eight studies conducted follow-up measurements, and 14 follow-up data points were analyzed. There was no significant difference in internalizing disorder scores between the intervention group and the

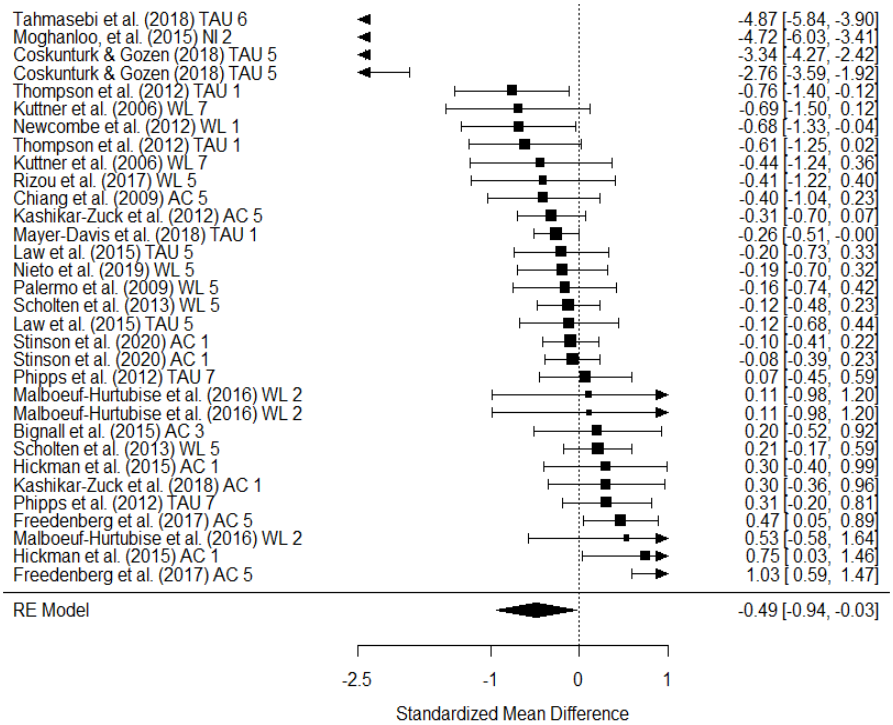

Figure 2: Results on Internalizing Disorders at the Post-Intervention

control group (d = 0.07, SE = 0.07, p = 0.32, 95% CI [-0.07, 0.21]) (Figure 3). The heterogeneity value was I^2 = 0.00%, and the homogeneity indicator was not significant (Q (9) = 6.47, p = 0.69), suggesting small variability among the studies.

No significant results were obtained regarding impact on internalizing disorders. This might be due to the limited data on interventions. It is possible that the number of studies might not be sufficient. Furthermore, the intervention effects are not being sustained over time, and that there is a potential for relapse occurrences.

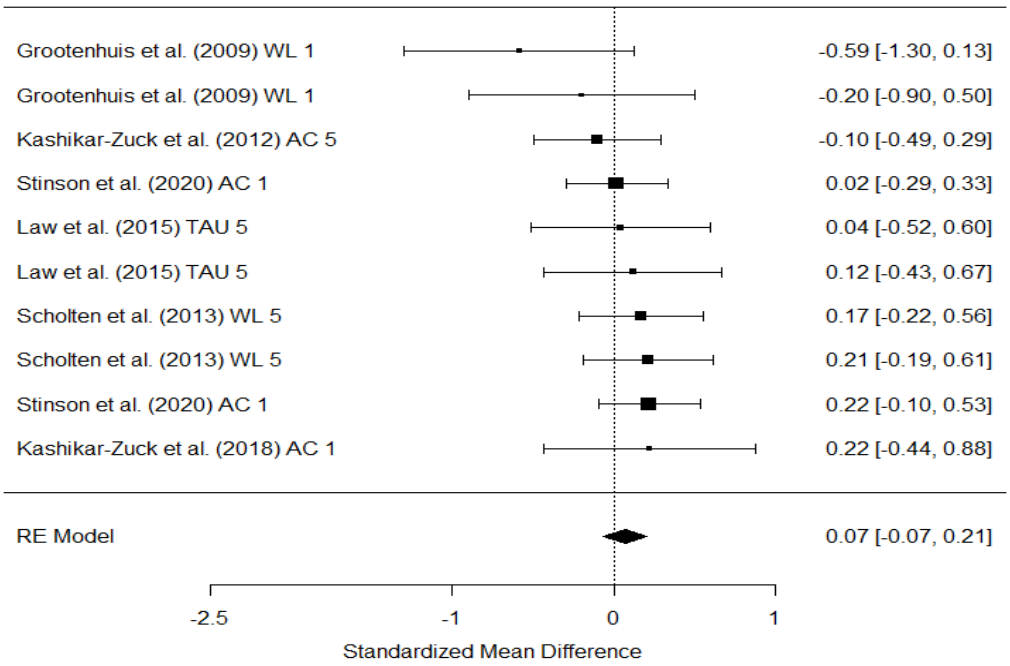

Figure 3: Results on Internalizing Disorders at the Follow-Up.

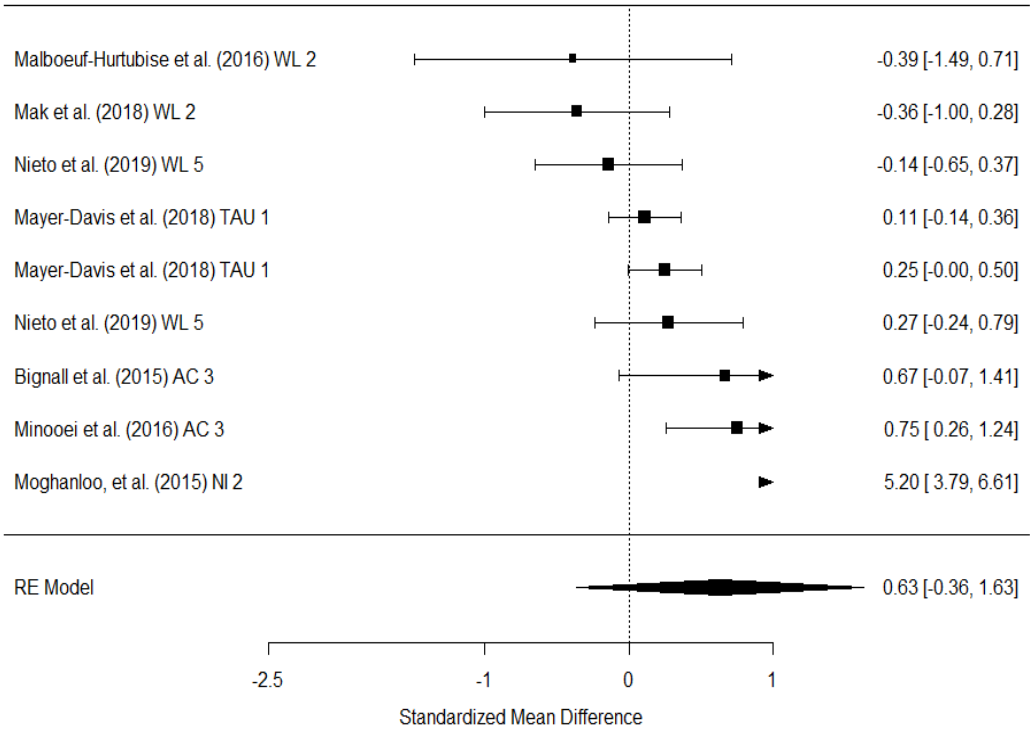

Figure 4: Results on QOL at the Post-Intervention

Thirteen data points were included in QOL analysis. At the post-intervention stage, there was no significant difference in QOL between the intervention and control groups ($d = 0.63$, $p = 0.21$, 95% CI [-0.36, 1.63]) (Figure 4). The heterogeneity value was $I^2 = 97.52\%$, and the homogeneity indicator was significant (Q (8) = 60.93, $p <$ .0001), indicating substantial variability among the studies regarding the effect of psychological interventions on QOL. As only two studies measured QOL at the follow-up stage, follow-up data were not analyzed.

No significant results were obtained regarding impact on QOL. This might be due to the limited data on interventions. The studies included in the current review focused on internalizing disorders (45 studies) and QOL (13 studies), indicating a focus on negative psychological factors in pediatric patients with chronic diseases. Considering the characteristics of chronic diseases, focusing on positive psychological factors such as QOL, which relate to how patients live with their diseases, is also an imperative.

Conclusion

The current study aimed to comprehensively review psychological interventions for children with chronic diseases and examine these interventions' effectiveness for treating internalizing disorders such as depression and anxiety and impact on QOL. This review highlights the challenges regarding research on psychological support for children with chronic diseases. Children with chronic diseases who also have internalizing problems may have mental health needs that are overlooked in favor of physical care [8]. Although the number of studies on psychological support provision for such children has increased since 2015, the limited number of studies in the current systematic review suggests establishing effective psychological support for children with chronic illnesses remains difficult. Future large-scale, rigorously controlled studies should explore the psychological adaptation of children with chronic diseases in order to establish such evidence. Additionally, for cognitive-behavioral interventions that are likely to be effective, it is necessary to address the unmet needs of children with chronic diseases by examining applicable methods when implemented alongside physical treatment.

Conflict of Interest

The author declares no conflict of interest.

Author's Contributions

All authors were involved in the conceptualization and design of the study, as well as the review procedures. KK and MM primarily handled the analysis, while SH and RM were responsible for creating the table. SH took the lead in writing the manuscript. All authors participated in reviewing the manuscript and approved the final version.

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