Neuropsychiatric Disease and Treatment

Childhood depression: a systematic review

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Abstract: As an important public health issue, childhood depression deserves special attention, considering the serious and lasting consequences of the disease to child development. Taking this into consideration, the present study was based on the following question: what practical contributions to clinicians and researchers does the current literature on childhood depression have to offer? The objective of the present study was to conduct a systematic review of articles regarding childhood depression. To accomplish this purpose, a systematic review of articles on childhood depression, published from January 1, 2010 to November 24, 2012, on MEDLINE and SciELO databases was carried out. Search terms were “depression” (medical subject headings [MeSH]), “child” (MeSH), and “childhood depression” (keyword). Of the 180 retrieved studies, 25 met the eligibility criteria. Retrieved studies covered a wide range of aspects regarding childhood depression, such as diagnosis, treatment, prevention and prognosis. Recent scientific literature regarding childhood depression converge to, directly or indirectly, highlight the negative impacts of depressive disorders to the children’s quality of life. Unfortunately, the retrieved studies show that childhood depression commonly grows in a background of vulnerability and poverty, where individual and familiar needs concerning childhood depression are not always taken into consideration. In this context, this review demonstrated that childhood-onset depression commonly leads to other psychiatric disorders and co-morbidities. Many of the retrieved studies also confirmed the hypothesis that human resources (eg, health care team in general) are not yet adequately trained to address childhood depression. Thus, further research on the development of programs to prepare health care professionals to deal with childhood depression is needed, as well as complementary studies, with larger and more homogeneous samples, centered on prevention and treatment of childhood depression.

Keywords: child, depression, depressive disorder, mental health, mental disorders

Introduction

The increasing incidence rates of psychiatric disorders have drawn attention of the scientific world to mental health research.¹-³ The World Health Organization (WHO) estimates that, until the year 2021, depression will be the second largest cause of the global disease burden.¹

However, cases of depressive disorders have increased not only among adults, but also among children,⁴-⁶ with a prevalence of 0.3% to 7.8% in children below 13 years old. In Brazil, the prevalence of childhood depression among children below 14 years old varies from 0.2% to 7.5%, according to the assessment method used.⁷

As a biopsychosocial phenomenon,²,⁷ childhood depression deserves special attention, considering the serious and lasting consequences of the disease to child
development, ranging from physiological changes to the impairment of social and cognitive functions.

In the short-term, depressive disorders might be a source of psychological suffering for these children, whereas in the long-term they can compromise social, cognitive, and emotional aspects of child development, becoming an important predictor of psychopathologies in adulthood.

Taking this into consideration, the present study was based on the following review question: What practical contributions to clinicians and researchers does the current literature on childhood depression have to offer? Considering that depression in children is an important public health issue, and in order to provide readers a panoramic view on the subject, this review aimed to assess currently existing evidence regarding different aspects (etiology/risk factors, diagnosis, treatment, prevention, and prognosis) of childhood depression, presenting a systematic review of the published studies regarding the subject. Our hypothesis is that, despite the growing interest in the theme, human resources (e.g., health care team in general) are not yet adequately trained to address childhood depression.

**Methods**

We performed a qualitative systematic review of articles about childhood depression published in previously chosen electronic databases. The qualitative approach was chosen because quantitative methods, such as meta-analysis, show that: (a) the necessary information in order to calculate result size is not available, and may limit this analysis to a small subset of studies; (b) age intervals regarding childhood vary greatly among studies included in the sample, making it difficult to adequately compare and to do proper statistical analyses.

A search of the literature was conducted via MEDLINE and SciELO online databases in November 2012 and was limited to articles published from January 1, 2010 to November 24, 2012. The reason for limiting the search to 2010–2012 was that, within this period, the invisibility of childhood depression was broken through a series of research based on the achievements of Psychiatric Reform.

From psychiatry to pediatrics, new forms of interaction between knowledge brought together more detailed information regarding socio-demographic data, epidemiologic-based clinical information, service regime, and procedures. Empirically, it is of note that from 2010 ethical worries about public policies for children and adolescent mental health have become the focus of research. In this sense, it is from 2010 to date when information about structure, composition, and functioning regarding mental health services for children were more clearly delineated, focusing on the search of a definition for childhood mental health care. The studies of interest regarding childhood mental health are thus centered on the period from 2010 to 2012, especially those relating to childhood depression.

Initially, the search terms browsed in MEDLINE database were:
1. “depression” (Medical Subject Headings [MeSH] term);
2. “child” (MeSH term); and
3. “childhood depression” (keyword).

The following searches were performed: 1 AND 2, 3. In addition to MeSH terms, we opted to add the keyword “childhood depression” to the search strategy, because, despite not being included in the MeSH thesaurus, it is frequently used to describe studies that deal with the theme object of the present review. The search strategy and the retrieved articles were reviewed on two separate occasions to ensure adequate sampling.

A similar search strategy was performed in the SciELO database, using the aforementioned terms and their correspondent terms in Portuguese.

In order to set a parameter for limiting the age group covered by the present review, the definition of “child” adopted in this study was MeSH’s; the National Library of Medicine’s controlled vocabulary thesaurus used for indexing articles for PubMed. Thus, when used in this study, the term “child” refers to a person from 6 to 12 years of age and, consequently, the term “childhood” refers to the state or time of being 6 to 12 years of age.

The article analysis followed previously determined eligibility criteria. We adopted the following inclusion criteria: (1) articles that included in the title at least one combination of terms described in the search strategy; (2) references written in English or Portuguese; (3) studies pertaining childhood depression; (4) original articles with online accessible full text available in CAPES (Higher Education Co-ordination Agency) Journal Portal, a virtual library linked to Brazil’s Ministry of Education and subjected to content subscription; and (5) prospective or retrospective observational (analytical or descriptive, except case reports), experimental, or quasi-experimental studies. Exclusion criteria were: (1) other designs, such as case reports, series of cases, review of literature, and commentaries; (2) non-original studies, including editorials, reviews, prefaces, brief communications, and letters to the editor.

Then, each paper in the sample was read in entirety, and data elements were then extracted and entered into a matrix that included authors, publication year, description of the
study sample, and main findings. Some of the studies dealt not only with depression in children, but also in adolescents and adults; because the focus of this study was on childhood depression, adolescent- or adult-related results were not recorded or analyzed for this study.

So as to provide a better analysis, the next phase involved comparing the studies and grouping, for heuristic reasons, the results regarding the studied subject into five categories: Etiology/Risk Factors; Diagnosis; Prevention; Prognosis; and Treatment.

Results
Initially, the aforementioned search strategies resulted in 180 references. After browsing the title and abstract of the retrieved citations for eligibility based on study inclusion criteria, 155 articles were excluded and 25 articles were further retrieved and included in the final sample (Figure 1). Only articles from MEDLINE database matched the inclusion criteria of the present study.

Table 1 provides an overview of all studies included in the final sample and of all data elements used during the data analysis process. Study designs included two experimental studies, one quasi-experimental study, and 22 nonexperimental studies. The 25 studies were distributed into the previously determined five categories as follows: Etiology/Risk Factors (nine studies); Diagnosis (two studies); Prevention (two studies); Prognosis (ten studies); and Treatment (two studies).

Discussion
Etiology/risk factors
Regarding etiology and risk factors for childhood depression, nine studies tried to relate depression in children with different aspects, such as general cognitive style and interparental conflict, sweet preferences and analgesia, child maltreatment and other adverse experiences, prenatal drug exposure, environmental processes, and functional connectivity of the amygdala.

Research on the mechanisms by which both general cognitive style and interparental conflict (IPC) affect childhood depression suggest that parental warmth/rejection mediated the relation between IPC and depression, and general cognitive style acted as a moderator. While analyzing effects of depression in sweet preferences and analgesia during childhood, Mennella et al show that depressive symptomatology alone was associated with greater liking for sweet-tasting foods and candies and increased pain sensitivity and that depression antagonized the analgesic properties of sucrose.

Other studies found that, in a low-income Brazilian schoolchildren sample, results point to multiple determinants of depressive behavior in children, as well as the potential contribution of psychological family violence. Prenatal drug
Table 1 Childhood depression: studies and main findings

<table>
<thead>
<tr>
<th>Author</th>
<th>Journal</th>
<th>Sample</th>
<th>Main findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etiology/risk factors</td>
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<tr>
<td>Avanci et al</td>
<td>Child and Adolescent Psychiatry and Mental Health</td>
<td>464 children (aged 6–10 years) from Rio de Janeiro, Brazil</td>
<td>The following variables are potential psychosocial factors associated with depression in childhood: average/poor relationship with the father, high frequency of victimization by psychological violence (humiliation), parental divorce, and externalizing behavior problems.</td>
</tr>
<tr>
<td>Buckingham-Howes et al</td>
<td>Journal of Developmental and Behavioral Pediatrics</td>
<td>76 prenatally drug exposed and 38 nonexposed adolescent-caregiver dyads</td>
<td>Prenatal drug exposure may interfere with emotion regulation, resulting in anxious/depressed behavior during childhood.</td>
</tr>
<tr>
<td>Lewis et al</td>
<td>Behavior Genetics</td>
<td>271 children/adolescents (aged 9–16 years) whose mothers had experienced at least two episodes of DSM-IV major depression and 165 controls (aged 12.25–16.67 years)</td>
<td>Recurrent maternal depression does not appear to interact with gene variants thought to be involved in the regulation of the stress response and predict symptoms of depression in children and adolescents in this sample.</td>
</tr>
<tr>
<td>Fite et al</td>
<td>Child Psychiatry and Human Development</td>
<td>276 children (aged 6–12 years) admitted to a child psychiatric inpatient facility</td>
<td>Relational aggression was associated with depressive symptoms. The link between relational aggression and suicidal ideation was fully accounted for by depressive symptoms.</td>
</tr>
<tr>
<td>Lewis et al</td>
<td>Journal of the American Academy of Child and Adolescent Psychiatry</td>
<td>852 families with a child born by assisted conception</td>
<td>Associations between parent and child depressive symptoms is due in part to environmental processes independent of inherited effects and is not accounted for by shared adversity measurements.</td>
</tr>
<tr>
<td>Luking et al</td>
<td>Journal of the American Academy of Child and Adolescent Psychiatry</td>
<td>51 children (aged 7–11 years)</td>
<td>The study found an attenuated relationship between the amygdala and cognitive control regions, which is consistent with a hypothesis of altered regulation of emotional processing in major depressive disorder with early-childhood-onset.</td>
</tr>
<tr>
<td>Tommyr et al</td>
<td>Journal of Adolescent Health</td>
<td>4,381 children (aged 10–15 years)</td>
<td>Child and family factors, and factors indicating social dislocation, play an important role in the child welfare workers’ identification of anxiety/depression in children. The association of emotional maltreatment with child anxiety/depression should be further explored.</td>
</tr>
<tr>
<td>Mennella et al</td>
<td>Addiction</td>
<td>300 children (aged 5–12 years)</td>
<td>The co-occurrence of having a family history of alcoholism and self-reports of depressive symptomatology was associated significantly with a preference for a more concentrated sucrose solution.</td>
</tr>
<tr>
<td>O’Donnell et al</td>
<td>Journal of Youth and Adolescence</td>
<td>88 children (5th and 6th graders) from two urban schools</td>
<td>Parental warmth/rejection mediated the relation between IPC and depression, and general cognitive style acted as a moderator.</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
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<tr>
<td>Lewis et al</td>
<td>Journal of Affective Disorders</td>
<td>287 parents with a history of recurrent depression and their adolescent offspring (aged 9–17 years)</td>
<td>Clinicians and researchers should give due consideration to parent ratings of their children’s depression symptoms, regardless of whether the parent suffers with depression.</td>
</tr>
<tr>
<td>Gaffrey et al</td>
<td>Journal of Affective Disorders</td>
<td>306 preschoolers (aged 3–5.11 years)</td>
<td>Preschoolers meeting all DSM-IV MDD criteria except for episode duration exhibit a clinically significant form of depression and experience a 2-year MDD outcome similar to those meeting full criterion.</td>
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<tr>
<td>Prevention</td>
<td></td>
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<tr>
<td>Kösters et al</td>
<td>BMC Public Health</td>
<td>Children aged 10–12 years from 20 primary schools in Amsterdam</td>
<td>‘FRIENDS for Life’ is effective as an indicated school-based prevention program for children with early or mild signs of anxiety or depression.</td>
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Lima et al

Neuropsychiatric Disease and Treatment 2019
<table>
<thead>
<tr>
<th>Study</th>
<th>Journal</th>
<th>Sample Description</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mihalopoulos et al</td>
<td>Pediatrics</td>
<td>Children and adolescents (aged 11–17 years) in the 2003 Australian population</td>
<td>After school screening, screening and the psychological intervention represent good value-for-money. Such an intervention needs to be seriously considered in any national package of preventive health services.</td>
</tr>
<tr>
<td>Banh et al</td>
<td>Journal of Abnormal Child Psychology</td>
<td>3,593 children (from 6th and 8th grades)</td>
<td>Although there may be differences in symptom endorsements among depressed individuals across racial/ethnic groups, these differences do not impact overall scores. The RCADS-DAN is a valid assessment tool for screening of anxiety and depression in Danish youth.</td>
</tr>
<tr>
<td>Esbjørn et al</td>
<td>PLoS One</td>
<td>667 youth from community schools (aged 8–16 years)</td>
<td>While anxiety and depression can be measured independently of each other in childhood, individual items for depression and anxiety may change in their strength as indicators of respective constructs across age.</td>
</tr>
<tr>
<td>Boylan et al</td>
<td>International Journal of Methods in Psychiatric Research</td>
<td>1,329 children (aged 4–7 years)</td>
<td>The PANAS-C-P PA and NA scale scores related to measures of anxiety and depression in a manner consistent with the tripartite model.</td>
</tr>
<tr>
<td>Esbesutani et al</td>
<td>Psychological Assessment</td>
<td>606 children and adolescents (aged 8–18 years) of public and private schools</td>
<td>Depressive episodes that begin in childhood or teenage years are associated with more comorbid diagnoses, a higher likelihood of Avoidant and Paranoid PD, a greater likelihood of attempted suicide, and poorer perceptions of paternal care.</td>
</tr>
<tr>
<td>Fernando et al</td>
<td>Comprehensive Psychiatry</td>
<td>372 participants (62 with childhood-onset, 101 with teenage-onset, and 209 with adult-onset depression)</td>
<td>Symptoms of conduct disorder tend to precede depression in girls during childhood and adolescence. Oppositional defiant disorder dimensions should be assessed when evaluating risk for comorbid depression in girls with conduct problems.</td>
</tr>
<tr>
<td>Hipwell et al</td>
<td>The Journal of Child Psychology and Psychiatry</td>
<td>2,451 girls (aged 5–8 years)</td>
<td>Highlight the potential pitfalls of assuming that only translation and back-translation can capture cultural differences in performance of mental health instruments.</td>
</tr>
<tr>
<td>Kohrt et al</td>
<td>BMC Psychiatry</td>
<td>162 children (aged 11–14 years) from one randomly selected school</td>
<td>Although psychological ill-health is associated with impaired endothelial function and CVD among adults, such processes may also be relevant to children.</td>
</tr>
<tr>
<td>Osika et al</td>
<td>Archives of Disease in Childhood</td>
<td>534 healthy school children (12–16 years old) from two schools in Göteborg region</td>
<td>Overall levels of depression (DSRS-C scores) were not as high as those reported in previous studies.</td>
</tr>
<tr>
<td>Wakimizu et al</td>
<td>BioScience Trends</td>
<td>118 family caregivers and 100 children with childhood cancer (aged 2–18 years)</td>
<td>RCADS-P possesses favorable psychometric properties in a sample of clinic-referred children and adolescents. The RCADS-P appears to be a valuable measure for identifying youths with depression and specific anxiety disorders.</td>
</tr>
<tr>
<td>Ebesutani et al</td>
<td>Journal of Abnormal Child Psychology</td>
<td>490 children and adolescents (aged 6–18 years) from two mental health clinics</td>
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<td>Kohrt et al</td>
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**Treatment**

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<tr>
<th>Study</th>
<th>Journal</th>
<th>Sample Description</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forbes et al</td>
<td>Journal of Child and Adolescent Psychopharmacology</td>
<td>66 children and adolescents (aged 8–16 years) diagnosed with MDD with comorbid anxiety, MDD only, or ANX.</td>
<td>A more typical profile of baseline affective functioning in natural settings (that is, lower NA and higher PA) and time with fathers, could provide a foundation for treatment response in children and adolescents.</td>
</tr>
<tr>
<td>Lenze et al</td>
<td>Depression and Anxiety</td>
<td>Eight parent-child dyads with depressed preschoolers</td>
<td>PCIT-ED seems to be a promising treatment for preschoolers with depression.</td>
</tr>
</tbody>
</table>

**Abbreviations:** DSM-IV, Diagnostic and Statistical Manual of Mental Disorders-IV; MDD, Major Depressive Disorder; RCADS-DAN, Revised Child Anxiety and Depression Scale, Danish version; PANAS-C-P, Positive and Negative Affect Schedule for Children-Parent Version; PA, positive affect; NA, negative affect; PD, personality disorder; CVD, cardiovascular disease; DSRS-C, Depression Self-Rating Scale for Children; RCADS-P, Revised Child Anxiety and Depression Scale – Parent Version; ANX, anxiety; PCIT-ED, Parent Child Interaction Therapy – Emotion Development; IPC, interparental conflict; BMC, BioMed Central.
exposure was also related to emotion regulation, resulting in anxious/depressed behavior during childhood. Relational aggression was also found to be related to depressive symptoms, which are linked to suicidal ideation within a clinical population.

Relating parent depression and child depressive/anxiety symptoms in an assisted conception design, it was highlighted that depression symptoms are due in part to environmental processes independent of inherited effects and are not accounted for by shared adversity measurements. Child maltreatment and other adverse experiences in childhood were related to anxiety and/or depression. Regarding genetic aspects of childhood depression, recurrent maternal depression does not appear to interact with gene variants thought to be involved in the regulation of the stress response and predict symptoms of depression in children and adolescents in this sample.

Finally, Luking et al highlight the correlation between corticolimbic functional connectivity alterations and the etiology of early-childhood-onset major depressive disorder (MDD). Using resting state functional magnetic resonance imaging (fMRI), in children aged 7 to 11 years old with a history of MDD during early childhood and/or a maternal history of depression, the study found an attenuated relationship between the amygdala and cognitive control regions, indicating a reduced connectivity within networks both positively (eg, limbic regions) and negatively (eg, dorsal frontal/parietal regions) correlated with the amygdala, thought to be important for the regulation of emotion. However, due to the reduced sample size, complementary studies are needed to confirm this evidence.

Diagnosis

Two of the retrieved studies, following different courses of action, dealt with diagnosis of depression in children. One of them mentions that clinically significant episodes of MDD can be identified and reliably diagnosed in preschoolers when age adjusted Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria are implemented. However, the same longitudinal study, with a subsample of Validation of Preschool Depression Study (PDS), suggests that the 2-week duration criteria may not be optimal for identifying all clinically relevant manifestations of depression in preschoolers.

Gaffrey et al pointed out that an adapted DSM (ie, 2-week criteria set aside) criteria for preschoolers might be considered in order to cover a group of children who, not yet diagnosed as MDD while using strict DSM criteria, would likely benefit from further clinical attention and are at risk for continued mood related impairment in the future. However, although the authors considered that their study used the largest sample of preschoolers to date, further studies are needed to confirm that episode duration should be given less “weight” in diagnostic decisions when dealing with preschoolers, being more accurately viewed dimensionally as an indicator of severity rather than dichotomously when defining “caseness” at the studied age group.

This cautious position is strengthened when we consider that the DSM group at follow up in the study represents a small sample, with a possibility of type II error. The last study investigates if baseline parental reports of child depression symptoms predicted new onset mood in children. The study shows that child and parent ratings of depression predict new onset child mood disorder (NOMD) to a similar degree. According to the study, for younger children, parent reports were significantly better at predicting NOMD compared to child reports, while for children older than 12 years old, there were no differences between parents’ and children’s reports.

However, considering the study’s intention of evaluating depressive parents’ reports, the conclusions must be analyzed with caution, since not all parents were currently experiencing an episode of depression at baseline. In addition, another possible bias results from the fact that the sample consisted predominantly of mothers, indicating that findings may not be applicable to fathers or families without a history of parental depression.

Prevention

Prevention of childhood depression was addressed by two studies. An experimental Dutch controlled trial (although non-randomized) presented ‘FRIENDS for Life’, a 10 weekly session (plus two booster session) program that has proven to be an effective school-based prevention program for children with early or mild signs of anxiety or depression. The program is based on cognitive behavioral therapy and involves psycho-education, relaxation exercises, exposure, problem-solving skills training, social support training, and cognitive restructuring exercises. The acronym ‘FRIENDS’ was generated from: Feelings; Remember to relax. Have quiet time; I can do it! I can try my best! Explore solutions and Coping Step Plans; Now reward yourself! You’ve done your best! Don’t forget to practice; Stay calm for life!

The other study, which used economic modeling techniques, showed that the population cost-effectiveness
of preventive interventions for childhood/adolescent depression is very favorable, although implementation issues, particularly around the acceptability to providers, need to be addressed before widespread adoption.\textsuperscript{20} Focusing on the screening of children in the 2003 Australian population, the study concluded that screening children for signs of depression and the provision of a psychological intervention to prevent a diagnosable case of MDD represents very good value for money, and must be taken into consideration in any national package of preventive health services.

**Prognosis**

Assessment tools for depression in children were the subject of five studies, all of which dealt with a different instrument. The Mood and Feelings Questionnaire (MFQ) and the measurement of its equivalence across racial/ethnic groups was addressed by a study among 6th and 8th grade students in the Seattle Public School District, suggesting that differences in MFQ scores across groups are unlikely to be caused by measurement non-equivalence.\textsuperscript{22} Positive affect (PA) and negative affect (NA) Schedule for Children – Parent Version (PANAS-C-P) was psychometrically analyzed in a school-based sample of children and adolescents.\textsuperscript{23}

Results from the cited study provide initial support for the PANAS-C-P as a parent-reported perspective of youth PA and NA among school-based youths. Ebesutani et al also conducted a psychometric analysis of the Revised Child Anxiety and Depression Scale – Parent Version in a clinical sample. The mentioned scale demonstrated favorable psychometric properties and the ability to distinguish between anxiety and depressive disorders, as well as between the targeted anxiety disorders.\textsuperscript{24}

In the cross-cultural field of childhood depression assessment, the Depression Self-Rating Scale and Child Post Traumatic Stress Disorder Symptom Scale were adapted in Nepali reality, showing that transcultural translation and alternative validation feasibility can be performed in low clinical resource settings through task-shifting the validation process to trained mental health paraprofessionals using structured interviews.\textsuperscript{25} The last retrieved study assessed the Revised Child Anxiety and Depression Scale (RCADS) in a national sample of Danish youths, providing convincing evidence that the RCADS-DAN is a valid assessment tool for screening anxiety in Danish youth.\textsuperscript{26}

As for depression-related psychiatric comorbidities, in a broader perspective, there is evidence, while analyzing a sample of depressed outpatients,\textsuperscript{5} that, later on, adult participants with a history of childhood-onset depression show greater Axis I comorbidity than those with adult-onset depression, more likely meeting criteria for comorbid DSM – Axis I diagnoses (especially anxiety disorders) and also meeting criteria for Avoidant and Paranoid personality disorders, as well as a greater likelihood of attempted suicide.

Specifically addressing the high degree of comorbidity between depression and anxiety in childhood, Boylan et al\textsuperscript{27} stated that anxiety and depression were highly correlated in each age group studied and in both boys and girls, suggesting that although they can be measured independently, they have significant shared variance.

Although the cohort used a large sample, the measurement stability of anxiety and depressive symptoms was done by mothers’ reports only, which could limit the results’ liability, and lend itself to over-reporting. Finally, another study\textsuperscript{28} investigated the role of oppositional defiant disorder (ODD) dimensions on the temporal unfolding of conduct disorder (CD) and depression in girls between childhood and adolescence. The study concluded that symptoms of CD tend to precede depression in girls during childhood and adolescence, and that emotion dysregulation and defiance aspects of ODD should be identified as targets for treatment in order to prevent depression in the future.

When it comes to medical depression-related comorbidities, Osika et al\textsuperscript{29} analyzed the association between psychological health (anger, depression, and anxiety) and endothelial function in childhood, emphasizing that psychosocial adversity in childhood might be a risk factor for subsequent cardiovascular diseases. The results of the study point to the relation between lower hyperaemia peripheral arterial tonometry scores (attenuated endothelial function) and self-assessed psychological health, in girls between 12 and 16 years of age. However, it is of note a possible selection bias resulting from the low participation rate, especially of boys, and of the fact that participants were younger than the control group. In the context of childhood cancer, Wakimizu et al\textsuperscript{30} analyzed the prevalence of depression and quality of life among Japanese pediatric cancer patients, finding that lower Pediatric Quality of Life Inventory (PedsQL) scores correlated with higher Birleson Depression Self-rating Scale for Children (DSRS-C) scores, indicating that an increased tendency for the child to experience depression was correlated with a low health-related quality of life for the child. However, possible sources of bias lie in the inclusion criteria, as the concept of a child of “primary school age” is not age-specific, and the criteria of “being able to complete a physical and psychological
questionnaire” does not specify if this ability is only cognitive-related or also related to the health state of the participant.

Treatment
Regarding treatment, novel treatments for depression in preschool children and the prediction of treatment response in childhood depression were searched. In the research of Lenze et al., an Emotional Development (ED) module, integrated with Parent Child Interaction Therapy (PCIT), was presented as a tool (PCIT-ED) designed to teach parents to facilitate the child’s emotional development and enhance emotion regulation. PCIT-ED includes three modules conducted over 14 sessions.

Standard PCIT targets the parent-child relationship using behavioral and play therapy techniques to enhance relationship quality and parent’s ability to set nurturing and effective limits with the child. PCIT-ED uses Child Directed Interaction (CDI) and Parent Directed Interaction (PDI) modules, limited to six sessions, plus a novel ED module, the latter focusing on teaching the parent to facilitate the child’s emotional development and enhance the child’s capacity for emotion regulation.

The first module (CDI) focuses on strengthening the parent-child relationship by teaching positive play techniques, whilst the PDI aims to decrease disruptive behavior by teaching the parent to give effective commands and training the parent in methods for handling noncompliance. Results of the use of PCIT-ED, in eight parent-child dyads with depressed preschoolers showed significant decreases in depression severity scores. Nonetheless, considering results were preliminary and this open trial used a small sample, a randomized controlled trial is needed to enhance the retrieved conclusions.

As for prediction of treatment response in childhood depression, the use of ecological momentary assessment of NA, PA, and companions in natural settings showed that a more typical profile of baseline affective functioning in natural settings (lower NA and higher PA) and time with parents could provide a foundation for treatment response in children.

Finally, it is important to highlight the methodological characteristics of the studies described in the present review, because methodological differences hamper the comparability and generalization of the results. The small samples with which most studies dealt with reinforce the importance of assessing the consistency of results found. There were also other methodological limitations, such as the absence of control groups. Although authors claim that these peculiarities do not affect the results, the generalization and reproducibility of findings may be impaired. As only two experimental studies were identified in the present review, it is of note the lack of experimental studies regarding childhood depression, which can be caused by the ethical barriers concerning experimental studies involving children.

Recent scientific literature regarding childhood depression converge to, directly or indirectly, highlight the negative impacts of depressive disorders to the children’s quality of life.

Unfortunately, the retrieved studies show that childhood depression commonly grows in a background of vulnerability and poverty, where individual and familiar needs concerning childhood depression are not always taken into consideration. In this context, this review demonstrated that childhood-onset depression commonly leads to other psychiatric disorders and co-morbidities, failing to be a warning for families to seek help while it is still possible to rapidly reverse the children’s unhealthy mental status.

Moreover, despite the growing interest toward this theme, human resources (eg, health care team in general) are not yet adequately trained to address childhood depression, which was confirmed by many of the retrieved studies. Taking this into account, an important area that requires further research is the development of programs that successfully prepare health care professionals to deal directly or indirectly with childhood depression in the clinical setting and being able to detect and correctly address the disease to halt its deleterious effects.

Acknowledgments
Public funding from the São Paulo Research Foundation – FAPESP, process 13/03270–9, supported this research.

Disclosure
The authors report no conflicts of interest in this work.

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