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SPECIAL ARTICLE

Guidelines for Adolescent Depression in Primary Care (GLAD-PC): II. Treatment and Ongoing Management

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Endorsements: The Canadian Paediatric Society, the Society for Adolescent Medicine, the Canadian Association for Adolescent Health, the National Association for Pediatric Nurse Practitioners, the Society for Developmental and Behavioral Pediatrics, the American Academy of Child and Adolescent Psychiatry, the Canadian Academy of Child Psychiatry, the Canadian Psychiatric Association, the College of Family Medicine of Canada, the National Alliance on Mental Illness, the Mental Health Association of New York City, the National Mental Health Association (now known as Mental Health America), the Depression and Bipolar Support Alliance, and the Federation of Families for Children's Mental Health have endorsed these guidelines. Endorsements from the American Academy of Pediatrics and the Canadian Psychological Association are pending. The American Academy of Family Physicians, the American Medical Association, and the American Psychological Association have been involved in the development of the guidelines but do not endorse external guidelines.

ABSTRACT

OBJECTIVES. To develop clinical practice guidelines to assist primary care clinicians in the management of adolescent depression. This second part of the guidelines addresses treatment and ongoing management of adolescent depression in the primary care setting.

METHODS. Using a combination of evidence- and consensus-based methodologies, guidelines were developed in 5 phases as informed by (1) current scientific evidence (published and unpublished), (2) a series of focus groups, (3) a formal survey, (4) an expert consensus workshop, and (5) revision and iteration among members of the steering committee.

RESULTS. These guidelines are targeted for youth aged 10 to 21 years and offer recommendations for the management of adolescent depression in primary care, including (1) active monitoring of mildly depressed youth, (2) details for the specific application of evidence-based medication and psychotherapeutic approaches in cases of moderate-to-severe depression, (3) careful monitoring of adverse effects, (4) consultation and coordination of care with mental health specialists, (5) ongoing tracking of outcomes, and (6) specific steps to be taken in instances of partial or no improvement after an initial treatment has begun. The strength of each recommendation and its evidence base are summarized.

CONCLUSIONS. These guidelines cannot replace clinical judgment, and they should not be the sole source of guidance for adolescent depression management. Nonetheless, the guidelines may assist primary care clinicians in the management of depressed adolescents in an era of great clinical need and a shortage of mental health specialists. Additional research concerning the management of youth with depression in primary care is needed, including the usability, feasibility, and sustainability of guidelines and determination of the extent to which the guidelines actually improve outcomes of youth with depression.

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Key Words
adolescents, depression, primary care, guidelines

Abbreviations
PC—primary care
MDD—major depressive disorder
AACAP—American Academy of Child and Adolescent Psychiatry
PCP—primary care provider
GLAD-PC—Guidelines for Adolescent Depression in Primary Care
FDA—Food and Drug Administration
RCT—randomized, controlled trial
CES-DC—Center for Epidemiological Studies Depression Scale for Children
MAOI—monoamine oxidase inhibitor
CBT—cognitive behavioral therapy
SSRI—selective serotonin reuptake inhibitor
IPT—interpersonal psychotherapy
CI—confidence interval

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STUDIES HAVE SHOWN that up to 9% of teenagers meet criteria for depression at any one time, with as many as 1 in 5 teens having a history of depression at some point during adolescence.[1–5] In primary care (PC) settings, point prevalence rates are likely higher, with rates up to 28%.[6–10] Taken together, epidemiologic and PC-specific studies have suggested that despite relatively high rates, major depressive disorder (MDD) in youth is underidentified and undertreated in PC settings.[11]

Because of barriers to adolescents receiving specialty mental health services, only a small percentage of depressed adolescents are treated by mental health professionals.[12] As a result, PC settings have become the de facto mental health clinics for this population, although most PC clinicians feel inadequately trained, supported, or reimbursed for the management of this disorder.[13–18] Although MDD management guidelines have been developed for specialty care settings (eg, see the American Academy of Child and Adolescent Psychiatry [AACAP] practice parameters[19]) or for related problems such as suicidal ideation or attempts,[20] it is clear that significant practice and clinician differences exist between the primary and specialty care settings that do not allow a simple transfer of guidelines from one setting to another.

Recognizing this gap in clinical guidance for PC providers (PCPs), a group of researchers from the United States and Canada established the Guidelines for Adolescent Depression in Primary Care (GLAD-PC), a North American collaborative, to develop guidelines for the management of adolescent depression in the PC setting. The development process of GLAD-PC is described in detail in our companion report.[21] This article describes the recommendations regarding treatment, ongoing management, and follow-up along with the supporting empirical evidence for those recommendations. Our companion article provides the corresponding evidence and resulting recommendations for depression identification, assessment and diagnosis, and initial management before the formal onset of specific treatments.[21]

METHODS

A full description of the methodology used for the development of GLAD-PC is included in our companion article.[21] In brief, the expert collaborative used a mix of qualitative (focus groups, expert consensus) and quantitative (survey, literature reviews) methods to inform the development of GLAD-PC. In view of space limitations, only the results of the literature reviews regarding available evidence pertaining to treatment, ongoing management, and follow-up procedures are presented in this article.

Literature Reviews

The literature-review approach used for all of the reviews was as follows. First, the GLAD-PC team identified the existence of high-quality, previously published, systematic evidence-based reviews that met the following criteria: (1) explicit definition of search terms and years covered; (2) exhaustive search of Medline; (3) reading of abstracts to determine relevance, followed by review of entire articles from relevant abstracts; (4) restriction to English-language journals only; (5) restriction to empirical articles; and (6) identification of any otherwise omitted citations from the reference sections from key reviews. In areas where there were no carefully executed and well-described systematic literature reviews had been recently conducted (ie, Food and Drug Administration [FDA], Cochrane), the GLAD-PC team conducted a systematic review for primary studies for each area by using Medline (from inception to 2004/2005 based on the 5 criteria described above.

Three literature reviews were conducted for the GLAD-PC recommendations presented in this article: (1) nonspecific psychosocial interventions in pediatric PC,[22] (2) antidepressant treatment,[23] and (3) the use of psychotherapy. For the first review, Stein et al[22] searched the literature (Medline, PsycINFO, and the Cochrane database) for articles that examined evidence for psychosocial interventions delivered in the PC setting. The reference lists of all relevant articles were searched for additional studies. In addition, experts in the field were consulted to identify additional studies. Given the paucity of randomized, controlled trials (RCTs) identified earlier in a review by Bower et al[24] in 2001, studies with simple before-and-after comparisons were also included.

In the second review, we examined the efficacy and safety of antidepressant medications in the pediatric population (aged 7–18). The studies were identified in 2 stages. Given the thorough reanalyses of safety data on both published and unpublished clinical trials completed by the FDA, all RCTs included in the FDA safety report were reviewed.[25] Second, to ensure that additional studies not reported to the FDA were not missed, Medline and PsycINFO were searched. For a full description of the review, please refer to the published review.[23]

In the final review, we searched the literature for depression trials that examined the efficacy of psychotherapy. The search included all forms of psychotherapy including both individual and group-based therapies. We not only identified individual studies but also high-quality systematic reviews given the extensive empirical literature in this area. Additional details on each of these searches, including search terms, number of abstracts selected, etc, are available from the authors on request.

Expert Consensus

Expert consensus was reached through 2 stages. First, expert participants completed a survey regarding adolescent depression management. Subsequently, the expert participants then met in a 2-day workshop to review the survey results to reach consensus on key issues regard-

ing identification and treatment of adolescent depression in PC. Overall, the guidelines only included recommendations that the experts agreed are highly appropriate and "first-line" practices.

RESULTS: LITERATURE REVIEWS

Psychosocial Interventions in PC

On behalf of the GLAD-PC team, Stein et al[22] reviewed the evidence for the efficacy of PC-delivered psychosocial interventions. The studies identified were divided into 2 categories of evidence: direct and indirect. Direct evidence included data from studies that evaluated interventions specific for adolescent depression, and indirect evidence included data from studies that examined PC interventions for adults with depression and PC interventions for other psychosocial problems in the pediatric population. Additional details about the review can be found in the Stein et al report.[22]

The literature review identified 4 articles that focused on depression interventions in the PC setting for adolescents,[26–29] all of which showed positive outcomes for the PC-delivered interventions. Walker et al conducted an RCT to evaluate the effectiveness of a PC-delivered consultation intervention that involved teens from 8 general practices in Britain. Teens were invited to discuss their health concerns with PC nurses who provided individual consultations.[22,26] The PC nurses also offered mental health referrals when appropriate. In those with high Center for Epidemiological Studies Depression Scale for Children (CES-DC) scores, those who were randomly assigned to PC nurse consultation had lower CES-DC scores on follow-up than adolescents with high CES-DC scores who were not randomly assigned to the consultation. The results suggest that PC-delivered intervention may be helpful in reducing depressive symptomology as measured by the CES-DC.

Stein et al[22] also identified 6 additional studies that focused on PC counseling, 4 that focused on improved patient outcomes for adult depression, and 2 that focused on improved parent-child relationships in postpartum depression. The adult depression in PC literature has shown that psychosocial support by a physician, nurse, or other staff, in the context of 15-minute problem-solving therapy, improves outcomes in depressed adults.[30–32]

With the pediatric PC literature, findings revealed that authors of previous studies have attempted to train pediatricians in various types of counseling such as anticipatory guidance or preventive counseling in a number of disorder areas. Before the Stein et al review,[22] the most recently published systematic review on the impact of psychosocial interventions in pediatric PC was conducted by Bower et al.[24] These investigators reviewed 25 studies in pediatric PC that demonstrated tremendous variability in the problems treated, clinician interventions, and outcomes studied.[24] As noted by Stein et al,[22] most studies did not compare the intervention group to a control group, and those that were RCTs did not provide enough information to judge the design. Thus, one must be cautious in stating that the "innovative" PC interventions were superior to usual care, although some positive effects were found. However, as shown in a review by Bass et al,[33] 18 studies have demonstrated positive effects of injury-prevention counseling in pediatric PC, and Stein et al[22] reviewed additional studies that suggested that modest educational counseling performed by pediatric PC staff can be useful.

Antidepressant Treatment

The treatment review for antidepressant safety and efficacy included RCTs of antidepressants in youth under the age of 19 with depression. This review has also been published elsewhere.[23] This GLAD-PC–initiated review identified 8 peer-reviewed articles in this area, including 4 trials with fluoxetine,[34–37] 1 with sertraline,[38] 1 with citalopram,[38] 1 with paroxetine,[39] and 1 with venlafaxine.[40] Older antidepressants (ie, monoamine oxidase inhibitors [MAOIs], tricyclic antidepressants) were not included in our review because the current controversy and the recent FDA review only involved newer classes of antidepressants and because of the known lack of efficacy (ie, tricyclic antidepressants) and clinical trials data (ie, MAOIs) for other classes of older antidepressants.[40] Finally, because of the continuing controversy around the disclosure of unpublished clinical research data, unpublished studies included in the FDA review were also reviewed. There were no completed yet unpublished studies identified that were excluded in the FDA analyses. For additional details regarding this review, see the Cheung et al report.[23]

Overall, both individual clinical trial evidence and evidence from systematic reviews support the use of antidepressants in adolescents with MDD. Bridge et al[41] conducted a meta-analysis of the clinical trials data and calculated the numbers needed to treated and numbers needed to harm. They concluded that 6 times more teens would benefit from treatment with antidepressants than would be harmed.[41] In reviewing the individual studies, the percentage of subjects who responded to antidepressants ranged from 47% to 69% and 33% to 57% for those on placebo (see Table 1). The majority of these studies found a significant difference between those on medication versus those on placebo. Overall, fluoxetine has had the largest number of studies with positive results, whereas paroxetine has had the largest number of studies with negative results.[34–37,39,42,43] However, methodologic differences may have played a role in these differing results.[23] The largest study, the Treatment for Adolescent Depression Study, involved subjects who were randomly assigned to receive placebo, cognitive behavioral therapy (CBT) alone, fluoxetine alone, or

TABLE 1 **Response Rates in RCTs of Antidepressants Based on Clinical Global Impression**

Medication	Drug, %	Placebo, %	*P*
Fluoxetine (March et al[36] [2004])[a]	56	33	.02
Fluoxetine (Emslie et al[89] [1997])	52	36.8	.03
Fluoxetine (Emslie et al[62] [2002])	61	35	.001
Paroxetine (Keller et al[39] [2001])[b]	66	48	.02
Paroxetine[c]	69	57.3	NS
Paroxetine[c]	65	46	.005
Citalopram (Wagner et al[38] [2004])	47	45	NS
Sertraline (Wagner et al[90] [2003])	63	53	.05
Escitalopram (Wagner et al[91] [2007])	63	52	NS

NS indicates not significant.
[a] Fluoxetine alone compared with placebo.
[b] Paroxetine compared with placebo.
[c] GlaxoSmithKline, unpublished data.

CBT with fluoxetine.[36] Subjects assigned to receive CBT with fluoxetine or fluoxetine alone showed significantly greater improvement in their depressive symptoms compared with those who received placebo or were treated with CBT alone (also see "Cognitive Behavioral Therapy").

Finally, available evidence from several large RCTs[23] suggests that adverse effects do emerge in depressed youth who are treated with antidepressants. Adverse effects (ie, nausea, headaches, behavioral activation, etc) occur in up to 93% of the subjects treated with these medications and in up to 75% of those treated with placebo when subjects are asked about specific adverse effects. Therefore, routine monitoring of the development of adverse events is critical for depressed youth who are treated with antidepressants.

Authors of several recent studies have used population data to evaluate the risks versus benefits of prescribing antidepressants. Olfson et al[44] focused specifically on youth aged 10 to 19 years; their study revealed decreased suicide rates in geographic areas where the rates of newer antidepressant prescriptions are increasing. Gibbons et al[45] reported similar findings when they conducted a study of children aged 5 to 14. Several other studies have focused on general populations that included significant numbers of children and adolescents.[46–49] Although one Australian study did identify a link between increased prescription rates of newer antidepressants and increased suicide rates in adolescents and young adults aged 15 to 24,[46] other American and international studies have indicated an inverse relationship between rates of selective serotonin reuptake inhibitor (SSRI) prescriptions and rates of suicide in adolescent populations.[48,49]

Still other studies have used large databases to carry out naturalistic studies of possible associations between antidepressant use and suicidality.[50–53] In the only 1 of these studies that focused exclusively on youth, Valuck et al[50] conducted a propensity-adjusted retrospective cohort study to examine links between antidepressant treatment and suicide attempts in depressed adolescents (aged 12–18) by using a community sample of managed care enrollees. They found no increase in suicide rates with treatment with SSRIs, other antidepressants, or multiple antidepressants after a diagnosis of MDD, finding instead that treatment for at least 6 months reduced the likelihood of suicide attempts compared with treatment for less than 8 weeks.

Psychotherapy

The final review conducted examined the efficacy of psychotherapy such as CBT, interpersonal psychotherapy (IPT), and nonspecific interventions such as counseling and support. Through our search, we were able to identify both individual studies and several high-quality meta-analyses/reviews that were recently conducted to examine the efficacy of psychotherapy in adolescent depression. A full description of the review is available from the authors on request.

Cognitive Behavioral Therapy

In 1998, Reinecke et al[54] and Harrington et al[55] conducted reviews of CBT trials and found improved outcomes. In addition to the above-mentioned meta-analytical studies, several systematic narrative reviews of CBT studies have been conducted. The most recent and comprehensive of these reviews was conducted by Compton et al[56] and included 12 studies published between 1990 and 2002. Although some of these studies showed negative results, Compton et al conclude that, in sum, they provided solid evidence of the effectiveness of CBT conducted by trained therapists for mild-to-moderate depression.

The effectiveness of CBT for adolescents with moderate to moderately severe depression was evaluated recently in the multicenter Treatment for Adolescents With Depression Study, which randomly assigned 439 depressed 12- to 17-year-olds to treatment with CBT, fluoxetine, CBT plus fluoxetine, or placebo.[36] According to Clinical Global Impressions severity scores, the posttreatment response rate to 15 sessions of CBT over 12 weeks (43.2% [95% confidence interval [CI]: 34–52]) was not significantly different ($P = .40$) from placebo (34.8% [95% CI: 26–44]). The authors attributed this relatively low response rate, in part, to the fact that the study population suffered from more severe and chronic depression than participants in previous studies and to a high rate of psychiatric comorbidity in their study participants.[36] Along with the fairly robust placebo-response rate, it is also possible that the nonspecific therapeutic aspects of this medication management could have successfully competed with the specific effects of the CBT intervention. As a consequence, one cannot and should not conclude that CBT was ineffective.

Although the Compton et al[56] review of studies pro-

vided evidence for the efficacy of CBT in specialty mental health clinics for adolescents with mild-to-moderate depression, more recent studies have helped determine the effectiveness of CBT in "real-world" situations. In 2003, Puskar et al[57] evaluated whether a group CBT intervention conducted in a high school by a masters-level nurse could improve depressive symptoms among 89 rural students with Reynold's Adolescent Depression Screen scores of ≥60. The 46 students who completed 10 weekly CBT group sessions had significantly better mean depressive scores immediately after treatment and at 6 months than those (n = 43) who were randomly assigned to receive usual care. In contrast, Kerfoot et al[58] studied the impact of training social workers in CBT methods (versus treatment as usual) on 52 depressed youth. The study showed no differences in depression scores across the 2 interventions, which was partially attributed to high drop-out rates.[58]

In yet another study with more difficult adolescents, Rohde et al[59] recently assessed the effectiveness of CBT in treating adolescents with comorbid MDD and conduct disorder by recruiting 13- to 17-year-olds (N = 93). After randomly assigning them to a CBT-based "Coping With Depression" course or a life skills tutoring control condition, 39% of the adolescents who "completed" the CBT course recovered compared with only 19% of the adolescents who participated in the life skills tutoring control group (odds ratio: 2.66; 95% CI: 1.03–6.85).

Finally, in the Youth Partners-in-Care study, Asarnow et al[27] evaluated the effectiveness of a quality improvement intervention that involved increasing access of PC clinicians and depressed youth to CBT and antidepressant medication. Participants (N = 418) were randomly assigned to usual care "enhanced" by an education intervention or the quality improvement intervention.[27] At the study's 6-month end point, subjects in the intervention group were significantly improved according to the study's 2 primary outcome variables as measured by the Center for Epidemiological Study Depression Scale. The intervention group had lower Center for Epidemiological Study Depression Scale scores and fewer youth scored in the severe range at the end of the study. Given the fact that the intervention and usual-care groups differed significantly only in their use of CBT (53% vs 36%, respectively; OR: 2.2; 95% CI: 1.3–3.9; P = .007), much of the intervention groups' improvement can be attributed to the availability of this treatment modality for patients screened and identified in PC settings.

Interpersonal Therapy

In terms of IPT, only a handful of studies have been conducted. First, Mufson et al[28] assigned 48 depressed adolescents to IPT for adolescents (IPT-A) or clinical monitoring. Those who received IPT-A reported fewer depressive symptoms and improved overall functioning. In the Rossello and Bernal[60] study, 71 depressed Puerto Rican adolescents were randomly assigned to receive IPT, CBT, or be placed on a waiting list. After 12 weeks, both IPT- and CBT-treated adolescents reported significantly fewer depressive symptoms. In the most recent study, 63 depressed adolescents (any depressive disorder) were randomly assigned to receive either 16 weeks of IPT-A or a treatment-as-usual condition (supportive counseling).[61] Subjects who were treated with IPT-A showed significantly greater symptom reduction and improved overall functioning.

GUIDELINES

Each of the recommendations listed below was graded on the basis of the level of supporting research evidence from the literature and the extent to which experts agreed that it is highly appropriate in PC. The level of supporting evidence for each recommendation is based on the Oxford Centre for Evidence-Based Medicine grades of evidence (A–D) system (see www.cebm.net/levels_of_evidence.asp).

Recommendation strength based on expert consensus was rated in 4 categories: very strong (>90% agreement), strong (>70% agreement), fair (>50% agreement), and weak (<50% agreement). The recommendations in the guidelines were developed only in areas of management that had at least "strong agreement" among experts (see Fig 1 for the treatment algorithm).

Treatment

Recommendation 1: After initial diagnosis, in cases of mild depression, clinicians should consider a period of active support and monitoring before starting other evidence-based treatment (grade of evidence: B; strength of recommendation: very strong).

After a preliminary diagnostic assessment, in cases of mild depression, clinicians should consider a period of active support and monitoring before recommending treatment (from 6 to 8 weeks of weekly or biweekly visits for active monitoring). Evidence from RCTs of antidepressants and CBT show that a sizable percentage of patients respond to nondirective supportive therapy and regular symptom monitoring.[34–40,62–65] However, if symptoms persist, treatment with antidepressants or psychotherapy should be offered. Active support and monitoring is also essential for cases in which depressed patients and/or their families/caregivers refuse other treatments. Active support and counseling for adolescents by pediatric PC clinicians have been evaluated for several different disorders including substance abuse and sleep disorders.[22]

Furthermore, expert opinion based on extensive clinical experience and qualitative research with families, patients, and clinicians indicate that these strategies are a crucial component of management by PC clinicians. For additional guidance on how to provide active sup-

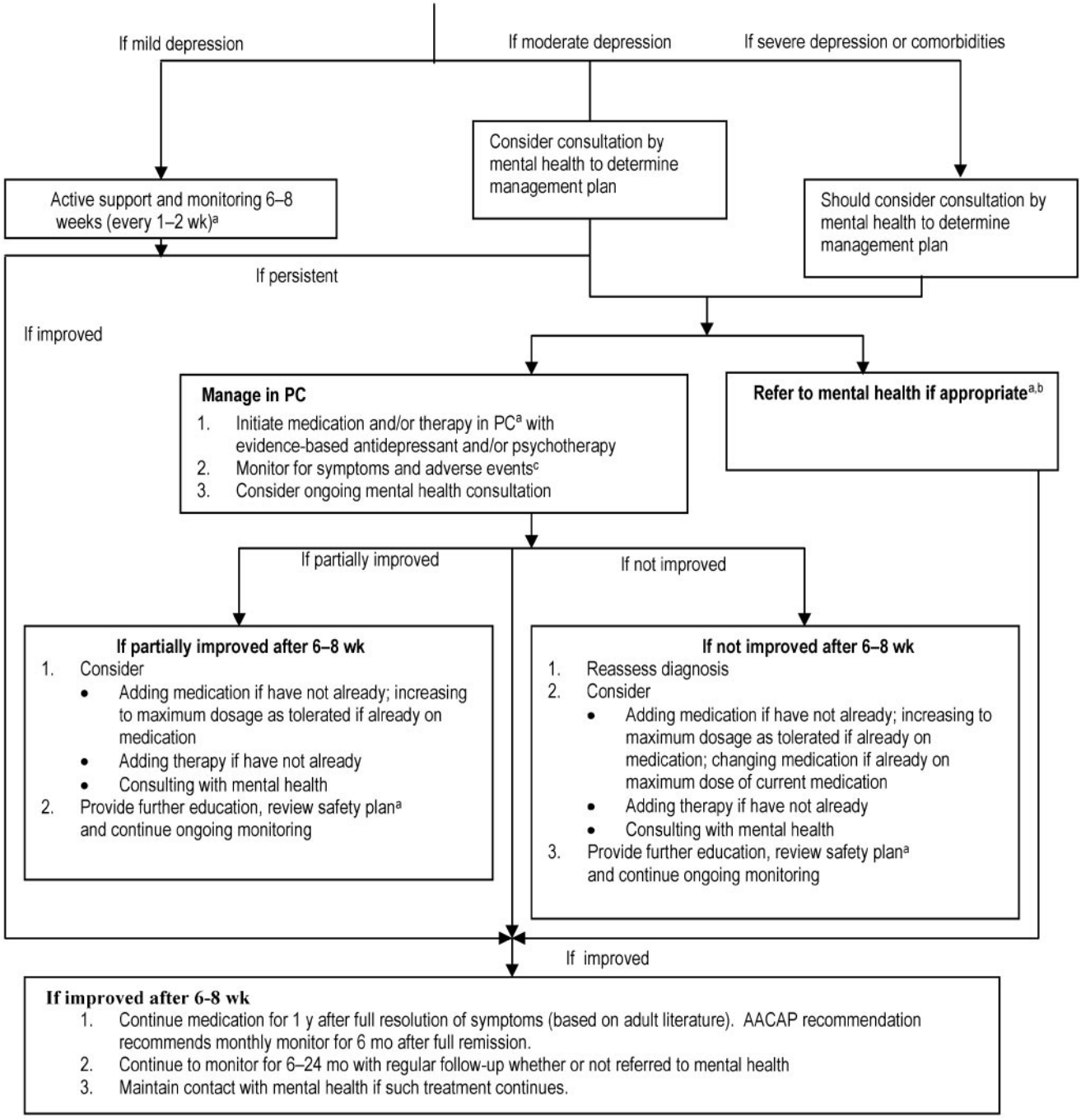

FIGURE 1

Clinical management flowchart. [a] Provide psychoeducation, provide supportive counseling, facilitate parental and patient self-management, refer for peer support, and regularly monitor for depressive symptoms and suicidality. [b] Negotiate roles/responsibilities between PC and mental health and designate case coordination responsibilities; continue to monitor in PC after referral; and maintain contact with mental health. [c] Clinicians should monitor for changes in symptoms and emergence of adverse events such as increased suicidal ideation, agitation, or induction of mania. For monitoring guidelines, refer to the GLAD-PC toolkit.

port, please refer to the GLAD-PC toolkit (available at www.glad-pc.org).

For moderate or severe cases, the clinician should recommend treatment, crisis intervention (as indicated), and mental health consultation immediately without a period of active monitoring.

Recommendation 2: If a PC clinician identifies an adolescent with moderate or severe depression or complicating factors/conditions such as coexisting substance abuse or psychosis, consultation with a mental health specialist should be considered (grade of evidence: C; strength of recommendation: strong). Appropriate roles and responsibilities for ongoing management by the PC and mental health clinicians should be communicated and agreed upon (grade of evidence: C; strength of rec-

ommendation: strong). The patient and family should be consulted and approve the roles of the PC and mental health professionals (grade of evidence: D; strength of recommendation: strong).

In adolescents with severe depression or comorbidities such as substance abuse, clinicians should consider consultation with mental health professionals and refer to such professionals when deemed necessary. In cases of moderate depression with or without comorbid anxiety, clinicians should consider consultation by mental health and/or treatment in the PC setting. Although the access barriers to mental health services need to be addressed by policy makers to make necessary mental health consultations more feasible, available, and affordable in underserviced areas, clinical judgment must prevail in the meantime; thus, the need for consultation should be based on the clinician's judgment. PC clinicians must also take into consideration the treatment preferences of patients/families, the severity and urgency of the case presentation, and the physician's level of training and experience.

Active support and treatment should also be started in cases in which there is a lengthy waiting list for mental health services. Once a referral is made, the PC clinician must remain involved in the follow-up. In particular, roles and responsibilities should be agreed upon between the PC clinician and mental health clinician(s), including the designation of case coordination responsibilities.[66–72]

Recommendation 3: PC clinicians should recommend scientifically tested and proven treatments (ie, psychotherapies such as CBT or IPT and/or antidepressant treatment such as SSRIs) whenever possible and appropriate to achieve the goals of the treatment plan (grade of evidence: A; strength of recommendation: very strong).

After providing education and support to the patient and family, the range of effective treatment including medications, psychotherapies, and family support options should be considered. The patient and family should be assisted to arrive at a treatment plan that is both acceptable and implementable while taking into account their preferences and availability of treatment services. The treatment plan should be customized according to the severity of disease, risk of suicide, and the existence of comorbid conditions. The GLAD-PC toolkit will provide more detailed guidance around the factors that may influence a treatment choice (ie, a patient with psychomotor retardation may not be able to actively engage in psychotherapy). The management of depression in youth is an emerging field, and new treatments may become available. However, common-sense approaches such as the prescription of physical exercise and adequate nutrition should also be used in the management of these patients.

As an aside, the majority of CBT and IPT studies that included patients with MDD also included patients with depression not otherwise specified, subthreshold depressive symptoms, or dysthymic disorder. In contrast, medication RCTs for depression in adolescents generally only included subjects with MDD. Thus, although these guidelines address the treatment of depression generally, medication-specific guidelines apply only to fully expressed MDD.

Psychotherapies

Both CBT and IPT have been adapted to address depression in adolescents and have been shown to be effective in treating adolescents with MDD in tertiary care and in community settings.[28,61,73] CBT has been used in the PC setting with positive preliminary results.[27,29] However, the results of a recent RCT demonstrated superior efficacy of combination therapy (medication and CBT) versus CBT alone.[36] For a brief description of the 2 therapies, see Table 2.

Antidepressant Treatment

Previous research has shown that up to 25% of pediatric PC clinicians and 42% of family physicians in the United States had recently prescribed SSRIs for more than 1 adolescent under the age of 18.[13] When indicated by clinical presentation (clear diagnosis of MDD with no comorbid conditions) and patient/family preference, an SSRI should be used. The selection of the specific SSRI should be based on the optimum combination of safety and efficacy data. The patient and family should be informed about the possible adverse effects (clinicians may use a checklist) including possible switch to mania or the development of behavioral activation or suicidal-behavior. Once the antidepressant is started, and if tol-

TABLE 2 Components of CBT and IPT for Adolescents

Therapy	Key Components
CBT	Thoughts influence behaviors and feelings, and vice versa. Treatment targets a patient's thoughts and behaviors to improve his or her mood.
	Essential elements of CBT include increasing pleasurable activities (behavioral activation), reducing negative thoughts (cognitive restructuring), and improving assertiveness and problem-solving skills to reduce feelings of hopelessness. CBT for adolescents may include sessions with parents/caregivers to review progress and increase compliance with CBT-related tasks.
IPT-A	Interpersonal problems may cause or exacerbate depression, and that depression, in turn, may exacerbate interpersonal problems. Treatment targets a patient's interpersonal problems to improve both interpersonal functioning and his or her mood.
	Essential elements of IPT include identifying an interpersonal problem area, improving interpersonal problem-solving skills, and modifying communication patterns.
	Parents/caregivers are involved in sessions during specific phases of the therapy.

Adapted from: Columbia University, Department of Child and Adolescent Psychiatry. *Columbia Treatment Guidelines Depressive Disorders (Version 2).* New York, NY: Columbia University; 2002.

erated, the clinician should ensure an adequate trial up to the maximum dose and duration.

Table 3 lists recommended antidepressants and dosages for use in youth with depression. These recommendations are based on the expert survey results and were also reviewed by our expert consensus panel. Generally, the effective dosages for antidepressants in adolescents are lower than would be found in adult guidelines. Note that only fluoxetine has been approved by the FDA for use in children and adolescents with depression. Clinicians should know the potential drug interactions with SSRIs. Further information on the use of antidepressants are described in the GLAD-PC toolkit. In addition, all SSRIs, with the exception of fluoxetine, should be slowly tapered when discontinued because of the risk of withdrawal effects. Details regarding the initial selection of a specific SSRI and possible reasons for initial drug choice can be found in the GLAD-PC toolkit.

Contact (either in person or by telephone with either the clinician or member of the clinical staff) should take place after the initiation of treatment to review the patient's and family's understanding of and adherence to the treatment plan. Issues such as the current status of the patient and the patient's/family's access to educational materials regarding depression should be discussed during follow-up conversations. For relevant educational resources for patients and/or families, refer to the GLAD-PC toolkit.

Recommendation 4: PC clinicians should monitor for the emergence of adverse events during antidepressant treatment (SSRIs) (grade of evidence: B; strength of recommendation: very strong).

Recent reanalyses of safety data from clinical trials of antidepressants have led to a black-box warning from the FDA regarding the use of these medications in children and adolescents and a recommendation for close monitoring. The exact wording of the FDA recommendation is, "all pediatric patients being treated with antidepressants for any indication should be observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases."

Although the frequency of monitoring has been controversial, the FDA further suggested that, "*Ideally, such observation would include at least weekly face-to-face contact with patients or their family members or caregivers during the first 4 weeks, then at biweekly visits for the next 4 weeks, then at 12 weeks, and as clinically indicated beyond 12 weeks. Additional contact by telephone may be appropriate between face-to-face visits.*" It should be noted, however, that there is no empirical evidence to support the requirement of weekly face-to-face meetings per se for the first 4 weeks after initiating antidepressant treatment. In fact, evidence from large population-based surveys show high reliability of telephone interviews with adolescent subjects for the diagnosis of depression.[74,75] Although obtaining a diagnosis is not the same as the elicitation of adverse events while in treatment, this evidence suggests that telephone contact may be just as effective in monitoring for adverse events. A regular and frequent monitoring schedule should be developed, and care should be taken to obtain input from the adolescents and families to ensure compliance with the monitoring strategy.[76,77] Recommendations endorsed by the AACAP have also highlighted the lack of research evidence to support weekly face-to-face visits. However, the AACAP does recommend that providers attempt to follow the FDA guidelines until other research findings become available.

ONGOING MANAGEMENT

Recommendation 1: Systematic and regular tracking of goals and outcomes from treatment should be performed, including assessment of depressive symptoms and functioning in several key domains: home, school, and peer settings (grade of evidence: D; strength of recommendation: very strong).

Goals should include both improvement in functioning status and resolution of depressive symptoms. Tracking of goals and outcomes from treatment should include function in several important domains (ie, home, school, peers). Evidence from large RCTs demonstrates that depressive symptoms and functional impairments may not improve at the same rate with treatment.[23,36] Therefore, symptoms and functioning should be tracked regularly during the course of treatment with information gathered from both the patients and their families when possible.

According to expert consensus, patients should be seen within 1 week of the initiation of treatment. At every visit, clinicians should inquire about ongoing de-

TABLE 3 **SSRI Titration Schedule**

Medication	Starting Dose, mg/d	Increments, mg	Effective Dose, mg	Maximum Dose, mg	Contraindication
Citalopram	10	10	20	60	MAOIs
Fluoxetine	10	10–20	20	60	MAOIs
Fluvoxamine	50	50	150	300	MAOIs
Paroxetine	10	10	20	60	MAOIs
Sertraline	25	12.5–25	50	200	MAOIs
Escitalopram	5	5	10	20	MAOIs

pressive symptoms, risk of suicide, possible adverse effects from treatment (including the use of specific adverse-effect scales), adherence to treatment, and new or ongoing environmental stressors.

Recently, Emslie et al[63] examined medication maintenance after response. The researchers randomly assigned those pediatric patients who had responded to fluoxetine by 19 weeks to placebo or to medication continuation for an additional 32 weeks. Of the 20 subjects who were randomly assigned to the 32-week medication relapse-prevention arm, 10 were exposed to fluoxetine for 51 weeks. Significantly fewer relapses occurred in the group of subjects who were randomly assigned to medication maintenance, which suggests that longer medication-continuation periods, possibly 1 year, may be necessary for relapse prevention. In addition, Emslie et al[63] found the greatest risk of relapse to be in the first 8 to 12 weeks after discontinuing medication, which suggests that after stopping an antidepressant, close follow-up should be encouraged for at least 2 to 3 months.

With the limited evidence in children and adolescents and the emerging evidence in the adult literature that suggests antidepressant medication should be continued for 1 year, the GLAD-PC and AACAP experts concluded that medication should be maintained for 6 to 12 months after the full resolution of depressive symptoms.[19,78]

However, regardless of the length of treatment, all patients should be monitored on a monthly basis for 6 to 12 months after the full resolution of symptoms.[19] If the depressive episode is a recurrence, clinicians are encouraged to monitor patients for up to 2 years given the high rates of recurrence as demonstrated in the adult literature, in which maintenance treatment in those with recurrent depression continue for up to 2 years after the full resolution of symptoms. Clinicians should obtain consultation from mental health if a teen develops psychosis, suicidal or homicidal ideation, or new or worsening of comorbid conditions.

Recommendation 2: Diagnosis and initial treatment should be reassessed if no improvement is noted after 6 to 8 weeks of treatment (grade of evidence: B; strength of recommendation: very strong). Mental health consultation should be considered (grade of evidence: D; strength of recommendation: very strong).

If improvement is not seen within 6 to 8 weeks of treatment, mental health consultation should be considered. Evidence of improvement may include reduction in the number of depressive symptoms, improved functioning in social or school settings, or improvement spontaneously reported by the adolescent and/or parent/caregiver. The clinician should also reassess the initial diagnosis, choice and adequacy of initial treatment, adherence to treatment plan, presence of comorbid conditions (eg, substance abuse) or bipolar symptoms that may influence treatment effectiveness, and new external stressors. If a patient has no response to maximum therapeutic dose of an antidepressant medication, the clinician should consider changing the medication. Alternatively, if the patient's condition fails to improve on antidepressant medication or therapy alone, the addition of, or switch to, the other modality should be considered.

Recommendation 3: For patients who achieve only partial improvement after PC diagnostic and therapeutic approaches have been exhausted (including exploration of poor adherence, comorbid disorders, and ongoing conflicts or abuse), a mental health consultation should be considered (grade of evidence: D; strength of recommendation: very strong).

If a patient only partially improves with treatment, mental health consultation should be considered. The clinician should also review the diagnosis and explore possible causes of partial response such as poor adherence to treatment, comorbid disorders, or ongoing conflicts and/or abuse. These causes may need to be managed first before changes to the treatment plan are made.

If a patient has been treated with an SSRI (maximum tolerated dosage) and has shown only partial improvement, the addition of an evidence-based psychotherapy should be considered if it has not previously been conducted. Other considerations may include the addition of another medication, an increase of the dosage above FDA-approved ranges, or a switch to another medication, preferably in consultation with a mental health professional. Likewise, if a patient's condition fails to improve after a trial of either CBT or IPT and has not yet begun medication, the clinician should consider a trial of SSRI antidepressant treatment. Strong consideration should also be given to a referral to mental health services.

Recommendation 4: PC clinicians should actively support depressed adolescents who are referred to mental health to ensure adequate management (grade of evidence: D; strength of recommendation: very strong). PC clinicians may also consider sharing care with mental health agencies/professionals when possible (grade of evidence: B; strength of recommendation: very strong). Appropriate roles and responsibilities regarding the provision and coordination of care should be communicated and agreed upon by the PC clinician and the mental health specialist (grade of evidence: D; strength of recommendation: very strong).

PC clinicians should continue follow-up with adolescents with depression who have been referred to mental health services for assessment and/or management. When possible, PC clinicians may consider sharing management of depressed adolescents with mental health agencies/professionals. There is emerging evidence from the adult literature about the greater effectiveness of "shared-care" models for the management of depression in the PC setting.[67–72,79–81] Similar evidence from case reports in the pediatric literature is emerging.[82]

DISCUSSION

The recommendations regarding treatment and ongoing management highlight the need for PC professionals to become familiar with the use of empirically tested treatments for adolescent depression including both antidepressants and psychotherapy. In particular, antidepressant treatments can be useful in certain clinical situations in the PC setting. However, in many of these clinical scenarios, PCPs need to ensure that there is systematic and regular follow-up and adequate mental health support if needed. The need for systematic follow-up, whether by the PCP or by a mental health provider, is especially important in light of the recent FDA warnings regarding the emergence of adverse events with antidepressant treatment.

Psychotherapy is also recommended as first-line treatment for depressed adolescents in the PC setting. Although the provision of psychotherapy may be less feasible and practical within the constraints (ie, time, availability of trained staff) of PC settings, there is some evidence that quality improvement projects that involve psychotherapy can improve the care of depressed adolescents.[27]

Another critical recommendation of the guidelines is the need for PCPs to establish connections to available mental health resources in the community, because PCPs will undoubtedly encounter complex cases in which mental health consultation or shared care may be required. Furthermore, increased coordination of care involving different providers are linked to improved outcomes for youth with both general medical and mental health disorders.[35,83–86] However, to increase linkages between PCPs and mental health specialists, changes in many existing health care systems need to occur (eg, mental health specialists to set aside time and be reimbursed for brief telephone consultations to PCPs).

The GLAD-PC was developed on the basis of the needs of PC clinicians who are faced with the challenge of caring for depressed adolescents and encounter many barriers including the shortage of mental health resources in most community settings. Although it is clear that more evidence and research in this area are needed, these guidelines represent a necessary step toward improving the care of depressed adolescents in the PC setting. Similar guidelines have also been produced for other health care contexts such as in the United Kingdom (www.nice.org.uk/pdf/CG028NICEguideline.pdf). The GLAD-PC and the toolkit reflects the coming together of available evidence and the consensus of a large number of experts representing a broad spectrum of specialties and advocacy organizations within the North American health care context. However, no improvements in care will be achieved if changes do not occur in the health care systems that would allow for increased training in mental health for PC clinicians and in collaborative models for both PC and specialty care clinicians. Therefore, it is critical that training programs for PCPs increase their focus on mental health issues and that trainees in both PC and specialty care areas be helped to hone their skills in working in collaborative care models. For providers who are currently practicing, continuing education for primary and specialty care professionals must strengthen skills in collaborative work, and specifically, for PCPs, increase skills and knowledge in the management of depression.

Limitations

Although these guidelines cover a range of issues regarding the management of adolescent depression in the PC setting, there were other controversial areas that were not addressed in these recommendations. These included such issues as universal screening, using a second antidepressant when patients' conditions fail to respond to an initial antidepressant, and the treatment of subthreshold symptoms. New emerging evidence may impact on the inclusion of such areas in future iterations of the guidelines and the accompanying toolkit. Many of these recommendations are made in the face of absence of evidence or lower levels of evidence.

Future Directions

Ample evidence exists to indicate that guidelines alone are insufficient in closing the gaps between recommended versus actual practices.[87,88] Thus, it will be necessary to identify effective methods for disseminating information and to provide assistance in changing practice to PC clinicians. Future studies of these guidelines must build on this work by piloting and evaluating methods, tools, and strategies to facilitate the adoption of these guidelines for the management of adolescent depression in PC settings. These studies must also explore optimal methods for helping clinicians and their organizations/practices address the range of obstacles that may interfere with adoption of necessary practices to yield sustainable management of adolescent depression in PC settings. Also, of course, such studies must show not only changes in PC clinicians' adolescent depression management but also improvements in outcomes of youth with depression.

Many jurisdictions have recognized the need to increase collaborative care to address the care of adolescents with mental illness. In Canada and the United States, models of care that involve mental health and PC are being implemented. However, the empirical support for these models is modest; therefore, additional research is urgently needed. Work has already begun in Massachusetts to implement GLAD-PC in pediatric practices with funding from AACAP. The findings from this and other studies will build the empirical base for new models of care in the pediatric setting.

APPENDIX: PART II TOOLKIT ITEMS

- Algorithm/flow sheet (Fig 1)
- Treatment choices: active support guide, psychotherapy guide, and medication guide and dosage charts
- Referral information
- Authorization to disclose protected health information between PCP and mental health professional
- Follow-up scripts for management
- Fact sheet/family education materials
- Self-management tools

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