STATEMENT OF ENDORSEMENT

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# Guidelines for Adolescent Depression in Primary Care (GLAD-PC): Part I. Practice Preparation, Identification, Assessment, and Initial Management

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## abstract

**OBJECTIVES:** To update clinical practice guidelines to assist primary care (PC) clinicians in the management of adolescent depression. This part of the updated guidelines is used to address practice preparation, identification, assessment, and initial management of adolescent depression in PC settings.

**METHODS:** By using a combination of evidence- and consensus-based methodologies, guidelines were developed by an expert steering committee in 2 phases as informed by (1) current scientific evidence (published and unpublished) and (2) draft revision and iteration among the steering committee, which included experts, clinicians, and youth and families with lived experience.

**RESULTS:** Guidelines were updated for youth aged 10 to 21 years and correspond to initial phases of adolescent depression management in PC, including the identification of at-risk youth, assessment and diagnosis, and initial management. The strength of each recommendation and its evidence base are summarized. The practice preparation, identification, assessment, and initial management section of the guidelines include recommendations for (1) the preparation of the PC practice for improved care of adolescents with depression; (2) annual universal screening of youth 12 and over at health maintenance visits; (3) the identification of depression in youth who are at high risk; (4) systematic assessment procedures by using reliable depression scales, patient and caregiver interviews, and *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* criteria; (5) patient and family psychoeducation; (6) the establishment of relevant links in the community; and (7) the establishment of a safety plan.

**CONCLUSIONS:** This part of the guidelines is intended to assist PC clinicians in the identification and initial management of adolescents with depression in an era of great clinical need and shortage of mental health specialists, but they cannot replace clinical judgment; these guidelines are not meant to be the sole source of guidance for depression management in adolescents. Additional research that addresses the identification and initial management of youth with depression in PC is needed, including empirical testing of these guidelines.

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## BACKGROUND

Major depression in adolescents is recognized as a serious psychiatric illness with extensive acute and chronic morbidity and mortality.[1–4] Research shows that only 50% of adolescents with depression are diagnosed before reaching adulthood.[5] In primary care (PC), as many as 2 in 3 youth with depression are not identified by their PC clinicians and fail to receive any kind of care.[6,7] Even when diagnosed by PC providers, only half of these patients are treated appropriately.[5] Furthermore, rates of completion of specialty mental health referral for youth with a recognized emotional disorder from general medical settings are low.[8]

In view of the shortage of mental health clinicians, the barriers to children's access to mental health professionals, the well-documented need for PC clinicians to learn how to manage this condition, the increasing evidence base that is available to guide clinical practice, the increased selective serotonin reuptake inhibitor–prescribing rates in pediatric PC,[9,10] and new evidence that a multifaceted approach with mental health consultation may improve the management of depression in PC settings,[8,10–16] guidance for the identification and management of depression in adolescents in PC were urgently needed. To address this gap as well as to meet the needs of PC clinicians and families who are on the front lines with few mental health resources available, in 2007, the Center for the Advancement of Children's Mental Health at Columbia University and the Sunnybrook Health Sciences Center at the University of Toronto joined forces with the New York Forum for Child Health, the New York District II Chapter 3 of the American Academy of Pediatrics (AAP), and the Resource for Advancing Children's Health (REACH) Institute along with leading experts across the United States and Canada to address the need for a synthesis of knowledge in this area. The result of this initiative was the development of the Guidelines for Adolescent Depression in Primary Care (GLAD-PC). These guidelines are based on available research and the consensus of experts in depression and PC. The two companion articles[17,18] constituted the first-ever evidence- and expert consensus–derived guidelines to guide PC clinicians' management of adolescent depression. The guidelines were also accompanied by a tool kit (available at no cost for download at http://www.gladpc.org).

In this article, we present the updated recommendations on the identification, assessment, and initial management of depression in PC settings and new recommendations on practice preparations (not previously in the GLAD-PC). In the accompanying report, we present the results of the reviews and recommendations on treatment (psychotherapy, psychopharmacology, and pediatric counseling) and ongoing management.

Major depressive disorder (MDD) is a specific diagnosis described in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5)[19] characterized by discrete episodes of at least 2 weeks' duration (although episodes can last considerably longer) and involving changes in affect, cognition and neurovegetative functions, and interepisode remissions. Other types of depression exist, such as persistent depressive disorder and premenstrual dysphoric disorder. It is important to note that depressive disorders have been separated from bipolar and related disorders in the DSM-5. Although the evidence for the psychopharmacology recommendations in the accompanying article focuses exclusively on MDD, the recommendations around identification, assessment, and initial management can be applied to other forms of depression as well.

Our guidelines also distinguish between mild, moderate, and severe forms of MDD. The DSM-5 depression criteria include 9 specific symptoms that have been shown to cluster together, run in families, and have a genetic basis,[20–24] and a large body of evidence accumulated over time now supports the internal consistency of depressive symptoms and the validity of the major depression construct.[20] According to the DSM-5, the severity of depressive disorders can be based on symptom count, intensity of symptoms, and/or level of impairment. This commonly used method to define depression severity has been used in large population-based studies[25] and may be particularly relevant in PC settings, in which less severe clinical presentations of depression may be more common. Thus, mild depression may be characterized on the basis of lower scores on standardized depression scales with a shorter duration of symptoms or meeting minimal criteria for depression. Following the DSM-5, mild depression might be defined as 5 to 6 symptoms that are mild in severity. Furthermore, the patient might experience only mild impairment in functioning.

In contrast, depression might be deemed severe when a patient experiences all of the depressive symptoms listed in the DSM-5. Depression might also be considered severe if the patient experiences severe impairment in functioning. Moderate depression falls between these 2 categories.

In general, however, even if not all 9 DSM-5–defined symptoms of depression are present, for the purposes of these guidelines, an adolescent with at least 5 criteria of MDD should be considered in the severe category if he or she presents with a specific suicide plan, clear intent, or recent attempt; psychotic symptoms; family history of first-degree relatives with bipolar disorder; or severe impairment in functioning (such as being unable to leave home).

These guidelines were developed for PC clinicians who are in a position to identify and assist youth with depression in their practice settings. Although the age range of 10 to 21 years may encompass preteenagers, adolescents, and young adults in specific instances, this age range was chosen to include those who might be considered developmentally adolescent. Research that supports adult depression guidelines includes adults 18 years and older. Much of the adolescent depression research focuses on children 18 years and younger. However, because adolescent medicine clinicians and school health clinicians often see patients until they are 21 years old, we have included the older adolescents. Furthermore, a PC clinician faced with an adolescent between the ages of 18 and 21 years can choose to use either adult or adolescent depression guidelines on the basis of the developmental status of the adolescent and his or her own comfort and familiarity with each set of guidelines.

## METHODS

The original GLAD-PC recommendations were developed on the basis of a synthesis of expert consensus– and evidence-based research review methodologies, as described in Zuckerbrot et al.[17] The 5-step process included conducting focus groups with PC clinicians, patients, and their families, a systematic literature review, a survey of depression experts to address questions that were not answered in the empirical literature,[26] an expert consensus workshop, and an iterative guideline drafting process with opportunity for input from all workshop attendees.

For the research update of the GLAD-PC, systematic literature reviews were conducted in the same 5 key areas of adolescent depression management in PC settings as the original guidelines: identification and assessment, initial management, safety planning, treatment, and ongoing management of youth depression. Consistent with the original review, the updated searches were conducted by using relevant databases (eg, Medline and PsycInfo), and all primary studies published since the original GLAD-PC reviews in 2005 and 2006 were examined. All update procedures were conducted with the input and guidance of the steering group, which is composed of clinical and research experts, organizational liaisons, and youth and families with lived experience. As in the original review, recommendations were graded on the basis of the University of Oxford's Centre for Evidence-Based Medicine grade of evidence (1–5) system, with 1 to 5 corresponding to the strongest to the weakest evidence respectively (see http://www.cebm.net/wp-content/uploads/2014/06/CEBM-Levels-of-Evidence-2.1.pdf). They were also rated on the basis of the strength of expert consensus among the steering group members that the recommended practice is appropriate. Recommendations with strong (>70%) or very strong (>90%) agreement are given here.

In addition, a new review on the topic of practice preparation was conducted given the emerging evidence for this area since the development of the original GLAD-PC guidelines. Electronic searches of relevant databases were conducted for English-language studies in which researchers examined practice preparation for treating youth depression in PC that were published between 1946 and September 2016. Search terms were grouped by categories and included the following: "child* or adolesc* or youth or teen* or juvenile" and "primary care or pediatr* or family prac* or general prac*" and "depress* or dysth* or mood or bipolar" and "collaborative care or integrat* health or medical-behavioral health care or behavioral health or medical home or shared care or facilita* or practice prepar*". Reference lists for relevant articles were also examined for additional studies that were not identified through search engines. A total of 135 abstracts were carefully examined. Studies that were conducted outside of PC facilities or that used solely adult populations were screened out, leaving a total of 8 relevant articles. A full report of all the literature reviews is available on request.

## RESULTS

### Literature Reviews

#### *Practice Preparation*

Once PC practices have buy-in from administrative and clinical staff to improve depression care for youth, 2 important steps are necessary. First, before practices embark on screening for or identifying youth who are at risk for depression, training in such issues as appropriate screening tools, assessment and diagnostic methods, safety planning, and so on is important. Second, it

is necessary to have access to community resources, such as mental health specialists (mental health specialists can include child and adolescent psychiatrists, psychiatric nurse practitioners, and therapists), not just as a potential referral resource but also for as-needed consultation for case patients that the PC clinicians choose to manage. We review the available evidence pertaining to these 2 areas (provider training and specialty consultation) below.

### *Effective Training Methods*

PC practices vary widely in their capacity to implement full-scale collaborative or integrative behavioral health programs to address psychological difficulties in youth. At minimum, providing PC providers with guidance, education, and training in key topic areas such as identification, evaluation of suicide risk, and initial management of adolescent depression can be a feasible and cost-efficient means of improving care delivery when comprehensive organizational restructuring efforts are out of reach. However, simply providing PC providers with relevant information is not enough because passive education strategies are usually inadequate for producing lasting change in provider behavior.[27]

Researchers in large-scale review studies suggest that the adoption of practice guidelines improves when training and implementation strategies are tailored to the PC practice (eg, training that is developed by primary mental health care specialists, such as the training provided by the REACH Institute [http://www.thereachinstitute.org/] and Child and Adolescent Psychology for Primary Care [http://www.cappcny.org/])[28] and/or use comprehensive training methods, such as varying information delivery methods and skill-building exercises, such as role-playing.[27] Evidence regarding which specific theory-driven training strategies are most effective at eliciting behavior change with PC providers, particularly related to mental health, is sparse, but 1 promising framework leverages principles from the theories of reasoned action and planned behavior to inform training methodology (see Perkins et al[29] for explanation and review). This approach posits 3 primary determinants of PC behavior change: attitudes toward the practice innovation, the strength of intention to adopt the new practice(s), and sense of self-efficacy in one's ability to continue the new behavior. Although no randomized trials in which researchers use this or other systematic frameworks for PC provider–training methodologies were identified, researchers in preliminary studies offer support for training approaches that incorporate basic science-guided behavior change theory and methods. There is increasing evidence that quality-improvement strategies and techniques can change PC practitioner behavior both in mental health and in other arenas.[30,31] The REACH Institute (which is committed to renewing and improving techniques for professionals and parents to treat children with behavioral and emotional needs) has developed and widely implemented a 3-day intensive training on evidence-based pediatric mental health assessment, diagnosis, and treatment practices (including for youth depression) that is guided by basic science behavior change principles, demonstrating long-term practice changes (eg, increased use of symptom scales) as well as favorable PC provider attitudes toward, intentions to follow, and self-efficacy to adhere to the clinical guidelines up to 1 year later.[32] In another study of the same training approach, participating PC providers showed higher levels of self-efficacy in diagnosing and managing youth depression and related disorders than those who received only more traditional continuing education programs (eg, lectures).[33]

An unrelated study demonstrated that provider attitudes toward youth mental health in PC impacts rates of identification. PC providers who viewed psychosocial treatment as burdensome were less likely to identify youth mental health problems.[34] A subsequent follow-up to the study revealed that providing PC staff with communication training enhanced their self-efficacy and willingness to discuss depression symptoms with patients and staff, and this was associated with long-term changes in practice behaviors, such as providing an agenda during the PC visit, querying for additional mental health concerns, and making encouraging statements to patients and families when symptoms are disclosed.[35] The small amount of available literature offers support for hands-on, interactive, and basic science theory–driven training strategies for PC clinicians, but more research is needed before a consensus can be reached on how best to optimize training and educational strategies for PC providers.

### *Access to Specialty Consultation*

In addition to obtaining relevant training, PC providers will benefit from having access to ongoing consultation with mental health specialists.[36,37] Consultation after training allows learning to be tailored to the PC provider's actual practice[38] and can increase provider comfort with diagnosing and treating mental health issues.[33,39] More than 25 states have established programs to promote collaboration between PC providers

and child psychiatrists by providing PC providers with education, rapid access to consultation, and referral options. Among the first psychiatric consultation programs was Targeted Child Psychiatry Services (TCPS) in the state of Massachusetts,[40,41] which offered regional providers access to real-time telephone consultation with a child psychiatrist and the option to refer a child to the psychiatry practice for a mental health evaluation, short-term psychosocial therapy, and/or pharmacotherapy. Program use data revealed that TCPS consultation support alone was sufficient to retain and treat in PC 43% of youth who potentially would have been referred to specialty services.[40] TCPS was subsequently expanded statewide and became known as the Massachusetts Child Psychiatry Access Project.[14] Similar programs in other states offer free training, telephone consultation, and referral advice to PC providers.[14,42,43] Participating PC providers consistently report being highly satisfied with the consultation they receive[14,42,43] and increasingly comfortable with treating mental health problems within the PC setting after consultation.[14,42,43] Additionally, consultation programs may improve access to mental health care not only by increasing its availability within PC but also by decreasing potentially unnecessary referrals to specialty care, which in turn makes specialty providers more available to treat complex or severe patients.[41,44]

### *Identification and Assessment*

In 2009, after the publication of the GLAD-PC, the United States Preventive Services Task Force (USPSTF) endorsed universal adolescent depression screening in teenagers ages 12 to 18 years.[45] This recommendation was based on evidence that there are validated depression screening tools that work in an adolescent PC population and the evidence that there are treatments that work for the identified population.[45,46] On the basis of our review to date, no researchers in a randomized control trial (RCT) have compared functional or depressive outcomes in a cohort of adolescents who were screened in PC by the PC providers themselves versus a cohort of adolescents who were not screened. This lack of evidence, which is also mentioned in the Canadian review of the literature in 2005,[47] the 2009 Williams et al[46] review performed for the USPSTF, the updated 2016 Forman-Hoffman et al[48] review for the USPSTF, and a 2013 systematic literature review published in *Pediatrics*,[49] becomes less relevant as more evidence accumulates regarding the specific steps in the process, such as the validity of PC screening, the feasibility of PC screening, the feasibility of implementing treatment in those who are identified as having depression, and the efficacy of treatment of those who received evidence-based treatments in PC. In our updated review in this area, we found 8 new articles that provide some psychometric data regarding the use of depression screens in the pediatric PC population (Supplemental Table 1) and 38 other articles that touch on screening issues that range from whether screening is taking place and whether screening impacts follow-up procedures or treatment to the specifics of screening, such as the use of mobile devices or gated procedures (Supplemental Table 2). Supplemental Tables 1 and 2 present the new evidence as well as the limitations for existing screening tools and protocols. Please see our original 2007 guidelines for the past review of screening tools and protocols.

During the original GLAD-PC development process, secondary to the paucity of data on the validity of screening tools in the adolescent PC population, the original GLAD-PC guideline was used to review instruments that are used in community and psychiatric populations as well.[17] Given that those screens are still in use and that their psychometric data still apply, in this current review, we focus only on new screening data in PC. Eight of the articles present psychometric data, such as sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), or area under the curve (Supplemental Table 1). Most relevant were the 2 publications by Richardson et al[56,57] in which they validated the Patient Health Questionnaire-2 (PHQ-2) and the Patient Health Questionnaire-9 (PHQ-9) in a PC sample against a gold standard diagnostic interview (the Diagnostic Interview Schedule for Children-IV [DISC-IV]). The PHQ-9, with a cut-point of 11, had a sensitivity and specificity of 89.5% and 77.5%, respectively, to DISC-IV MDD with a PPV of 15.2% and NPV of 99.4%. A PHQ-2 cut score of 3 had a sensitivity and specificity of 73.7% and 75.2%, respectively, to DISC-IV MDD.

Researchers have looked at brief depression-specific screening questions that stand alone (eg, the PHQ-2),[51,57,65,75,79,82,85] longer depression-specific scales that stand alone (eg, the PHQ-9, the Mood and Feelings Questionnaire, the Columbia Depression Scale, and the PHQ-9: Modified for Teens),[58,62,63,66,67,70,74,78,80–82,86–88] brief depression screening questions that are part of a larger psychosocial tool (eg, the Guidelines for Adolescent Preventive Services [GAPS] questionnaire and the Pediatric Symptom Checklist [PSC]),[53,54,64,68,69] and brief screening questions or longer depression-specific scales that are combined with other screens for

either other psychiatric disorders (eg, Screen for Child Anxiety Related Disorders-5) and/or screens for other high-risk behaviors (eg, substance use and sexual activity) to make a more multidimensional tool or packet in 1 (eg, the behavioral health screen [BHS]).[50,52,55,59–61,76,77,83,84,89] Not all of the screens in these studies have specific psychometric validation data (eg, 2 depression questions on the GAPS). Clinicians may also consider the use of tools that can be used to screen for depression and other risk behaviors or more disorders. Although no researchers have compared the functional or depressive outcomes of a cohort of adolescents who were initially screened only for depression with a cohort of adolescents who were initially screened for an array of high-risk behaviors and emotional issues, some hint at the possibility that too much information may overwhelm the clinician and result in positive depression screening questions being overlooked in the morass of issues needing to be addressed.[52,53,59–61,64,76,80,82–84,89] Therefore, clinicians should base the selection of a depression-specific tool versus a more general tool on their own expertise and clinical supports in their practices. For example, a solo practitioner starting to address depression care in his or her practice may choose to start with screening for depression alone before moving to more general screening for riskier behaviors or disorders.

There is limited evidence to evaluate whether one can use a general parent questionnaire as a gated entry for adolescent self-report depression screening. Researchers in 1 study of general mental health screening used the parent- or youth-completed Pediatric Symptom Checklist-35 alone to screen for internalizing disorders, but this provides no psychometric data,[69] whereas others used the Parent Pediatric Symptom Checklist-17 (PSC-17) along with other, more depression-specific child and parent scales.[54,56,57,82] One of these studies reveals adequate psychometric data for the parent PSC-17 internalizing subscale as compared with the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS) MDD module, performing as well as the Children's Depression Inventory but only with children aged 8 to 15 years.[54] Richardson et al[56,57,82] suggest some correlation with adolescent depression self-report tools, with the adolescent scores that are higher on the PHQ-9 or PHQ-2 being associated with higher mean on the parent PSC-17 internalizing subscale, with a correlation of 0.21 ($P$ = .02). However, the data presented do reveal that some teenagers who scored above the cutoffs on the self-reports would have parents who score below the cutoff of 5 on the internalizing subscale of the PSC-17. The authors do not present the data regarding how many teenagers would be missed by using the internalizing subscale as a gate and whether those teenagers met DISC-IV MDD criteria. Lastly, researchers in 1 study looked at the correlation of the PSC-17 internalizing subscale between the parent- and youth-completed PSC-17 but only among subjects whose parents were already positive.[53] The data revealed low agreement, with a κ of 0.15 (95% confidence interval of 0.00–0.30). However, those adolescents who did match with their parents were of higher severity than those parents who were positive but did not match with their negative-scoring teenagers. In addition, the parent PSC-17 in general has usually been studied with the younger adolescent cohort and not the older adolescent cohort. Once again, there is no RCT in which researchers compare the outcomes of a cohort of adolescents who were universally screened with an adolescent depression self-report versus a cohort that was only screened with self-reports after a positive parent PSC result. All of these data reveal that there is limited evidence in the older teenage cohort about using parent reports alone, that parent information may be helpful if used in conjunction with child reports when a clinician is available to resolve discrepant data, and that if used alone, parent reports may only account for the adolescents with the most severe conditions, but those data are unclear.

Researchers have also looked at paper screens, Internet-based screens, and electronic screens that are accessed through a mobile or personal digital assistant device. Although there appears to be no evidence of researchers comparing such screening methods to each other, all methods seem to be equally successful (in that adolescents rarely refuse screening) and equally problematic (obstacles to universal screening exist with every method). See Supplemental Tables 1 and 2 for more specific information.

Some researchers report adaptive (brief initial questions and, if gated questions have positive results, then automated additional questions)[61] as well as algorithmic screening, in which a positive PHQ-2 result or the equivalent triggers a person to then administer a PHQ-9 or the equivalent.[65,75,79,85] Although evidence for this type of gated screening is limited, researchers in 1 study compared the psychometric data of the PHQ-2 versus the PHQ-9 in the same population.[57]

One limitation of brief depression screening may be the loss of the suicide questions if one focuses

only on brief questions on the basis of criterion A for MDD. The validation study of the PHQ-2 found that 19% of teenagers who did endorse suicidality did not screen positive on the PHQ-2, suggesting that in a real-world setting, they would have been missed.[57] Several studies in which researchers used brief or long depression-specific screenings that did not include a suicide question did add a suicide question for this reason.[60,70,83,84,89] In this review, we did not review the suicide screening in pediatric PC literature but are aware of the USPSTF decision not to endorse suicide screening secondary to its conclusion for the lack of evidence for PC intervention for suicidal adolescents.[90] However, we do note which depression screening studies also looked for suicide as well as the rates of suicidality that were found (Supplemental Tables 1 and 2).

One other area that was examined in the review is the definition of depression when screening for depression. The definition of depression affects the psychometric properties and evidence for the use of a screen given that trying to find only MDD versus trying to find any depressive symptoms requires different specificities and sensitivities, and using the same screens for both purposes would result in choosing different cutoffs. Again, whereas the USPSTF comments on screening for MDD, the screening literature seems to be more unfocused. Richardson et al[79] used a score of 2 as the initial gate and a score of 10 on the PHQ-9 as a positive score for entry into the next step. Forty percent of the sample did not meet the criteria for MDD but were deemed to be impaired enough with depressive symptoms to enter the study. When Lewandowski et al[74] studied the large-scale use of the PHQ-9 modified in the health maintenance organization (HMO), they looked at whether any depressive disorder was identified, even adjustment disorder, rather than just MDD. The Youth Partners in Care (YPIC) intervention[11,58] also included teenagers without MDD who had clinically significant and current depressive symptoms. Van Voorhees et al,[91] in a series of small studies and now in a large RCT, have been purposely screening to account for depressive symptoms and depressive disorders other than MDD because the Competent Adulthood Transition with Cognitive-behavioral, Humanistic and Interpersonal Training (CATCH-IT) prevention model was developed for teenagers with depressive symptoms and disorders other than MDD.[65] Thus, the evidence for choosing instruments and cutoff scores may depend on what depression end point a PC provider is pursuing and what intervention the clinician wishes to put in place.

Although the USPSTF clearly endorsed screening at age 12 years, the literature in which researchers look at depression screening includes studies that have starting ages ranging from age 8 to 14 years and later ages ranging from 15 to 24 years. Most of the younger-age studies include depression as part of a broader psychosocial screening effort, with the researchers looking specifically at depression screening that focuses on some of the older age ranges (Supplemental Tables 1 and 2). With that said, there is no evidence to compare outcomes in a cohort of adolescents who were screened at age 11 years versus age 12 years versus age 13 years.

The last guideline review included the YPIC study, which did reveal that an identification program in PC, when combined with high-quality depression treatment, actually yields better outcomes than treatment-as-usual conditions (when no high-quality depression treatment is available).[11] Two follow-up publications from the same intervention[58,87] are included in this review and once again show that identified youth who receive evidence-based treatment do have better outcomes. More recently, Richardson and colleagues, in their collaborative care for adolescent depression RCT, compared controls who screened positive and whose positive results were given to both parents and PC clinicians with subjects who were screened and placed in a collaborative care intervention.[79] Those in the collaborative care intervention had a greater chance of response and remission at 12 months and a greater likelihood of receiving evidence-based treatments. The researchers only tracked outcomes in those who were screened; although it is possible that those who were screened did better than those adolescents with depression who were not screened, the study does reveal that screening alone is not likely to improve outcomes by much given how much better those in the group that had screening combined with an intervention in place did and how much more likely they were to receive care than those who were only screened.

Although much of the literature on identification crosses both the area of screening and assessment in that the PC provider can use the screening tool to aid in the assessment, we found some studies that focused less on the screening tools and more on the assessment of depression in pediatric PC. These studies included those in which researchers used standardized patients to help with depression and suicide assessment as well as a protocol to teach PC clinicians how to do a therapeutic interview during the assessment process.[62,63,71–73]

In summary, no perfect depression screening and/or assessment tool exists, and no perfect screening algorithm or systematic protocol exists, but a number of adolescent depression assessment instruments do possess adequate psychometric properties to recommend their use in depression detection and assessment, and there is a limited amount of evidence to support some differing methods of implementation (Supplemental Table 3). Thus, it is reasonable to expect that depression detection in PC can be improved by the use of adolescent self-report checklists with or without parent self-reports. Reliance on adolescent self-report depression checklists alone will lead to substantial numbers of false-positive and false-negative cases. Screening and detection are only the first step to making a diagnosis. Instead, optimal diagnostic procedures should combine the use of depression-specific screening tools as diagnostic aids, buttressed by follow-up clinical interviews in which one obtains information from other informants (eg, parents) as legally permissible and uses either other tools or interviews to assess for other psychiatric diagnoses as well, reconciling discrepant information to arrive at an accurate diagnosis and impairment assessment before treatment. Although screening parents may not be required, gathering information from third-party collaterals to make a diagnosis is important. Teenagers should be encouraged to allow their parents to access their information, and the importance of including parents in the diagnostic discussion should be emphasized. For more information about rating scales and cutoff scores, please refer to the GLAD-PC tool kit.

### *Initial Management of Adolescent Depression*

On behalf of the initial GLAD-PC team, Stein et al[92] reviewed the literature on psychosocial interventions for anticipatory guidance. No RCTs or evidence-based reviews were found. Citing earlier literature reviews in the area of injury prevention[93] and anticipatory guidance,[94] Stein et al[92] found some limited evidence that anticipatory guidance strategies, such as education and counseling, in the PC setting can be effective.

Another area reviewed by Stein et al[92] involved psychosocial interventions for improved adherence. In an evidence review on asthma adherence, Lemanek et al[95] suggested that some educational and behavioral strategies are probably efficacious in creating change. In addition, a study in which researchers used cognitive behavioral strategies revealed that diabetic adherence can also be improved.[95]

For this update, our team searched the Cochrane Database of Systematic Reviews for all types of interventions that were implemented in the adherence arena. These reviews[96–98] revealed that only complex, multifaceted approaches that include convenient care, patient education, reminders, reinforcement, counseling, and additional supervision by a member of the care team were effective in improving adherence in different chronic medical conditions, including asthma, hypertension, diabetes, and adult depression. In the pediatric literature, research regarding adherence commonly involved interventions that targeted both patients and their families.[99] Several key components have been identified that may improve compliance and/or adherence, including patient self-management and/or monitoring, patient and/or family education and/or support, and the setting and supervision of management goals.[100,101] The identification and periodic review of short- and long-term goals provides an individualized plan that both the provider and the patient and family can follow over time.[100,101] Specifically in the area of youth depression, however, current research evidence reveals that only more complex interventions are likely to have the greatest impact on both adherence and treatment outcomes. This kind of coordinated care, which is often described as collaborative care or integrated behavioral health, is discussed further in the accompanying report on depression treatment and ongoing management.[102]

### *Safety Planning*

Safety planning with adolescent patients who have depression and are suicidal or potentially suicidal usually consists of instructing the family to remove lethal means, instructing the family to monitor for risk factors for suicide (including sexual orientation and intellectual disability), engaging the potentially suicidal adolescent in treatment, providing adolescents with mutually agreeable and available emergency contacts, and establishing clear follow-up. In our updated review of the literature, we found no trials in which researchers have studied the impact of or how to conduct any of these aspects of safety planning with adolescents with depression. Once again, no studies were found in which researchers examined the benefits or risks of a safety contract. Researchers in several articles reviewed what little literature is available regarding the use of suicide safety contracts, and all concluded that these should not be used in clinical practice because there is no empirical evidence that they actually prevent suicide.[103–107] Multiple authors also asserted that contracts have numerous flaws, which could actually be harmful to the clinician-patient alliance. Some alternatives to a contract have been proposed (for example, the commitment to treatment statement discussed by Rudd et al[107]), but none have been tested in a clinical trial. Some studies have suggested that

limiting access to firearms or other lethal means can decrease suicide by those methods, but the evidence is still unclear as to whether, on a broader population level, restricting access to certain lethal methods results in an overall decrease of suicide rates.[108–116] In addition, Brent et al[117] found that the families of adolescents with depression are frequently noncompliant with recommendations to remove firearms from the house. Yet, a small prospective follow-up of patients who were seen in an emergency department (ED) for mental health concerns found that the majority of their families removed or secured lethal means (firearms, alcohol, prescription medications, and over the counter medications) after injury-prevention education in the ED.[117] Some limited evidence suggests that quick and consistent follow-up and/or treatment with a team approach will be most helpful in increasing compliance and engagement among patients who are suicidal.[118–120]

## GUIDELINES

The strength of the evidence on which each recommendation is based has been rated 1 (strongest) through 5 (weakest) according to the Centre for Evidence-Based Medicine levels of evidence and paired with the strength of the recommendation (strong or very strong).

### Practice Preparation

**Recommendation 1:*PC clinicians are encouraged to seek training in depression assessment, identification, diagnosis, and treatment if they are not previously trained (grade of evidence: 5; strength of recommendation: very strong).***

Consistent with the original GLAD-PC guidelines, PC clinicians who manage adolescent depression are advised to pursue additional education in identification, assessment, diagnosis, treatment and follow-up, consent and confidentiality, safety risk assessment and management, liability, and billing practices. Appropriate training on the assessment, diagnosis, and treatment of adolescent depression enhances PC providers' attitudes and self-efficacy to treat youth depression within their practices, thereby making it more likely that psychological disorders will be identified in the patient population.[34] The REACH Institute and Child and Adolescent Psychology for Primary Care are examples of organizations that provide training opportunities to PC clinicians. In addition to high-quality content, studies of PC provider training reveal that effective information delivery methods are important to the successful uptake of new practice behaviors. Such training methods include a succinct presentation of high-priority information, interactive content delivery methods, hands-on learning activities (eg, role-plays), and cultivating peer leaders to champion new practices. Additionally, access to ongoing consultation after training allows learning to be tailored to the PC provider's actual practice[38] and can increase comfort with diagnosing and treating mental health issues.[33,39] Clinicians also need to practice self-care by using supports for themselves as they take on more responsibilities of caring for youth with depression because engaging with this population can prove to be emotionally challenging.

***Recommendation 2: PC clinicians should establish relevant referral and collaborations with mental health resources in the community, which may include patients and families who have dealt with adolescent depression and are willing to serve as a resource for other affected adolescents and their family members. Consultations should be pursued whenever available in initial cases until the PC clinician acquires confidence and skills and when challenging cases arise. In addition, whenever available, these resources may also include state-wide or regional child and adolescent psychiatry consultation programs (grade of evidence: 5; strength of recommendation: very strong).***

The lack of linkages among relevant services within a system of care is a large gap in the management of chronic disorders in young people.[121] Furthermore, family-based interventions have been shown to help youth with mental illness.[122] Therefore, establishing mental health referral and collaboration resources in the local community for adolescents with depression and their families is essential to ensuring timely and effective access to needed services.[11,123] Such linkages may include mental health sites to which patients can be referred for specialty care services, such as comprehensive evaluations, psychosocial treatment, pharmacotherapy, and crises intervention services (in the event of suicidality). In highly underserved areas, these linkages may also include paraprofessionals who are tasked with providing the bulk of supportive counseling services to local residents. To reduce barriers to care, PC providers may arrange to have standing agreements with these practices regarding referral, the exchange of clinical information, points of contact, and so on. Schools play a critical role, especially if therapeutic support is available. Clinicians should connect to any available resources in the school system. PC providers should also work with the patient and/or family to establish an individual education plan to provide supports for the teenager in the school setting. Other linkages may include online or in-person support groups, advocacy groups (eg, the American

Foundation for Suicide Prevention), and family partner organizations (ie, patients and/or caregivers who have experience dealing with adolescent depression and serve as a resource for affected adolescents and families whenever these services are available).

To provide support to PC providers, >25 states have established programs to promote collaboration between PC providers and child psychiatrists by providing PC providers with education, rapid access to consultation, and referral options. PC sites may wish to search registries such as the National Network of Child Psychiatry Access Programs (www.nncpap.org) to identify any regional or state-wide programs that are available in their areas.

### Identification and Surveillance

***Recommendation 1: Adolescent patients ages 12 years and older should be screened annually for depression (MDD or depressive disorders) with a formal self-report screening tool either on paper or electronically (universal screening) (grade of evidence: 2; strength of recommendation: very strong).***

Given the high prevalence of adolescent depression (lifetime prevalence is estimated to be ~ 20% by age 20 years), the evidence that adolescent depression can be persistent, the fact that adolescence is a time of significant brain maturation, and longitudinal studies that reveal that adolescents with depression have significant problems as adults, it is important to try to identify and treat adolescents with depression early in the course of the disorder. Although most PC clinicians believe it is their responsibility to identify depression in their adolescent patients, evidence suggests that only a fraction of these youth are identified when presenting in PC settings even after the USPSTF mandate on screening.[45] Extant evidence does suggest that screening with a systematic tool will identify more adolescents with depressive disorders than not screening at all. Providers should choose a tool with at least minimal validation data. Given that more evidence is needed to guide the choice of a depression screening tool, at this point, providers should choose a depression-only tool or a combined tool, a short tool as a gate or a longer initial tool, and an adaptive screening or a paper screen on the basis of what they believe will work better for their practices, patients, and health organizations. Furthermore, the current literature does reveal that screening and scoring before the provider is in the room with the patient can be most helpful to the workflow. Although both the USPSTF and the AAP support the universal use of an adolescent self-report screen, using a parent-completed PSC as an initial gate may be acceptable given the limited evidence. However, 1 limitation to gated depression screening, using either a short self-report or a longer parent psychosocial report as the initial gate, is the loss of the suicide questions that are part of longer adolescent self-reports. Given the high rate of suicidal ideation and attempts among adolescents and the fact that not all adolescents who are suicidal will have MDD, it seems likely that screening for suicidality may be helpful as well, so providers should consider including suicide questions. Choosing a cutoff score for the selected tool will need to depend on the practice's expected prevalence rates as well as the practice's available and accepted pathways for intervention. Although there is no evidence to suggest how often a teenager should be screened, screening once per year seems reasonable until more evidence is amassed, whether this takes place at health maintenance visits or at the next available sick visit. Finally, this recommendation should not discourage PC providers who regularly speak with their teenagers about their moods from continuing to do so and should not dissuade clinicians from learning how to better identify teens with depression through interview, but we merely endorse universal adolescent depression self-report instruments as an initial screening tool.

***Recommendation 2: Patients with depression risk factors (eg, a history of previous depressive episodes, a family history, other psychiatric disorders, substance use, trauma, psychosocial adversity, frequent somatic complaints, previous high-scoring screens without a depression diagnosis, etc) should be identified (grade of evidence: 2; strength of recommendation: very strong) and systematically monitored over time for the development of a depressive disorder by using a formal depression instrument or tool (targeted screening) (grade of evidence: 2; strength of recommendation: very strong).***

As part of overall health care, PC clinicians should routinely monitor the psychosocial functioning of all youth because problems in psychosocial functioning may be an early indication of a variety of problems, including depression. Risk factors that clinicians may use to identify those who are at high risk for depression include a previous history or family history of (1) depression, (2) bipolar disorder, (3) suicide-related behaviors, (4) substance use, and (5) other psychiatric illness; (6) significant psychosocial stressors, such as family crises, physical and sexual abuse, neglect, and other trauma history; (7) frequent somatic complaints; as well as (8) foster care and adoption.[124–126] Research evidence shows that patients who present with such risk factors are likely to experience future depressive episodes.[22,127–133] There are recent

data as well that reveal that those who score high on depression screening instruments, even when they are not initially diagnosed with depression, may be at risk for a depression diagnosis within 6 months.[66] Although these at-risk teenagers may be screened annually as part of the practice's universal depression screening, they may also require a more frequent, systematic, targeted screening during other health care visits (ie, well-child visits and urgent care visits). Following the chronic care model, teens with depression, past depression, frequent somatization, or other risk factors may need to be included in a registry and managed more closely over time.

### Assessment and/or Diagnosis

***Recommendation 1: PC clinicians should evaluate for depression in those who screen positive on the formal screening tool (whether it is used as part of universal or targeted screening), in those who present with any emotional problem as the chief complaint, and in those in whom depression is highly suspected despite a negative screen result. Clinicians should assess for depressive symptoms on the basis of the diagnostic criteria established in the* DSM-5 *or the* International Classification of Diseases, 10th Revision *(grade of evidence: 3; strength of recommendation: very strong) and should use standardized depression tools to aid in the assessment (if they are not already used as part of the screening process) (grade of evidence: 1; strength of recommendation: very strong).***

Scoring high on a screening tool alone does not make for a diagnosis of MDD, especially given that in a low-risk PC population, the PPV of a positive screen result may be low. However, as discussed earlier, a positive screen result can also indicate a different depressive disorder or subthreshold depression. On the other hand, in youth who are suspected of having depression on the basis of other initiating triggers, such as risk factors, somatic complaints, or other emotional chief complaints, assessing for depression (regardless of whether there is a positive screen result) may be in order. PC clinicians should probe for the presence of any of several depressive disorders, including MDD, persistent depressive disorder (dysthymia), and other specified or unspecified depressive disorders by using systematic, rigorous assessment methods. Although standardized instruments should be used to help with diagnosis, they should not replace direct interview by a clinician.[134–136] Because adolescents with depression may not be able to clearly identify depressed mood as their presenting complaint, providers need to be aware of common presenting symptoms that may signal MDD. These may include irritability, fatigue, insomnia or sleeping more, weight loss or weight gain, decline in academic functioning, family conflict, and other symptoms of depressive disorders.[137]

***Recommendation 2: Assessment for depression should include direct interviews with the patients and families and/or caregivers (grade of evidence: 2; strength of recommendation: very strong) and should include the assessment of functional impairment in different domains (grade of evidence: 1; strength of recommendation: very strong) and other existing psychiatric conditions (grade of evidence: 1; strength of recommendation: very strong). Clinicians should remember to interview an adolescent alone.***

Evidence of the core symptoms of depression and functional impairment should be obtained from the youth as well as from families and/or caregivers separately.[138–140] The involvement of the family is critical in all phases of management and should be included in the assessment for depressive disorders. If family involvement is determined to be detrimental, then involving another responsible adult would be appropriate. Family relationships may also affect the presentation of depression in adolescents. However, despite the importance of family involvement and the imperative to try to include family, adolescents value their sense of privacy, confidentiality, and individuality. It is important to remember that adolescents should be interviewed alone about their depressive symptoms, suicidality, and psychosocial risk factors and circumstances. The cultural backgrounds of the patients and their families should also be considered during the assessments because they can impact the presentation of core symptoms.[141] Collateral information from other sources (eg, teachers) may also be obtained to aid in the assessment. Given the high rates of comorbidities, clinicians should assess for the existence of comorbid conditions that may affect the diagnosis and treatment of the depressive disorder.[2,22,142,143] These comorbidities may include 1 or more of the following conditions: substance use, anxiety disorder, attention-deficit/hyperactivity disorder, bipolar disorder, physical abuse, and trauma. Instruments that assess for a range of common comorbid mental health conditions should be considered as well during this assessment phase if they were not used in the initial screening protocol. Clinicians should also assess for impairment in key areas of functioning, including school, home, and peer settings.[144] Subjective distress should be evaluated as well. Regardless of the diagnostic impression or any further treatment plans, a safety assessment, including

for suicidality, should be completed by the clinician (see recommendation 3 in Initial Management of Depression).

### Initial Management of Depression

***Recommendation 1: Clinicians should educate and counsel families and patients about depression and options for the management of the disorder (grade of evidence: 5; strength of recommendation: very strong). Clinicians should also discuss the limits of confidentiality with the adolescent and family (grade of evidence: 5; strength of recommendation: very strong).***

Management should be based on a plan that is developed with the understanding that depression is often a recurring condition. As seen in studies of depression interventions, families and patients need to be educated about the causes and symptoms of depression, impairments associated with it, and the expected outcomes of treatment.[145–148] Information should be provided at a developmentally appropriate level and in a way that the patient and family can understand the nature of the condition and the management plan. Communication that is developmentally appropriate should facilitate the ability of parents and patients to work with the clinicians to develop an effective and achievable treatment plan. To establish a strong therapeutic alliance, the clinicians should also take into account cultural factors that may affect the diagnosis and management of this disorder.[141] Clinicians should also be aware of the negative reactions of family members to a possible diagnosis of depression in a teen (ie, sadness, anger, and denial). Sample materials are available in the GLAD-PC and include resources for patients and parents. Because the symptoms of depression can also affect many areas of an adolescent's life, other ongoing partnerships may need to be established with personnel in schools and other settings (eg, extracurricular activities). Confidentiality should also be discussed with the adolescent and his or her family. Adolescents and families should be aware of the limits of confidentiality, including the need to involve parents or legal authorities when the risk of harm to the adolescent or others may be imminent. Clinicians should be aware of state laws regarding confidentiality (for additional information, see www.advocatesforyouth.org).

***Recommendation 2: After appropriate training, PC clinicians should develop a treatment plan with patients and families (grade of evidence: 5; strength of recommendation: very strong) and set specific treatment goals in key areas of functioning, including home, peer, and school settings (grade of evidence: 5; strength of recommendation: very strong).***

From studies of chronic disorders in youth, it is suggested that better adherence to treatment is associated with the identification and tracking of specific treatment goals and outcomes. Written action plans in asthma management have some evidence for improved outcomes.[149] Similarly, studies of adolescents with depression reveal greater adherence and outcomes when they were assessed to be ready for change and received their treatment of choice.[11,86] If a patient presents with moderate-to-severe depression or has persistent depressive symptoms, treatment goals and outcomes should be identified and agreed on via close collaboration with the patient and family at the time of treatment initiation. Treatment goals may include the establishment of a regular exercise routine, adequate nutrition, and regular meetings to resolve issues at home. In the adult depression literature, monitoring appears to be most effective when it is implemented through designated case managers who monitor patients' clinical status and treatment plan adherence.[12] The benefits of such programs may be enhanced through the use of electronic medical records (EMRs) and the development of patient registries. Technologies such as apps are being used more commonly in clinical practice, and there is emerging evidence for their effectiveness.[150]

***Recommendation 3: All management should include the establishment of a safety plan, which includes restricting lethal means, engaging a concerned third party, and developing an emergency communication mechanism should the patient deteriorate, become actively suicidal or dangerous to others, or experience an acute crisis associated with psychosocial stressors, especially during the period of initial treatment, when safety concerns are the highest (grade of evidence: 3; strength of recommendation: very strong). The establishment and development of a safety plan within the home environment is another important management step.***

Suicidality, including ideation, behaviors, and attempts, is common among adolescents with depression. In studies of completed suicide, more than 50% of the victims had a diagnosis of depression.[151] Therefore, clinicians who manage this disorder should develop an emergency communication mechanism for handling increased suicidality or acute crises. After assessing a patient for suicidality, the clinician should obtain information from a third party, assess that adequate adult supervision and support are available, have an adult agree to help remove lethal means (eg, medications and firearms) from the premises, warn the patient of the disinhibiting effects of drugs and alcohol, put contingency planning

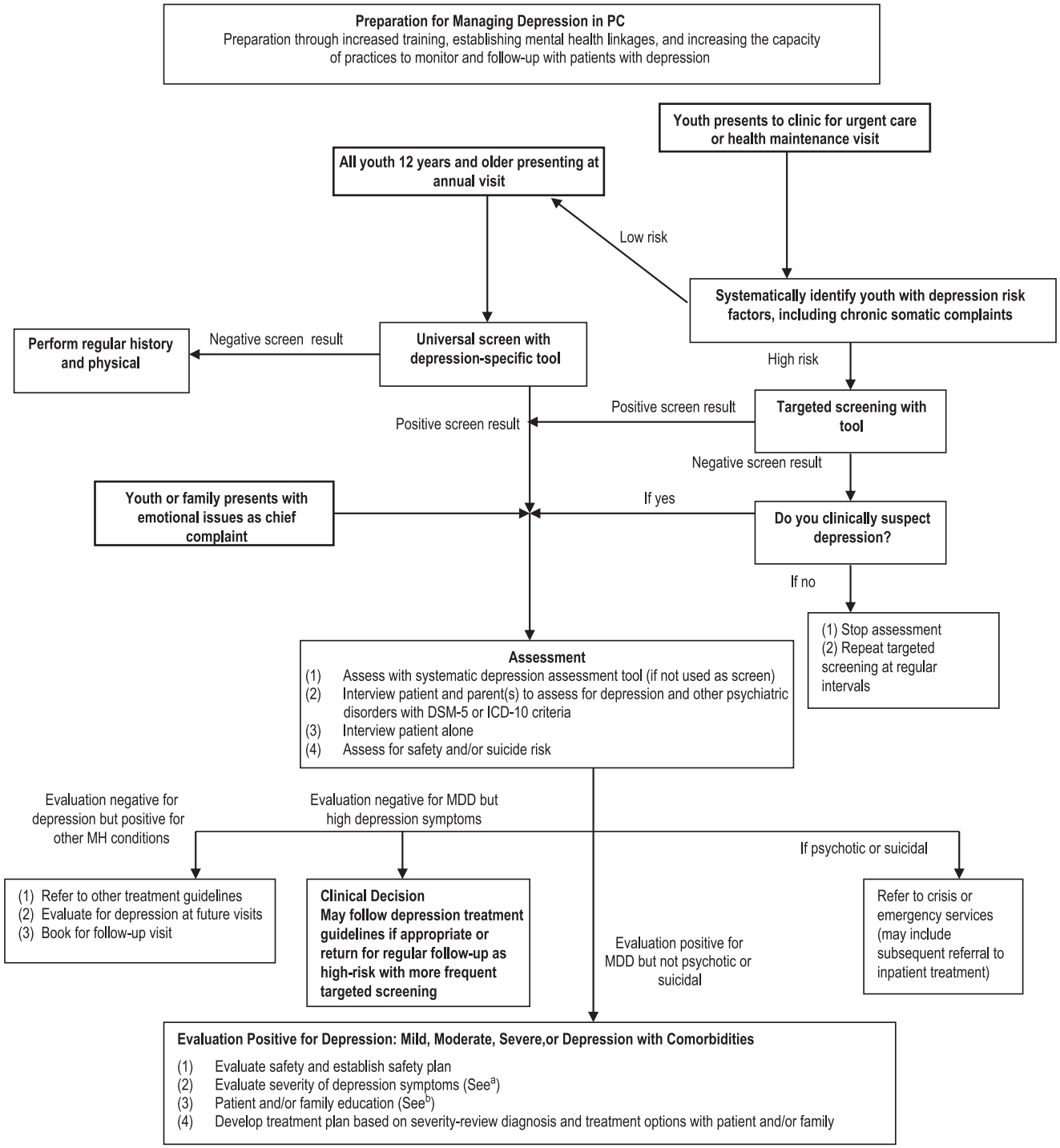


**FIGURE 1**

Clinical assessment flowchart. ICD-10, *International Classification of Diseases, 10th Revision*; MH, mental health. [a] See part I of the guidelines for definitions of mild, moderate, and severe depression. Please consult the tool kit for methods that are available to aid clinicians in distinguishing among mild, moderate, and severe depression. [b] Psychoeducation, supportive counseling, facilitation of parental and patient self-management, referring for peer support, and regular monitoring of depressive symptoms and suicidality.

in place, and establish follow-up within a reasonable period of time.[109,120,152,153] This plan should be developed with adolescents (and with their families and/or caregivers if possible) and should include a list of persons and/or services for the adolescent to contact in case of acute crisis or increased suicidality. The establishment of this plan is especially important during the period of diagnosis and initial

treatment, when safety concerns are the highest. It is critical for PC clinicians to make linkages with their closest crisis support and hospital services so that they are supported in crisis situations when caring for youth with depression. Clinicians may also work with schools to develop an emergency plan for all students who may experience acute suicidal crises. This global approach may prevent, in some instances, having to label a specific child as suicidal when providers are merely trying to ensure that safety measures are in place in case the child decompensates. Components of a safety plan may also include a list of persons who are aware of the adolescents' issues and will be able to assist if contacted during an acute crisis (Fig 1).

## DISCUSSION

Although not definitive and subject to modification on the basis of the ongoing accumulation of additional evidence, this part of the updated guidelines is intended to help address the lack of recommendations regarding practice preparation, screening, diagnosis, and initial management of depression in adolescents aged 10 to 21 years in PC settings in the United States and Canada. As such, these guidelines are intended to assist PC clinicians in family medicine, pediatrics, nursing, and internal medicine, who may be the first (and sometimes only) clinicians to identify, manage, and possibly treat adolescent depression. These guidelines may also be helpful to allied health professionals who care for adolescents.

Although not all the steps involved in identifying, diagnosing, and initially managing the care for adolescent depression in PC have been (or even can be) subject to rigorous RCTs, there is sound reason to believe that existing tools and management protocols for adolescent depression can be applied in the PC setting. Although more research is needed, we suggest that these components of the identification and initial management of adolescent depression in PC can be done. The recommendations were developed and updated on the basis of areas that had at least strong agreement among experts.

### Should These Guidelines Be Universally Deployed?

One might question whether PC clinicians should identify and diagnose the problem of adolescent depression if the lack of psychiatric services prevents them from referring these youth.[154] This caution notwithstanding, the increasingly prevailing recommendation is that at a minimum, PC clinicians should be provided the necessary guidance to support the initial management of adolescent depression.[155,156] Nonetheless, because practitioners and their clinical practice settings vary widely in their degree of readiness in identifying and managing adolescent depression, it is likely that a good deal of time and flexibility will be required before these guidelines are adopted systematically or as a universal requirement. It is conceivable that integrated health care systems with EMRs, tracking systems, and access to specialty mental health backup and consultation will be most ready and able to fully implement the guidelines. The second part of the guidelines, the companion article, addresses the treatment of depression. Practices that do identify adolescent depression and have nowhere to refer patients to may benefit from the guidance offered in the next set of recommendations.

### Preparatory Steps

Because the management of adolescent depression may constitute a new or major challenge for some PC practices, a number of important considerations should be kept in mind when preparing to implement the guidelines given the findings from studies in the adult literature; input from our focus groups of clinicians, families, and patients; and the experience of members of the GLAD-PC Steering Committee. Specifically, PC clinicians who manage adolescent depression should pursue the following: (1) additional training regarding issues such as advances in screening, diagnosis, treatment, follow-up, liability, consent, confidentiality, and billing; (2) practice and systems changes, such as office staff training and buy-in, EMRs, and automated tracking systems, whenever available; and (3) establishing linkages with mental health services.

Linkages with community mental health resources are necessary to both meet the learning needs of the PC clinicians and to facilitate consultation for and/or referral of difficult cases. Practice and systems changes are useful in increasing clinicians' capacity to facilitate monitoring and follow-up of patients with depression. For example, staff training may help prioritize calls from adolescent patients who may not state the nature of their call. Specific tools and/or templates have been developed that offer examples of how to efficiently identify, monitor, track, and refer teenagers with depression. These materials are available in the GLAD-PC tool kit. The tool kit addresses how each of the recommendations might be accomplished without each practice necessarily having to "reinvent the wheel."

## CONCLUSIONS

Review of the evidence suggests that PC clinicians who have appropriate training and are attempting to deliver comprehensive health care should be able to identify

and initiate the management of adolescent depression. This will likely require real changes in existing systems of care. As health care models such as the medical home indicate, comprehensive health care should include assessment and coordination of care for both physical and behavioral health issues. This first part of the guidelines for adolescent depression in PC may enable providers to pull together the current best evidence and deliver the best available, high-quality care even in instances when they are not in a position to treat such youth. Mounting evidence suggests that pediatric providers can and should identify and coordinate depression care in their adolescent populations.

## APPENDIX: PART I TOOLKIT ITEMS

- Screening/assessment instruments (i.e., Columbia Depression Scale)
- Information sheet on the developmental considerations in the diagnosis of depression
- Assessment Algorithm/Flow Sheet (Fig 1)
- Fact sheet/family education materials
- Educational materials on suicide prevention/safety planning

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## ABBREVIATIONS

AAP: American Academy of Pediatrics
BHS: Behavioral Health Screen
CATCH-IT: Competent Adulthood Transition with Cognitive-behavioral, Humanistic and Interpersonal Training
DISC-IV: Diagnostic Interview Schedule for Children-IV
DSM-5: *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*
ED: emergency department
EMR: electronic medical record
GAPS: Guidelines for Adolescent Preventive Services
GLAD-PC: Guidelines for Adolescent Depression in Primary Care
HMO: health maintenance organization
K-SADS: Kiddie Schedule for Affective Disorders and Schizophrenia
MDD: major depressive disorder
NPV: negative predictive value
PC: primary care
PHQ-2: Patient Health Questionnaire-2
PHQ-9: Patient Health Questionnaire-9
PPV: positive predictive value
PSC: Pediatric Symptom Checklist
PSC-17: Pediatric Symptom Checklist-17
RCT: randomized controlled trial
REACH: Resource for Advancing Children's Health
TCPS: Targeted Child Psychiatry Services
USPSTF: United States Preventive Services Task Force
YPIC: Youth Partners in Care

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# Guidelines for Adolescent Depression in Primary Care (GLAD-PC): Part I. Practice Preparation, Identification, Assessment, and Initial Management

Rachel A. Zuckerbrot, Amy Cheung, Peter S. Jensen, Ruth E.K. Stein, Danielle Laraque and GLAD-PC STEERING GROUP

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

Amy H. Cheung, MD,[a] Rachel A. Zuckerbrot, MD,[b] Peter S. Jensen, MD,[c] Danielle Laraque, MD,[d] Ruth E.K. Stein, MD,[e] GLAD-PC STEERING GROUP

## abstract

**OBJECTIVES:** To update clinical practice guidelines to assist primary care (PC) in the screening and assessment of depression. In this second part of the updated guidelines, we address treatment and ongoing management of adolescent depression in the PC setting.

**METHODS:** By using a combination of evidence- and consensus-based methodologies, the guidelines were updated in 2 phases as informed by (1) current scientific evidence (published and unpublished) and (2) revision and iteration among the steering committee, including youth and families with lived experience.

**RESULTS:** These updated guidelines are targeted for youth aged 10 to 21 years and offer recommendations for the management of adolescent depression in PC, including (1) active monitoring of mildly depressed youth, (2) treatment with evidence-based medication and psychotherapeutic approaches in cases of moderate and/or severe depression, (3) close monitoring of side effects, (4) consultation and comanagement 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 the grade of its evidence base are summarized.

**CONCLUSIONS:** The Guidelines for Adolescent Depression in Primary Care cannot replace clinical judgment, and they should not be the sole source of guidance for adolescent depression management. Nonetheless, the guidelines may assist PC 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 depressed youth in PC is needed, including the usability, feasibility, and sustainability of guidelines, and determination of the extent to which the guidelines actually improve outcomes of depressed youth.

FREE

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**FINANCIAL DISCLOSURE:** In the past 2 years, Dr Jensen has received royalties from the following publishing companies: Random House, Oxford, and APPI, Inc. He also is a part owner of a consulting company,

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## BACKGROUND

Studies have revealed that up to 9% of teenagers meet criteria for depression at any one time, with as many as 1 in 5 teenagers having a history of depression at some point during adolescence.[1–7] In primary care (PC) settings, point prevalence rates are likely higher, with rates up to 28%.[8–12] Taken together, in epidemiologic and PC-specific studies it is suggested that despite relatively high rates, major depressive disorder (MDD) in youth is underidentified and undertreated in PC settings.[13,14]

Because adolescents face barriers to receive specialty mental health services, only a small percentage of depressed adolescents are treated by mental health professionals.[15] 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 depression.[14–21] Although MDD management guidelines have been developed for specialty care settings (eg, the American Academy of Child and Adolescent Psychiatry[22]) or related problems such as suicidal ideation or attempts,[23] 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, in 2007, a group of researchers and clinical experts from the United States and Canada established 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 Part I of the original GLAD-PC articles.[24,25] In this article, we describe the updated recommendations regarding treatment, ongoing management, and follow-up, along with the supporting empirical evidence for these recommendations. In our companion article, we provide a detailed description of the update process as well as the corresponding updated recommendations for GLAD-PC regarding practice preparation, depression identification, assessment, and diagnosis, and initial management before formal treatment.

## METHODS

A full description of the methodology used for the update of GLAD-PC is included in our companion article. In brief, the expert collaborative used a mix of qualitative (expert consensus) and quantitative (literature reviews) methods to inform the update of GLAD-PC. In view of space limitations, only the methods and results of the updated literature reviews regarding available evidence for treatment and ongoing management are presented in this article.

The following 3 literature reviews were conducted for the updated GLAD-PC recommendations: (1) nonspecific psychosocial interventions in pediatric PC, including studies pertaining to integrated behavioral health and collaborative care models; (2) antidepressant treatment; and (3) psychotherapy interventions.

For the first review, we searched the literature (PubMed, PsycInfo, and the Cochrane Database) for articles published from 2005 to the present in which researchers examined evidence for psychosocial interventions delivered in the PC setting to update the previous review conducted by Stein et al.[26] The "related articles" function was used to search for articles similar to Asarnow et al[14] and Richardson et al.[27] In addition, reference lists of all relevant articles were also examined for other relevant studies.

In the second updated review, we examined the efficacy and safety of antidepressant medications in the pediatric population (under the age of 18 years). This review was used to update the findings from the US Food and Drug Administration (FDA) safety report[28] and the previously published GLAD-PC review on antidepressants in youth depression.[29] Studies in which researchers examined the management of depression with the use of antidepressants as both monotherapy and combination therapy were included.

In the third review, we searched the literature for depression trials in which researchers examined the efficacy of psychotherapy for the management of depression in children and adolescents. The search included all forms of psychotherapy, including both individual and group-based therapies. We not only identified both individual studies but also high-quality systematic reviews, given the extensive empirical literature in this area. In both the second and third reviews, the literature searches were conducted by using Medline and PsycInfo to find studies published between 2005 to the present. To ensure additional articles were not missed, reference lists of included articles were hand-searched for other relevant studies. A full description of the 3 reviews is available on request.

## RESULTS

### Organizational Adoption of Integrative Care

Within the past decade, there has been a shift in medicine and in mental health away from the "traditional" model of autonomous individual providers and toward delivering empirically supported interventions in a team-based manner. This followed a growing recognition that complex chronic conditions, such as depression,

are more successfully managed with proactive, multidisciplinary patient-centered care teams. Ongoing changes in the health care landscape helped to solidify support for this revolution. Systems are enacting top-down changes designed to make the entire delivery system (organizations, clinics, and providers) more effective, efficient, safe, and satisfying to both patients and providers.

Proposed integrated care models include "chronic care management," "integrated behavioral health care," "collaborative care," and "medical home." Here, the term "integrative care" will be used to collectively refer to models such as these. These complex care models share multiple features, such as an emphasis on systematically identifying and tracking target populations, multidisciplinary patient care, structured protocols for symptom management, regular follow-ups, decreasing fragmentation across the care team, and enhancing the patient's ability to self-manage their condition.[30] The following list represents many of the components described in 1 or more of these health care models:

1. a treatment team that includes the patient, the family, and access to mental health expertise;
2. education (including decision tools) for PC providers, patients, and family;
3. tools and/or procedures to systematically identify, assess, and diagnose patients who are at risk or are currently experiencing depressive symptoms;
4. a care plan for target patients (which may involve the family when possible and includes resources at other agencies or in the community);
5. improved communication and coordination of care across providers and/or between patient, family, and provider;
6. case management and/or patient and family support;
7. routine tracking of patient progress, with appropriate follow-up action as needed;
8. routine evaluation of staff performance metrics to inform ongoing quality improvement efforts; and
9. increased patient and family motivation and capacity to self-manage symptoms, including education, feedback, etc.

A variety of integrative care models have been proposed or discussed in the literature,[31,32] but few studies have actually been conducted to examine whether they ultimately improve care for children and adolescents with mental health disorders, broadly speaking, or depression, specifically. In the present review, only 3 randomized clinical trials were identified. In the first, Asarnow et al[14] found that adolescents treated for depression at PC clinics engaging in a quality improvement initiative received higher rates of mental health care and psychosocial therapy, endorsed fewer depressive symptoms, reported a greater quality of life, and expressed greater satisfaction with their care than comparison adolescents in a usual care condition. In a second study, researchers examined the additive benefits of providing brief (4-session) cognitive behavioral therapy (CBT) for depression in conjunction with antidepressant medication compared with medication alone in a collaborative care practice with embedded care managers and found a weak but positive benefit for adjunctive CBT.[33] Finally, Richardson et al[27] randomly assigned adolescents to either an integrative care condition, in which patients chose from a treatment menu of antidepressant medication alone, brief CBT alone, or a combination of the 2, versus usual care. Results revealed that integrative care was associated with significant decreases in depression scores and improved response and remission rates at 12 months compared with treatment as usual.[27] The results of a cost-effectiveness analysis of this trial revealed that the integrative care condition was more effective at reducing depression symptoms for adolescents, resulting in incremental cost savings given the quality of life years gained from improved functioning.[34]

Although research studies offer support for the impact of integrative or collaborative health care delivery models as a whole,[35] multiple changes to the practice setting are being evaluated simultaneously. The components of integrative health care models have largely been identified through practice-based research[36] or "best ideas" about how to solve identified problems, without a clear theoretical or empirical basis for these components individually or in combination. Thus, it is unknown what "active ingredients" account for the greatest proportion of variance in patient improvement because no dismantling studies have been conducted in which the relative impact of the individual components was examined. Given that integrated health care approaches are resource-intensive to implement and maintain, it may not be feasible for many PC practices to fully adopt such a model. Some states and communities have attempted to implement "wraparound services" under the "systems of care model"; however, unfortunately, these services are usually restricted to severely impaired children with chronic mental health problems. Nonetheless, such services are available if PC providers are interested.[37,38] Unfortunately, there is relatively little information to help guide prioritization and decision-making for PC clinics that wish to improve patient care within the constraints

of highly limited human and/or financial resources.

## Antidepressant Treatment

The updated treatment review for antidepressant safety and efficacy included randomized controlled trials (RCTs) of antidepressants in youth with depression. In this GLAD-PC review, we identified 27 peer-reviewed articles in this area, including trials with fluoxetine, sertraline, citalopram, paroxetine, duloxetine, and venlafaxine. In addition, in several studies, the switch from a selective serotonin reuptake inhibitor (SSRI) to venlafaxine, a serotonin norepinephrine reuptake inhibitor, was explored.[39–41] Older antidepressants (ie, monoamine oxidase inhibitors, tricyclic antidepressants) were not included in our updated review because of several reasons. First, the 2004 FDA review that was used for the development of the guidelines only involved newer classes of antidepressants. Second, older antidepressants are not used because of the lack of efficacy demonstrated in clinical trials data for other classes of older antidepressants.[42]

Overall, both individual clinical trial evidence and evidence from systematic reviews still support the use of antidepressants in adolescents with MDD. Bridge et al[43] conducted a meta-analysis of the clinical trials data and calculated the numbers needed to treat and numbers needed to harm. They concluded that 6 times more teenagers would benefit from treatment with antidepressants than would be harmed.[43] In reviewing the individual studies, the percentage of subjects who responded to antidepressants ranged from 47% to 69% and from 33% to 57% for those on placebo (see Table 1). The majority of these studies revealed a significant difference between those on medication versus those on placebo. Similarly, on the basis of the updated review, fluoxetine still has the most evidence to support its use in the adolescent population.[44]

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

| Medication | Drug, % | Placebo, % | *P* |
|---|---|---|---|
| Fluoxetine[45,a] | 56 | 33 | .02 |
| Fluoxetine[46] | 52 | 37 | .03 |
| Fluoxetine[47] | 61 | 35 | .001 |
| Paroxetine[48,b] | 66 | 48 | .02 |
| Paroxetine[49] | 69 | 57 | NS |
| Paroxetine[49] | 65 | 46 | .005 |
| Citalopram[50] | 47 | 45 | NS |
| Citalopram[51] | 51 | 53 | NS |
| Sertraline[52] | 63 | 53 | .05 |
| Escitalopram[53] | 63 | 52 | .14 |
| Escitalopram[54] | 64 | 53 | .03 |

NS, not significant.
[a] Fluoxetine alone compared with placebo.
[b] Paroxetine compared with placebo.

The largest study, the Treatment of Adolescent Depression Study, involved subjects who were randomly assigned to receive placebo, CBT alone, fluoxetine alone, or a combination treatment of CBT with fluoxetine.[45] Subjects assigned to receive combination treatment or fluoxetine alone showed significantly greater improvement in their depressive symptoms compared with those on placebo or those treated with CBT alone (also see subsection "CBT"). There is also a more rapid initial response when medication is initiated first or in combination with therapy.[55] The superiority of combination therapy is also demonstrated in adolescents with anxiety.[56,57] However, a few trials have revealed little extra benefit to combination therapy, but these findings might be confounded by the control therapy intervention (ie, routine specialist care).[58–60]

Combination therapy has also been evaluated in adolescents with treatment-resistant depression. In the Treatment of SSRI-resistant Depression in Adolescents study, researchers examined treatment options for adolescents aged 12 to 18 whose depression had not improved after 1 adequate trial of an SSRI.[39–41,49,61–63] Subjects were randomly assigned to 4 possible interventions: (1) switch to a different SSRI (citalopram, fluoxetine, paroxetine), (2) switch to a second SSRI in combination with CBT, (3) switch to venlafaxine, or (4) switch to venlafaxine in combination with CBT. Patients who received CBT and changed their medication to a second SSRI or venlafaxine had a higher response rate (54.8%; 95% confidence interval [CI]: 47%–62%) than changing the medication alone (40.5%; 95% CI: 33%–48%; $P = .009$). Additionally, there was no difference in response rate between venlafaxine and a second SSRI (48.2%; 95% CI: 41%–56%; and 47%; 95% CI: 40%–55%; $P = .83$) as well as no significant differences among Children's Depression Rating Scale–Revised improvements between treatment options.

Finally, with available evidence from RCTs, it is suggested that adverse effects do emerge in depressed youth who are treated with antidepressants.[45] Adverse effects (ie, nausea, headaches, behavioral activation, etc) were found to occur in most adolescents treated with antidepressants, with duloxetine, venlafaxine, and paroxetine as the most intolerable.[45] Therefore, routine monitoring of the development of adverse events is critical for depressed youth treated with antidepressants.

The most significant adverse effect of antidepressants is the emergence of

new onset or worsening suicidality, which was demonstrated in the FDA review in 2004.[29] The estimated risk of suicidality is 4% in those on medication versus 2% in those on placebo. However, further analyses of clinical trials data revealed that there is overall improvement in suicidality in subjects treated with antidepressants, with only a few subjects reporting worsening or new onset suicidality.[49] In the FDA review, it was also suggested that paroxetine and venlafaxine have a significantly higher risk for suicidality compared with other serotonergic antidepressants.

The doubling of risk of suicidality was also confirmed in population level studies.[63] However, studies have also revealed that almost all adolescents who die by suicide do not test positive for antidepressants in postmortem toxicology tests despite being prescribed these drugs.[64] Furthermore, Olfson et al[65] found an inverse relationship between rates of SSRI prescriptions and rates of suicide in adolescent populations.

## Psychotherapy

In the third review conducted, we examined the efficacy of psychotherapy, such as CBT, interpersonal psychotherapy for adolescents (IPT-A), as well as nonspecific interventions such as counseling and support. Through our search, we were able to identify both individual studies as well as several high-quality meta-analyses and/or reviews that were recently conducted to examine the efficacy of psychotherapy in adolescent depression.

### *CBT*

Numerous meta-analyses and reviews have been conducted on CBT in the treatment of adolescent depression and showed improved outcomes for subjects treated with CBT.[66–68] There are also several ongoing studies in which researchers are evaluating CBT in youth up to age 21.[69]

The effectiveness of CBT for adolescents with moderate to moderately severe depression was also evaluated in Treatment of Adolescent Depression Study, in which researchers randomly assigned 439 12- to 17-year-olds who were depressed to treatment with CBT, fluoxetine, CBT plus fluoxetine, or placebo.[45,70] According to Clinical Global Impressions severity scores, the posttreatment response rate to 15 sessions of CBT over 12 weeks (43.2%; 95% 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. Along with the fairly robust placebo-response rate, it is also possible that the nonspecific therapeutic aspects of the 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 is ineffective.

In another study with adolescents with depression, Fleming et al[71] evaluated the effectiveness of a computerized cognitive behavioral therapy (CCBT) intervention called SPARX in treating adolescents aged 13 to 16 years excluded from mainstream education ($n = 20$). After randomly assigning them to CCBT or the waitlist control, it was found that there were significantly greater reductions in Children's Depression Rating Scale and Reynolds Adolescent Depression Scale scores from baseline to week 5 for the intervention group compared with those who waited. In addition, the SPARX group was significantly more likely to be in remission or have a significant reduction in symptoms.

In several other studies, researchers have evaluated CCBT interventions and have also found similar results, with 1 study conducted in the PC setting.[72,73]

### *IPT-A*

In terms of IPT-A, only a handful of studies have been conducted. First, Tang et al[74] randomly assigned 347 adolescents who were depressed to receive IPT-A in schools or treatment as usual. IPT-A was found to have significantly higher effects on reducing severity of depression, suicidal ideation, and hopelessness compared with treatment as usual. In Gunlicks-Stoessel et al's[75] study, 63 adolescents who were depressed were randomly assigned to IPT-A or treatment as usual. Adolescents who were depressed who reported higher baseline levels of interpersonal difficulties showed a greater and more rapid reduction in depressive symptoms if treated with IPT-A compared with treatment as usual. In the most recent study,[76] 57 adolescents with depressive symptoms were randomly assigned to receive either 8 weeks of interpersonal therapy–adolescent skills training or supportive school counseling. Adolescents who were treated with interpersonal therapy–adolescent skills training showed significantly greater rates of change compared with adolescents who received school counseling on the Center for Epidemiologic Studies Depression Scale ($t[215] = -2.56$, $P = .01$), Children's Depression Rating Scale-Revised ($t[169] = -3.09$, $P < .01$), and the Children's Global Assessment Scale ($t[168] = 3.24$, $P < .01$).

## GUIDELINES

Each of the recommendations 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[1–5] system, with 1 to 5 corresponding to strongest to weakest evidence (see http://www.cebm.net/wp-content/uploads/2014/06/CEBM-Levels-of-Evidence-2.1.pdf/).

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 a "strong agreement" among experts (see Fig 1 for the treatment algorithm).

## Treatment

***Recommendation 1: PC clinicians should work with administration to organize their clinical settings to reflect best practices in integrated and/or collaborative care models (eg, facilitating contact with psychiatrists, case managers, embedded therapists). (grade of evidence: 4; strength of recommendation: very strong).***

There is a growing recognition that complex chronic conditions, such as depression, are most successfully managed with proactive, multidisciplinary, patient-centered care teams.[77,78] Proposed integrated care models include chronic care management, integrated behavioral health care, collaborative care, and medical home. These complex care models have been shown to be more effective in improving outcomes and share multiple features, such as an emphasis on systematically identifying and tracking target populations, decreasing fragmentation across the care team, and enhancing the patient's ability to self-manage their condition.

***Recommendation 2: After initial diagnosis, in cases of mild depression, clinicians should consider a period of active support and monitoring before starting evidence-based treatment (grade of evidence: 3; 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 with antidepressants and CBT show that a sizable percentage of patients respond to nondirective supportive therapy and regular symptom monitoring.[42,43,45,48,50,70,79] However, if symptoms persist, treatment with antidepressants or psychotherapy should be offered, whether provided by PC or mental health. Active support and monitoring is also essential in cases in which depressed patients and/or their families and/or 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 indicates that these strategies are a crucial component of management by PC clinicians. For further guidance on how to provide active support, please refer to the GLAD-PC toolkit (http://www.gladpc.org).

For moderate or severe cases, the clinician should recommend treatment; crisis intervention; patient and family support services, such as in-home or skill-building services (as indicated); and mental health consultation immediately, without a period of active monitoring.

***Recommendation 3: If a PC clinician identifies an adolescent with moderate or severe depression or complicating factors and/or conditions such as coexisting substance abuse or psychosis, consultation with a mental health specialist should be considered (grade of evidence: 5; strength of recommendation: strong). Appropriate roles and responsibilities for ongoing comanagement by the PC clinician and mental health clinician(s) should be communicated and agreed on (grade of evidence: 5; strength of recommendation: strong). The patient and family should be active team members and approve the roles of the PC and mental health clinicians (grade of evidence: 5; 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 mental health consultations more feasible, available, and affordable in underserviced areas, clinical judgment should prevail in the meantime; thus, the need for consultation should be based on the clinician's judgment. PC providers should also take into consideration the treatment preferences of patients and/or families, the severity and urgency of the case presentation, and the PC provider'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

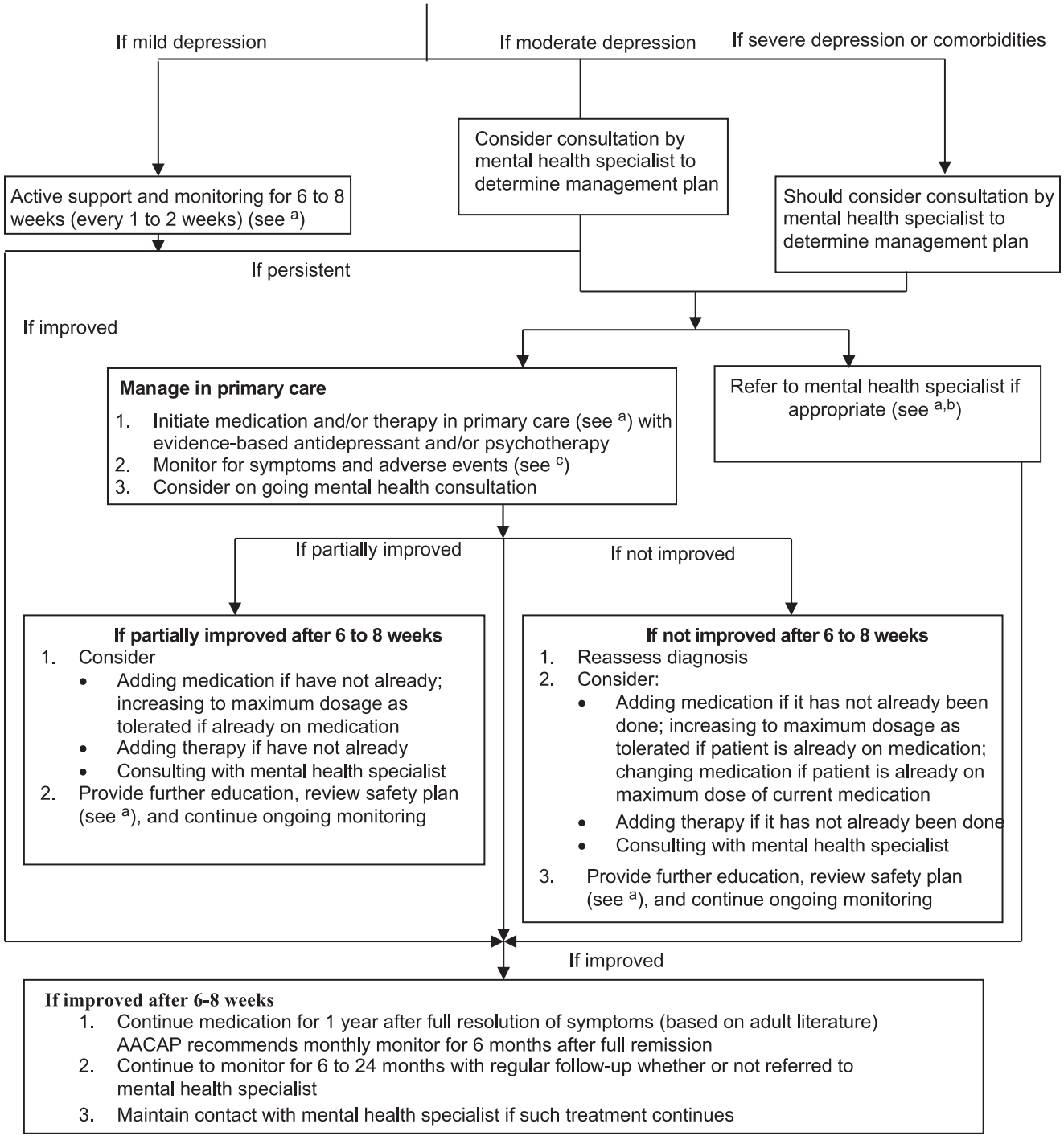


**FIGURE 1**

Clinical management flowchart. [a]Psychoeducation, supportive counseling, facilitate parental and patient self-management, refer for peer support, and regular monitoring of depressive symptoms and suicidality. [b]Negotiate roles and/or 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, please refer to the guidelines and/or toolkit. AACAP, American Academy of Child and Adolescent Psychiatry.

referral is made, comanagement of treatment should take place with the PC clinician remaining involved in follow-up. In particular, roles and responsibilities should be agreed on between the PC clinician and mental health clinician(s), including the designation of case coordination responsibilities.[48,50,77,78,80,81] It is critical for PC clinicians to make linkages with their closest crisis support and hospital services so that

they are supported in crisis situations when caring for depressed youth.

***Recommendation 4: PC clinicians should recommend scientifically tested and proven treatments (ie, psychotherapies, such as CBT or IPT-A, and/or antidepressant treatment, such as SSRIs) whenever possible and appropriate to achieve the goals of the treatment plan[82] (grade of evidence: 1; strength of recommendation: very strong).***

After providing education and support to the patient and family, the range of effective treatment options, including medications, psychotherapies, and family support should be considered. The patient and family should be assisted to arrive at a treatment plan that is both acceptable and implementable, taking into account their preferences and the 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 (www.gladpc.org) provides more detailed guidance around the factors that may influence treatment choices (ie, a patient with psychomotor retardation may not be able to actively engage in psychotherapy). A "common factors" approach is focused on evidence-based practices, which are common across therapies. Common factors include better communication skills, to be supportive, to take advantage of therapeutic alliance, and to engage in shared decision-making.[83] Common sense approaches such as the prescription of physical exercise, sleep hygiene, and adequate nutrition should also be used in the management of these patients.

As an aside, the majority of CBT and IPT-A studies in which researchers 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 the general treatment of depression is addressed in these guidelines, medication-specific guidelines apply only to fully expressed MDD.

**TABLE 2** Components of CBT and IPT-A

| Therapy | Key Components |
|---|---|
| CBT | Thoughts influence behaviors and feelings and vice versa. Treatment targets patient's thoughts and behaviors to improve his or her mood.<br>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 and/or caregivers to review progress and to 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 patient's interpersonal problems to improve both interpersonal functioning and his or her mood.<br>Essential elements of interpersonal therapy include identifying an interpersonal problem area, improving interpersonal problem-solving skills, and modifying communication patterns.<br>Parents and/or caregivers are involved in sessions during specific phases of the therapy. |

## Psychotherapies

Both CBT and IPT-A have been adapted to address depression in adolescents and have been shown to be effective in treating adolescents with MDD in tertiary care as well as community settings.[57,84] CBT has been used in the PC setting with preliminary positive results.[33,35] Also suggested in emerging evidence is the superior efficacy of combination therapy (medication and CBT) versus CBT alone.[43] 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.[15] When indicated by clinical presentation (ie, clear diagnosis of MDD with no comorbid conditions) and patient and/or 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. Deliberate self-harm and/or suicide risk is more likely to occur if the SSRI is started at higher doses (rather than normal starting doses).[85] The patient and family should be informed about the possible adverse effects (clinicians may use checklist), including possible switch to mania or the development of behavioral activation or suicide-related events. Once the antidepressant is started, and if tolerated, the clinician should support an adequate trial up to the maximum dose and duration.

In Table 3, recommended antidepressants and dosages for use in adolescents with depression are listed. These recommendations are based on the updated literature review and reviewed by the GLAD-PC Steering Committee. 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, and only escitalopram has been approved for use in adolescents aged 12 years and older. Clinicians should know the potential drug interactions with SSRIs. Further information on the use of antidepressants is described in the GLAD-PC toolkit (www.gladpc.org). In addition, all SSRIs should be slowly tapered when discontinued because of 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.

**TABLE 3** SSRI Titration Schedule

| Medication | Starting Dose (qd/od), mg | Increments, mg | Effective Dose, mg | Maximum Dosage, mg | Contraindicated |
|---|---|---|---|---|---|
| Citalopram | 10 | 10 | 20 | 60 | MAOIs |
| Fluoxetine | 10 | 10–20 | 20 | 60 | MAOIs |
| Fluvoxamine | 50 | 50 | 150 | 300 | MAOIs |
| Paroxetine[a] | 10 | 10 | 20 | 60 | MAOIs |
| Sertraline | 25 | 12.5–25 | 50 | 200 | MAOIs |
| Escitalopram | 10 | 5 | 10 | 20 | MAOIs |

MAOI, monoamine oxidase inhibitor; qd/od, every day once daily.
[a] Not recommended to be started in PC.

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 and/or family's access to educational materials regarding depression should be discussed during follow-up conversations. For relevant educational resources for patients and/or families, please refer to the GLAD-PC toolkit (www.gladpc.org).

***Recommendation 5: PC clinicians should monitor for the emergence of adverse events during antidepressant treatment (SSRIs) (grade of evidence: 3; strength of recommendation: very strong).***[82]

Re-analysis of safety data from clinical trials of antidepressants led to a black-box warning from the FDA regarding the use of these medications in children and adolescents in 2004 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.*

It should be noted, however, that there is no empirical evidence to support the requirement of face-to-face meetings per se. In fact, evidence from large population-based surveys reveals high reliability of telephone interviews with adolescent subjects for the diagnosis of depression.[86,87] Although obtaining a diagnosis is not the same as the elicitation of adverse events while in treatment, with this evidence, it is suggested that telephone contact may be just as effective in monitoring for adverse events. More importantly, a regular and frequent monitoring schedule should be developed, taking care to obtain input from the adolescents and families to ensure compliance with the monitoring strategy.[88,89] This may include monitoring of depressive symptoms, risky behaviors, and also functioning in the school setting, especially if an individualized education program is in place. Working closely with the family will ensure appropriate monitoring and help-seeking by caregivers.

## Ongoing Management

The strength of evidence on which each recommendation is based has been rated 1 (strongest) through 5 (weakest), according to the Oxford Centre for Evidence-Based Medicine levels of evidence, and paired with the strength of recommendation (Very strong [>90% agreement]), Strong [>70% agreement], Fair [>50% agreement], Weak [<50% agreement]).

***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. These include home, school, and peer settings (grade of evidence: 4; strength of recommendation: very strong).***

Goals should include both improvement in functioning 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 reveals that depressive symptoms and functional impairments may not improve at the same rate with treatment.[28,70] 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, it is ideal that patients are assessed in person within 1 week of the initiation of treatment. At every assessment, clinicians should inquire about each of the following: (1) ongoing depressive symptoms, (2) risk of suicide, (3) possible adverse effects from treatment (including the use of specific adverse-effect scales), (4) adherence to treatment, and (5) new or ongoing environmental stressors. In several studies, researchers have examined medication maintenance after response.[90–93] Emslie et al[93] randomly assigned 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 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 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[93] 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. Other studies have revealed similar benefits of prolonged treatment after acute response.[90–93]

With the limited evidence in children and adolescents and the emerging evidence in the adult literature in which it is suggested that antidepressant medication should be continued for 1 year after remission, both GLAD-PC and the American Academy of Child and Adolescent Psychiatry concluded that medication be maintained for 6 to 12 months after the full resolution of depressive symptoms.[22,90–93]

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.[22,93,94] 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 continues for up to 2 years after the full resolution of symptoms. Clinicians should obtain consultation from mental health professionals if a teenager develops psychosis, suicidal or homicidal ideation, and 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: 4; strength of recommendation: very strong). Mental health consultation should be considered (grade of evidence: 4; 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 or 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 a maximum therapeutic dose of an antidepressant medication, the clinician should consider changing the medication. Alternatively, if the patient has failed to improve on antidepressant medication or therapy alone, the addition of or switch to the other modality should be considered.

***Recommendation 3: For patients achieving 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: 4; 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 a SSRI (maximum tolerated dosage) and has shown only partial improvement, the addition of an evidence-based psychotherapy should be considered, if not previously initiated. Other considerations may include the addition of another medication, an increase of the dosage above FDA-approved ranges, or a switch to another medication as suggested in the Treatment of SSRI-resistant Depression in Adolescents study,[39] preferably done in consultation with a mental health professional. Likewise, if a patient's condition fails to improve after a trial of either CBT or IPT-A 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 referred to mental health services to ensure adequate management (grade of evidence: 5; strength of recommendation: very strong). PC clinicians may also consider sharing care with mental health agencies and/or professionals where possible (grade of evidence: 1; strength of recommendation: very strong). Appropriate roles and responsibilities regarding the provision and comanagement of care should be communicated and agreed on by the PC clinician and the mental health clinician(s) (grade of evidence: 4; 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.[95] Where possible, PC clinicians may consider sharing management of depressed adolescents with mental health agencies and/or professionals. There is emerging evidence from the literature about the greater effectiveness of "shared-care" models for the management of depression in the PC setting.[27,31,95–97] There is also increasing evidence to support that quality improvement strategies and techniques can change PC

practitioner behavior both in mental health and in other arenas.[98,99]

## DISCUSSION

The recommendations regarding treatment and ongoing management highlight the need for PC providers 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. In many of these clinical scenarios, PC providers should schedule systematic and routine follow-up, including mental health support when appropriate. The need for systematic follow-up, whether by PC provider or by mental health provider, is especially important in light of the FDA black-box warnings regarding the emergence of adverse events with antidepressant treatment.

Psychotherapy is also recommended as first-line treatment of adolescents who are depressed 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 to support that quality improvement projects involving psychotherapy can improve the care of adolescents who are depressed.[35]

GLAD-PC was developed and now updated on the basis of the needs of PC clinicians who are faced with the challenge of caring for depressed adolescents as well as 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 updated 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 (https://www.nice.org.uk/guidance/cg28). The updated GLAD-PC guidelines and the toolkit (www.gladpc.org) reflect the coming together of available evidence and the consensus 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 primary and specialty care clinicians. Therefore, it is critical that training programs for PC providers 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[89] (see http://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/Mental-Health/Pages/implementing_mental_health_priorities_in_practice.aspx). For providers who are currently practicing, continuing education should strengthen skills in collaborative work, and specifically, for PC providers, increase skills and knowledge in the management of depression.

## LIMITATIONS

Although the guidelines covered 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 the use of augmenting agents and treatment of subthreshold symptoms. New emerging evidence may impact on the inclusion of such areas in future iterations of the guidelines and the toolkit (available for download at www.gladpc.org). Many of these recommendations are made in the face of an absence of evidence or at lower levels of evidence.

## FUTURE DIRECTIONS

Ample evidence exists to support the notion that guidelines alone are insufficient in closing the gaps between recommended versus actual practices.[100,101] Thus, it will be necessary to identify effective methods for disseminating information and provide assistance to PC clinicians in changing practice. Researchers should 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. Researchers should also explore optimal methods for helping clinicians and their clinical settings address the range of obstacles that may interfere with the adoption of necessary practices to yield sustainable management of adolescent depression in PC settings.

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 involving mental health and PC are being implemented (National Network of Child Psychiatry Access Programs: www.nncpap.org; Massachusetts Child Psychiatry Access Program: https://www.mcpap.com/; Partnership Access Line; Training and Education for the Advancement of Children's Health).[102–106] However, the empirical support for these models is modest internationally; therefore, additional research is urgently needed.

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### ABBREVIATIONS

CBT: cognitive behavioral therapy
CCBT: computerized cognitive behavioral therapy
CI: confidence interval
FDA: Food and Drug Administration
GLAD-PC: Guidelines for Adolescent Depression in Primary Care
IPT-A: interpersonal psychotherapy for adolescents
MDD: major depressive disorder
PC: primary care
RCT: randomized controlled trial
SSRI: selective serotonin reuptake inhibitor

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