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International Committee on Mental Health in Cystic Fibrosis: Cystic Fibrosis Foundation and European Cystic Fibrosis Society consensus statements for screening and treating depression and anxiety

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ABSTRACT

Studies measuring psychological distress in individuals with cystic fibrosis (CF) have found high rates of both depression and anxiety. Psychological symptoms in both individuals with CF and parent caregivers have been associated with decreased lung function, lower body mass index, worse adherence, worse health-related quality of life, more frequent hospitalisations and increased healthcare costs. To identify and treat depression and anxiety in CF, the CF Foundation and the European CF Society invited a panel of experts, including physicians, psychologists, psychiatrists, nurses, social workers, a pharmacist, parents and an individual with CF, to develop consensus recommendations for clinical care. Over 18 months, this 22-member committee was divided into four workgroups: Screening; Psychological Interventions; Pharmacological Treatments and Implementation and Future Research, and used the Population, Intervention, Comparison, Outcome methodology to develop questions for literature search and review. Searches were conducted in PubMed, PsychINFO, ScienceDirect, Google Scholar, Psychiatry online and ABData by a methodologist at Dartmouth. The committee reviewed 344 articles, drafted statements and set an 80% acceptance for each recommendation statement as a consensus threshold prior to an anonymous voting process. Fifteen guideline recommendation statements for screening and treatment of depression and anxiety in individuals with CF and parent caregivers were finalised by vote. As these recommendations are implemented in CF centres internationally, the process of dissemination, implementation and resource provision should be closely monitored to assess barriers and concerns, validity and use.

INTRODUCTION

Original studies, meta-analyses and systematic reviews have shown that adults and children with chronic conditions, as well as parent caregivers, are at higher risk for depression and anxiety in comparison with community samples^{1 2} (see online supplementary appendix A). Cystic fibrosis (CF), a common genetic, life-shortening chronic illness, leading to frequent infections and progressive

Key messages

What is the key question?

► Given the high prevalence of depression and anxiety among individuals with cystic fibrosis (CF) and parent caregivers, the International Committee on Mental Health in CF (ICMH) tackled the question of how we can change clinical practice to improve mental health outcomes.

What is the bottom line?

► The ICMH is recommending that when annual screening shows elevated levels of depression and anxiety, clinical diagnostic procedures should be implemented, followed by evidence-based psychological and/or pharmacological interventions, if needed.

Why read on?

► International implementation of the guidelines, which were developed over nearly 3 years by a number of international experts, will address the needs of individuals with CF and parent caregivers, and will likely improve their health outcomes and quality of life.

failure of most organ systems (eg, lungs, pancreas) was the focus of our study.³ Despite recent advances in diagnosis and treatment, management of CF requires a complex, time-consuming daily regimen taking 2–4 h/day.⁴ Thus, CF continues to be one of the most difficult chronic conditions to manage.

There is strong consensus that depression is defined as “a mood disorder that affects the way a person feels, thinks or behaves, which impairs social or occupational functioning” (ref., 5 p.775). Central to this is depressed mood or loss of interest in most activities.⁶ Risk for suicide is a core component of depression, is a major cause of death among adolescents and adults in the general population and in recent Cystic Fibrosis Foundation (CFF) Registry data, 1.6% of deaths were



categorised as explicit suicide.⁷ Anxiety is a “state of intense apprehension, uncertainty, and fear resulting from the anticipation of a threatening event or situation to the degree that normal physical and psychological functioning is disrupted.”⁸ Procedural anxiety, which is particularly important for individuals with CF, has been defined as an acute and excessive fear of a medical or surgical procedure that results in acute stress or avoidance. Patients may experience anxiety in anticipation of or during procedures. Avoidance due to procedural anxiety can have negative health consequences.⁹

Studies measuring psychological distress in individuals with CF have found high rates of both depression and anxiety. The prevalence of depression ranges from 8% to 29% among children and adolescents, and 13–33% among adults;^{10–11} anxiety in adults has ranged from 30% to 33%.⁷ Caregivers have also reported elevations in depression scores ranging from 20% to 35%.¹² A recent study in nine countries screened 6088 patients with CF ages 12 years through adulthood and 4102 parents.¹³ Elevated symptoms of depression were found in 130 adolescents (10%), 913 adults (19%), 1165 mothers (37%), and 305 fathers (31%). Anxiety was reported by 281 adolescents (22%), 1503 adults (32%), 1496 mothers (48%), and 343 fathers (36%). Elevations were 2–3 times those reported in community samples. High rates of comorbidity were found between depression and anxiety symptoms across patient and parent samples. Further, among 1122 parent–teen dyads, adolescents were more than twice as likely to report elevated depression or anxiety if either parent was elevated.

Importantly, psychological symptoms in both patients and parents have been associated with decreased lung function,¹⁴ lower body mass index,¹⁵ worse adherence,^{10–16} worse health-related quality of life,¹⁷ more frequent hospitalisations and increased healthcare costs¹⁵ (see online supplementary appendix B). Given these high rates of depression and anxiety and their effects on quality of life and key health outcomes, the CFF and the European Cystic Fibrosis Society (ECFS) supported the formation of an International Committee on Mental Health in CF (ICMH).

METHODS

The CFF and ECFS formed a 22-member multidisciplinary committee including professionals, parents of individuals with CF and an adult with CF by invitation. They met in May 2013 and elected to focus on the assessment and treatment of depression and anxiety. Four workgroups were created: Screening; Psychological Interventions; Pharmacological Treatments and Implementation and Future Research. Each workgroup developed topic-specific questions using the Population, Intervention, Comparison, Outcome (PICO) format.¹⁸ These questions were reviewed and approved by the entire committee before literature searches were conducted.

The PICO questions were used to guide literature searches in PubMed, PsychINFO, ScienceDirect, Google Scholar, Psychiatry online and ABData conducted by a methodologist at the Dartmouth Institute of Health Policy and Clinical Practice at the Geisel School of Medicine at Dartmouth. Searches were limited to the English language and the period of 1960–2015. Standard textbooks were also consulted. Additional topic-relevant guidelines and reviews targeting general, chronically ill and CF-specific populations were identified through searches of the websites of organisations, including American Thoracic Society, Cochrane Collaboration, American Academy of Pediatrics, Agency for Healthcare Research and Quality, National Health and Medical Research Council, Canadian Psychiatric Association, National Institute for Health Care Excellence,

American Academy of Child and Adolescent Psychiatry, American Psychiatric Association, British Association for Psychopharmacology, World Federation of Societies of Biological Psychiatry and US Department of Veterans Affairs.

In April 2014, the committee reconvened to finalise the recommendation statements. A threshold consensus vote of 80% acceptance for each statement was set prior to the meeting. At the meeting, each workgroup presented draft recommendation statements and rationale to the full committee. After review and discussion of each statement, committee members voted anonymously. Review and voting continued until the 80% or higher acceptance rate was reached for each statement.

A preliminary version of the manuscript was distributed for public comment to the CF clinical, parent and patient communities in Europe and the USA. Feedback and comments were collected via a web-based survey. The committee reviewed and responded to this feedback.

RESULTS

A total of 21 756 references were retrieved in the creation of these recommendation statements. Of those, 980 abstracts and books were reviewed, and 344 articles were chosen for more in-depth review. Articles were excluded if they focused on children under the age of 7 because there is less evidence supporting screening and treatment of depression and anxiety in this age group. However, attention to the mental health of families from the time of diagnosis is recommended by other guidelines¹⁹ and in this review, we included articles on parents of children with CF from birth to adulthood. After review, key articles were selected to address the PICO questions under consideration by the committee. Articles not referenced in this document appear in the online supplementary appendices. Fifteen guideline recommendation statements for screening and treatment of depression and anxiety in individuals with CF and parent caregivers were finalised by vote (table 1).

PREVENTION

In the course of routine care, all individuals with CF and caregivers should be offered education and preventative, supportive interventions to promote effective coping skills and disease management. Care teams should provide support in a sensitive and empathic manner, paying attention to individual and family functioning, encouraging habits that promote good physical and mental health—including CF centres that are already using preventive interventions every day from the time of first diagnosis through the end of life, in the form of providing education about CF in a sensitive and empathetic manner, paying attention to individual and family functioning and coping and encouraging habits that promote good physical *and* mental health—including exercise, good nutrition, sleep hygiene and finding ways to balance the demands of CF with education, work and pleasurable activities that make life satisfying and meaningful.²⁰ Specific preventive strategies may be developed to reduce the risk of anxiety and depression in CF. For example, training in specific problem-solving and cognitive behavioural skills can decrease anxiety and improve resilience.^{9–21} See Recommendation 1 in table 1.

In addition, there are a number of painful medical procedures experienced by patients with CF, including blood draws and intravenous or peripherally inserted central catheter insertions, and behavioural approaches can reduce distress related to these procedures.⁹ For individuals with CF undergoing medical procedures, the ICMH recommends that behavioural approaches be used to reduce the risk of distress. See Recommendation 2 in table 1.

Table 1 Consensus statements

| Recommendation statement | Consensus (%) |
|--|---------------|
| Prevention | |
| 1. For all individuals with CF and caregivers, the CFF/ECFS International Committee on Mental Health in CF (ICMH) recommends that ongoing education and preventative, supportive interventions, such as training in stress management and the development of coping skills, aligned with appropriate developmental stage and disease events be offered. | 100 |
| 2. For all individuals with CF undergoing medical procedures, the ICMH recommends that behavioural approaches be used to reduce the risk of distress. | 100 |
| Screening | |
| 3. The ICMH recommends that children with CF ages 7–11 be clinically evaluated for depression and anxiety when caregiver depression or anxiety scores are elevated, or when significant symptoms of depression or anxiety in the child are reported or observed by patients, caregivers or members of the CF multidisciplinary team. | 100 |
| 4. The ICMH recommends annual screening for depression and anxiety with the PHQ-9 and GAD-7 for adolescents and adults with CF (ages 12–adulthood). | 100 |
| 5. The ICMH recommends offering annual screening for depression and anxiety to <i>at least</i> one primary caregiver of children and adolescents with CF (ages 0–17) using one of the following approaches listed below, depending on staffing and resources: | 100 |
| ▶ Screening with the PHQ-9 and GAD-7 | |
| ▶ Screening with the PHQ-8 and GAD-7 | |
| ▶ Screening with the PHQ-2 and GAD-2 | |
| Clinical Assessment | |
| 6. The ICMH recommends that any treatment for depression and anxiety in individuals with CF and caregivers be based on clinical diagnosis. | 100 |
| ▶ A healthcare provider with appropriate training and expertise should evaluate the clinical significance of elevated screening scores and presenting symptoms to perform a differential diagnosis before initiating treatment. | |
| 7. For caregivers of individuals with CF who have clinically significant symptoms of depression/anxiety, the ICMH recommends referral for treatment to primary care or mental health services after initial assessment with the CF team. | 100 |
| Intervention | |
| 8. For all individuals with CF and symptoms of depression/anxiety, the ICMH recommends a flexible, stepped care model of clinical intervention developed and implemented in close collaboration with patients and caregivers, the multidisciplinary CF team and other treatment providers or consultants, such as primary care or mental health specialists. | 100 |
| ▶ CF teams must identify who will be responsible to initiate and coordinate care and monitor treatment effects. | |
| 9. The ICMH recommends that in children with CF ages 7–11, who have clinically significant depression or anxiety, evidence-based psychological interventions are recommended as the first-line treatment. | 100 |
| 10. For individuals with CF ages 12–adulthood and mild depression or anxiety symptoms, the ICMH recommends education about depression/anxiety, preventative or supportive interventions and rescreening at the next clinic visit. | 100 |
| 11. For individuals with CF ages 12–adulthood and moderate depression or anxiety, the ICMH recommends offering or providing a referral for evidence-based psychological interventions, including CBT or IPT. | 100 |
| ▶ When psychological intervention is unavailable, declined or not fully effective, antidepressant treatment should be considered. | |
| 12. For individuals with CF ages 12–adulthood and severe depression, the ICMH recommends use of combined evidence-based psychological interventions and antidepressant pharmacotherapy. | 100 |
| 13. For individuals with CF ages 12–adulthood and severe anxiety, the ICMH recommends offering exposure-based CBT. | 100 |
| ▶ When exposure-based CBT is unavailable, declined or not fully effective, antidepressant medications can be considered. | |
| 14. The ICMH recommends that the SSRIs citalopram, escitalopram, sertraline and fluoxetine are appropriate first-line antidepressants for most individuals with CF, ages 12–adulthood, requiring pharmacotherapy. | 100 |
| ▶ In selecting an antidepressant and adjusting its dosage, close monitoring of therapeutic effects, adverse effects, drug–drug interactions and medical comorbidities is recommended. | |
| 15. The ICMH recommends that lorazepam be considered for short-term use in individuals with CF with moderate-to-severe anxiety symptoms, associated with medical procedures, who have not responded to behavioural approaches. | 100 |

CBT, cognitive behavioural therapy; CF, cystic fibrosis; CFF, Cystic Fibrosis Foundation; ECFS, European Cystic Fibrosis Society; GAD, Generalised Anxiety Disorder Questionnaire; IPT, interpersonal therapy; PHQ, Patient Health Questionnaire; SSRIs, selective serotonin reuptake inhibitors.

SCREENING

Care pathways and provision of high-quality care for depression/anxiety should be in place *prior* to implementation of a screening programme.²² Given that models of healthcare delivery and availability of resources differ worldwide, it is difficult to specify the qualifications and training of the team member who will assess and treat mental health issues.²² In Europe, CF teams can consult the ECFS Standards of Care documents,²⁰ but in the USA this document does not exist and the designated professional may be a social worker, nurse practitioner, psychologist or psychiatrist. Before initiating annual screening, CF Teams should (1) identify a clinician with specialised expertise and training in mental health (e.g., licensed social worker, psychologist, psychiatrist), (2) develop educational materials on the importance of assessing and treating depression and anxiety and (3) develop a list of referral sources within the hospital and surrounding community. A plan to address suicidal ideation,

which can be associated with depression, should also be established (eg, clinical assessment or interview, visit to emergency department). See online supplementary appendix C for a Manual of Procedures and Toolkit for Implementation.

Evidence from The International Depression Epidemiological Study (TIDES) indicated that when a parent reported elevated depressive or anxious symptoms, the adolescent with CF was more than twice as likely to also experience depression and anxiety.¹³ There is limited guidance on routine screening of younger children below age 12. Thus, for children with CF, ages 7–11, whose parents score in the elevated range or who themselves have clinical concerns, referrals for screening or clinical assessment for these younger children should be made to mental health experts in the CF team, in the hospital or in the community. See Recommendation 3 in table 1.

The US Screening Guidelines recommend universal screening for depression in adolescents and adults and the UK

recommends screening for high-risk populations.^{6 5 23–26} In addition, chronic disease practice guidelines⁹ recommend mental health screening because of their link to worse health outcomes. These practice guidelines, in combination with recent screening evidence in CF,¹³ support our recommendation for annual screening of depression and anxiety in patients with CF ages 12 years and older and parent caregivers of children with CF aged from birth to 17 years of age.

Internationally, more than 48 different screening tools were in use at CF centres.²² To standardise the screening process using reliable, valid measures that yield clinically relevant scores, the committee recommends the use of the Patient Health Questionnaire 9 (PHQ-9), which includes an item to assess suicide risk, and Generalised Anxiety Disorder 7-item (GAD-7) Scale for annual screening of adolescents (ages 12 years and older) and adults with CF and offered annually to at least one primary caregiver of children with CF (ages 0–17 years). The PHQ-9 and GAD-7 are free, brief, reliable and valid, with optimal cut-off scores for detecting psychological symptoms, map onto current diagnostic criteria Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5)⁸ and are available in all major languages.

Guidelines from US and UK societies advocate for the use of PHQ-9 when appropriate diagnostic, treatment and follow-up services are available.^{6 24 25 27} The PHQ-9 is also recommended for depression severity assessment.⁸ When screening anxiety, UK societies endorse the use of the GAD-7.²⁸ Figure 1 outlines the meta-strategy for screening and treating depression and anxiety.

A brief explanation and discussion of the rationale for screening mental health issues is recommended for all patients and parent caregivers, followed by administration of the PHQ-9 and GAD-7 (<http://www.phqscreeners.com/>). For caregivers, centres that do not have the resources or expertise to assess suicidality may choose to omit the question on the PHQ-9 that assesses self-harm and administer the PHQ-8. An alternative approach is to use two items from the PHQ-9 on low mood and anhedonia (PHQ-2, http://www.cqaimh.org/pdf/tool_phq2.pdf) and two items from the GAD-7 on feeling anxious/nervous and not being able to stop or control worrying (GAD-2, http://depression.acponline.org/content/all/tools/dcg_o11.pdf). See Recommendations 4 and 5 in table 1.

CLINICAL ASSESSMENT

We recommend that a mental health specialist (eg, a licensed social worker, psychologist, psychiatrist) perform the screening. However, there may be other providers (eg, nurse, physician), with additional training or consultation, who can conduct the screening. Individuals with CF who screen positive for depression/anxiety must have a clinical assessment prior to initiation of or referral for treatment to identify the presence, duration and severity of these symptoms, as well as prior history and risk factors. Severity of CF, prior history of depression or anxiety, previous treatment and response to treatment(s), family history of psychiatric illnesses, comorbid psychiatric diagnoses and the presence of other chronic illnesses should be assessed. Treatment decisions should be based on clinical diagnosis and not solely on the screening results. CF healthcare professionals should decide when referral to a trained mental health professional is required.

All caregivers who screen positive and have clinically significant symptoms of depression/anxiety should be advised to follow up with their primary care provider or mental health services (outside the CF centre), with provision of referrals as needed. Although some CF centres may have the expertise and

resources to treat parental depression and anxiety within their centre, this will not be the case in a majority of countries. Thus, we are recommending provision of psychological services for parents outside the CF team.

For patients or caregivers who screen positive for suicide risk (Question 9 on the PHQ-9), the designated mental health expert in the CF team should follow up immediately to determine the severity. This should include a clinical interview or further assessment. There are formal tools, such as the Columbia Suicide Severity Rating Scale (C-SSRS; <http://www.ccrs.columbia.edu/ccsrs.html>), which can also be used to evaluate this risk. This measure is free, well validated and available in over 100 languages. This tool was designed for use by ‘lay professionals’ (eg, teacher, law enforcement) and has an on-line training course and certification available. It is appropriate for children, adolescents and adults.²⁹ See Recommendations 6 and 7 in table 1.

INTERVENTION

A variety of international authorities and professional associations have issued evidence-based guidelines for the treatment of depression and anxiety in the general population and in those with chronic illness (see online supplementary appendix D tables 1 and 2). Given that minimal research has specifically examined the treatment of depression and anxiety in CF,³⁰ the ICMH used developmentally appropriate, existing guidelines to frame CF-specific recommendations. Although treatment plans should consider potential adverse effects and overall burden of care, the risks of *not* treating depression or anxiety are often heightened in individuals with CF leading to worse adherence to CF treatments and increased healthcare utilisation and costs.^{10 15 17}

Treatment plans for depression/anxiety must be developed and implemented in close collaboration with patients and caregivers, the multidisciplinary CF healthcare professionals and other providers, such as primary care or mental health specialists. Figures 2 and 3 illustrate a flexible stepped care model for prevention, screening and intervention for individuals with CF and caregivers. Factors such as patient age, screening scores, clinical assessment, functional impairment and safety should be considered in developing a treatment plan. In addition, interventions should be adjusted to account for patient/caregiver preferences, medical status, psychiatric comorbidities, treatment history, resource availability, access to treatments and local practice patterns. See Recommendation 8 in table 1.

The PHQ-9 and GAD-7 can be used both to screen these symptoms and to assess and monitor treatment response and adequacy of the treatment plan. If depression or anxiety symptoms continue to be elevated or functioning remains impaired 12 weeks later, additional or alternative interventions should be offered until symptoms return to within normal range.

Depending on the clinical context, the differential diagnosis in individuals with symptoms of depression and anxiety may include bipolar disorder, post-traumatic stress disorder, delirium, substance abuse or disease-related factors, such as fatigue, sleep disturbance, dyspnoea, pain³¹ and vitamin D deficiency.³² Concomitant CF symptoms should be actively treated while depression and anxiety are being addressed. CF pulmonary exacerbations may worsen depression and anxiety through multiple biopsychosocial mechanisms, including the adverse impact of demoralisation, stress and inflammation.³³

Considering the limited evidence for psychopharmacological treatment of depression and anxiety in children, psychological interventions tailored to individual and family needs are

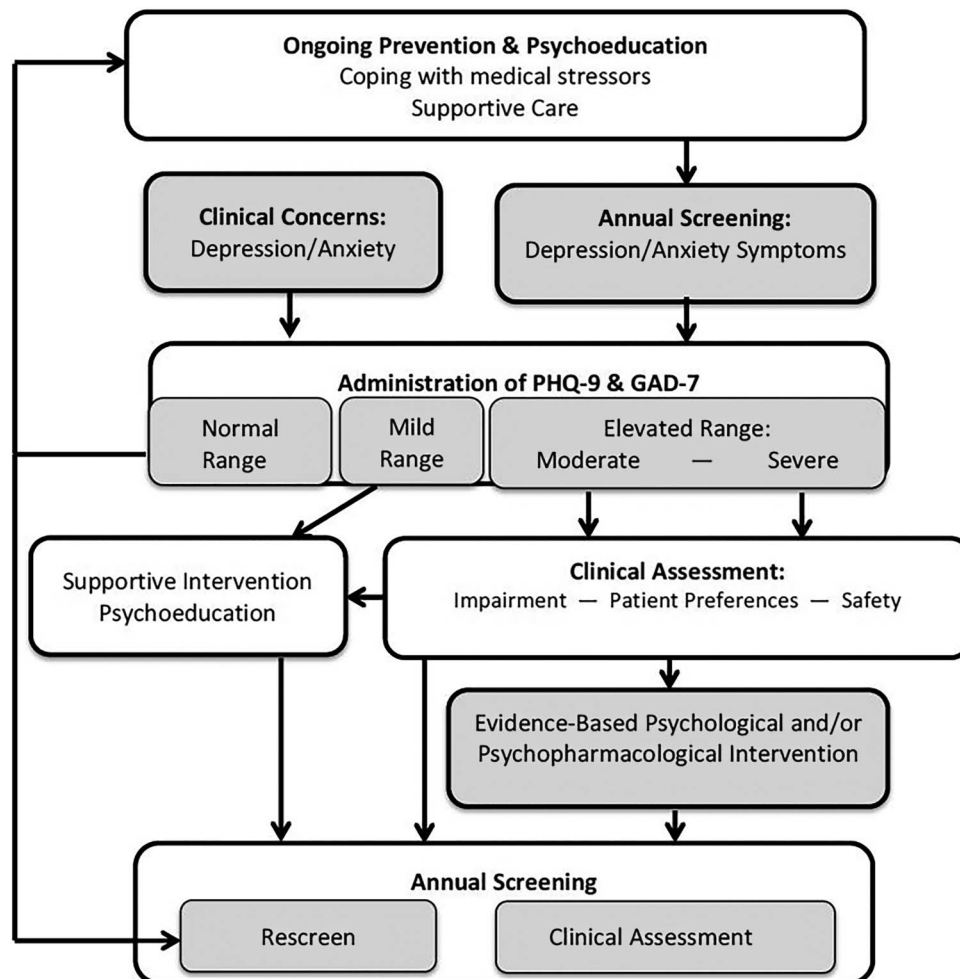


Figure 1 A flexible, stepped-care model for assessing and treating depression and anxiety.

recommended as the first-line approach in all children with CF ages 7–11 who require treatment. Specialised consultation should be obtained if psychological interventions are not sufficiently effective. See Recommendation 9 in [table 1](#).

Psychological interventions

Adolescents and adults with CF (ages 12 and above) whose depression or anxiety is in the mild range should receive education, preventive or supportive psychological interventions and rescreening at the next CF visit. Evidence-based psychological interventions should be offered to all adolescents and adults with CF whose depression or anxiety is of at least moderate severity. An extensive body of literature supports the efficacy and effectiveness of cognitive behavioural therapy (CBT) for the treatment of both depression and anxiety, whereas some evidence indicates that interpersonal therapy (IPT) is an effective treatment for depression (see online supplementary appendix D [tables 1–3](#)).⁶ CBT is a psychotherapeutic approach that addresses dysfunctional emotions, behaviours and cognitions. It combines cognitive interventions (ie, challenge and replace negative thoughts with more functional cognitions) with the principles of behaviour modification (eg, training of skills and behaviours, using classical and operant learning principles).³⁴ See Recommendations 10 and 11 in [table 1](#).

Education and cognitive restructuring are included in CBT interventions for both depression and anxiety, whereas behavioural activation (eg, engaging in pleasant activities) is an

additional core ingredient of most CBT manuals for the treatment of depression. Relaxation training and gradual exposure to triggers of anxiety are considered essential components of anxiety-specific CBT. IPT is a short-term treatment that encourages patients to regain control of mood and functioning. It is based on a treatment alliance in which the therapist empathically engages the patient, helps the patient feel understood and structures success experiences.³⁵ Comparisons of CBT and IPT suggest there is broader empirical support, dissemination and training and worldwide adoption of CBT versus IPT. CBT has also demonstrated efficacy in treating comorbid depression and anxiety, which occur commonly among those with CF.¹³

Pharmacological interventions

In individuals with CF, antidepressant medication should generally be prescribed in conjunction with psychological interventions, as part of a comprehensive treatment plan. For those with severe depression, evidence supports the combined use of antidepressants and psychological interventions as the most effective initial therapy.³⁶ For adolescents and adults with CF who report moderate depression or moderate-to-severe anxiety, antidepressant medication should be considered when psychological interventions are not feasible or fully effective (see [figures 2 and 3](#)). See Recommendations 11, 12 and 13 in [table 1](#).

When pharmacotherapy is needed, the selective serotonin reuptake inhibitors (SSRIs) citalopram, escitalopram, sertraline

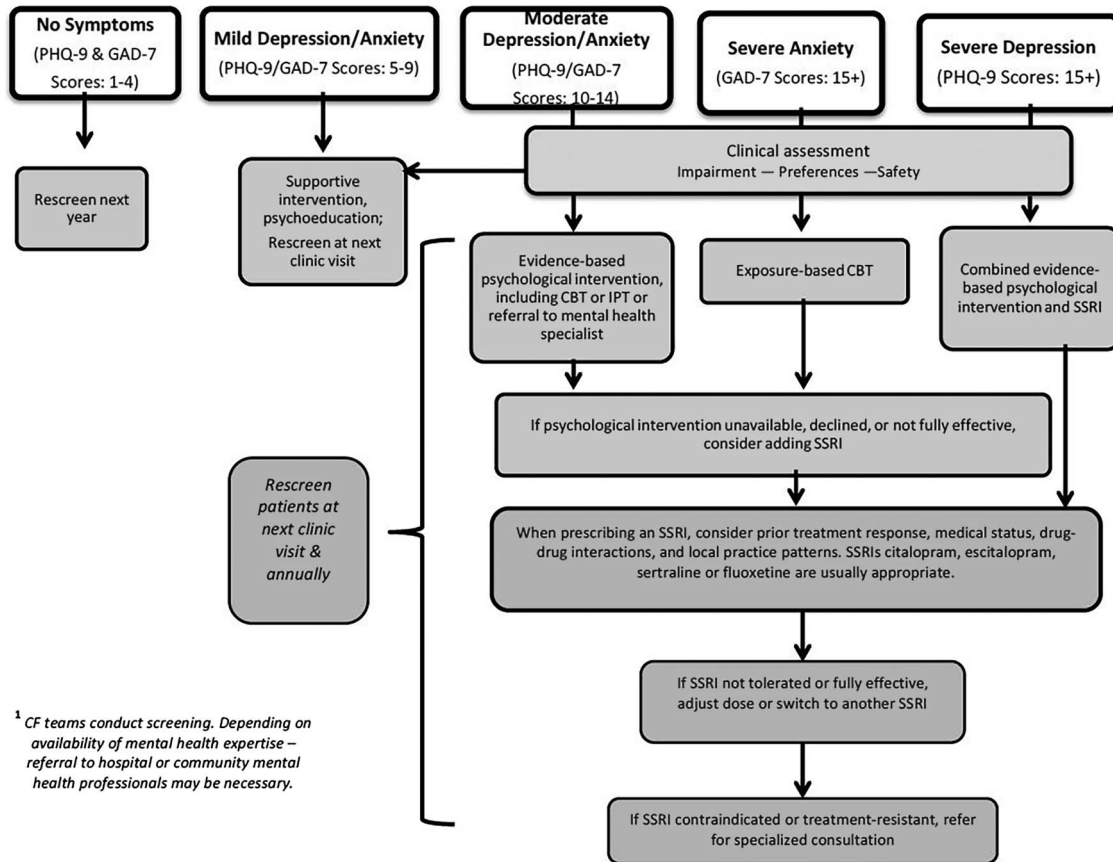


Figure 2 Screening and treatment of depression and anxiety: algorithm for individuals with cystic fibrosis (CF) (ages 12–adulthood). CBT, cognitive behavioural therapy; GAD-7, Generalised Anxiety Disorder 7-item Scale; IPT, interpersonal therapy; PHQ-9, Patient Health Questionnaire 9; SSRI, selective serotonin reuptake inhibitor.

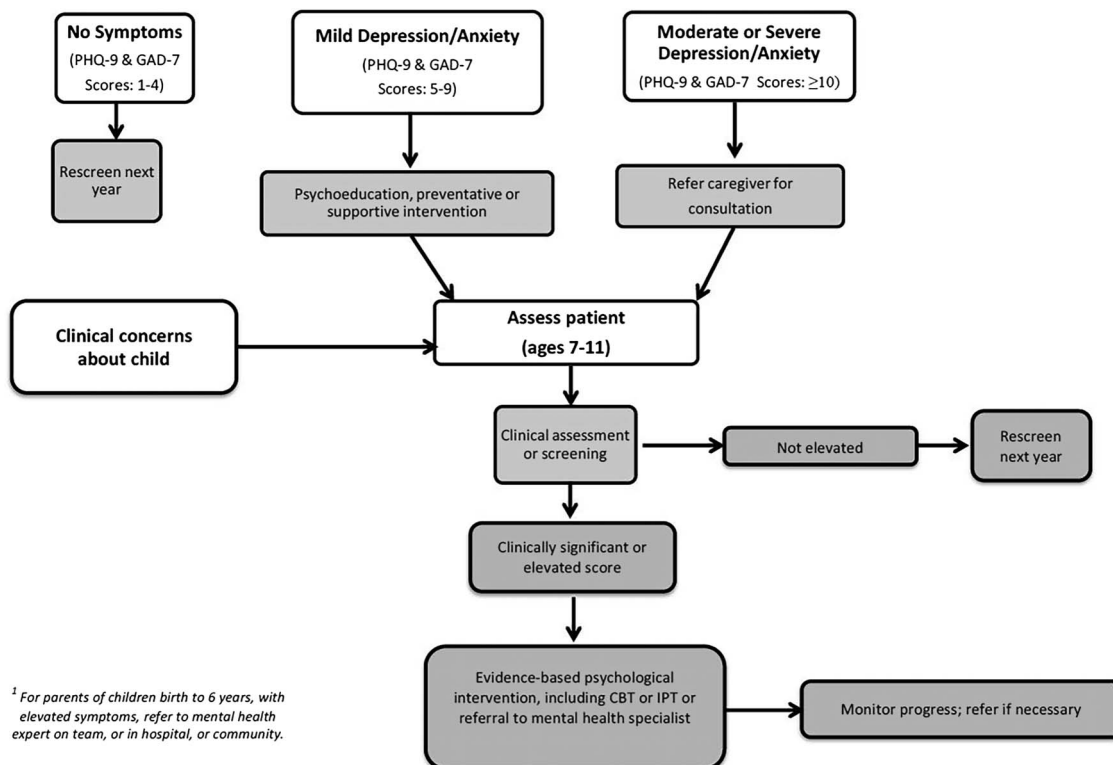


Figure 3 Screening and treatment of depression and anxiety: algorithm for parents/caregivers. CBT, cognitive behavioural therapy; GAD-7, Generalised Anxiety Disorder 7-item Scale; IPT, interpersonal therapy; PHQ-9, Patient Health Questionnaire 9.

and fluoxetine are appropriate initial choices for most adolescents and adults with CF (see online supplementary appendix D and table 4). The ICMH sought to identify a short list of medications with strong evidence for their use in medical populations. SSRIs, although commonly referred to as antidepressants, are recommended by virtually all published guidelines as first-line medications for *both* depression and anxiety. Given the frequent co-occurrence of depression and anxiety in CF,¹³ the effectiveness of SSRIs in treating either condition or both simultaneously is advantageous; this has not been demonstrated for many alternative antidepressants or anti-anxiety agents. Among the SSRIs and alternative agents, citalopram, escitalopram, sertraline and fluoxetine are more likely to be available inexpensively in many countries, covered by health plans, have regulatory approvals in a variety of age groups and minimise the potential for medication interactions and side effects. See Recommendation 14 in table 1.

Since the pharmacokinetics of medications may be altered in CF and may be variable across individuals, optimal dose adjustment of psychopharmacological agents requires close monitoring of therapeutic benefits, adverse effects and medical status. In CF, pulmonary, gastrointestinal/hepatic, renal and nutritional changes are particularly salient. Dose reduction may be required in individuals with renal or hepatic impairment, treatment-emergent adverse effects or drug–drug interactions. Dose increases may be required for those with impaired absorption or enhanced hepatic metabolism, partial response to treatment or drug–drug interactions. Therapeutic drug monitoring of blood levels, when available, may supplement clinical monitoring of psychotropic medication dosing. See Recommendation 14 in table 1.

To reduce the risk of drug–drug interactions, prescribing clinicians should be informed of all medications used daily, regularly cycled or used periodically for CF exacerbations. For example, when used with lumacaftor, the doses of citalopram, escitalopram and sertraline may need to be increased. Linezolid is not recommended for use with serotonergic antidepressants when alternatives are readily available. When both are clinically necessary, the lowest effective doses should be used, with informed consent and monitoring for serotonin syndrome. QTc prolongation, while not usually clinically significant, is more likely with citalopram than other SSRIs; electrocardiogram (EKG) and electrolyte monitoring can be considered when simultaneous use of multiple medications known to prolong the QTc is clinically necessary.³⁷

Anxiety in relation to medical procedures

For moderate-to-severe episodic anxiety associated with medical procedures that have not responded to behavioural approaches, the benzodiazepine lorazepam may be considered for short-term use. Benzodiazepines require additional caution and monitoring for those with a history of substance abuse, depression or an elevated risk for respiratory depression, and local practice patterns differ regarding their use to treat anxiety. Benzodiazepines are preferable to SSRIs primarily when rapid onset of action is needed or when serotonergic agents are contraindicated. Lorazepam is available in both oral and intravenous forms, and its duration of action is short enough to avoid a prolonged period of sedation following a procedure. It is renally excreted with no hepatic metabolism, which reduces medication interactions and may be useful in the context of CF liver disease. However, dose reduction may be necessary in patients who develop renal insufficiency. See Recommendation 15 in table 1.

Medications used for treatment-resistant depression or anxiety, which may carry increased risks of drug–drug interactions and adverse effects in individuals with CF, are outside the scope of this guideline. When necessary, they should be prescribed and monitored by a psychiatric specialist in close collaboration with the CF team. Specialised consultation should also be obtained when the psychiatric diagnosis is uncertain, the complexity of the case exceeds the CF team's level of training and experience or when an urgent safety risk is identified.

RECOMMENDATIONS FOR IMPLEMENTATION AND FUTURE RESEARCH

As screening for depression and anxiety is implemented in CF centres internationally, the process of dissemination, implementation and resource provision should be closely monitored to address barriers and concerns. As many international healthcare providers do not have a colleague trained in mental health,²² implementation will require providing CF healthcare professionals with (1) training, easy access to resources and a 'toolkit' to facilitate implementation of annual mental health screening (see online supplementary appendix D); (2) training in the provision of preventive and supportive interventions and (3) development of referral networks within the hospital and community for subsequent psychological and/or pharmacological management of clinically diagnosed depression and anxiety. Many initiatives directly tied to these recommendations are in process. For example, the CFF in the USA recently convened a Task Force on Mental Health, which outlined both the challenges and the importance of implementing these new guidelines, is sponsoring short courses and conference sessions on this topic at the North American CF Conference and is launching a 'request for applications' to provide resources to CF centres that implement screening and treatment. Addressing mental health issues systematically is likely to improve health outcomes, quality of life and reduce healthcare utilisation.^{10 38}

Despite evidence in the TIDES study¹³ that a new diagnosis of CF-related diabetes, and events such as haemoptysis and pneumothorax, may precede elevations in symptoms of depression and anxiety, little is also known about the 'triggers' of psychological symptoms, or how mood affects health outcomes in this complex disease. The development of preventative strategies will be enhanced by research which identifies psychosocial and clinical risk factors, such as maladaptive coping, social isolation, CF clinical complications, markers of inflammation or vitamin deficiencies that predict the onset of depression or anxiety in individuals with CF. Large-scale studies are also required to examine how psychological symptoms affect disease management (eg, adherence) and health outcomes. In terms of cutting edge questions, new evidence in other chronic conditions (eg, cardiovascular disease) indicates that depression, independent of disease state, can increase inflammation and lead directly to a worsening of disease.³⁹ New studies in CF are actively testing this hypothesis, which if supported, adds urgency to the initiation of both screening and treatment.

Although psychotherapy and medication treatments for depression and anxiety are already used in CF,^{13 14} these interventions require further systematic research to inform future recommendations. A recent Cochrane Review of psychological treatments for individuals with CF found no controlled studies evaluating interventions that address depression and anxiety in either individuals with CF or parent caregivers.³⁰ Randomised, comparative effectiveness studies of psychotherapeutic and psychopharmacological interventions for depression and anxiety in CF are recommended. Additional studies are needed to

understand not only the efficacy of cognitive behavioural interventions, but also the pharmacokinetics, the frequency of gastrointestinal or pulmonary side effects or beneficial weight gain. To understand the full potential of psychological and pharmacological treatments to improve care, beyond the reduction of symptoms of depression and anxiety, studies evaluating changes in adherence to CF treatments and/or medical outcomes, as well as the indirect effects of mental health treatment on parental caregivers, should be investigated. Multicentre studies are recommended to increase sample sizes and enhance statistical power in trials of a rare condition, such as CF.

Finally, the inclusion of screening data, as well as intervention efforts, in our national registries will greatly facilitate answers to such pressing questions, including (1) evaluation of the prevalence of psychological symptoms by age, gender and disease severity, (2) identification of the predictors of elevated symptoms, (3) outcomes of both the screening and intervention processes, (4) consequences of psychological symptoms on adherence and health outcomes and (5) impact of psychological distress on healthcare utilisation and cost. Novel forms of service delivery, such as integrated care models or internet-based education and treatment, are also worthy of investigation.^{40 41}

CONCLUSION

Robust evidence indicates that adolescents, adults with CF and parent caregivers report elevations in depression and anxiety that should be identified and treated. Data also suggest that these symptoms affect both disease management and health outcomes. Systematic screening of these symptoms, with appropriate intervention, offers the opportunity to significantly improve the quality of life and health of individuals with CF and their parent caregivers.

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Table 1. Prevalence of depression and anxiety in patients and parent caregivers across chronic conditions

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Location | Review | Matched Healthy | Notes |
|--|----------------------------|------------------------|---|---|---|------------------|--------|---------------------------|--|
| Psychological Medicine (Goodwin et al., 2004)¹ | Asthma Children & Teens | N= 183, 16-18 years | CIDI (Composite International Diagnostic Interview) | 33.90% | 23.00% | New Zealand | No | Yes | |
| Journal of Asthma (Goodwin et al., 2005)² | Asthma Children & Teens | N= 74 5-11 years | DISC Predictive Scales | 2.70% | 4.10% | New York | No | No | |
| Adolescent Health (Katon et al., 2007)³ | Asthma Children & Teens | N= 781 11-17 years | DISC, ASI | 7.2% vs. 4.0% | 2.20% | Washington State | No | Yes, controls | |
| General Hospital Psychiatry (Richardson et al., 2008)⁴ | Asthma Children & Teens | N= 767 11-14 years | Interview, DISC, PCDS | 2.5% met criteria for a depressive disorder alone | 8.9% met criteria for an anxiety disorder alone | Washington State | No | Yes for health care costs | 16.2% of youth with asthma met DSMIV criteria for >1 anxiety or depressive disorders in the last 12 months and 4.8% met criteria for both an anxiety and a depressive disorder |

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Location | Review | Matched Healthy | Notes |
|---|---|---|---------------------------------|-------------------|--------------|---------------------|--------|-----------------|---|
| European Journal of Cancer (Allen et al., 1997)⁵ | Cancer Children & Teens | N= 42 12-20 years vs N= 173 controls | BDI, STAI | 38% vs 29% | 9% vs. 15% | U.K. | No | Yes | |
| Acta Pñdiatr (Von Essen et al., 2000)⁶ | Cancer Children & Teens | N= 51 8-18 years | CDI, RCMAS | 14% | N/A | Sweden | No | Yes | Children and adolescents on treatment did not differ from their healthy Swedish peers |
| J Pediatr Hematol Oncol (Hedstrom et al., 2005)⁷ | Cancer Children & Teens | N= 56 13-19 years | HADS, Interview, SF-36 | 21% | 12% | Sweden | No | No | |
| International Council of Nurses (Matziou et al., 2008)⁸ | Cancer Children & Teens | N= 80 cancer 6-17 years N= 84 control | CDI | 7.5% vs. 11.9% | N/A | Greece | No | Yes | |
| J Pediatr Hematol Oncol (Kersun et al., 2009)⁹ | Cancer Children & Teens | N=41 12-18 years | BYI (Beck Youth Inventory) | 17.10% | 21.9 | US | No | No | |
| Pediatric Blood & Cancer (Deyell et al., 2013)¹⁰ | Cancer Children, Adolescents, Young Adults | N= 2,389 Mean age= 28.8 | Anti-depressant Prescription | 21.6% | NA | British Colombia | No | Yes | |

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Location | Review | Matched Healthy | Notes |
|---|---------------------------------------|--------------------------|------------|---|---|---------------|--------|-----------------|---------------------------|
| Journal of Advanced Nursing (Wu et al., 2013)¹¹ | Cancer, Adolescents | N= 131 Mean age+ 14.7 | RCMAS | NA | 11.5% | Taiwan | No | No | |
| Cancer (Myers et al., 2013)¹² | Acute Lymphoblastic Leukemia Children | N= 159 Mean age= 4.9 | BASC-2 PRS | 5 % 1 month post-diagnosis 6.4% % 6 months post-diagnosis 6.8% % 12 months post-diagnosis | 10.4% 1 month post-diagnosis 8.7% 6 months post-diagnosis 4.5% 12 months post-diagnosis | United States | No | Yes | |
| Children's Healthcare (Key et al., 2001)¹³ | Chronic Illness Children & Teens | N= 125 13-18 years | BDI | Total 13.4% CF= 7.1% vs. 5% | N/A | US | No | Yes | NO differences, low power |
| Psychosomatic Research (Grey et al., 2002)¹⁴ | Diabetes Children & Teens | | | 20% vs. 7% | N/A | US | Yes | Yes | |
| Pediatrics (Lawrence et al., 2006)¹⁵ | Diabetes Children & Teens | N= 2,672 10-21 years | CES-D | 22% | N/A | US | No | Yes | |

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Location | Review | Matched Healthy | Notes |
|---|---|---|---|--|--------------|----------|--------|-----------------|-------|
| Diabetes Care (Hood et al., 2006)¹⁶ | Diabetes Children & Teens | N= 145 10-18 years | CDI, Family Conflict Scale, Diabetes Family Responsibility Questionnaire , Blood Glucose Monitoring Comm. Ques. | 15.20% | N/A | US | No | No | |
| Pediatric Diabetes (Colton et al., 2013)¹⁷ | Diabetes Children & Teens (Girls) | N=98, 9-14 year at baseline, 14-18 5 yr later | K-SADS interview | 30% (at year 5, longitudinal design) | N/A | U.S. | No | No | |
| Clinical Pediatrics (Bernstein et al., 2013)¹⁸ | Children and young adults | N=150, M=17 | BDI, SCARED | 11.3% | 21.3% | U.S. | No | No | |
| Current Diabetes Reports (Pinhas-Hamiel et al., 2013)¹⁹ | Diabetes Children older than 10 | N/A | N/A | 18% vs 5% in boys, 20% vs 9% in girls | N/A | U.S. | Yes | Yes | |

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Location | Review | Matched Healthy | Notes |
|--|---|---|--|---------------------------------------|--------------|----------|--------|-----------------|-------|
| Journal of Child Neurology (Banihani et al., 2015)²⁰ | Duchenne muscular dystrophy Children & Teens (Boys) | N=59 | Diagnostic and Statistical Manual of Mental Disorders criteria | N/A | 27% | US | No | No | |
| Child Neurology (Oguz et al., 2002)²¹ | Epilepsy Children & Teens | N= 35 7-18 Years N= 35 controls 7-18 years | STAI, CDI | 28% vs. 8% | N/A | Turkey | No | Yes | |
| Epilepsy & Behavior (Baki et al., 2004)²² | Epilepsy Children & Teens | N= 35 w/ Epilepsy 7-19 Years N= 35 controls 8-17 years | CDI, STAI, BDI, STAI | 12% vs. 9% | 51-49% | Turkey | No | Yes | |
| Epilepsia (Caplan et al., 2005)²³ | Epilepsy Children & Teens | N= 171 5-16 years | K-SADS, CDI | 33% affective and anxiety vs 6% | Combined | US | No | Controls | |
| Seizure (Reilly et al., 2011)²⁴ | Epilepsy Children & Teens | | | 12-14% | N/A | USA/UK | Yes | No | |

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Location | Review | Matched Healthy | Notes |
|---|---------------|---------------------------|--|--|---|-------------|--------|-----------------|-------|
| Psychological Medicine (Goodwin et al., 2004)¹ | Asthma Adults | N= 203 18-21 years | CIDI | 31.00% | 19.20% | New Zealand | No | Yes | |
| PLOS ONE (Liu et al., 2014)²⁵ | Asthma Adults | N= 261, 18-79 years | SAS (Self Rating Anxiety Scale), SDS (Self Rating Depression Scale) | 13.41% | 11.88% | China | No | No | |
| Cancer (Kugaya et al., 2000)²⁶ | Cancer Adults | N=107 Mean age = 61 | HADS | 15.9% with history of MDD; 3.7% with current MDD | 13.1% (4.7% anxiety only + 8.4% anxiety and depressed mood) | Japan | No | No | |
| Psychosomatics (Brintzenhofe-Szoc et al., 2009)²⁷ | Cancer Adults | N= 8,175 Mean age= 54 | BSI | 18.30% | 24.00% | US (JHU) | No | No | |
| Affective Disorders (Linden et al., 2012)²⁸ | Cancer Adults | N= 10,153 Mean age= 59 | PSSCAN | 12.90% | 19% | Canada | No | No | |

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Location | Review | Matched Healthy | Notes |
|---|----------------------------|--|--|--|--|---------------|--------|-----------------|-------|
| The Lancet Oncology (Mitchell et al., 2013)²⁹ | Cancer Survivors Adults | N= 51, 381 with depression N= 48, 964 with anxiety Mean age range= 50-73.9 | CES-D, HADS-D, HADS-A, CIDI, DSM-IV diagnosis, ICD-9-CM diagnosis, consultation, prescription, | RR of depression in cancer survivors vs. controls: CES-D: 1.86 (p<.05) HADS: 0.93 (p=0.56) Overall prevalence (both measures): 11.6% in cancer survivors to 10.2% in health controls (RR=1.11, p=0.17) | 17.9% in cancer survivors vs. 13.9% in controls (RR=1.27, p<.01) | International | Yes | Yes | |
| Psycho- Oncology (Carlson et al., 2011)³⁰ | Cancer Adults | N= 877 Mean age=62.3 | PSSCAN | 10.7% | 25.9% | Canada | No | No | |
| Support Care Cancer (Hong & Tian, 2013)³¹ | Cancer Adults | N= 1,217 Mean age= 51.24 | HADS | 66.72% | 6.49% | China | No | No | |
| Journal of Clinical Oncology (Boyes et al., 2013)³² | Cancer Survivors Adults | N= 1,154 Ages 18-80 | HADS | 13% (6mo and 12mo post-dx) | 22% (6mo post-dx)/21% (12mo post-dx) | Australia | No | No | |

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Location | Review | Matched Healthy | Notes |
|--|---|------------------------------------|--|--|--|---------------|--------|-----------------|-------|
| Annals of Oncology (Walker et al., 2013)³³ | Cancer Adults | N= 100-3938 Ages 18 and older | DSM-IV/ICD criteria based on clinical interview | 4-11% | NA | International | Yes | No | |
| Psycho-Oncology (Stafford et al., 2013)³⁴ | Breast and Gynaecologic Cancer Adults | N= 167 Ages 18 and older | CES-D, HADS-A | 7.5 | 23.4 | Australia | No | No | |
| Psycho-Oncology (Krebber et al., 2014)³⁵ | Cancer Adults | N= 238 cohorts Age not included | HADS-D, CES-D, Diagnostic Interviews based on DSM-III(-R)/ICD-10 | 8-24% | NA | International | Yes | No | |
| Psycho-Oncology (Singer et al., 2013)³⁶ | Cancer Adults | N= 502 Mean age= 57.63 | SCID | 7.6% | 8.4% | Germany | No | Yes | |
| Support Care Cancer (Mackenzie et al., 2013)³⁷ | Cancer, undergoing radiation Adults | N= 454 Mean age= 61.2 | HADS-3, HADS-A, HADS-T | 5.7% | 15% | Australia | No | No | |
| Psycho-Oncology (Neilson et al., 2013)³⁸ | Head and Neck Cancer, treated with radiotherapy Adults | N= 101 Mean age= 63 | HADS | 15% baseline, 29% 3 weeks post-treatment | 20% baseline, 17% 3 weeks post-treatment | Australia | No | No | |

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Location | Review | Matched Healthy | Notes |
|--|---|------------------------------------|--|--|--|---------------|--------|-----------------|-------|
| British Journal of Cancer (Brinkman, et al., 2013)³⁹ | Cancer Adult Survivors of Childhood Cancer | N= 4569 Mean age= 27 | BSI-18 | 8.9% | 4.8% | United States | No | No | |
| BMJ Open (Watts et al., 2014)⁴⁰ | Prostate Cancer Adult | N= 4494 Mean age= 66.3 | HADS, STAS, CESD, Symptom Checklist, BDI, Self-Rating Anxiety Scale, Self-Rating Depression Scale, BSI, CIDI, Memorial Anxiety Scale for Prostate Cancer and the Effects of Prostate Cancer on Lifestyle Questionnaire | 17.24% pre-treatment 14.70% on-treatment 14.70% post-treatment | 27.04% pre-treatment 15.09% on-treatment 18.49% post-treatment | International | Yes | No | |
| BMC Cancer (Yang et al., 2013)⁴¹ | Cancer Adults | N= 3497 Mean age range= 35.3-67 | DSM-IV or CCMD diagnosis, HRSD/HRSA, other self-report questionnaires | 54.90% | 49.69% | China | Yes | Yes | |

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Location | Review | Matched Healthy | Notes |
|--|--|---------------------------------|--|--|--------------|---|--------|--------------------------|-------|
| The Lancet, Psychiatry (Walker et al., 2014)⁴² | Lung, gynecological, breast, colorectal, or genitourinary cancer Adults | N= 21,151 Mean age= 64.4 | HADS, SCID | 4.5-13.1% | NA | Scotland | No | No | |
| Respiratory Care (Willgoss & Yohannes, 2013)⁴³ | COPD | Study N=20-204 (Total N=691) | ND, CIDI, SCID, ADIS-IV, F-DIPS, or GMSS | N/A | 10-55% | 8 countries (Nigeria, Turkey, New Zealand, United States, Germany, Canada, Australia, United Kingdom) | Yes | | |
| Diabetes Care (Anderson et al., 2001)⁴⁴ | Diabetes Adults | | | Twice as common in Diabetes group than in Comparison group | N/A | US | Yes | Yes, half of studies did | |
| Diabetes Care (Li, et al. 2008)⁴⁵ | Type 1/2 Diabetes Adults | N=18,814 Mean age = 62 | PHQ-8 | 16.6% (8.3% major depression, 8.3% minor depression) | N/A | US (data from 2006 Behavior Risk Factor Surveillance Survey, BRFSS) | No | No | |

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Location | Review | Matched Healthy | Notes |
|--|---------------------------|--------------------|----------------|--|--------------|-----------------|--------|-----------------|--|
| Diabetic Medicine (Ali et al., 2006)⁴⁶ | Type 2 Diabetes Adults | Meta-analysis | | 17.6% (diabetes) vs. 9.8% (healthy controls) | N/A | Various | Yes | Yes | Odds ratio for having depression given T2D status = 1.6 |
| Diabetic Medicine (Barnard et al., 2005)⁴⁷ | Diabetes Adults | Review | | 12% vs. 3.2% | N/A | | Yes | Yes | |
| Journal of Intellectual Disability Research (De Winter et al., 2015)⁴⁸ | Diabetes Adults & Elderly | N= 2322 M= 61.1 | IDS-SR; SDL-ID | 16.8 | 16.3 | The Netherlands | No | Yes | There was a significant association between increased anxiety symptoms and diabetes. |
| Psychosomatics (Smith & Schmitz, 2014)⁴⁹ | Diabetes Adults | N=1701 | WHO DAS II | 2.4 | 5.8 | The Netherlands | No | No | Results indicate that elevated anxiety and depression symptoms are important factors associated with increased functional disability and frequent disability days in people with diabetes. |

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Location | Review | Matched Healthy | Notes |
|--|---|------------------------------------|----------------|---|--------------|----------|--------|-----------------|-------|
| Journal of Psychosomatic Research (Deschenes et al., 2015) ⁵⁰ | Diabetes Adults | N= 1730 30-79 | WMH-CIDI | | | Canada | No | No | |
| Journal of Psychosomatic Research (Mezuk et al., 2013) ⁵¹ | Diabetes Adults | N= 512,891 30-79 | CIDI-SF | .9 vs .6 | .3 vs .2 | China | No | Yes | |
| Journal of Affective Disorders (Tanenbaum et al., 2013) ⁵² | Diabetes Adults | N=70 Mean age=56 | CES-D, DDS | ? | ? | | | | |
| BMC Psychiatry (Niraula et al., 2013) ⁵³ | Diabetes Adults | N=348 Mean age=52 | BDI-I | 40.3% of the population | N/A | Nepal | No | No | |
| Journal of Affective Disorders (Windle & Windle, 2013) ⁵⁴ | Cardiovascular Disease or Diabetes Adult | Wave 6 N=557 Way 7 N= 506 | WHO-CIDI | 20.3% recurrent MDD, 19% single episode MDD | N/A | US | No | No | |
| Psychoneuroendocrinology (Meyers et al., 2013) ⁵⁵ | Diabetes Adults | N=145 M=49 | QIDS-SR, PHQ-9 | 37.9% | N/A | US | No | No | |
| JAMA Psychiatry (Sullivan et al., 2013) ⁵⁶ | Diabetes Adults | N=2977 M= | PHQ-9 | 18% | N/A | US | No | No | |

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Location | Review | Matched Healthy | Notes |
|--|---------------------------|------------------|--|-----------------|--------------|-----------|--------|-----------------|-------|
| Asian journal of psychiatry (Gehlawat et al., 2013)⁵⁷ | Diabetes Adults | N=410 M=51 | HAM-D | | | India | No | No | |
| Journal of Affective Disorders (Akena et al., 2015)⁵⁸ | Diabetes Adults | N=437 M=51 | MINI, MNSI, WHO-QOL | 34.8% | N/A | Uganda | No | No | |
| Journal of Behavioral Science (Mayberry et al., 2014)⁵⁹ | Diabetes Adults | N=314 M=52 | PHQ-9 | 24% | N/A | US | No | No | |
| Journal of Behavioral Science (Carper et al., 2014)⁶⁰ | Type 2 Diabetes Adults | N=146 M=56 | QOLI, DDS, MADRS | 56.8% | N/A | US | No | No | |
| Journal of Nursing Research (Wu et al., 2013)⁶¹ | Type 2 Diabetes Adults | N=111 | Beck depression inventory, Beck anxiety inventory | 12.6% | 27% | Taiwan | No | No | |
| Iranian Red Crescent Medical Journal (Palizgir et al., 2013)⁶² | Type 2 Diabetes Adults | N=184, 22- 78 | Beck depression inventory, Beck anxiety inventory | 70.7% | 69.9% | Iran | No | No | |
| BMJ open (Ganasegeran et al., 2014)⁶³ | Type 2 Diabetes Adults | N=169 M=37 | HADS | 40.3% | 31.4% | Malaysia | No | No | |
| Medical science monitor: Int'l Med journal of experimental and clinical research (Mikaliukstiene et al., 2014)⁶⁴ | Type 2 Diabetes Adults | N=1022 M=59 | HADS | 28.5% | 42.4% | Lithuania | No | No | |

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Location | Review | Matched Healthy | Notes |
|---|--------------------------------------|--------------------------|-----------------------|---|--------------|---------------|--------|---------------------------|-------|
| Epilepsy & Behavior (Mensah et al., 2006)⁶⁵ | Epilepsy Adults | N=515 | HADS | 27.8% (includes borderline and clinical) | N/A | US | No | No | |
| Epilepsy & Behavior (Thapar et al., 2009)⁶⁶ | Epilepsy Adults | N=443 | HADS | 10.9% for those currently experiencing seizures vs. 4.4% of those who were currently seizure-free | N/A | US | No | No | |
| Chest (Schneider et al., 2010)⁶⁷ | COPD Adults | N= 35,722 vs. Controls | Diagnosis in Database | odds ratio 1.44 23.1% vs 16.8% | N/A | UK | No | Yes | |
| Chronic Respiratory Disease (Akhtar et al., 2013)⁶⁸ | Idiopathic Pulmonary Fibrosis Adults | N= 118 34-96 years | WDI | 49.20% | N/A | Scotland | No | National Prevalence: 2.6% | |
| Archives of Neuropsychiatry (Aysal et al., 2013)⁶⁹ | Myasthenia gravis Adults | N=42, ages 18-78, M=42.6 | BDI, BAI | 40.5% | 9.5% | Turkey | No | No | |
| National Medical Association (Hasan et al., 2003)⁷⁰ | Sickle Cell Adults | N= 60 21-64 years | BDI | 44% | N/A | Washington DC | No | No | |

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Location | Review | Matched Healthy | Notes |
|--|-----------------------------|--|-----------|--|--|-------------|--------|-----------------|-------|
| Journal of Pediatric Psychology (Feldman et al., 2013)⁷¹ | Asthma Parents & Caregivers | N= 97 7-11 years old (mean age 9.45) | SCID | 28.1% (any current depressive disorder) | 37.5% (any current anxiety disorder) | US | No | No | |
| Journal of Nervous and Mental Disease (Feldman et al., 2011)⁷² | Asthma Parents & Caregivers | N=641 10-25 years old (mean age 16.31 for asthma group; mean age 17.68 in healthy controls) | CIDI | 19.38% for caregivers of youth who had EVER had an asthma attack; 7.42% for caregivers of youth who had NEVER had an asthma attack (sig difference - p<.0001) | 11.89% for caregivers of youth who had EVER had an asthma attack; 7.71% for caregivers of youth who had NEVER had an asthma attack (ns) | Puerto Rico | No | Yes | |
| Pediatric Allergy & Immunology (Szabo et al., 2010)⁷³ | Asthma Parents & Caregivers | N=108 parents of children with asthma and N=27 parents of children with chronic renal disease Total N = 135 Ages 7-17 years | BDI, STAI | For caregivers of children with asthma: Men: 39%, women: 33%. For caregivers of children with renal disease: Men: 14%, women: 50% | Not reported | Hungary | No | No | |

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Location | Review | Matched Healthy | Notes |
|--|-----------------------------|---|--|--|--|-------------|--------|-----------------|---|
| Journal of Asthma (Martinez et al., 2009)⁷⁴ | Asthma Parents & Caregivers | N=221 mean age 7.35 years old (range 5-12 years old) | CES-D | 33% | N/A | Puerto Rico | No | No | Similar prev. of dep. among community samples of women in PR from low SES areas |
| Journal of Pediatric Psychology (Dahlquist et al., 1993)⁷⁵ | Cancer Parents & Caregivers | N=134 Mean age 6.88 years old; range: 3 months - 17 y 2 months | BDI, STAI | 13% mothers, 8% fathers | State: 13% mothers, 12% fathers; Trait: 12% mothers, 3% fathers | US | No | No | |
| Journal of Pediatric Psychology (Manne et al., 1995)⁷⁶ | Cancer Parents & Caregivers | N= 59 Mean age 11.6 years old; range 3-18 years | BDI | 58% immediately post-diagnosis; 51% at 3-month follow-up (no intervention given) | N/A | US | No | No | |
| Journal of Pediatric Psychology (Van Dongen-Melman et al., 1995)⁷⁷ | Cancer Parents & Caregivers | N= 133 range: 8-12 years old | STAI, Self-Rating Depression Scale (SDS; Zung, 1965) | 31% | 42% | Netherlands | No | No | |

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Location | Review | Matched Healthy | Notes |
|--|-------------------------------------|--|----------------|--|---------------------------|----------|--------|-----------------|-------|
| Journal of Pediatric Oncology Nursing (Elkin et al., 2007)⁷⁸ | Cancer Parents & Caregivers | N=27 Mean age 12.78 years old | BDI-II | 30% | N/A | US | No | No | |
| Journal of Pediatric Psychology (Greening & Stoppelbein, 2008)⁷⁹ | Cancer Parents & Caregivers | N=150 Mean age 11.51 years old; range 6-18 years old | BDI-II, STAI-S | 1% | 7% | US | No | No | |
| Psycho-Oncology (Fotiadou et al., 2008)⁸⁰ | Cancer Parents & Caregivers | N=100 study group; N=117 control group Mean 8 years old; Range 0-16 years old | HADS | 27% of women, 17% of men | 68% for women, 37% of men | UK | No | Yes | |
| Journal of Pediatric Psychology (Rodriguez et al., 2013)⁸¹ | Cancer Parents & Caregivers | N=94 Mean age 10.4 years old; range 5-18 years old | BDI-II | 45% | N/A | US | No | No | |
| Journal of Pediatric Psychology (Manuel et al., 2003)⁸² | Cerebral palsy Parents & Caregivers | N=270 1.1-17.8 years old | CES-D | 30% of mothers had depressive symptoms above the cut off | N/A | US | No | No | |

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Location | Review | Matched Healthy | Notes |
|---|--------------------------------------|--|-------------|--|--|----------|--------|-----------------|-------|
| American Journal of Hospice and Palliative Medicine (Fauman et al., 2011)⁸³ | Chronic Illness Parents & Caregivers | N=61 18 months-18 years old | BDI-II | 56.3% of mothers, 20.9% of fathers | N/A | US | No | No | |
| Journal of Pediatric Psychology (Driscoll et al., 2010)⁸⁴ | Type 1 Diabetes Parents & Caregivers | N=108 Mean age 8.14 years old | CES-D | 33.30% | N/A | US | No | No | |
| Children's Health Care (Jaser et al., 2009)⁸⁵ | Type 1 Diabetes Parents & Caregivers | N=67 1-8 years old (mean age 4.77) | CES-D, STAI | 24% of mothers clinically significant depression | 21% mothers clinically significant anxiety | US | No | No | |
| Journal of Pediatric Psychology (Jaser et al., 2008)⁸⁶ | Type 1 Diabetes Parents & Caregivers | N=108 (mothers only) 8-12 years old (mean 9.94 years old) | CES-D | 22.20% | N/A | US | No | No | |
| Hellenic Journal of Nursing Science (Albani et al., 2010)⁸⁷ | Type 1 Diabetes Parents & Caregivers | N=83 Range: 6-10 years old | STAI | N/A | 51.8% (state), 53% (trait) | Greece | No | No | |
| Child: Care, Health, and Development (Hilliard et al., 2010)⁸⁸ | Type 1 Diabetes Parents & Caregivers | N=73 (2-6 years old)M age 4.4 years | STAI | N/A | 21% | US | No | No | |

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Location | Review | Matched Healthy | Notes |
|---|--------------------------------------|---|-------------|-----------------|--------------|----------|--------|-----------------|-------|
| Diabetic Medicine (Williams et al., 2009)⁸⁹ | Type 1 Diabetes Parents & Caregivers | N=187 Mean age 14.4 years old; range 10-17.9 years old | CES-D, STAI | 22% | 24% | US | No | No | |
| Journal of Pediatric Psychology (Hood, 2009)⁹⁰ | Type 1 Diabetes Parents & Caregivers | N=187 Mean age 14.4 years old (10-18) | CES-D | 22% | N/A | US | No | No | |
| Health Psychology (Mackey et al., 2014)⁹¹ | Diabetes Parents & Caregivers | N=225 (mothers and their young adolescents M=13) | BDI-II | 21% | N/A | US | No | No | |
| Maternal and Child Health Journal (Jaser et al., 2014)⁹² | Diabetes Parents & Caregivers | N=118 | CES-D, STAI | 18% | 13% | U.S. | No | No | |
| Journal for Specialists in Pediatric Nursing (Shore et al., 2002)⁹³ | Epilepsy Parents & Caregivers | N=115 Range: 11-18 years old | CES-D | 36% | N/A | US | No | No | |

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Location | Review | Matched Healthy | Notes |
|--|-------------------------------|--|----------|---|--------------|--------------|--------|--|-------|
| Acta Neurologica Scandinavica (Lv et al., 2009)⁹⁴ | Epilepsy Parents & Caregivers | N=263 Range: 6-18 years old | ZDS, ZAS | 38.40% | 21.67% | China | No | Yes - anxiety and depression prevalence were significantly higher in parents of epileptic children compared to parents of healthy children | |
| Biomedical and Environmental Sciences (Li et al., 2008)⁹⁵ | Epilepsy Parents & Caregivers | N=340 4-8 years old (M age 9.1) | HADS | N/A | 56.20% | China | No | No | |
| Neurosciences (Shariff et al., 2013)⁹⁶ | Epilepsy Parents & Caregivers | N=31 Mean age 6.49 years old; range 8 months - 13 years old | HADS | 38.70% | 55.00% | Saudi Arabia | No | No | |
| Social Psychiatry and Psychiatric Epidemiology (Ferro & Speechley, 2012)⁹⁷ | Epilepsy Parents & Caregivers | N=210 Mean age 7.6 years; range = 4-12 years old | CES-D | 38% immediately after diagnosis 30% at 6 months post-diagnosis 32% at 12 months post-diagnosis 30% at 24 months post-diagnosis | N/A | Canada | No | No | |

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Table 1. Prevalence of depression and anxiety in cystic fibrosis patients and parent caregivers.

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Country | Review | Matched Healthy | Notes |
|---|--------------------------|--------------------------------|--------------|--|--|---|--------|-----------------|--|
| Thorax (Quittner et al., 2014)¹ | Adults | N=4739 | HADS, CES-D | HADS: 13% CES-D: 29% | 32% | 9 countries (US, UK, Spain, Belgium, Turkey, Germany, Italy, Netherlands, Sweden) | No | No | |
| Psychosomatics (Quon et al, 2014)² | Adults | N=153 | PHQ-9, GAD-7 | 7% (Symptom definition) 22% (composite definition) | 5% (symptom definition) 10% (composite definition) | US | No | No | 5% endorsed suicidality item on PHQ-9 |
| Health Psychology (Hilliard et al., 2014)³ | Adults Mean age: 29.2 | N=128 | CES-D | 23% | N/A | US | No | No | |
| J Cyst Fibros (Duff et al., 2014)⁴ | Adults | N=1780(CF) N=1788 (Control) | HADS | Men(CF):13.1% Women(CF):11.9% Men(non-CF): 9% Women(non-CF):14% | Men(CF):30.1% Women(CF):38.5% Men(non-CF):27% Women(non-CF):39% | UK | No | Yes | For men (but not women): significant differences between CF and non-CF on anxiety and depression |
| J Cyst Fibros (Latchford et al., 2013)⁵ | Adults | N=232 | HADS, PHQ-9 | 5.6% (HADS) 33.4% (PHQ-9) | N/A | UK | No | No | 10.4% endorsed suicidality item on PHQ-9 |
| Journal of Affective Disorders (Kopp et al., 2013)⁶ | Adults Mean age: 26.1 | N=30 | CES-D | 50% | N/A | US | No | No | Hospitalized patients |

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Country | Review | Matched Healthy | Notes |
|---|---|-----------------------------------|--|---|---|---------|--------|-----------------|--|
| Respiratory Care (Yohannes et al., 2012)⁷ | Adults 18-70 years | N=121 | CF-QOL, HADS | 17% (HADS) | 33% | UK | No | No | |
| Chest (Goldbeck et al., 2010)⁸ | Adults with CF Mean age: 23.1 years Adults (Control) Mean age: 24.6 | N=670 (CF) N=2629 (Control) | HADS | Ages 21-30: 11.3% (CF) v. 7.0% (non- CF) (ns) Ages 31-50: 14.0% (CF) v. 16.4% (non-CF)(ns) | Ages 21-30: 18.5%(CF) v. 9.5%(non-CF) (p<.05) Ages 31-50: 27.3%(CF) v. 19.2%(non-CF) (p<.05) | Germany | No | Yes | Overall depression rate: 9.6%(CF) Anxiety rate: 20.6%(CF) |
| J Cyst Fibros (Havermans et al., 2008)⁹ | Adults Mean age=26.7 | N=57 | HADS | 13% | 30% | Belgium | No | No | |
| Chest (Riekert et al., 2007)¹⁰ | Adults Mean age=30.6 | N=76 | BDI | 30.3% | N/A | US | No | No | |
| Chest (Anderson et al., 2001)¹¹ | Adults Mean age= 28.5 | N=34 | MMPI-2 | 5.9% | 5.9% | US | No | No | Prevalence of anxiety and depression were similar to general population |
| J of Child & Adolescent Psychiatry (Pearson et al., 1991)¹² | Adults Mean age=24.8 | N=36 | STAI, Self- report depression inventory | 42.4% | 22.2% | US | No | No | |

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Country | Review | Matched Healthy | Notes |
|--|---|-------------|-----------------|--------------------------------------|--------------|---|--------|-----------------|---|
| Thorax (Quittner et al., 2014)¹ | Adolescents | N=1286 | HADS, CES-D | HADS:5% CES-D: 19% | 22% | 9 countries (US, UK, Spain, Belgium, Turkey, Germany, Italy, Netherlands, Sweden) | No | No | |
| Psychosomatics (Smith et al., 2014)¹³ | Children/ Adolescents 7-17 years | N=38 | CDI | 28% | N/A | US | No | No | Vitamin D insufficiency associated with depressive symptoms |
| Annals of Pharmacotherapy (Ploessl et al., 2013)¹⁴ | Children/ Adolescents 6-18 years | N=190 | ICD-9 codes | 9% | N/A | US | No | No | Depressed patients had lower lung function and more hospitalizations |
| J Cyst Fibros (Besier et al., 2011)¹⁵ | Children/ Adolescents 12-17 years | N=162 | HADS, CES-D | 7.4% | 12.3% | Germany | No | No | |
| Pediatr Pulmonology (Smith et al., 2010)¹⁶ | Children/ Adolescents 7-17 years | N=39 | CDI, CES-D, DPD | 29% total 7-12: 33% 12-17: 25% | N/A | US | No | No | Depressive symptoms significantly predicted adherence to airway clearance |
| J Child Adolesc Psychiatry (Burke et al., 1989)¹⁷ | Children/ Adolescents | N=52 | K-SADS | 11.5% | 11.5% | US | No | No | |

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Country | Review | Matched Healthy | Notes |
|--|------------|------------------------------|---------------|--|------------------------------|---|--------|-----------------|-------|
| Thorax (Quittner et al., 2014)¹ | Parents | N= 3127 Mothers, 975 Fathers | HADS, CES-D | Mothers HADS: 20%, CES-D: 34% Fathers HADS: 18%, CES-D: 25% | Mothers: 48% Fathers: 36% | 9 countries (US, UK, Spain, Belgium, Turkey, Germany, Italy, Netherlands, Sweden) | No | No | |
| J Cyst Fibros (Ltluczek et al., 2013)¹⁸ | Parents | N=72 (CF=33, non-CF=39) | CES-D | Children diagnosed from newborn screening: 58% Standard diagnosis: 27% Non-CF: 22% | N/A/ | US | No | Yes | |
| Pediatr Pulmonol (Besier et al., 2011)¹⁵ | Parent | N=650 | CES-D HADS | 28% | 37.2% | Germany | No | No | |
| J Cyst Fibros (Besier & Goldbeck, 2011)¹⁹ | Parent | N=162 | HADS CES-D | 26.4% | 37.7% | Germany | No | No | |
| J of Pediatr Psychol (Driscoll et al., 2010)²⁰ | Parent | N=87 | CES-D | 32.2% | N/A | US | No | No | |

| Journal (Authors) | Population | Sample Size | Measures | Depression Rate | Anxiety Rate | Country | Review | Matched Healthy | Notes |
|---|----------------------------------|---|---------------|---|--------------|---------|--------|-----------------|-------|
| Pediatr Pulmonol (Smith et al., 2010)¹⁶ | Parent | N=39 | CES-D | Mothers: 35% Fathers: 23% | N/A | US | No | No | |
| Pediatr Pulmonol (Driscoll et al., 2009)²¹ | Parent (100 mothers, 22 fathers) | N=122 | CES-D HADS | Mothers: 28%(CES-D), 20%(HADS) Fathers: 31%(CES-D), 14%(HADS) | N/A | US | No | No | |
| Health Psychology (Quittner et al., 1998)²² | Parent | 33 couples with child with CF 33 control couples | CES-D | Women (CF): 36.4% Women (non-CF): 21% Men (CF):12% Men (non-CF): 15% | N/A/ | US | No | Yes | |

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Appendix C: Manual of procedures and tool kit for implementation

**International Committee on Mental Health in Cystic Fibrosis:
Cystic Fibrosis Foundation and European Cystic Fibrosis Society's
Guide to Implementing Depression and Anxiety Screening in CF Centers**

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This guide was adapted from A Guide to Depression Screening developed at the Cystic Fibrosis Center of University at Buffalo at Women & Children's Hospital of Buffalo by Beth Smith, M.D., Carla Frederick, M.D., Danielle Goetz, M.D., Lynne Fries, PA-C, MPAS, DPT, Kimberly Rand, LMSW, Christine M. Roach, RN, BSN, and Drucy S. Borowitz, M.D.

How to Get Started:

Before you get started with depression and anxiety screening, identify a core group of people who are interested. "It takes a village" to move this forward and it's **important that this does not land on the shoulders of just one or two people.**

Identify:

- **Who** are the integral players for depression and anxiety screening and assessment in your center?
- **What** specifically will each of them do and do they have the knowledge and skills to do it?

The Main Ideas:

- **All patients 12 years and older receive annual screening for depression and anxiety.**
- **Parent caregivers of patients aged 0-17 years are *offered* annual screening for depression and anxiety.**
- **A stepped process** for prevention, screening, assessment and intervention is recommended. Please refer to the Cystic Fibrosis Foundation and European Cystic Fibrosis Society Consensus Statements for Screening and Treating Depression and Anxiety Figure 1: Assessing & Treating Depression & Anxiety in CF.

Step 1 Screening:

For Depression: Administer the Patient Health Questionnaire-9 (PHQ-9) to adult patients and parent caregivers (appendix 1) and the PHQ-9 *or* PHQ-9 Modified for Teens to adolescent patients 12-17 years (appendix 2). The PHQ-9 informs on depression severity and diagnostic criteria of major depression based on the Diagnostic and Statistical Manual of Mental Disorders (DSM).

For Anxiety: Administer the Generalized Anxiety Disorder Questionnaire (GAD-7) to adolescents, adults and parent caregivers (appendix 3).

These forms are in the appendix however can also be downloaded free with a full instruction manual at www.phqscreeners.com.

Step 2 Assessment:

Assessment: If the PHQ-9 and/or the GAD-7 score ≥ 10 the patient needs an assessment.

- Assessment should be the shared responsibility of the team however the team must designate who is expected to conduct the assessment per the scope of practice. This may be a mental health specialist on your team or another CF professional with sufficient mental health training and comfort.
- Some teams may decide to refer to psychiatry, psychology, or the patient's primary care physician for further assessment based on the team's resources. For example, teams may choose to refer all patients scoring in the moderate to severe range or patients with certain risk factors.
- An assessment should include risk factors, pertinent history, severity/extent of symptoms and level of impairment, which leads to different interventions using a stepped care approach.
- Patient and parent preference is also considered.

Screening Tools:

- Identify if you will use paper/pencil or computer based questionnaires.
- Who will administer the tools?
- Who will score them?
- Consider when you will screen.

An example could be to screen patients annually in a certain quarter of the year, as many patients are seen quarterly. Here are some tips if you choose this method:

- If a patient is not seen in that quarter of the year, screen them at their next outpatient visit.
 - If a patient is non-adherent to outpatient appointments or was not seen in that quarter of the year consider screening at the end of an inpatient admission.
 - Begin the next cycle in the same quarter so you do not have to track when individual patients are due for their next screen.
 - Additionally, the team may choose to screen patients **any time** significant symptoms of depression or anxiety are reported or observed by patients, caregivers, or members of the CF multidisciplinary team.
 - **All patients, whether or not they had a positive screen the year before, are screened again the following year.**
- **PHQ-9 and GAD-7 total scores, together with an assessment, lead to different interventions using a stepped care approach. Patient and parent preference is also considered.**
 - The **PHQ-9 total score** puts the patient into categories:
 1. **No or minimal depression:** Total Score 0-4
 2. **Mild depression:** Total Score 5-9
 3. **Moderate depression:** Total Score 10-14
 4. **Severe depression:** Total Score ≥ 15
 - The **GAD-7 total score** puts the patient into categories:
 1. **No or minimal anxiety:** Total Score 0-4
 2. **Mild anxiety:** Total Score 5-9
 3. **Moderate anxiety:** Total Score 10-14
 4. **Severe anxiety:** Total Score ≥ 15

- Refer to www.phqscreeners.com for full scoring instructions for the PHQ and GAD-7 and to Appendix 4 for examples of different scoring methods for the PHQ-9 and PHQ-9 Modified for Teens and appendix 5 for scoring the GAD-7.
- **All patients with a positive screen (Score ≥ 10) receive a follow-up assessment.**
- The PHQ-9 and GAD-7 total score helps assess depression and anxiety severity; however, an **assessment** provides additional information to help **further categorize the severity** and clinical significance of symptoms based on factors such as prior history of depression and/or anxiety, depression/anxiety treatment, stressors, history of comorbid psychiatric diagnoses, severity of CF, and presence of complications.
- There is an **algorithm** of how to manage each of the categories of depression and anxiety severity for individuals with CF 12 years and older. Please refer to the Cystic Fibrosis Foundation and European Cystic Fibrosis Society Consensus Statements for Screening and Treating Depression and Anxiety Figure 2 (Screening & Treatment for Depression & Anxiety: Algorithm for Individuals with CF ages 12-Adulthood). It is important to confirm a clinical diagnosis prior to initiating treatment and use independent clinical judgment and skills in the context of individual clinical circumstances.
- There is also an **algorithm** for managing parent/caregiver depressive and anxiety symptoms. Please refer to the Cystic Fibrosis Foundation and European Cystic Fibrosis Society Consensus Statements for Screening and Treating Depression and Anxiety Figure 3 (Screening & Treatment for Depression & Anxiety: Algorithm for Parents/Caregivers).
- Remember there is a suicidality question in the PHQ-9 (question #9). This is addressed below.

The work before the work” – The PLAN part of the P-D-S-A Cycle:

1. The key to beginning screening is to have a plan for what you will do with a positive screen:

- You will want to have **educational materials on hand for patients with depression and anxiety**. Offer support, help coping with stress, and provide education and information about depression/anxiety and its management for all patients with a PHQ-9 or GAD-7 score ≥ 5 . Depression and anxiety education is an important part of ongoing prevention, as well as an intervention for all levels of depression and anxiety severity.
- Examples of sample handouts/educational materials are found in Appendix 5. Some additional resources include:
 - A comprehensive resource for adolescent depression tools can be found in a toolkit that accompanies the Guidelines for Adolescent Depression in Primary Care (GLAD-PC) and can be downloaded free at www.glad-pc.org.
 - Additional educational materials and screening tools for other mental health issues, such as substance abuse, ADHD, oppositional-defiant disorder, and a variety of behavioral health problems are available at www.cappcnny.org.
 - For adolescent patients the American Academy of Child and Adolescent Psychiatry has developed facts for families, which are concise handouts with up-to-date information on a variety of topics that affect children. (www.aacap.org)

- For pediatric patients, the Massachusetts General Hospital School Psychiatry Program/Mood and Anxiety Disorders Institute has developed resources aimed at parents, teachers, and clinicians for implementing school-based interventions for depression, anxiety, and other mental health disorders (www.schoolpsychiatry.org).
 - For adult patients the American Academy of Psychiatry has "Let's Talk Brochures" on psychiatric disorders and their treatments (www.psychiatry.org).
- **You will need to identify available resources in your institution and community for the treatment of depression and anxiety for patients with moderate - severe symptoms**
 - *Even if your CF team already includes a mental health provider/clinician with appropriate skills and training, it is likely that some individual patients, such as those travelling long distances to their CF center, will need to access additional community resources..*
 - **This step must be completed prior to implementing screening and will likely take the most time.**

Here are some thoughts about how to do this:

- Contact Psychology/Psychiatry Departments at your university and ask for resources or contact psychology or consult liaison psychiatry services within your hospital and ask for resources.
 - Contact the local office of mental health in your county or region.
 - It is recommended when referring patients that you educate the patients/parents on what to ask for. For example: evidence based therapies for depression include Cognitive Behavioral Therapy (CBT) and Interpersonal Therapy (IPT) and evidence based treatment for anxiety includes exposure based CBT. Handouts about CBT for depression and anxiety are found in appendix 6 (www.abct.org). Information about IPT can be found at <http://interpersonalpsychotherapy.org>. It is also important to educate our referral resources about CF. Appendix 7 has a general handout about cystic fibrosis for mental health care providers.
- **You will need to develop a plan for patients with suicidality.**
 - For patients or parents/caregivers who screen positive for suicide risk (Question 9 on the PHQ-9), the designated mental health expert on the CF team should follow up immediately to determine how serious the risk is. This should include a clinical interview or further assessment. There are formal assessment tools, such as the Columbia Suicide Severity Rating Scale (C-SSRS; <http://www.ccrs.columbia.edu/ecssrs.html>), which can also be used to evaluate this risk.
 - Appendix 7 has the Columbia Suicide Severity Rating Scale (CSSRS) for assessing and managing patients with suicidal ideation. This scale or an alternate assessment, should be completed on every patient with a positive response to question 9 on the PHQ-9. This scale is administered in person and is not handed to the patient.
 - If using the CSSRS, we recommend members of your team complete the free online training. All members of your team involved in screening are encouraged to complete this training and will receive a certificate of completion.
 - Appendix 8 has POSSIBLE triage responses to the Columbia Suicide Severity Rating Scale and suggested interventions however these need to be modified based on your local practice patterns and resources. Other responses are available on the training web-site and again may differ in your algorithm depending on local practices and resources.
 - Appendix 9 has an example of an Adult Safety Plan.
 - Appendix 10 has an example of a Pediatric Safety Plan.

2. Your team will need to figure out how to **communicate with patients and parents/caregivers that screening will be starting**. It is important for patients and parents to be aware of the process.

- Will you send a letter to patients?
- Do you have a newsletter?
- Will you do an educational webinar?
- Other

3. **Establish your process for screening in clinic**. Decide who will do specific tasks.

- Who will hand out the screening tools (PHQ-9 and GAD-7)?
- Who will score the PHQ-9 and GAD-7?
- How will the treating clinician know what was completed and the results?
- How do patients with positive PHQ-9 and/or GAD-7 receive an assessment?
- What is the process for looking at question #9 (suicidality) on the PHQ-9 and intervening if necessary? One possibility: The clinician seeing the patient looks at question 9 and if positive intervenes with the help of the social worker/psychologist.
- Who gets the PHQ-9 and GAD-7 forms at the end of clinic?
- Are the forms scanned into the patient's electronic medical record?
- Consider discussing each patient with a positive score at your team's next multidisciplinary team meeting.

Implementing the Program – the “DO” part of the P-D-S-A Cycle:

- Now that you've prepared your team and your patients/parents, **get started!**
- You've decided who is doing what in clinic, but you also need to decide who is doing what after clinic.
 - **How will you keep track of screening scores?**
 - Who will enter this data at your site?
 - **How will you track the patients who screened positive for suicidality**, especially those who have an intervention in clinic?
- **How will you track that the required follow-up and re-assessment has been completed?**
- **How will you track patient adherence with recommendations/treatment?** It is common for patients with symptoms of depression to not follow through on treatment referrals and/or comply with treatment recommendations. One suggestion is calling patients with moderate to severe depression and/or anxiety after their clinic visit to assess follow-through and compliance with recommendations/treatment and any perceived barriers to either the referral or treatment. Alternatively one could assess follow-through at the next clinic visit.
- **Routinely discuss patients who screen positive as part of your weekly pre-clinic/post-clinic team meeting.**

Evaluating the Program: The “STUDY” Part of the P-D-S-A cycle:

- **Examine your tracking tools to see if you are accomplishing your initial goals:**
 - All patients get screened with PHQ-9 and GAD-7 at least once a year.
 - All patients with a positive answer to question #9 (suicidality) have an intervention.
 - All patients with a PHQ-9 or GAD-7 score ≥ 10 have an assessment and an intervention based on their level of depression and/or anxiety.
- **Examine your tracking tools to see if you are achieving longer-term goals:**
 - Are you re-assessing patients and repeating the PHQ-9 and GAD-7 for those with mild depression/anxiety at the next visit?

- Are you ensuring follow-up for patients with PHQ-9 or GAD-7 score ≥ 10 ?
- If the patient is receiving psychological or psychopharmacological treatment within the center more frequent reassessment may be required for optimal management. For those patients who are referred for psychological/psychiatric treatment, are you re-assessing/repeating the PHQ-9 or GAD-7 for those patients with moderate-severe symptoms at the next clinic visit? Consider whether and how you will communicate the initial and regular rescreening results to clinicians providing mental health treatment within or outside your CF team.
- On reassessment, if the PHQ-9 or GAD-7 score is < 5 then rescreen at the next annual assessment period.
- **Will you elicit feedback from patients/parents on your depression and anxiety screening protocol?**
 - If so, how does that alter what you will do next?

Improving your processes: The “ACT” Part of the P-D-S-A cycle:

- **As a team, decide what part of your processes should change.**
 - Work together as a team to put your new processes in place. Meet periodically to review the process and seek feedback from your team to improve the process.
 - Decide if you need to change or improve your protocol or tracking tools so you can continue to measure the effectiveness of your screening.
- **Share your experience, resources and tools generously with other CF Centers**

Appendix 1: Depression Screening Tool - The PHQ-9

PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)

Over the **last 2 weeks**, how often have you been bothered by any of the following problems?

(Use "✓" to indicate your answer)

| | Not at all | Several days | More than half the days | Nearly every day |
|---|------------|--------------|-------------------------|------------------|
| 1. Little interest or pleasure in doing things | 0 | 1 | 2 | 3 |
| 2. Feeling down, depressed, or hopeless | 0 | 1 | 2 | 3 |
| 3. Trouble falling or staying asleep, or sleeping too much | 0 | 1 | 2 | 3 |
| 4. Feeling tired or having little energy | 0 | 1 | 2 | 3 |
| 5. Poor appetite or overeating | 0 | 1 | 2 | 3 |
| 6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down | 0 | 1 | 2 | 3 |
| 7. Trouble concentrating on things, such as reading the newspaper or watching television | 0 | 1 | 2 | 3 |
| 8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual | 0 | 1 | 2 | 3 |
| 9. Thoughts that you would be better off dead or of hurting yourself in some way | 0 | 1 | 2 | 3 |

FOR OFFICE CODING 0 + + +
=Total Score:

If you checked off **any** problems, how **difficult** have these problems made it for you to do your work, take care of things at home, or get along with other people?

| Not difficult at all | Somewhat difficult | Very difficult | Extremely difficult |
|--------------------------|--------------------------|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

Appendix 2: Depression Screening Tool- PHQ-9: Modified for Teens

PHQ-9 modified for Adolescents (PHQ-A)

Name: _____ Clinician: _____ Date: _____

Instructions: How often have you been bothered by each of the following symptoms during the past **two weeks**? For each symptom put an "X" in the box beneath the answer that best describes how you have been feeling.

| | (0) Not at all | (1) Several days | (2) More than half the days | (3) Nearly every day |
|--|----------------------|------------------------|---|-------------------------------|
| 1. Feeling down, depressed, irritable, or hopeless? | | | | |
| 2. Little interest or pleasure in doing things? | | | | |
| 3. Trouble falling asleep, staying asleep, or sleeping too much? | | | | |
| 4. Poor appetite, weight loss, or overeating? | | | | |
| 5. Feeling tired, or having little energy? | | | | |
| 6. Feeling bad about yourself – or feeling that you are a failure, or that you have let yourself or your family down? | | | | |
| 7. Trouble concentrating on things like school work, reading, or watching TV? | | | | |
| 8. Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you were moving around a lot more than usual? | | | | |
| 9. Thoughts that you would be better off dead, or of hurting yourself in some way? | | | | |

In the **past year** have you felt depressed or sad most days, even if you felt okay sometimes?
 Yes No

If you are experiencing any of the problems on this form, how **difficult** have these problems made it for you to do your work, take care of things at home or get along with other people?
 Not difficult at all Somewhat difficult Very difficult Extremely difficult

Has there been a time in the **past month** when you have had serious thoughts about ending your life?
 Yes No

Have you **EVER**, in your WHOLE LIFE, tried to kill yourself or made a suicide attempt?
 Yes No

***If you have had thoughts that you would be better off dead or of hurting yourself in some way, please discuss this with your Health Care Clinician, go to a hospital emergency room or call 911.*

Office use only: _____ **Severity score:** _____

Modified with permission from the PHQ (Spitzer, Williams & Kroenke, 1999) by J. Johnson (Johnson, 2002)

Appendix 3: Anxiety Screening Tool - GAD-7

GAD-7

| Over the <u>last 2 weeks</u>, how often have you been bothered by the following problems? | Not at all | Several days | More than half the days | Nearly every day |
|--|-------------------|---------------------|--------------------------------|-------------------------|
| <i>(Use "✓" to indicate your answer)</i> | | | | |
| 1. Feeling nervous, anxious or on edge | 0 | 1 | 2 | 3 |
| 2. Not being able to stop or control worrying | 0 | 1 | 2 | 3 |
| 3. Worrying too much about different things | 0 | 1 | 2 | 3 |
| 4. Trouble relaxing | 0 | 1 | 2 | 3 |
| 5. Being so restless that it is hard to sit still | 0 | 1 | 2 | 3 |
| 6. Becoming easily annoyed or irritable | 0 | 1 | 2 | 3 |
| 7. Feeling afraid as if something awful might happen | 0 | 1 | 2 | 3 |

(For office coding: Total Score T_____ = _____ + _____ + _____)

Appendix 4: Depression Scoring Tool
PHQ-9 Scoring Worksheet

Scoring the PHQ-9 and PHQ-9 Modified for Teens

Scoring the PHQ-9 or the PHQ-9 Modified for Teens is easy but involves thinking about several different aspects of depression.

To use the PHQ-9 as a diagnostic aid for Major Depressive Disorder:

- Questions 1 and/or 2 need to be endorsed as a “2” or “3”
- Need five or more positive symptoms (positive as defined by a “2” or “3” in questions 1-8 and by a “1”, “2”, or “3” in question 9).
- The functional impairment question (How difficult...) needs to be rated at least as “somewhat difficult.”

To use the PHQ-9 to aid in the diagnosis of dysthymia:

- The dysthymia question (In the past year...) should be endorsed as “yes.”

To use the PHQ-9 to screen for suicide risk:

- All positive answers to question 9 MUST be followed up by a clinical interview.

To use the PHQ-9 to obtain a total score and assess depressive severity:

- Add up the numbers endorsed for questions 1-9 and obtain a total score.
- See Table below:

| Total Score | Depression Severity |
|--------------------|----------------------------|
| 0-4 | No or minimal depression |
| 5-9 | Mild depression |
| 10-14 | Moderate depression |
| ≥ 15 | Severe depression |

Appendix 5: Anxiety Scoring Tool
GAD-7 Scoring Worksheet

Scoring the GAD-7

To use the GAD-7 to obtain a total score and assess the severity of anxiety:

- Add up the numbers endorsed for questions 1-9 and obtain a total score.
- See Table below:

| Total Score | Severity of Anxiety |
|--------------------|----------------------------|
| 0-4 | No or minimal anxiety |
| 5-9 | Mild anxiety |
| 10-14 | Moderate anxiety |
| ≥ 15 | Severe anxiety |

FACTS *for* FAMILIES

No. 66

May 2005

Helping Teenagers Deal with Stress

Teenagers, like adults, may experience stress everyday and can benefit from learning stress management skills. Most teens experience more stress when they perceive a situation as dangerous, difficult, or painful and they do not have the resources to cope. Some sources of stress for teens might include:

- school demands and frustrations
- negative thoughts and feelings about themselves
- changes in their bodies
- problems with friends and/or peers at school
- unsafe living environment/neighborhood
- separation or divorce of parents
- chronic illness or severe problems in the family
- death of a loved one
- moving or changing schools
- taking on too many activities or having too high expectations
- family financial problems

Some teens become overloaded with stress. When it happens, inadequately managed stress can lead to anxiety, withdrawal, aggression, physical illness, or poor coping skills such as drug and/or alcohol use.

When we perceive a situation as difficult or painful, changes occur in our minds and bodies to prepare us to respond to danger. This "fight, flight, or freeze" response includes faster heart and breathing rate, increased blood to muscles of arms and legs, cold or clammy hands and feet, upset stomach and/or a sense of dread.

The same mechanism that turns on the stress response can turn it off. As soon as we decide that a situation is no longer dangerous, changes can occur in our minds and bodies to help us relax and calm down. This "relaxation response" includes decreased heart and breathing rate and a sense of well being. Teens that develop a "relaxation response" and other stress management skills feel less helpless and have more choices when responding to stress.

Parents can help their teen in these ways:

- Monitor if stress is affecting their teen's health, behavior, thoughts, or feelings
- Listen carefully to teens and watch for overloading
- Learn and model stress management skills
- Support involvement in sports and other pro-social activities

Helping Teenagers Deal with Stress, “Facts for Families,” No. 66 (05/05)

Teens can decrease stress with the following behaviors and techniques:

- Exercise and eat regularly
- Avoid excess caffeine intake which can increase feelings of anxiety and agitation
- Avoid illegal drugs, alcohol and tobacco
- Learn relaxation exercises (abdominal breathing and muscle relaxation techniques)
- Develop assertiveness training skills. For example, state feelings in polite firm and not overly aggressive or passive ways: (“I feel angry when you yell at me” “Please stop yelling.”)
- Rehearse and practice situations which cause stress. One example is taking a speech class if talking in front of a class makes you anxious
- Learn practical coping skills. For example, break a large task into smaller, more attainable tasks
- Decrease negative self talk: challenge negative thoughts about yourself with alternative neutral or positive thoughts. “My life will never get better” can be transformed into “I may feel hopeless now, but my life will probably get better if I work at it and get some help”
- Learn to feel good about doing a competent or “good enough” job rather than demanding perfection from yourself and others
- Take a break from stressful situations. Activities like listening to music, talking to a friend, drawing, writing, or spending time with a pet can reduce stress
- Build a network of friends who help you cope in a positive way

By using these and other techniques, teenagers can begin to manage stress. If a teen talks about or shows signs of being overly stressed, a consultation with a child and adolescent psychiatrist or qualified mental health professional may be helpful.

For additional information see *Facts for Families*:

[#4 The Depressed Child](#)

[#47 The Anxious Child](#)

[#24 When to Seek Help](#)

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FACTS *for* FAMILIES

No. 04

July 2013

The Depressed Child

Not only adults become depressed. Children and teenagers also may have depression, as well. The good news is that depression is a treatable illness. Depression is defined as an illness when the feelings of depression persist and interfere with a child or adolescent's ability to function.

About 5 percent of children and adolescents in the general population suffer from depression at any given point in time. Children under stress, who experience loss, or who have attentional, learning, conduct or anxiety disorders are at a higher risk for depression. Depression also tends to run in families.

The behavior of depressed children and teenagers may differ from the behavior of depressed adults. Child and adolescent psychiatrists advise parents to be aware of signs of depression in their youngsters.

If one or more of these signs of depression persist, parents should seek help:

- Frequent sadness, tearfulness, crying
- Decreased interest in activities; or inability to enjoy previously favorite activities
- Hopelessness
- Persistent boredom; low energy
- Social isolation, poor communication
- Low self-esteem and guilt
- Extreme sensitivity to rejection or failure
- Increased irritability, anger, or hostility
- Difficulty with relationships
- Frequent complaints of physical illnesses such as headaches and stomachaches
- Frequent absences from school or poor performance in school
- Poor concentration
- A major change in eating and/or sleeping patterns
- Talk of or efforts to run away from home
- Thoughts or expressions of suicide or self-destructive behavior

A child who used to play often with friends may now spend most of the time alone and without interests. Things that were once fun now bring little joy to the depressed child. Children and adolescents who are depressed may say they want to be dead or may talk about suicide. Depressed children and adolescents are at increased risk for committing suicide. Depressed adolescents may abuse alcohol or other drugs as a way of trying to feel better.

The Depressed Child, "Facts for Families," No. 4 (5/08)

Children and adolescents who cause trouble at home or at school may also be suffering from depression. Because the youngster may not always seem sad, parents and teachers may not realize that troublesome behavior is a sign of depression. When asked directly, these children can sometimes state they are unhappy or sad.

Early diagnosis and treatment are essential for depressed children. Depression is a real illness that requires professional help. Comprehensive treatment often includes both individual and family therapy. For example, cognitive behavioral therapy (CBT) and interpersonal psychotherapy (IPT) are forms of individual therapy shown to be effective in treating depression. Treatment may also include the use of antidepressant medication. For help, parents should ask their physician to refer them to a qualified mental health professional, who can diagnose and treat depression in children and teenagers.

Also see the following Facts for Families:

#8 Children and Grief

#10 Teen Suicide

#21 Psychiatric Medication for Children

#38 Bipolar Disorder in Teens

#86 Psychotherapies for Children and Adolescents

#00 Definition of a Child and Adolescent Psychiatrist

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FACTS *for* FAMILIES

No. 47

November 2012

The Anxious Child

All children experience anxiety. Anxiety in children is expected and normal at specific times in development. For example, from approximately age 8 months through the preschool years, healthy youngsters may show intense distress (anxiety) at times of separation from their parents or other persons with whom they are close. Young children may have short-lived fears, such as fear of the dark, storms, animals, or a fear of strangers. Anxious children are often overly tense or uptight. Some may seek a lot of reassurance, and their worries may interfere with activities. Parents should not dismiss a child's fears. Because anxious children may also be quiet, compliant and eager to please, their difficulties may be missed. Parents should be alert to the signs of severe anxiety so they can intervene early to prevent complications. There are different types of anxiety in children.

Symptoms of separation anxiety include:

- constant thoughts and intense fears about the safety of parents and caretakers
- refusing to go to school
- frequent stomachaches and other physical complaints
- extreme worries about sleeping away from home
- being overly clingy
- panic or tantrums at times of separation from parents
- trouble sleeping or nightmares

Symptoms of phobia include:

- extreme fear about a specific thing or situation (ex. dogs, insects, or needles)
- the fears cause significant distress and interfere with usual activities

Symptoms of social anxiety include:

- fears of meeting or talking to people
- avoidance of social situations
- few friends outside the family

Other symptoms of anxious children include:

- many worries about things before they happen
- constant worries or concerns about family, school, friends, or activities
- repetitive, unwanted thoughts (obsessions) or actions (compulsions)
- fears of embarrassment or making mistakes

The Anxious Child, "Facts for Families," No. 47 (11/12)

- low self-esteem and lack of self-confidence

Severe anxiety problems in children can be treated. Early treatment can prevent future difficulties, such as loss of friendships, failure to reach social and academic potential, and feelings of low self-esteem. Treatments may include a combination of the following: individual psychotherapy, family therapy, medications, behavioral treatments, and consultation to the school.

If anxieties become severe and begin to interfere with the child's usual activities (for example separating from parents, attending school and making friends) parents should consider seeking an evaluation from a qualified mental health professional or a child and adolescent psychiatrist.

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FACTS *for* FAMILIES

No. 10

May 2008

Teen Suicide

Suicides among young people continue to be a serious problem. Each year in the U.S., thousands of teenagers commit suicide. Suicide is the third leading cause of death for 15-to-24-year-olds, and the sixth leading cause of death for 5-to-14-year-olds.

Teenagers experience strong feelings of stress, confusion, self-doubt, pressure to succeed, financial uncertainty, and other fears while growing up. For some teenagers, divorce, the formation of a new family with step-parents and step-siblings, or moving to a new community can be very unsettling and can intensify self-doubts. For some teens, suicide may appear to be a solution to their problems and stress.

Depression and suicidal feelings are treatable mental disorders. The child or adolescent needs to have his or her illness recognized and diagnosed, and appropriate treatment plans developed. When parents are in doubt whether their child has a serious problem, a psychiatric examination can be very helpful.

Many of the signs and symptoms of suicidal feelings are similar to those of depression.

Parents should be aware of the following signs of adolescents who may try to kill themselves:

- change in eating and sleeping habits
- withdrawal from friends, family, and regular activities
- violent actions, rebellious behavior, or running away
- drug and alcohol use
- unusual neglect of personal appearance
- marked personality change
- persistent boredom, difficulty concentrating, or a decline in the quality of schoolwork
- frequent complaints about physical symptoms, often related to emotions, such as stomachaches, headaches, fatigue, etc.
- loss of interest in pleasurable activities
- not tolerating praise or rewards

A teenager who is planning to commit suicide may also:

- complain of being a bad person or feeling rotten inside
- give verbal hints with statements such as: I won't be a problem for you much longer, nothing matters, It's no use, and I won't see you again

- put his or her affairs in order, for example, give away favorite possessions, clean his or her room, throw away important belongings, etc.
- become suddenly cheerful after a period of depression
- have signs of psychosis (hallucinations or bizarre thoughts)

If a child or adolescent says, I want to kill myself, or I'm going to commit suicide, always take the statement seriously and immediately seek assistance from a qualified mental health professional. People often feel uncomfortable talking about death. However, asking the child or adolescent whether he or she is depressed or thinking about suicide can be helpful. Rather than putting thoughts in the child's head, such a question will provide assurance that somebody cares and will give the young person the chance to talk about problems.

If one or more of these signs occurs, parents need to talk to their child about their concerns and seek professional help from a physician or a qualified mental health professional. With support from family and appropriate treatment, children and teenagers who are suicidal can heal and return to a more healthy path of development.

For more information, see Facts for Families:

#3 Teens: Alcohol and Other Drugs

#4 The Depressed Child

#37 Children and Firearms

#38 Bipolar Disorder in Children and Teens

#00 Definition of a Child and Adolescent Psychiatrist

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What is Psychotherapy?

Psychotherapy is a treatment that involves a relationship between a therapist and patient. It can be used to treat a broad variety of mental disorders and emotional difficulties. The goal of psychotherapy is to eliminate or control disabling or troubling symptoms so the patient can function better. Therapy can also help build a sense of well-being and healing.

Problems helped by psychotherapy include difficulties in coping with daily life, the impact of trauma, medical illness, or loss, like the death of a loved one, and specific mental disorders, like depression or eating disorders. Psychiatrists and other mental health professionals can provide psychotherapy.

One out of five Americans will experience a mental illness severe enough to require treatment at some time in their lives. Mental illnesses and emotional distress do not discriminate. They affect men and women of all ages, ethnic groups and socioeconomic statuses. These disorders impair how people feel, think, and act. They can interfere with how people function at work or school and affect their relationships with friends and family.

Therapy Sessions

The goals of treatment and arrangements for how often and how long to meet are planned jointly by the patient and therapist. Most sessions are 45 – 60 minutes long. Psychotherapy can be short-term, dealing with immediate issues, or long-term, dealing with longstanding and complex issues. Therapy may be conducted in an individual, family, couples, or group setting, and can be used by adults, children, or adolescents.

Medication is often used in addition to psychotherapy, and for some disorders the combined treatment is better than either alone. This is a decision to be made by a patient in consultation with the therapist.

Confidentiality is a basic requirement of psychotherapy. Also, although patients share personal feelings and thoughts, intimate physical contact with a therapist is never appropriate, acceptable, or useful.

Does Psychotherapy Work?

Research shows that most patients who receive psychotherapy experience symptom relief and are better able to function in their lives. Psychotherapy has been shown to improve emotions and behaviors and to be linked with positive changes in the brain and body. The benefits also include fewer sick days, less disability, fewer medical problems, and more job stability.

The cost of not treating mental disorders can often be greater personal anguish, substance abuse, poor work performance, broken relationships with family and friends, or death by suicide.

Types of Psychotherapy

Psychiatrists and other mental health professionals use several types of therapy. The choice of therapy type depends on the patient's particular illness and circumstances, and the patient's preference.

Common types of therapy include:

- * **Cognitive behavioral therapy, which helps patients identify and change thinking and behavior patterns that are harmful or ineffective, replacing them with more accurate thoughts and functional behaviors. It often involves practicing new skills in the "real world."**
- * **Interpersonal therapy, which is used to help patients understand underlying interpersonal issues that are troublesome, like unresolved grief, changes in social or work roles, conflicts with significant others, and problems relating to others.**
- * **Psychodynamic therapy, which is based on the idea that behavior and mental well-being are influenced by childhood relationships and experiences, psychological conflicts, and unproductive or inappropriate repetitive thoughts or feelings that are often outside of the person's awareness. It uses the**

relationship with the therapist to work on understanding oneself more fully and to change old patterns so a person can more fully take charge of his or her life.

- * **Psychoanalysis, which is a more intensive form of psychodynamic therapy. Sessions are conducted three or more times a week.**

Choosing a psychotherapist

Psychiatrists, psychologists, social workers, and some others may have specialized training in psychotherapy. However, only psychiatrists are also trained in medicine and are able to prescribe medications.

Psychiatrists are medical doctors who are specially trained to treat individuals for a broad range of emotional and behavioral problems. They are uniquely qualified to diagnose and treat emotional difficulties because they understand the mind, brain and body and their interactions. They are trained to use psychotherapy, medications, and the two in combination.

Finding a psychiatrist or other therapist with whom an individual can work well is important. Good sources of referrals include family physicians, local psychiatric societies, medical schools, and community health centers.

What Is Depression?

Depression is a serious medical illness that negatively affects how you feel, the way you think and how you act.

Depression has a variety of symptoms, but the most common are a deep feeling of sadness or a marked loss of interest or pleasure in activities. Other symptoms include:

- ✱ Changes in appetite that result in weight losses or gains unrelated to dieting
- ✱ Insomnia or oversleeping
- ✱ Loss of energy or increased fatigue
- ✱ Restlessness or irritability
- ✱ Feelings of worthlessness or inappropriate guilt
- ✱ Difficulty thinking, concentrating, or making decisions
- ✱ Thoughts of death or suicide or attempts at suicide.

Depression is common. It affects nearly one in 10 adults each year—nearly twice as many women as men. It's also important to note that depression can strike at any time, but on average, first appears during the late teens to mid-20s. Depression is also common in older adults.

Fortunately, depression is very treatable.

How Depression and Sadness Are Different

The death of a loved one, loss of a job, or the ending of a relationship are difficult experiences for a person to endure. It is normal for feelings of sadness or grief to develop in response to such stressful situations. Those experiencing trying times often might describe themselves as being "depressed."

But sadness and depression are not the same. While feelings of sadness will lessen with time, the disorder of depression can continue for months, even years. Patients who have experienced depression note marked differences between normal sadness and the disabling weight of clinical depression.

Postpartum Depression

Postpartum depression—an illness associated with the delivery of a child—is caused by changes in hormones and

can run in families. It is distinguished from "baby blues"—an extremely common reaction following delivery—both by its duration and the debilitating effects of indifference the mother has about herself and her children. About one in 10 new mothers experience some degree of postpartum depression; women with severe premenstrual syndrome are more likely to suffer from it.

Women with postpartum depression love their children but may be convinced that they are not able to be good mothers.

What Causes Depression?

Depression can affect anyone—even a person who appears to live in relatively ideal circumstances.

But several factors can play a role in the onset of depression:

Biochemistry. Abnormalities in two chemicals in the brain, serotonin and norepinephrine, might contribute to symptoms of depression, including anxiety, irritability and fatigue. Other brain networks undoubtedly are involved as well; scientists are actively seeking new knowledge in this area.

Genetics. Depression can run in families. For example, if one identical twin has depression, the other has a 70% chance of having the illness sometime in life.

Personality. People with low self-esteem, who are easily overwhelmed by stress, or who are generally pessimistic appear to be vulnerable to depression.

Environmental factors. Continuous exposure to violence, neglect, abuse or poverty may make people who are already susceptible to depression all the more vulnerable to the illness.

Also, a medical condition (e.g., a brain tumor or vitamin deficiency) can cause depression, so it is important to be evaluated by a psychiatrist or other physician to rule out general medical causes.

How Is Depression Treated?

For many people, depression cannot always be controlled for any length of time simply by exercise, changing diet, or taking a vacation. It is, however, among the most treatable of mental disorders: between 80% and 90% of people with

depression eventually respond well to treatment, and almost all patients gain some relief from their symptoms.

Before a specific treatment is recommended, a psychiatrist should conduct a thorough diagnostic evaluation, consisting of an interview and possibly a physical examination. The purpose of the evaluation is to reveal specific symptoms, medical and family history, cultural settings and environmental factors to arrive at a proper diagnosis and to determine the best treatment.

Medication: Antidepressants may be prescribed to correct imbalances in the levels of chemicals in the brain. These medications are not sedatives, "uppers" or tranquilizers. Neither are they habit-forming. Generally antidepressant medications have no stimulating effect on those not experiencing depression.

Antidepressants may produce some improvement within the first week or two of treatment. Full benefits may not be realized for two to three months. If a patient feels little or no improvement after several weeks, his or her psychiatrist will alter the dose of the medication or will add or substitute another antidepressant.

Psychiatrists usually recommend that patients continue to take medication for six or more months after symptoms have improved. After two or three episodes of major depression, long-term maintenance treatment may be suggested to decrease the risk of future episodes.

Psychotherapy: Psychotherapy, or "talk therapy," is sometimes used alone for treatment of mild depression; for moderate to severe depression, it is often used in combination with antidepressant medications.

Psychotherapy may involve only the individual patient, but it can include others. For example, family or couples therapy can help address specific issues arising within these close relationships. Group therapy involves people with similar illnesses.

Depending on the severity of the depression, treatment can take a few weeks or substantially longer. However, in many cases, significant improvement can be made in 10 to 15 sessions.

Conclusion

Depression is never normal and always produces needless suffering. With proper diagnosis and treatment, the vast majority of people with depression will overcome it.

Adolescence can be a turbulent time. Teenagers deal with a vast array of new experiences during this transitional period, such as new relationships, decisions about the future, and physical changes that are taking place in their bodies.

A considerable number of teenagers are dealing with depression, an illness with significant long-term consequences, including an increased risk for suicide.

Other teenagers are simply overwhelmed by the uncertainties of adolescence and feel they have nowhere to turn. Their search for answers may lead them to begin "self-medicating" their pain by abusing drugs or alcohol. Or they might express their rage and frustration by engaging in acts of violence. They don't want to talk about their emotions or problems because they may think that will make them a burden, or that others will make fun of them. Too often, these troubled teens opt instead to take their own lives.

Suicide Signals

The strongest risk factors for attempted suicide in youth are depression, alcohol or drug abuse, aggressive or disruptive behaviors, and a previous suicide attempt. If several of the following symptoms, experiences, or behaviors are present, a mental health professional or another trusted adult, such as a parent or a school counselor, should be consulted:

- * Depressed mood
- * Substance abuse
- * Frequent episodes of running away or being incarcerated
- * Family loss or instability; significant problems with parents
- * Expressions of suicidal thoughts, or talk of death or the afterlife during moments of sadness or boredom
- * Withdrawal from friends and family
- * Difficulties in dealing with sexual orientation
- * No longer interested in or enjoying activities that once were pleasurable
- * Unplanned pregnancy
- * Impulsive, aggressive behavior or frequent expressions of rage

Adolescents who consider suicide generally feel alone, hopeless and rejected. They are especially vulnerable to these feelings if they have experienced a loss, humiliation or trauma of some kind: poor performance on a test; breakup with a boyfriend or girlfriend; parents with alcohol or drug problems or who are abusive; or a family life affected by parental discord, separation or divorce. However, a teenager still may be depressed or suicidal even without any of these adverse conditions.

Teenagers who are planning suicide may "clean house" by giving away favorite possessions, cleaning their rooms, or throwing things away. After a period of depression, they may also become suddenly cheerful because they think that by deciding to end their lives they have "found the solution."

Young people who have attempted suicide in the past or who talk about suicide are at greater risk for future attempts. Listen for hints like "I'd be better off dead" or "I won't be a problem for you much longer."

Some Suicide Statistics

While the teen suicide rate has declined by over 25 percent since the early 1990s, suicide is the third leading cause of death among young people ages 15 to 24.

- * It is estimated that depression increases the risk of a first suicide attempt by at least 14-fold.
- * Over half of all kids who suffer from depression will eventually attempt suicide at least once, and more than seven percent will die as a result.
- * Four times as many men as women die by suicide, but young women attempt suicide three times more frequently than young men.
- * Firearms are used in a little more than half of all youth suicides.

What Can Be Done?

Teens aren't helped by lectures or by hearing all the reasons they have to live. What they need is to be reassured that they have someone to whom they can turn—be it family, friends, school counselor, physician, or teacher—to discuss their feelings or problems. It must be a person who is willing to listen and who is able to reassure the individual that depression and suicidal tendencies are treatable.

Treatment is of utmost importance and may involve medications, talk therapy or a combination of the two. Help can be found in a variety of places: through local mental health associations, family physicians, a county medical society, a local hospital's department of psychiatry, a community mental health center, a mood disorders program affiliated with a university or medical school, or a family service/social agency.

In short, simply taking the time to talk to troubled teenagers about their emotions or problems can help prevent the senseless tragedy of teen suicide. Let them know help is available.

DEPRESSION

Depression is a common psychological problem, experienced by many people at some time during their lives. One member of most families has experienced an episode of depression severe enough to require formal treatment. Depressed mood is costly to individuals and society as a whole, both economically as well as in terms of quality of life.

Major Characteristics

The primary feature of depression is a sad mood state, which, in its most severe form, is experienced as a feeling of helplessness, hopelessness, and despair.

When people experience depressed mood, it is common for them also to experience a decrease in social activities, problems with relationships, and an increase in crying or "a desire to cry even if you cannot get the tears out" (called dry tears depression).

Cognitive Characteristics

There are also several cognitive features of depression that may include a loss of concentration and memory; a belief that you are becoming worthless; a belief that things cannot be made better, have gotten bad, and will get worse; and a focus on negative things about yourself without enough attention on positive things about yourself.

Biological Characteristics

The biological characteristics of depression include disrupted sleep (especially trouble falling sleep and a pattern of waking up very early in the morning), loss of appetite, loss of sexual desire or lack of interest in sexual activity, and fatigue or tiredness during the day. It is also important to know that depression may happen along with increased anxiety and feelings of anger or hostility. In about 10% of cases, depression will be followed by problems with alcohol or drugs.

Frequency

Depression severe enough to require formal treatment occurs in about 6% of the women and 3% of the men in this country. Depression can occur, although at lower rates, among children. During adolescence, the rates gradually increase, so that by age 14 or 15 they equal those of adults. Among the elderly, the rates decrease slightly, but depression remains a frequent and serious problem among this age group.

Causes

Life Events

Although no definitive and final answer exists to the question of what causes depression, much is known. Depression may be caused by major negative life events – for example, the death of a loved one, a divorce, a severe financial setback, or even a move to a different neighborhood or part of the country. Other factors that may cause depression include trouble having and keeping social relationships and trouble keeping your everyday life in line with your values in life.

What Is Cognitive Behavior Therapy?

Behavior Therapy and Cognitive Behavior Therapy are types of treatment that are based firmly on research findings. These approaches aid people in achieving specific changes or goals.

Changes or goals might involve:

- **A way of acting:** like smoking less or being more outgoing;
- **A way of feeling:** like helping a person to be less scared, less depressed, or less anxious;
- **A way of thinking:** like learning to problem-solve or get rid of self-defeating thoughts;
- **A way of dealing with physical or medical problems:** like lessening back pain or helping a person stick to a doctor's suggestions; or
- **A way of coping:** like training developmentally disabled people to care for themselves or hold a job

Behavior Therapists and Cognitive Behavior Therapists usually focus more on the current situation and its solution, rather than the past. They concentrate on a person's views and beliefs about their life, not on personality traits. Behavior Therapists and Cognitive Behavior Therapists treat individuals, parents, children, couples, and families. Replacing ways of living that do not work well with ways of living that work, and giving people more control over their lives, are common goals of behavior and cognitive behavior therapy.

HOW TO GET HELP: If you are looking for help with depression, either for yourself or someone else, you may be tempted to call someone who advertises in a local publication or on the Internet. You may, or may not, find a competent therapist in this manner. It is wise to check on the credentials of a psychotherapist. It is expected that competent therapists hold advanced academic degrees and are trained in techniques for treating depression. They should be listed as members of professional organizations, such as the Association for Behavioral and Cognitive Therapies or the American Psychological Association. Of course, they should be licensed to practice in your state. You can find competent specialists who are affiliated with local universities or mental health facilities or who are listed on the websites of professional organizations. You may, of course, visit our website (www.abct.org) and click on "Find a CBT Therapist."

The Association for Behavioral and Cognitive Therapies (ABCT) is an interdisciplinary organization committed to the advancement of a scientific approach to the understanding and amelioration of problems of the human condition. These aims are achieved through the investigation and application of behavioral, cognitive, and other evidence-based principles to assessment, prevention, and treatment.

Thinking Patterns

Depression also may be related to faulty thinking patterns. These might include magnifying how badly things are going for you, drawing negative conclusions from life events even when it doesn't make good sense to do so, and generally having a negative view of oneself, the world, and the future.

Biochemical Imbalances

There are several types of biochemical imbalances that may occur in depression. Depression may develop when a biological predisposition to depression is activated by an event. This predisposition is activated when one experiences a major life event (or a sequence of more minor negative life events) and/or develops a negative cognitive pattern of evaluating oneself and one's life events. It is believed that the biological characteristics of depression (sleep disturbance, appetite loss, loss of sexual interest, and tiredness) are related to this biochemical imbalance.

Treatment

During the past few years, very effective treatments have been developed for depression. The majority of people experiencing depression can expect to experience considerable relief from depression within 3 or 4 weeks of effective treatment, and long-lasting relief within 3 to 6 months of treatment.

Behavioral and Cognitive Behavioral Therapies

Behavior therapy and cognitive behavior therapy are among the treatments that have been most extensively evaluated and that have been shown through research to be effective. Behavioral treatments help a person to engage in healthy life activities, particularly activities that are consistent with one's life values. Behavior therapy also helps people to develop skills and abilities to cope with major life events and to learn social relationship skills when these are missing. Cognitive behavior therapy includes the development of behavioral skills, but focuses more on correcting the faulty thinking patterns of depression. Most people experiencing depression will profit from participating in cognitive behavioral therapy that is widely available from mental health professionals.

Some severe depressions, especially those involving severe biological symptoms, may require antidepressant medications. Such medications are available, and many produce quick and effective relief of depression. When antidepressant medication is necessary, it may be combined with behavior therapy or cognitive behavior therapy to produce effective and long-lasting treatment results. Some people believe that depression will gradually go away, or that if you "just get yourself in gear" you can get over it yourself. Indeed, in some small percentage of cases that may be true. Unfortunately, depression usually does not go away without treatment. Therefore, if you are experiencing a severe, acute depression or a chronic lower level depression, it is best and wise to seek and participate in therapy. Fortunately, there are treatments available to lessen depression and the life difficulties that come along with it.

For more information or to find a therapist:

ASSOCIATION for BEHAVIORAL and COGNITIVE THERAPIES

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ANXIETY DISORDERS

Anxiety is a normal emotion and common experience, and it represents one of the most basic of human emotions. At one time or another, all of us are likely to be “stressed out,” worried about finances or health or the children, fearful in certain situations (such as when on a ladder or just before an operation), and concerned about what other people think. In general, anxiety serves to motivate and protect an individual from harm or unpleasant consequences.

For many people, however, constant or excessive anxiety disrupts their daily activities and quality of life; for others, panic, which seems to come out of nowhere, can cause terrible physical symptoms, such as faintness, chills, and even extreme chest pains. Anxiety disorders are so common that more than 1 in every 10 Americans will suffer with one at some point in their lives. Fortunately, anxiety disorders can be treated, generally with short-term, effective, and cost-efficient methods.

Types of Anxiety Disorders

There are a number of different disorders that fall under the category of anxiety. They include Panic, Generalized Anxiety, Obsessive-Compulsive Disorder (or OCD), various Phobias (including Social Phobia and Agoraphobia), and Posttraumatic Stress Disorder (or PTSD). Each of these is described below.

PANIC DISORDER

On his way home from work, John is driving through his neighborhood when suddenly a child darts out into the street in front of the car. John slams on the brakes and swerves, just missing the child. As he pulls over, John’s heart is beating furiously, and he is breathless, sweating, and shaking. He could have killed that child. It is several long minutes before he is able to continue home. This is a normal reaction to a potentially catastrophic situation. Our nervous systems are equipped with an alarm system, much like a fire alarm, that alerts us to danger. This system is triggered by impending danger, and it instantaneously prepares our body to “fight or flee” and ultimately protects us from harm. For some individuals, the alarm system rings at inappropriate times, when there is no danger present. Imagine sitting at home, watching television, and, from out of nowhere, this alarm reaction occurs. A panic attack is the physical sensations of the alarm system and includes sensations such as a racing heart, rapid breathing, tingling or numbing sensations, hot or cold flashes, sweating, trembling, and similar sensations. Individuals who experience unexpected alarms develop a fear of these sensations, and often attribute the attacks to major medical problems, such as a heart attack or stroke. When no physical cause is identified, the individual begins to fear losing control, or even think that he or she is going crazy. The more a person fears these intense sensations, the more aware he or she becomes of the sensations. The fear of the panic attacks ultimately can cause the attacks to become more intense and frequent. Fear of panic attacks, then, often becomes the cause of the panic attack.

What Is Cognitive Behavior Therapy?

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Changes or goals might involve:

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- A way of feeling, like helping a person to be less scared, less depressed, or less anxious;
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- A way of coping, like training developmentally disabled people to care for themselves or hold a job.

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SOCIAL PHOBIA

Giving a talk in front of a group, walking into a room full of strangers, or meeting with the boss can make anyone somewhat anxious, but for the person with social phobia, such situations cause intense fear and even panic attacks. Individuals with social phobia fear being evaluated negatively by others, and worry excessively about embarrassing themselves. This overwhelming fear often leads the person to avoid social situations. Social phobia is not the normal nervousness a person has before meeting new people, it is an intense fear that causes that person to avoid that situation, significantly disrupting the person's life. Social phobia is one of the most common forms of anxiety disorder, and is often accompanied by depression. In addition, some individuals with social phobia develop alcoholism or other substance abuse problems. Social phobia may be present in all social situations or it may appear in only certain situations, such as speaking in public.

GENERALIZED ANXIETY DISORDER (GAD)

Everyone worries from time to time about finances, the job, health, or family matters. For individuals with GAD, the worry is excessive, difficult to control, and unrealistic. In addition, GAD is accompanied by a range of physical symptoms, such as muscle aches, tension, soreness, sleepless nights, irritability, concentration difficulties, and restlessness. The worry and physical symptoms of GAD can persist for six months or longer, thus reinforcing the person's feelings of helplessness and anxiety. Individuals with GAD are also more likely to develop additional anxiety disorders and depression.

SPECIFIC PHOBIAS AND AGORAPHOBIA

Dogs, spiders, injections, small rooms, thunderstorms, blood, elevators, crowds, driving, heights, and deep water can all cause a certain degree of unease in most individuals. It is relatively easy for most individuals to think about a particular situation or object that they would prefer to avoid. However, when that fear is persistent, or the individual's life is disrupted when trying to avoid the cause of that fear, this is considered a specific phobia. Although individuals with specific phobias recognize that their fear is way out of proportion to the actual threat of the situation, they are unable to control the fear and may experience an anxiety attack when encountering the feared situation or object. As an example, individuals with a specific phobia of blood often faint when they see blood; the anxiety and, especially, fainting, make simple medical or dental procedures overwhelming. Agoraphobia, which is closely linked with panic attacks, is particularly disruptive because the person fears most any open space, thereby making simple tasks, such as grocery shopping, or even seeing a therapist, anxiety-provoking.

OBSESSIVE-COMPULSIVE DISORDER (OCD)

Ever wonder if you locked the doors or left the stove on? Ever have the feeling that something terrible was about to happen? Do you have certain routines that you follow in the morning or evening? These thoughts and simple routines are not unusual. However, for the person with OCD, these thoughts and routines occur repeatedly, and the individual feels unable to stop them. Moreover, these thoughts and behaviors cause significant distress and interference in the individual's life. When "checking behavior" or other compulsive

sions take hours, not minutes, of a person's day, therapists consider this to be OCD. Typical obsessions include fears of contamination or poisoning, religious themes, doubts, and thoughts of sex. Compulsions are often desperate attempts to "neutralize" the obsession and anxiety, and involve repeating some behavior such as washing, checking, counting, tapping or touching things repeatedly.

POSTTRAUMATIC STRESS DISORDER (PTSD)

Terrible events can cause extreme feelings of helplessness, horror, and fear. These events might include physical or sexual assault, car accidents, natural disasters, robbery, and war. People with PTSD develop anxiety and intrusive thoughts about the event, and may feel at times as though the event were happening again. Classic symptoms of PTSD include nightmares, being easily startled, anger outbursts, feelings of detachment, and hopelessness about the future. PTSD can occur within one month of the event, or may be delayed for many years after the trauma.

How Can Cognitive and Behavior Therapy Help People With Anxiety Disorders?

There is hope for individuals with anxiety disorders, because these problems can be effectively treated with cognitive therapy and behavior therapy. In some cases, treatment of a specific phobia takes only one session, while most programs for the other anxiety disorders take, on average, 12 to 18 sessions. Cognitive behavioral treatments typically involve four main components.

Education about the nature of anxiety helps the individual understand his or her responses and teaches the individual ways to more effectively cope with anxiety. **Somatic management skills** teach relaxation and breathing techniques, which help the individual manage the physical symptoms and discomfort of anxiety. **Cognitive skills** address the individual's beliefs and thoughts, and focus on teaching more adaptive, realistic thinking styles. And, all treatments for anxiety involve some form of **behavioral exposure**, a gradual, step-by-step confrontation of the fear with mastery and skill.

For many people, behavior therapy and cognitive therapy alone will be enough to overcome or manage the various anxiety disorders. For some individuals, however, medication, in combination with cognitive behavioral therapy, can foster a return to a full and satisfying life. Programs combining pharmacology and behavior therapy are available for the range of anxiety disorders.

For more information or to find a therapist:

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Appendix 7: Educational Tool for Mental Health Providers.

This handout was provided by Carla Frederick, M.D. You can use this, modify/update this template, or create your own.

Overview of Cystic Fibrosis

What Is Cystic Fibrosis?

Cystic fibrosis (CF) is an inherited chronic disease that affects the lungs and digestive system of about 30,000 children and adults in the United States (70,000 worldwide). Patients with CF have two copies of a defective gene located on chromosome 7. The defective gene results in a defective protein called CFTR (cystic fibrosis transmembrane regulator) which cause the body to produce unusually thick, sticky mucus that:

- clogs the lungs and leads to life-threatening lung infections; and
- obstructs the pancreas and stops natural enzymes from helping the body break down and absorb food.

In the 1950s, few children with cystic fibrosis lived to attend elementary school. Today, advances in research and medical treatments have further enhanced and extended life for children and adults with CF. Many people with the disease can now expect to live into their 30s, 40s and beyond.

Symptoms of Cystic Fibrosis

People with CF can have a variety of symptoms, including:

- very salty-tasting skin
- persistent coughing, at times with phlegm
- frequent lung infections
- wheezing or shortness of breath
- poor growth/weight gain in spite of a good appetite
- frequent greasy, bulky stools or difficulty in bowel movements

Statistics

- About 1,000 new cases of cystic fibrosis are diagnosed each year.
- More than 70% of patients are diagnosed by age two.
- More than 45% of the CF patient population is age 18 or older.
- The predicted median age of survival for a person with CF is in the mid-30s.

The Cystic Fibrosis Foundation

Since 1955, the Cystic Fibrosis Foundation has been the driving force behind the pursuit of a cure. Thanks to the dedication and financial backing of our supporters--patients, families and friends, clinicians, researchers, volunteers, individual donors, corporations and staff, we are making a difference.

CF Foundation-Accredited Care Centers

- The Cystic Fibrosis Foundation provides funding for and accredits more than 110 cystic fibrosis care centers and 55 affiliate programs nationwide, including 96 programs for treating adults with CF.

- The high quality of specialized care available throughout the care center network has led to the improved length and quality of life for people with CF. Located at teaching and community hospitals across the country, these care centers offer the best care, treatments, and support for those with CF.

Much more information can be found on www.cff.org. There are articles, videos, and a variety of other links meant for patients, caregivers, and CF providers. Check it out!

Treatment of Cystic Fibrosis

A CF care center is made up of physicians, physician's assistants, nurses, respiratory therapists, dietitians, social workers, pharmacists, and medical assistants. Everyone truly plays a critical role in giving each patient with CF the best possible care. At each clinic visit and while patients are in the hospital, these CF team members each perform their specific role of expertise as they see the patient.

CF is multisystem disease. It's not just the lungs that are affected – the GI tract, endocrine system, sinuses, muscles and joints and sometimes mental health of each patient also have problems related to the disease that need to be monitored regularly. Below are the main treatment categories that we pay attention to every time we see a patient with CF.

Pulmonary

End stage lung disease is the eventual cause of death in most patients with cystic fibrosis. The disease has seen great advances over the last 20 years allowing our patients to live longer and healthier lives. Advances and adherence to pulmonary therapies that are proven to be effective are responsible for a large part of this improvement in the health of patients with CF. Pulmonary treatment consists of airway clearance, bronchodilators, inhaled medications, and antibiotics.

Airway Clearance Techniques

Airway clearance techniques (ACTs) are treatments that help people with cystic fibrosis (CF) stay healthy and breathe easier. ACTs loosen thick, sticky lung mucus so it can be cleared by coughing or huffing. Clearing the airways reduces lung infections and improves lung function. There are many ACTs. ACTs move mucus from small to large (more central) airways to be coughed or huffed out.

Types of ACT

- **Coughing** is the most basic ACT. It is a reflex. It clears mucus with high-speed airflow. But sometimes mucus cannot be cleared just with a lot of coughing. Coughing a lot can make you feel more short of breath and worse, not better. **Huffing** is a type of cough. It also involves taking a breath in and actively exhaling. It is more like “huffing” onto a mirror or window to steam it up. It is not as forceful as a cough but can work better and be less tiring.
- **Oscillating Positive Expiratory Pressure (Oscillating PEP)** is an ACT where the person blows all the way out many times through a device. Types of Oscillating PEP devices include the Flutter™, Acapella™, Cornet™ and Intrapulmonary Percussive

Ventilation (IPV). Breathing with these devices vibrates the large and small airways. This vibration thins, dislodges and moves mucus. After blowing through the device many times, the person coughs or huffs. This cycle is repeated many times.

- **High-frequency Chest Wall Oscillation** also is called the Vest or Oscillator. An inflatable vest is attached to a machine that vibrates it at high frequency. The vest vibrates the chest to loosen and thin mucus. Every five minutes the person stops the machine and coughs or huffs.

A little more about mucus...

The lungs make mucus to help defend against germs. CF changes the mucus, making it thick and hard to clear. This mucus is where infections can occur. Infections cause inflammation or swelling of the lungs. Both infections and inflammation cause more mucus to be made. More mucus in the lungs can lead to more infections. This cycle of infection, inflammation and more mucus can hurt the lungs and lower lung function. Antibiotics treat infections. They make you feel better but, over time, the damage builds. This is why your CF care team may say to do ACTs even when you are well. When you get sick, do them more often.

How does mucus move out of the lungs?

Mucus moves three ways:

- Tiny hairs, called cilia, line bronchi. Cilia move back and forth. Mucus is carried on top of cilia. Cilia cannot carry thick, extra mucus as well.
- Mucus builds and lines the bronchi walls. ACTs increase air flow through the bronchi. As air rushes over the mucus in the bronchi, the mucus is pulled toward the large airways. This is like wind on the water making a crest on waves, or wind across a dry plain blowing dust. The faster the air flows, the better it moves mucus.
- If air gets behind thick mucus, it can push it into larger airways. More air behind mucus means more air flowing over it, pulling the mucus along. If air does not get behind mucus, mucus is hard to move.

Bronchodilators

Albuterol is a medication called a bronchodilator. It is inhaled and acts on the small muscles in the respiratory tract (bronchioles) to cause them to dilate or get bigger. This medication is used prior to inhaled medications to open the airways as much as possible, prevent bronchospasm or irritation that can be caused by some inhaled medications. Some patients use their albuterol aside from treatments if they have a component of their cystic fibrosis that is like asthma. (Asthma and CF are similar in that they both affect the respiratory tract and are treated in part by albuterol but overall are very different diseases.)

Inhaled Medications

Inhaled drugs are commonly used in cystic fibrosis care because they reach the airways quickly and easily. Inhaled treatments can be given by aerosol—a mist made from liquid medicines. The medicines go into a cup (nebulizer) that is attached to a small air compressor. The compressor blows air through the cup and makes a mist. People with cystic fibrosis breathe the mist in through a mouthpiece or mask for several minutes. Some medicines can also be given as metered dose inhalers (MDI), which deliver one dose of medicine at a time.

There are several kinds of inhaled medications used to treat CF symptoms:

- Mucolytics like **Pulmozyme® (DNase)** to thin mucus so people can cough it out easier.
- Antibiotics to treat infections. Inhaled **TOBI®** (tobramycin solution for inhalation) is a widely used antibiotic treatment. TOBI can be effective against the most common source of chronic lung infections, a bacterium called *Pseudomonas aeruginosa*. **Cayston** (aztreonam for inhalation solution) also is used to improve respiratory symptoms in people with CF who have *Pseudomonas aeruginosa*. A third inhaled antibiotic is called **Coly-Myxin** (colistin).
- **Hypertonic saline** to draw more water into the airways and make it easier to cough out the mucus.

Antibiotics

Antibiotics are used to fight infection-causing bacteria. Infections are common in the lungs of people with cystic fibrosis, so antibiotics are an important part of regular care. The most common bacteria that colonizes (lives in) the lungs of patients with CF are *pseudomonas aeruginosa* and *staphylococcus aureus*. The antibiotic drug, the dosage, and the length of time to take the drug, all vary from person to person. The infection-causing bacteria can become **resistant** to some drugs.

Antibiotics come in three different forms:

- **Oral antibiotics** – liquids, tablets or capsules that must be swallowed.
- **Intravenous (IV) antibiotics** – liquid medicine that goes directly into the blood through an IV catheter. An IV may require a hospital stay, but can also be done at home.
- **Inhaled antibiotics** – an aerosol or mist that can reach the airways directly.
- [Azithromycin](#), a common antibiotic, was shown to have special benefits for some people with cystic fibrosis. It does not kill the bacteria in the lungs but helps to reduce chronic inflammation that is present in the airways. The drug helped to preserve and improve lung function in research trials as well as reduced the number of hospital stays.

Gastrointestinal

Nutrition & Eating Right

- Nutrition needs change with age—especially for people with cystic fibrosis. Dietitians at cystic fibrosis [care centers](#) offer specially tailored dietary programs for each stage of life.
- All patients should eat a high-calorie diet, including supplements when needed
- Children and teens with cystic fibrosis need extra calories to grow and develop. Everyone with CF, no matter their age, needs good nutrition to stay strong against lung infections and other challenges. Occasionally, patients need to take nutrition through a tube ("[tube-feeding](#)") to provide extra calories that help the body grow and stay strong.
- Body Mass Index, or “BMI” is a calculation used to assess how healthy an individual’s weight is relative to their height. It has been shown in numerous investigations that patient’s with a BMI that is at goal have better lung health.
- Good nutrition can help to prevent or lessen the impact of other health problems like CF related diabetes and osteoporosis.

Pancreatic Enzyme Replacement

The pancreas is responsible for producing enzymes to digest fats, carbohydrates, and proteins as well as making insulin for the body. Both of these functions are affected in many patients with CF. More than 90 percent of people with CF take pancreatic enzymes with every meal and snack they eat to improve digestion and growth because their body does not make secrete the proper amount of enzymes. About 40% of patients with CF have a problem secreting insulin and have what is called CF related diabetes.

Endocrine

What is Cystic Fibrosis-Related Diabetes?

Cystic Fibrosis-Related Diabetes (CFRD) is a unique type of diabetes. It is not the same as diabetes in people without CF. The diagnosis and treatment are not exactly the same. CFRD is extremely common in people with CF especially as they get older. CFRD is found in 35 percent of adults aged 20 to 29 and 43 percent for those over 30 years old.

Causes of CFRD

There are two types of diabetes in the non-CF population - **Type I diabetes** (known as “insulin-dependent diabetes”) and **Type II diabetes** (known as “non-insulin dependent diabetes”).

CFRD has some features of both types of diabetes. People with CF do not make enough insulin. This is a result of scarring in the pancreas.

Insulin resistance is another reason people develop CFRD. Insulin resistance means your body does not use insulin normally.

Symptoms of CFRD

Common symptoms, such as increased thirst and increased urination, are caused by high blood sugar levels (hyperglycemia). Other symptoms of CFRD are excessive fatigue, weight loss and unexplained decline in lung function.

Screening and Diagnosis

Many people with CFRD do not know they have it until they are tested for diabetes. Since many people with CF have no symptoms, this is the best way to find out if someone has CF-related diabetes.

People with CFRD who receive treatment for diabetes often start to feel better, gain weight and improve their lung function.

Treatment of CFRD

Insulin is the medication used to treat CFRD. It allows sugars and proteins to move from the blood into the body’s cells. It is used for energy and to build muscle.

Keeping blood glucose levels at a normal or near-normal level helps you gain weight, feel better and have more energy. It also lowers the risk of problems caused by diabetes.

Mental Health

Individuals with chronic diseases are at increased risk for symptoms of depression and anxiety. The connection between cystic fibrosis and depression has been studied in over 6000 patients (12

years of age and older) and 4000 parent caregivers in an epidemiological study across nine countries.

How many people with CF experience depression and anxiety?

Depression and anxiety are common in individuals with CF. One in three patients twelve years and older have high levels of anxiety and 17% have symptoms of depression. Specifically, in adult patients, 32% are anxious and 19% have elevated symptoms of depression. In adolescents, symptoms of anxiety are found in 22% of patients and depression found in 10% of adolescents.

For parent caregivers, the statistics are even higher. Half of mothers of children (0-17 years) with CF have elevated levels of anxiety, and 37% of moms have elevated symptoms of depression. One third of fathers have elevated rates of anxiety and depressive symptoms. These rates are much higher than in the general population.

What are the causes of anxiety and depression in people with CF and their caregivers?

There is no single cause of depression — for the general population — or for people with cystic fibrosis. However, some of the issues that people with CF and their caregivers face may be contributing factors. In any complex chronic condition that requires a time consuming treatment regimen and the potential for health to worsen, symptoms of anxiety and depression are more common. In CF, treatments can take up to 2 to 4+ hours per day, making it difficult to balance the things they want to do and also manage the disease. Because CF is a deteriorating condition, people with the disease and their families often struggle to cope with the uncertainty of the future. Some level of stress or anxiety is, at times, to be expected. In other words, it is not a sign of a medical condition, but a normal response to a very difficult situation.

What do higher rates of anxiety and depression mean for those with CF?

A person who feels overwhelmed, anxious or sad may not adjust well to the CF diagnosis. Individuals with CF who are depressed are less likely to adhere to their treatments. In addition, if you have a lot of anxiety, you may be less able to take care of yourself or your loved one. Too much anxiety, particularly in caregivers, can be very draining and exhausting.

Lung Transplantation

- Lung transplantation is a difficult and personal decision. The Cystic Fibrosis Foundation has prepared the following general information about lung transplantation to help guide discussions between people with cystic fibrosis (CF) and their CF care teams.
- **When is it time for a lung transplant? What is involved in the evaluation process?**
- When someone with CF develops severe lung disease, the CF care team may discuss the option of lung transplantation with the person. The doctor can refer the person to a lung transplant center for evaluation. The transplant center evaluates the person's health to determine if a lung transplant is necessary and timely. Tests examine how well the lungs, heart, and kidneys function, the types of bacteria in the lungs, and, because of the serious health care implications of transplantation, the person's psychological well-being. The transplant center also will evaluate the person's social support system including family, friends, and professional support. Most components of the evaluation are standard, but

each center can have some specific requirements. The staff's decision to accept a person for a transplant is specific to that center.

Appendix 8: Columbia Suicide Severity Rating Scale

| SUICIDE IDEATION DEFINITIONS AND PROMPTS: | Past month | |
|---|------------|----|
| Ask questions that are bolded and underlined. | YES | NO |
| Ask Questions 1 and 2 | | |
| <p>1) Wish to be Dead: Person endorses thoughts about a wish to be dead or not alive anymore, or wish to fall asleep and not wake up. <u>Have you wished you were dead or wished you could go to sleep and not wake up?</u></p> | | |
| <p>2) Suicidal Thoughts: General non-specific thoughts of wanting to end one's life/commit suicide, <i>"I've thought about killing myself" without general thoughts of ways to kill oneself/associated methods, intent, or plan.</i> <u>Have you actually had any thoughts of killing yourself?</u></p> | | |
| <p>If YES to 2, ask questions 3, 4, 5, and 6. If NO to 2, go directly to question 6.</p> | | |
| <p>3) Suicidal Thoughts with Method (without Specific Plan or Intent to Act): Person endorses thoughts of suicide and has thought of a least one method during the assessment period. This is different than a specific plan with time, place or method details worked out. <i>"I thought about taking an overdose but I never made a specific plan as to when where or how I would actually do it....and I would never go through with it."</i> <u>Have you been thinking about how you might kill yourself?</u></p> | | |
| <p>4) Suicidal Intent (without Specific Plan): Active suicidal thoughts of killing oneself and patient reports having <u>some intent to act on such thoughts</u>, as opposed to <i>"I have the thoughts but I definitely will not do anything about them."</i> <u>Have you had these thoughts and had some intention of acting on them?</u></p> | | |
| <p>5) Suicide Intent with Specific Plan: Thoughts of killing oneself with details of plan fully or partially worked out and person has some intent to carry it out. <u>Have you started to work out or worked out the details of how to kill yourself? Do you intend to carry out this plan?</u></p> | | |
| <p>6) Suicide Behavior Question <u>"Have you ever done anything, started to do anything, or prepared to do anything to end your life?"</u> Examples: Collected pills, obtained a gun, gave away valuables, wrote a will or suicide note, took out pills but didn't swallow any, held a gun but changed your mind or it was grabbed from your hand, went to the roof but didn't jump; or actually took pills, tried to shoot yourself, cut yourself, tried to hang yourself, etc. If YES, ask: <u>How long ago did you do any of these?</u> <input type="checkbox"/> Over a year ago? <input type="checkbox"/> Between three months and a year ago? <input type="checkbox"/> Within the last three months?</p> | | |

Appendix 9: Responses to Columbia Suicide Severity Rating Scale

Administer this scale if there is a score of 1 or greater on question 9 of PHQ-9 (the suicide item).

Item 1 – Safety Plan and Mental Health Referral

Item 2 – Safety Plan and Mental Health Referral

Item 3 – Safety Plan and Urgent Referral

Item 4 – Emergent Referral

Item 5 – Emergent Referral

Item 6 –

- If one week ago or less- Emergent Referral
- If between 1 week and 3 months- Urgent Referral
- Over 3 months ago- Routine Mental Health Referral

Disposition: You should consider having these things in your “toolbox”

- Safety Plan (See examples of an adult and teen safety plan in appendix 10 and 11 respectively)
- Urgent Mental Health Referrals
- Contact information for Local Crisis Services and a suicide hotline
- Know how to make a referral for an Emergency Evaluation (e.g., Psychiatric Emergency Room)

Appendix 10: Adult Safety Plan

If I begin to have thoughts or intentions of hurting or killing myself, or if I am at risk of being in an unsafe situation, I will take the following steps:

1. Things I can do to calm down or keep myself safe:

2. Talk about my feelings with someone that I trust. Specifically, I can talk to the following people:

3. I or someone else will call (_____) at (_____).

4. If I am unable to find someone to talk with, I can contact:
My therapist/psychiatrists if I have one at _____.
The Crisis Hotline at 1-800-273-TALK.
Crisis Services at _____.

5. If I am not able to stay safe, then I will go immediately to the Psychiatric Emergency Program at _____.
The address is _____. The Phone number there is _____.

6. Patients/Families should be sure that all firearms are either removed from the home or are locked away and secured. Access to medications and sharp objects (e.g., kitchen knives) should also be monitored and restricted.

7. Families should also be sure patients are not left alone if they are having suicidal thoughts.

8. Other considerations:

9. I agree to follow the above actions as necessary to maintain my safety:

Patient: _____ Date: _____

Provider: _____ Date: _____

Appendix 11: Teen Safety Plan

Safety Plan for Adolescent Patient: _____

If I begin to have thoughts and/or intentions of hurting or killing myself, or if I am at risk of being in an unsafe situation, I will take the following steps:

1. Talk about my feelings with someone that I trust. Specifically, I can talk to the following people:

2. I or someone else will call (_____) at (_____).

3. If I am unable to find someone to talk with, I can also call the Crisis Hotline number which is 800-273-TALK or _____ (ADD YOUR RESOURCES HERE).

4. If I am not able to stay safe, then I will go immediately to the Psychiatric Emergency Room (or another emergency resource in your area). The address _____ (Again add your resources here).

5. Parents should be sure that all firearms are either removed from the home or are locked away and secured. Access to medications and sharp objects (e.g., kitchen knives) should also be monitored and restricted.

6. Parents should also be sure children are not left alone if they are having suicidal thoughts.

7. Other considerations:

8. I agree to follow the above actions as necessary to maintain my safety:

Adolescent: _____ Date: _____

Parent: _____ Date: _____

Provider: _____ Date: _____

Appendix D: Intervention

Table 1. English-Language National/International Guidelines for the Treatment of Depression*

| Guideline (Country, year) | Depression Subtypes | Age Groups | Settings/Special Population | First-line medications when pharmacologic intervention is needed | Psychological Interventions | Reference |
|---|---|---------------------------|--|---|---|--|
| AACAP pediatric depression (US, 2007) | MDD or dysthymia | Children & adolescents | Psychiatric care in unspecified settings --Adapt therapies to account for any comorbid physical illness | SSRI, especially fluoxetine | --CBT or IPT --Psychodynamic therapy, family or school-based interventions as appropriate (less evidence) | Birmaher B, Brent D, and the AACAP Work Group on Quality Issues, American Academy of Child and Adolescent Psychiatry. Practice Parameter for the Assessment and Treatment of Children and Adolescents with Depressive Disorders. J Am Acad Child Adolesc Psychiatry 2007; 46(11):1503-1526. |
| AACAP Psychiatric Management of physically ill children and adolescents (US, 2009) | Depression as a non- categorical target symptom | Children & adolescents | Physical illness | Options include: --SSRI --SNRI --Stimulant Medication selection and dosing should consider pharmacokinetics, pharmacodynamics, organ systems affected by medical illness | Options include: --Supportive therapy --Narrative therapy --CBT --Behavior modification --Coping skills and play strategies for procedures --Group therapy --Family therapy --Address symptoms in parents | DeMaso DR, Martini DR, Cahen LA, and the Work Group on Quality Issues (WGQI), American Academy of Child and Adolescent Psychiatry. Practice Parameter for the Psychiatric Assessment and Management of Physically Ill Children and Adolescents. J Am Acad Child Adolesc Psychiatry 2009; 48(2): 213-233. |

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|--|--------------------------------------|--|--|--|---|---|
| <p>AACAP psychotropic medication (US, 2009)</p> | <p>MDD</p> | <p>Children & adolescents</p> | <p>Prescription of medication to children & adolescents in unspecified settings</p> | <p>--SSRIs fluoxetine, sertraline, citalopram have more evidence</p> <p>Before prescribing medication:</p> <p>Psychiatric evaluation, medical history, collaboration between health care providers, ensure availability of follow up, consent/assent process</p> | <p>--Combined medication plus CBT is first line for moderate to severe depression in adolescents</p> | <p>Walkup J, and the Work Group on Quality Issues, American Academy of Child and Adolescent Psychiatry. Practice Parameter on the Use of Psychotropic Medication in Children and Adolescents. J Am Acad Child Adolesc Psychiatry; 2009; 48(9): 961-73.</p> |
| <p>APA depression in adults (US, 2010)</p> | <p>MDD</p> | <p>Adults</p> | <p>Psychiatric care settings</p> <p>--Adapt therapies to account for any comorbid physical illness</p> | <p>--SSRI, SNRI, mirtazapine or bupropion for most patients</p> <p>--Of the SSRIs, sertraline, citalopram, escitalopram have fewer drug-drug interactions</p> <p>--SNRI or TCA possibly preferable for patients with comorbid chronic pain</p> | <p>--CBT or IPT</p> <p>--Psychodynamic psychotherapy (less evidence)</p> <p>--Problem solving therapy in mild cases</p> <p>--Couples or family therapy when appropriate</p> | <p>Gelenberg A Freeman M, Markowitz J. Rosenbaum J. Thase M. Trivedi M. Van Rhoads R. American Psychiatric Association Practice Guideline: Treatment of Patients with Major Depressive Disorder. American Psychiatric Association. 2010.</p> |
| <p>BAP anti-depressant use (UK, 2008)</p> | <p>Unipolar depressive disorders</p> | <p>Primarily adults; also children & adolescents, elderly, medical illness</p> | <p>Depression treatment by physicians of any specialty, including primary care and psychiatry</p> | <p>For adults:</p> <p>--SSRI</p> <p>--TCA, escitalopram or venlafaxine more effective in severe depression</p> <p>For children & adolescents:</p> | <p>For adults:</p> <p>--CBT or behavior therapy/activity scheduling</p> <p>--IPT</p> <p>For children & adolescents:</p> | <p>Anderson IM, Ferrier IN, Baldwin RC, Cowen PJ, Howard L, Lewis G, Matthews K, McAllister-Williams RH, Peveler RC, Scott J, Tylee A. Evidence-based guidelines for treating depressive disorders with antidepressants: a revision of the 2000 British Association for Psychopharmacology guidelines. J Psychopharmacol 2008 Jun;22(4):343-96. Epub 2008 Apr 15.</p> |

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| | | | | <p>For comorbid medical illness:</p> <p>Consider drug-drug interactions, adverse effects</p> | <p>--CBT if no response to structured supportive treatment</p> | |
| <p>Beyondblue adolescent & young adult depression</p> <p>(Australia, 2011)</p> | <p>MDD, dysthymia, bipolar disorder</p> | <p>Adolescents (age 13-18) & young adults (age 19-24)</p> | <p>Diverse health care settings</p> | <p>For moderate or severe MDD:</p> <p>The SSRI fluoxetine, used with CBT or IPT</p> <p>--Australian Adverse Drug Reactions Advisory Committee (ADRAC) advises that the SSRIs fluoxetine, fluvoxamine and sertraline are approved in this age group for OCD but not for depression.</p> | <p>For dysthymia:</p> <p>--Nondirective support</p> <p>--Group CBT/IPT</p> <p>For MDD:</p> <p>--CBT</p> <p>--IPT</p> | <p>McDermott B, Baigent M, Chanen A, Graetz B, Hayman N, Newman L, Parikh N, Peirce B, Proimos J, Smalley T, Spence S; beyondblue Expert Working Committee. Clinical practice guidelines: depression in adolescents and young adults. Melbourne: beyondblue: the national depression initiative; 2011 Feb. bspg.com.au Guideline approved by the Australian Government National Health and Medical Research Council.</p> |
| <p>CANMAT MDD in adults</p> <p>(Canada, 2009)</p> | <p>MDD</p> | <p>Adults; also children & adolescents</p> | <p>Primarily treatment by psychiatrists and other mental health specialists; also primary care settings</p> | <p>For adults, select from wide variety of first line agents based on clinical situation:</p> <p>--SSRI</p> <p>--SNRI</p> <p>--"Newer" agents including agomelatine, bupropion, mianserin, mirtazapine, moclobemide, reboxetine, tianeptine</p> | <p>--CBT</p> <p>--IPT</p> | <p>Kennedy SH, Lam RW, Parikh SV, Patten SB, Ravindran AV. Canadian Network for Mood and Anxiety Treatments (CANMAT) clinical guidelines for the management of major depressive disorder in adults. Introduction. J Affect Disord. 2009 Oct;117 Suppl 1:S1-2. Epub 2009 Aug 13.</p> <p>Parikh SV, Segal ZV, Grigoriadis S, Ravindran AV, Kennedy SH, Lam RW, Patten SB. Canadian Network for Mood and Anxiety Treatments (CANMAT) clinical guidelines for the management of major depressive disorder in adults. II. Psychotherapy alone or in combination with antidepressant medication. J Affect</p> |

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|--|---------------------------------|--|--|--|--|--|
| | | | | <p>--Superior efficacy for escitalopram, sertraline, venlafaxine</p> <p>--Superior tolerability for escitalopram, sertraline</p> <p>--Weight gain with mirtazapine, paroxetine</p> <p>--Fewest drug-drug interactions with citalopram, desvenlafaxine, escitalopram, mirtazapine, venlafaxine</p> <p>For children & adolescents:</p> <p>--The SSRIs fluoxetine and citalopram are first line (combined with CBT)</p> | | <p>Disord 2009 Oct;117 Suppl 1:S15-25. Epub 2009 Aug 13.</p> <p>Lam RW, Kennedy SH, Grigoriadis S, McIntyre RS, Milev R, Ramasubbu R, Parikh SV, Patten SB, Ravindran AV.</p> <p>Canadian Network for Mood and Anxiety Treatments (CANMAT) clinical guidelines for the management of major depressive disorder in adults. III. Pharmacotherapy. J Affect Disord 2009 Oct;117 Suppl 1:S26-43. Epub 2009 Aug 11.</p> |
| <p>CANMAT mood disorders and comorbid medical conditions (Canada, 2012)</p> | <p>Depressive symptoms, MDD</p> | <p>Medically ill populations; focus on cardiovascular disease, cancer, HIV/hepatitis C, migraine, multiple sclerosis, epilepsy, osteoporosis</p> | <p>Specialized medical clinics; multidisciplinary care teams</p> | <p>--Level of evidence differs by specific medical disorder</p> <p>--When evidence in specific medical disorder is limited, consult general treatment guidelines</p> <p>--Consider drug-drug interactions and drug-illness interactions</p> <p>--Of the SSRIs, citalopram, escitalopram, and sertraline</p> | <p>--CPT</p> <p>--IPT</p> <p>--Problem solving therapy</p> | <p>Ramasubbu R, Beaulieu S, Taylor VH, Schaffer A, McIntyre RS; Canadian Network for Mood and Anxiety Treatments (CANMAT) Task Force. The CANMAT task force recommendations for the management of patients with mood disorders and comorbid medical conditions: diagnostic, assessment, and treatment principles. <i>Ann Clin Psychiatry</i>. 2012 Feb;24(1):82-90.</p> <p>Ramasubbu R, Taylor VH, Samaan Z, Sockalingham S, Li M, Patten S, Rodin G, Schaffer A, Beaulieu S, McIntyre RS; Canadian Network for Mood and Anxiety Treatments (CANMAT) Task Force. The Canadian Network for Mood and Anxiety Treatments (CANMAT) task force recommendations for the management</p> |

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| | | | | <p>have fewer drug-drug interactions</p> <p>--Supplement vitamin D and consider bone density monitoring when SSRI use >2 years</p> | | <p>of patients with mood disorders and select comorbid medical conditions. Ann Clin Psychiatry. 2012 Feb;24(1):91-109.</p> |
| <p>GLAD-PC adolescent depression primary care (US and Canada, 2007)</p> | <p>For psychological intervention:</p> <p>MDD, depression not otherwise specified, dysthymic disorder, subthreshold symptoms</p> <p>For medication:</p> <p>MDD</p> | <p>Adolescents & young adults (age 10-21)</p> | <p>Primary care</p> | <p>--SSRI</p> | <p>For mild cases:</p> <p>--Active support and monitoring</p> <p>For moderate to severe cases:</p> <p>--CBT</p> <p>--ITP</p> | <p>Cheung AH, Zuckerbrot RA, Jensen PS, Ghalib K, Laraque D, Stein REK, and the GLAD-PC Steering Group. Guidelines for Adolescent Depression in Primary Care (GLAD-PC): II. Treatment and Ongoing Management. Pediatrics 2007; 120(5)e1313-e1326.</p> <p>Zuckerbrot RA, Cheung AH, Jensen PS, Stein REK, Laraque D. Guidelines for Adolescent Depression in Primary Care (GLAD-PC): I. Identification, Assessment, and Initial Management. Pediatrics 2007; 120(5) e1299-e1312.</p> |
| <p>NICE depression in adults (UK, 2009)</p> | <p>MDD, or persistent sub-threshold MDD/dysthymia</p> | <p>Adults (age 18+)</p> | <p>Primary and secondary care (stepped care model)</p> | <p>--SSRI</p> | <p>--CBT or IPT</p> <p>--Behavioral activation (less evidence)</p> <p>--Couples therapy when appropriate</p> | <p>National Collaborating Centre For Mental Health (UK). Treatment and Management of Depression in Adults. Leicester (UK): National Institute for Health and Care Excellence (NICE); 2009 (Clinical guideline; no. 90)</p> |

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| NICE depression in adults with chronic physical health problem (UK, 2009) | MDD, or persistent subthreshold MDD (dysthymia) | Adults (age 18+) | chronic physical illness (stepped care model) | --SSRI, especially citalopram or sertraline (fewer drug-drug interactions) | --CBT --Couples therapy when appropriate | National Collaborating Centre for Mental Health. Depression in adults with a chronic physical health problem. Treatment and management. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 Oct. (Clinical guideline; no. 91). |
| NICE pediatric depression (UK, 2005) | Mild depression or dysthymia; Moderate to severe depression; psychotic depression | Children (age 5-11) & adolescents (age 12-17) | Primary care, community care, secondary care settings | --The SSRI fluoxetine for moderate to severe depression unresponsive to psychological interventions --The SSRIs sertraline or citalopram are second line agents for severe depression | --Supportive therapy, group CBT or guided self-help first line for mild symptoms --CBT, IPT, or family therapy first line for moderate to severe symptoms | National Institute for Health and Care Excellence (NICE). Depression in children and young people: identification and management in primary, community, and secondary care. NICE; 2005 Sept. Guidance.nice.org.uk/cg28. (Clinical guideline; no. 28) |
| Spanish National Health System MDD in adults (Spain, 2008) | MDD | Adults (age 18+) | Primary and specialized care | --SSRI | --CBT --IPT as alternative --Problem-solving or supportive counseling in mild cases --Couples or family therapy when appropriate | Working Group on the Management of Major Depression in Adults. Clinical Practice Guideline on the Management of Major Depression in Adults. Madrid: National Plan for the SHN of the MHCA. Agencia de Avaluacion de Tecnoloxias Sanitarias de Galicia (avalialia-t); 2008. Clinical Practice Guidelines in the Spanish SHN: avalialia-t no 2006/06. |
| Spanish National Health System MDD in children & adolescents | MDD | Children (age 5-11) & Adolescents (age 12-18) | Primary care and specialty child & adolescent mental health care in Spanish National Health System | For moderate to severe MDD: --SSRI: Fluoxetine has most evidence and the only approval of Spanish Agency of Medicines and Medical | For mild to moderate MDD in adolescents: --CBT --Family therapy | Working group of the clinical practice guideline on the Management of Major Depression in Childhood and Adolescence. Clinical practice guideline on major depression in childhood and adolescence. Quality Plan for the National Health System of the Ministry of Health and Social Policy. Agencia de Avaluacion de Tecnoloxias Sanitarias de Galicia (avalialia-t); 2009. Clinical |

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| (Spain, 2009) | | | | <p>Devices for pediatric depression</p> <p>--Sertraline, citalopram and escitalopram are first line alternatives based on clinical situation including family history</p> | <p>--IPT</p> <p>For severe MDD in adolescents:</p> <p>--CBT</p> <p>In children:</p> <p>--CBT</p> <p>--Family therapy</p> | <p>Practice Guidelines in the SNS: avalia-t no. 2007/09. www.sergas.es/docs/Avalia-t</p> |
| USPTF adult depression screening (US, 2009) | MDD, dysthymia, minor depression (non-bipolar) | Adults | Primary care | <p>--If using medication, consider selecting antidepressant other than SSRI for age 18-29 (increased risk for not-fatal suicidal behavior, highest with paroxetine) or over age 70 (increased risk of upper gastrointestinal bleeding)</p> | <p>--Options include CBT or brief psychosocial counseling</p> | <p>US Preventive Services Task Force. Screening for depression in adults: US Preventive Services Task Force recommendation statement. Ann Intern Med 2009;151:784-792.</p> <p>O'Connor EA, Whitlock EP, Beil TL, Gaynes BN. Screening for depression in adult patients in primary care settings: a systematic evidence review. Ann Intern Med 2009;151:793-803.</p> <p>O'Connor EA, Whitlock EP, Gaynes B, Beil TL. Screening for Depression in Adults and Older Adults in Primary Care: An Updated Systematic Review [Internet]. Rockville MD: Agency for Healthcare Research and Quality (US); 2009 Dec. Report No.: 10-05143-EF-1. US Preventive Services Task Force Evidence Syntheses, formerly Systematic Evidence Reviews.</p> |
| USPTF pediatric depression (US, 2009) | MDD | Children (age 7-11) & adolescents (age 12-18) | Primary care | <p>For adolescents:</p> <p>SSRI (fluoxetine, citalopram, paroxetine, escitalopram, sertraline)</p> | <p>For adolescents:</p> <p>--CBT</p> <p>--IPT</p> | <p>US Preventive Services Task Force. Screening and treatment for major depressive disorder in children and adolescents: US Preventive Services Task Force recommendation statement. Pediatrics 2009; 123: 1223-1228.</p> <p>Williams SB, O'Connor EA, Eder M,</p> |

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| | | | | For children: The SSRI fluoxetine | For children: Inadequate evidence | Whitlock EP. Screening for child and adolescent depression in primary care settings: a systematic evidence review for the US Preventive Services Task Force. Pediatrics 2009;123:e716-735. |
| VA/DoD MDD (US, 2009) | MDD | Adults | Primary care providers and other healthcare professionals | --SSRI except fluvoxamine --SNRI --bupropion --mirtazapine Preferred in primary care: --SSRI (except fluvoxamine) or the SNRI venlafaxine | --CBT --IPT --Problem solving therapy --Couples/marital-focused therapy first line if relationship distress | The Management of MDD Working Group. VA/DoD clinical practice guidelines for management of major depressive disorder (MDD). Department of Veterans Affairs, Department of Defense 2008; Version 2.0: 1-203. |
| WFSBP unipolar depression (international, 2013) | MDD, moderate to severe unipolar depressive episode | Primarily adults; also elderly, comorbid medical illness | Biological treatment by physician of any specialty | --SSRI --SNRI --“Newer” antidepressants including mirtazapine, agomelatine, bupropion but not reboxetine --TCA also a first-line option for severe depression --Consider drug-drug interactions --Treat underlying medical illness first when possible | --CBT --IPT --Alternative: training non-specialists in problem-solving therapy | Bauer M, Pfennig A, Severus E, Whybrow PC, Angst J, Moller HJ on behalf of the Task Force on Unipolar Depressive Disorders. World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for Biological Treatment of Unipolar Depressive disorders, Part 1: Update 2013 on the acute and continuation treatment of unipolar depressive disorders. World J Biol Psychiatry 2013 Jul; 14(5): 334-85. |

*Inclusion criteria: English-language guidelines issued between 2005-2014 by national governments or national/international medical professional associations addressing psychopharmacologic and/or psychotherapeutic intervention for unipolar depressive disorders in children, adolescents, and/or adults in the general population or with chronic medical illness were included. Guidelines issued by regional governments or other organizations (ex: Texas Medication Algorithm Project, Institute for Clinical Systems Improvement) were excluded. Guidelines focusing solely on bipolar depression were excluded. Guidelines addressing the treatment of depression in individuals with a specific medical illness other than CF (ex: cancer, HIV) were excluded. No previous guidelines focusing on the treatment of depression in individuals with CF were identified.

CBT: Cognitive behavioral therapy

ER: Extended release

IPT: Interpersonal therapy

MDD: Major depressive disorder

SNRI: Serotonin norepinephrine reuptake inhibitor

SSRI: Selective serotonin reuptake inhibitor

TCA: Tricyclic antidepressant

Table 2. English-Language National/International Guidelines for the Treatment of Anxiety*

| Guideline (Country, year) | Anxiety Subtypes | Age Groups | Settings/ Special Population | First-line medications when pharmacologic intervention is needed | Psychological Interventions | Reference |
|--|--|------------------------|--|--|---|--|
| AACAP anxiety (US, 2007) | All anxiety disorders except OCD, PTSD | Children & adolescents | Psychiatric care in unspecified settings | SSRI | --Exposure-based CBT --Psychodynamic psychotherapy (less evidence) --Parent-child, family therapy | Connolly S, Bernstein G, and the Work Group on Quality Issues, American Academy of Child and Adolescent Psychiatry. Practice Parameter for the Assessment and Treatment of Children and Adolescents with Anxiety Disorders. J Am Acad Child Adolesc Psychiatry 2007; 46(2): 267-283. |
| AACAP Psychiatric Management of physically ill children and | Anxiety as a non-categorical | Children & adolescents | Physical illness | Options include: --Benzodiazepine --Antidepressant | Options include: --Supportive therapy --Narrative therapy | DeMaso DR, Martini DR, Cahen LA, and the Work Group on Quality Issues (WGQI), American Academy of Child and Adolescent Psychiatry. Practice Parameter for the Psychiatric Assessment and Management of Physically Ill Children and Adolescents. J Am Acad Child Adolesc Psychiatry 2009; 48(2): 213-233. |

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|---|---|---|--|---|--|---|
| adolescents (US, 2009) | target symptom | | | --Buspirone --Gabapentin --Clonidine Medication selection and dosing should consider pharmacokinetics, pharmacodynamics, organ systems affected by medical illness | --CBT --Behavior modification --Coping skills and play strategies for procedures --Group therapy --Family therapy --Address symptoms in parents | |
| AACAP psychotropic medication (US, 2009) | Anxiety disorders including separation anxiety, social phobia, GAD; OCD | Children & adolescents | Prescription of medication to children & adolescents in unspecified settings | --SSRI for OCD --SSRI often used “off label” for non-OCD anxiety disorders Before prescribing medication: Psychiatric evaluation, medical history, collaboration between health care providers, ensure availability of follow up, consent/assent process | --CBT or combined medication plus CBT is first line for OCD | Walkup J, and the Work Group on Quality Issues, American Academy of Child and Adolescent Psychiatry. Practice Parameter on the Use of Psychotropic Medication in Children and Adolescents. J Am Acad Child Adolesc Psychiatry; 2009; 48(9): 961-73. |
| APA panic (US, 2010) | Panic disorder | Primarily adults; also children & adolescents | Psychiatric care setting --Adapt therapies to account for | --SSRI preferred, especially for adolescents --SNRI (venlafaxine ER) --TCA effective but more side effects | --CBT --Panic-focused psychodynamic psychotherapy in some cases | Stein M, Goin M, Pollack M, Roy-Byrne P, Sareen J, Simon N, Campbell-Sills L. American Psychiatric Association Practice Guideline: Treatment of Patients with Panic Disorder. Second Edition. American Psychiatric Association. 2010. |

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| | | | any comorbid physical illness | -Benzodiazepines (alprazolam, clonazepam, diazepam, lorazepam) preferred when rapid symptom control needed | --Couples or family therapy when appropriate (not as monotherapy) | |
| BAP anxiety (UK, 2014) | GAD, panic disorder, specific phobia, social anxiety disorder, PTSD, OCD, Separation anxiety, illness anxiety disorder | Primarily adults (age 18-65); also children & adolescents, elderly/medically ill patients | Primary, secondary, and tertiary care settings | For adults: --SSRI Fluoxetine and paroxetine more likely to have drug interactions in medically ill patients --Benzodiazepines first line only for short-term use For children and adolescents: --SSRI, fluoxetine may be preferable --Consider reserving medication for second-line use after psychotherapy | --Exposure therapy, CBT --Psychodynamic psychotherapy (less evidence) | Baldwin DS, Anderson IM, Nutt DJ, Allgulander C, Bandelow B, den Boer JA, Christmas DM, Davies S, Fineberg N, Lidbetter N, Malizia A, McCrone P, Nabarro D, O'Neill C, Scott J, van der Wee N, Wittchen HU. Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive-compulsive disorder: a revision of the 2005 guidelines from the British Association for Psychopharmacology . J Psychopharmacol. 2014 May;28(5):403-39. Epub 2014 Apr 8. |
| BAP/RCP benzo-diazepines (UK, 2013) | GAD, panic disorder, social anxiety disorder, OCD, PTSD | Unspecified; includes elderly and medically ill patients | Unspecified clinical care settings | --Benzodiazepines are first line for short term use (up to 4 weeks) or severe anxiety --Consider benzodiazepines for long term use in panic disorder, social anxiety disorder, or GAD when SSRI, SNRI, and/or pregabalin are | --Consider psychological interventions (ex: CBT) as alternatives to benzodiazepine use | Baldwin DS, Aitchison K, Bateson A, Curran HV, Davies S, Leonard B, Nutt DJ, Stephens DN, Wilson S. Benzodiazepines: risks and benefits. A reconsideration. J Psychopharmacol 2013 Nov;27(11):967-71. Epub 2013 Sep 24. --A joint guideline of the British Association for Psychopharmacology and the Psychopharmacology Special Interest Group of the Royal College of Psychiatrists |

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| | | | | <p>ineffective or contraindicated due to medical comorbidities</p> <p>--Not for use in OCD, PTSD</p> | | |
| <p>ADAC anxiety (Canada, 2014)</p> | <p>Panic disorder, agoraphobia, specific phobia, social anxiety disorder, GAD, OCD, PTSD</p> | <p>Adults; children & adolescents or elderly; comorbid conditions</p> | <p>Primary care, psychiatric care, multidisciplinary care team</p> | <p>For adults:</p> <p>--SSRI for most anxiety disorders</p> <p>--SNRI for most anxiety disorders, not first line for OCD</p> <p>--Also pregabalin for social anxiety disorder, GAD</p> <p>--Also agomelatine for GAD</p> <p>--Benzodiazepines for short term use during acute crises or antidepressant treatment initiation</p> <p>--Medications less useful for specific phobia</p> <p>For children & adolescents:</p> <p>SSRI</p> | <p>--Exposure-based CBT, mindfulness-based cognitive therapy, or other forms of CBT first line for most anxiety disorders</p> <p>--IPT an alternative for social anxiety (less effective)</p> <p>--ACT an alternative for OCD (less evidence)</p> <p>--EMDR or DBT alternatives for PTSD</p> <p>--Include parent/family component for children and adolescents</p> | <p>Katzman MA, Bleau P, Blier P, Chokka P, Kjernisted K, Van Ameringen M; Canadian Anxiety Guidelines Initiative Group on behalf of the Anxiety Disorders Association of Canada/Association Canadienne des troubles anxieux and McGill University.</p> <p>Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive-compulsive disorders. BMC Psychiatry. 2014;14 Suppl 1:S1. Epub 2014 Jul 2.</p> |
| <p>CPA anxiety (Canada, 2006)</p> | <p>Panic disorder, agoraphobia,</p> | <p>Adults; children & adolescents</p> | <p>Primary care, psychiatric care</p> | <p>For adults:</p> | <p>--CBT</p> | <p>Swinson RP, Antony MM, Bleau P, Chokka P, Craven M, Fallu A, Katzman M, Kjernisted K, Lanius R, Manassis K, McIntosh D, Plamondon J, Rabheru K, Van Ameringen M, Walker JR. Canadian Psychiatric</p> |

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| | phobia, specific phobia, social anxiety disorder, OCD, GAD, PTSD | | | --SSRI for most anxiety disorders (less data for specific phobia) --SNRI venlafaxine ER a first-line alternative for panic, GAD, social anxiety, PTSD --Benzodiazepines for short term use For children & adolescents: --SSRI | | Association. Clinical Practice Guidelines: Management of Anxiety Disorders. Can J Psychiatry, 2006, 51; Suppl 2. |
| NICE anxiety in adults (UK, 2011) | GAD, panic disorder | Adults (age 18+) | Primary, secondary, community care (stepped care model) | --SSRI, especially sertraline due to low cost --Benzodiazepine acceptable only for short term crisis | CBT or applied relaxation | National Collaborating Centre for Mental Health, National Collaborating Centre for Primary Care. Generalised anxiety disorder and panic disorder (with or without agoraphobia) in adults. Management in primary, secondary and community care. London (UK): National Institute for Health and Clinical Excellence (NICE); 2011 Jan. (Clinical guideline; no. 113). |
| NICE social anxiety (UK, 2013) | Social anxiety disorder | Adults (age 18+); Children & adolescents (age 5-17) | Primary and secondary care, educational settings | For adults only: --SSRI (escitalopram or sertraline) | --CBT; parent involvement for pediatric patients --Short term psychodynamic psychotherapy for social phobia is a less effective alternative, for ages 15+ only | National Collaborating Centre for Mental Health. Social anxiety disorder: recognition, assessment and treatment. London (UK): National Institute for Health and Care Excellence (NICE); 2013 May. (Clinical guideline; no. 159). |
| Spanish National Health System anxiety | GAD, panic disorder | Adults | Primary care | --SSRI | --CBT | Guideline Working Group for the Treatment of Patients with Anxiety Disorders in Primary Care. Madrid: National Plan for the NHS of the MSC. Health Technology Assessment unit. Lain Entralgo Agency. |

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| <p>adults in primary care (Spain, 2008)</p> | | | | <p>--SNRI (venlafaxine ER) --TCA (chlor)impramine --Benzodiazepines mainly for short term use or need for rapid response; alprazolam or lorazepam for acute panic attack</p> | <p>--Other techniques as appropriate</p> | <p>Community of Madrid; 2008. Clinical Practice Guidelines in the NHS. UETS No. 2006/10.</p> |
| <p>WFSBP anxiety in primary care (international, 2012)</p> | <p>GAD, panic disorder, agoraphobia, specific phobia, social anxiety disorder, OCD, PTSD</p> | <p>Primarily adults; also children & adolescents</p> | <p>Primary care (See Bandelow, 2008, re: complex care in other settings)</p> | <p>For adults: --SSRI for most anxiety disorders, OCD, PTSD --SNRI for most anxiety disorders or PTSD (but not OCD) --Pregabalin for generalized anxiety disorder --Benzodiazepines only first line if used short term, during SSRI/SNRI treatment initiation or for a specific stressor For children and adolescents: SSRIs with careful monitoring</p> | <p>--All patients require supportive psychotherapy --Consider CBT/exposure therapy as alternative or addition to medication</p> | <p>Bandelow B, Sher L, Bunevicius R, Hollander E, Kasper Siegfried, Zohar J, Moller HJ, WFSBP Task Force on Mental Disorders in Primary Care and WFSBP Task Force on Anxiety Disorders, OCD, and PTSD. Guidelines for the pharmacological treatment of anxiety disorders, obsessive-compulsive disorder and posttraumatic stress disorder in primary care. International Journal of Psychiatry in Clinical Practice. World Federation of Societies of Biological Psychiatry Guidelines. 2012. 16; 77-- 84. For additional supporting detail, see: Bandelow B, Zohar J, Hollander E, Kasper S, Moller HJ, and WFSBP Task Force on Treatment Guidelines for Anxiety Obsessive-Compulsive Post-Traumatic Stress Disorders. World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the pharmacological treatment of anxiety, obsessive-compulsive and post-traumatic stress disorders—first revision. World J Biol Psychiatry 2008; 9(4):248-312.</p> |

*Inclusion criteria: English-language guidelines issued between 2005-2014 by national governments or national/international medical professional associations addressing psychopharmacologic and/or psychotherapeutic intervention for anxiety disorders (primarily GAD, social phobia, and panic disorder) in children, adolescents, and/or adults in the general population or with chronic medical illness were included. Guidelines issued by regional governments or other organizations (ex: Texas Medication Algorithm Project, Institute for Clinical Systems Improvement) were excluded. Guidelines focusing solely on OCD, PTSD, or specific phobia were excluded. Guidelines addressing the treatment of anxiety in individuals with a specific medical illness other than CF (ex: cancer, HIV) were excluded. No previous guidelines focusing on the treatment of anxiety in individuals with CF were identified.

ACT: Acceptance and commitment therapy

CBT: Cognitive behavioral therapy

DBT: Dialectical behavior therapy

EMDR: Eye movement desensitization and reprocessing

ER: Extended release

GAD: Generalized anxiety disorder

OCD: Obsessive compulsive disorder

PTSD: Posttraumatic stress disorder

SNRI: Serotonin norepinephrine reuptake inhibitor

SSRI: Selective serotonin reuptake inhibitor

TCA: tricyclic antidepressant

Table 3. Selected English-Language Textbooks, Reviews and Meta-analyses of Depression or Anxiety Prevention and Intervention

| Year | Depression or Anxiety | Age Groups | Settings/Special Population | First-line medications when pharmacologic intervention is needed | Psychological Interventions | Reference |
|------|------------------------|------------|-----------------------------|--|--|---|
| 2011 | Depression and anxiety | Adults | Patients with COPD | n/a | --Psychological interventions had small effects in reducing anxiety symptoms, but findings unclear | Baraniak A, Sheffield D. The efficacy of psychologically based interventions to improve anxiety, depression and quality of life in COPD: A systematic review and meta-analysis. Patient Education and Counseling 2011; 83: 29-36. |

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| 2014 | Depression | Adults | Review and meta-analysis; 19 RCTs of psychological intervention and/or psychopharmacologic treatment in individuals with diabetes | --SSRIs improved depression severity and glycemic control | --Psychological interventions improved depression severity --Insufficient evidence regarding medical outcomes | Baumeister H, Hutter N, Bengel J. Psychological and pharmacological interventions for depression in patients with diabetes mellitus and depression: an abridged Cochrane review. Diabet Med 2014;31:773-786. |
| 2013, 2014 | | | --Review and meta-analysis of QTc prolongation with psychotropic medications | --Dose-dependent QTc prolongation with SSRIs small (6.1 ms), less than TCA --Among SSRIs, more prolongation with citalopram than sertraline, paroxetine, fluvoxamine | n/a | Beach SR, Celano CM, Noseworthy PA, Januzzi JL, Huffman JC. QTc prolongation, torsades de pointes, and psychotropic medications. Psychosomatics 2013;54:1-13. Beach SR, Kostis WJ, Celano CM, Januzzi JL, Ruskin JN, Noseworthy PA, Huffman JC. Meta-analysis of selective serotonin reuptake inhibitor-associated QTc prolongation. J Clin Psychiatry. 2014 May;75(5):e441-9. |
| 2014 | Depression | Adults; children & adolescents; | Review of systematic reviews and meta-analysis in 156 trials, n= 56,158 including general and high risk populations; physical illness | n/a | --Psychological and educational interventions effective to prevent depression with small to medium effect sizes --Insufficient evidence to compare types of intervention | Bellón JA, Moreno-Peral P, Motrico E, Rodríguez-Morejón A, Fernández A, Serrano-Blanco A, Zabaleta-Del-Olmo E, Conejo-Cerón S. Effectiveness of psychological and/or educational interventions to prevent the onset of episodes of depression: A systematic review of systematic reviews and meta-analyses. Prev Med. 2014 Nov 20. http://dx.doi.org/10.1016/j.ypmed.2014.11.003 . [Epub ahead of print] |
| 2005 | Anxiety (unspecified) | | Patients with epilepsy | --SSRI | --CBT | Beyenburg S, Mitchell AJ, Schmidt D, Elger CE, Reuber M. Anxiety in patients with epilepsy: Systematic review and suggestions for clinical management. Epilepsy & Behavior 2005;7:161-171. |

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|------|------------------------|---------------------|--|---|--|--|
| 2012 | Depression and anxiety | | Patients with COPD | <p>--SSRI for depression and COPD</p> <p>--Antidepressants and benzodiazepines for anxiety and COPD</p> | <p>--CBT for depression and anxiety</p> <p>--Pulmonary rehabilitation is recommended because of improvement in quality of life, reduction in fatigue and dyspnea</p> <p>-More focus on interpersonal psychotherapy, self-management programs because of promising effects in other populations</p> | <p>Cafarella PA, Effing TW, Usmani ZA, Frith PA. Treatments for anxiety and depression in patients with chronic obstructive pulmonary disease: A literature review. <i>Respirology</i> 2012;17:627-638.</p> |
| 2009 | Depression and anxiety | Children and adults | Patients with various chronic diseases | <p>--SSRI for depression in patients with cancer</p> | <p>--CBT for reducing depression and anxiety symptoms in patients with diabetes, heart disease or cancer and in children with asthma</p> <p>--Biofeedback</p> <p>--Relaxation training</p> | <p>Clarke DM, Currie KC. Depression, anxiety and their relationship with chronic diseases: a review of the epidemiology, risk and treatment evidence. <i>Medical Journal of Australia</i> 2009;190: S54-S60.</p> |
| 2011 | Anxiety and depression | | Patients with cardiovascular disease | <p>--SSRI</p> | <p>--CBT for patients with coronary artery and depression, which includes stress management, relaxation training and health education</p> <p>--CBT for patients with anxiety, which includes relaxation techniques and exposure training</p> | <p>Compare A, Germani E, Proietti R, Janeway D. Clinical psychology and cardiovascular disease: an up-to-date clinical practice review for assessment and treatment of anxiety and depression. <i>Clinical Practice & Epidemiology in Mental Health</i> 2011;7: 148-156.</p> |

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|------|---|-----------------------------------|---|---|--|---|
| 1994 | Depression | | | n/a | --Review of IPT | Cornes CL, Frank E. Interpersonal psychotherapy for depression. The Clinical Psychologist 1994;47(3), 9-10. |
| 2013 | Anxiety and depression | Adults | Patients with COPD | n/a | --Exercise training with or without psychological components | Coventry PA, Bower P, Keyworth C, Kenning C, Knopp J, Garrett C, et al. The Effect of Complex Interventions on Depression and Anxiety in Chronic Obstructive Pulmonary Disease: Systematic Review and Meta-Analysis. PLoS ONE 2013;8:1-22. |
| 2008 | Mild-to-moderate anxiety and depression | Adults (age 18+) | Patients with COPD | n/a | --Some evidence for CBT in combination with exercise and education | Coventry PA, Gellatly JL. Improving outcomes for COPD patients with mild-to-moderate anxiety and depression: A systematic review of cognitive behavioural therapy. British Journal of Health Psychology 2008;13: 381-400. |
| 2014 | MDD | Children & adolescents (age 6-18) | Review and meta-analysis; 11 RCTs of psychotherapy and/or antidepressant treatment in pediatric populations | --Insufficient evidence | --Insufficient evidence | Cox GR , Callahan P , Churchill R , Hunot V , Merry SN , Parker AG , Hetrick SE . Psychological therapies versus antidepressant medication, alone and in combination for depression in children and adolescents. Cochrane Database Syst Rev. 2014 Nov 30;11:CD008324. |
| 2007 | Anxiety and panic | Adults | Patients with asthma | n/a | --CBT | Deshmukh V M, Toelle BG, Usherwood T, O'Grady B, Jenkins CR. Anxiety, panic and adult asthma: a cognitive-behavioral perspective. Respiratory Medicine 2007;101: 194-202. |
| 2009 | Anxiety and depression | Children & adolescents | Patients with epilepsy | --SSRI | --CBT --Relaxation techniques --Coping skills for improving self-concept | Ekinci O, Titus JB, Rodopman AA, Berkem M, Trevathan E. Depression and anxiety in children and adolescents with epilepsy: Prevalence, risk factors, and treatment. Epilepsy & Behavior 2009;14: 8-18. |
| 2005 | Mood disorders | | Patients with various physical illnesses | --SSRI | --CBT | Evans DL, Charney DS, Lewis L, Golden RN, Gorman JM, Krishnan KRR, et al. Mood disorders in the medically ill: Scientific review and recommendations. Biological Psychiatry 2005; 58: 175-189. |
| 2015 | Anxiety, depressive syndromes, | Adults; chapters focusing on | Textbook of psychiatry in medically ill patients, including chapters on | --Reviews pharmacokinetics in patients with medical | --Reviews psychological interventions in medically ill, including CBT, family | Fogel B, Greenberg D, eds. Psychiatric Care of the Medical Patient, 3 rd Edition. |

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|------|--|------------------------|--|--|--|---|
| | other neuro-psychiatric symptoms | children & adolescents | pulmonary disease, dyspnea, pain, transplant | illness (Mascarenas et al.) | therapy, adherence interventions | New York: Oxford University Press, 2015 (In press). |
| 2010 | Anxiety and depression | Children | Patients with diabetes | n/a | --Distraction --Hypnosis --CBT --Operant learning procedures with positive reinforcement | Fritsch SL, Overton MW, Robbins DR. The interface of child mental health and juvenile diabetes mellitus. <i>Child & Adolescent Psychiatric Clinics of North America</i> 2010; 19: 333-352. |
| 2011 | Depression | | Patients with COPD | --SSRI is preferred --TCA (more side effects) | --CBT | Fritzsche A, Clamor A, von Leupoldt A. Effects of medical and psychological treatment of depression in patients with COPD—a review. <i>Respiratory Medicine</i> 2011; 105:1422-1433. |
| 2014 | Anxiety, depression, other psychiatric disorders | Children & Adolescents | Textbook of pharmacotherapy in pediatric populations | --Review of principles of neuropsychopharmacology --Review of risks and benefits of SSRIs, including serotonin syndrome, suicidality, bleeding. | n/a | Gerlach M, Warnke A, Greenhill L. <i>Psychiatric Drugs in Children and Adolescents</i> . New York: Springer-Verlag Wien, 2014. |
| 2014 | Anxiety, depression, or other psychological outcomes | All ages | Review of 16 RCTs in individuals with CF or their family members | n/a | --Insufficient evidence regarding psychological interventions to treat depression or anxiety in CF | Goldbeck L, Fidika A, Herle M, Quittner AL. Psychological interventions for individuals with cystic fibrosis and their families. <i>Cochrane Database of Systematic Reviews</i> . 2014;Art. No.: CD003148 |
| 2013 | Depression | | Patients with diabetes | --SSRI | --Stepped care model --CBT | Hermanns N, Caputo S, Dzida G, Khunti K, Meneghini LF, Snoek F. Screening, evaluation and management of depression in people with diabetes in primary care. <i>Primary Care Diabetes</i> 2013; 7: 1-10. |

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|------|------------------------|----------|---|--|--|--|
| 2013 | Depression and Anxiety | All ages | Review of 67 key articles evaluating collaborative care interventions in primary care and specialized medical populations --systematic assessment --care management --stepped care process | --Specific interventions vary by study | --Specific interventions vary by study | Huffman JC, Niazi SK, Rundell JR, Sharpe M, Katon WJ. Essential articles on collaborative care models for the treatment of psychiatric disorders in medical settings: a publication by the Academy of Psychosomatic Medicine Research and Evidence-Based Practice Committee . Psychosomatics. 2014 Mar-Apr;55(2):109-22. Epub 2013 Dec 25. |
| 2008 | Anxiety and depression | Adults | Patients with cancer | --n/a | --Behavioral interventions --Education --Counseling --Relaxation training | Jacobsen PB, Jim HS. Psychosocial interventions for anxiety and depression in adult cancer patients: achievements and challenges. CA: A Cancer Journal for Clinicians 2008; 58: 214-230. |
| 2008 | Depression | | Patients with coronary heart disease | --SSRI | --CBT --Aerobic exercise and cardiac rehabilitation | Lichtman JH, Bigger JT, Blumenthal JA, Frasure-Smith N, Kaufmann PG, Lesperance F., et al. Depression and coronary heart disease: recommendations for screening, referral, and treatment: a science advisory from the American Heart Association Prevention Committee of the Council on Cardiovascular Nursing, Council on Clinical Cardiology, Council on Epidemiology and Prevention, and Interdisciplinary Council on Quality of Care and Outcomes Research: endorsed by the American Psychiatric Association. Circulation 2008; 118:1768-1775. |
| 2004 | Anxiety and depression | | Patients with COPD | --SSRI (but poor compliance) --Partial 5HT1A-receptor agonist buspirone | --CBT with relaxation exercises, cognitive components and exposure | Mikkelsen RL, Middelboe T, Pisinger C, Stage KB. Anxiety and depression in patients with chronic obstructive pulmonary disease (COPD). A review. Nordic Journal of Psychiatry 2004; 58: 65-70. |

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|------|--|---|---|--|---|--|
| 2012 | Anxiety | | Review of drug interactions for medications used to treat anxiety | --Among SSRIs, fluoxetine, fluvoxamine, paroxetine most prone to drug-drug interactions | n/a | Muscattello MR, Spina E, Bandelow B, Baldwin DS. Clinically relevant drug interactions in anxiety disorders. Hum Psychopharmacol Clin Exp 2012; 27:239-253. |
| 2003 | Depression | Adults | Patients with diabetes types 1 and 2 | --SNRI and SSRI --TCA (and MAOI) | --CBT | Musselman DL, Betan E, Larsen H, Phillips LS. Relationship of depression to diabetes types 1 and 2: epidemiology, biology, and treatment. Biological Psychiatry 2003; 54: 317-329. |
| 2012 | Depression | | Review of use of antidepressants in patients with renal disease | --SSRI | n/a | Nagler EV , Webster AC , Vanholder R , Zoccali C . Antidepressants for depression in stage 3-5 chronic kidney disease: a systematic review of pharmacokinetics, efficacy and safety with recommendations by European Renal Best Practice (ERBP). Nephrol Dial Transplant 2012 Oct;27(10): 3736-45. Epub 2012 Aug 1. |
| 2015 | Depression | | Patients with HIV | --SSRI, especially fluoxetine --TCA --Less data for testosterone, stimulants, dehydroepiandrosterone | --CBT and cognitive therapy --Collaborative care/stepped care improve depression, HIV health outcomes, costs | Nanni MG, Caruso R, Mitchell AJ, Meggiolaro E, Grassi L. Depression in HIV infected patients: a review. Curr Psychiatry Rep 2015; 17:530. |
| 2009 | Mental disorders and behavioral problems including | Children, adolescents, young adults (to age 25) | Prevention in family, community, school-based, legal, and health care systems | n/a | --Prevention programs derived from CBT for anxiety/depression | O'Connell ME, Boat T, Warner KE., eds. Preventing Mental, Emotional, and Behavioral Disorders Among Young People: Progress and Possibilities. National Research Council and Institute of Medicine of the National Academies. Washington DC:National Academies Press, 2009. www.nap.edu |

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|------|--|------------------------|--|--|---|---|
| | depression and anxiety | | | | --Family intervention for prevention of depression in high risk adolescents | |
| 2007 | | | Review of cognitive behavioral therapy | | --CBT | Rachman, S. The evolution of cognitive behaviour therapy. In Clark, D, Fairburn, CG & Gelder, MG. <i>Science and practice of cognitive behaviour therapy</i> . Oxford: Oxford University Press, 2007: pp. 1–26. |
| 2010 | Depression: MDD, adjustment disorder, dysthymia | Adults | Review and meta-analysis; 51 RCTs of antidepressants in physically ill populations | --TCA and SSRI both more effective than placebo in pooled efficacy analysis of 1674 patients | n/a | Rayner L , Price A , Evans A , Valsraj K , Higginson IJ , Hotopf M . Antidepressants for depression in physically ill people. <i>Cochrane Database Syst Rev</i> . 2010 Mar 17;(3): CD007503. |
| 2010 | Depression: MDD, adjustment disorder, dysthymic disorder | Adults | Review and meta-analysis; 25 RCTs of antidepressants in individuals with “life threatening illness”: cancer, renal failure, COPD, heart failure, HIV Parkinson’s, multiple sclerosis | --TCA and SSRI both more effective than placebo in meta-analysis --Mianserin and mirtazapine also more effective than placebo, but with fewer studies | n/a | Rayner L , Price A , Evans A , Valsraj K , Hotopf M , Higginson IJ . Antidepressants for the treatment of depression in palliative care: systematic review and meta-analysis. <i>Palliat Med</i> . 2011 Jan;25(1):36-51. Epub 2010 Oct 8. |
| 2014 | Depression | Adults | Systematic review and meta-analysis supporting reduction of depressive symptoms by physical activity in patients with mental illness | n/a | n/a | Rosenbaum S, Tiedemann A, Sherrington C, Curtis J, Ward PB. Physical activity interventions for people with mental illness: a systematic review and meta-analysis. <i>J Clin Psychiatry</i> . 2014 Sep;75(9):964-74. |
| 2012 | Anxiety, depression, other psychiatric disorders | Children & Adolescents | Textbook of pharmacotherapy in pediatric populations | --Reviews principles of clinical psychopharmacology --Reviews use of antidepressants in | n/a | Rosenberg DR, Gershon S, eds. <i>Pharmacotherapy of Child and Adolescent Psychiatric Disorders</i> . Third edition. West Sussex: Wiley-Blackwell, 2012. |

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| | | | | children and adolescents | | |
| 2011 | Depression | | Patients with diabetes | --SSRI | --CBT | Rustad JK, Musselman DL, Nemeroff CB. The relationship of depression and diabetes: pathophysiological and treatment implications. <i>Psychoneuroendocrinology</i> 2011; 36: 1276-1286. |
| 2013 | Mood disorders and anxiety | Adults | Patients with HIV | n/a | --CBT reduced symptoms of depression and anxiety | Spies G, Asmal L, Seedat S. Cognitive-behavioural interventions for mood and anxiety disorders in HIV: a systematic review. <i>Journal of Affective Disorders</i> 2013; 150:171-180. |
| 2008, 2015 | Depression, anxiety, other psychiatric disorders | Adults; chapters focusing on children & adolescents; elderly | Textbook of clinical psychiatry, including patients with comorbid medical illness | --Reviews use and risks of antidepressants, drug-drug interactions | --Reviews psychological interventions including in medically ill | Stern TA, Rosenbaum JF, Fava M, Biederman J, Rauch SL, eds. <i>Massachusetts General Hospital Comprehensive Clinical Psychiatry</i> . Philadelphia: Mosby/Elsevier, 2008. Stern TA, Fava M, Wilens T, Rosenbaum JF, eds. <i>Massachusetts General Hospital Comprehensive Clinical Psychiatry</i> , 2 nd edition. Elsevier, 2015 (in press). |
| 2005 | Depression | Children and adolescents | Patients with diabetes | n/a | --Family interventions | Stewart SM, Rao U, White P. Depression and diabetes in children and adolescents. <i>Current Opinion in Pediatrics</i> 2005;17: 626-631. |
| 2012 | Anxiety | | Patients with cancer | --SSRIs are preferred | --CBT and/or stress management | Traeger L, Greer JA, Temel JS, Fernandez-Robles C, Pirl WF. Evidence-based treatment of anxiety in patients with cancer. <i>Journal of Clinical Oncology</i> 2012;30: 1197-1205. |
| 2013 | Distress, pain | Children and adolescents | Patients undergoing medical procedures using needles | n/a | --Distraction --Hypnosis | Uman LS, Birnie KA, Noel M, Parker JA, Chambers CT, McGrath PJ, Kisely SR (2013) Psychological interventions for needle-related procedural pain and distress in children and adolescents. <i>Cochrane Database Syst Rev</i> . 2013 Oct 10;10:CD005179. |
| 2011 | Anxiety | Adults (age 40+) | Review of 4 studies in individuals with COPD (n=40) | --Insufficient evidence | n/a | Usmani ZA , Carson KV , Cheng JN , Esterman AJ , Smith BJ . Pharmacological interventions for the treatment of anxiety disorders in chronic obstructive pulmonary disease. <i>Cochrane</i> |

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| | | | | | | Database Syst Rev. 2011 Nov 9;(11):CD008483. |
| 2010 | Dysthymic disorder or significant depressive symptoms | Adults | Patients with diabetes | --Pharmacotherapy showed some effects on depression, but the number of subjects was small | --CBT --Supportive therapy | van der Feltz-Cornelis C, Nuyen J, Stoop C, Chan J, Jacobson AM, Katon W, et al. Effect of interventions for major depressive disorder and significant depressive symptoms in patients with diabetes mellitus: a systematic review and meta-analysis. <i>General Hospital Psychiatry</i> 2010;32: 380-395. |
| 2013 | Depression | Children, adolescents, adults | Patients with diabetes | n/a | --CBT | Verma R, Balhara Y. Management of depression in diabetes: A review of psycho-social interventions. <i>Journal of Social Health and Diabetes</i> 2013;1: 22-26. |
| 2014 | | | Review of liver injury associated with antidepressants | --Lower risk of liver injury with citalopram, escitalopram, paroxetine, fluvoxamine | n/a | Voican CS, Corruble E, Naveau S, Perlemuter G. Antidepressant-induced liver injury: a review for clinicians. <i>Am J Psychiatry</i> 2014; 171:404-415. |
| 2013 | | | Review of serotonin syndrome with use of linezolid and SSRIs or other serotonergic medications | --SSRI/linezolid interaction may be severe but concomitant use is not necessarily contraindicated | n/a | Woytowish MR, Maynor LM. Clinical relevance of linezolid-associated serotonin toxicity. <i>Ann Pharmacother</i> 2013; 47:388-397. |
| 2010 | Depression and anxiety | | Patients with heart failure and COPD | n/a | --CBT --Pulmonary rehabilitation reduces symptoms in patients with COPD | Yohannes AM, Willgoss TG, Baldwin RC, Connolly MJ. Depression and anxiety in chronic heart failure and chronic obstructive pulmonary disease: prevalence, relevance, clinical implications and management principles. <i>International Journal of Geriatric Psychiatry</i> 2010;25: 1209-1221. |

CBT: Cognitive behavioral therapy

CF: Cystic Fibrosis

COPD: Chronic obstructive pulmonary disease

HIV: Human immunodeficiency virus

MAOI: Monoamine oxidase inhibitor

MDD: Major depressive disorder

RCT: Randomized controlled trial

SNRI: Serotonin norepinephrine reuptake inhibitor

SSRI: Selective serotonin reuptake inhibitor

QTc: Corrected QT interval (on electrocardiogram)

TCA: Tricyclic antidepressant

Comparison of First-Line Medications Recommended to Treat Depression and/or Anxiety in Individuals with CF ages 12-Adulthood

| | CITALOPRAM | ESCITALOPRAM | FLUOXETINE | SERTRALINE |
|--|---|--|---|--|
| BASIC CHARACTERISTICS | | | | |
| Neurochemical class | SSRI | SSRI; active <i>S</i> -isomer of citalopram | SSRI | SSRI |
| Selected trade names | --Akarin --Celexa --Cipramil | --Cipralext --Lexapro --Seroplex | --Adofen --Fluctine --Prozac | --Gladem --Lustral --Zoloft |
| | CITALOPRAM | ESCITALOPRAM | FLUOXETINE | SERTRALINE |
| DOSING | | | | |
| Reduced starting dose --For pediatric or medically complex individuals | Start at 5-10 mg/day | Start at 2.5-5 mg/day | Start at 5-10 mg/day | Start at 12.5-25 mg/day |
| Dose increase --Assess clinical response, considering repeat GAD-7 and/or PHQ-9 and functional improvement --Assess adherence to medication | Increase by 5-10 mg every 1-4 weeks if needed | Increase by 2.5-5 mg every 1-4 weeks if needed | Increase by 5-10 mg every 1-4 weeks if needed | Increase by 12.5-25 mg every 1-4 weeks if needed |

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|---|-----------------|-----------------|-----------------|------------------|
| <p>--If symptoms persist and side effects are tolerable, consider dose increase</p> | | | | |
| <p>Typical target dose</p> <p>--To minimize the risk of relapse, consider continuing SSRI for one year following an episode of treatment before tapering gradually</p> <p>--Patients with recurrent symptoms may need longer-term treatment</p> | 20-40 mg/day | 10-20 mg/day | 20-60 mg/day | 50-200 mg/day |
| <p>Elevated dose (off-label)</p> <p>--High doses may be required in cases of partial response, poor absorption, enhanced hepatic metabolism, CYP genetic polymorphism, drug-drug interaction</p> <p>--Consider change in SSRI or referral for specialized consultation</p> | Up to 80 mg/day | Up to 40 mg/day | Up to 80 mg/day | Up to 250 mg/day |

| | | | | |
|---|--|--|--|--|
| Dose adjustment for renal impairment | none | none | none | Consider reducing maximum dose in severe renal impairment |
| Dose adjustment for hepatic impairment | Maximum 20 mg/day | Maximum 10 mg/day | Reduce dose (50% reduction in severe hepatic impairment) | Reduce dose |
| TDM target blood level (ng/ml) --TDM is not routinely used for SSRIs --Consider TDM when elevated doses are required, or drug-drug interactions or CYP genetic polymorphisms are suspected | 50-110 | 15-80 | 120-500 | 10-150 |
| | CITALOPRAM | ESCITALOPRAM | FLUOXETINE | SERTRALINE |
| DRUG-DRUG INTERACTIONS | | | | |
| CYP metabolism of SSRI | Major substrates: 2C19 3A4 Minor substrates: 2D6 | Major substrates: 2C19 Minor substrates: 3A4 2D6 | Major substrates: 2C9 2D6* *metabolite norfluoxetine is exclusive substrate of CYP2D6, increasing clinical significance Minor substrates: 1A2 | Major substrates: 2C19 3A4 Minor substrates: 2B6 2C9 2D6 |

| | | | | |
|----------------------------------|---------------------------------------|---------------------------------------|--|---|
| | | | 2B6 2C19 3A4 | |
| Inhibition of CYP by SSRI | Weak to moderate inhibitor of: 2D6 | Weak to moderate inhibitor of: 2D6 | Strong inhibitor of: 2D6 Weak to moderate inhibitor of: 1A2 2B6 2C9 2C19 2D6 3A4 | Weak to moderate inhibitor of: 1A2 2B6 2C9 2C19 2D6 3A4 |

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|---|------------------|--|------------------|-----------------------------|
| Selected CYP-mediated drug-drug interactions: Medications commonly used in CF that may require dose reduction of SSRI or of CF medication | 2C19 inhibitors: | 2C19 inhibitors: | 2C9 inhibitors: | 2C19 inhibitors: |
| | Cimetidine | Cimetidine | Fluconazole | Cimetidine |
| | Fluconazole | Fluconazole | Miconazole | Fluconazole |
| | Esomeprazole | Esomeprazole | | Esomeprazole |
| | Omeprazole | Omeprazole | 2D6 inhibitors: | Omeprazole |
| | Voriconazole | Voriconazole | Cimetidine | Voriconazole |
| | | | Methadone | |
| | 3A4 inhibitors: | 3A4 inhibitors: | Metoclopramide | 3A4 inhibitors: |
| | Clarithromycin | Clarithromycin | | Clarithromycin Itraconazole |
| | Itraconazole | Itraconazole | 2D6 substrates: | Ketoconazole |
| | Ketoconazole | Ketoconazole | Dextromethorphan | Voriconazole |
| | Voriconazole | Voriconazole | Hydroxycodone | Posaconazole |
| | Posaconazole | Posaconazole | Ondansetron | Fluconazole |
| | Fluconazole | Fluconazole | Morphine | Erythromycin |
| | Erythromycin | Erythromycin | Codeine* | Ivacaftor (weak) |
| Ivacaftor (weak) | Ivacaftor (weak) | Tramadol* | | |
| | | *analgesic effect may be reduced by 2D6 inhibition | 3A4 inducers: | |
| 3A4 inducers: | 3A4 inducers: | | Lumacaftor | |
| Lumacaftor | Lumacaftor | | Rifampin | |
| Rifampin | Rifampin | | | |

| | | | | |
|--|--|-----------------------------|-------------|-----------------------------|
| | 3A4 substrate: Ivacaftor | 3A4 substrate: Ivacaftor | | 3A4 substrate: Ivacaftor |
| <p>QTc prolongation</p> <p>--Modest dose-dependent increases in QTc are unlikely to be clinically significant unless QTc is high (>500 ms)</p> <p>--May consider EKG monitoring when used with other medications that prolong QTc:</p> <ul style="list-style-type: none"> • Antifungals: fluconazole, ketoconazole • Macrolides: erythromycin, clarithromycin, azithromycin • Methadone • Quinolones: levofloxacin, moxifloxacin | <p>Carries FDA warning:</p> <p>http://www.fda.gov/Drugs/DrugSafety/ucm297391.htm</p> <p>--Discontinue use if QTc>500 ms persistently</p> <p>--Correct hypokalemia, hypomagnesemia</p> | Less likely | Less likely | Less likely |

| | | | | |
|--|---|-----------|-----------|-----------|
| <p>Serotonin syndrome</p> <p>--Potentially fatal syndrome includes change in mental status; autonomic instability (sweating, tachycardia, fever); tremor, myoclonus, hyperreflexia; abdominal pain and diarrhea</p> <p>--Relative contraindication of SSRI use with linezolid; when alternatives are unavailable, use with informed consent and clinical monitoring</p> | linezolid | linezolid | linezolid | linezolid |
| | | | | |
| ADVERSE EFFECTS | | | | |
| Common SSRI side effects | <p>--Nausea, diarrhea, sexual dysfunction, insomnia, restlessness, and headache may occur with any SSRI</p> <p>--May improve with time, slower dose titration, dose reduction, or change in medication</p> <p>--Insufficient evidence exists regarding effects of SSRIs in CF on bone density, hemoptysis, or weight gain</p> | | | |
| Suicidal thoughts and/or behaviors | <p>--Depression and anxiety can themselves be associated with suicidal thoughts and/or behavior</p> <p>--Concerns have been raised regarding increased risk of suicidal thoughts and/or behavior with the use of antidepressant medications, particularly when starting medication in pediatric and young adult patients</p> <p>--The risk/benefit ratio remains in favor of using SSRIs when clinically appropriate</p> <p>--Regardless of treatment modality, good clinical practice supports ongoing surveillance of suicidal thoughts in order to properly intervene, particularly at times of higher stress or when initiating or changing treatment</p> | | | |
| SSRI discontinuation syndrome | <p>--When discontinuing an SSRI, taper down gradually whenever possible to avoid discontinuation symptoms</p> <p>--May include nausea, headache, dizziness, paresthesias, and insomnia</p> | | | |

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| | --Fluoxetine is least likely to cause discontinuation syndrome due to its longer half-life |
|--|--|

CF: Cystic fibrosis

CYP: Cytochrome P450 isoenzyme

EKG: Electrocardiogram

GAD-7: Generalized Anxiety Disorder-7 (anxiety rating scale)

FDA: United States Food and Drug Administration

PHQ-9: Patient Health Questionnaire-9 (depression rating scale)

SSRI: Selective serotonin reuptake inhibitor

TDM: Therapeutic drug monitoring

QTc: Corrected QT interval on EKG

Appendix E: Screening Measures

Table 1: Depression Screening Measures

| Depression Screening Measures | | | | | | | |
|---|---|--|----------------------|------------------------|---|----------------------------------|-----------------------------|
| Tool | Description | # of Items/Format | Ages | Time | Psychometric Properties | Languages/Cultural Consideration | Cost |
| BDI-II (Beck Depression Inventory)^{1,2} | Measures symptoms of depression | 21 items Self-administered or verbally by trained administrator | 13+ | 5 min | Sensitivity: 84% Specificity: 81% Coefficient alpha: .92 | English, Spanish | \$125/kit |
| BDI-FS (Beck Depression Inventory-FastScreen for Medical Patients)³ | Screens for depression, while omitting items that may be due to medical condition | 7 items | 13+ | <5 min | Sensitivity: 91% Specificity: 91% Cronbach's alpha: .84 | English | \$99/kit |
| Beck Hopelessness Scale⁴⁻⁶ | Measures negative attitudes about the future | 20 true/false | 12 to 22 | 5-10 min | Reliability: 0.93 Cronbach's alpha: 0.92 ⁴ | English Finnish Spanish | \$125/kit |
| | | | 17 to 25 in Pakistan | | Cronbach's alpha: 0.81 ⁵ | Urdu | |
| BYI (Beck Youth Inventories)^{7,8} | Screens for depression, anxiety, anger, disruptive behavior, and self-concept | 5 separate 20-item self-report inventories | 7 to 18 | 5 min/ inventory | Cronbach's alpha: 0.83 to 0.94 Test-retest reliability: 0.61 to 0.87 | English | \$265/kit or \$55/inventory |
| CDI-2 (Child Depression Inventory)⁹⁻¹² | Measures symptoms of depression | Parent: 17 items Teacher: 12 items Youth: 28 items | 7 to 17 | 5-10 min (youth items) | Cronbach's alpha: 0.71 to 0.89 test-retest range 0.74 to 0.83 | English, Spanish | \$289/kit |

| | | | | | | | |
|---|--|------------------------|----------------------------|-----------|--|------------------------------|----------------------|
| CDI 2 Short ¹³ | Short version of CDI 2 | 10 items | 7 to 17 | 5 min | Sensitivity: 93% Specificity: 71% | English Spanish German | \$55/short version |
| CDRS-R (Children's Depression Rating Scale- Revised) ¹⁴ | Semi structured interview for depression | 17 items | 6 to 17 | 15-20 min | Cronbach's alpha: Initial screening: 0.79 Baseline: 0.74 Exit: 0.92 | English | \$107/kit |
| CES-D (Center for Epidemiological Studies - Depression Scale) ¹⁵⁻²⁰ | Screens for depression, modified version for children and adolescents | 20 items | 6 to 17 | 5-10 min | Cronbach's alpha: 0.89 | English Spanish | Public domain |
| | | 12 items short version | 7th, 9th, 10th, 12th grade | | Cronbach's alpha: 0.85 | | |
| Columbia Depression Scale ²¹ | Depression stem questions from the Diagnostic Interview Schedule for Children (DISC) | 22 yes/no items | 11+ | <5 | Cronbach's alpha: 0.87 | English | Free with permission |

| | | | | | | | |
|---|--|--|--|----------|---|---|----------------------|
| HADS (Hospital Anxiety and Depression Scale)²²⁻²³ | Brief assessment of anxiety and depression in medical populations. | 14 items (7 anxiety, 7 depression) | 13+ | 2-5 min | Cronbach's alpha: 0.71 (anxiety) 0.76 (depression) Significant relationship between acceptance (Illness Cognition Questionnaire) and depressive symptoms | English, Arabic, Dutch, French, German, Hebrew, Swedish, Italian, Spanish | Free |
| KADS (Kutcher Adolescent Depression Scale)²⁴⁻²⁵ | Measures symptoms of depression | 6, 11, or 16 items | 12 to 17 | 5 min | Sensitivity: 92% Specificity: 71% | English | Free with permission |
| MFQ (Mood and Feeling Questionnaire)²⁶⁻²⁷ | Measures symptoms of depression, available as child self-report, parent report on child, and adult self-report | Youth: 33 items Parent: 34 items Adult: 33 items | 7+ research subjects & clinic patients | 5-10 min | MFQ-C Cronbach's alpha: 0.95 Test-retest: .80; AUC: .85 Optimal cut point: 29 PPV: 21% Sensitivity: 68% Specificity: 88% <hr/> MFQ-P: Cronbach's alpha: .96 Test-retest: .80; Optimal cut point: 27 PPV: 23% Sensitivity: 61% Specificity: 85% | English Norwegian | Free |

| | | | | | | | |
|--|--|---|--|--------------|--|---|-----------------------------|
| <p>MFQ - Short Version (SMFQ)²⁸⁻³⁰</p> | <p>Measures symptoms of depression</p> | <p>Youth: 13 items Parent: 13 items Adult: 13 items</p> | <p>7+</p> | <p>5 min</p> | <p>Child score AUC: 0.73 Parent score AUC: 0.74 Combined child + parent score: AUC =0.86 At cut point of 10: Sensitivity: 76% Specificity: 78%</p> | <p>English</p> | <p>Free</p> |
| <p>PHQ-9³¹⁻³⁴</p> | <p>Measures symptoms of depression and suicidality</p> | <p>9 plus severity items</p> | <p>Adolescent</p> | <p>5 min</p> | <p>Cronbach's alpha: 0.79-.89 Overall 88% sensitivity and 88% specificity</p> | <p>English + over 30 more languages</p> | <p>Free with permission</p> |
| | | | <p>Newly medically admitted in- and outpatients aged 13-16 in Pediatric Hospitals in Munich, Germany</p> | | <p>Dimensional algorithm: Optimal cut point score of 8 or greater Cronbach's alpha: 0.82 Sensitivity: 90% Specificity: 86.5% PPV: 48.6%; NPV: 98.4% AUC= 93.2%</p> | <p>German</p> | |
| | | | <p>13 to 17</p> | | <p>Optimal cut point score of 11 or greater Sensitivity: 89.5% Specificity: 77.5% PPV: 15.2%; NPV: 99.4% AOC: 0.88</p> | <p>English</p> | |

| | | | | | | | |
|---|---|----------------|---|------------------|---|--|-------------|
| <p>PHQ-A Depression Screen³⁵⁻³⁶</p> | <p>Abbreviated screen specifically for depression</p> | <p>9 items</p> | <p>12 to 18</p> | <p><5 min</p> | <p>Sensitivity: 87.1% Specificity: 79.7% PPV: 39.7% NPV: 97.58% AOC: .939 Cronbach's alpha: .835</p> | <p>Available in multiple languages</p> | <p>Free</p> |
| <p>PHQ-2 (Patient Health Questionnaire 2)³⁷</p> | <p>First items of PHQ-9</p> | <p>2 items</p> | <p>13-16 year old in- and outpatients in pediatric hospitals in Munich, Germany</p> | <p><5 min</p> | <p>Optimal cut point score of 2 or greater. Sensitivity: 85% Specificity: 79.4% PPV: 37% NPV: 97.4% AUC: 87.2%</p> | <p>German</p> | <p>Free</p> |
| | | | <p>13 to 17</p> | | <p>Optimal cut point score of 2 or greater. Sensitivity: 74% Specificity: 75% AOC: 0.84</p> | <p>English</p> | |

Table 2: Anxiety Screening Measures

| Anxiety Screening Measures | | | | | | | |
|--|---|-------------------|---------------------|--------|---|--|-----------|
| Tool | Description | # of Items/Format | Ages | Time | Psychometric Properties | Languages | Cost |
| MASC (Multidimensional Anxiety Scale for Children)³⁸⁻³⁹ | Broad dimensions of anxiety-physical symptoms, harm avoidance, social anxiety, and separation/panic | 39 items | 8 to 19 | 15 min | Gender: girls scored higher across all scale than boys. | English, Taiwanese | \$189/kit |
| | | | 8 to 13 in Sydney | | Cronbach's alpha: .89 (child) Cronbach's alpha: .90 (parent) Parent Child concordance: range .20 to .36 | English | |
| GAD-7 (Generalized Anxiety Disorder Scale)⁴⁰ | Self-report anxiety scale | 7 items | Adolescent to adult | <5 min | Cronbach's alpha: .92 Test-retest reliability: intraclass correlation: .83 | English + over 30 more languages | Free |
| SCARED (Self-Report for Childhood Anxiety Related Emotional Disorders)⁴¹ | Child and parent self-report for childhood anxiety | 41 items | 8 to 18 | 10 min | Coefficient alpha: 0.90 | English, Arabic, Chinese, French, German, Italian, Portuguese, Spanish | Free |

| | | | | | | | |
|--|--|----------|---------------------|--------|---|---|------|
| Spence Children's Anxiety Scale ⁴²⁻⁴⁴ | Self-report that assess six domains of anxiety | 44 items | 8 to 12 | 10 min | Coefficient alpha: 0.9 to 0.92 Test-retest 0.60 to 0.63 | Available in 22 languages | Free |
| Penn State Worry Questionnaire (PSWQ) ⁴⁶ | Self-report worry severity questionnaire | 16 items | Adolescent to adult | <5 min | Cronbach's alpha: 0.95 Test-retest reliability: $r = 0.92$ Internal consistency = .91 | English, Korean, French, Dutch, Chinese, German, Greek, Italian, Thai | Free |
| Penn State Worry Questionnaire – Children (PSWQ-C) ⁴⁷⁻⁴⁸ | Self-report worry severity questionnaire | 14 items | 6 to 18 | 5 min | Test-retest reliability: 0.92 Internal Consistency: 0.89 | English, Korean, French, Dutch, Chinese, German, Greek, Italian, Thai | Free |

AAP, American Academy of Pediatrics; MCHB, Maternal and Child Health Bureau; NA, not applicable; PPV, positive predictive value; NPV, negative predictive value; ROC, receiver operator curve; *DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*; ADHD, attention-deficit/hyperactivity disorder; ODD, oppositional-defiant disorder; CD, conduct disorder; OCD, obsessive-compulsive disorder; PTSD, post-traumatic stress disorder; *DSM-III-R, Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised*; *ICD-10, International Classification of Diseases, 10th Edition*.

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