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.

AACAP psychotropic medication **(US, 2009)**	MDD	Children & adolescents	Prescription of medication to children & adolescents in unspecified settings	--SSRIs fluoxetine, sertraline, citalopram have more evidence Before prescribing medication: Psychiatric evaluation, medical history, collaboration between health care providers, ensure availability of follow up, consent/assent process	--Combined medication plus CBT is first line for moderate to severe depression in adolescents	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 depression in adults **(US, 2010)**	MDD	Adults	Psychiatric care settings --Adapt therapies to account for any comorbid physical illness	--SSRI, SNRI, mirtazapine or bupropion for most patients --Of the SSRIs, sertraline, citalopram, escitalopram have fewer drug-drug interactions --SNRI or TCA possibly preferable for patients with comorbid chronic pain	--CBT or IPT --Psychodynamic psychotherapy (less evidence) --Problem solving therapy in mild cases --Couples or family therapy when appropriate	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.
BAP anti-depressant use **(UK, 2008)**	Unipolar depressive disorders	Primarily adults; also children & adolescents, elderly, medical illness	Depression treatment by physicians of any specialty, including primary care and psychiatry	For adults: --SSRI --TCA, escitalopram or venlafaxine more effective in severe depression For children & adolescents:	For adults: --CBT or behavior therapy/activity scheduling --IPT For children & adolescents:	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.

				For comorbid medical illness: Consider drug-drug interactions, adverse effects	--CBT if no response to structured supportive treatment	
Beyondblue adolescent & young adult depression **(Australia, 2011)**	MDD, dysthmia, bipolar disorder	Adolescents (age 13-18) & young adults (age 19-24)	Diverse health care settings	For moderate or severe MDD: The SSRI fluoxetine, used with CBT or IPT --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.	For dysthymia: --Nondirective support --Group CBT/IPT For MDD: --CBT --IPT	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.
CANMAT MDD in adults **(Canada, 2009)**	MDD	Adults; also children & adolescents	Primarily treatment by psychiatrists and other mental health specialists; also primary care settings	For adults, select from wide variety of first line agents based on clinical situation: --SSRI --SNRI --"Newer" agents including agomelatine, bupropion, mianserin, mirtazapine, moclobemide, reboxetine, tianeptine	--CBT --IPT	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. 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

				--Superior efficacy for escitalopram, sertraline, venlafaxine --Superior tolerability for escitalopram, sertraline --Weight gain with mirtazapine, paroxetine --Fewest drug-drug interactions with citalopram, desvenlafaxine, escitalopram, mirtazapine, venlafaxine For children & adolescents: --The SSRIs fluoxetine and citalopram are first line (combined with CBT)		Disord 2009 Oct;117 Suppl 1:S15-25. Epub 2009 Aug 13. Lam RW, Kennedy SH, Grigoriadis S, McIntyre RS, Milev R, Ramasubbu R, 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. III. Pharmacotherapy. J Affect Disord 2009 Oct;117 Suppl 1:S26-43. Epub 2009 Aug 11.
CANMAT mood disorders and comorbid medical conditions **(Canada, 2012)**	Depressive symptoms, MDD	Medically ill populations; focus on cardio-vascular disease, cancer, HIV/ hepatitis C, migraine, multiple sclerosis, epilepsy, osteoporosis	Specialized medical clinics; multidisciplinary care teams	--Level of evidence differs by specific medical disorder --When evidence in specific medical disorder is limited, consult general treatment guidelines --Consider drug-drug interactions and drug-illness interactions --Of the SSRIs, citalopram, escitalopram, and sertraline	--CPT --IPT --Problem solving therapy	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. Ann Clin Psychiatry. 2012 Feb;24(1):82-90. 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

				have fewer drug-drug interactions --Supplement vitamin D and consider bone density monitoring when SSRI use >2 years		of patients with mood disorders and select comorbid medical conditions. Ann Clin Psychiatry. 2012 Feb;24(1):91-109.
GLAD-PC adolescent depression primary care **(US and Canada, 2007)**	For psycho-logical intervention: MDD, depression not otherwise specified, dysthymic disorder, subthreshold symptoms For medication: MDD	Adolescents & young adults (age 10-21)	Primary care	--SSRI	For mild cases: --Active support and monitoring For moderate to severe cases: --CBT --ITP	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. 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.
NICE depression in adults **(UK, 2009)**	MDD, or persistent sub-threshold MDD/ dysthymia	Adults (age 18+)	Primary and secondary care (stepped care model)	--SSRI	--CBT or IPT --Behavioral activation (less evidence) --Couples therapy when appropriate	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)

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. Axencia de Avaliacion de Tecnoloxias Sanatarias de Galicia (avalia-t); 2008. Clinical Practice Guidelines in the Spanish SHN: avalia-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. Axencia de Avaliacion de Tecnoloxias Sanatarias de Galicia (avalia-t); 2009. Clinical

(Spain, 2009)				Devices for pediatric depression --Sertraline, citalopram and escitalopram are first line alternatives based on clinical situation including family history	--IPT For severe MDD in adolescents: --CBT In children: --CBT --Family therapy	Practice Guidelines in the SNS: avalia-t no. 2007/09. www.sergas.es/docs/Avalia-t
USPTF adult depression screening (US, 2009)	MDD, dysthymia, minor depression (non-bipolar)	Adults	Primary care	--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)	--Options include CBT or brief psychosocial counseling	US Preventive Services Task Force. Screening for depression in adults: US Preventive Services Task Force recommendation statement. Ann Intern Med 2009;151:784-792. 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. 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.
USPTF pediatric depression (US, 2009)	MDD	Children (age 7-11) & adolescents (age 12-18)	Primary care	For adolescents: SSRI (fluoxetine, citalopram, paroxetine, escitalopram, sertraline)	For adolescents: --CBT --IPT	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. Williams SB, O'Connor EA, Eder M,

				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.

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.

			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

				ineffective or contraindicated due to medical comorbidities --Not for use in OCD, PTSD		
ADAC anxiety **(Canada, 2014)**	Panic disorder, agora-phobia, specific phobia, social anxiety disorder, GAD, OCD, PTSD	Adults; children & adolescents or elderly; comorbid conditions	Primary care, psychiatric care, multidisciplinary care team	For adults: --SSRI for most anxiety disorders --SNRI for most anxiety disorders, not first line for OCD --Also pregabalin for social anxiety disorder, GAD --Also agomelatine for GAD --Benzodiazepines for short term use during acute crises or antidepressant treatment initiation --Medications less useful for specific phobia For children & adolescents: SSRI	--Exposure-based CBT, mindfulness-based cognitive therapy, or other forms of CBT first line for most anxiety disorders --IPT an alternative for social anxiety (less effective) --ACT an alternative for OCD (less evidence) --EMDR or DBT alternatives for PTSD --Include parent/family component for children and adolescents	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. 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.
CPA anxiety (Canada, 2006)	Panic disorder, agora-	Adults; children & adolescents	Primary care, psychiatric care	For adults:	--CBT	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 Amerigen M, Walker JR. Canadian Psychiatric

	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.

adults in primary care (Spain, 2008)				--SNRI (venlafaxine ER) --TCA (chlor)impramine --Benzodiazepines mainly for short term use or need for rapid response; alprazolam or lorazepam for acute panic attack	--Other techniques as appropriate	Community of Madrid; 2008. Clinical Practice Guidelines in the NHS. UETS No. 2006/10.
WFSBP anxiety in primary care (international, 2012)	GAD, panic disorder, agora-phobia, specific phobia, social anxiety disorder, OCD, PTSD	Primarily adults; also children & adolescents	Primary care (See Bandelow, 2008, re: complex care in other settings)	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	--All patients require supportive psychotherapy --Consider CBT/exposure therapy as alternative or addition to medication	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.

*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: Dialetical 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.

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.

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

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, 3rd Edition.

	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. Child & Adolescent Psychiatric Clinics of North America 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. Respiratory Medicine 2011; 105:1422-1433.
2014	Anxiety, depression, other psychiatric disorders	Children & Adolescents	Texbook of pharmacotherapy in pediatric populations	--Review of principles of neuropsycho-pharmacology --Review of risks and benefits of SSRIs, including serotonin syndrome, suicidality, bleeding.	n/a	Gerlach M, Warnke A, Greenhill L. Psychiatric Drugs in Children and Adolescents. 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. *Cochrane Database of Systematic Reviews.* 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. Primary Care Diabetes 2013; 7: 1-10.

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.

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	Muscatello 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**

	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. *Science and practice of cognitive behaviour therapy*. 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. Cochrane Database Syst Rev. 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. Palliat Med. 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. J Clin Psychiatry. 2014 Sep;75(9):964-74.
2012	Anxiety, depression, other psychiatric disorders	Children & Adolescents	Texbook of pharmacotherapy in pediatric populations	--Reviews principles of clinical psycho-pharmacology --Reviews use of antidepressants in	n/a	Rosenberg DR, Gershon S, eds. Pharmacotherapy of Child and Adolescent Psychiatric Disorders. Third edition. West Sussex: Wiley-Blackwell, 2012.

				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. Psychoneuroendocrinology 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. Journal of Affective Disorders 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. Massachusetts General Hospital Comprehensive Clinical Psychiatry. Philadelphia: Mosby/Elsevier, 2008. Stern TA, Fava M, Wilens T, Rosenbaum JF, eds. Massachusetts General Hospital Comprehensive Clinical Psychiatry, 2nd 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. Current Opinion in Pediatrics 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 Ttreatment of anxiety in patients with cancer. Journal of Clinical Oncology 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. Cochrane Database Syst Rev. 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. Cochrane

						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. General Hospital Psychiatry 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. Journal of Social Health and Diabetes 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. Am J Psychiatry 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. Ann Pharmacother 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. International Journal of Geriatric Psychiatry 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 *S*-isomer of citalopram	SSRI	SSRI
Selected trade names	--Akarin --Celexa --Cipramil	--Cipralex --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 reponse, 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 by12.5-25 mg every 1-4 weeks if needed

--If symptoms persist and side effects are tolerable, consider dose increase				
Typical target dose --To minimize the risk of relapse, consider continuing SSRI for one year following an episode of treatment before tapering gradually --Patients with recurrent symptoms may need longer-term treatment	20-40 mg/day	10-20 mg/day	20-60 mg/day	50-200 mg/day
Elevated dose (off-label) --High doses may be required in cases of partial response, poor absorption, enhanced hepatic metabolism, CYP genetic polymorphism, drug-drug interaction --Consider change in SSRI or referral for specialized consultation	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 3A4	Weak to moderate inhibitor of: 1A2 2B6 2C9 2C19 2D6 3A4

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

	3A4 substrate: Ivacaftor	3A4 substrate: Ivacaftor		3A4 substrate: Ivacaftor
QTc prolongation --Modest dose-dependent increases in QTc are unlikely to be clinically significant unless QTc is high (>500 ms) --May consider EKG monitoring when used with other medications that prolong QTc: • Antifungals: fluconazole, ketoconazole • Macrolides: erythromycin, clarithromycin, azithromycin • Methadone • Quinolones: levofloxacin, moxifloxacin	Carries FDA warning: http://www.fda.gov/Drugs/DrugSafety/ucm297391.htm --Discontinue use if QTc>500 ms persistently --Correct hypokalemia, hypomagnesemia	Less likely	Less likely	Less likely

Serotonin syndrome --Potentially fatal syndrome includes change in mental status; autonomic instability (sweating, tachycardia, fever); tremor, myoclonus, hyperreflexia; abdominal pain and diarrhea --Relative contraindication of SSRI use with linezolid; when alternatives are unavailable, use with informed consent and clinical monitoring	linezolid	linezolid	linezolid	linezolid

ADVERSE EFFECTS	
Common SSRI side effects	--Nausea, diarrhea, sexual dysfunction, insomnia, restlessness, and headache may occur with any SSRI --May improve with time, slower dose titration, dose reduction, or change in medication --Insufficient evidence exists regarding effects of SSRIs in CF on bone density, hemoptysis, or weight gain
Suicidal thoughts and/or behaviors	--Depression and anxiety can themselves be associated with suicidal thoughts and/or behavior --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 --The risk/benefit ratio remains in favor of using SSRIs when clinically appropriate --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
SSRI discontinuation syndrome	--When discontinuing an SSRI, taper down gradually whenever possible to avoid discontinuation symptoms --May include nausea, headache, dizziness, paresthesias, and insomnia

	--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