

Quality Improvement Guidelines

Depression Screening and Follow-Up Plan

Purpose

To provide a guide for primary care clinicians when screening patients for depression and selfharm and when creating a follow-up plan for patients who screen positive for depression.

Scope

This document applies to patients being treated by BSWQA primary care clinicians in family medicine and internal medicine.

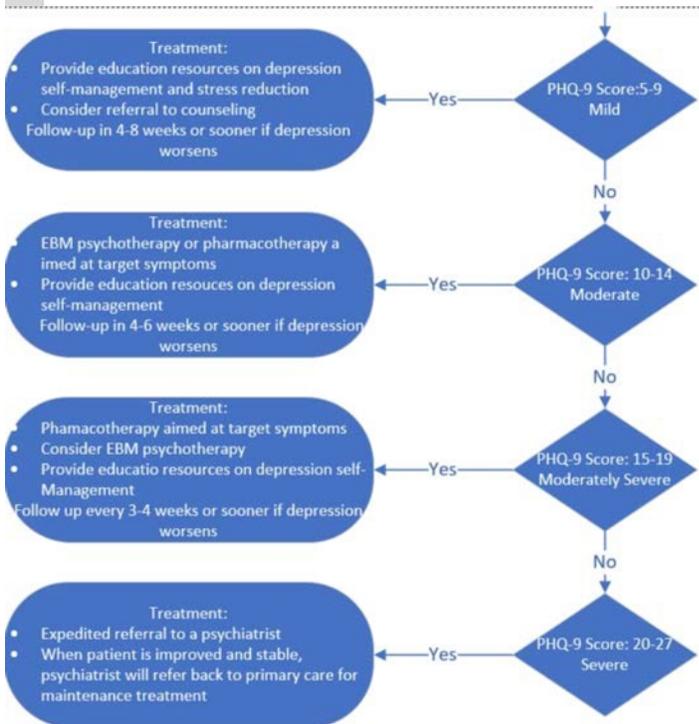
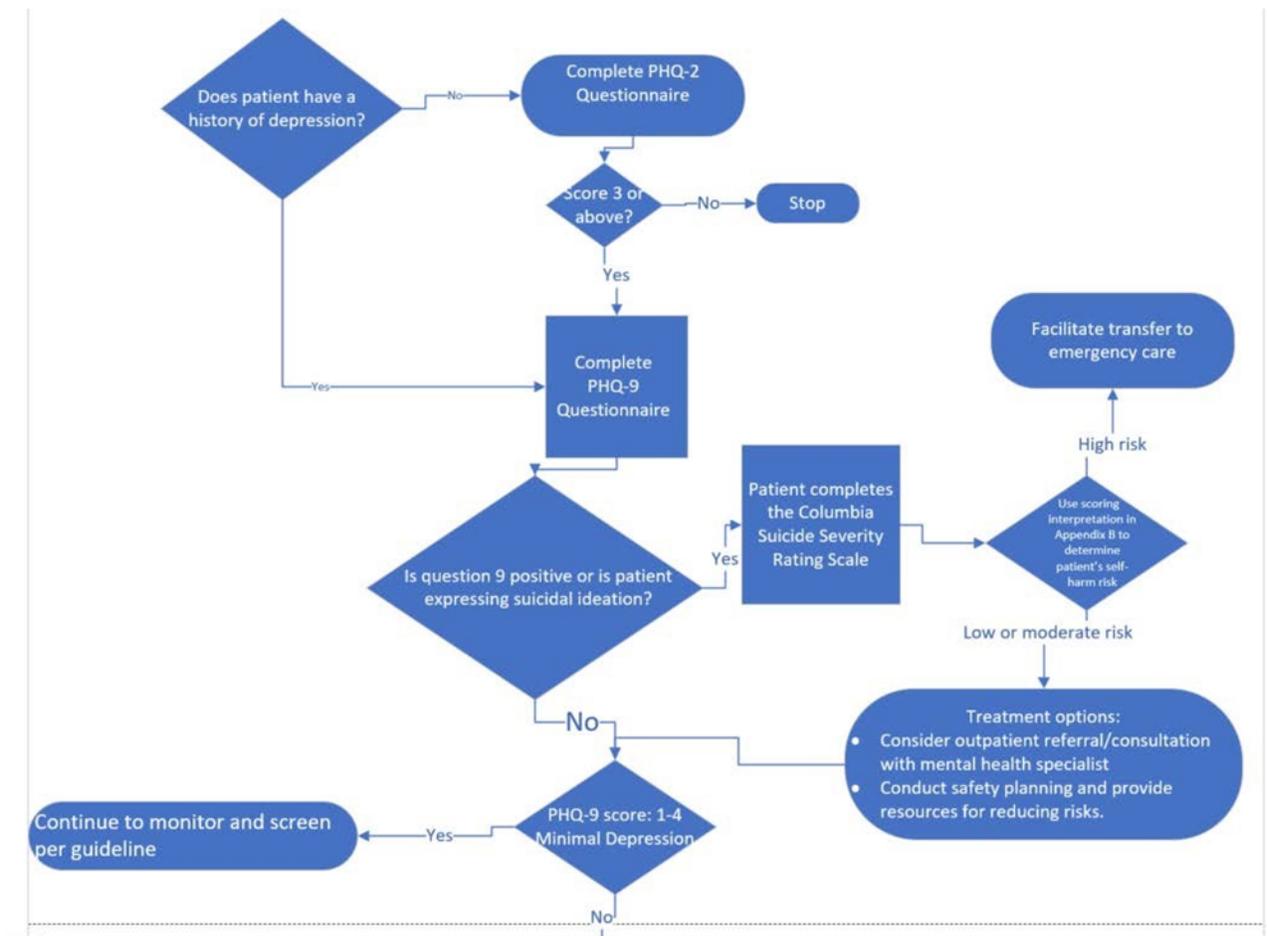
This document does not apply to:

- Patients receiving treatment for moderate to severe depressive disorder within a psychiatric inpatient facility or a specialty behavioral health outpatient clinic.
- Patient or patient's legal guardian who does not consent.
- Patients with severe mental and/or physical incapacity with impaired decisional capacity where the person is unable to express himself/herself in a manner understood by others. For example, cases such as delirium, major neurocognitive disorder, or other illnesses with severe cognitive impairment, where depression cannot be accurately assessed through use of nationally recognized standardized assessment tools.
- Pediatric patients under 18 years old.

Guideline

Definitions

- EBM – Evidence-based medicine treatment
- PHQ – Patient Health Questionnaire
- Medical Clearance - The process required to reach the point, with reasonable clinical confidence, at which any remaining systemic medical problems can be treated on an outpatient basis. This is the point at which a qualified primary or specialty medical provider has made the determination that it is medically appropriate to discharge the patient or transfer to a psychiatric facility.
- Mental Health Specialist - A specially trained clinician who evaluates the patient in order to recommend appropriate mental health treatment and/or disposition
- Qualified Provider - Staff including Registered Nurses ("RN"), APPs, Licensed Masters Level Social Workers or Counselors, and others who have been trained in providing selfharm risk assessments



Depression and Self-Harm (Suicide) Risk

BSWQA providers in clinics and ambulatory patient care departments will screen patients for depression and imminent risk of harm to self. All primary care clinical staff are reminded that suicide risk is increased for illnesses other than depression (e.g., psychotic disorders, substance use disorders, PTSD) Staff will provide an appropriate environment for patients at risk of self-harm based upon physician orders. Staff will conduct further assessment or refer to a Mental Health Specialist/other qualified provider for further assessment, when a patient has been determined to be imminent risk of harm to self.

Locations

Clinic and ambulatory screening will occur at the following clinics:

- Family Medicine
- Internal Medicine

Timing and Frequency

- Patients will be screened for depression **at least annually***.
- Patients with a current diagnosis of depression should be monitored at least quarterly.

Screening Questions

Staff members screen patients for depression and imminent risk of harm to self by utilizing standardized screening tools. Below is an example of screening with the Patient Health Questionnaire (PHQ).

1. PHQ-2

- The PHQ-2 is composed of the first two questions of the PHQ-9(see *Appendix A* for the questions).

2. PHQ-2 Positive Screening

- The patient screens positive when he/she scores a total of 3 or greater. If a patient screens positive, the provider may take appropriate steps, as deemed necessary by the provider, including but not limited to, further utilizing the PHQ-9 or personal and direct referrals and provide resources for outpatient mental/behavioral health and other providers for follow-up care.

3. PHQ-9

- The PHQ-9 can be used for screening and monitoring of depression (see *Appendix B* for questionnaire and scoring instructions). The treatment algorithm above outlines recommendations based on depression severity/score.

4. PHQ-9 Positive Screening for Self-Harm

- If a patient screens positive for item 9, the provider may take appropriate steps, as deemed necessary by the provider, including further assessment utilizing the Columbia-Suicide Severity Rating Scale (“CSSRS”) (see *Appendix C*). Refer to BSWH Outpatient Suicide system policy by following this [LINK](#).

*Evidence of depression is defined by symptom duration of at least two weeks. Therefore, it is recommended that screening be administered more frequently than once a year. It is appropriate to obtain a PHQ2/PHQ9 at each visit or at least bi-annually if possible

Depression Follow-up Recommendations

For patients who screen positive for depression, but are not at immediate risk, a follow-up plan must be documented in the medical record on the day of the screening. Follow-up recommendations can include:

- Additional evaluation for depression
- Referral to a mental health specialist who can diagnose and treat depression
- Pharmacological and neuromodulation interventions
- Other interventions or follow-up for the diagnosis or treatment of depression

The follow-up plan will vary depending on the patient's score (see algorithm on *page 2*). See *Appendix D* to learn more about the Pearls of Treatment and *Appendix E* for a list of resources for patients in crisis.

Pharmacologic Treatment

Antidepressants should be started as initial treatment for patients with moderate and severe major depressive disorder. All primary care providers (PCPs) should document antidepressant medication use on the patient's medication list and update the medication list when changes are made to antidepressant medication therapy.

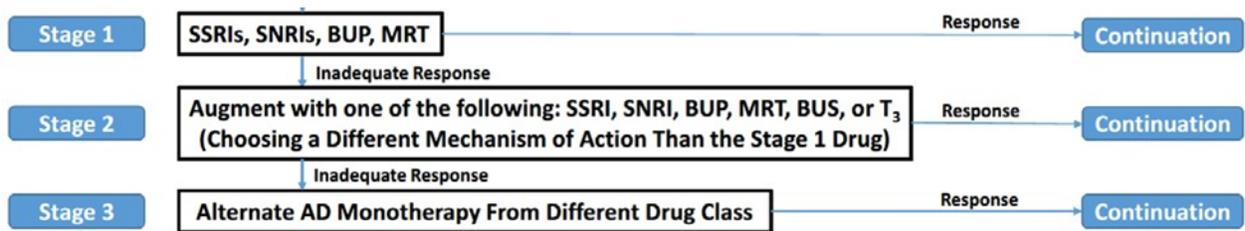
Acute Phase Treatment

Acute Phase Treatment is/are the intervention(s) required for the patient to achieve remission, or at least response. There are various factors to be considered when choosing the right antidepressant for the patient (see *Appendices F, G and H* for selection considerations). The initial dose should be incrementally increased until one of the following occurs: remission is achieved, a maximum FDA approved dose is reached with validated medication compliance, or treatment-limiting significant side effects are encountered. Remission is defined as a PHQ-9 score of ≤ 5 on 2 consecutive assessments. Response is a 50% decrease in the PHQ-9 score from baseline.

Response	PHQ-9 at each follow-up contact	Treatment Plan
Responsive	Drop of > 5 points from previous PHQ-9 and PHQ-9 score is <10	No treatment change needed. Follow up in 4 more weeks.
Partially Responsive	Drop of 2-4 points from previous PHQ-9 or PHQ-9 score is > 10	Consider upward titration of current antidepressant +/- adding another medication or referring for psychotherapy
Non-responsive	Drop of 1 point or no change or increase in PHQ-9 score relative to previous PHQ-9 score.	Consider the following: <ul style="list-style-type: none">• Antidepressant if receiving psychotherapy alone• Adjust dose of the medication• A different class of antidepressant• Augmentation strategy• Adding psychotherapy• Psychiatric consultation

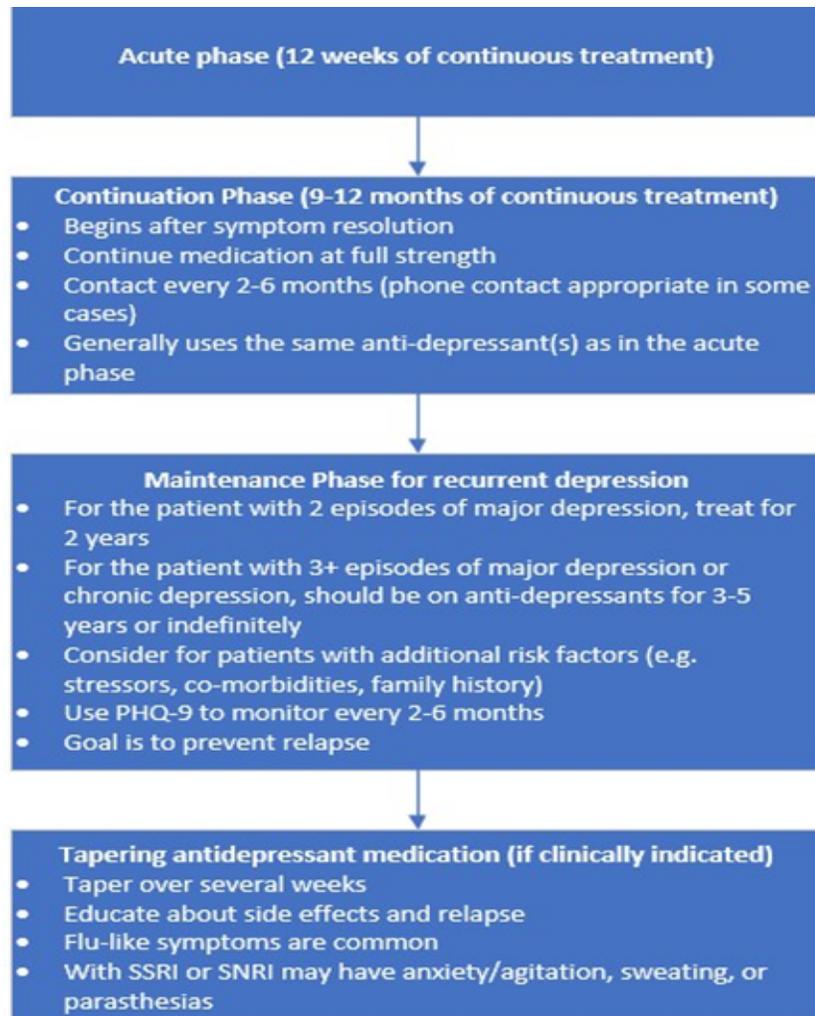
Below are some treatment recommendations:

- Although some patients will see improvements in the first 2 weeks, the full benefits are not achieved at a dose until the patient has been taking it for ≥ 8 weeks.
- Recent evidence suggests a very low probability of improvement if the patient does not experience a 20% improvement in symptoms (decrease in baseline PHQ-9 score) after 2 weeks. If this early improvement is not observed by 2 weeks, a change in the antidepressant regimen should occur. Refer to below diagram.
- For the elderly population, dosing should start low and be titrated up slowly.



Continuation Phase Treatment

The Continuation Phase consists of at least 9 to 12 months of continuous treatment on the same antidepressant regimen and dosage(s) after achievement of remission. The provider should monitor the patient's symptoms and assess response using standardized assessments, such as the PHQ-9.



Additionally, see the following appendices for more information on specific topics or tools:

- **Appendix F: Pharmacological Therapy**
- **Appendix G: Shared Decision-Making Aid**
- **Appendix H: Serious Side Effects of Antidepressants**
- **Appendix I: Antidepressant Cost Analysis**
- **Appendix J: Discontinuation Syndrome Patient Handout**

Appendices:

Appendix A: PHQ-2 Questions and Scoring Interpretation

The Patient Health Questionnaire-2 (PHQ-2)

Patient Name _____ Date of Visit _____

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

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Appendix B: PHQ-9 Questions and Scoring Interpretation

PATIENT HEALTH QUESTIONNAIRE (PHQ-9)

NAME: _____ DATE: _____

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	0	1	2	3

add columns + +

(Healthcare professional: For interpretation of TOTAL, please refer to accompanying scoring card). TOTAL:

10. 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	_____

PHQ-9 Patient Depression Questionnaire

For initial diagnosis:

1. Patient completes PHQ-9 Quick Depression Assessment.
2. If there are at least 4 ✓s in the shaded section (including Questions #1 and #2), consider a depressive disorder. Add score to determine severity.

Consider Major Depressive Disorder

- if there are at least 5 ✓s in the shaded section (one of which corresponds to Question #1 or #2)

Consider Other Depressive Disorder

- if there are 2-4 ✓s in the shaded section (one of which corresponds to Question #1 or #2)

Note: Since the questionnaire relies on patient self-report, all responses should be verified by the clinician, and a definitive diagnosis is made on clinical grounds taking into account how well the patient understood the questionnaire, as well as other relevant information from the patient.

Diagnoses of Major Depressive Disorder or Other Depressive Disorder also require impairment of social, occupational, or other important areas of functioning (Question #10) and ruling out normal bereavement, a history of a Manic Episode (Bipolar Disorder), and a physical disorder, medication, or other drug as the biological cause of the depressive symptoms.

To monitor severity over time for newly diagnosed patients or patients in current treatment for depression:

3. Patients may complete questionnaires at baseline and at regular intervals (e.g., every 2 weeks) at home and bring them in at their next appointment for scoring or they may complete the questionnaire during each scheduled appointment.
4. Add up ✓s by column. For every ✓: Several days = 1 More than half the days = 2 Nearly every day = 3
5. Add together column scores to get a TOTAL score.
6. Refer to the accompanying PHQ-9 Scoring Box to interpret the TOTAL score.
7. Results may be included in patient files to assist you in setting up a treatment goal, determining degree of response, as well as guiding treatment intervention.

Scoring: add up all checked boxes on PHQ-9

For every ✓ Not at all - 0; Several days - 1,
More than half the days = 2; Nearly every day = 3

Interpretation of Total Score

Total Score	Depression Severity
1-4	Minimal depression
5-9	Mild depression
10-14	Moderate depression
15-19	Moderately severe depression
20-27	Severe depression

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Appendix C: CSSRS Questions and Scoring Interpretation

COLUMBIA-SUICIDE SEVERITY RATING SCALE

Screening Version - Since Last Visit

SUICIDE IDEATION DEFINITIONS AND PROMPTS	Since Last Visit	
Ask questions that are bold and <u>underlined</u>	YES	NO
Ask Questions 1 and 2		
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. <i><u>Have you wished you were dead or wished you could go to sleep and not wake up?</u></i>		
2) Suicidal Thoughts: General non-specific thoughts of wanting to end one's life/die by suicide, "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></i>		
If YES to 2, ask questions 3, 4, 5, and 6. If NO to 2, go directly to question 6		
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 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></i>		
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 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></i>		
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. <i><u>Have you started to work out or worked out the details of how to kill yourself and do you intend to carry out this plan?</u></i>		
6) Suicide Behavior <i><u>Have you done anything, started to do anything, or prepared to do anything to end your life?</u></i> 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.		

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COLUMBIA-SUICIDE SEVERITY RATING SCALE
Primary Care Screen with Triage Points

SUICIDE IDEATION DEFINITIONS AND PROMPTS:	Past month	
	YES	NO
Ask questions that are in bold and underlined.		
Ask Questions 1 and 2		
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>		
2) Suicidal Thoughts: General non-specific thoughts of wanting to end one's life/die by suicide, "I've thought about killing myself" without general thoughts of ways to kill oneself/associated methods, intent, or plan." <u>Have you had any actual thoughts of killing yourself?</u>		
If YES to 2, ask questions 3, 4, 5, and 6. If NO to 2, go directly to question 6.		
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 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." <u>Have you been thinking about how you might do this?</u>		
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 oppose to "I have the thoughts but I definitely will not do anything about them." <u>Have you had these thoughts and had some intention of acting on them?</u>		
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>		
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>Was this within the past 3 months?</u>		Lifetime
		Past 3 Months

Response Protocol to C-SSRS Screening (Linked to last item marked "YES")

Item 1 Behavioral Health Referral
Item 2 Behavioral Health Referral
Item 3 Behavioral Health Consult (Psychiatric Nurse/Social Worker) and consider Patient Safety Precautions
Item 4 Behavioral Health Consultation and Patient Safety Precautions
Item 5 Behavioral Health Consultation and Patient Safety Precautions
Item 6 Behavioral Health Consult (Psychiatric Nurse/Social Worker) and consider Patient Safety Precautions
Item 6 3 months ago or less: Behavioral Health Consultation and Patient Safety Precautions

Appendix D: Pearls of Treatment

Shared Decision Making:

- Provide education on diagnosis
- Review treatment options (based on PHQ-9 score)
- Discuss treatment barriers: family/work responsibilities, insurance, transportation
- Discuss treatment plan
- Set timeline: response, side effects and treatment duration
- Educate on importance of adherence
- Develop safety plan for suicidal ideation
- See *Appendix G* for shared decision-making tool

Promote Healthy Behaviors

- Exercise
- Social support
- Faith/spiritual support
- Healthy sleep pattern
- Healthy diet
- Alcohol only in moderation
- Cessation of tobacco and illicit drug use
- Engagement in positive activities
- Stress management
- Educational books and online resources

Additional Considerations

- Current or planned pregnancy: psychotherapy preferred if symptoms tolerable
- Start with lower dose for panic/anxiety or the elderly
- Level of functioning/activities of daily living
- Psychiatry consultation, including ECT, ketamine or rTMS evaluation
- Consider pharmacogenetic testing when appropriate (see *Appendix I* for more information)

Consider Prompt Referral or Consult

- Suicidal or homicidal
- Bipolar disorder
- Substance abuse
- Psychotic features
- Cognitive impairment
- Multiple Meds

Appendix E: Crisis Resources

What to do if there is a crisis with a person or patient in the clinic?

For a concern that the patient/person might hurt others or themselves while in the clinic

- **Call 911**
- State your name and location and describe the situation, description of the patient, patient's address, etc. The dispatcher will guide you, so don't worry if you can't remember every detail. *The important thing is to remember to call 911.*

Crisis Text Line: A national 24/7 service; patients can utilize this service by texting 741741 or through a Facebook message. Find out more at www.crisistextline.org

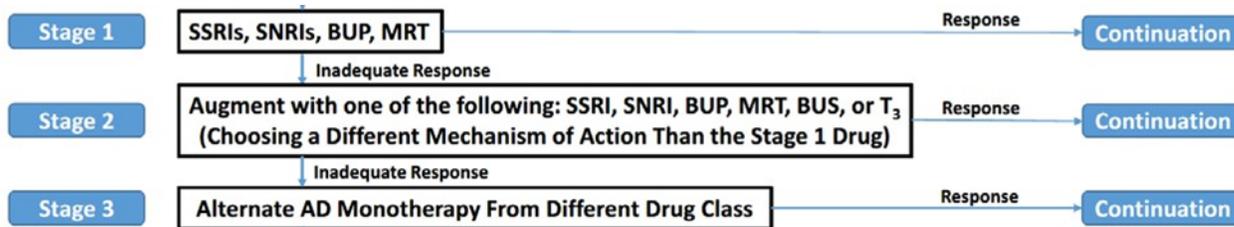
National Suicide Prevention Lifeline: A national 24/7 crisis line. Phone number is 1-800-273-TALK (8255). Find out more at www.suicidepreventionlifeline.org

CSSRS Training: Anyone can complete this training and become a screener. The training takes between 30-60 minutes. Find out more at <http://cssrs.columbia.edu/training/training-options/>

Appendix F: Pharmacological Therapy

There is insufficient evidence to recommend one antidepressant medication over another for all patients. Choosing an antidepressant agent depends on depressive symptoms, side effect profile, personal or family response history, drug interactions, comorbid medical conditions, and cost.

- SSRIs, SNRIs, bupropion, or mirtazapine are generally regarded as the first-line treatment for depression
- Augment with one of the following: SSRI, SNRI, mirtazapine, buspirone, or T₃ (choosing a different mechanism of action than the Stage 1 drug)
- If the augmentation strategy is ineffective, the patient should be placed on an antidepressant from a different antidepressant class than what was initiated in the inaugural trial while maintaining the augmentation strategy or referred to Psychiatry for evaluation
- Refer to psychiatry for more complex augmentation strategies (e.g., anticonvulsants, antipsychotics, lithium)



- Patients who do not respond to Stage 3 interventions should be referred to the Treatment-Resistant Depression Clinic in Temple for evaluation and consideration of either transcranial magnetic stimulation (TMS) or Esketamine (Spravato).
- See Appendix G for a list of antidepressants and the most common considerations to assist in tailoring treatment and Appendix H for medication cost analysis. Costs are based on the average claims paid for the drugs across all BSWQA contracts (Scott & White Health Plan, United Health Care, Cigna, Aetna, Humana Medicare Advantage, and Scott & White Medicare Advantage). The date range is February 2019 to January 2020. There were no claims for some drugs, which is noted as “no claims” in the table.

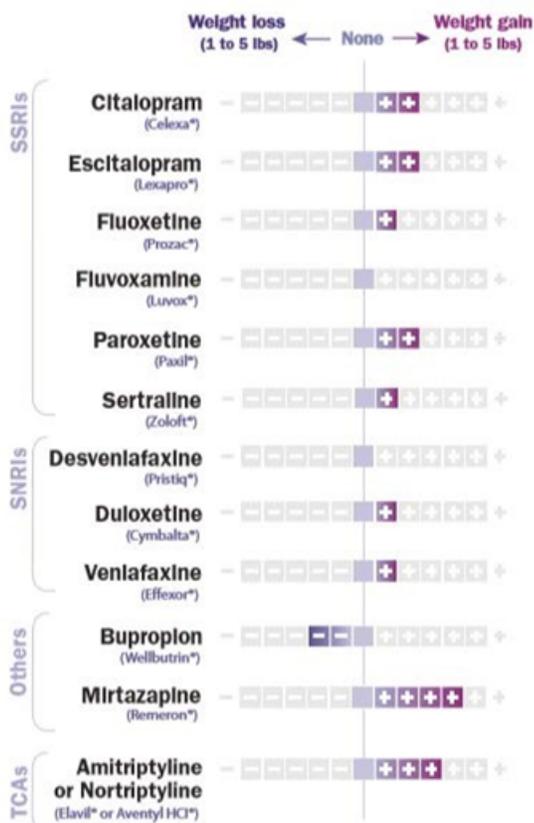
If safety and efficacy are equivalent, the more cost-effective option is preferred.

Appendix G: Shared Decision-Making Aid

Shared decision making can be used to tailor treatment to the individual patient. Mayo Clinic has developed a Shared Decision-Making Depression Medication Choice Decision Aid. It contains considerations for the most common antidepressants including: weight changes, sexual issues, sleep, cost, stopping approach, and things to keep in mind. Below is an example of the aid:

Weight Change

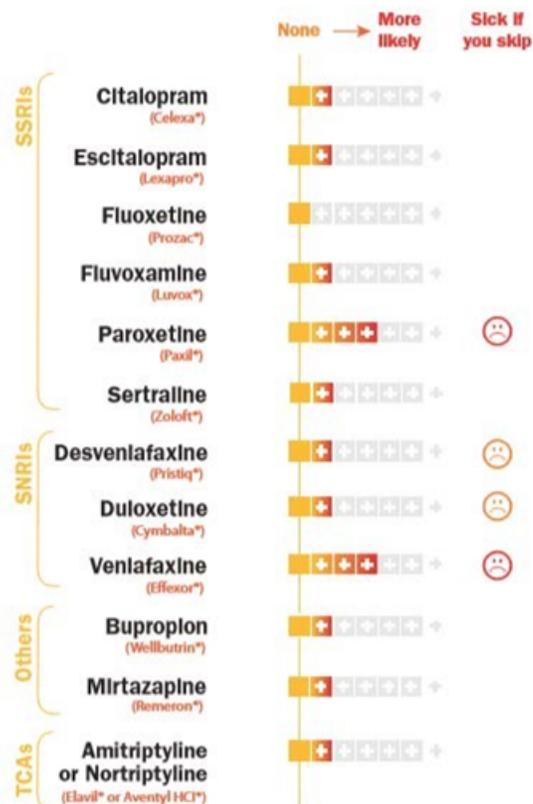
Some people may experience weight change. It is most likely to occur over six to twelve months and depends on your actual weight. The chart below is based on a 150 lb person.



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Stopping Approach

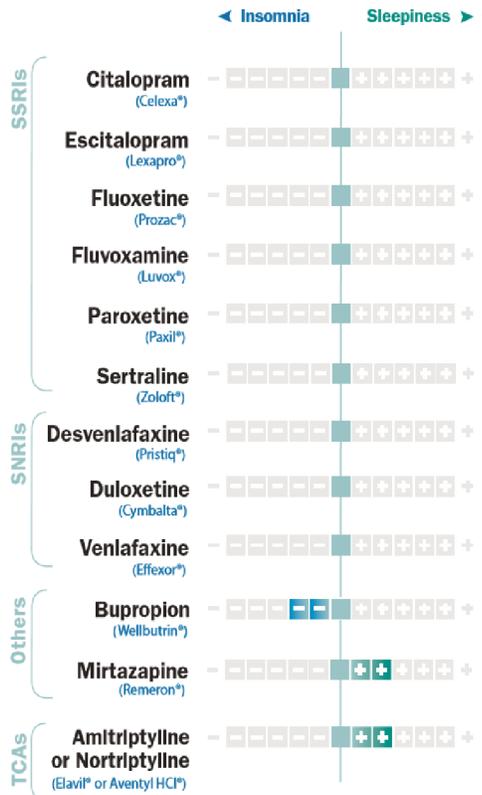
Quitting your medicine all at once can make you feel sick, as if you had the flu (e.g. headache, dizziness, light-headedness, nausea or anxiety).



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Sleep

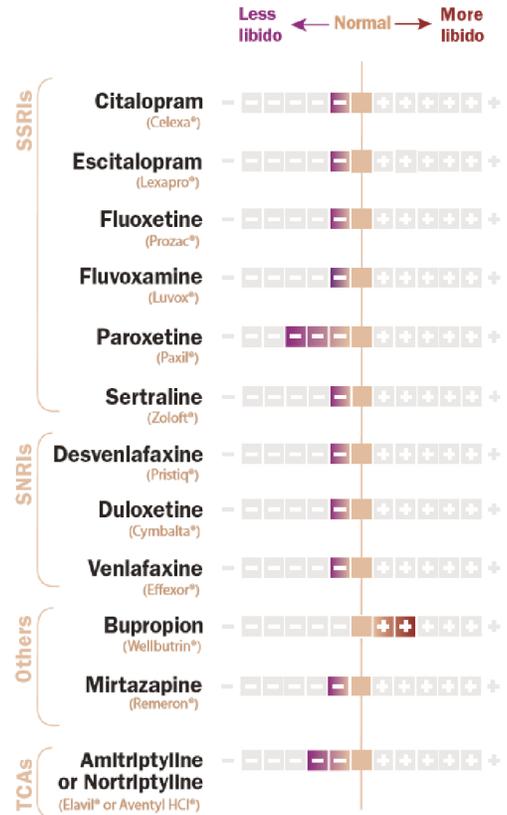
Some people may experience sleepiness or insomnia because of their antidepressant.



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Sexual Issues

Some people may experience loss of sexual desire (libido) or loss of ability to reach orgasm because of their antidepressant.



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This aid is available in English and Spanish as a take-home brochure. To access the aids, please go to this link: <http://shareddecisions.mayoclinic.org/decision-aid-information/decision-aids-for-chronic-disease/depressionmedication-choice/>

Appendix H: Serious Side Effects of Antidepressants

Classification	Specific Medication	Side Effects
SSRI	<ul style="list-style-type: none"> • Citalopram • Escitalopram 	Prolonged QTc
SSRI	<ul style="list-style-type: none"> • Fluoxetine • Paroxetine • Fluvoxamine 	Drug to drug interactions
SSRI/SNRI/TCA	ALL	Bleeding SIADH Serotonin syndrome
SNRI	<ul style="list-style-type: none"> • Venlafaxine 	HTN
SNRI	<ul style="list-style-type: none"> • Duloxetine 	Hepatotoxicity
TCA	ALL	Delirium Sedation Orthostatic hypotension Lethal in overdose due to cardiac conduction abnormalities
	<ul style="list-style-type: none"> • Bupropion 	Seizure
	<ul style="list-style-type: none"> • Mirtazapine 	Sedation Increased appetite
	<ul style="list-style-type: none"> • Trazodone 	Priapism

Appendix I: Antidepressant Cost Analysis

Drug Class	Generic Name	Brand Name		Drug Class	Generic Name	Brand Name
Antidepressants, other	Bupropion \$	Wellbutrin \$\$\$\$\$\$ Forfivo \$\$\$\$		SSRI's	Citalopram \$	*
	Chlordiazepoxide- amitriptyline \$\$\$	*			Escitalopram \$	Lexapro \$\$\$\$
	Mirtazapine \$	*			Fluoxetine \$	*
	Nefazodone \$\$	*			Fluvoxamine \$\$	*
	Trazodone \$	*			Paroxetine \$	Paxil \$\$\$
	*	Trintellix \$\$\$\$			Sertraline \$	Zoloft \$\$\$\$
	*	Viibryd \$\$\$				
TCA's	Amitriptyline \$	*		SNRI's	Desvenlafaxine \$\$	Pristiq \$\$\$\$
	Desipramine \$\$	*			Duloxetine \$	Cymbalta \$\$\$
	Doxepin \$\$	Silenor \$\$\$\$			Venlafaxine \$	Effexor \$\$\$\$\$
	Imipramine \$	*			*	<u>Savella</u> \$\$\$\$
	Nortriptyline \$	*			*	Fetzima \$\$\$\$

<\$20 = \$
 \$21-\$100 = \$\$
 \$101-300 = \$\$\$
 \$301-\$500 = \$\$\$\$
 \$501-\$1000 = \$\$\$\$\$
 >\$1000 = \$\$\$\$\$\$

*No claims available



Antidepressant Discontinuation Syndrome

What is Discontinuation Syndrome?

Discontinuation Syndrome can happen if you suddenly stop taking an antidepressant medicine. It is not dangerous, but it can be uncomfortable and upsetting.

What are the signs of Discontinuation Syndrome?

The symptoms of Discontinuation Syndrome happen within 1 to 2 days after stopping or lowering the dose of an antidepressant medication.

You may feel:

- dizzy
- shaky
- sweaty
- irritable or agitated
- anxious or nervous

You may have:

- a headache
- nausea or vomiting
- flu-like symptoms
- trouble-sleeping, nightmares, or lots of dreams

Call your doctor for instructions if you have symptoms of Discontinuation Syndrome and you stopped taking or lowered the dose of an antidepressant medicine in the last few days.



Which medicines cause Discontinuation Syndrome?

Stopping any antidepressant medicine can cause Discontinuation Syndrome.

The most common antidepressants that can cause Discontinuation Syndrome are:

- venlafaxine (Effexor[®])
- duloxetine (Cymbalta[®])
- desvenlafaxine (Pristiq[®])
- paroxetine (Paxil[®])
- escitalopram (Lexapro[®])
- sertraline (Zoloft[®])
- citalopram (Celexa[®])

How is Discontinuation Syndrome treated?

You may need to restart the antidepressant medicine. Talk with your doctor about why you stopped taking the antidepressant. If you and your doctor decide you should stop the medicine, you may need to slowly take less medicine over time until you stop completely.

How can you protect yourself from dangerous reactions to medicines?

- Tell all your doctors and pharmacists about all the prescription and over-the-counter medicines, vitamins, and supplements you take.
- Talk to your doctor before stopping any medicine and make a plan to do it safely. If you have to stop a medicine for a short time, restart it as soon as possible.

The information provided herein is considered educational and should not be used during any medical emergency or for the diagnosis or treatment of any medical condition. A licensed medical professional should be consulted for diagnosis and treatment of any and all medical conditions. Call 911 for all medical emergencies.

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You may access this patient handout in English by following this link:

https://bswhealth.sharepoint.com/sites/BSWClinicalLearning/Patient%20Learning%20Materials/Medication%20Information/Antidepressant_Discontinuation_Syndrome_2018.pdf

Appendix J: Pharmacogenetic Testing in Antidepressant Therapy

Background

Pharmacogenomics, the study of how genes influence an individual's response to a drug, may help identify patients who are at an increased risk of nonresponse or experiencing adverse reactions to a medication.

Pharmacogenomic testing does not help identify which antidepressant will be effective. Genetic variation may alter pharmacokinetic and pharmacodynamic parameters of a medication, influencing the response to the medication. The testing may identify poor, normal/extensive, rapid and ultrarapid metabolizers - which translates into efficacy of a drug and its propensity to accumulate and cause side effects. Pharmacogenetic testing may be pre-emptive (prior to prescribing) or reactive (post-prescribing).

Clinical Pharmacogenetics Implementation Consortium (CPIC)* classifies gene–drug groupings into those that are likely actionable based on categories assigned by PharmGKB.** There are currently CPIC guidelines for 12 antidepressant gene drug pairs. The current CPIC guidelines, PharmGKB categorization and FDA labeling information is summarized below and is provided as an example of the current state of pharmacogenomic data for antidepressant therapy.

Table 1

Gene Biomarker	Drug	CPIC Guideline	FDA label categories by PharmGKB (see table 2 for definitions)
CYP2D6 CYP2C19	Amitriptyline Clomipramine Doxepin Imipramine Trimipramine	Clinical Pharmacogenetics Implementation Consortium guideline for <i>CYP2D6</i> and <i>CYP2C19</i> genotypes and dosing of tricyclic antidepressants	Actionable pharmacogenetics
CYP2D6	Desipramine Nortriptyline	Clinical Pharmacogenetics Implementation Consortium guideline for <i>CYP2D6</i> and <i>CYP2C19</i> genotypes and dosing of tricyclic antidepressants	Actionable pharmacogenetics
CYP2C19	Citalopram Escitalopram	Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for <i>CYP2D6</i> and <i>CYP2C19</i> genotypes and dosing of selective serotonin reuptake inhibitors.	Actionable pharmacogenetics
CYP2C19	Sertraline	Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for <i>CYP2D6</i> and <i>CYP2C19</i> genotypes and dosing of selective serotonin reuptake inhibitors.	Not Applicable - No Information
CYP2D6	Fluvoxamine Paroxetine	Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for <i>CYP2D6</i> and <i>CYP2C19</i> genotypes and dosing of selective serotonin reuptake inhibitors.	Actionable pharmacogenetics
CYP2D6	Paroxetine	Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for <i>CYP2D6</i> and <i>CYP2C19</i> genotypes and dosing of selective serotonin reuptake inhibitors.	Informative pharmacogenetics

Recommendation

Current literature supports use of pharmacogenetic testing in a reactive fashion for antidepressant therapy. Routine Pre-emptive (prior to prescribing) pharmacogenetic testing is not recommended at this time.

Genetic testing is not currently recommended or required in the FDA approved drug label of any antidepressant medication. Several antidepressant medications do have informative or actionable pharmacogenetic information in the product labeling.

Consider pharmacogenetic testing of antidepressant therapy for patients with at least one of the following conditions:

- Patients who have had two – three trials of antidepressants with little or no success.
- Patients who experience unusual or excessive side effects.
- Patients who have history of extreme sensitivity to medications.

Additional Information

*Clinical Pharmacogenetics Implementation Consortium (CPIC) is an international group of individuals from government, academia, and industry that provide peer-reviewed freely available evidence-based clinical practice guidelines to assist in the implementation of pharmacogenetics into clinical practice.

**PharmGKB is an NIH-funded resource that provides information about how human genetic variation affects response to medications. PharmGKB collects, curates and disseminates knowledge about clinically actionable gene-drug associations and genotype-phenotype relationships.

Table 2 FDA label categories by PharmGKB

Level	Definition
Testing Required	The label states or implies that some sort of gene, protein or chromosomal testing, including genetic testing, functional protein assays, cytogenetic studies, etc., should be conducted before using this drug. This requirement may only be for a particular subset of patients. PharmGKB considers labels that state the variant is an indication for the drug, as implying a test requirement. If the label states a test "should be" performed, this is also interpreted as a requirement
Testing Recommended	The label states or implies that some sort of gene, protein or chromosomal testing, including genetic testing, functional protein assays, cytogenetic studies, etc., is recommended before using this drug. This recommendation may only be for a particular subset of patients. PharmGKB considers labels that say testing "should be considered" to be recommending testing.
Actionable pharmacogenetics	The label does not discuss genetic or other testing for gene/protein/chromosomal variants, but does contain information about changes in efficacy, dosage or toxicity due to such variants. The label may mention contraindication of the drug in a particular subset of patients but does not require or recommend gene, protein or chromosomal testing
Informative pharmacogenetics	The label mentions a gene or protein is involved in the metabolism or pharmacodynamics of the drug, but there is no information to suggest that variation in these genes/proteins leads to different response.

Guideline and FDA labeling information is regularly updated and may be found at:

<https://cpicpgx.org/guidelines/>

<https://www.fda.gov/Drugs/ScienceResearch/ucm572698.htm> and

<https://www.pharmgkb.org/page/drugLabelLegend>

Guideline Developers: BSWH NTX Behavioral Health Advisory Council and BSWQA Primary Care Subcommittee

Approved By: BSWQA Primary Care Subcommittee, BSWQA Quality Committee, and BSWQA Board of Managers

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