Introduction to VA/DoD Clinical Practice Guideline for the Management of Bipolar Disorder

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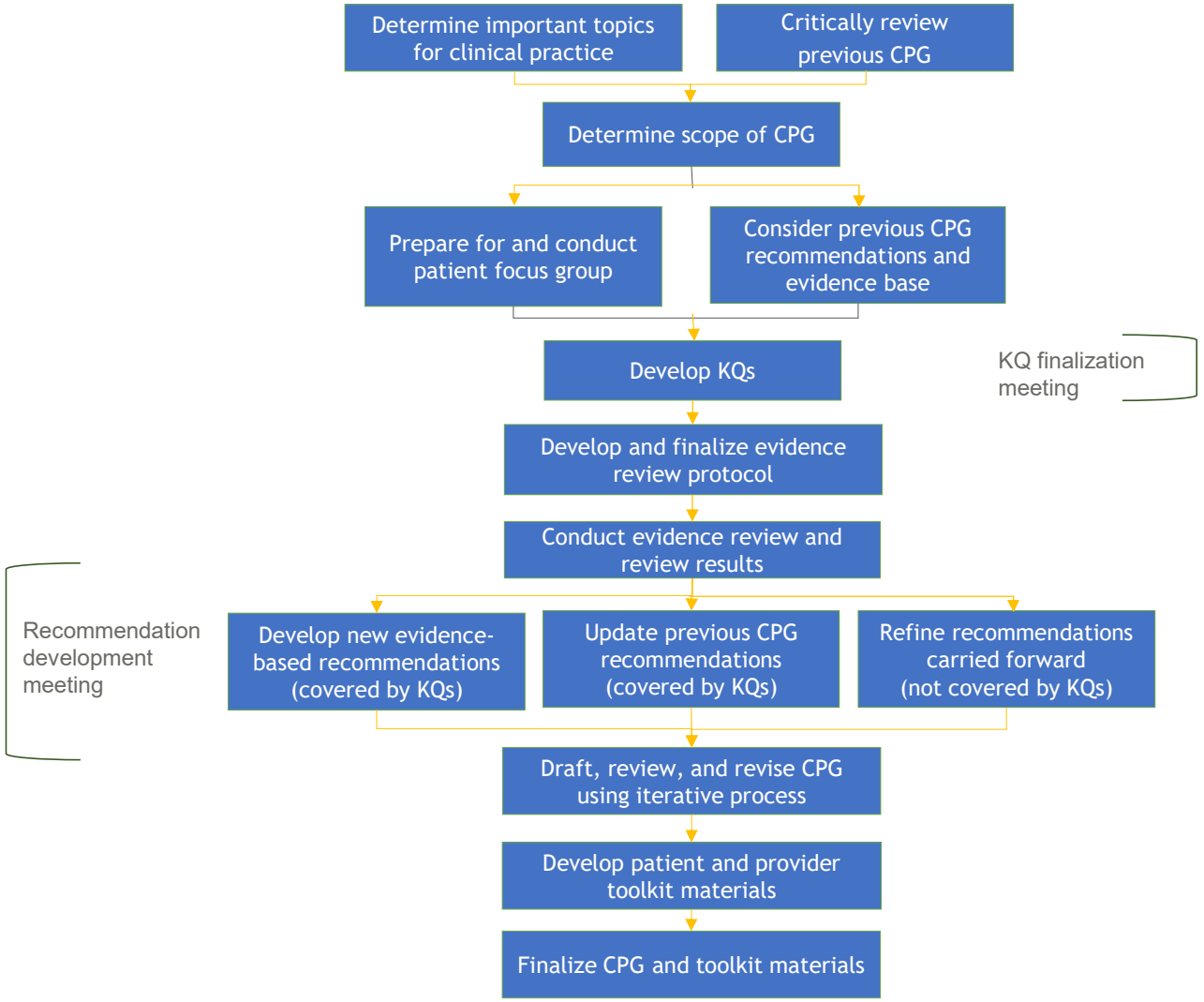
Overview of CPG Development Process



Grading Recommendations - GRADE

- Evidence-based clinical practice recommendations were developed based on the:
  - Evidence review, which was informed by 12 key questions
  - GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodology and use of four decision domains to determine strength (*Strong* or *Weak*) and direction (*For* or *Against)* of each recommendation:
    - Confidence in the quality of evidence
    - Balance of desirable and undesirable outcomes
    - Values and preferences
    - Other implications, as appropriate (e.g., resource use)

Strength of a Recommendation

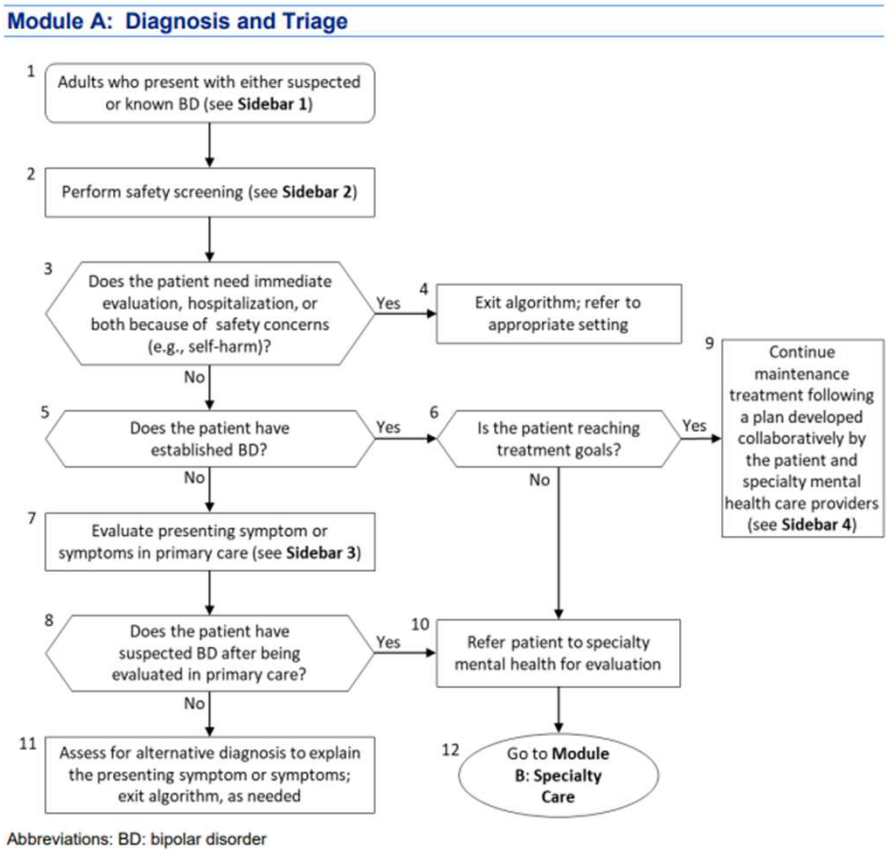
- Strength of a recommendation on a continuum:
  - ***Strong for*** (or "*We recommend*…")
  - ***Weak for*** (or "*We suggest*…")
  - ***Neither for nor against*** (or "*There is insufficient evidence*…")
  - ***Weak against*** (or "*We suggest against*…")
  - ***Strong against*** (or "*We recommend against*…")

Background and Statistics

- Bipolar disorder (BD) is a serious mental health concern affecting more than 40 million people worldwide
- Lifetime prevalence for BD is around 1% in United States with varying rates
- Globally, rates range as high as 2.4%
- While relatively uncommon compared to major depressive disorder, BD has a sizable impact on measures of disability and years lost to disability
- Patients with a Bipolar Disorder may have a myriad of presentations.
  - Major depressive episodes
  - Manic episodes
  - Hypomanic episodes
  - Or combination of manic and depressive symptoms (mixed episode)
- This CPG is intended for patients currently displaying a manic, hypomanic, mixed episode, or acute bipolar depression

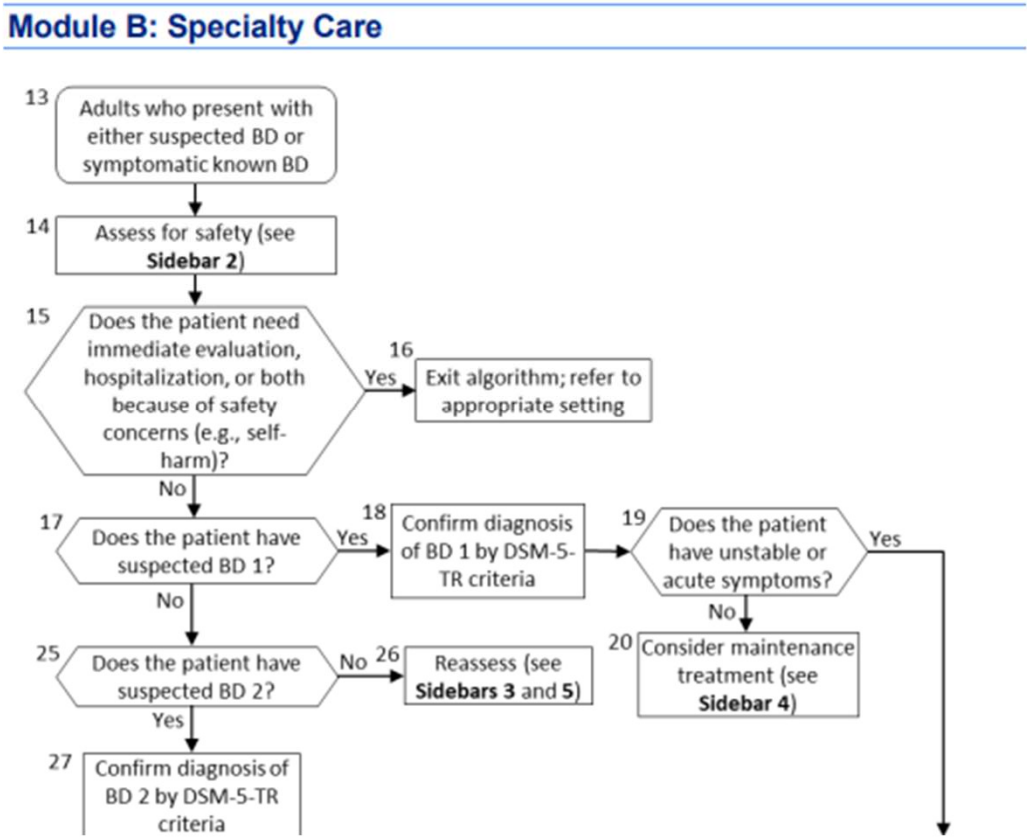
Diagnosis

- When there is suspicion for bipolar disorder:
  - Screen the patient with a validated instrument
    - Bipolar Spectrum Diagnostic Scale
    - Hypomania Checklist
    - Mood Disorder Questionnaire
  - Screen when starting an antidepressant
- Refer to specialty care if positive
- DSM-5-TR is the standard for full diagnostic assessment



Diagnosis

- In specialty care the diagnosis is confirmed
  - Screening tools to suspect BD
  - BP 1 vs BD 2
  - Confirm diagnosis
- DSM-5-TR is the standard for full diagnostic assessment
- Diagnosis is essential for established the correct acute and maintenance treatment



Poll Question: Treatment considerations

When there is suspicion of bipolar disorder, the VA/DoD CPG for the Management of Bipolar Disorder suggests using a validated instrument (e.g., Bipolar Spectrum Diagnostic Scale, Hypomania Checklist, Mood Disorder Questionnaire) to support decision making about the diagnosis.

A. True
B. False

Pharmacologic Therapies in Bipolar Disorder

- **Basic Principle:** Bipolar disorder is a **lifelong disorder** that requires maintenance treatment and the **choice of acute treatments should be informed** by need for maintenance treatment.
- The Work Group first examined the evidence for the effectiveness of medications used in the **maintenance phase of treatment**, considering prevention of mania and of bipolar depression as separate outcomes.
- After identifying those that were effective for maintenance, the Work Group examined the evidence for **treatment of acute phases**.
- The Work Group then structured the recommendations for monotherapies for the acute treatment phases to recognize those medications that demonstrated **efficacy for both the acute and maintenance phases**.

Pharmacologic Therapies – Acute Mania

	Recommendation	Strength
5.	We suggest **lithium** or **quetiapine** as **monotherapy** for acute mania.	Weak for
6.	If lithium or quetiapine is not selected based on patient preference and characteristics, we suggest **olanzapine**, **paliperidone**, or **risperidone** as **monotherapy** for acute mania.	Weak for
7.	If lithium, quetiapine, olanzapine, paliperidone, or risperidone is not selected based on patient preference and characteristics, we suggest **aripiprazole**, **asenapine**, **carbamazepine**, **cariprazine**, **haloperidol**, **valproate**, or **ziprasidone** as **monotherapy** for acute mania.	Weak for

Pharmacologic Therapies – Acute Mania

	Recommendation	Strength
8.	We suggest **lithium or valproate in combination with haloperidol, asenapine, quetiapine, olanzapine, or risperidone** for acute mania symptoms in individuals who had an **unsatisfactory response or a breakthrough episode on monotherapy**.	Weak for

Pharmacologic Therapies – Acute Mania

	Recommendation	Strength
9.	We suggest *against* **brexpiprazole, topiramate, or lamotrigine** as a monotherapy for acute mania.	Weak against
10.	We suggest *against* the addition of **aripiprazole, paliperidone, or ziprasidone after unsatisfactory response to lithium or valproate monotherapy** for acute mania.	Weak against
11.	There is *insufficient evidence* to recommend for or against other **first-generation antipsychotics or second-generation antipsychotics, gabapentin, oxcarbazepine, or benzodiazepines** as monotherapy or in combination for acute mania	Neither for nor against

Pharmacologic Therapies – Acute Bipolar Depression

	Recommendation	Strength
12.	We recommend **quetiapine as monotherapy** for acute bipolar depression.	Strong for
13.	If quetiapine is not selected based on patient preference and characteristics, we suggest **cariprazine, lumateperone, lurasidone, or olanzapine as monotherapy** for acute bipolar depression.	Weak for
15.	We suggest **lamotrigine in combination with lithium or quetiapine** for acute bipolar depression.	Weak for

Pharmacologic Therapies – Acute Bipolar Depression

	Recommendation	Strength
14.	There is *insufficient evidence to recommend for or against* **antidepressants or lamotrigine as monotherapy** for acute bipolar depression	Neither for nor against
16.	There is *insufficient evidence to recommend for or against* **ketamine or esketamine as either a monotherapy or an adjunctive therapy** for acute bipolar depression	Neither for nor against
17.	There is *insufficient evidence to recommend for or against* **antidepressants to augment treatment with second-generation antipsychotics or mood stabilizers** for acute bipolar depression	Neither for nor against

Pharmacologic Therapies – Prevention of Recurrence of Mania

	Recommendation	Strength
18.	We recommend **lithium or quetiapine** for the prevention of recurrence of mania.	Strong for
19.	If lithium or quetiapine is not selected based on patient preference and characteristics, we suggest **oral olanzapine, oral paliperidone, or risperidone long-acting injectable** for the prevention of recurrence of mania.	Weak for
22.	We suggest aripiprazole, olanzapine, quetiapine, or ziprasidone in combination with lithium or valproate for the prevention of recurrence of mania.	Weak for

Pharmacologic Therapies – Prevention of Recurrence of Mania

	Recommendation	Strength
20.	There is *insufficient evidence to recommend for or against* **other first-generation antipsychotics, second-generation antipsychotics, and anticonvulsants (including valproate)** for the prevention of recurrence of mania. (See Recommendations 18, 19, and 30).	Neither for nor against
21.	We suggest *against* **lamotrigine as monotherapy** for the prevention of recurrence of mania.	Weak against

Pharmacologic Therapies – Prevention of Recurrence of Bipolar Depression

	Recommendation	Strength
23.	We recommend **lamotrigine** for the prevention of recurrence of bipolar depressive episodes.	Strong for
24.	We suggest **lithium or quetiapine as monotherapy** for the prevention of recurrence of bipolar depressive episodes.	Weak for
25.	If lithium or quetiapine is not selected based on patient preference and characteristics, we suggest **olanzapine as monotherapy** for the prevention of recurrence of bipolar depressive episodes.	Weak for
26.	We suggest **olanzapine, lurasidone, or quetiapine in combination with lithium or valproate** for the prevention of recurrence of bipolar depressive episodes.	Weak for

Pharmacologic Therapies – Prevention of Recurrence of Bipolar Depression

	Recommendation	Strength
27.	There is *insufficient evidence to recommend for or against* **other first-generation antipsychotics, other second-generation antipsychotics, and anticonvulsants (including valproate) as monotherapies** for the prevention of recurrence of bipolar depressive episodes.	Neither for nor against
28.	There is *insufficient evidence to recommend for or against* **other first-generation antipsychotics, other second-generation antipsychotics, and anticonvulsants in combination with a mood stabilizer** for the prevention of recurrence of bipolar depressive episodes.	Neither for nor against

Pharmacologic Therapies – Pregnancy/Childbearing Potential

	Recommendation	Strength
29.	For *individuals with bipolar disorder who are or might become pregnant* and are **stabilized on lithium**, we suggest **continued treatment with lithium at the lowest effective dose** in a framework that includes psychoeducation and shared decision making.	Weak for
30.	We recommend *against* **valproate, carbamazepine, or topiramate** in the treatment of bipolar disorder in *individuals of child-bearing potential*	Strong against

Other Somatic Therapies

	Recommendation	Strength
31.	For individuals with *bipolar 1 disorder with acute severe manic symptoms*, we suggest **electroconvulsive therapy in combination with pharmacotherapy** when there is a need for rapid control of symptoms.	Weak for
32.	In individuals with bipolar 1 or bipolar 2 disorder, we suggest offering **short-term light therapy as augmentation to pharmacotherapy** for treatment of bipolar depression.	Weak for
33.	For individuals with bipolar disorder who have demonstrated *partial or no response to pharmacologic treatment for depressive symptoms*, we suggest offering **repetitive transcranial magnetic stimulation** as an adjunctive treatment.	Weak for

Non-Pharmacologic Therapies

	Recommendation	Strength
	Psychosocial and Recovery-Oriented Therapy	
34.	For individuals with bipolar 1 or bipolar 2 disorder who are not acutely manic, we suggest offering psychotherapy as an adjunct to pharmacotherapy, including **cognitive behavioral therapy, family or conjoint therapy, interpersonal and social rhythm therapy, and non-brief psychoeducation** (not ranked).	Weak for
35.	For individuals with bipolar 1 or bipolar 2 disorder, there is insufficient evidence to recommend for or against **any one specific psychotherapy** among cognitive behavioral therapy, family or conjoint therapy, interpersonal and social rhythm therapy, and non-brief psychoeducation.	Neither for nor against

Non-Pharmacologic Therapies Continued

	Recommendation	Strength
	Psychosocial and Recovery-Oriented Therapy	
36.	For individuals with bipolar 2 disorder, there is insufficient evidence to recommend for or against **meditation** as an adjunct to other effective treatments for depressive episodes or symptoms.	Neither for nor against
37.	In individuals with bipolar disorder, there is insufficient evidence to recommend for or against augmenting with **nutritional supplements**, including nutraceuticals, probiotics, and vitamins, for reduction of depressive or manic symptoms.	Neither for nor against
38.	For individuals with bipolar disorder, there is insufficient evidence to recommend for or against **any particular phone application or computer- or web-based intervention**.	Neither for nor against

Non-Pharmacologic Therapies Continued

	Recommendation	Strength
	Supportive Care/Models of Care	
39.	There is insufficient evidence to recommend **any specific supported housing intervention** over another for individuals with bipolar disorder experiencing housing insecurity.	Neither for nor against
40.	For individuals with bipolar disorder who require vocational or educational support, we suggest **Individual Placement and Support or Individual Placement and Support Enhanced**.	Weak for
41.	For individuals with bipolar disorder, we suggest **caregiver support programs** to improve mental health outcomes.	Weak for
42.	For individuals with bipolar disorder, we suggest that clinical management should be based on the **collaborative care model**.	Weak for

Non-Pharmacologic Therapies Continued

	Recommendation	Strength
	Co-Occurring Conditions	
43.	For individuals with bipolar 1 or bipolar 2 disorder and tobacco use disorder, we suggest offering **varenicline** for tobacco cessation, with monitoring for increased depression and suicidal behavior.	Weak for
44.	For individuals with bipolar 1 or bipolar 2 disorder and co-occurring substance use disorder, there is insufficient evidence to recommend for or against any specific pharmacotherapy or psychotherapy intervention. See **VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorder**.	Neither for nor against
45.	For individuals with fully or partially remitted bipolar disorder and with residual anxiety symptoms, we suggest **cognitive behavioral therapy**.	Weak for

Hypothetical Case Study (Page 1 of 2)

- XX is a 25-year-old man who comes to the VA for the first time three years after separating from the military.
  - He first experienced depression two years ago.
  - He has had several entry-level jobs, but lost them due to erratic performance marked by periods of intense effort followed by absenteeism.
  - Moved back in with his parents after experiencing conflict with his roommates and finding himself unable to pay rent based on frequent job losses.

Hypothetical Case Study (Page 2 of 2)

- He had briefly been prescribed sertraline for depression by a community psychiatrist, but missed several appointments and decided to stop the medication once his mood improved.
- Currently, he spends significant time isolating in his parents' house, but has periods where he feels "right as rain" marked by increased social activity and reckless spending on retail websites.
- He smokes marijuana to help "calm himself down" but does not drink alcohol or use other drugs.
- His isolation, marijuana use, and overspending have contributed to significant conflict with his parents, who have encouraged him to seek care within VA.

- What should be considered in planning his treatment?

Poll Question: Treatment considerations

Which **pharmacotherapy** as monotherapy should be initiated for this patient?

A. cariprazine
B. quetiapine
C. lumateperone
D. lamotrigine
E. lithium

Poll Question: Treatment considerations

Which **nonpharmacologic** recommendations could be suggested for this patient?

A. Psychotherapy as an adjunct to pharmacotherapy
B. Caregiver support programs
C. Individual Placement Support or Individual Placement Support Enhanced
D. All the above

Poll Question: Treatment considerations

If you were to offer this Veteran psychotherapy, which would you offer first?

A. Cognitive Behavioral Therapy (CBT)
B. Family or Conjoint Therapy
C. Interpersonal and Social Rhythm Therapy (IPSRT)
D. Psychoeducation of 6+ sessions

Resources

Category	Questions or Mental Health Need	Mental Health Reference Materials and Websites to Learn More
Education	Do I need help?	Determine how BD symptoms impact daily living https://www.nimh.nih.gov/health/publications/my-mental-health-do-i-need-help?utm_campaign=shareNIMH&utm_medium=Portal&utm_source=NIMHwebsite
	Diagnosis and Treatment Can Help	Overview of BD: diagnosis, symptoms, risk factors, and treatments https://www.nimh.nih.gov/health/topics/bipolar-disorder?utm_campaign=shareNIMH&utm_medium=Portal&utm_source=NIMHwebsite
	Coping with BD	Help yourself manage BD and provide information for family and friends https://www.nami.org/About-Mental-Illness/Mental-Health-Conditions/Bipolar-Disorder/Support
	Veterans Seeking Help with BD: Overview and Treatments	Information about BD and seeking care at VA https://www.mentalhealth.va.gov/mentalhealth/bipolar/index.asp
	VA VISN 5 MIRECC	Mission is to maximize the recovery and community functioning of Veterans with SMIs https://www.mirecc.va.gov/visn5/
	VA VISN 22 MIRECC	Improve the long-term functional outcome of Veterans with psychotic mental disorders https://www.mirecc.va.gov/visn22/

Resources

Category	Questions or Mental Health Need	Mental Health Reference Materials and Websites to Learn More
Support Groups and Online Help	Online Support Groups for BD	Help locate an online support group https://www.dbsalliance.org/support/chapters-and-support-groups/online-support-groups/ https://www.dbsalliance.org/support/chapters-and-support-groups/find-a-support-group/
	Parent Support Community	Online support community for parents and caregivers of those with BD https://community.dbsalliance.org/
	Ask a Doc about BD	Ask a mental health provider your questions online https://www.dbsalliance.org/education/ask-the-doc/?filter=bipolar-disorder
	Free, Online Problem-Solving Therapy	Online treatment to help with problem solving https://www.veterantraining.va.gov/movingforward/
Hotline	Military/Veteran Crisis Line	Acute care for Veterans, Service members, and civilians Veterans' Crisis Line (988 or 1-800-273-8255, option 1; text 838255; online chat: https://www.veteranscrisisline.net/get-help-now/chat/) National Suicide Prevention Lifeline (988 or 1-800-273-8255) https://mhanational.org/crisisresources

http://www.healthquality.va.gov

Audience Q&A