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Psychiatry and Addictions Case Conference

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INITIAL TREATMENT FOR MAJOR DEPRESSIVE DISORDER

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SPEAKER DISCLOSURES

- ✓ No conflicts of interest

OBJECTIVES

1. Review the diagnosis of Major Depressive Episodes.
2. Identify initial treatments for Major Depressive Episodes.
3. Discuss when you would not prescribe antidepressants.
4. Highlight essential prescribing practices for antidepressants for people with MDD.

DSM-5 MAJOR DEPRESSIVE EPISODE

- A. 5 (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least 1 of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.
- Depressed mood most of the day, nearly every day, as indicated by either subjective report (eg, feels sad, empty, hopeless) or observations made by others (eg, appears tearful). (NOTE: In children and adolescents, can be irritable mood.)
 - Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation).
 - Significant weight loss when not dieting or weight gain (eg, a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. (NOTE: In children, consider failure to make expected weight gain.)
 - Insomnia or hypersomnia nearly every day.
 - Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
 - Fatigue or loss of energy nearly every day.
 - Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
 - Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by their subjective account or as observed by others).
 - Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.
- B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- C. The episode is not attributable to the direct physiological effects of a substance or to another medical condition.

OTHER CAUSES OF DEPRESSIVE SYMPTOMS

- Persistent depressive disorder
- Premenstrual dysphoric disorder
- Substance induced depressive disorder
- PTSD
- Seasonal Affective Disorder
- Depressive disorder due to a medical condition (ex: sleep apnea, thyroid, anemia, hormonal changes, dementia)
- Adjustment disorder
- Bipolar Disorder
 - ***The majority of presentations of bipolar disorder to primary care are depressive phase!***
 - ***Need to rule out bipolar disorder as most antidepressants do not work for BPD or make it worse, trigger hypo/mania***

WHAT IS THE PREVALENCE OF MAJOR DEPRESSION EPISODE IN US?

2020

- Major depression episode
 - 21.0 million adults
 - 8.4%
- Major depression episode with impairment
 - 14.8 million adults
 - 6.0%

<https://www.nimh.nih.gov/health/statistics/major-depression>

DEPRESSION IN PRIMARY CARE?

- Epidemiology:
 - Primary care: 5% to 25% of patients with depressive sx's
 - 60% of people with depression don't get treatment
 - *if they do, up to 50% get treatment in primary care!*

SCREENING

- USPSTF, AAFP: universal, if adequate mgmt and follow up in place
- Screening tools:
 - Depression: PHQ-2 vs PHQ9
 - Substances: AUDIT C and DAST-10
 - Perinatal: Edinburgh Postnatal Depression Scale or PHQ-9 in pregnant/postpartum people
 - Bipolar Disorder: CIDI to rule out bipolar disorder (MDQ less specific)
 - Labwork: TSH, CBC, B12, Vit D, folate, BMP
 - Sleep apnea: STOP-BANG, sleep study
- ***Suicide risk screening***: PHQ-9, VA Algorithm, Columbia (CSSRS), SAFE-T card (<https://sprc.org/settings/primary-care/toolkit/>)
 - All Patient's Safe: Basic, Advanced, Firearm risk:
<https://www.apsafe.uw.edu/>

<https://www.healthquality.va.gov/guidelines/mh/srb/>

MAJOR DEPRESSION TREATMENTS

101

DO ANTIDEPRESSANTS WORK FOR: MAJOR DEPRESSIVE DISORDERS?

- Yes
- And...SNRIs and Mirtazapine work a little better
- And...there will be a range of responses (average 2-4 pt improvement on HAM-D)

Levkovitz Y, Tedeschi E, Papakostas GI. Efficacy of antidepressants for dysthymia: a meta-analysis of placebo-controlled randomized trials. *J Clin Psychiatry*. 2011 Apr;72(4):509-14. doi: 10.4088/JCP.09m05949blu. PMID: 21527126.

Thase, M.E. The Small Specific Effects of Antidepressants in Clinical Trials: What Do They Mean to Psychiatrists?. *Curr Psychiatry Rep* 13, 476–482 (2011). <https://doi-org.offcampus.lib.washington.edu/10.1007/s11920-011-0235-x>

DO ANTIDEPRESSANTS **ONLY** WORK FOR: SEVERE DEPRESSION?

- No
 - they work in mild to severe depression to the same degree

Cipriani A, Barbui C, Butler R, Hatcher S, Geddes J. Depression in adults: drug and physical treatments. *BMJ Clin Evid*. 2011 May 25;2011:1003. PMID: 21609510; PMCID: PMC3217759.

Gibbons RD, Hur K, Brown CH, Davis JM, Mann JJ. Benefits from antidepressants: synthesis of 6-week patient-level outcomes from double-blind placebo-controlled randomized trials of fluoxetine and venlafaxine. *Arch Gen Psychiatry*. 2012 Jun;69(6):572-9. doi: 10.1001/archgenpsychiatry.2011.2044. PMID: 22393205; PMCID: PMC3371295.

HOW **FAST** CAN ANTIDEPRESSANTS WORK?

- 1-2 weeks
- Change dose every 2-4 weeks

Taylor MJ, Freemantle N, Geddes JR, Bhagwagar Z. Early onset of selective serotonin reuptake inhibitor antidepressant action: systematic review and meta-analysis. Arch Gen Psychiatry. 2006 Nov;63(11):1217-23. doi: 10.1001/archpsyc.63.11.1217. PMID: 17088502; PMCID: PMC2211759.

HOW **LONG** SHOULD I WAIT BEFORE CHANGING MEDS?

- 6-12 weeks
 - Potentially sooner if no response

Rush AJ. STAR*D: what have we learned? Am J Psychiatry. 2007 Feb;164(2):201-4. doi: 10.1176/ajp.2007.164.2.201. PMID: 17267779.

Taylor MJ, Freemantle N, Geddes JR, Bhagwagar Z. Early onset of selective serotonin reuptake inhibitor antidepressant action: systematic review and meta-analysis. Arch Gen Psychiatry. 2006 Nov;63(11):1217-23. doi: 10.1001/archpsyc.63.11.1217. PMID: 17088502; PMCID: PMC2211759.

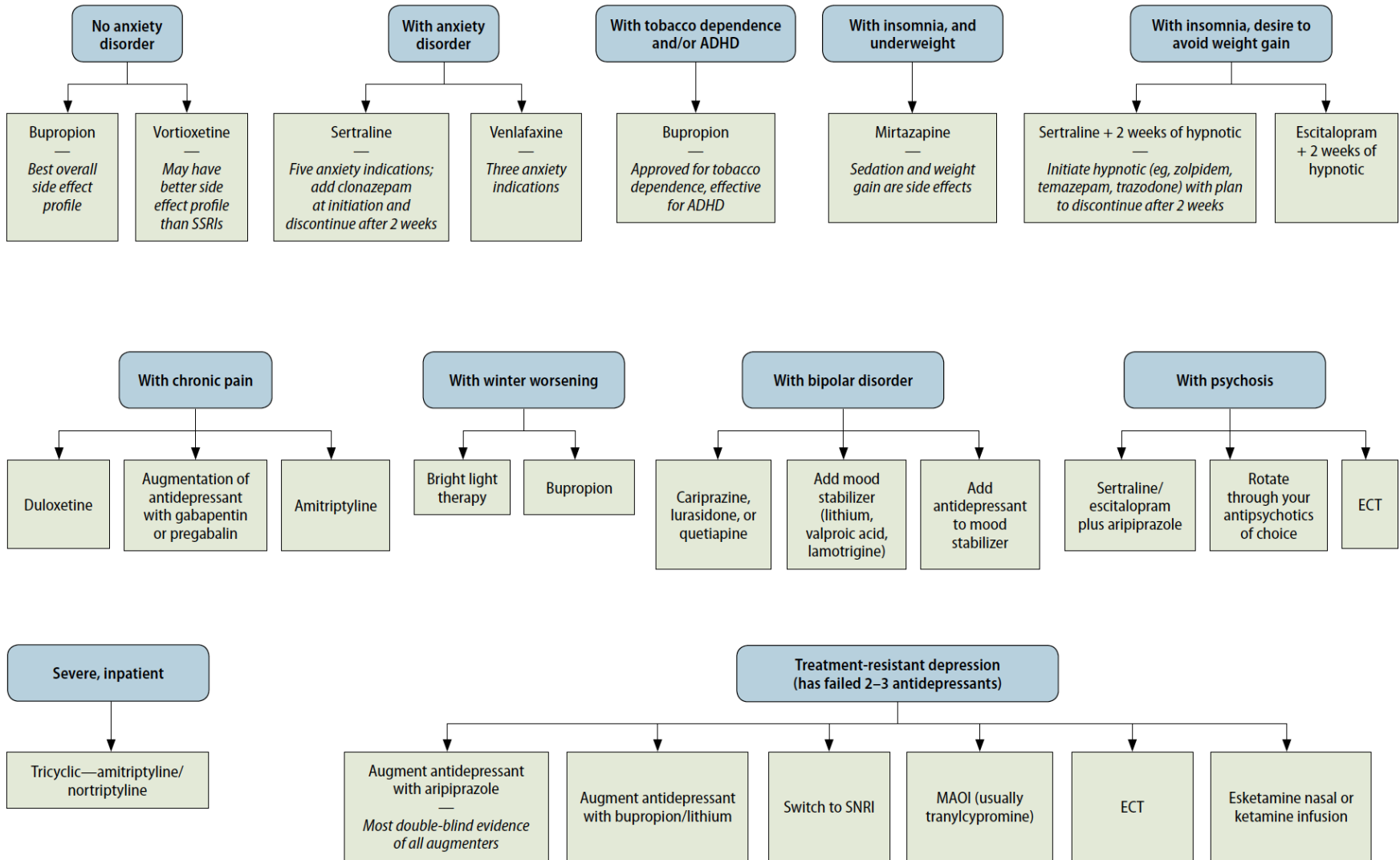
ARE THERE THINGS TO DO TO MAKE ANTIDEPRESSANTS WORK BETTER?

- See patients frequently at the beginning of treatment
- Continue to titrate as needed
- Provide education about the illness and treatments
- Build therapeutic alliance
 - Be curious
 - Validate
 - Listen

CHOOSING AN ANTIDEPRESSANT

- Anticipated side effects
- Pharmacologic properties (half-life, med interactions)
- Past response to med
- Family history of response
- Depressive symptoms
- Comorbid illnesses

TREATMENT ALGORITHM: Depression



DOES THERAPY WORK FOR: MAJOR DEPRESSIVE DISORDERS?

- Yes
- And results may persist after acute course of treatment ends

Taylor MJ, Freemantle N, Geddes JR, Bhagwagar Z. Early onset of selective serotonin reuptake inhibitor antidepressant action: systematic review and meta-analysis. Arch Gen Psychiatry. 2006 Nov;63(11):1217-23. doi: 10.1001/archpsyc.63.11.1217. PMID: 17088502; PMCID: PMC2211759.

Parikh SV, Segal ZV, Grigoriadis S, Ravindran AV, Kennedy SH, Lam RW, Patten SB; Canadian Network for Mood and Anxiety Treatments (CANMAT). 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 Disord. 2009 Oct;117 Suppl 1:S15-25. doi: 10.1016/j.jad.2009.06.042. Epub 2009 Aug 13. PMID: 19682749.

DOES THERAPY WORK ONLY FOR: SEVERE DEPRESSION?

- No, it can work for the range of severity

Farah WH, Alsawas M, Mainou M, Alahdab F, Farah MH, Ahmed AT, Mohamed EA, Almasri J, Gionfriddo MR, Castaneda-Guarderas A, Mohammed K, Wang Z, Asi N, Sawchuk CN, Williams MD, Prokop LJ, Murad MH, LeBlanc A. Non-pharmacological treatment of depression: a systematic review and evidence map. Evid Based Med. 2016 Dec;21(6):214-221. doi: 10.1136/ebmed-2016-110522. Epub 2016 Nov 11. PMID: 27836921.

IS COMBINATION MEDS AND THERAPY THE BEST?

- Yes (but the effect size is small)

Parikh SV, Segal ZV, Grigoriadis S, Ravindran AV, Kennedy SH, Lam RW, Patten SB; Canadian Network for Mood and Anxiety Treatments (CANMAT). 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 Disord. 2009 Oct;117 Suppl 1:S15-25. doi: 10.1016/j.jad.2009.06.042. Epub 2009 Aug 13. PMID: 19682749.

THERAPY FOR MAJOR DEPRESSIVE EPISODES

- Also behavioral activation, problem solving therapy

SIDEBAR 3

EMPIRICALLY SUPPORTED TREATMENT RECOMMENDATIONS

- **Recommend** behavioral therapy, cognitive therapy, cognitive-behavioral therapy (CBT), interpersonal psychotherapy (IPT), mindfulness-based cognitive therapy, psychodynamic therapy, or supportive therapy.
- **Recommend** second-generation antidepressant medications (ADMs).
- If considering combined treatment, **recommend** CBT or IPT plus a second-generation ADM.

To view the full set of recommendations, including conditional recommendations and recommendations against treatments, please refer to [Table 3](#) of the full guideline document.

WHEN WOULD YOU RECOMMEND AN ANTIDEPRESSANT FOR FIRST TIME DEPRESSIVE SYMPTOMS?

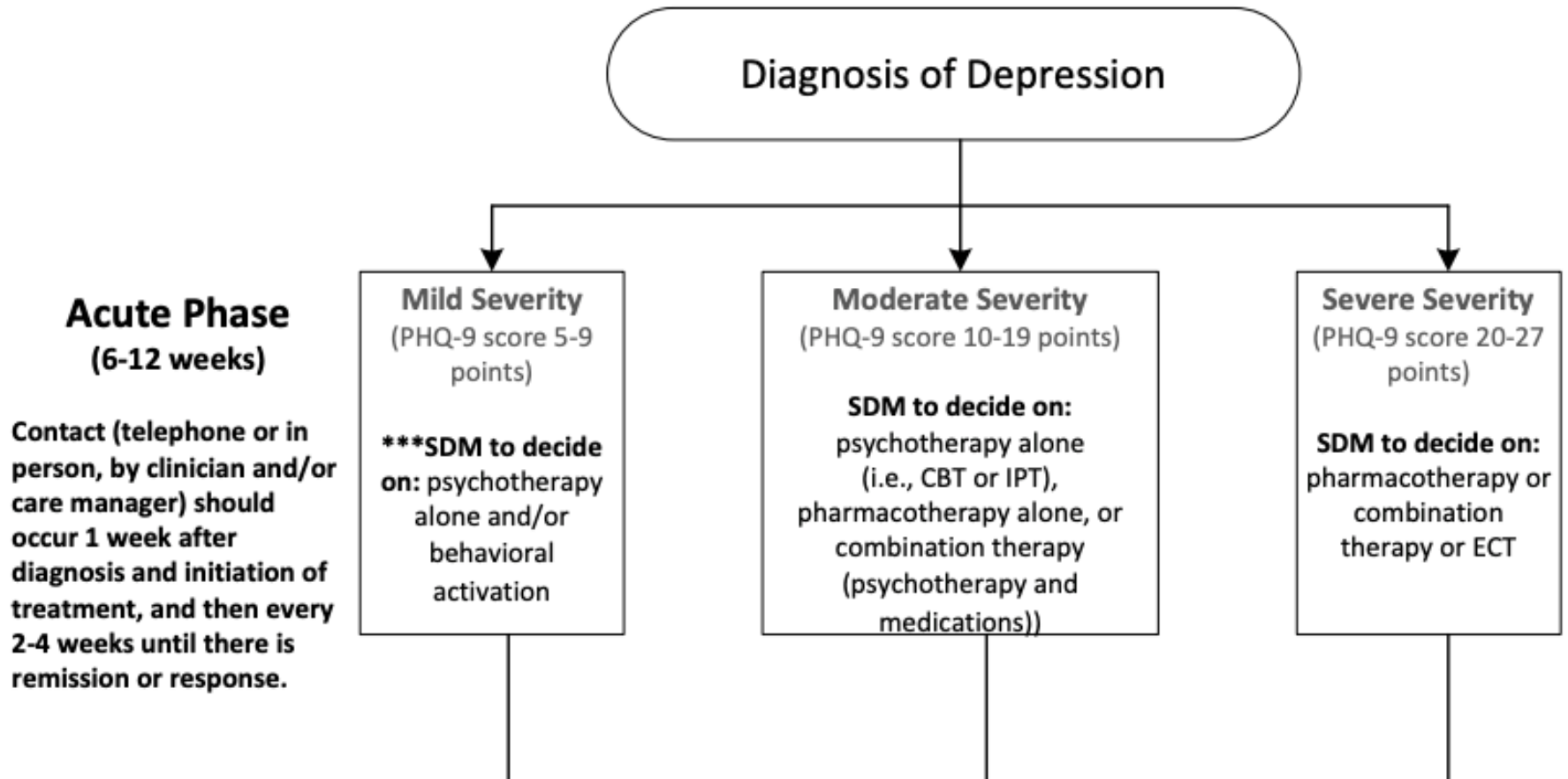
- A. For a PHQ9>20, irrespective of cause
- B. For a **mild** major depressive episode (per DSM5)
- C. For a **moderate or severe** major depressive episode (per DSM5)
- D. Any level** of severity of a major depressive episode
- E. I would always refer to therapy first

TREATMENT GUIDELINES REVIEW

- Veterans Affairs
- Dartmouth
- UK NICE

****Common Theme: Shared Decision Making****

APPENDIX 2: Depression Treatment in Adults Algorithm



Dartmouth: <https://www.dartmouth-hitchcock.org/sites/default/files/2021-02/depression-clinical-practice-guideline.pdf>

2022 UK NICE TREATMENT GUIDELINES

**Less Severe
Depression**

VS

**More Severe
Depression**

- **Less Severe
Depression**
– PHQ < 16

- **More Severe
Depression**
– PHQ > 16

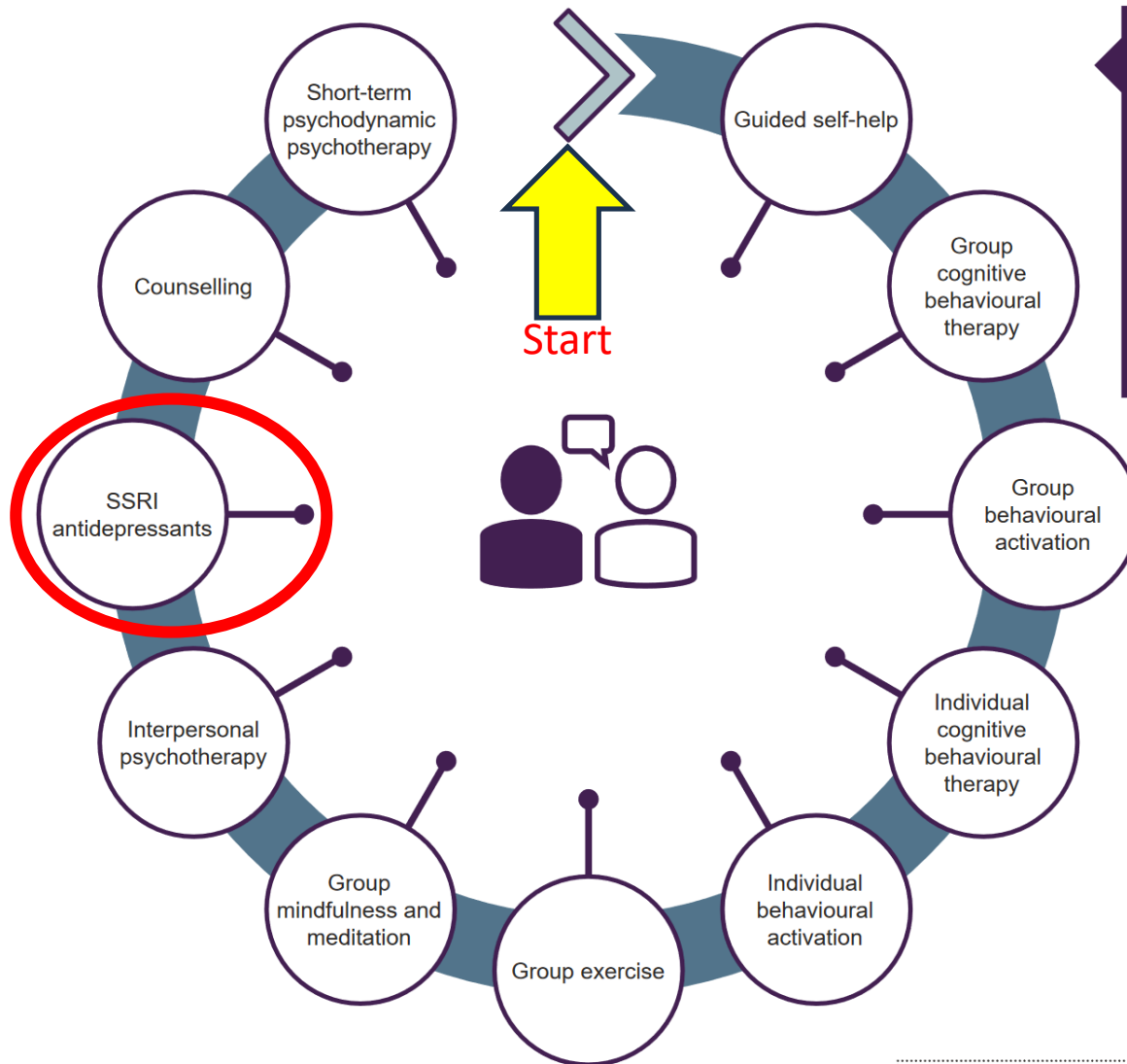
<https://www.nice.org.uk/guidance/ng222/chapter/recommendations#less-severe-depression>

Depression in adults: discussing first-line treatments for less severe depression

Discuss treatment options and match the choice of treatment to clinical needs and preferences, taking into account that any option can be used as first line, but consider the least intrusive and least resource intensive treatment first (guided self-help).

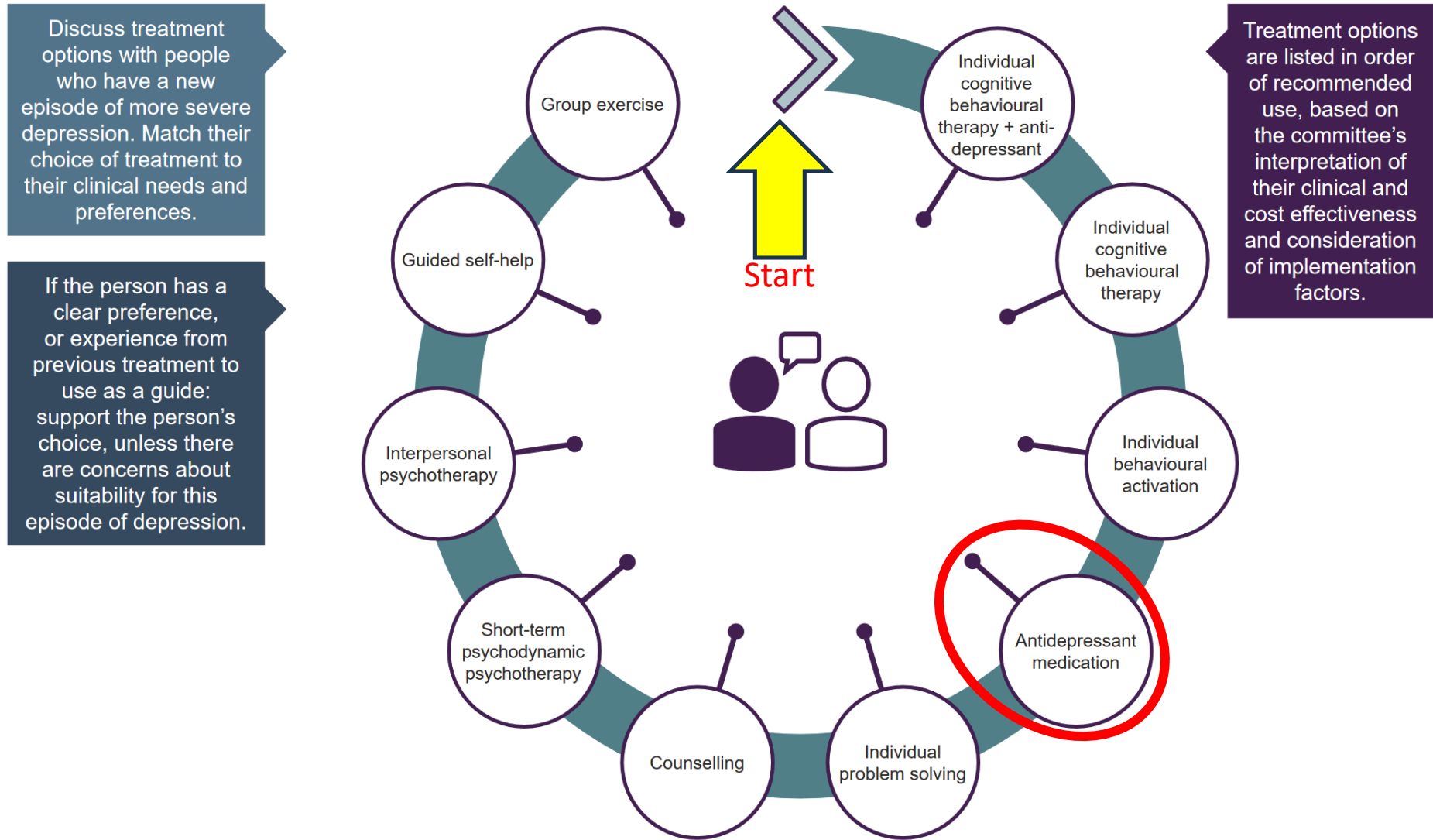
If the person has a clear preference, or experience from previous treatment to use as a guide: support the person's choice, unless there are concerns about suitability for this episode of depression.

Do not routinely offer antidepressants as a first-line treatment, unless that is the person's preference.



Treatment options are listed in order of recommended use, based on the committee's interpretation of their clinical and cost effectiveness and consideration of implementation factors.

Depression in adults: discussing first-line treatments for more severe depression



VA TREATMENT GUIDELINES

Uncomplicated
or restart of
past effective
treatment

VS

Severe or partial
or limited
response to
treatment

- **Complicated**

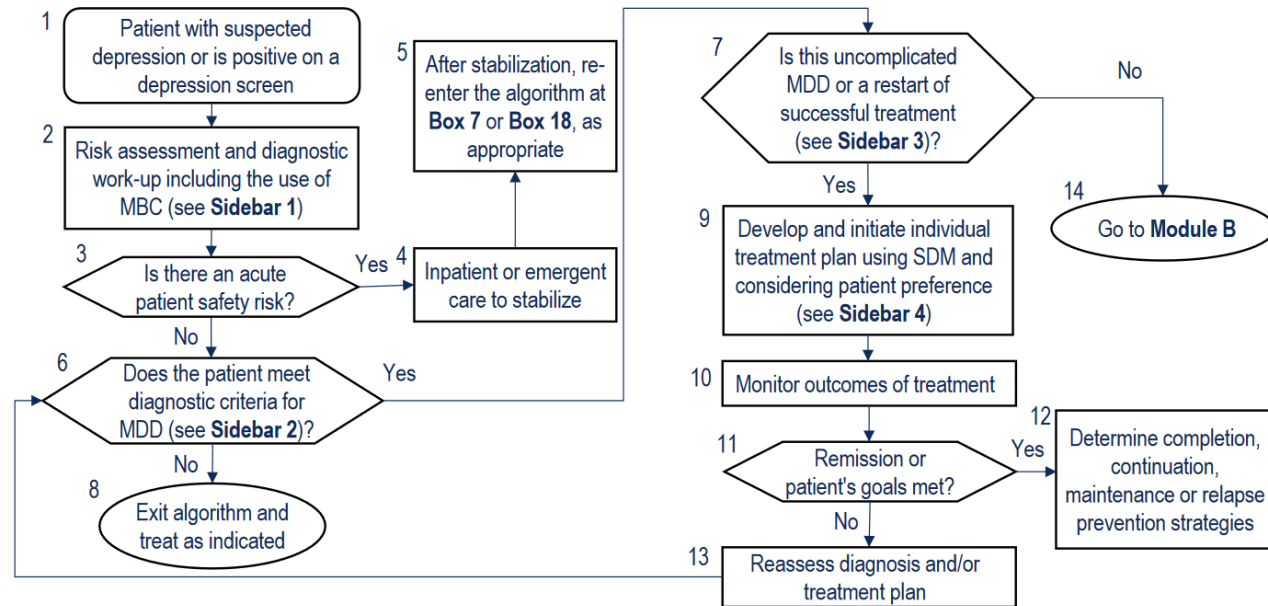
- Treatment resistant (if applicable)
- More severe (PHQ9>???)
- Persistent
- Co-morbid disorders (substance use, other MH, medical)
- High suicide risk
- Psychosis
- Catatonic
- Low functional status

- <https://www.healthquality.va.gov/guidelines/MH/mdd/>



Management of Major Depressive Disorder (MDD)

Module A: Initial Assessment and Treatment



Sidebar 1: Risk Assessment and Work-up

- Functional status, medical history, past treatment history, and relevant family history
- Consider administration of PHQ-9
- Evaluate for suicidal and homicidal ideation and history of suicide attempts, and consult the VA/DoD Assessment and Management of Patients at Risk for Suicide CPG, as appropriate
- Rule out depression secondary to other causes (e.g., hypothyroidism, vitamin B-12 deficiency, syphilis, pain, chronic disease)
- Incorporate MBC principles in the initial assessment

Sidebar 3: Factors to be Considered in Treatment Choice

- Prior treatment response
- Severity (e.g., PHQ-9)
- Chronicity
- Comorbidity (e.g., substance use, medical conditions, other psychiatric conditions)
- Suicide risk
- Psychosis
- Catatonic or melancholic features
- Functional status

Sidebar 2: DSM-5 Criteria

- Criterion A:** Five or more of the following symptoms present during the same 2-week period; at least one of the symptoms is either (1) depressed mood or (2) loss of interest/pleasure:
- Depressed mood most of the day, nearly every day
 - Markedly diminished interest or pleasure in almost all activities most of the day, nearly every day
 - Significant weight loss when not dieting or weight gain
 - Insomnia or hypersomnia nearly every day
 - Psychomotor agitation or retardation nearly every day
 - Fatigue or loss of energy every day
 - Feelings of worthlessness or excessive inappropriate guilt
 - Diminished ability to think, concentrate, or indecisiveness, nearly every day
 - Recurrent thought of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide
- Criterion B:** The symptoms cause significant distress or functional impairment
- Criterion C:** The episode is not attributable to the physiological effects of a substance or another medical condition

Sidebar 4: Considerations in Treatment of Uncomplicated MDD

- For initial treatment, select pharmacotherapy, psychotherapy, or both based on SDM
- If previous treatment was successful, consider restarting this approach
- Based on patient preferences, consider self help with exercise (e.g., yoga, tai chi, qi gong, resistance, aerobics), light therapy, patient education, and bibliotherapy
- Include patient characteristics (e.g., treatment of co-occurring conditions, pregnant patients, geriatric patients) in SDM
- Consider collaborative care in primary care for appropriate patients

Access to the full guideline and additional resources is available at: <https://www.healthquality.va.gov/>.

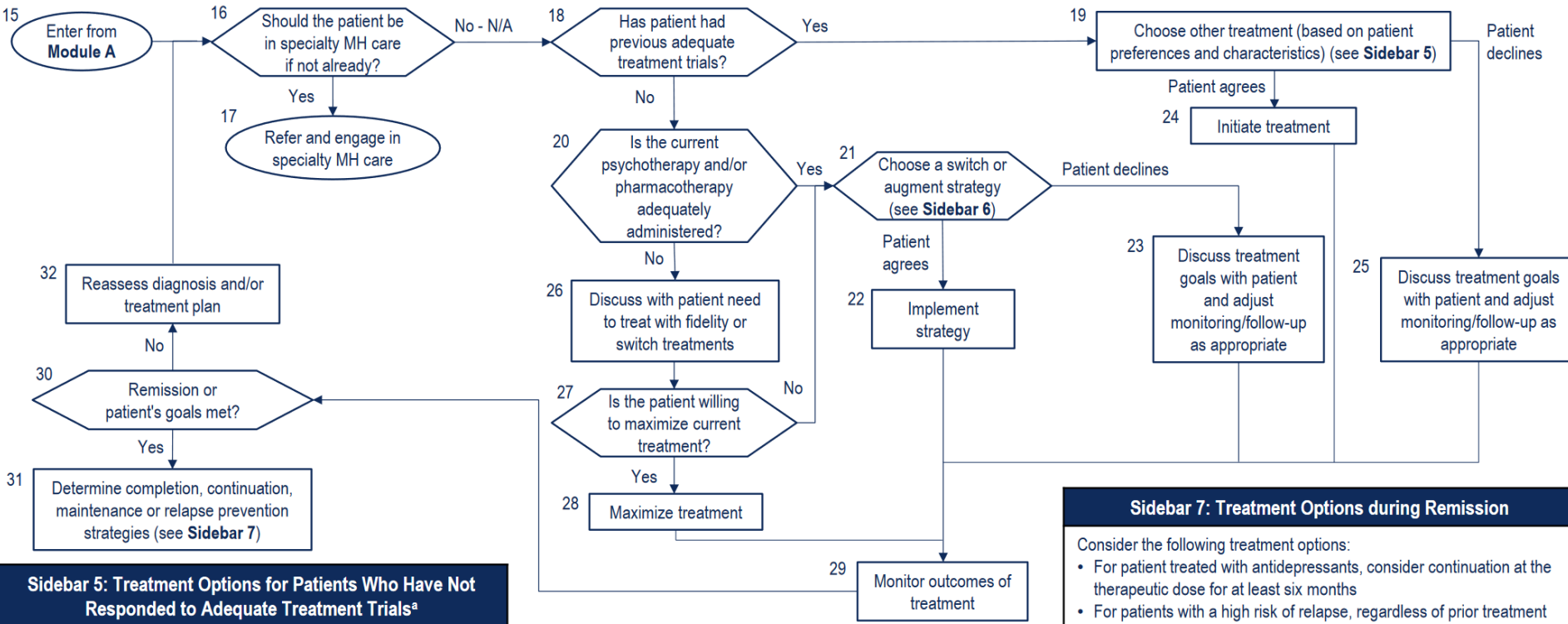


2022 VA MDD TREATMENT GUIDELINE

Sidebar 4: Considerations in Treatment of Uncomplicated MDD

- For initial treatment, select pharmacotherapy, psychotherapy, or both based on SDM
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- Based on patient preferences, consider self help with exercise (e.g., yoga, tai chi, qi gong, resistance, aerobics), light therapy, patient education, and bibliotherapy
- Include patient characteristics (e.g., treatment of co-occurring conditions, pregnant patients, geriatric patients) in SDM
- Consider collaborative care in primary care for appropriate patients

Module B: Advanced Care Management



Sidebar 5: Treatment Options for Patients Who Have Not Responded to Adequate Treatment Trials^a

- Consider the following treatment options:
- Consider other pharmacotherapy options (e.g., MAOIs, TCAs) (see Recommendation 16)
 - ECT (see Recommendation 20)
 - rTMS (see Recommendation 17)
 - Ketamine/esketamine (see Recommendation 19)

Sidebar 6: Treatment Options for Switching or Augmenting

- Consider the following treatment options:
- Adding psychotherapy or pharmacotherapy
 - Switching to a different treatment (e.g., switch between psychotherapy or pharmacotherapy, switch to a different focus of psychotherapy or different antidepressant)
 - Augmenting with a different class of medication (e.g., adding an SGA)

Sidebar 7: Treatment Options during Remission

- Consider the following treatment options:
- For patient treated with antidepressants, consider continuation at the therapeutic dose for at least six months
 - For patients with a high risk of relapse, regardless of prior treatment received, consider offering a course of CBT

Abbreviations: CBT: cognitive behavioral therapy; CPG: clinical practice guideline; DoD: Department of Defense; DSM-5: Diagnostic and Statistical Manual of Mental Disorders, 5th edition; ECT: electroconvulsive therapy; MAOI: monoamine oxidase inhibitor; MBC: measurement-based care; MDD: major depressive disorder; MH: mental health; PHQ-9: Patient Health Questionnaire-9; rTMS: repetitive transcranial magnetic stimulation; SDM: shared decision-making; SGA: second-generation antipsychotics; TCA: tricyclic antidepressant; VA: Department of Veterans Affairs

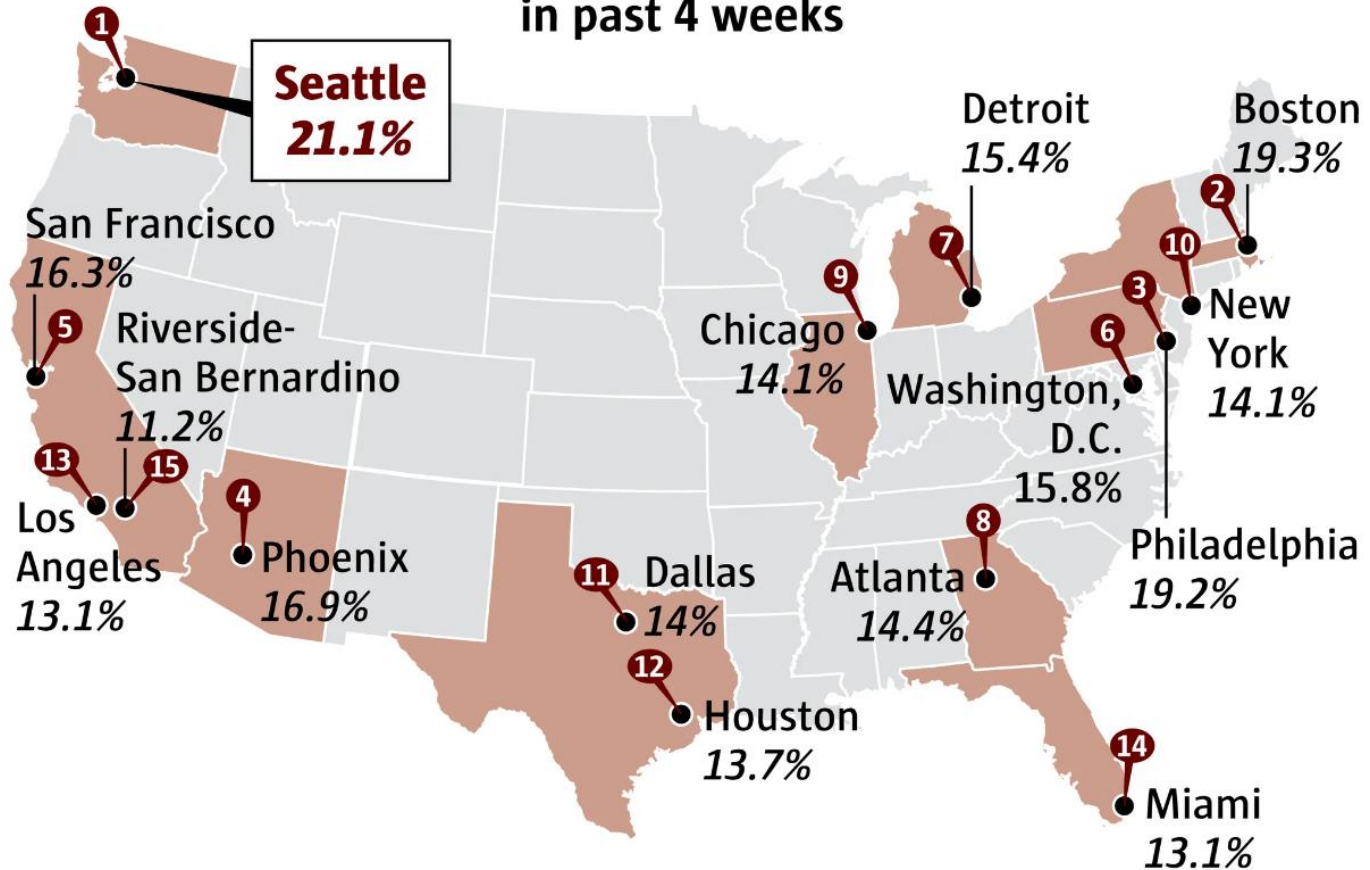
^a Patients who have demonstrated partial or no response to initial pharmacologic monotherapy (maximized) after a minimum of four to six weeks of treatment

OVERMEDICATED?

For “emotions, concentration, behavior, or mental health”.

WA: 24.7%

Took prescription medicine in past 4 weeks

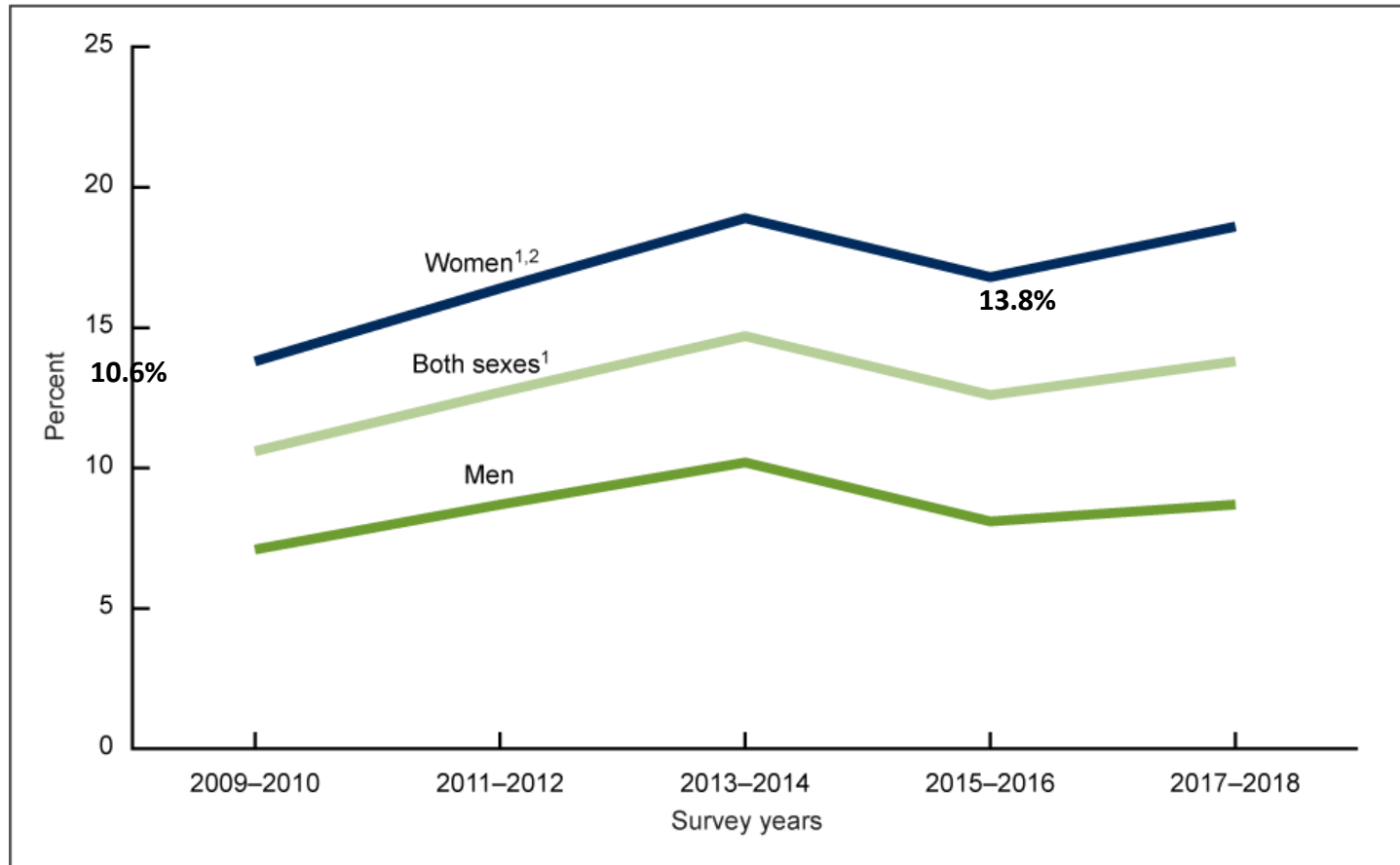


Source: Household Pulse Survey (Seattle), Dec. 1-13, U.S. Census Bureau

[Seattle ranks as most medicated metro for mental health reasons | The Seattle Times](#)

ANTIDEPRESSANTS IN THE US

Figure 4. Trends in antidepressant use over past 30 days among adults aged 18 and over, by sex: United States, 2009–2018



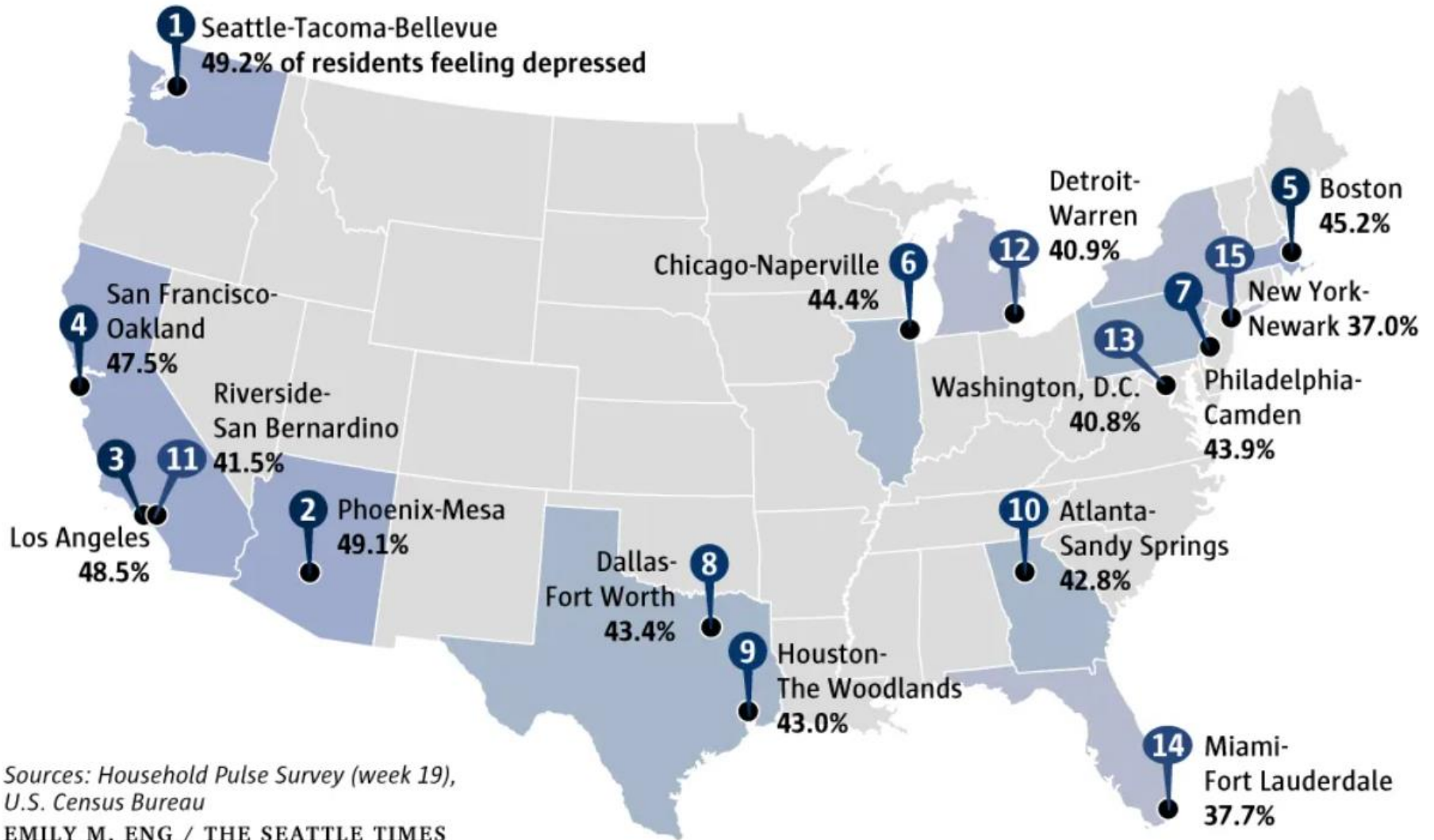
¹Significantly increasing linear trend.

²Significantly higher percentage than men in all years.

NOTE: Access data table for Figure 4 at: <https://www.cdc.gov/nchs/data/databriefs/db377-tables-508.pdf#4>.

SOURCE: National Center for Health Statistics, National Health and Nutrition Examination Survey, 2009–2018.

DEPRESSION IN SEATTLE



Sources: Household Pulse Survey (week 19),
U.S. Census Bureau

EMILY M. ENG / THE SEATTLE TIMES

[Seattle was the saddest metro area in the nation last month, survey shows | The Seattle Times](#)

33YO F WITH DEPRESSIVE SYMPTOMS

- Endorses low mood x 2 weeks. Broke up with partner about 1 month ago. Work is stressful. No past psych history. Poor sleep. Medicaid. Daily cannabis.
- PHQ9: 15. No SI.
- Patient would like some help and wonders if meds will help.

What would you offer?

- A. Start an antidepressant
- B. Refer to community mental health for therapy
- C. Recommend an online therapy option
- D. Recommend a supplement
- E. Recommend she reduce her cannabis and have her come back in 4 weeks because this is likely an adjustment disorder or substance induced

DSM-5 ADJUSTMENT DISORDER

The presence of emotional or behavioral symptoms in response to an identifiable stressor(s) occurring within 3 months of the onset of the stressor(s)

- Distress that is out of proportion with expected reactions to the stressor
- Symptoms must be clinically significant—they cause marked distress and impairment in functioning
- Distress and impairment are related to the stressor and are not an escalation of existing mental health disorders
- The reaction isn't part of normal bereavement
- Once the stressor is removed or the person has begun to adjust and cope, the symptoms must subside within six months.

33YO F WITH HIGH DEPRESSIVE SYMPTOMS

What would you offer?

A. Start an antidepressant

Is there a role for antidepressants in adjustment disorders?

- Evidence is too weak to recommend.
- Maybe for severe symptoms?
 - Suicidal behaviors OR 1.8
 - Death by suicide OR 0.12

O'Donnell ML, Metcalf O, Watson L, Phelps A, Varker T. A Systematic Review of Psychological and Pharmacological Treatments for Adjustment Disorder in Adults. *J Trauma Stress*. 2018 Jun;31(3):321-331. doi: 10.1002/jts.22295. PMID: 29958336.

Constantin D, Dinu EA, Rogozea L, Burtea V, Leasu FG. Therapeutic Interventions for Adjustment Disorder: A Systematic Review. *Am J Ther*. 2020 Jul/Aug;27(4):e375-e386. doi: 10.1097/MJT.0000000000001170. PMID: 32520732.

Fegan J, Doherty AM. Adjustment Disorder and Suicidal Behaviours Presenting in the General Medical Setting: A Systematic Review. *Int J Environ Res Public Health*. 2019 Aug 18;16(16):2967. doi: 10.3390/ijerph16162967. PMID: 31426568; PMCID: PMC6719096.

33YO F WITH HIGH DEPRESSIVE SYMPTOMS

What would you offer?

A. Recommend an online therapy option

Is online therapy the answer?

2022 VA Guidelines for Treatment of Uncomplicated MDD

- For patients with mild to moderate MDD, we suggest offering clinician-guided computer/internet-based cognitive behavioral therapy either as an adjunct to pharmacotherapy or as a first-line treatment, based on patient preference.

- Strength of Evidence: **Weak**

!!!Warning!!!

Privacy Issues



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Business Blog

FTC says online counseling service BetterHelp pushed people into handing over health information – and broke its privacy promises

By: Lesley Fair | March 3, 2023 | [f](#) [t](#) [in](#)

33YO F WITH HIGH DEPRESSIVE SYMPTOMS

What would you offer antidepressants for possible substance induced depressive disorder?

- Setting: SUD treatment center
- Initial Evaluation
 - Substance-induced Depression: 51%
 - Co-occurring Major Depression: 49%
- 1 year follow-up
 - 32% of substance induced depression reclassified as having independent MDD

O'Donnell ML, Metcalf O, Watson L, Phelps A, Varker T. A Systematic Review of Psychological and Pharmacological Treatments for Adjustment Disorder in Adults. *J Trauma Stress*. 2018 Jun;31(3):321-331. doi: 10.1002/jts.22295. PMID: 29958336.

Constantin D, Dinu EA, Rogozea L, Burtea V, Leasu FG. Therapeutic Interventions for Adjustment Disorder: A Systematic Review. *Am J Ther*. 2020 Jul/Aug;27(4):e375-e386. doi: 10.1097/MJT.0000000000001170. PMID: 32520732.

ANTIDEPRESSANT WITHDRAWAL

F	• Flu-like symptoms
I	• Insomnia
N	• Nausea
I	• Imbalance
S	• Sensory disturbances
H	• Hyperarousal (anxiety/agitation)

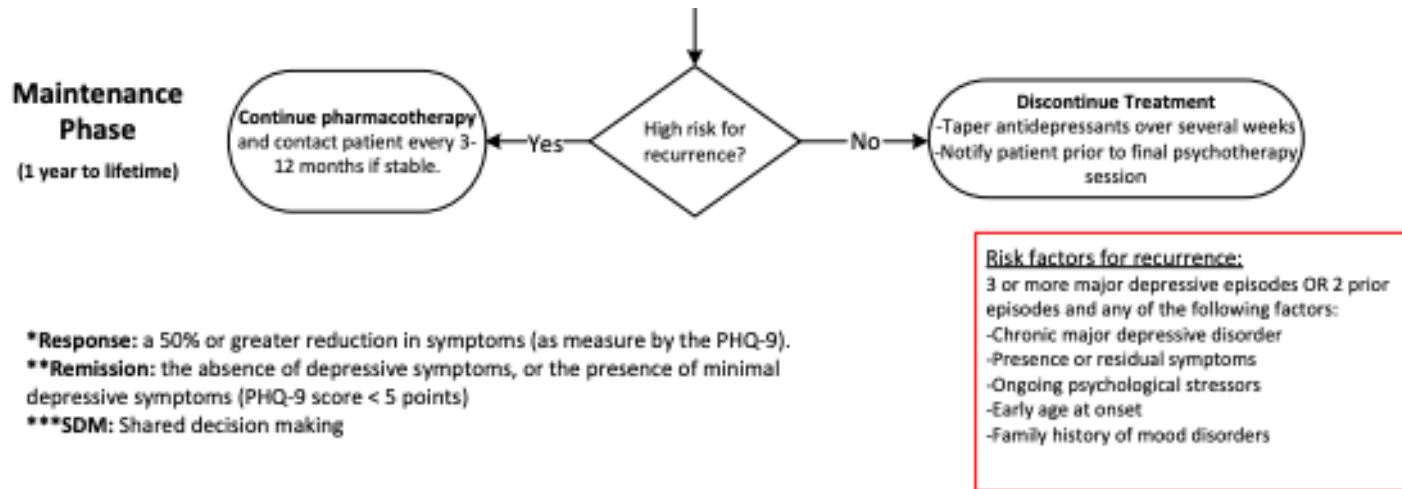
- Aka discontinuation syndrome (ADS)
- Higher risk: shorter half-life, abrupt or more rapid taper
- Evidence for CBT, maintenance antidepressants

• Maund E, Stuart B, Moore M, Dowrick C, Geraghty AWA, Dawson S, Kendrick T. Managing Antidepressant Discontinuation: A Systematic Review. *Ann Fam Med*. 2019 Jan;17(1):52-60. doi: 10.1370/afm.2336. PMID: 30670397; PMCID: PMC6342590.

• Fornaro M, Cattaneo CI, De Berardis D, Ressico FV, Martinotti G, Vieta E. Antidepressant discontinuation syndrome: A state-of-the-art clinical review. *Eur Neuropsychopharmacol*. 2023 Jan;66:1-10.

• Gabriel M, Sharma V. Antidepressant discontinuation syndrome. *CMAJ*. 2017 May 29;189(21):E747. doi: 10.1503/cmaj.160991. PMID: 28554948; PMCID: PMC5449237.

HOW LONG SHOULD I CONTINUE ANTIDEPRESSANTS?



Depression Management Adult, Ambulatory Clinical Practice Guideline
Copyright © 2017 Dartmouth-Hitchcock Knowledge Map™. Updated: January 2017

17

- NEJM 2021: DB RCT in UK, 150 clinics
 - Inclusion: 478 pts: 2+ depressive episodes OR antidepressants for 2+ years
 - Discontinuation group had higher relapse rate vs maintenance over 1 year period (56% vs 39%, respectively)

CHOOSING INITIAL TREATMENT SUMMARY

- Treatments for depression work best for Major Depressive Disorder.
- Therapy and medications are effective treatment for Major Depressive Disorder
- Choice of treatment should be driven by shared decision making
- Close follow-up at the start will help support your treatment recommendations