Differentiating between symptoms of MDD and adverse effects of antidepressants

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Learning Objectives

Upon completion of this activity, participants should be better able to:

- Apply validated screening tools to identify symptoms and diagnosis of MDD and and communication strategies to document preferences
- Utilize longitudinal assessment from baseline throughout treatment to differentiate severity and efficacy outcomes in MDD vs adverse effects of antidepressant medications
- Implement management strategies for persistent symptoms of MDD and for adverse effects to medications

MDD, major depressive disorder

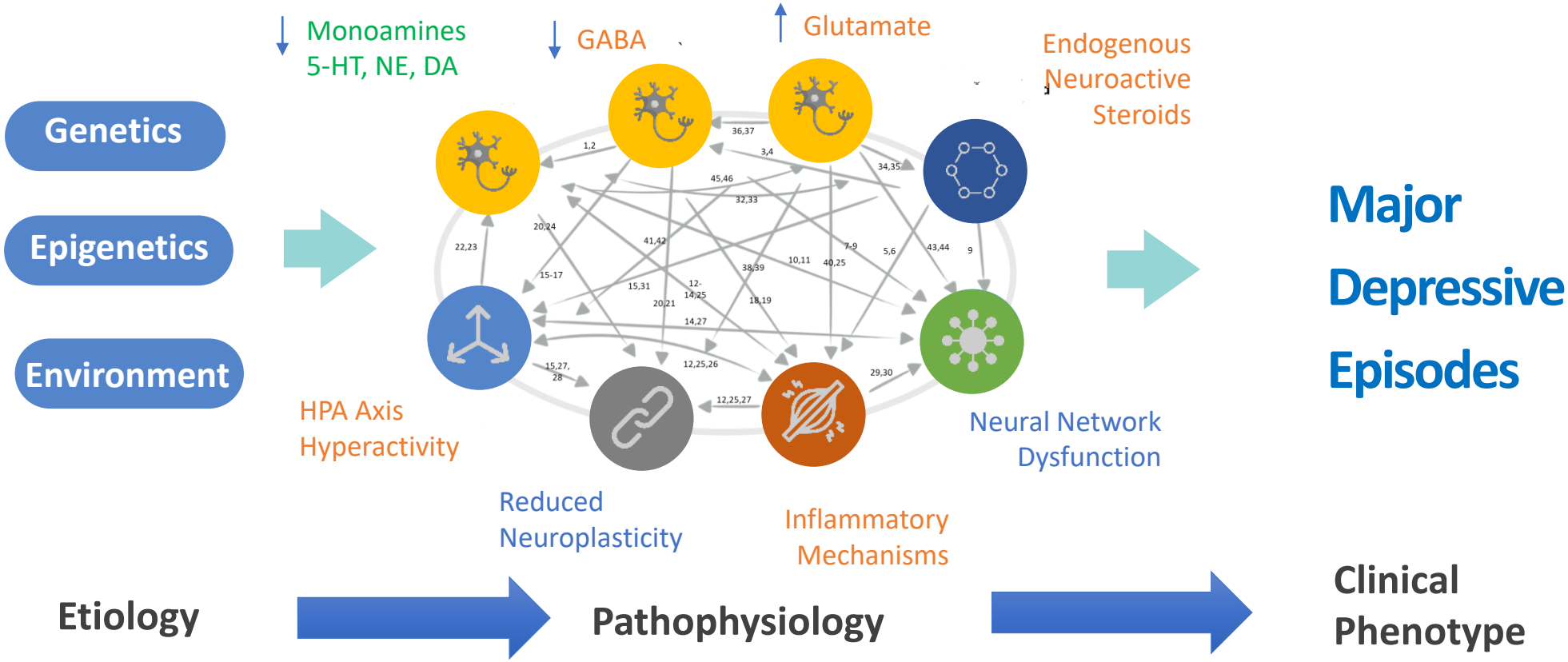
MDD: Common, Costly, Disabling

- In the United States, MDD has a[1]
  - 12-month prevalence of ~10%
  - Lifetime prevalence of ~21%
- Direct and indirect costs of MDD[2]
  - Estimated $210.5 billion annually
- Worldwide, MDD is a leading cause of disability[3]
- MDD predicts decreases in role functioning, social relationships, and quality of life[4-6]
- MDD is also associated with physical illnesses[1,7]
  - Cardiovascular disease, stroke
  - Diabetes
  - Fibromyalgia
  - Dementia
  - Cancer
  - Obstructive sleep apnea
  - Migraine
  - Sexual dysfunctions

[1]Hasin DS et al. *JAMA Psychiatry*. 2018;75:336. [2]Greenberg PE et al. *J Clin Psychiatry*. 2015;76:155.[3]GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. *Lancet*. 2018;392:1789. [4]Amos TB et al. *J Clin Psychiatry*. 2018;79:17m11725. [5]Whisman MA. *J Abnorm Psychol*. 2007;116:638.[6] IsHak WW et al. *Harv Rev Psychiatry*. 2011;19:229-239. [7]Goodwin GM. *Dialogues Clin Neurosci*. 2006;8:259.

Unified Theory of Depression

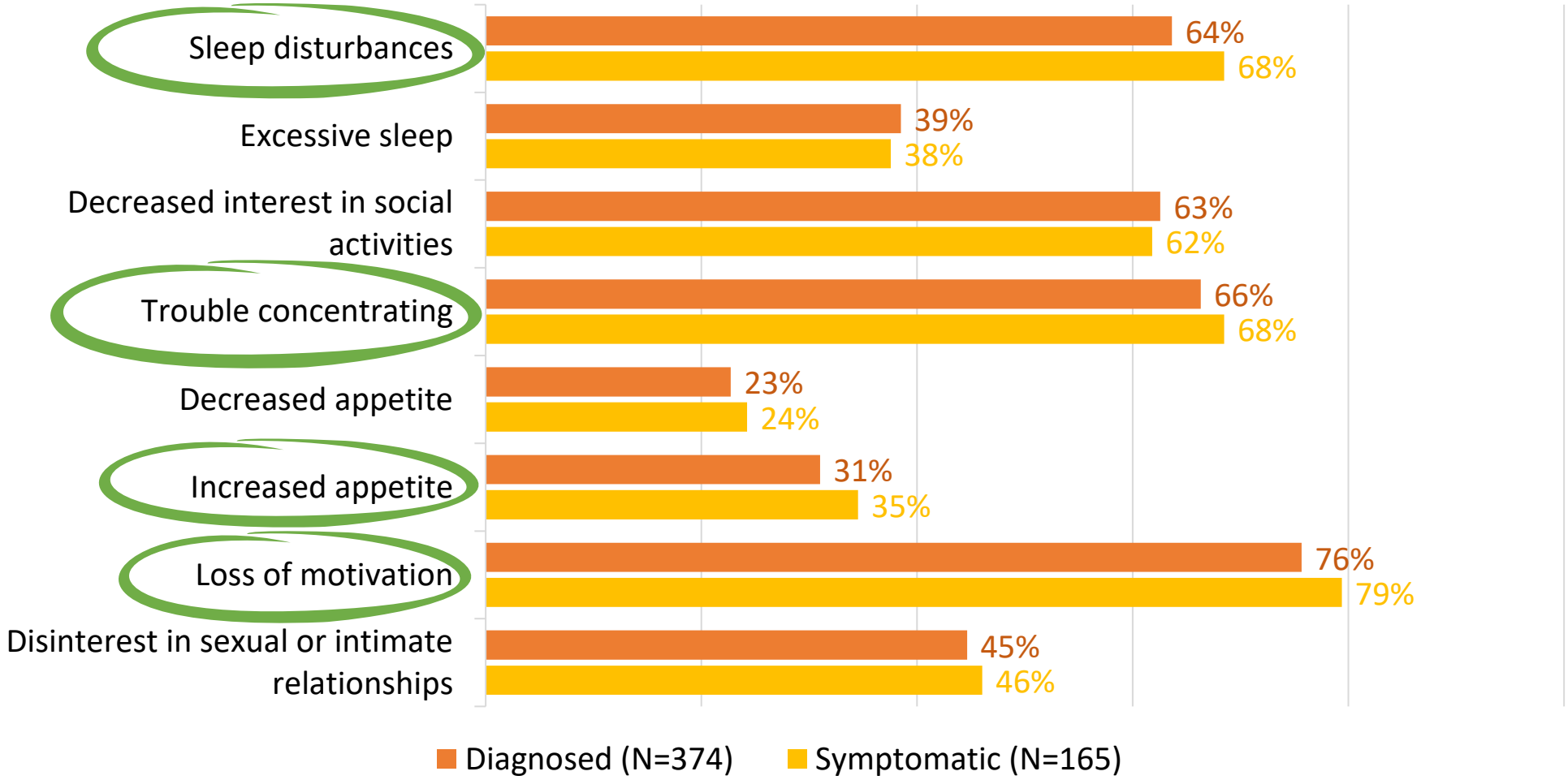
Synaptic Dysfunction Mechanisms



5-HT, 5-hydroxytryptamine; DA, dopamine; GABA, gamma-aminobutyric acid; HPA, hypothalamic-pituitary-adrenal; NE, norepinephrine
Adapted from Dean J, Keshavan M. *Asian J Psychiatr.* 2017;27:101-111

Impact of MDD on QoL

- **% Patients Bothersome/Very Bothersome**

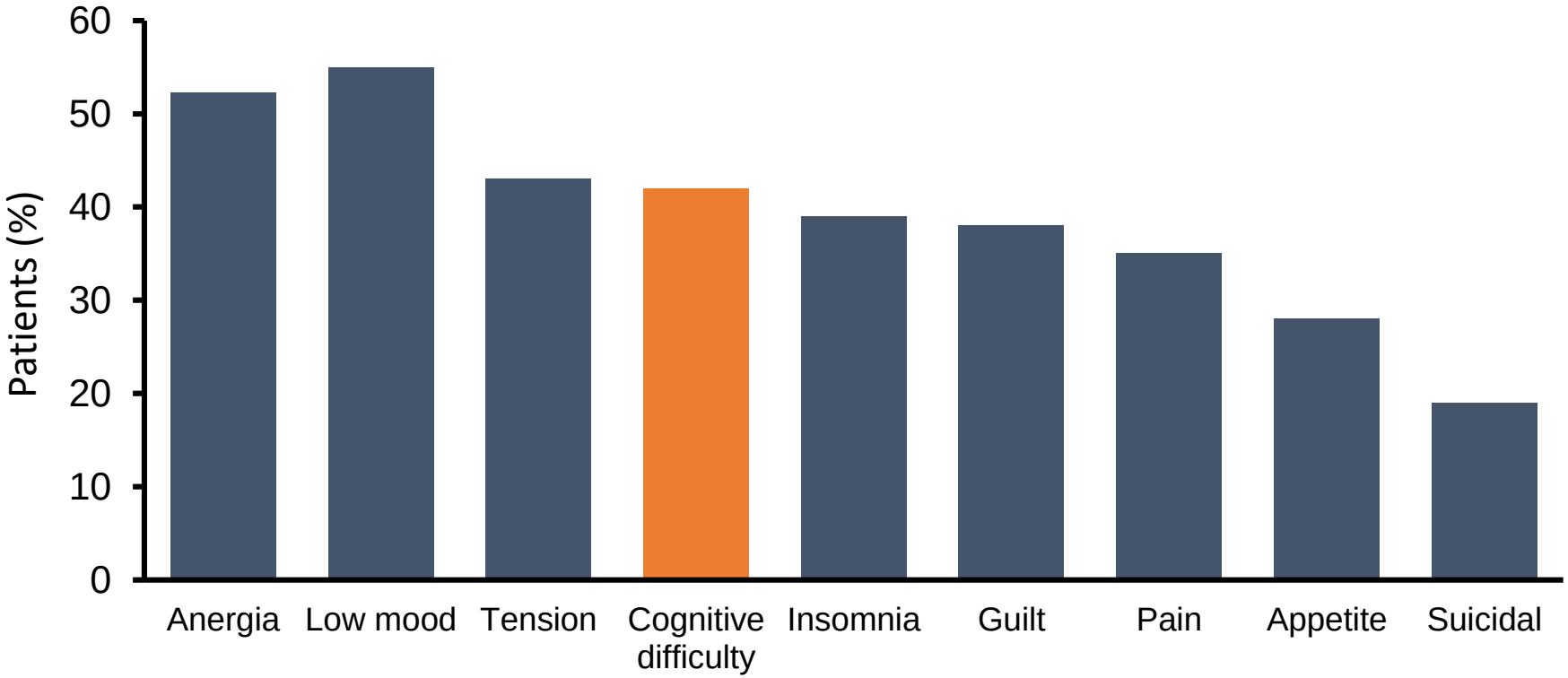


QoL, quality of life.
Results of the WebMD Depression Survey results

Depressive Symptoms and Work Functioning Impairment

>40% of depressed patients report anergia, low mood, tension and cognitive difficulty severely interfere with their work

% reporting interference with work functioning "Very much" or "So much that I had to stop working"



Anergia = lack of motivation, low energy, physically slowed down, sleepy during day
Tension = anxious/tense/nervous, irritability/anger
Cognitive difficulty = trouble concentrating, trouble with memory

Lam RW, et al. Depress Res Treat. 2012;2012:630206.

Treatment of MDD Should be Personalized

- Patient factors guiding treatment selection:
  - **Clinical features** (eg cormorbidities, specific symptoms, etc.)
  - **Severity of depression, functional impairment**
  - Treatment history, **preferences**, goals, expectations
- Characteristics of antidepressant
  - Efficacy
  - Safety (**tolerability/adverse events**) data which may compromise effectiveness, tolerability, and/or adherence

APA. MDD Practice Guidelines. 2010; Oluboka OJ et al. *Int J Neuropsychopharmacol*. 2018;21(2):128-144

Measurement-Based Care

Systematic use of validated measurement tools for screening, to monitor outcomes and to support clinical decision-making

Meta-analysis with random-effects models found no difference between MBC and comparison groups in response rates

But found significant differences in outcomes of greater remission rates
OR: 1.83 (*P*=.015)

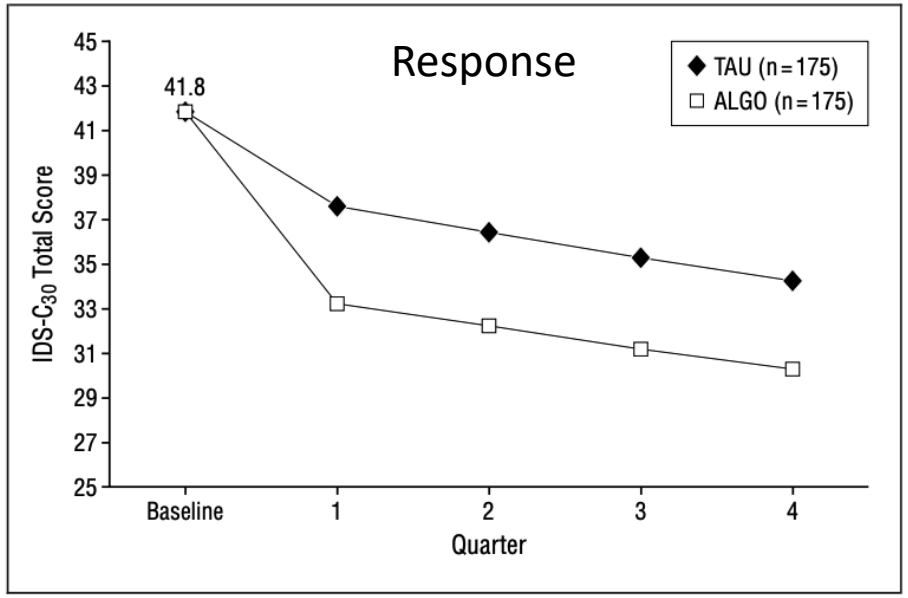
Lower end point severity, standard mean difference: 0.53 (*P*=.026)
Greater medication adherence, OR: 1.68 (*P*=.001)

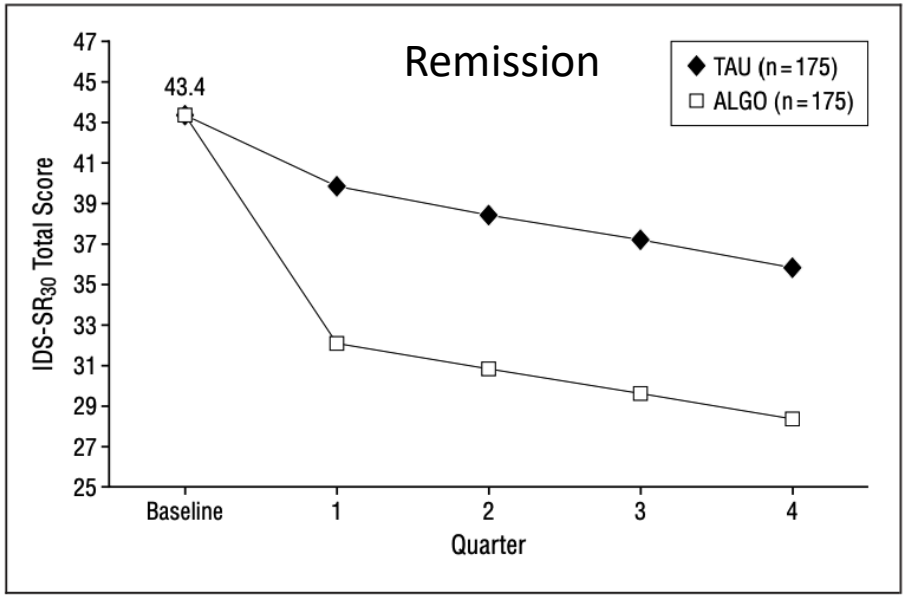
MBC, measurement-based care

Lam RW, et al;CANMAT Depression Work Group. *Can J Psychiatry.* 2016;61(9):510-523; Kurian BT, et al. *Curr Psychiatry Rep*. 2012;14(4):370-375; Morris DW, Trivedi MH. *Curr Psychiatry Rep*. 2011;13(6):446-458; Zhu M, et al. *J Clin Psychiatry*. 2021;82(5):21r14034

MBC: Improving Patient Outcomes

- Prospective trial evaluating clinical outcomes for patients with MDD (N=350) receiving Algorithm-guided treatment (AGT) or Treatment as usual (TAU)





- MBC broadly improves health outcomes of patients living with depression
- PROs show greater benefit than clinician-administered measures
- Functional improvement was also significantly greater with ALGO on the SF-12 (*P*=.046)

IDS-C_{30}, 30-item Inventory of Depressive Symptomatology-Clinician-Rated scale; IDS-SR_{30}, 30-item Inventory of Depressive Symptomatology-Self-Report scale; PRO, patient-reported outcome measure; SF-12, 12-Item Short Form Health Survey; TAU, treatment as usual; *IDS-C30 threshold for depression > 13; **IDS-SR30 threshold for depression > 18

PHQ-9 for MDD

Review period is over the past 2 weeks

Responses

- 0: Not at all
- 1: Several days
- 2: More than half the days
- 3: Nearly every day

Interpretation of total score

- 1 to 4: Minimal depression
- 5 to 9: Mild depression
- 10 to 14: Moderate depression
- 15 to 19: Moderately severe depression
- 20 to 27: Severe depression

Kroenke K, et al. *J Gen Intern Med*. 2001;16(9):606-613
Spitzer RL, et al. Patient Health Questionnaire-9. Accessed March 7, 2023. https://www.apa.org/depression-guideline/patient-health-questionnaire.pdf

PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)

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

FOR OFFICE CODING 0 + _____ + _____ + _____

=Total Score: _____

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

Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult
☐	☐	☐	☐

GAD-7

GAD-7

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

(For office coding: Total Score T____ = ____ + ____ + ____)

If you checked any problems, how difficult have they 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
☐	☐	☐	☐

Scoring GAD-7 Anxiety Severity

Review period is over last 2 weeks

This is calculated by assigning scores of 0, 1, 2, and 3 to the response categories, respectively, of "not at all," "several days," "more than half the days," and "nearly every day." GAD-7 total score for the seven items ranges from 0 to 21.

0–4: minimal anxiety

5–9: mild anxiety

10–14: moderate anxiety

15–21: severe anxiety

Spitzer RL, et al. *Arch Intern Med*. 2006;166(10):1092-1097
Spitzer RL, et al. GAD-7 anxiety. Accessed March 7, 2023. https://adaa.org/sites/default/files/GAD-7_Anxiety-updated_0.pdf

MDQ for Bipolar Disorder

Review period is essentially ever

Responses: Yes/No

Positive screen

- Yes to ≥ 7 of the 13 items in #1
- Yes to #2
- Moderate or serious to #3

Next step is comprehensive evaluation for bipolar spectrum disorder

Mood Disorder Questionnaire (MDQ)

Name: _____ Date: _____

Instructions: Check (✓) the answer that best applies to you.
Please answer each question as best you can.

	Yes	No
1. Has there ever been a period of time when you were not your usual self and...		
...you felt so good or so hyper that other people thought you were not your normal self or you were so hyper that you got into trouble?	◯	◯
...you were so irritable that you shouted at people or started fights or arguments?	◯	◯
...you felt much more self-confident than usual?	◯	◯
...you got much less sleep than usual and found you didn't really miss it?	◯	◯
...you were much more talkative or spoke faster than usual?	◯	◯
...thoughts raced through your head or you couldn't slow your mind down?	◯	◯
...you were so easily distracted by things around you that you had trouble concentrating or staying on track?	◯	◯
...you had much more energy than usual?	◯	◯
...you were much more active or did many more things than usual?	◯	◯
...you were much more social or outgoing than usual, for example, you telephoned friends in the middle of the night?	◯	◯
...you were much more interested in sex than usual?	◯	◯
...you did things that were unusual for you or that other people might have thought were excessive, foolish, or risky?	◯	◯
...spending money got you or your family in trouble?	◯	◯
2. If you checked YES to more than one of the above, have several of these ever happened during the same period of time? *Please check 1 response only.*	◯	◯
3. How much of a problem did any of these cause you — like being able to work; having family, money, or legal troubles; getting into arguments or fights? *Please check 1 response only.* ◯ No problem ◯ Minor problem ◯ Moderate problem ◯ Serious problem		
4. Have any of your blood relatives (ie, children, siblings, parents, grandparents, aunts, uncles) had manic-depressive illness or bipolar disorder?	◯	◯
5. Has a health professional ever told you that you have manic-depressive illness or bipolar disorder?	◯	◯

Adapted from Hirschfeld R, Williams J, Spitzer RL, et al. Development and validation of a screening instrument for bipolar spectrum disorder: the Mood Disorder Questionnaire. *Am J Psychiatry*. 2000;157:1873-1875. Isometsä E, et al. *BMC Psychiatry*. 2003;3:8; Wang HR, et al. *Depress Anxiety*. 2015;32(7):527-538; Hirschfeld RM, et al. Mood disorder questionnaire. Accessed March 7, 2023. https://www.ohsu.edu/sites/default/files/2019-06/cms-quality-bipolar_disorder_mdq_screener.pdf

Oxford Depression Questionnaire (ODQ)

	Section 1
1	All my emotions, both “pleasant” and “unpleasant”, are “toned down”
2	I don’t fully enjoy things that should give me pleasure, such as beautiful places or things or music
3	I care less about other people’s feelings than I think I should
4	Because I don’t care so much about things, I’m having problems at home
5	Unpleasant emotions, such as sadness, disappointment, and distress, feel toned down or different in some way
6	I don’t look forward to things with eager anticipation
7	I don’t have much sympathy for people
8	I feel “spaced out” and distant from the world around me
9	My emotions lack intensity
10	I don’t have the passion and enthusiasm for life that I should
11	Other people being distressed doesn’t affect me
12	Because I don’t care so much about things, I’m having problems at work or school
	Section 2
13	Day-to-day life just doesn’t have the same emotional impact on me that it did before my illness/problem
14	I don’t experience pleasant emotions as much as I did before I developed my illness/problem
15	I don’t react to other people’s emotions (such as their sadness, anger or distress) as much as I did before my illness/problem
16	I don’t care as much about my day-to-day responsibilities as I did before I developed my illness/problem
17	My emotions are numbed/dulled/flattened compared to before I developed my illness/problem
18	I don’t get as much of a “high” from good things in my life as I did before my illness/problem
19	I don’t have as much sympathy for other people as I did before my illness/problem
20	I just don’t care about things as much as I did before my illness/problem
	Section 3
21	The antidepressant is preventing me from feeling my emotions in some way
22	The antidepressant seems to make me just not care about things that should matter to me
23	The antidepressant seems to make me feel emotionally disconnected from people around me
24	The antidepressant is preventing me from feeling pleasant emotions
25	The antidepressant changes the way I experience my emotions in a way that is unhelpful (not helpful) to me
26	I have considered stopping (or have already stopped) my antidepressant because of its emotional side effects

Disagree	Disagree a little	Neither agree nor disagree	Agree a little	Agree

Oxford Depression Questionnaire (ODQ) Scoring

All items are scored: 1-5 = Disagree - Agree

Four dimensions can then be scored:

GR = *General reduction in emotions*
Items 1 + 5 + 9 + 13 + 17

RP = *Reduction in positive emotions*
Items 2 + 6 + 10 + 14 + 18

ED = *Emotional detachment from others*
Items 3 + 7 + 11 + 15 + 19

NC = *Not caring* = 4 + 8 + 12 + 16 + 20

Total = GR + RP + ED + NC

If required, a further attributional dimension can be scored:

AC = *Antidepressant as cause*
Items 21 + 22 + 23 + 24 + 25 + 26

Spitzer RL, et al. *Arch Intern Med*. 2006;166(10):1092-1097
Spitzer RL, et al. GAD-7 anxiety. Accessed March 7, 2023.
https://adaa.org/sites/default/files/GAD-7_Anxiety-updated_0.pdf

Measurement Tools: Caveats

- Tools should not replace clinician judgment
- Not everything with depressive symptoms and mood lability is MDD (Bipolar disorder, borderline personality disorder)
- Tools can be combined:
  - PHQ-9 and GAD-7 for MDD and comorbid anxiety
  - PHQ-9 and MDQ to rule out bipolar disorder
  - PHQ-9 and Oxford Depression Questionnaire (ODQ) to determine continued depression vs. emotional blunting
  - PHQ-9 and Sexual function questionnaire eg ASEX or CSFQ

Measurement-Based Care

- MBC is more than assessing symptoms. We also assess:
- Medication side effects
    - Acute
    - Chronic/Long-term (measure at baseline and follow-up):
        - Weight gain (measure weight)
        - Sexual function/dysfunction
        - Cognitive effects
        - Insomnia
        - At follow-up with symptoms of emotional blunting vs anhedonia (ODQ); use with PHQ-9 for additional specificity (depression severity)
- Patient adherence to medications: monitor refills and assessment
- Safety/Suicidality: specific questions

ODQ, Oxford Depression Questionnaire

Morris DW, Trivedi MH. *Curr Psychiatry Rep*. 2011;13(6):446-458.

Shared Decision Making

- Communication with the patient is important
- Encourage patient to share preferences/needs
- Maintaining trust and buy-in to the treatment plan will improve adherence

MDD Symptoms

- **SSRIs, SNRIs, and atypical antidepressants** (bupropion, mirtazapine, trazodone, vilazodone, vortioxetine) for MDD without psychosis or bipolar diathesis (use PHQ-9 at baseline and for changes/outcomes). **Avoid TCAs** due to safety concerns, alone or with SRIs
- First step: Consider personal and family past response, hx of adverse effects, cost, comorbidities and **patient preferences**
  - Mild MDD: Monotherapy with above medications or psychotherapy
  - Moderate – severe MDD: Monotherapy +/- psychotherapy
  - Assess for **efficacy** and **adverse effects** (atypical antidepressants are far less likely to be associated with sexual dysfunction, emotional blunting, weight gain, cognitive dysfunction**,** etc.) over 4-8 weeks. **A trial at inadequate doses for <6-8 weeks is not a Tx failure**
- If needed: Switch medications (**AD with different MOA)** or augment (**AD with different MOA**, atypical antipsychotic, buspirone, and if comfortable, lithium, thyroid supplementation)

Taylor RW, et al. *International Journal of Neuropsychopharmacology*. 2020;23(9):587-625

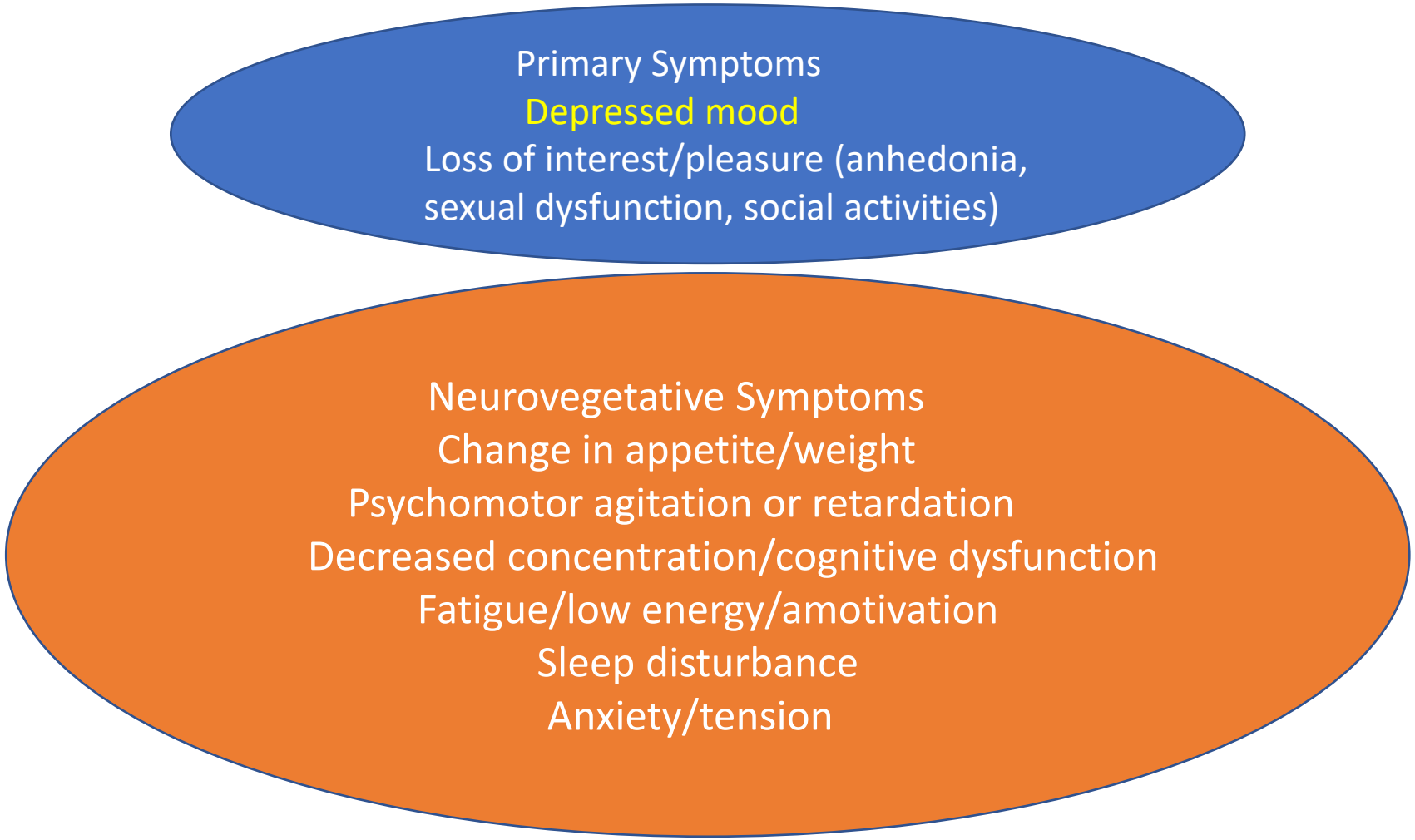
Overall Strategies for Interventions with MDD

Combination Treatments	Use of 2 ADs preferably with different MOA or AD augmentation strategies (eg, antipsychotics, buspirone, lithium, thyroid supplementation)
Psychotherapy	Effective alone for mild–moderate depression Use with antidepressants for combination treatment
Lifestyle Changes	Exercise, sleep, diet, avoid ETOH, supplements (eg, vitamin B100 complex, omega-3 fatty acids, folate), meditation
Manage Comorbidities	Persistent untreated or under-treated comorbidities (eg, OSA, DM, migraine, substance use disorder, obesity) contribute to poor response

AD, antidepressant; DM, diabetes mellitus; MOA, mechanism of action; OSA, obstructive sleep apnea

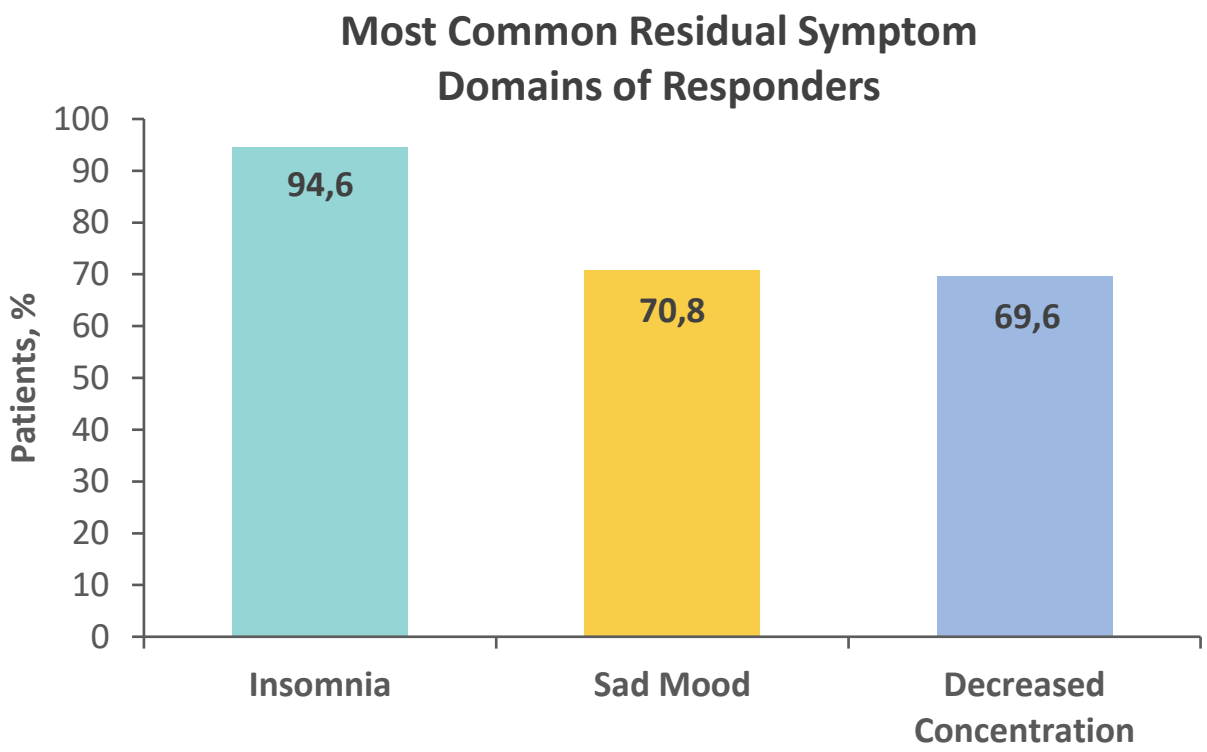
Solmi M, et al. *Braz J Psychiatry*. 2020;43(2):189-202; Ferguson JM. *Prim Care Companion J Clin Psychiatry*. 2001;3(1):22-27; Cartwright C, et al. *Patient Prefer Adherence*. 2016;10:1401-1407

Overlap of Symptoms of MDD and Antidepressant AEs



Managing Symptoms and Treatment Decisions

- Managing **residual symptoms** is key, as they predispose to relapse
- For mild - moderate MDD, informed treatment selection can be accomplished
  - MBC approach can help guide management in these cases
  - Tracking both insomnia and sexual dysfunction also provide benefit



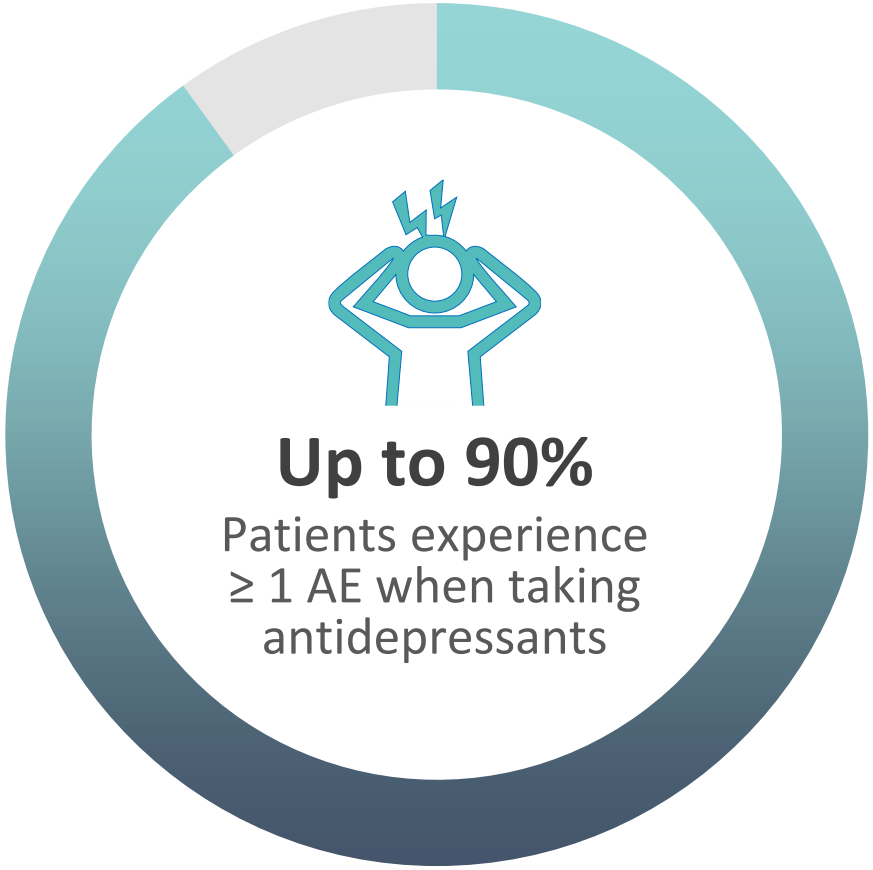
The care model a clinician and the team implements should be directed toward the patient's individual needs and symptoms

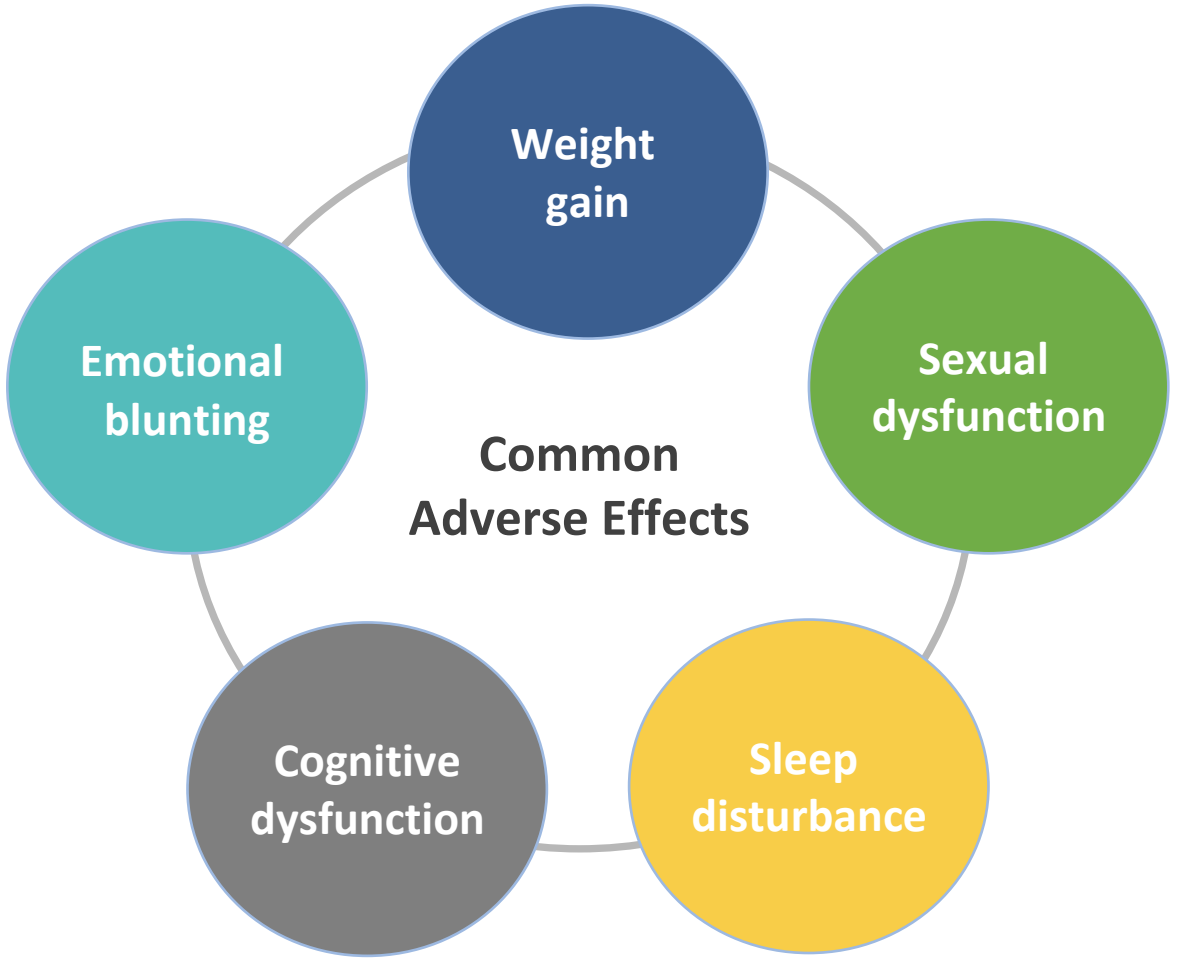
AE, adverse event

Conradi HJ, et al. *Psychol Med*. 2011;41(6):1165-1174; Lam RW, et al. *Depress Res Treat*. 2012;2012:630206; McClintock SM, et al. *J Clin Psychopharmacol*. 2011;31(2):180-186

Current SOC Antidepressants: Distinct Tolerability Profiles

Undesirable side effects are greatest with SSRIs > SNRIs > atypical antidepressants

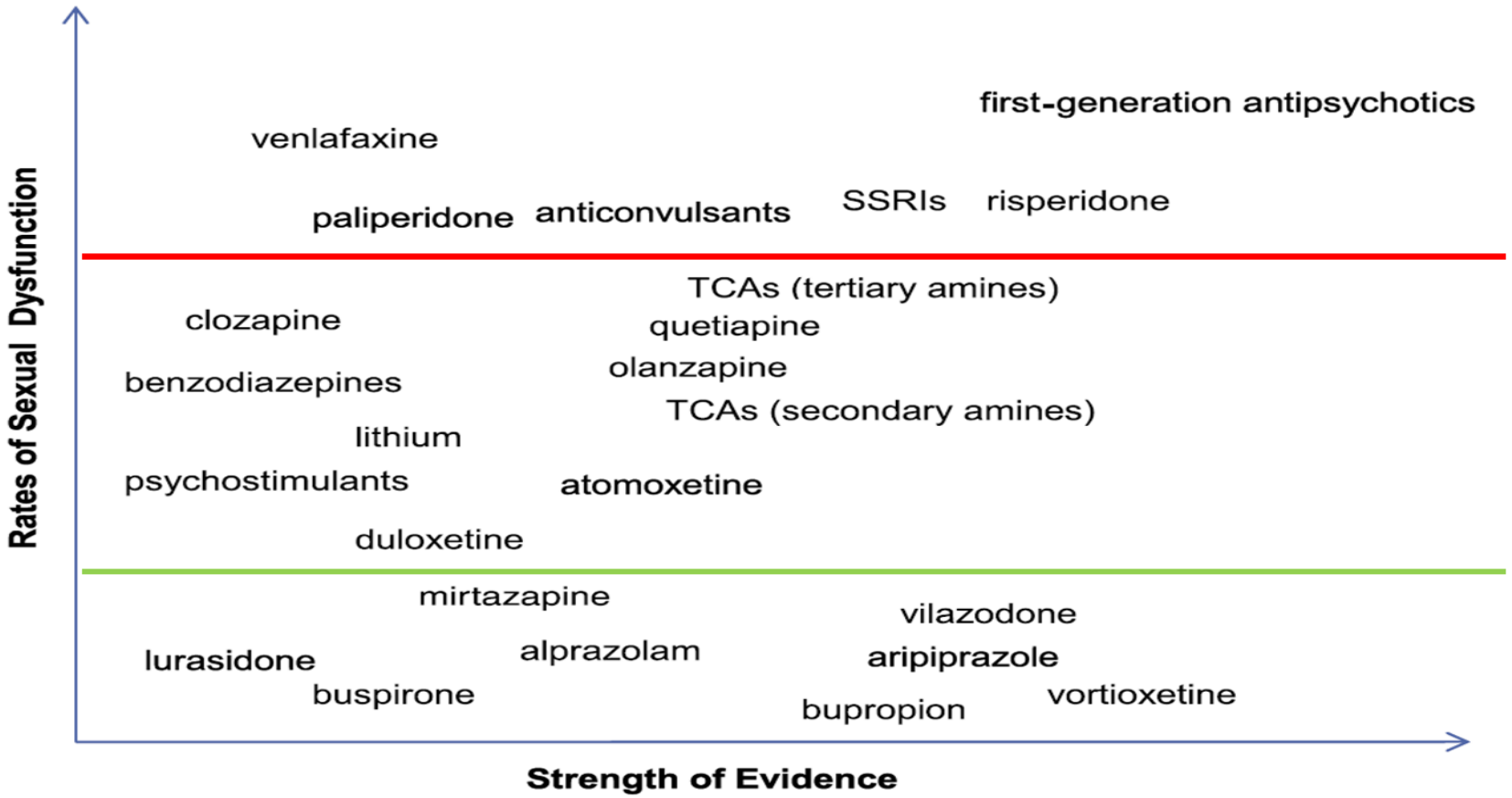




GI, gastrointestinal; SOC, standard of care; SSRI, selective serotonin reuptake inhibitor; SNRI, serotonin and norepinephrine reuptake inhibitor

Solmi M, et al. *Braz J Psychiatry*. 2020;43(2):189-202; Ferguson JM. *Prim Care Companion J Clin Psychiatry*. 2001;3(1):22-27; Cartwright C, et al. *Patient Prefer Adherence*. 2016;10:1401-1407

Rates of SD with Psychotropics



Clayton AH, et al. Sexual dysfunction due to psychotropic medications, *Psychiatric Clinics of North America 2016;39:*427-463

Emotional Blunting

- Among patients receiving SSRIs/SNRIs 30-60% reported emotional blunting
- Among 316 patients with MDD, 35% discontinued their medication due to emotional blunting patients
- Emotional blunting can lead to other symptoms such as decreased sexual desire/drive, social motivation, mental or cognitive energy/abilities, physical energy/fatigue

Antidepressant	Patients with emotional blunting
Citalopram	46%
Venlafaxine	46%
Fluoxetine	47%
Sertraline	45%
Paroxetine	43%
Escitalopram	43%
Bupropion	33%
Duloxetine	75%
Amitriptyline	47%
Mirtazapine	42%
Desvenlafaxine	56%
Others	48%
Total (N = 669)	**46%**

Read J et al. *Curr Drug Saf.* 2018;13(3):176-186; Goodwin GM et al. *J Affect Disord*. 2017;221:31-35; Read J et al. *Psychiatry Res*. 2014;216(1):67-73; Price J et al. *Br J Psychiatry*. 2009;195(3):211-217; Bolling et al. *Psychother Psychosom*. 2004;73(6):380-385. Rosenblat JD et al. *J Affect Disord*. 2019;243:116-120; Ishak WW et al. *J Affect Disord*. 2013;151(1):59-65. Fagiolini A et al. *J Affect Disord.* 2021;283: 472–479

Differentiating Anhedonia and Emotional Blunting

Anhedonia

- Reduced ability to experience positive feelings
- Increased experience of negative feelings
- SSRI/SNRIs may be beneficial; although suboptimal treatment

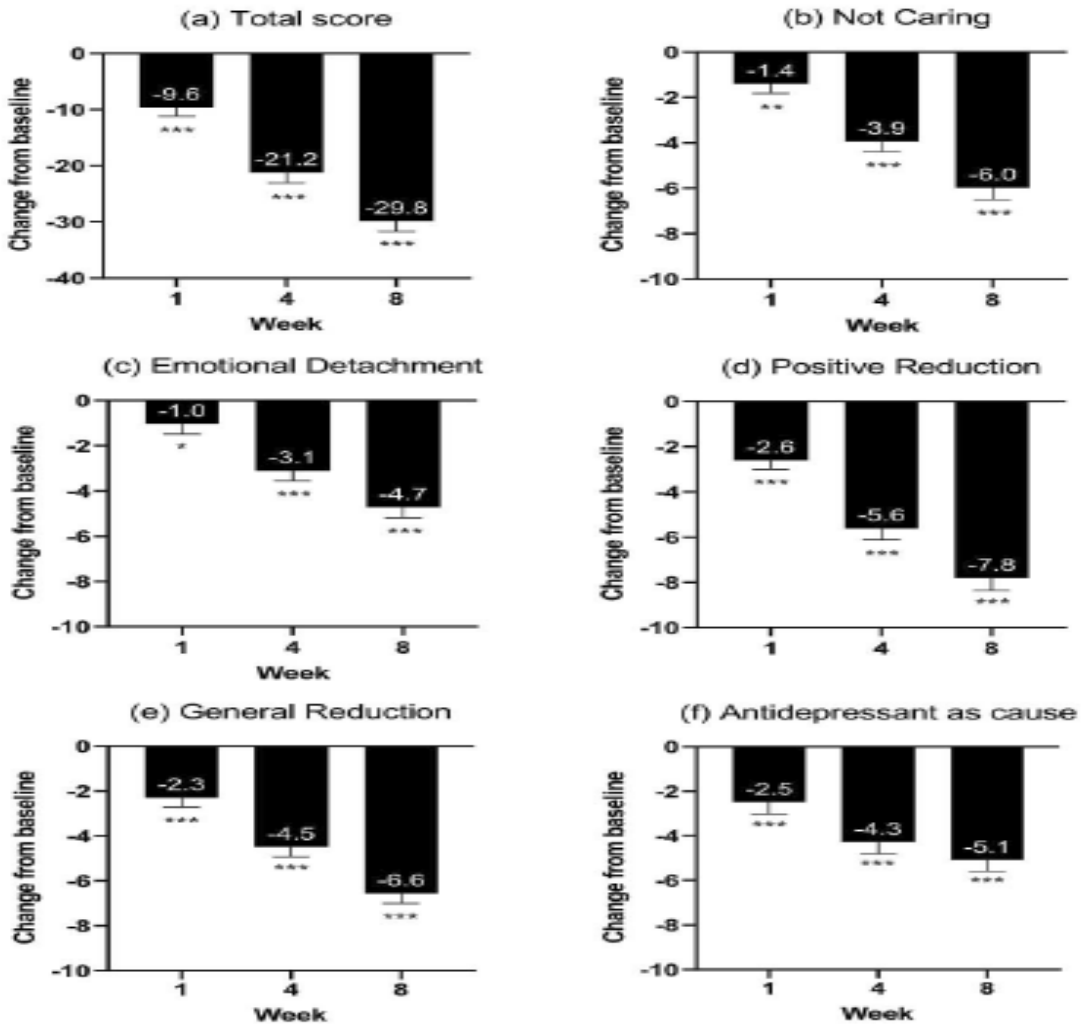
Emotional Blunting

- Defined as restriction in both positive and negative emotions, e.g. apathy, emotional indifference and detachment, loss of empathy
- May be manifested by decreased intensity/range of emotion, decreased laughing and crying, loss of motivation/drive, diminished feelings in interpersonal relationships, etc.
- SSRI/SNRIs may cause/worsen the condition; benefits with lowering the dose, augmentation, alternative antidepressant

Fagiolini A et al. *J Affect Disord*. 2021;283:472-479.

Change from Baseline in Oxford Depression Questionnaire

In a recent multicenter study (2019-2020), at week 8, serotonin modulator vortioxetine showed an improvement in ODQ total score in patients with MDD who had **inadequate response** to SSRI/SNRI treatment, and 50% reported no emotional blunting in response to standardized screening question.



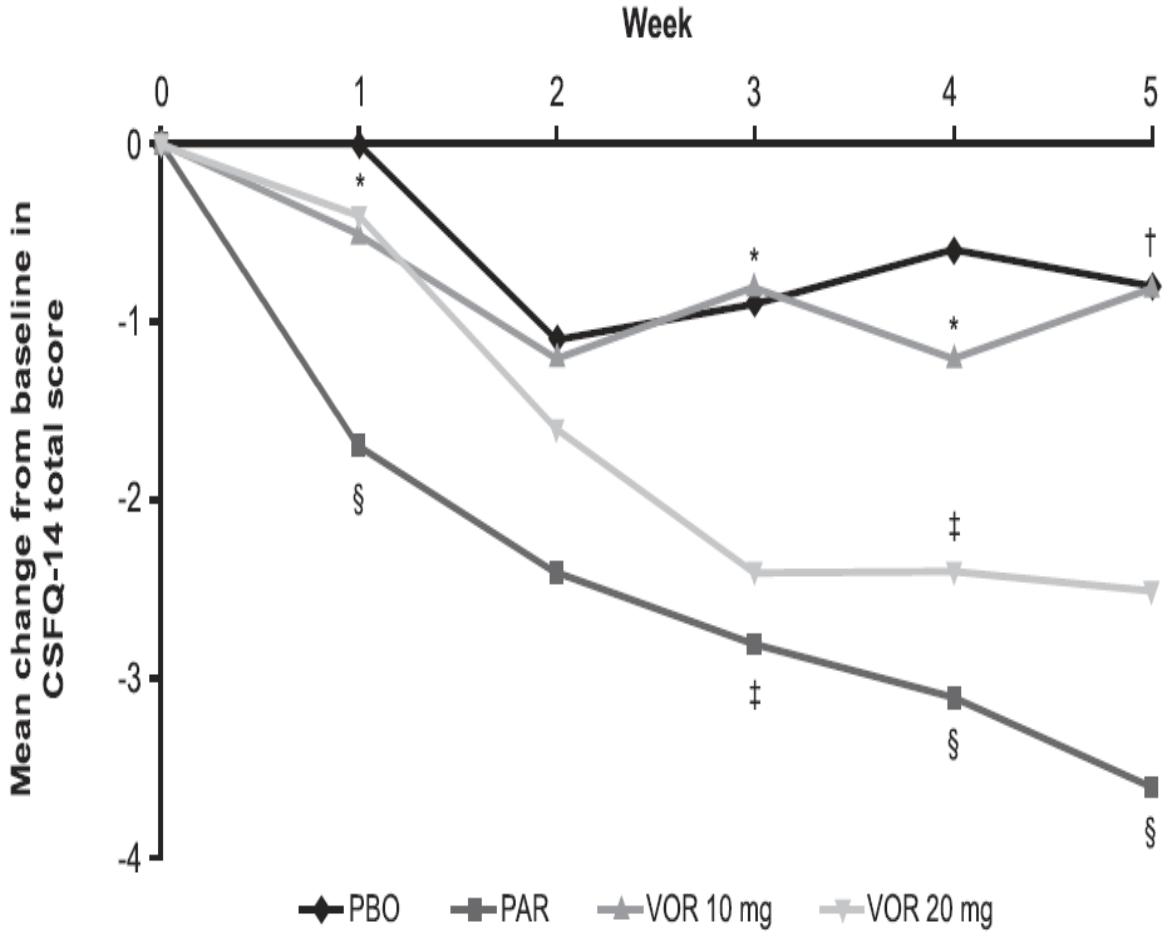
Fagiolini A et al. *J Affect Disord.* 2021;283: 472–479

Manage Efficacy and Adverse Effects of Antidepressants

- Identify response of MDD to treatment
- Measure and manage adverse effects
- Interventions
  - When inadequate MDD response, discontinue/**switch** to drug with different MOA
    - SNRI, atypical antidepressant (bupropion, vortioxetine, vilazodone, mirtazapine)
  - When + efficacy response to current AD and/or associated AEs a**ugment** with atypical antidepressants or buspirone or atypical antipsychotics eg aripiprazole, lurasidone
- Target full functional recovery and minimize adverse effects across cognitive, physical, and emotional domains

Vortioxetine vs Paroxetine in Sexual Dysfunction

- 5 week RTC in healthy adult controls. Vortioxetine (10 mg QD and placebo demonstrated significantly less TESD than paroxetine (20 mg QD), showing assay sensitivity. Neither dose of vortioxetine differed from placebo in TESD.



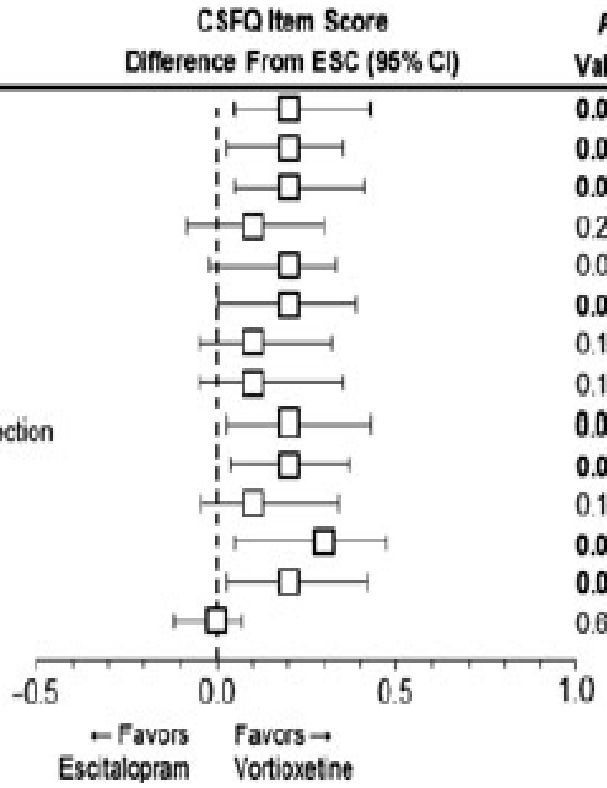
Least Square Mean Changes from Baseline CSFQ-14 Total Score

*$P \leq 0.05$ VOR vs PAR; † $P \leq 0.01$ VOR vs PAR; ‡ $P \leq 0.05$ PAR/VOR 20mg vs PLA; § $P \leq 0.01$ PAR vs PLA

Jacobsen, et al. *J Sex Med*. 2019;16(10):1638-1649

TESD with Vortioxetine vs Escitalopram

Patients with well-treated depressive symptoms with SSRIs, but experiencing TESD
Least Square Mean Difference 8 weeks after switching to vortioxetine or escitalopram



CSFQ Item	CSFQ Item Score Difference From ESC (95% CI)	*P* Value	VOR, *n*	VOR Change From Baseline (±SE)	ESC, *n*	ESC Change From Baseline (±SE)
Pleasure in Sexual Life		**0.015**	165	0.9 (0.07)	174	0.7 (0.07)
Frequency of Sexual Activity		**0.022**	165	0.5 (0.06)	174	0.3 (0.05)
Desire for Sexual Activity		**0.014**	165	0.7 (0.07)	174	0.5 (0.07)
Frequency of Sexual Thoughts		0.255	165	0.6 (0.07)	174	0.5 (0.07)
Enjoyment of Sexual Content		0.081	165	0.4 (0.06)	174	0.2 (0.05)
Pleasure Thinking About Sex		**0.049**	165	0.8 (0.07)	174	0.6 (0.07)
Become Sexually Aroused		0.143	165	0.7 (0.07)	174	0.5 (0.07)
Easily Aroused / Get an Erection		0.134	165	0.7 (0.07)	174	0.6 (0.07)
Become Lubricated / Maintain an Erection		**0.022**	165	0.8 (0.07)	174	0.6 (0.07)
Lose Interest / Painful Erection		**0.016**	165	0.4 (0.06)	174	0.2 (0.05)
Experience Orgasm / Ejaculation		0.130	165	0.7 (0.07)	174	0.6 (0.07)
Orgasm / Ejaculate When Desired		**0.015**	165	0.9 (0.06)	174	0.6 (0.05)
Pleasure / Enjoyment From Orgasm		**0.022**	165	0.7 (0.07)	173	0.5 (0.07)
Painful Orgasm		0.614	165	0.1 (0.04)	174	0.1 (0.03)

Sexual functioning was assessed by the Changes in Sexual Functioning Questionnaire-14 (CSFQ-14)
Treatment-emergent sexual dysfunction (TESD)

Jacobsen PL et al. *CNS Spectr*. 2020;25(1):50-63.

Conclusions

- Measurement-based care with validated screening tools to identify symptoms and diagnosis of MDD and employing communication strategies regarding patient preferences inform initial treatment
- Utilize longitudinal assessment from baseline and throughout treatment to differentiate MDD severity and efficacy outcomes vs adverse effects of antidepressant medications
- Implement strategies to manage persistent symptoms of MDD and adverse effects to medications

MDD, major depressive disorder

Q&A