Treatment of Major Depressive Disorder in the Patient-Centered Medical Home

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MDD

Disclosures

Dr. Gallant has indicated he has nothing to disclose relevant to this presentation

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Learning Objectives

At the conclusion of this program you should be able to:

1. Describe the current understanding of MDD as a bio-psychosocial illness
2. Describe the serotonergic system and its role in MDD
3. Describe the DSM-5 diagnostic criteria for MDD

Learning Objectives (Con't)

At the conclusion of this program you should be able to:

4. Select appropriate pharmacologic/non-pharmacologic therapies for patients with MDD and monitor treatment efficacy

5. Assess for, and, if necessary, treat residual symptoms of MDD

6. Recognize significant potential differences in presentation and treatment response that may exist in older adults with MDD compared with younger adults

Unique Opportunity

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To Register:

- See course representative at the back of the room
- Register yourself – The URL is listed on the session poster

MDD

Overview

- A minority of those with MDD are adequately treated[1]
- PCPs manage roughly ⅓ to ½ of depressed younger adults and nearly ⅔ of depressed older adults[2]
- As a bio-psychosocial disorder, MDD is most effectively treated with a multi-modal approach that includes non-pharmacological strategies
- The PCMH model can be more effective than usual care for the management of MDD[3]

1. Kessler RC, et al. *JAMA.* 2003;289(23):3095-3105.
2. Harman JS, et al. *J Gen Int Med.* 2006;21(9):926-930.
3. Unutzer J, et al. *JAMA .* 2002;288(22):2836-2845.

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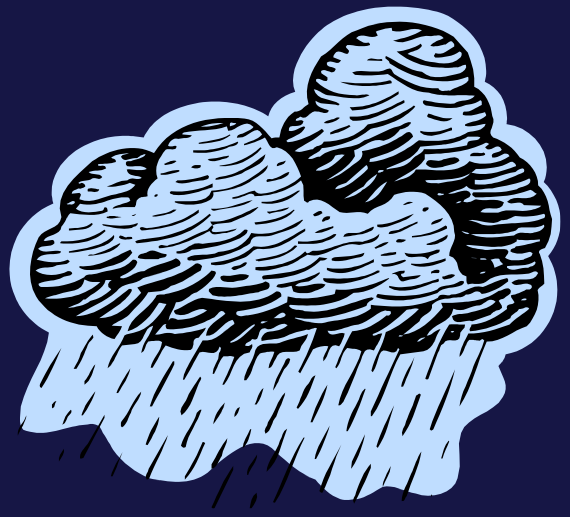
The Reality of Depression

"That the word 'indescribable' should present itself is not surprising, since it has to be emphasized that if the pain were readily describable most of the countless sufferers from this ancient affliction would have been able to confidently depict for their friends and loved ones (even their physicians) some of the actual dimensions of their torment."



William Styron,
Darkness Visible

MDD: Under-recognized & Under-treated

14 million U.S. adults

7.2M treated

6.8M untreated

3.2M adequately treated

4M poorly served

Inadequate response
Intolerant to side effects

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Etiology

- Depression recognized since ancient times
- Early 20th century: Adolf Meyer coins “psychobiology”
- Freud’s psychotherapeutic perspective
- 1950s: rise of biogenic amine theory
- Late 20th century: serotonin hypothesis
- Stress cortisol hypothesis

Etiology—Current Understanding

- Many non-monoaminergic molecular mechanisms are being explored
- NMDA antagonists show rapid alleviation of depressive symptoms
- Depression is a highly heterogeneous condition with multiple and complexly-interacting etiologies

MDD in Context of DSM-5

- Disruptive mood dysregulation disorder
- Major Depressive Disorder
- Persistent Depressive Disorder (formerly dysthymia)
- Premenstrual dysphoric disorder
- Substance/medication-induced depressive disorder
- Depressive disorder due to another medical condition
- Unspecified depressive disorder

Bipolar disorders are not included with depressive disorders in DSM-5

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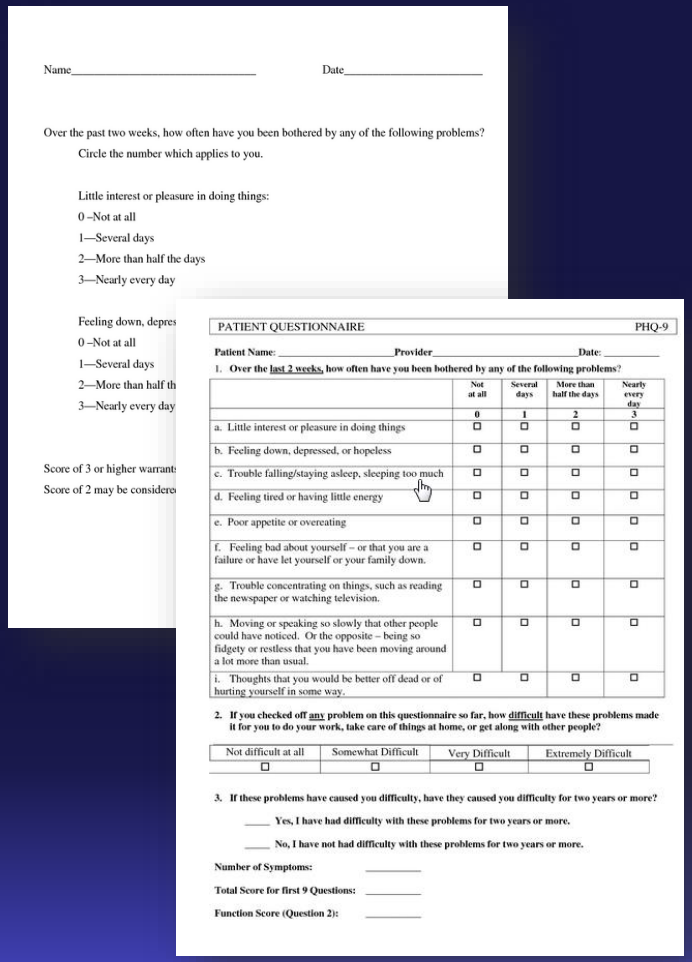
DSM-5 and Bereavement

- The “Bereavement Exclusion” was eliminated in DSM-5 because:

  - Normal grief often lasts longer than 2 mo.
  - Bereavement may precipitate a major depressive episode in vulnerable individuals
  - Bereavement-related depression responds to the same psychosocial and medication Tx as non-bereavement-related depression

Screening & Assessment of MDD

- **PHQ-2:** two simple questions about mood and anhedonia
  - 38% positive predictive value
  - 93 % negative predictive value
- **PHQ-9** commonly used for confirmation
  - 2-5 minutes to complete
  - 61 % sensitivity
  - 94 % specificity



Name_____ Date_____

Over the past two weeks, how often have you been bothered by any of the following problems?
Circle the number which applies to you.

Little interest or pleasure in doing things:
0 –Not at all
1—Several days
2—More than half the days
3—Nearly every day

Feeling down, depres
0 –Not at all
1—Several days
2—More than half th
3—Nearly every day

Score of 3 or higher warrant
Score of 2 may be considere

PATIENT QUESTIONNAIRE PHQ-9

Patient Name: _____ **Provider**_____ **Date:** _____

1. **Over the last 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
	0	1	2	3
a. Little interest or pleasure in doing things	☐	☐	☐	☐
b. Feeling down, depressed, or hopeless	☐	☐	☐	☐
c. Trouble falling/staying asleep, sleeping too much	☐	☐	☐	☐
d. Feeling tired or having little energy	☐	☐	☐	☐
e. Poor appetite or overeating	☐	☐	☐	☐
f. Feeling bad about yourself – or that you are a failure or have let yourself or your family down.	☐	☐	☐	☐
g. Trouble concentrating on things, such as reading the newspaper or watching television.	☐	☐	☐	☐
h. 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.	☐	☐	☐	☐
i. Thoughts that you would be better off dead or of hurting yourself in some way.	☐	☐	☐	☐

2. **If you checked off any problem on this questionnaire so far, 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
☐	☐	☐	☐

3. **If these problems have caused you difficulty, have they caused you difficulty for two years or more?**

____ **Yes, I have had difficulty with these problems for two years or more.**

____ **No, I have not had difficulty with these problems for two years or more.**

Number of Symptoms: _____

Total Score for first 9 Questions: _____

Function Score (Question 2): _____

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DSM-5 Diagnostic Criteria for MDD

Depressed mood or anhedonia + 4 or more symptoms most of the day, nearly every day, during a 2 week period:

- Significant weight loss (when not dieting), or weight gain, or a marked increase *or* decrease in appetite nearly every day
- Excessive sleepiness *or* insomnia
- Agitation and restlessness
- Fatigue
- Feelings of worthlessness or excessive and inappropriate guilt nearly every day
- Diminished ability to think, concentrate, or make decisions
- Recurrent thoughts of death or suicide

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Differential Diagnosis

Symptoms of depression can be caused by:

- Unrecognized thyroid disease
- Structural brain diseases such as stroke or tumor
- Parkinson's disease
- Metabolic conditions (e.g., vitamin B_{12} deficiency)
- Infections (e.g., HIV)
- Certain cancers (e.g., pancreatic cancer)

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Differential Diagnosis

- Alcohol
- Amphetamines
- Antihypertensive drugs
- Barbiturates
- Benzodiazepines
- Beta-adrenergic blockers
- Chemotherapy agents
- Cimetidine
- Corticosteroids
- Metronidazole
- Fluoroquinolone antibiotics
- H2-receptor antagonists
- Opioid pain medications
- Oral contraceptives
- Transplant anti-rejection agents

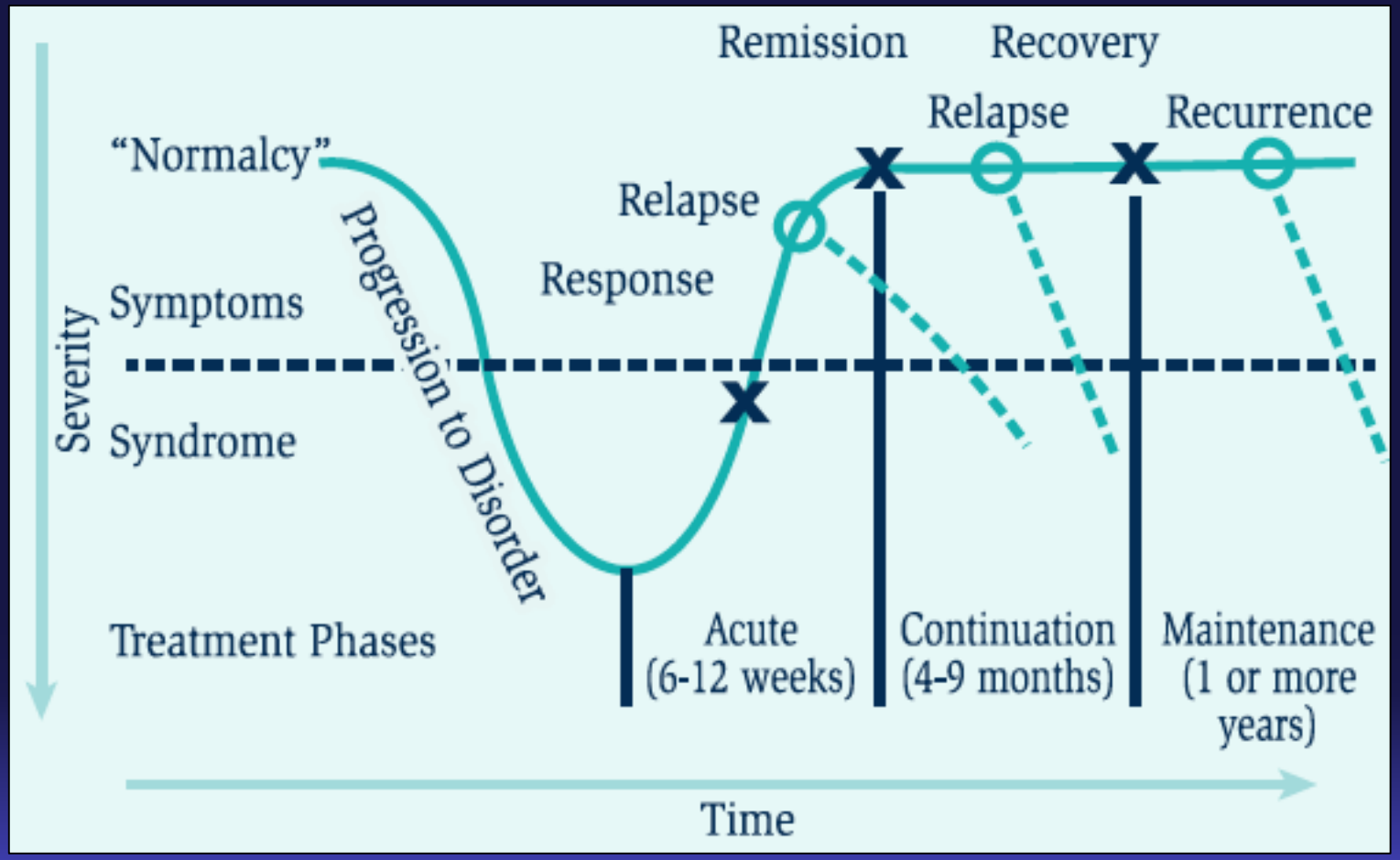
Depression & Dementia

- Patients in early phase of dementia may present with signs of depression
- Patients who are depressed may be misdiagnosed as having dementia
- Clinical features can help distinguish MDD from dementia:
  - On cognitive tasks, depressed patients generally exert less effort and report greater incapacity than patients with dementia
  - Depressed patients are more likely to report being unable to think or remember
- *If in doubt, consult a specialist in geriatric psychology*

Evaluating Suicide Risk

- Suicide risk factors:
  - Male gender, especially age ≥ 60
  - Being single or living alone
  - Prominent feelings of hopelessness
  - Psychotic features
  - Other significant psychiatric disorders
  - Access to means of suicide and the lethality of those means
  - Alcohol or other substance use

Phases of Treatment



Kupfer DJ. J Clin Psych. 1991;52S:28-34.

MDD Treatment Overview

Treatment goal: full remission of symptoms and restoration of psychosocial functioning

- Choice of initial approach depends on the severity and nature of the symptoms
- Options include:
  - ✓ Psychotherapy
  - ✓ Pharmacotherapy
  - ✓ Somatic therapies (e.g., exercise, light therapy, electro-convulsive therapy, other devices)

The Value of Psychotherapy

- Mild-to-moderate MDD - psychotherapy may be as effective as pharmacotherapy
- Psychotherapy can play a vital supporting role for more serious forms of MDD
- Different forms of psychotherapy may help address complications such as addiction or difficulty with interpersonal relationships
- Rebuilding lives often requires treating complex emotional and lifestyle issues
- Greater psychological resilience cannot be obtained by a medication

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“Prescribing” Psychotherapy

- Solid evidence supports the following types of therapy for MDD:
  - Cognitive-behavioral therapy (CBT)
  - Interpersonal psychotherapy (IPT)
  - Behavioral activation (BA)
- However, one meta-analysis found no large differences in long-term efficacy between 7 common types of psychotherapy[5]
- Psychotherapies generally have longer-lasting effects than antidepressants

5. Cuijpers P, van Straten A, Andersson G, van Oppen P. Psychotherapy for depression in adults: a meta-analysis of comparative outcome studies. *Journal of Consulting and Clinical Psychology.* 2008;76(6):909-922.

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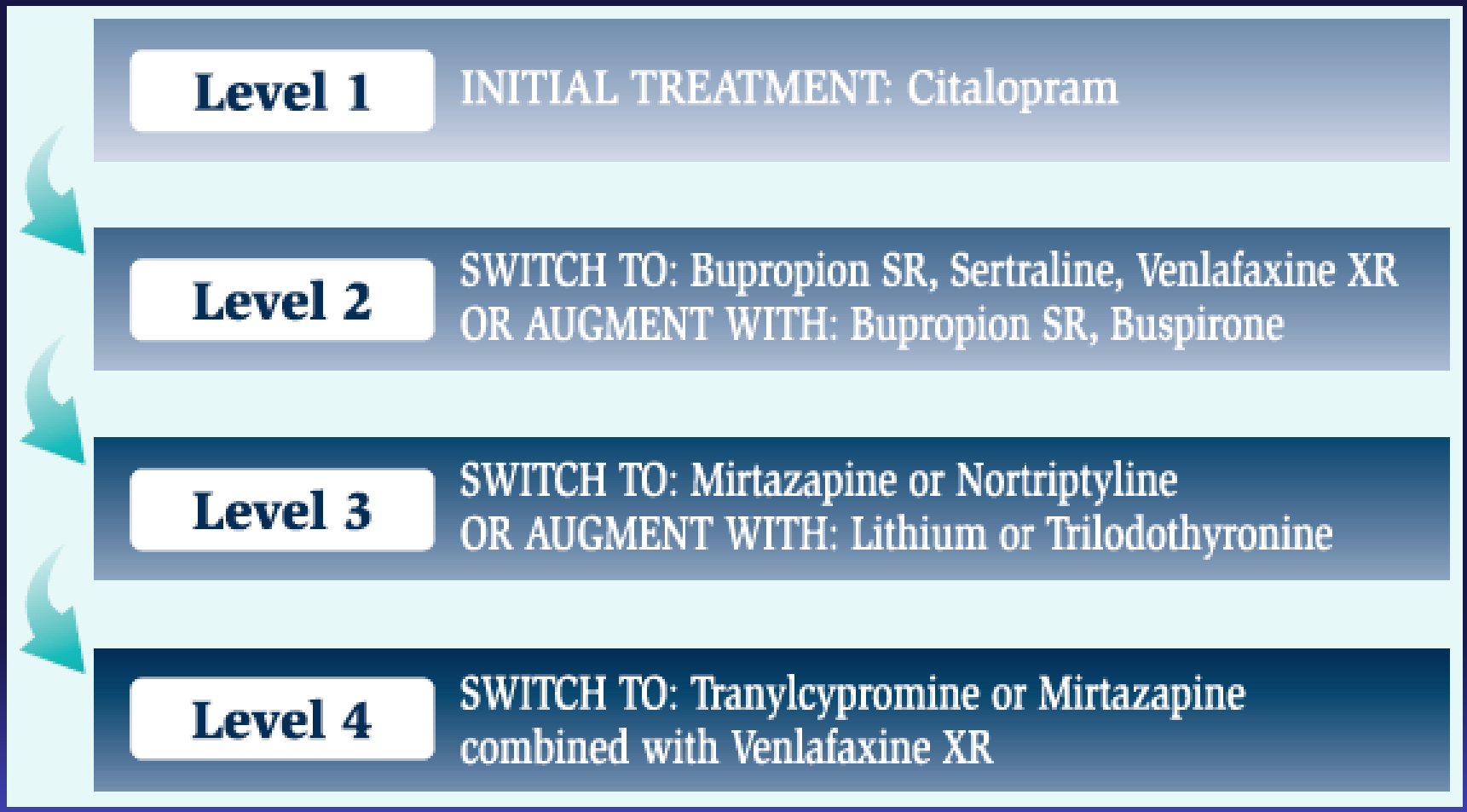
Pharmacotherapy for MDD

- Antidepressants are:
  - An option for mild-to-moderate MDD
  - Recommended for moderate-to-severe MDD (unless patient is expected to undergo ECT)

- Decision must be weighed carefully because:
  - Side effects may occur
  - Average efficacy is relatively modest
  - Discontinuation is seldom as easy as initiation

Lessons From STAR*D



1. Rush AJ. Am J Psychiatry. 2006;163(11):1905-1917.

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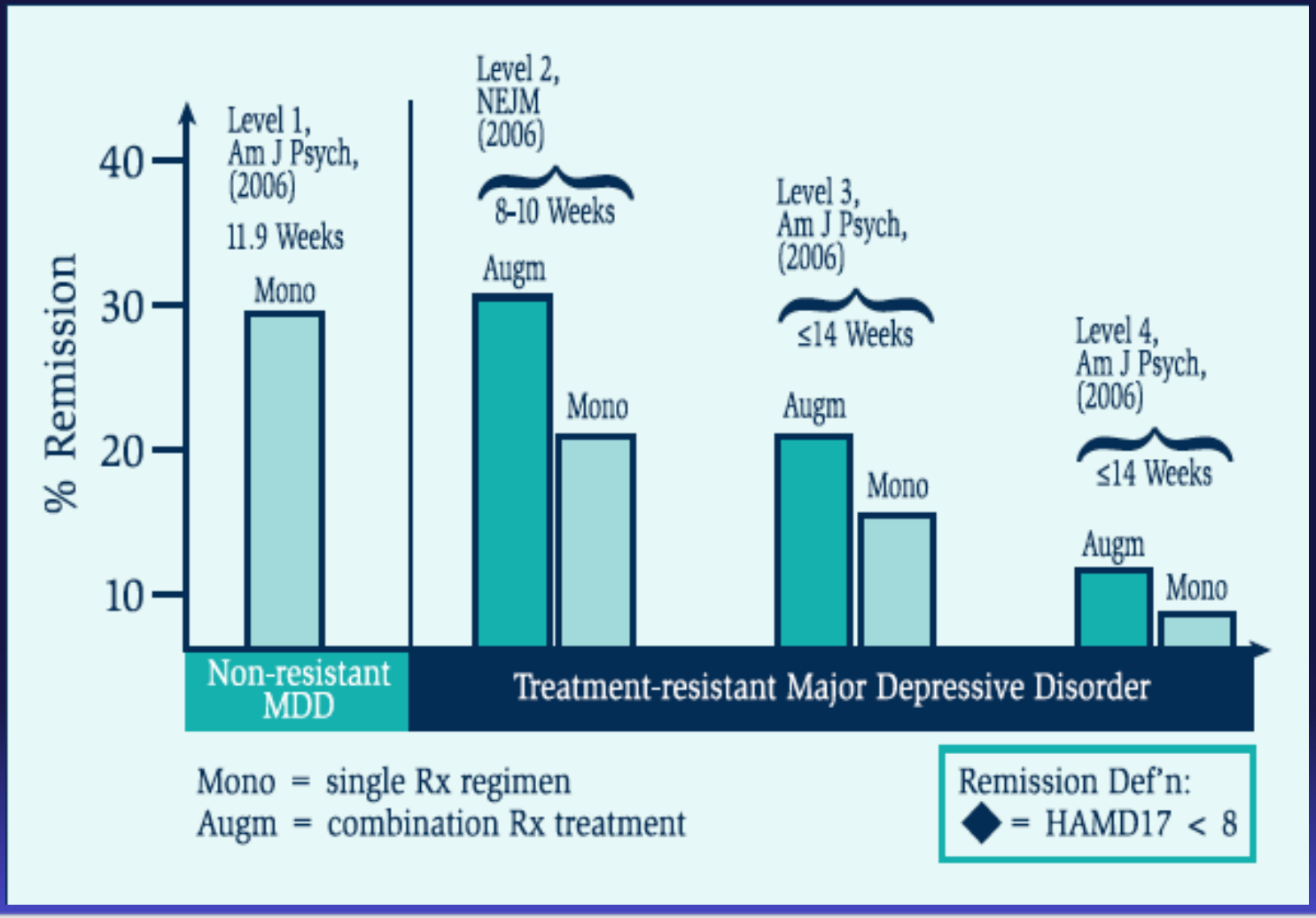
Lessons From STAR*D



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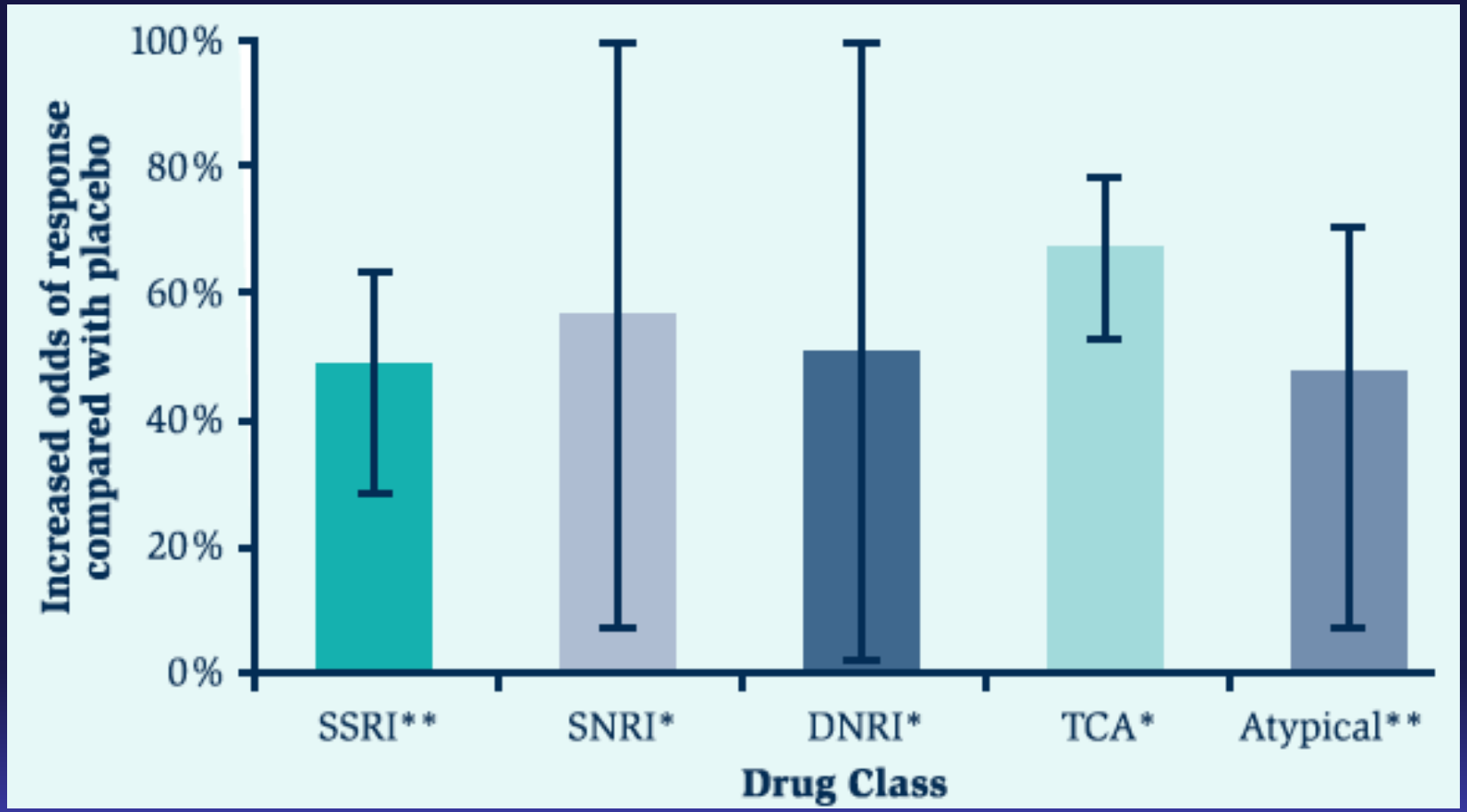
Pharmacologic Treatments: Overview



* Nelson JC, et al. Am J Geriatric Psych. 2008;16:558-567.
** Wilson K, et al. Cochrane Database Syst Rev. 2001;2:CD000561.

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Choosing an Antidepressant

Factors to consider

- Side effect profile
- Patient preference
- Nature of prior response to medication
- Safety and tolerability
- Co-occurring psychiatric/general medical conditions
- Potential drug interactions
- Half-life
- Cost

Selective Serotonin Reuptake Inhibitors

Currently-available SSRIs:

- Fluoxetine (Prozac)
- Sertraline (Zoloft)
- Paroxetine (Paxil)
- Fluvoxamine (Luvox)
- Citalopram (Celexa)
- Escitalopram (Lexapro)
- Vilazodone (Viibryd)
- Vortioxetine (Brintellix)

Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)

Currently-available SNRIs:

- Venlafaxine (Effexor, Efexor)
- Desvenlafaxine (Pristiq)
- Duloxetine (Cymbalta)

Dopamine-Norepinephrine Reuptake Inhibitors (DNRIs)

Currently-available DNRI:

- Bupropion (Wellbutrin)

Other Antidepressants

Currently-available:

- Mirtazapine (Remeron, others)
- Nefazodone (available as generic)
- Trazodone (Desyrel, others)

Combination Treatment

- Adding a second antidepressant of a different class can be beneficial
- Most commonly-studied combination is an SSRI with a TCA
- Some studies have found benefit with combination of an SSRI with venlafaxine, bupropion, or mirtazapine

Adjunctive Agents

- Lithium
- Thyroid hormone supplementation (even in euthyroid patients)
- Atypical antipsychotics
- Psychostimulants

Treatment-Resistance/Residual Symptoms

Contributing Factors [6]

- Patient –non adherence
- Inadequate treatment
- Undesirable/intolerable side effects
- Genetic variations in drug responses
- Incorrect diagnosis
- Comorbid substance abuse; comorbid personality disorder; history of physical, sexual, or emotional abuse
- Cognitive impairment; neurological disease
- Biological treatments do not address all symptoms or all types of depression

6. Salzman C. *JAMA.* 2006;295:318–323.

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Strategies To Address Treatment-Resistance/Residual Symptoms

- Look for environmental/ social stresses that might be exacerbating/ contributing to symptoms
- Consider optimizing (typically raising) medication dose or intensity of psychotherapy
- Re-screen for substance use, bipolar, and anxiety disorders
- Switch to a different antidepressant
- Augment with another medication
- Change to/augment with psychotherapy
- Consider psychiatric consultation

Biomedical Devices for MDD

- Electroconvulsive Therapy
- Transcranial Magnetic Stimulation
- Vagus Nerve Stimulation

Patient-Centered Management of MDD

Supportive data from:

- PRISMe study
- Nurse Telehealth study
- IMPACT study

Mental health professionals can be integrated into practice by:

- Hiring a psychiatric nurse practitioner, either full or part-time
- Using “physician extenders” such as mental health social workers, psychologists, or counselors

Case Study #1: Marquesa

Age: 42
BMI: borderline underweight
PHQ-9 score: 11
Non-smoker, moderate alcohol (~1-2 drinks/day)

Complaint: weight loss, “*ataque de nervios*”

Notes: takes “herbs” for symptoms

Case Study #1: Marquesa

Question 1: Which of the following would *not* be recommended as a next step?

A. Administer the PHQ-2 or PHQ-9 in either English or Spanish, depending on patient preference
B. Take a detailed psychosocial history
C. Prescribe an SSRI antidepressant with a relatively long half-life
D. Provide a patient-education handout about depression in either English or Spanish, depending on patient preference

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D. Provide a patient-education handout about depression in either English or Spanish, depending on patient preference

Answer: C

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Case Study #1: Marquesa

- You provide advice about nutrition, exercise, sleep, and avoiding alcohol. Ask her to return in 4 weeks
- Marquesa is subdued. Reports marital problems
- Supplement she takes contains ephedra
- You recommend:
  - Consult with psychiatric nurse
  - Stopping supplement
  - Generic citalopram, 20 mg/day

Case Study #1: Marquesa

Discussion Questions

1. What cultural barriers might exist that could affect Marquesa's ability to adhere to the medication regimen?
2. What kinds of follow-up attention could you or a "physician extender" provide to support Marquesa?
3. What behavioral counseling recommendations could you make?

Case Study #1: Marquesa

- Rx refill because husband flushed her medications down the toilet
- At 5 weeks, Marquesa appears more energetic, but struggling
- Asks for a sleeping pill

Case Study #1: Marquesa

Question 2: Which of the following would be an appropriate way to respond to Marquesa's request?

A. Switch from citalopram to trazodone
B. Suggest she try over-the-counter melatonin and advise about sleep hygiene
C. Prescribe zolpidem 5 mg/prn
D. Lower the dose of citalopram

Case Study #1: Marquesa

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D. Lower the dose of citalopram

Answer: B

Case Study #2: Flora

Age: 71
BMI: normal
PHQ-9 score: 16
O_2 saturation: normal

Complaint: Diffuse aches and pains; fatigue

Co-morbid conditions: COPD
Medications:

- ✓ Long-acting inhaled anticholinergic
- ✓ Short-acting beta-agonist

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Case Study #2: Flora

Question 1: Which of the following might be a reasonable first choice of antidepressant for this patient?

A. Phenelzine
B. Imipramine
C. Nefazodone
D. Fluoxetine

Case Study #2: Flora

Question 1: Which of the following might be a reasonable first choice of antidepressant for this patient?

A. Phenelzine
B. Imipramine
C. Nefazodone
D. Fluoxetine

Answer: D

Case Study #2: Flora

- You start Flora fluoxetine (10 mg/day), titrated to 20 mg/day after 2 weeks
- PHQ-9 after four weeks: 7
- You raise the dose to 40 mg/day
- After another month, Flora says she feels somewhat better, though not sleeping well, joints hurt, and doesn’t feel like exercising

Case Study #2: Flora

Question 2: What next-step strategy might be appropriate for Flora at this point?

A. Cross-titrate to trazodone
B. Increase fluoxetine to 60mg and add trazodone
C. Augment with zolpidem 5 mg/prn
D. Focus on pulmonary function by prescribing an antibiotic and theophylline

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Answer: B

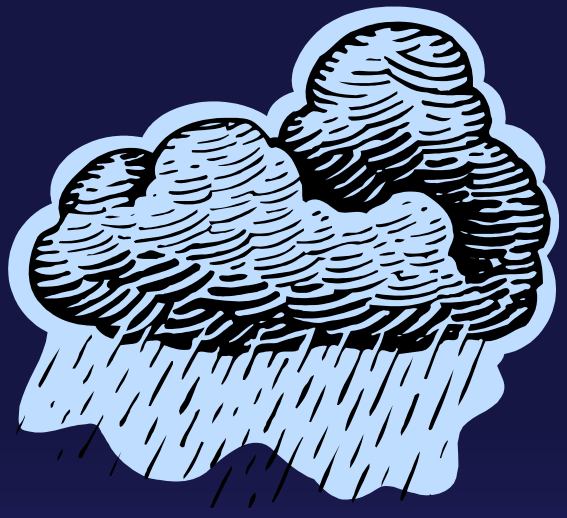
Conclusions

1. MDD is a challenge and an opportunity for family physicians, who manage more than half of adults treated for MDD

2. Management of MDD in the context of a PCMH can be implemented without adding burden

3. A wide range of psychotherapeutic, pharmacologic, and medical device options exist to treat MDD

Discussion



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