

Depression: Diagnosis and Treatment

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Diagnosis

Depressive Syndromes (DSM V)

- Major Depressive Disorder
- Persistent Depressive Disorder (Dythymia)
- Premenstrual Dysphoric Disorder
- Substance-Induced Depressive Disorder
- Depression due to General Medical Condition
- Disruptive Mood Dysregulation Disorder
- Other Specified Depressive Disorder

Major Depressive Episode

- Depressed Mood
and/or
- Loss of interest/pleasure (anhedonia)
- Weight loss/gain
- Insomnia/hypersomnia
- Psychomotor agitation/retardation
- Loss of energy
- Feelings of worthlessness, excessive guilt
- Diminished concentration
- Recurrent thoughts of death/suicide

Major Depressive Disorder

Symptoms of a Major Depressive Episode

Duration: \geq 2 weeks

Depressed Mood and/or Anhedonia

(and \geq 4 other symptoms)

A change from previous functioning

Not due to General Medical Condition,

Substance Use/Abuse

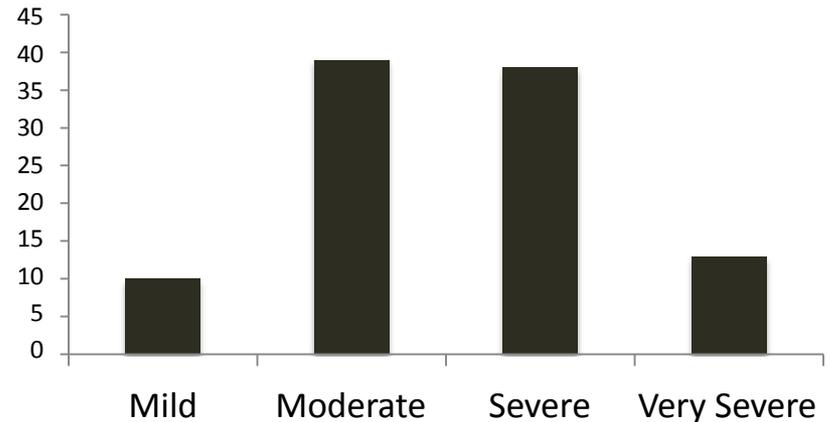
MDD Specifiers

- With anxious distress
- With mixed features
- With melancholic features
- With atypical features
- With psychotic features
 - Mood congruent
 - Mood incongruent
- With catatonia
- With peripartum onset
- With seasonal pattern

MDD

US lifetime prevalence: 16%
US 12 month prevalence: 6.6%

| | |
|-------------|-----|
| Mild | 10% |
| Moderate | 39% |
| Severe | 38% |
| Very Severe | 13% |



Degree of role impairment: 59% severe/very severe

Mean duration of an MDD episode: 16 weeks

52% were treated

42% of these were adequately treated

22% of total had adequate treatment

Risks *for* Depression

- Genetics
- Environment
- Situation
 - Loss
 - Role transition
- Medical illness
- History of trauma as a child
- Personality style/disorder (neuroticism)
- Drug abuse

Risks *of* Depression

Poor compliance with medical treatment

Cardiovascular

1.8 RR for future CHD in depressed pt

1.8 RR for hypertension

Incr risk of CVA

Metabolic/Endocrine

3.15 RR of depression leading to diabetes spectrum

Dementia

Late life depression associated with dementia:

All causes 1.85; Alzheimers 1.65; Vascular Dementia 2.5

Persistent Depressive Disorder (Dysthymia)

Amalgam of two DSM IV diagnoses:

Dysthymic Disorder + Chronic Major Depressive Episode

Depressed mood for ≥ 2 years

With ≥ 2 symptoms:

- Poor appetite/overeating

- Insomnia/hypersomnia

- Anergia

- Low self-esteem

- Poor concentration

- Feeling of hopelessness

Dysthymia



Dysthymia + Major Depressive Episode = 'Double Depression'



Premenstrual Dysphoric Disorder

- Depressive Symptoms (≥ 5) associated with the majority of menstrual cycles over ≥ 12 months

Primary Symptoms

≥ 1

- Marked affective lability
- Marked irritability/anger
- Marked depressed mood

Secondary Symptoms

≥ 1

- Anhedonia
- Difficulty with concentration
- Anergia
- Change in appetite
- Hypersomnia/Insomnia
- Sense of being overwhelmed
- Physical sx (breast tenderness, joint pain, bloating, weight gain)

Substance-Induced Depressive Disorder

- Depressive symptoms *persist* beyond the expected physiological effect.
- Onset of symptoms is *within one month* of last use.
- Types: Alcohol, phencyclidine, other hallucinogens, inhalants, opioids, sedative-hypnotics, amphetamine/other stimulants, cocaine, other.
- Differential Dx: Substance intoxication or withdrawal

Substance-induced Depressive Disorder¹⁴

- Iatrogenic: due to prescribed medications
 - Interferon
 - Steroids
 - Betablockers
 - Isotretinoin/Accutane
 - Chemotherapy

Depression Due to General Medical Condition

- Prominent and persistent period of depressed mood and/or anhedonia
- Specifiers:
 - With depressive features
 - With Major Depressive-like features
 - With Mixed features

Depression Due to General Medical Condition¹⁶

- Neurological
 - CVA
 - Parkinson's
 - Huntington's
 - Multiple Sclerosis
 - TBI
- Endocrine
 - Hypothyroidism
 - Cushing's

Other

- SLE
- Liver disease

Other Specified Depressive Disorder

- Recurrent Brief Depression
 - 2-13 days
 - At least once a month (not associated with menses)
 - For >12 months
- Short-duration Depressive Episodes
 - 2-13 days
 - ≥ 4 symptoms of MDE
- Depressive Episodes with Insufficient Symptoms
 - Depressed Affect + ≥ 1 symptom of MDE

Demoralization

- Persistent inability to cope
- Feelings of hopelessness, helplessness, meaninglessness, subjective incompetence, low self-esteem
- Feel powerless to change
- Giving up-Given up (Engel)
- Less associated with anhedonia (MDE)

Mnemonic for Depression: 'Sig E Caps'

- Sleep
- Interest
- Guilt

- Energy

- Concentration
- Appetite
- Psychomotor
- Suicidality

Screening Instruments

Self Report

PHQ-9

Beck Depression
Inventory

Clinician-completed

Hamilton Depression
Rating Scale

Patient Health Questionnaire (PHQ-9)

Name: _____ Date: _____

Over the *past 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 |

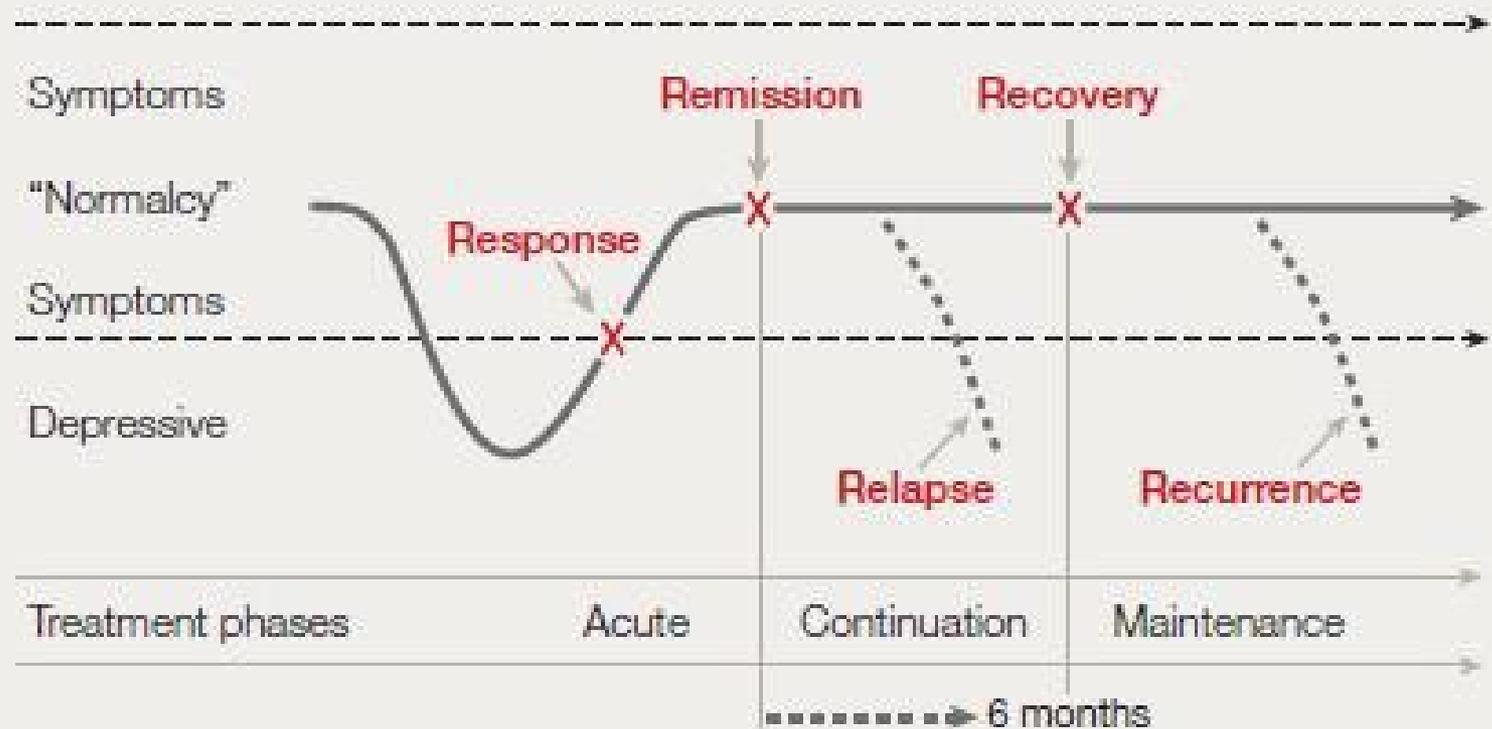
add columns: + +

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

0-4 remission
5-9 mild
10-14 moderate
15-19 moderately severe
20-27 severe

Treatment

Response, Remission, Recovery, Relapse, Recurrence



Treatment of Depression

- Somatic Treatments

- Medications
- ECT
- Phototherapy
- Vagal Nerve Stimulation
- Transcranial Magnetic Stimulation

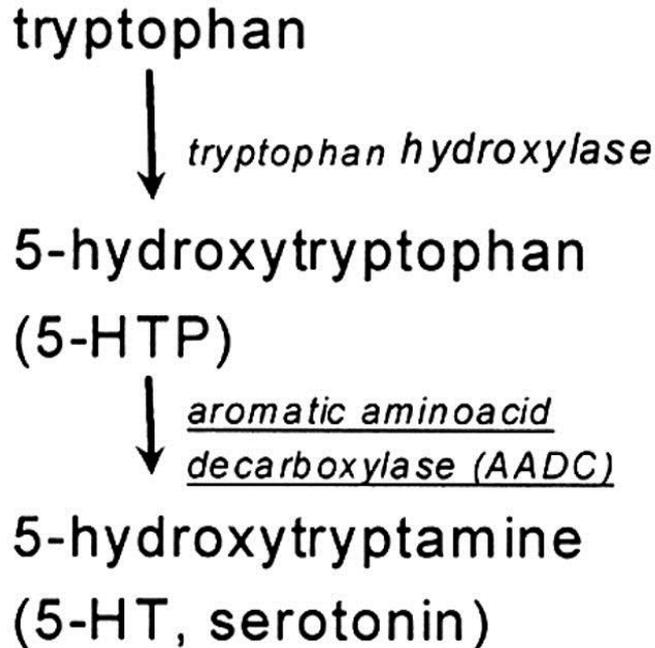
Psychotherapy

- Cognitive Therapy
- Interpersonal Psychotherapy

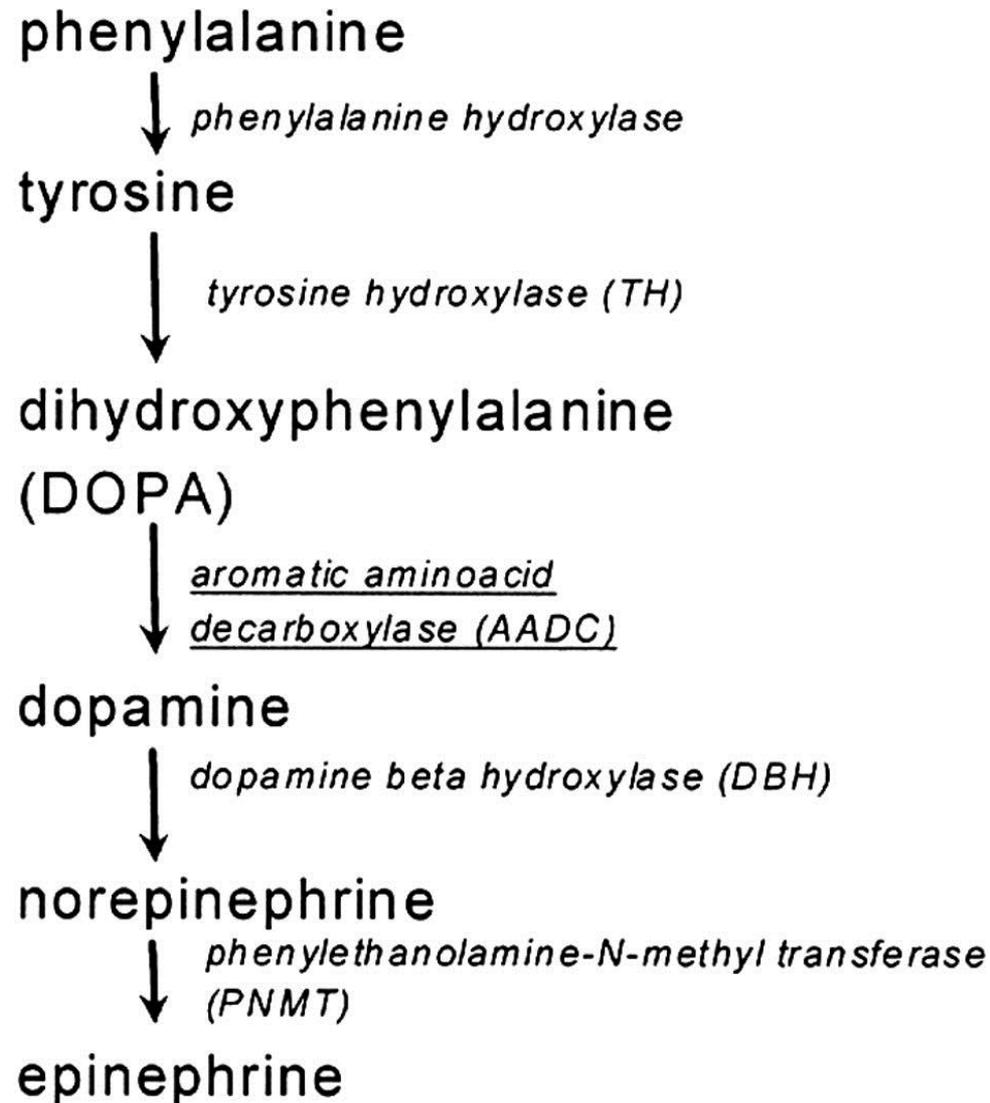
Antidepressant Medication Classes

- Tricyclic Antidepressants (TCAs)
- Monoamine Oxidase Inhibitors (MAOIs)
- Serotonin-Specific Reuptake Inhibitors (SSRIs)
- Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs)
- Norepinephrine and Dopamine Reuptake Inhibitors (NDRIs)
- Serotonin Antagonist-Reuptake Inhibitors (SARIs)
- Alpha 2 Adrenergic Blockers

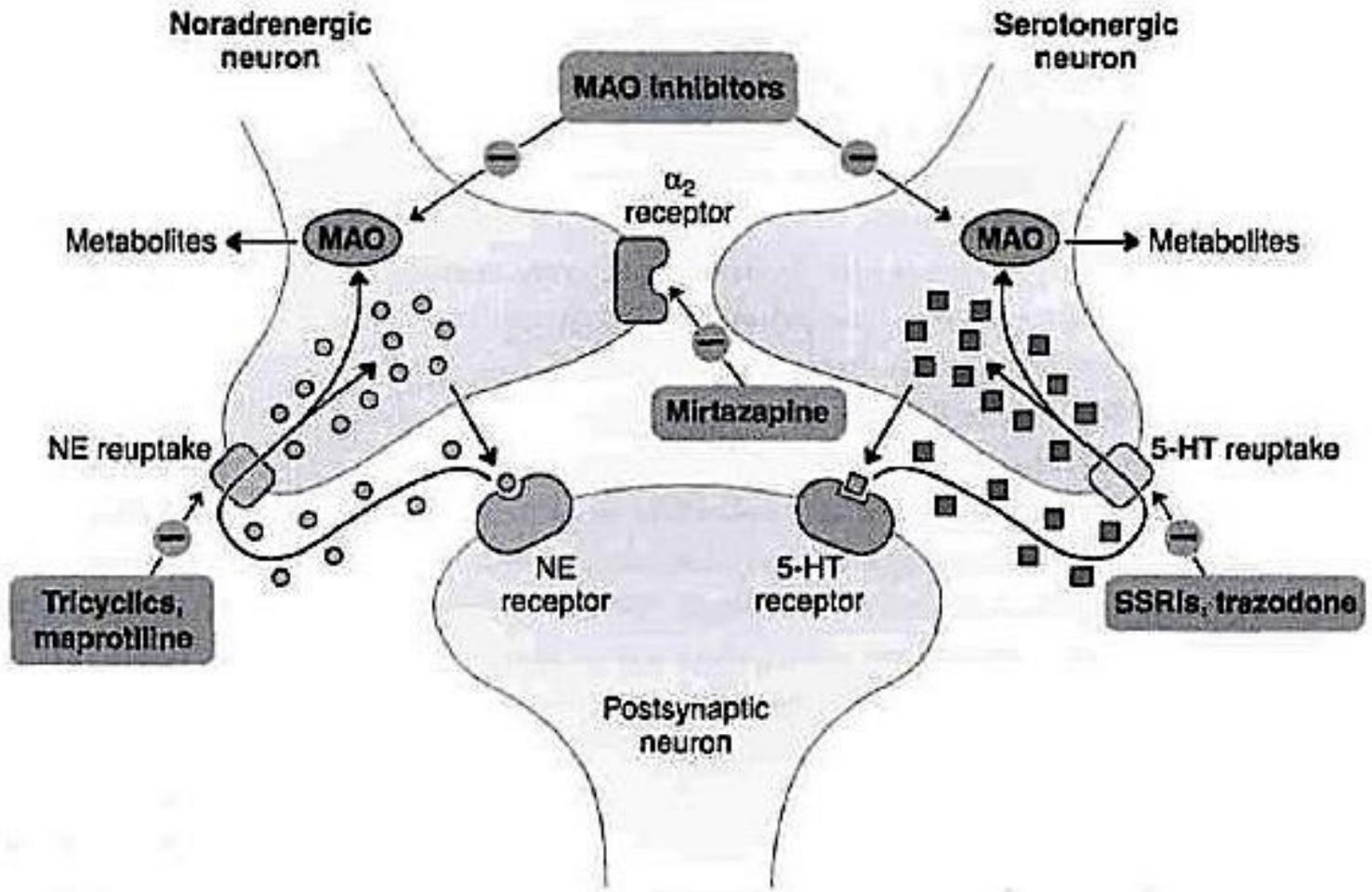
Serotonin synthesis



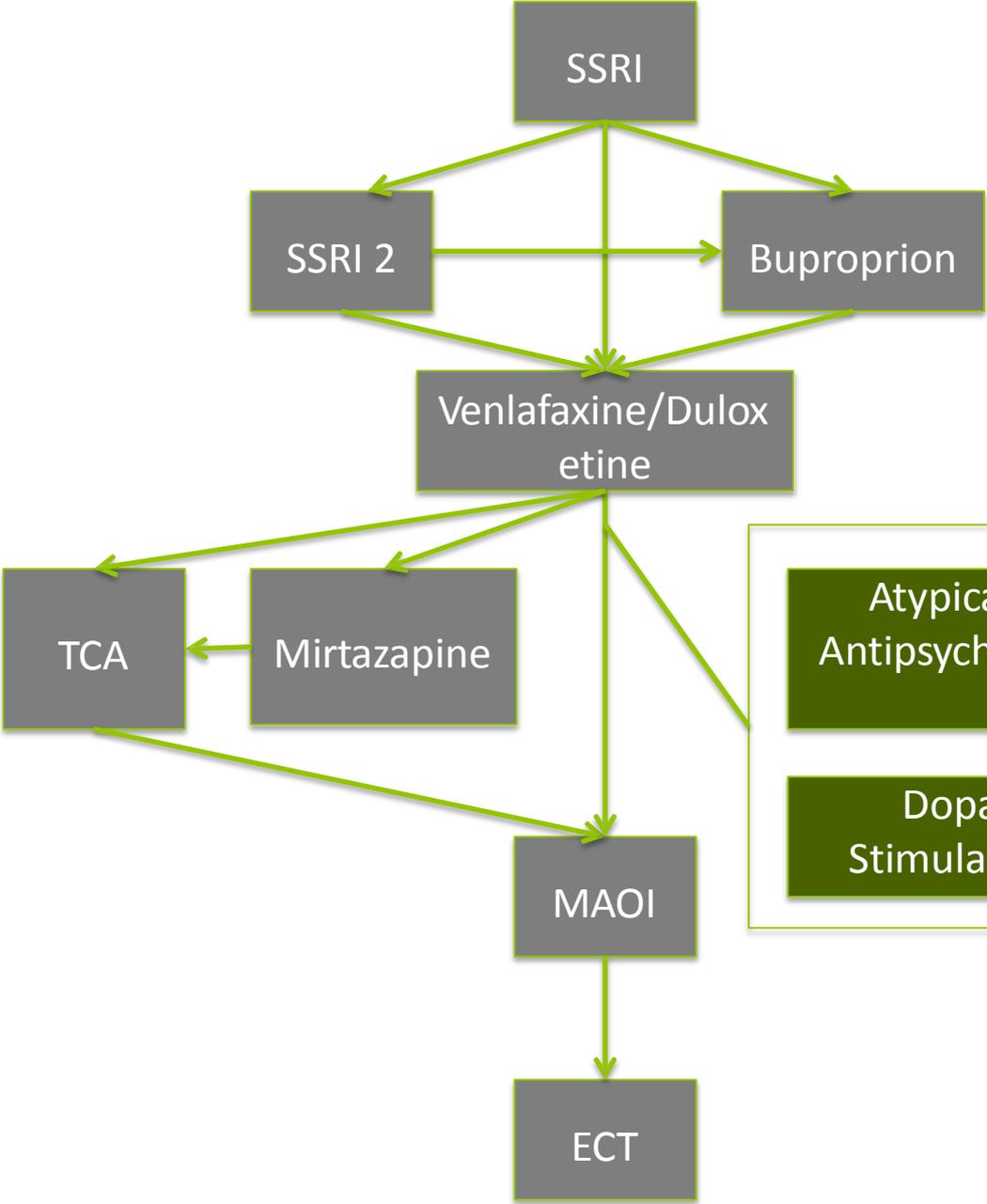
Catecholamine synthesis



Sites of Antidepressant Drug Action



MDD Algorithm



Augmentation Agents

| | | |
|--|----------------------|---------|
| Atypical Antipsychotic | Thyroid hormone (T3) | Lithium |
| Dopamine agent: Stimulant, Pramipexole | L-methylfolate | |

Serotonin-Selective Reuptake Inhibitors

- Fluoxetine/Prozac (20-60 mg/d)
- Sertraline/Zoloft (50-200 mg/d)
- Paroxetine/Paxil (20-60 mg/d)
- Fluvoxamine/Luvox (50-200 mg/d)
- Citalopram/Celexa (20-40 mg/d)
- Escitalopram/Lexapro (10-20 mg/d)

Serotonin Syndrome

- Abdominal pain
- Diarrhea
- Elevated blood pressure
- Delirium
- Myoclonus
- Increased motor activity
- Irritability/
Hostility
- Mood change

- Hyperpyrexia
- Cardiovascular Shock
- Death

Norepinephrine and Serotonin Reuptake Inhibitors (SNRIs)

- Venlafaxine/Effexor (75-225 mg/d; Extended Release)
 - Duloxetine/Cymbalta (60-120 mg/d)
- Side Effects
- Weight gain, sexual dysfunction, headaches, GI, elevated
 - blood pressure
 - Discontinuation Syndrome

Norepinephrine and Dopamine Reuptake Inhibitor (NDRI)

- **Bupropion/Wellbutrin** SR 150-450 mg/d
XL 300 mg/d

Side effects

- Seizures (caution in eating disorders, h/o seizure do)

Alpha 2 Adrenergic Blockers

- Mirtazapine/Remeron (15-45 mg/d)

Side Effects: Sedation, weight gain

Tricyclic Antidepressants (TCAs)

- Imipramine/Tofranil
- Amitriptyline/Elavil
- Clomipramine/Anafranil
- Doxepin/Sinequan

- Desipramine/Norpramin
- Nortriptyline/Pamelor
- Protriptyline/Vivactil

- Maprotiline/Ludiomil
- Amoxapine/Asendin
- Trimipramine/Surmontil

Monoamine Oxidase Inhibitors (MAOIs)

- Phenelzine/Nardil (45 -90 mg/d)
- Tranylcypromine/Parnate (30-60 mg/d)
- Isocarboxazid/Marplan (30-60 mg/d)

Effective antidepressants (third-line)

Side effects: weight gain, orthostasis, sexual dysfunction, dry mouth, headache, insomnia/somnolence

Risks: lethal in overdose; hypertensive crisis, stroke.

Drug-Drug Issues:

Food/drink with Tyramine (hypertensive crises)

meperidine/Demerol and SSRIs (Serotonergic Syndrome)

Stimulants, cold remedies (hypertensive crisis)

Phenylalanine

Tyrosine

Tyramine

HPA

Tyramine-rich diet

Catecholamine release
DA, NE, EP

Hypertensive
Crisis

Aged cheese
Dry Sausage
Beer/Red wine
Fava beans
Smoked fish
Liver

MAO A

Augmentation Strategies

- Lithium (600-1200 mg/d)
- Thyroid hormone (T3) (12.5-50 mcg/d)
- Dopamine agonists
 - Stimulant
 - Pramipexole/Mirapex (0.25-5 mg/d)
- Antipsychotic
 - Aripiprazole (2.5-10 mg/d)
 - Olanzapine (+ Fluoxetine) (6/12.5-12/50 mg/d)
- L-methylfolate/Deplin (7.5-15 mg/d)
- TCAs

STAR*D RESULTS

| STEP | TREATMENT | REMISSION RATE |
|------|-----------|----------------|
|------|-----------|----------------|

| | | |
|---|------------|-------|
| 1 | Citalopram | 36.8% |
|---|------------|-------|

| | | |
|---|---|-------|
| 2 | Switch: Bupropion, CT, Sertraline, Venlafaxine Augment: Bupropion, Buspirone, CT | 30.6% |
|---|---|-------|

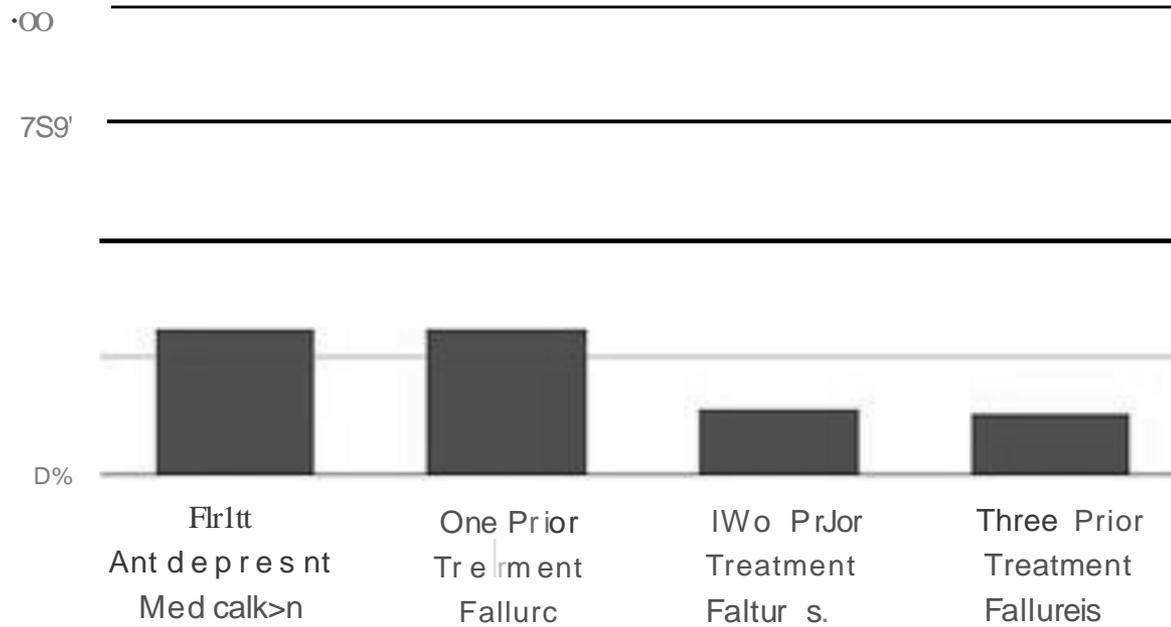
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|---|---|-------|
| 3 | Switch: Mirtazapine, Nortriptyline Augment: lithium, thyroid hormone | 13.7% |
|---|---|-------|

| | | |
|---|--|-------|
| 4 | Switch: Tranylcypromine, Venlafaxine + Mirtazapine | 13.0% |
|---|--|-------|

STAR 0 Study Results Demonstrate Limited Rates of Remission with Current Antidepressant Medications

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*Determined by
QIDS-SR 16 Rating
Scale



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