

# 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

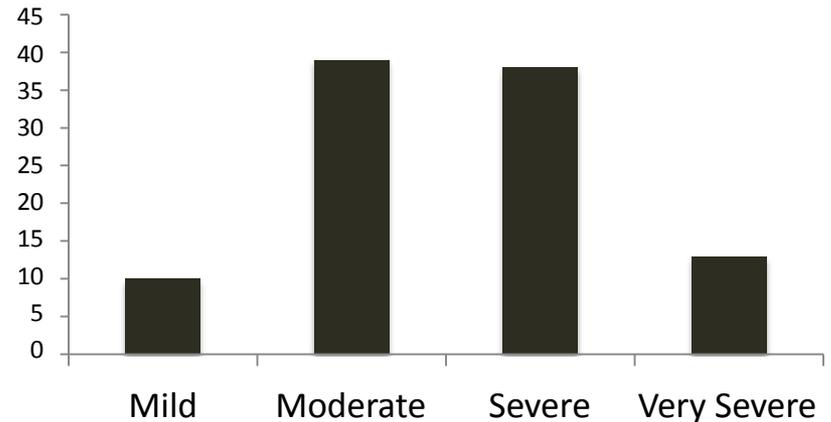
# MDD Specifiers

- 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  $\geq 2$  years

With  $\geq 2$  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 ( $\geq 5$ ) associated with the majority of menstrual cycles over  $\geq 12$  months

## Primary Symptoms

$\geq 1$

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

## Secondary Symptoms

$\geq 1$

- 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 Disorder<sup>14</sup>

- 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 Condition<sup>16</sup>

- 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
  - $\geq 4$  symptoms of MDE
- Depressive Episodes with Insufficient Symptoms
  - Depressed Affect +  $\geq 1$  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

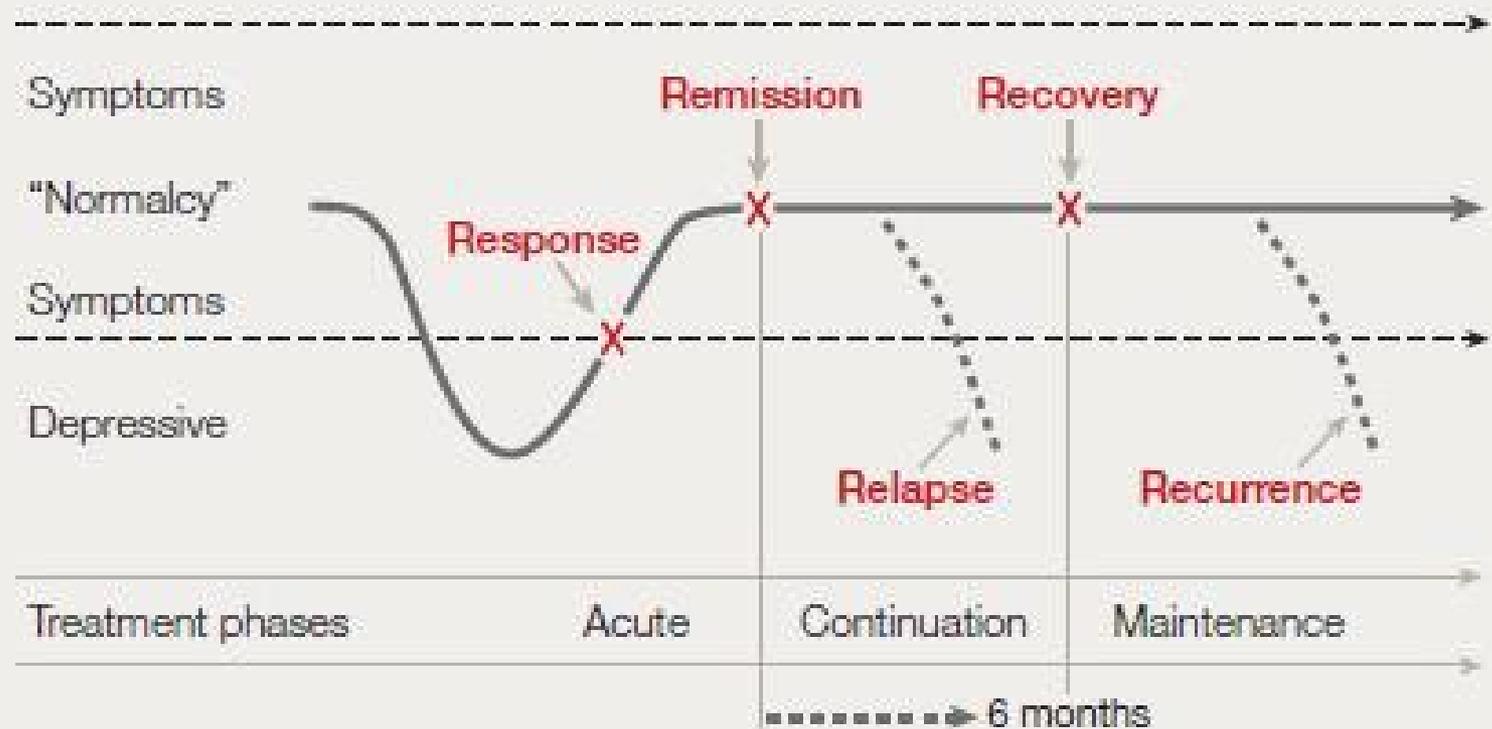
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(Healthcare professional: For interpretation of TOTAL, please refer to accompanying scoring card.) Total:

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

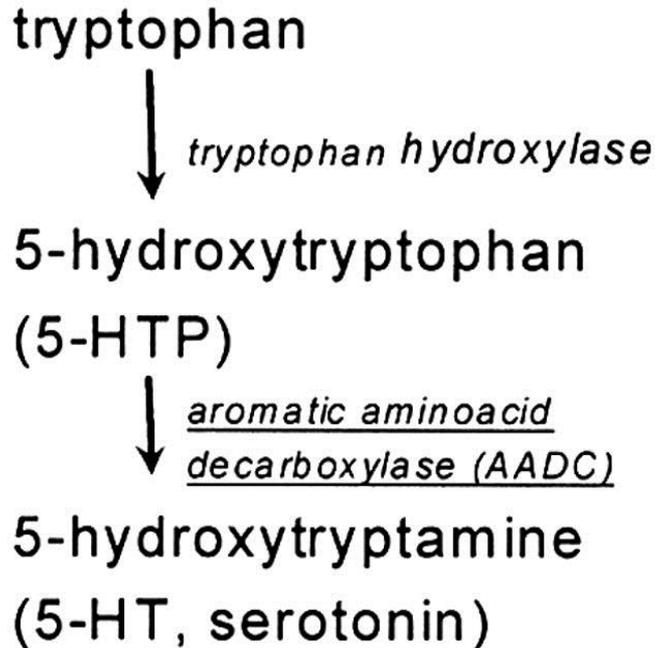
## Psychotherapy

- Cognitive Therapy
- Interpersonal Psychotherapy

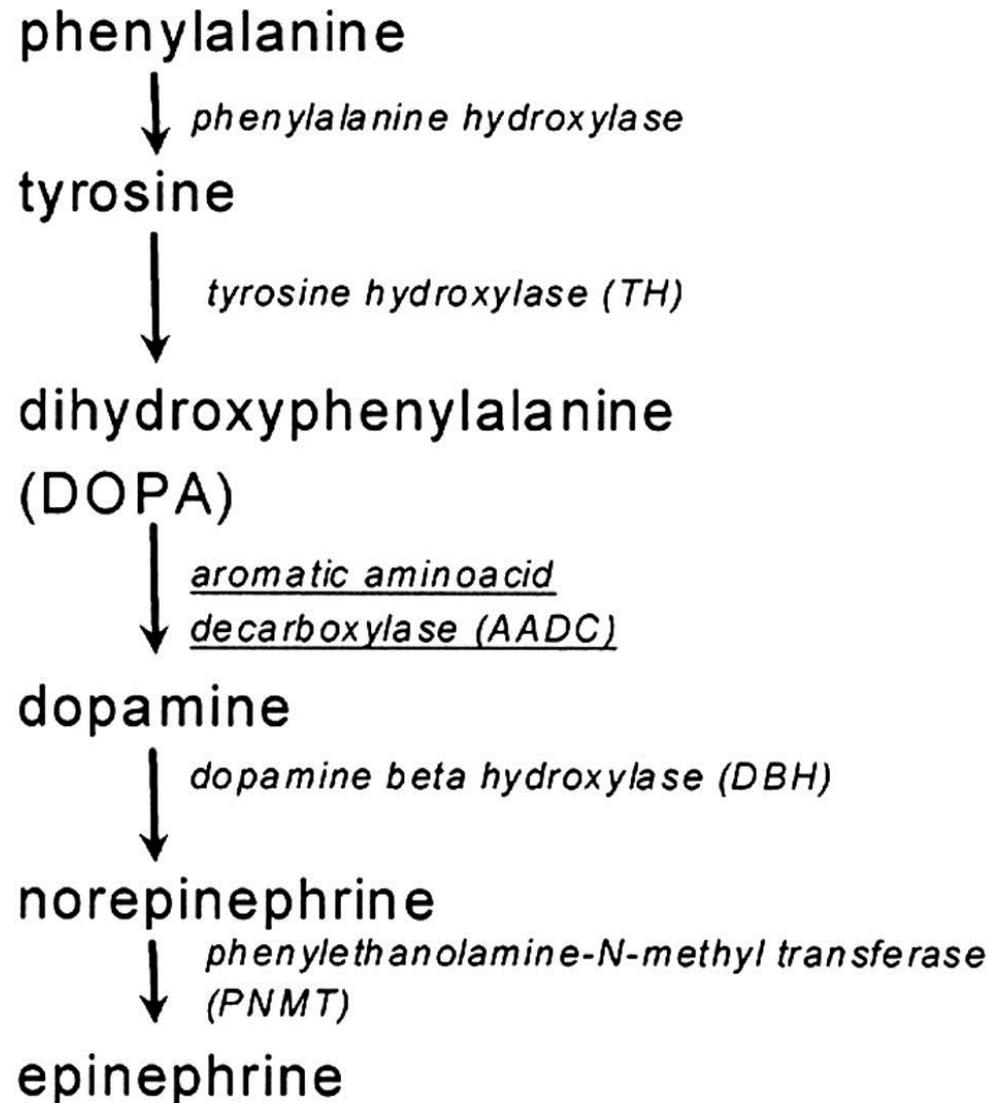
# Antidepressant Medication Classes

- 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

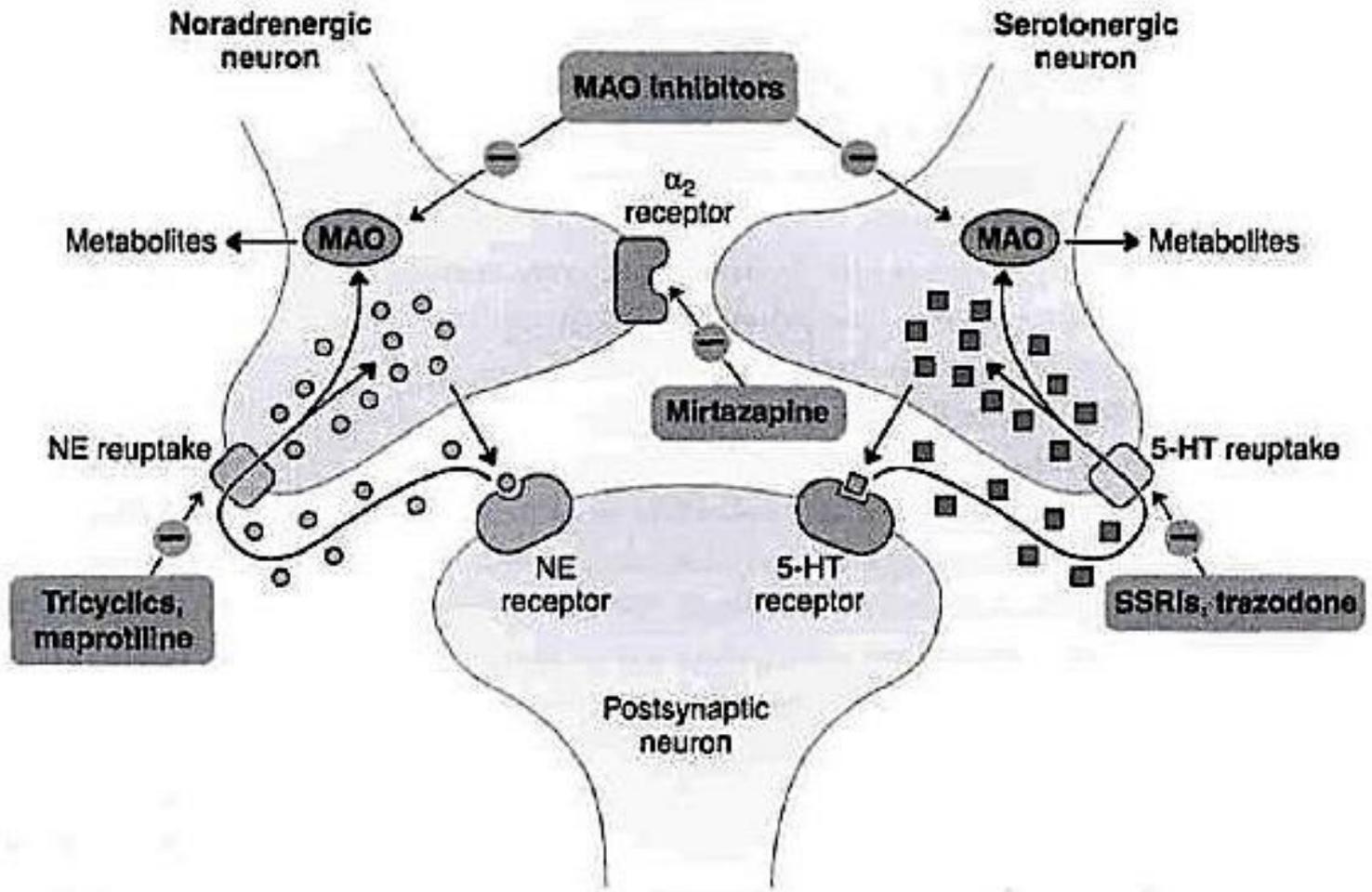
## Serotonin synthesis



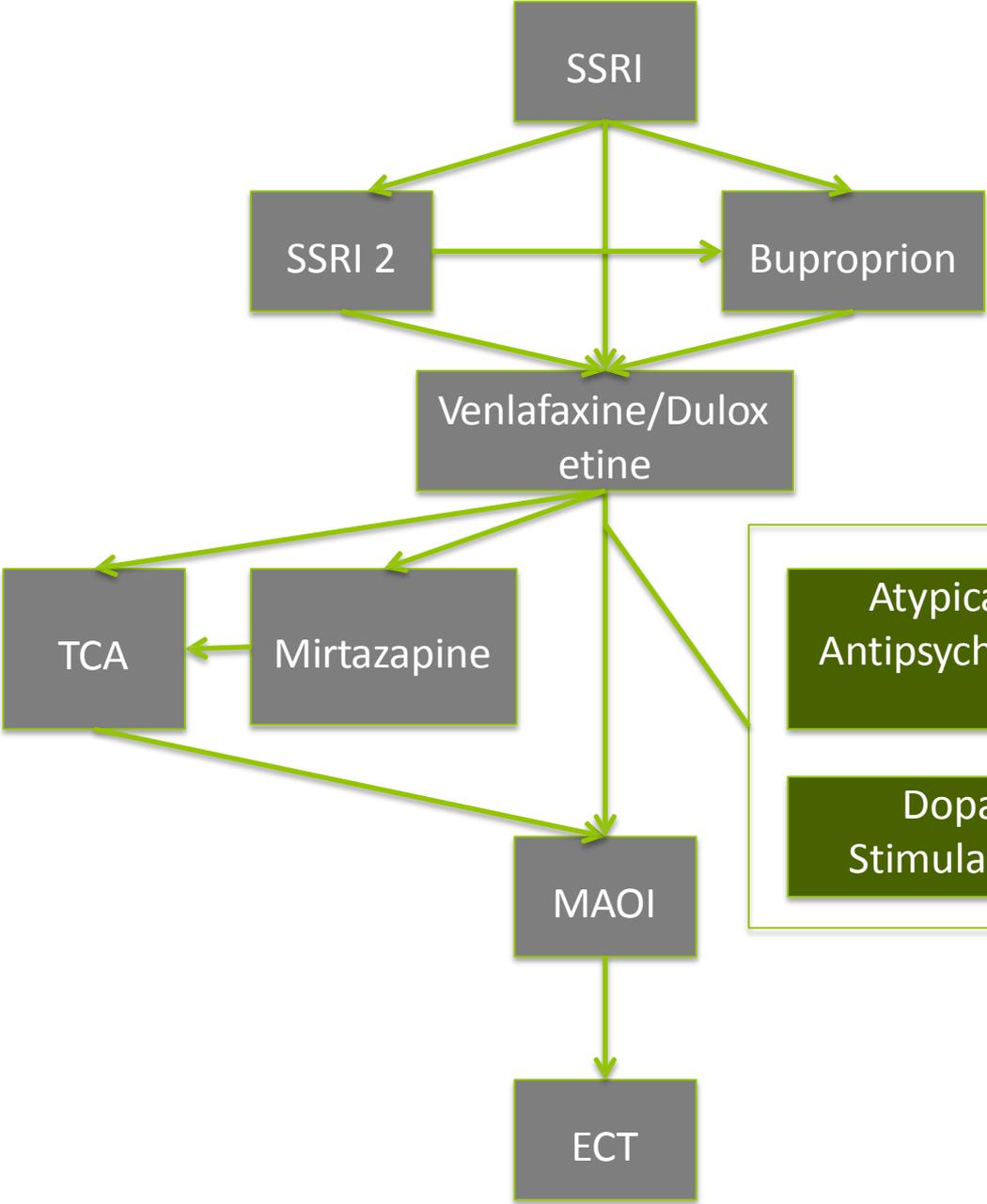
## Catecholamine synthesis



# 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

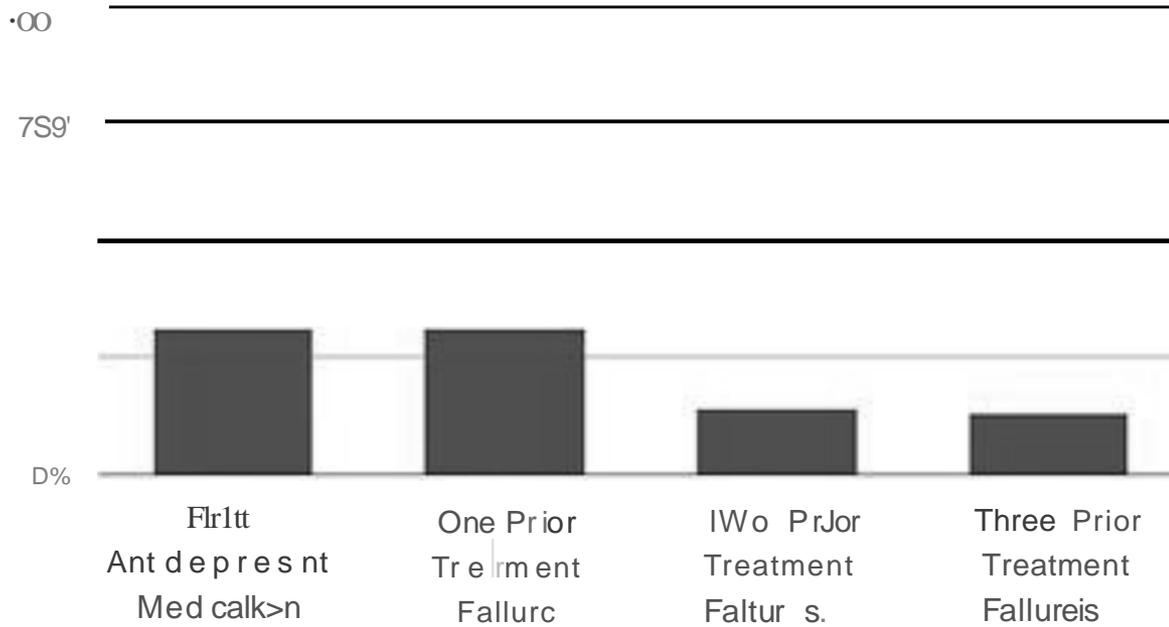
# STAR\*D RESULTS

STEP	TREATMENT	REMISSION RATE
1	Citalopram	36.8%
2	Switch: Bupropion, CT, Sertraline, Venlafaxine Augment: Bupropion, Buspirone, CT	30.6%
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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