

# Antidepressants – Choosing the Right One

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**Psychological Wellness**

# Case Study

- 32 year old Chinese female
- Married with one daughter
- Accountant
- Chief complaints: **headaches** and **poor sleep**
- As a result → **unable to concentrate** at work
- Cannot make decisions at work
- Irritable

# What is Depression

## **Table 1: DSM IV-TR criteria for Major Depressive Episode and Major Depressive Disorder\***

Depressed mood and/or loss of interest or pleasure in life activities for at least 2 weeks and at least five of the following symptoms that cause clinically significant impairment in social, work, or other important areas of functioning almost every day.

1. Depressed mood most of the day.
2. Diminished interest or pleasure in all or most activities.
3. Significant unintentional weight loss or gain.
4. Insomnia or sleeping too much.
5. Agitation or psychomotor retardation noticed by others.
6. Fatigue or loss of energy.
7. Feelings of worthlessness or excessive guilt.
8. Diminished ability to think or concentrate, or indecisiveness.
9. Recurrent thoughts of death

*\* Major Depressive Disorder requires two or more major depressive episodes.*

# What is Depression

**Table 2: Mnemonic “IN SAD CAGES”**

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**I**N -- Interest (loss of)  
**S** -- Sleep disturbances  
**A** -- Appetite and weight disturbances  
**D** -- Dysphoric mood  
**C** -- Concentration poor  
**A** -- Activity (either decreased or agitated)  
**G** -- Guilt  
**E** -- Energy decreased  
**S** -- Suicidal Ideations

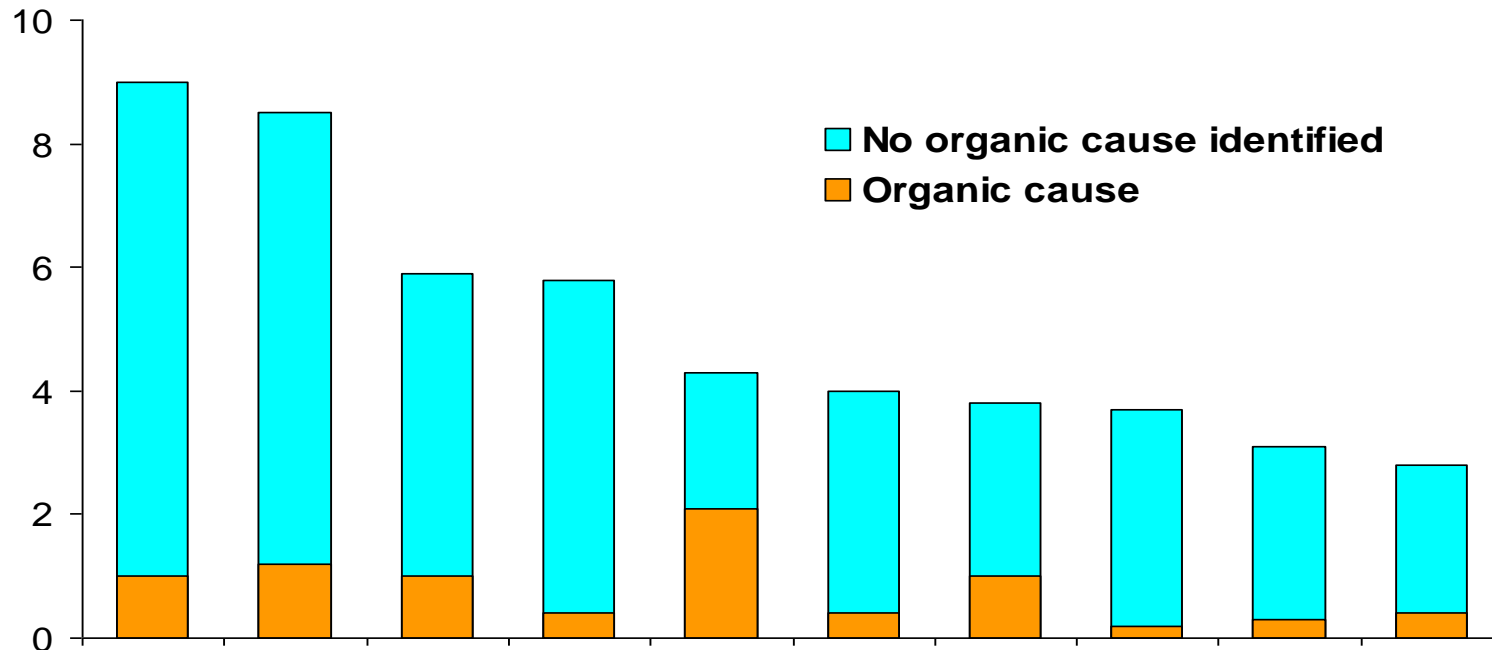
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# Presentation in Primary Care

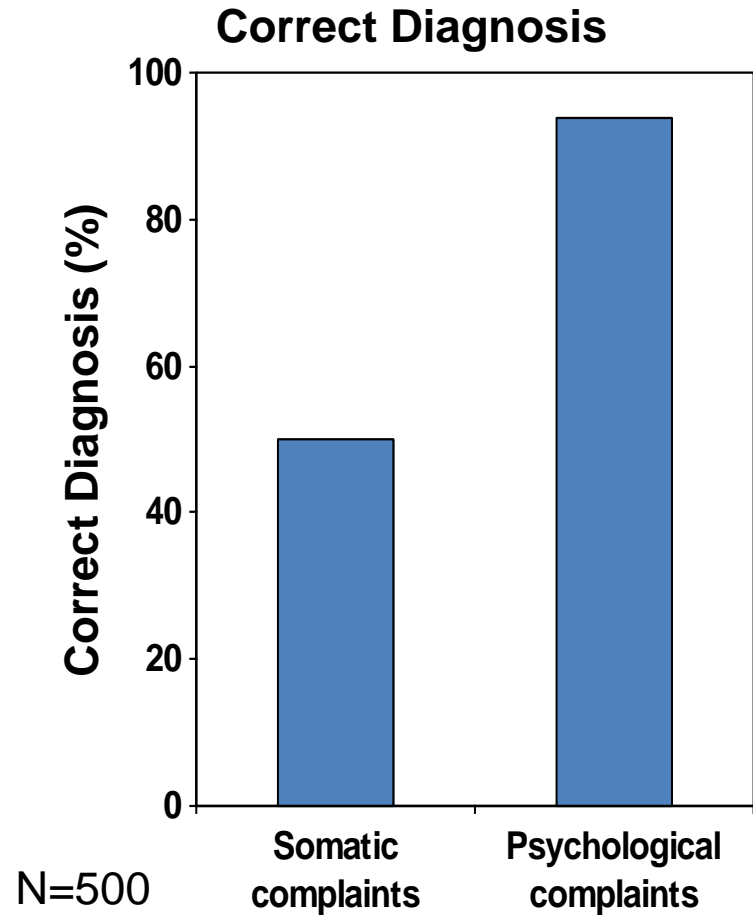
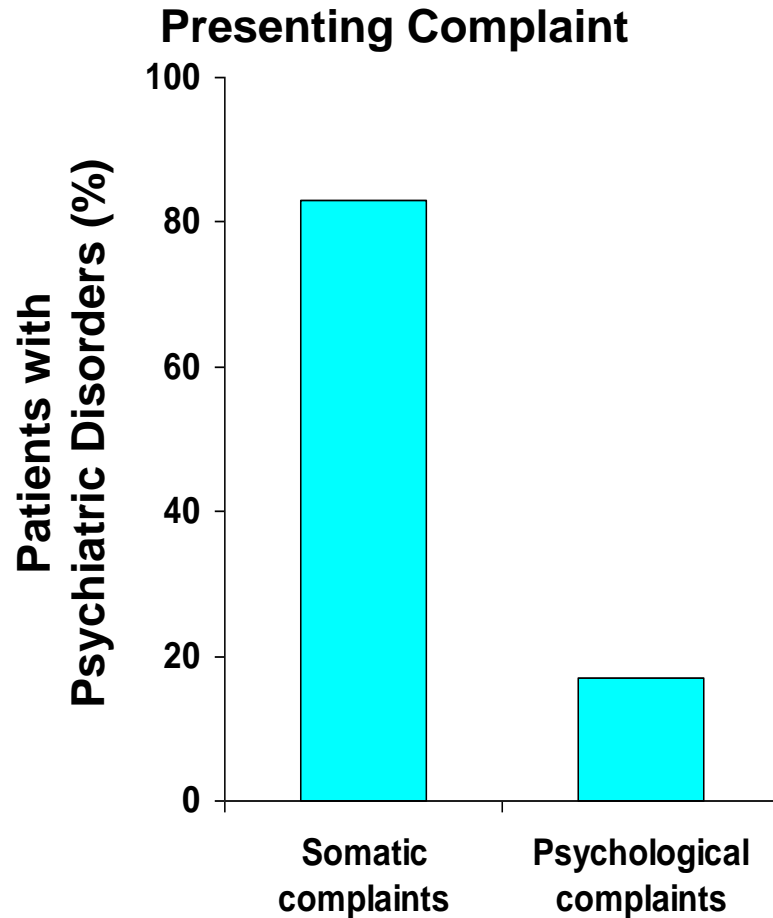
- Unlikely to complain of sadness
- More likely to present with physical / somatic symptoms

# Physical complaints are rarely organic



Kroenke K, Mangelsdorff AD. *Am J Med.* 1989;86:262-266.

# Presentation in Primary Care



Bridges KW, Goldberg DP. *J Psychosom Res.* 1985;29:563-569.

# Case Study

- 32 year old Chinese female
- Married with one daughter (2 year old)
- HR officer
- Chief complaints: **headaches** and **poor sleep**
- As a result → **fatigue** and **unable to concentrate** at work
- Cannot make decisions at work



# Case Study

- Precipitated by sudden increase in workload
- Ruminates and anxious about work esp during bed time
- Loss of interest
- Feelings that life is meaningless
- Passive suicidal thoughts but no active plans
- Feels husband is not understanding
- Stays with in-laws and bugging her for another grandchild

# Suicide Assessment

## **Mnemonic “SAD PERSONS”**

S -- Sex (male)

A -- Age (elderly or adolescent)

D -- Depression

P -- Previous suicide attempts

E -- Ethanol abuse

R -- Rational thinking loss (psychosis)

S -- Social supports lacking

O -- Organised plan to commit suicide

N -- No spouse (divorced > widowed > single)

S -- Sickness (physical illness)

# Treatment

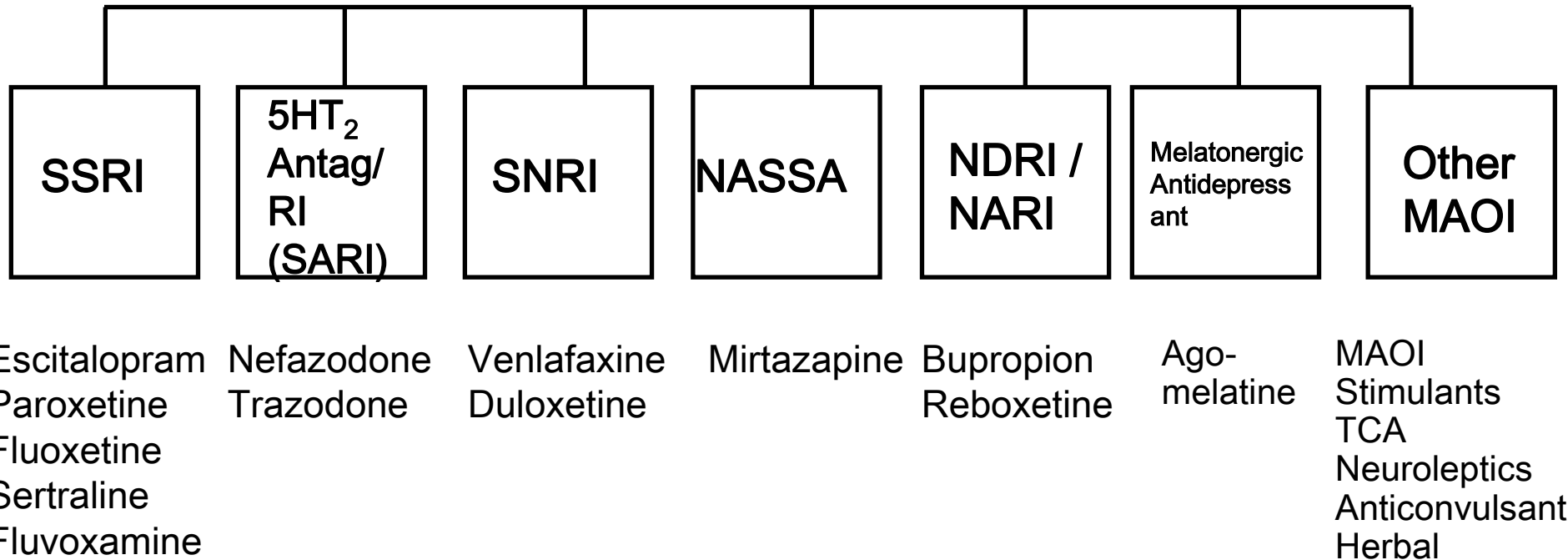
- **Bio-Psycho-Social**
- Psychological: Cognitive Behavioral Therapy
- Social: Getting family involvement, psycho-educating family, medical leave (respite)

# Antidepressants



- Used in both anxiety and depression
- Effective in mild, moderate or severe depression
- 60 -70% response rate in depression
- Effectiveness comparable between and within classes
- Improvements seen in 2 weeks; sometimes up to 4-8 weeks

# Antidepressants



# Factors Affecting Choice of Antidepressants

## **PITS**

- 1. Patient Factors**
- 2. Illness Factors**
- 3. Treatment Factors**
- 4. Social Factors**

# Factors Affecting Choice of Antidepressants

## Patient Factors

- Age
  - child / adolescents to 24 yo / adults / geriatrics
- Gender
  - Male
  - Female: Pregnancy / Breast feeding / Weight gain
- Family History of response and non response
- Polypharmacy?

# Factors Affecting Choice of Antidepressants

## Patient Factors – Age

- **Child:** Fluoxetine and Escitalopram FDA indicated. Start at half dose
- **Adolescents to 24 yo:** black box warning of increase of suicidality, but not completed suicide
- **Adults:** Child bearing age?
- **Geriatrics:** Escitalopram, Mirtazapine and Fluvoxamine commonly used. Start low (half dose), go slow.



# Factors Affecting Choice of Antidepressants

## Patient Factors - Gender

- Male: May be more worried about sexual side effects
- Female:
  - Pregnancy →
    - SSRIs can cause Persistent Pulmonary Hypertension of the Newborn (PPNH), older antidepressants like TCAs safer in pregnancy.
    - To advise pts about planning pregnancy
  - Breast feeding →
    - **Setraline** most commonly used, level in breast milk very low
  - Weight gain →
    - May be adverse to antidepressants causing wt gain especially **Mirtazapine**

# Factors Affecting Choice of Antidepressants

## Patient Factors -

- Family History of response and non response
  - Use antidepressants family members tolerated and found effective
- Polypharmacy?
  - If having multiple drug regime, Escitalopram least likely to have drug-drug interaction

# Factors Affecting Choice of Antidepressants

## **Illness Factors - Symptomatology**

- Poor sleep: use sedating antidepressants like mirtazapine or fluvoxamine
- Suicide risk: avoid TCAs, cardiotoxic in overdose
- Obsessive symptoms, prominent anxiety: use antidepressants with strong serotonergic effects  
→ ie. SSRIs, clomipramine. (Bupropion and Agomelatine may not be effective)

# Factors Affecting Choice of Antidepressants

## Illness Factors

- Past History:
  - Response and non response
  - Tolerability
  - Use previously successful regime and dosage

# Factors Affecting Choice of Antidepressants

## Treatment Factors

- Medication side effects

# Medication side effects

<i>Class</i>	<i>Examples</i>	<i>Action</i>	<i>Precautions</i>
<b>Tricyclic antidepressants</b>	Amitriptyline, Imipramine, Clomipramine, Nortriptyline, Dothiepin	Inhibit serotonin & NE uptake; anticholinergic-antimuscarinic; alpha1-adrenergic antagonist; antihistamine	Anticholinergic effects, postural hypotension, confusion, weight gain, CVS effects, toxicity in overdose
<b>MAOIs</b>	Phenelzine, Tranylcypromine	MAO inhibition causes NE accumulation	Postural hypotension, dietary restrictions, drug interactions, sexual dysfunction
<b>SSRIs</b>	Fluoxetine, Fluvoxamine, Paroxetine, Escitalopram, Sertraline	Selectively inhibits 5HT reuptake	Agitation, akathisia, anxiety, insomnia, sexual dysfunction, GI effects, withdrawal effects

<i>Class</i>	<i>Examples</i>	<i>Action</i>	<i>Precautions</i>
<b>SNRI</b>	Venlafaxine Duloxetine	Inhibits 5HT and NE reuptake	Same as SSRIs (low doses), hypertension, insomnia, agitation, headache (high doses)
<b>SARI</b>	Trazodone	Serotonin antagonist & reuptake inhibitor	Sedation, postural hypotension, nausea
<b>NaSSA</b>	Mirtazapine	Alpha2, 5HT1, 5HT2, H1 antagonism → Enhances NE & 5HT neurotransmission	H1 antagonism – sedation, weight gain
<b>NDRI</b>	Bupropion	NE and Dopamine reuptake inhibitor	Stimulation, agitation, nausea, insomnia, seizures (4/1000)

# SSRI

- 1<sup>st</sup> line for depression
- Safer in overdose
- Less problematic side-effects
- Broad spectrum of activity
  - Depression
  - Anxiety
  - OCD
  - PTSD





# SSRI

<i>Generic name</i>	<i>Trade name(s)</i>	<i>Dose (mg/day)</i>
Fluoxetine	Prozac, Magrilan	20-60
Fluvoxamine	Faverin, Luvox	50-300
Lexapro	Escitalopram	10-20
Sertraline	Zoloft	50-200
Paroxetine	Seroxat, Paxil	20-60

# SSRI

- Nausea, GI discomfort
- Anxiety, restlessness during initiation
- Drowsiness, lethargy
- Insomnia
- Sexual / erectile dysfunction

# Tricyclics

- Older and time-tested, cheap
- Problems of anticholinergic side-effects, postural hypotension and sedation
- Toxic in overdose; cardiac effects
- Imipramine, amitriptyline, clomipramine and dothiepin (prothiaden)
- Dose 10 – 150 mg/day
- Usual effective dose 25-100 mg/day
- Once daily at night; titrate up 25 mg/day



# SNRI

- Dual Mechanism of action
- Useful as second line drug
- Also useful in painful somatic symptoms
- Examples Duloxetine, Venlaflexine
- Side effects similar to SSRIs
- Need to monitor BP for Venlaflexine
- Duloxetine has approval for diabetic neuropathy

# NASSA

- Mirtazepine (Remeron)
- 15mg to 30mg
- Alpha-2 adrenergic receptors that normally inhibit the release of the neurotransmitters norepinephrine (noradrenaline) and serotonin, thereby increasing active levels in the synapse
- Mirtazapine is a potent antagonist of 5-HT<sub>2</sub> and 5-HT<sub>3</sub> receptors. Reducing side effects of sexual dysfunction and GI effects
- Prominent anti-histamine effect. Weight gain and sedation prominent
- Sedation effects paradoxical, higher dose less sedating

# New Class

- Newest class
- Melatonin Agonist, Agomelatine
- Can be considered if first line treatment failed
- Resynchronizes circadian rhythm
- LFT at initiation, **6,12,24 weeks**
- Metabolized by CYP450 1A2 – avoid ciprofloxacin and faverin

# Factors Affecting Choice of Antidepressants

## Treatment Factors

- Medication side effects
- Duration of onset
  - Antidepressants work after two weeks
  - Escitalopram: evidence of onset as fast as Day 7
- Dosing Schedule

[Int Clin Psychopharmacol.](#) 2006 Mar;21(2):105-10. Onset of action of escitalopram compared with other antidepressants: results of a pooled analysis. [Kasper S](#), [Spadone C](#), [Verpillat P](#), [Angst J](#).

# Factors Affecting Choice of Antidepressants

## Social Factor

- Costs
- Dr's experience and personal preference



# Case Study

- Major Depressive Episode
- With features of poor sleep, irritability and anxiety
- Sister had depression treated with SSRI – but cannot remb name
- Keen to try medication but worried about weight gain+++

# 1<sup>st</sup> Line with SSRI

	Fluoxetine	Setraline	Escitalopram	Fluvoxamine	Paroxetine
<b>Sedation</b>	1	1	3	5	5
<b>Activation</b>	5	4	3	1	1
<b>Weight gain</b>	2	2	3	5	5
<b>Sexual dysfunction</b>	3	3	3	5	5

**1**-Least, **3**- moderate, **5**-most

Stephen M. Stahl, M. (2008). *Stahl's Essential Psychopharmacology* (3rd ed.). New York, NY: Cambridge University Press.

# Initiating Medication

- May start with *full* dose or *half*-dose
- May need to cover with *short-term* BZPs to manage anxiety and insomnia initially
- Response takes 10 to 21 days, sometimes longer
- Side effects usually settle within a week
- Beware the “one-dose” patient

# Management Guidelines

- Acute treatment: 8 to 12 weeks
- Maintenance treatment: 6-12 months symptom-free

*“The dose that makes them well is the dose that keeps them well”*

- Prophylaxis at full dose for recurrent depression
  - 2 or more episodes
  - Prominent family history
  - Significant suicide risk

# Q and A

