

ANTIDEPRESSANT ADVERSE EFFECTS

Casey Gallimore, PharmD, MS

Learning Objectives

- List common and serious adverse effects of individual antidepressant agents, and recognize characteristics that make patients more or less susceptible (i.e. anticholinergic effects in elderly patients).
- Predict onset and duration of adverse effects associated with antidepressants (i.e. What is time to onset for each adverse effect? If an adverse effect occurs, is it expected to be transient or chronic?)
- Provide recommendations to minimize or manage antidepressant adverse effects.

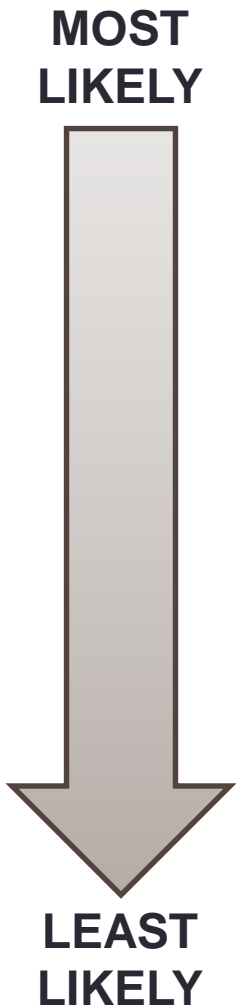
General Antidepressant Adverse Effects

**63% of patients in trials experienced ≥ 1 adverse effect

Clinical Course		
Transient*	Chronic	Rare
GI effects (upset, N/V/C) Dizziness Headache Sedation / Insomnia Anxiety / jitteriness	Sweating Tremor Anticholinergic effects BP/HR changes Vivid dreams Weight changes Sexual side effects	Worsening mood / suicide Asthenia EPS (akathisia/dyskinesia) Bruxism QT prolongation Reduced seizure threshold Bone fracture? Serotonin syndrome Hyponatremia (SIADH)

*Transient: effect tends to be worst following initiation or dosage increases, often minimizes with time (1-4 weeks at consistent dose) or slower taper, but in some patients may not entirely go away

(SIADH) syndrome of inappropriate antidiuretic hormone (EPS) extrapyramidal symptoms



Sedation
TCAs Mirtazapine Trazodone
Paroxetine Fluvoxamine Venlafaxine MAO-Is
SSRIs SNRIs Bupropion Vilazodone Vortioxetine

Insomnia / agitation
Fluoxetine Sertraline Bupropion Vilazodone
SSRIs SNRIs MAO-Is
TCAs Mirtazapine Trazodone Vortioxetine

Increased BP/HR
SNRIs MAO-Is
Bupropion Duloxetine Mirtazapine TCAs
SSRIs Vilazodone Vortioxetine

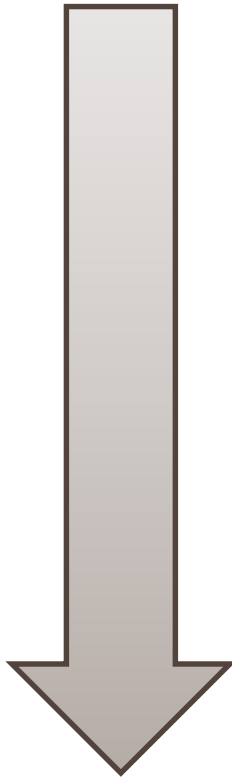
Orthostatic Hypotension
TCAs Trazodone MAO-Is
Paroxetine Mirtazapine
SSRIs SNRIs Bupropion Vilazodone Vortioxetine

Anticholinergic
TCAs
MAO-Is Mirtazapine Paroxetine
SSRIs SNRIs Bupropion Trazodone Vilazodone Vortioxetine

UpToDate®: Side Effects of Antidepressants (table)

Goldberg JF, Ernst CL. (2019). Managing the side effects of psychotropic medications (2nd ed.). Washington DC:American Psychiatric Association.

**MOST
LIKELY**



**LEAST
LIKELY**

GI Toxicity
SNRIs (N, C) Bupropion (N) Trazodone (N) Vilazodone (N,D) Vortioxetine (N,C) Sertraline* (N,D)
SSRIs (N,D) Paroxetine (N,D,C) TCAs (C) MAO-Is
Mirtazapine (C)

N = nausea
D = diarrhea
C = constipation

Weight Change
TCAs + Mirtazapine + Paroxetine +
SSRIs + Bupropion - Trazodone + MAO-Is +
SNRIs Vilazodone Vortioxetine

+ weight gain
- weight loss

Sexual Side Effects
SSRIs Venlafaxine TCAs MAO-Is
SNRIs Vilazodone Vortioxetine
Bupropion Mirtazapine Trazodone†

†priapism

QT Prolongation
TCAs Trazodone
Citalopram Escitalopram Fluoxetine Bupropion Mirtazapine Venlafaxine
SSRIs SNRIs MAO-Is Vilazodone Vortioxetine

Seizure
TCAs Bupropion
SSRIs SNRIS Trazodone Mirtazapine Vilazodone Vortioxetine MAO-Is

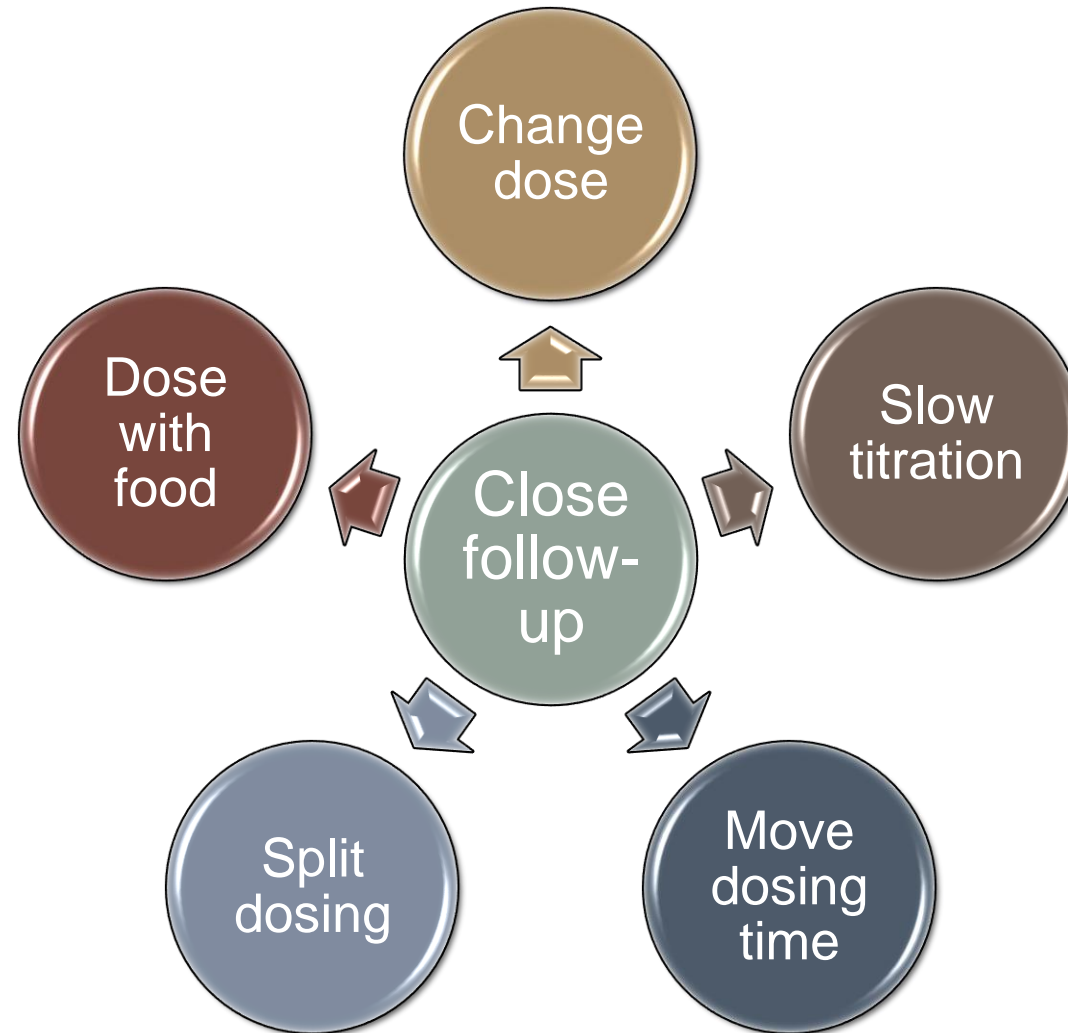
Tricyclic Antidepressants

Responsible receptors	Muscarinic	Histamine		Alpha-adrenergic		5-HT2
	Anticholinergic	Drowsiness	Weight Gain	Hypotension	QT prolongation	Sexual Dysfunction
Tertiary Amines						
Amitriptyline	++	++	++	++	++	++
Clomipramine	++	++	++	+	+	++
Doxepin	++	++	++	+	++	++
Imipramine	++	++	++	++	++	++
Triimipramine	++	++	++	++	+	++
Secondary Amines						
Desipramine	+	+	+	+	++	++
Nortriptyline	+	+	+	+	++	++
Protriptyline	+	+	+	+	++	++
Miscellaneous						
Amoxapine	+	+	+	+	+	++
Maprotiline	+	+	+	+	++	++

++ high risk, + moderate risk

Adapted from UpToDate®: Side Effects of Antidepressants (table)

Side Effect Management



Sexual Side Effects

~25-80% of patients taking antidepressants experience sexual side effects

- Low sexual desire or libido
- Arousal difficulties (lubrication in women and erectile function in men)
- Lack of orgasm

- Mesolimbic dopaminergic system involved in maintenance of sexual desire, arousal and orgasm
- SSRIs and venlafaxine decrease dopaminergic transmission by acting as agonists at 5HT-2 receptors

Sexual Side Effect Management Options

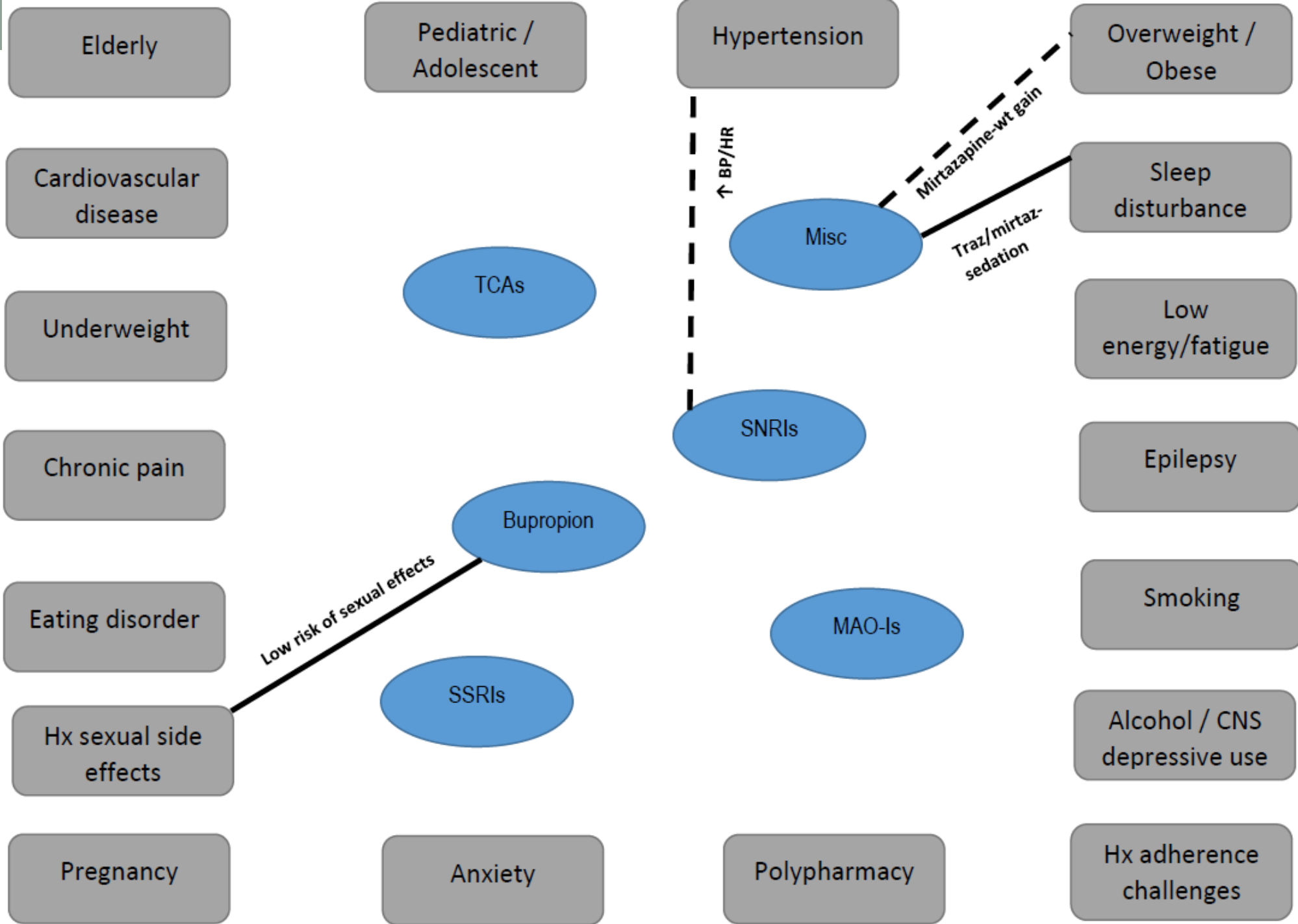
- Drug holiday
 - Dose reduction
 - Psychological interventions
 - Mechanical devices
 - Switch antidepressant**
- Augmentation
 - Bupropion**
 - Mirtazapine
 - Sildenafil, tadalafil**
 - Granisetron
 - Ginkgo biloba
 - Buspirone
 - Olanzapine
 - Amantadine
 - Yohimbine

**supporting evidence from RCT

Concept Map

Good choice

- - - - -
Poor choice



Questions??

- Casey.Gallimore@wisc.edu