



Antidepressants: Advancing Past the Single SSRI Trial

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Disclosures

No disclosures

The Serotonin Synapse

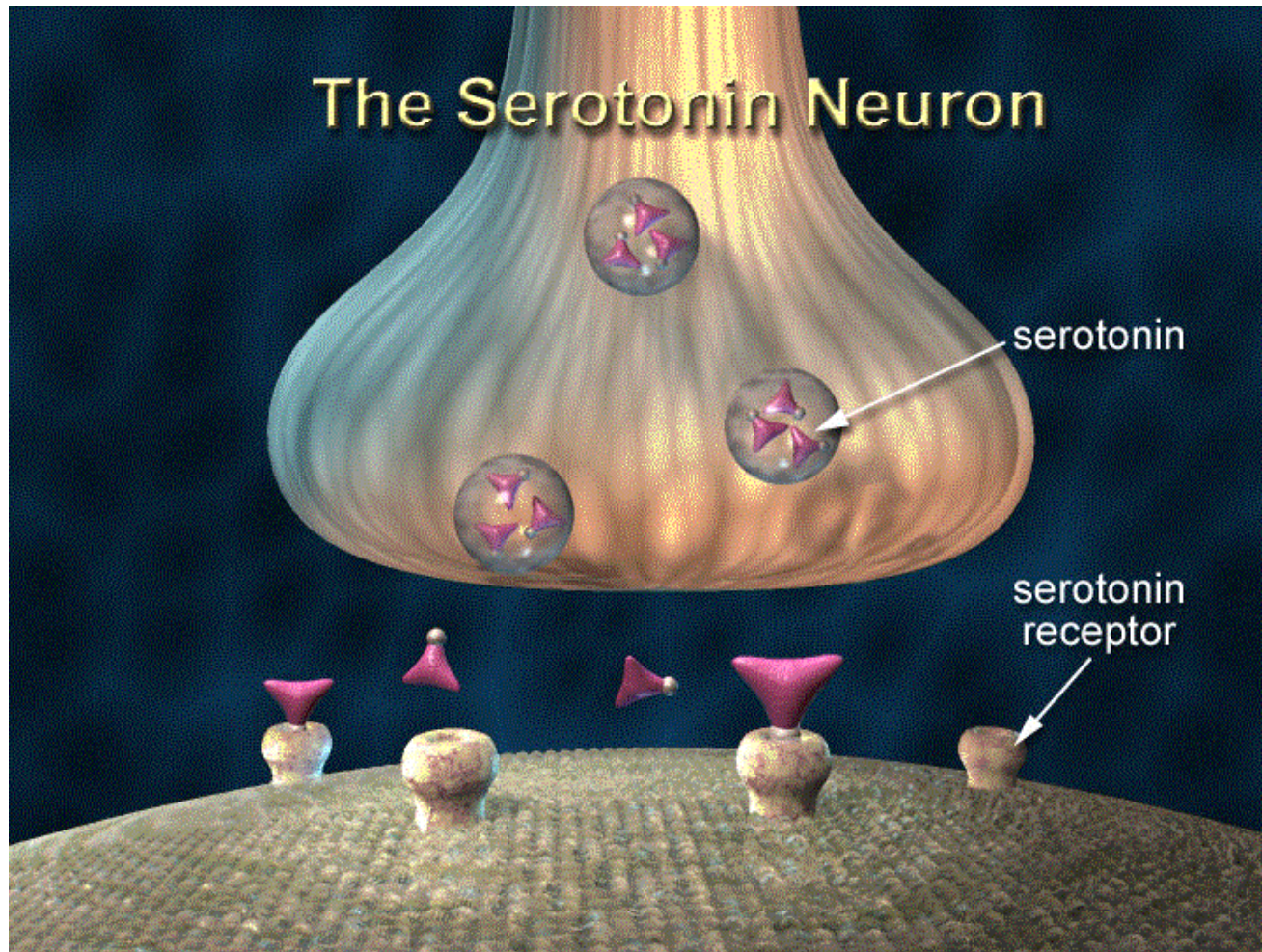
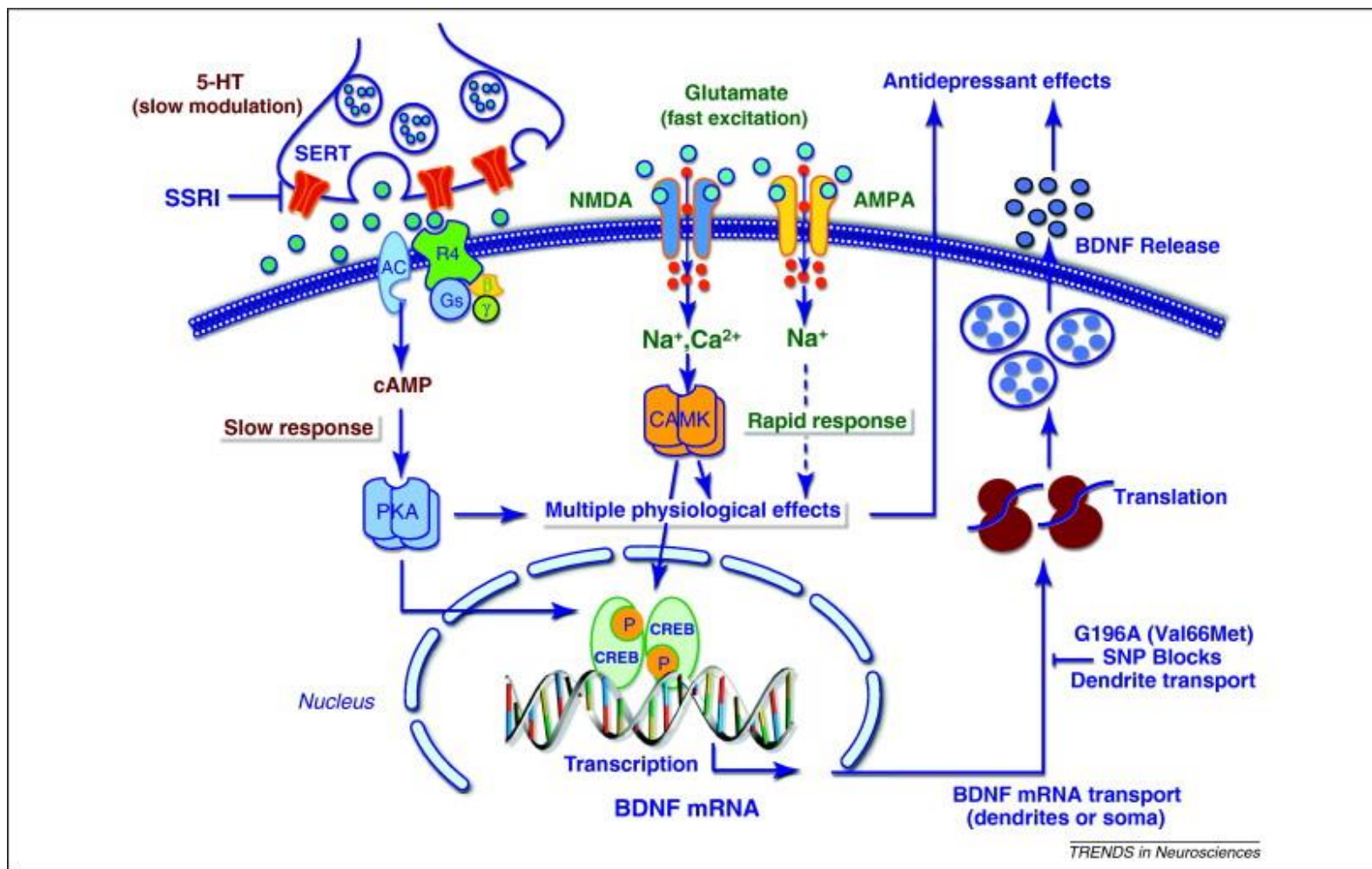


Image Credit: National Institute on Drug Abuse

The Serotonin Neuron



Duman & Volieti (2012)

A Post-mortem on Lack of Efficacy of the First SSRI Trial



Image Credit: Paul Rogers, New York Times, April 17, 2017

A Post-mortem on Lack of Efficacy of the First SSRI Trial: Side Effects

- Temporary:
 - Worsening anxiety
 - Sleep disturbance
 - Nausea
 - Headache
- Persistent/Serious:
 - Sexual side effects
 - QT prolongation
 - Mania
 - Suicidality

A Post-mortem on Lack of Efficacy of the First SSRI Trial: Dose and Duration

TABLE 1
SEROTONERGIC AGENTS: APPROVED AND STUDIED DOSAGES

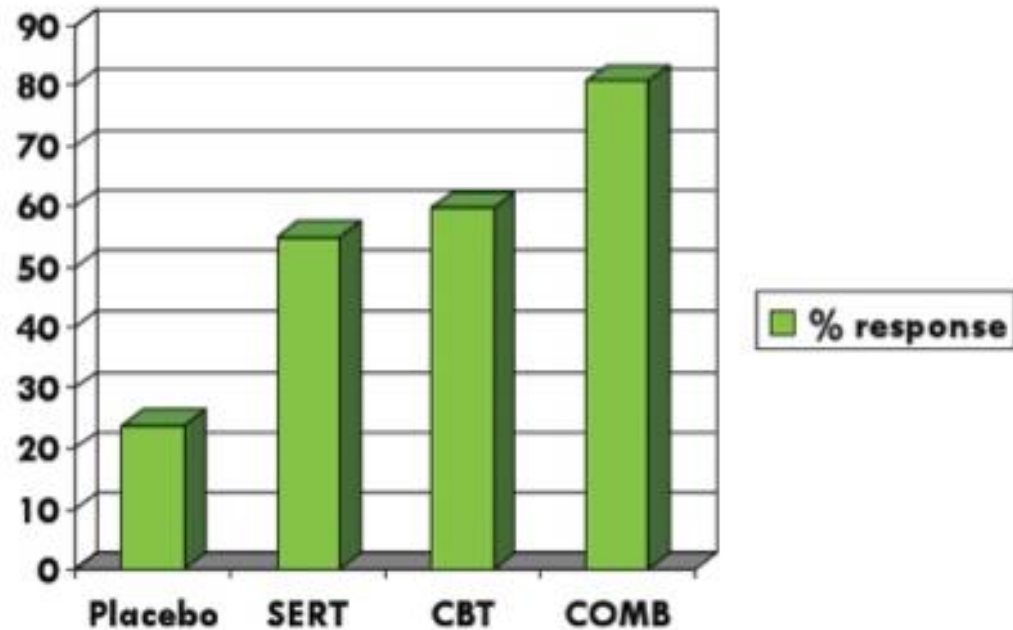
Medication	Indication	FDA Approved?	FDA-Approved Dose	Supported Dose (mg /day)	Minimum Supported Effective Dose
Fluoxetine	SAD	No	N/A	(45)	(45)
	GAD	No	N/A	N/A	N/A
	Panic disorder	Yes	ITD: 20, Max: 60	10–20	10
Fluvoxamine	SAD	Yes	ITD: 100, Max: 300	(150–202)	(150)
	GAD	No	N/A	N/A	N/A
	Panic disorder	No	N/A	150–(230)	150
Paroxetine	SAD	Yes	ITD: 20, Max: 60	20–60	20
	GAD	Yes	ITD: 20, Max: 20	20–50	20
	Panic disorder	Yes	ITD: 40, Max: 60	20–40	20
Paroxetine CR	SAD	Yes	12.5–37.5	(32)	(32)
	GAD	N/A	N/A	N/A	N/A
	Panic disorder	Yes	12.5–75	(50)	(50)
Sertraline	SAD	Yes	ITD: 50, Max: 200	(99)–200	(99)
	GAD	No	N/A	50–150	50
	Panic disorder	Yes	ITD: 50, Max: 200	50–200	50
Citalopram	SAD	No	N/A	N/A	N/A
	GAD	No	N/A	N/A	N/A
	Panic disorder	No	N/A	20–60	20
Escitalopram	SAD	No	N/A	5–20	5
	GAD	Yes	ITD: 10, Max: 20	10–20	10
	Panic disorder	No	N/A	(11)	(11)
Venlafaxine ER	SAD	Yes	ITD: 75, Max: 75	75–225	75
	GAD	Yes	ITD: 75, Max: 225	37.5–225	37.5
	Panic disorder	Yes	ITD: 75, Max: 225	75–225	75
Duloxetine	SAD	No	N/A	N/A	N/A
	GAD	Yes	ITD: 60, Max: 120	20–120	20
	Panic disorder	No	N/A	N/A	N/A

Parentheses “0” indicate average dose in a flexible-dose study. This is used unless separate statistical analysis is performed for a given dose.

FDA=Food and Drug Administration; SAD=social anxiety disorder; N/A=not applicable; GAD=generalized anxiety disorder; ITD=initial target dose as recommended by the FDA; Max=maximum dose; CR=controlled release; ER=extended release.

White MP. *Primary Psychiatry*. Vol 16, No 10. 2009.

Next step



SERT=sertraline, CBT=cognitive-behavioral therapy, COMB=combination

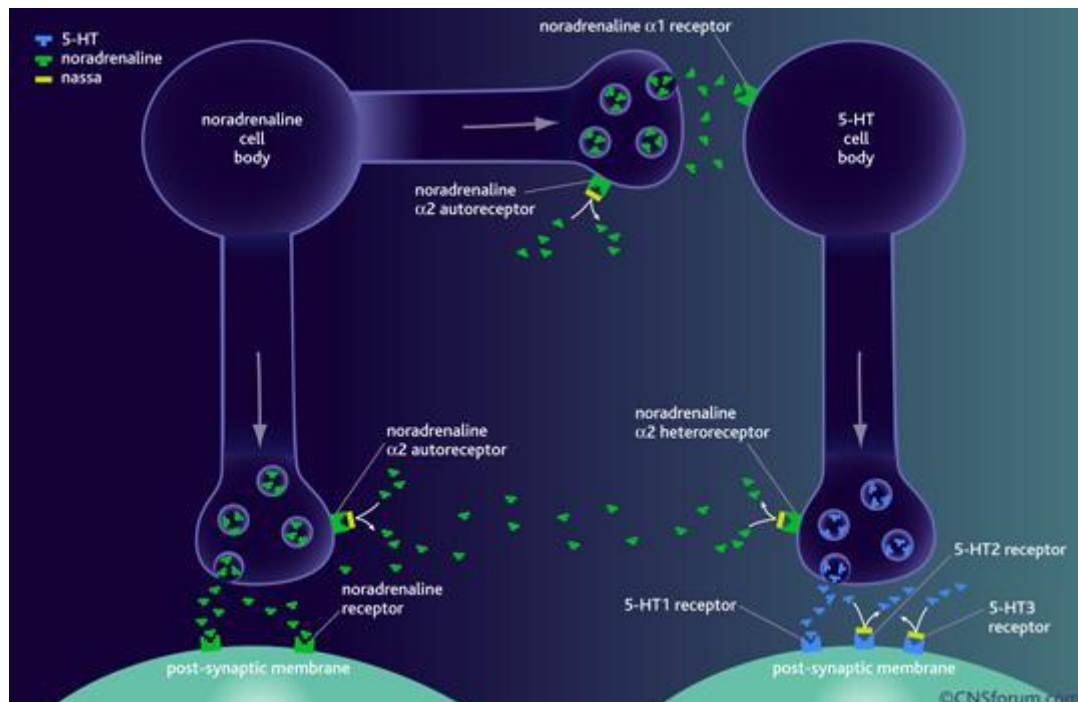
Walkup JT et al, *N Engl J Med*, 2008;359:2753-2766

SNRIs

- Venlafaxine (Desvenlafaxine)
 - Generalized Anxiety Disorder (I)
 - Panic Disorder (II)
 - Social Anxiety Disorder (II)
 - Obsessive Compulsive Disorder (II)
- Duloxetine
 - Generalized Anxiety Disorder (I)
- Levomilnacipran

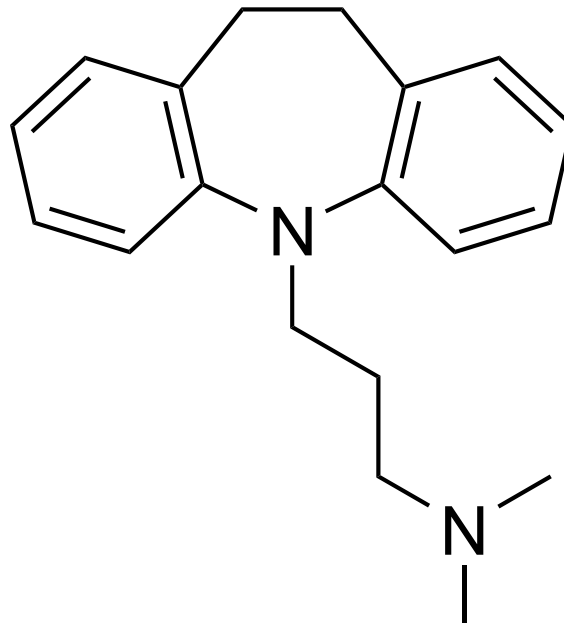
Mirtzapine

- Panic Disorder (II)
- Post-Traumatic Stress Disorder (II)
- Generalized Anxiety Disorder (IV)



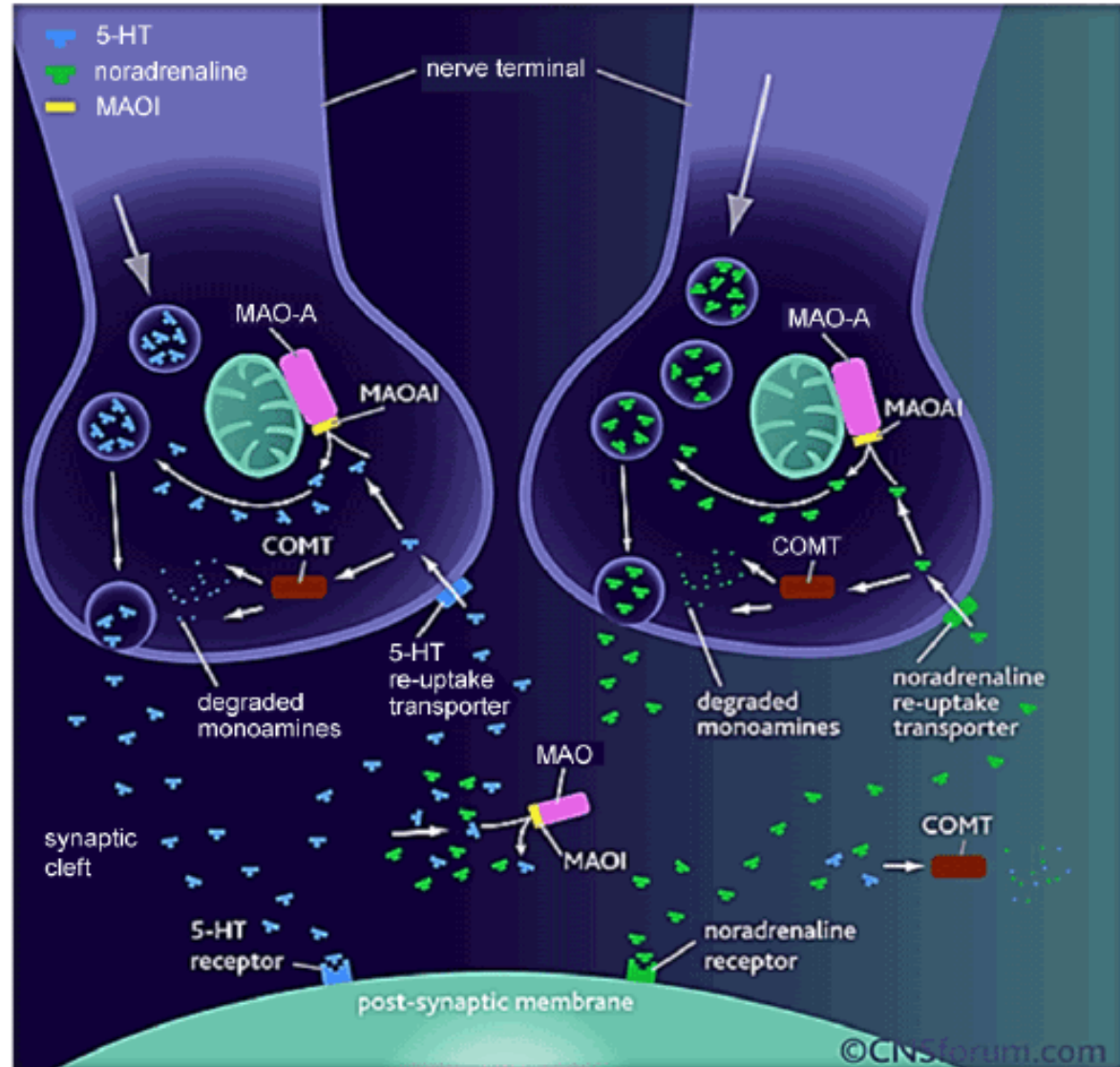
Tricyclic Antidepressants

- Panic Disorder (I, II)
- Obsessive-Compulsive Disorder (I)
- Generalized Anxiety (II)
- Post-Traumatic Stress disorder (II)



- Monoamine Oxidase Inhibitors

Panic Disorder (II)
Social Anxiety Disorder (II)
Post-Traumatic Disorder(II)



MAOIs



MAOI Diet

Food	Allowed	Limit	Avoid
Beverages	<ul style="list-style-type: none"> Milk Decaf coffee and tea Carbonated drinks 	<ul style="list-style-type: none"> Chocolate drinks Coffee, tea, and other caffeinated drinks White wine and clear spirits (limit two 8 oz. servings) 	<ul style="list-style-type: none"> Alcoholic drinks, especially beer, ale, wine (Chianti, burgundy, sherry, vermouth, sauterne), and nonalcoholic beer and wine Acidophilus milk
Bread	<ul style="list-style-type: none"> Whole-wheat enriched white breads, rolls, crackers, and quick breads 	<ul style="list-style-type: none"> None 	<ul style="list-style-type: none"> Cheese breads Crackers Sourdough and fresh, homemade, yeast-leavened breads
Cereals	<ul style="list-style-type: none"> Cooked and dry cereals 	<ul style="list-style-type: none"> None 	<ul style="list-style-type: none"> None
Cheese and Dairy Products	<ul style="list-style-type: none"> Cottage cheese, farmer or pot cheese, cream cheese, ricotta cheese, and processed cheese 	<ul style="list-style-type: none"> Buttermilk (limit to 4 oz.), sour cream, yogurt (national brands only-limit to 4 oz. per day) 	<ul style="list-style-type: none"> All other cheese: aged cheese, Camembert, cheddar, Gouda, Gruyere, mozzarella, Parmesan, provolone, Roquefort, and Stilton
Desserts	<ul style="list-style-type: none"> Cakes and cookies Gelatins Ice cream and sherbets Pastries Puddings 	<ul style="list-style-type: none"> Chocolate desserts 	<ul style="list-style-type: none"> Cheese-filled desserts and cheesecake
Eggs	<ul style="list-style-type: none"> All 	<ul style="list-style-type: none"> None 	<ul style="list-style-type: none"> Quiche with cheese
Fats	<ul style="list-style-type: none"> All 	<ul style="list-style-type: none"> None 	<ul style="list-style-type: none"> None
Fruits	<ul style="list-style-type: none"> Fresh, frozen, or canned fruits and juices 	<ul style="list-style-type: none"> None 	<ul style="list-style-type: none"> Banana peel extract Overripe and spoiled fruits
Meats, Fish, and Poultry	<ul style="list-style-type: none"> All fresh or frozen meats, fish, or poultry 	<ul style="list-style-type: none"> Aged meats and frankfurters Fresh sausage and pepperoni Canned sardines Canned meats Fish roe (caviar) and paté (limit to 1 oz.) 	<ul style="list-style-type: none"> Caviar (more than 1 oz.) Chicken and beef liver Dried, salted, and pickled fish Fermented and dry sausages Salami Dried meats and meat extracts
Potatoes and Substitutes	<ul style="list-style-type: none"> White and sweet potatoes Grits, pasta, and rice 	<ul style="list-style-type: none"> None 	<ul style="list-style-type: none"> None
Soups	<ul style="list-style-type: none"> All cream and broth soups, except those on the "Avoid" list 	<ul style="list-style-type: none"> None 	<ul style="list-style-type: none"> Soups from Italian broad beans and fava beans Cheese soup Soup made with beer or wine Any soup cubes or meat extract Packet soups and packaged soups Miso soup
Sweets	<ul style="list-style-type: none"> Sugars, hard candies, honey, molasses, and syrups 	<ul style="list-style-type: none"> Chocolate candies and chocolate syrups 	<ul style="list-style-type: none"> Imported chocolate
Vegetables	<ul style="list-style-type: none"> All fresh, frozen, canned or dried vegetables and vegetable juices, except those on the "Avoid" list 	<ul style="list-style-type: none"> None 	<ul style="list-style-type: none"> Chinese pea pods Fava beans and Italian broad beans Sauerkraut Fermented soybean products miso and some tofu products)
Miscellaneous	<ul style="list-style-type: none"> Salt Nuts and peanut butter Spices, herbs, and flavorings 	<ul style="list-style-type: none"> Soy sauce (limit to 1/4 cup) and teriyaki sauce (limit to 1/4 cup) Brewer's yeast 	<ul style="list-style-type: none"> Marmite (vegetable extracts) Yeast concentrates Vitamin supplements with brewer's yeast Monosodium glutamate (MSG) All aged products

Conclusions

- The most common failed SSRI is the SSRI not taken
- Management of expectations as important as that based on side-effect profiles, individual tolerability, comorbidity and past trials
- Multiple empirically based alternatives – SNRIs, Mirtazapine, TCAs and MAOIs