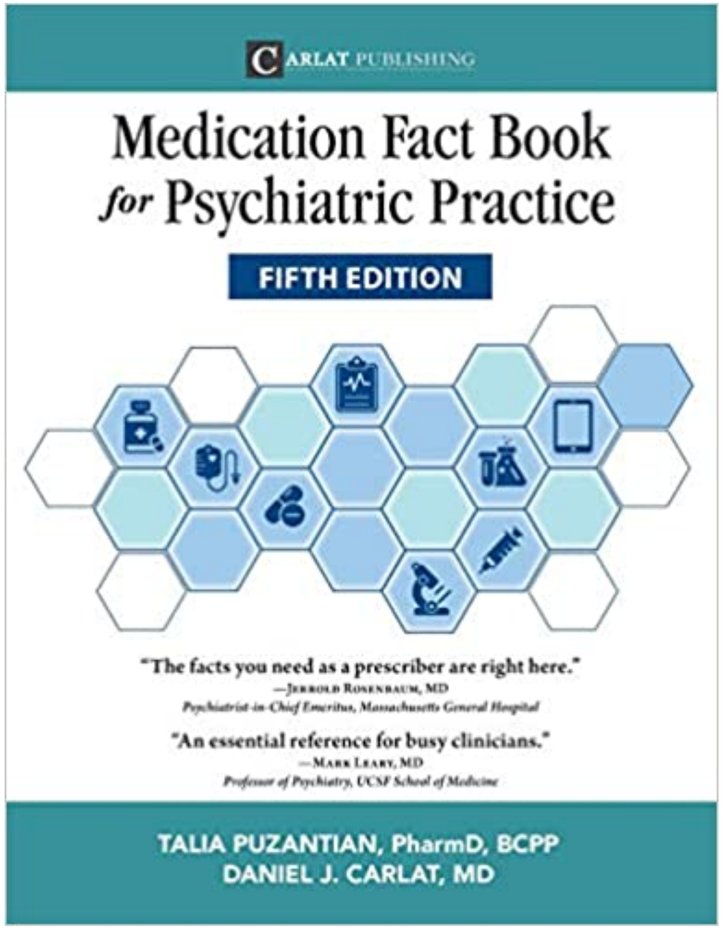
WHICH TO USE, WHICH TO LOSE?

PSYCHIATRIC MEDS '21

KENNETH S. ARFA, MD

HOUSTONPSYCHIATRY.COM

REFERENCES



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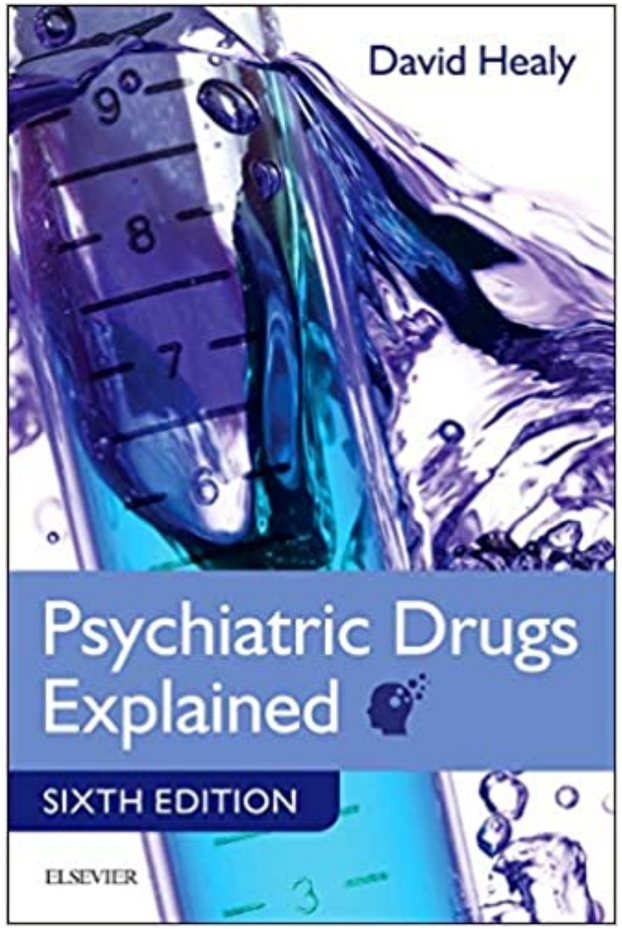

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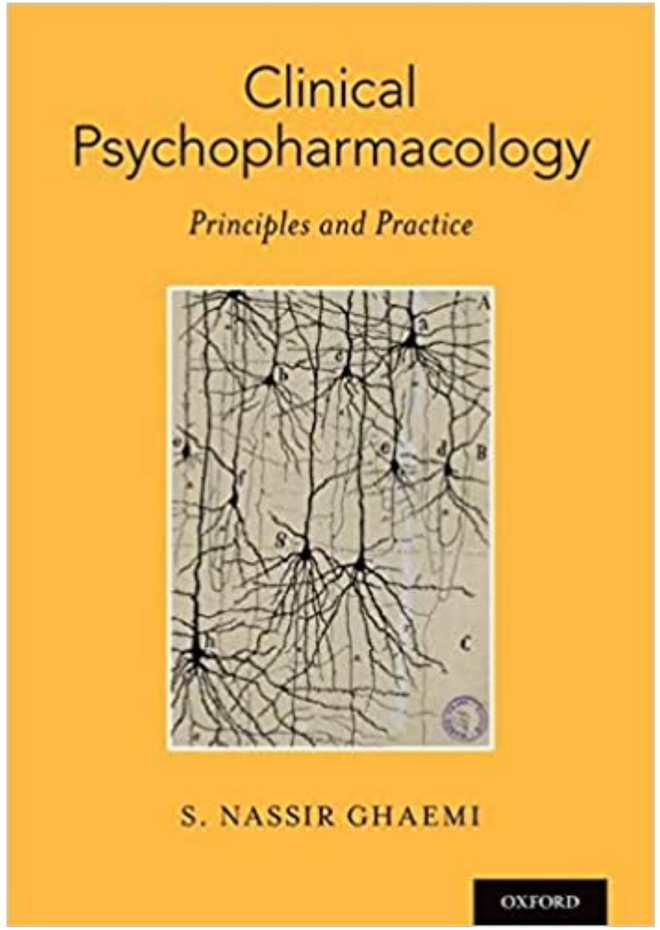

Ghaemi

TODAY'S TALK

1. Antidepressants
2. Sex
3. Somatic treatments
4. Antipsychotics
5. Mood stabilizers
6. Anxiety, sleep
7. ADHD
8. Dementia
9. Natural tx
10. Pregnancy
11. Gene testing

FOCUS

- The best meds in each category
- Comment on the newest
- Use brand names except with oldest drugs

DISCLAIMERS

Dollars for Docs

How Industry Dollars Reached Your Doctors

By Mike Tigas, Ryann Grochowski Jones, Charles Ornstein, and Lena Groeger, ProPublica. Updated October 17, 2019

Pharmaceutical and medical device companies are required by law to release details of their payments to a variety of doctors and U.S. teaching hospitals for promotional talks, research and consulting, among other categories. Use this tool to search for general payments (excluding research and ownership interests) made from August 2013 to December 2018. | About the Dollars for Docs Data → | Read the entire series →

Has Your Doctor Received Drug or Device Company Money?

For example: Andrew Jones, Boston, 10013

All States | Search

Archive: Search our older data for payments made by 17 drug companies between 2009 and 2013.

Get Updates

Sign up to be notified when Dollars for Docs is updated, and get more of ProPublica's stories in your inbox.

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KENNETH ARFA

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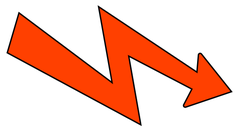
2018 Payments: At a Glance



0

PAYMENTS

$0

PAYMENT TOTAL

0

COMPANIES PAID THIS DOCTOR

Types of Payments

CATEGORY	PAYMENTS	PAYMENT VALUE

2017 Payments At a Glance

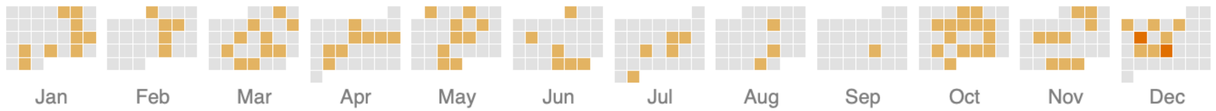
211	$2,521,446	13
PAYMENTS	PAYMENT TOTAL	COMPANIES PAID THIS DOCTOR

Payment Calendar in 2017

This doctor received a payment on **87** days in 2017.

Each box below represents a single day during the disclosure period. A gray box indicates no payments. The darker the color, the more payments a doctor received that day.

2017



Types of Payments in 2017

CATEGORY	PAYMENTS	PAYMENT VALUE
PROMOTIONAL SPEAKING/OTHER	47	$2.15M
CONSULTING	26	$324K
TRAVEL AND LODGING	77	$34,882
HONORARIA	1	$5,444
FOOD AND BEVERAGE	53	$4,233
GIFT	6	$295
EDUCATION	1	$38

The New York Times

Study Finds a Link of Drug Makers to Psychiatrists

By Benedict Carey

April 20, 2006

More than half the psychiatrists who took part in developing a widely used diagnostic manual for mental disorders had financial ties to drug companies before or after the manual was published, public health researchers reported yesterday.

The researchers found that 95 -- or 56 percent -- of 170 experts who worked on the 1994 edition of the manual, called the Diagnostic and Statistical Manual, or D.S.M, had at least one monetary

The New York Times

Psychiatric Group Faces Scrutiny Over Drug Industry Ties

By Benedict Carey and Gardiner Harris

July 12, 2008

It seemed an ideal marriage, a scientific partnership that would attack mental illness from all sides. Psychiatrists would bring to the union their expertise and clinical experience, drug makers would provide their products and the money to run rigorous studies, and patients would get better medications, faster.

But now the profession itself is under attack in Congress, accused of allowing this relationship to become too cozy. After a series of stinging investigations of individual doctors' arrangements with drug makers, Senator Charles E. Grassley, Republican of Iowa, is demanding that the American Psychiatric Association, the field's premier professional organization, give an accounting of its financing.

The association is the voice of establishment psychiatry, publishing the field's major journals and its standard diagnostic manual.

The New York Times

Top Psychiatrist Didn't Report Drug Makers' Pay

By Gardiner Harris

Oct. 3, 2008

One of the nation's most influential psychiatrists earned more than $2.8 million in consulting arrangements with drug makers from 2000 to 2007, failed to report at least $1.2 million of that income to his university and violated federal research rules, according to documents provided to Congressional investigators.

The psychiatrist, Dr. [redacted] University is

ANTIDEPRESSANTS

AGENDA

1. Choosing
2. TRD
3. Suicide and other risks
4. Best & newest
5. Ketamine

45 ANTIDEPRESSANT MEDS

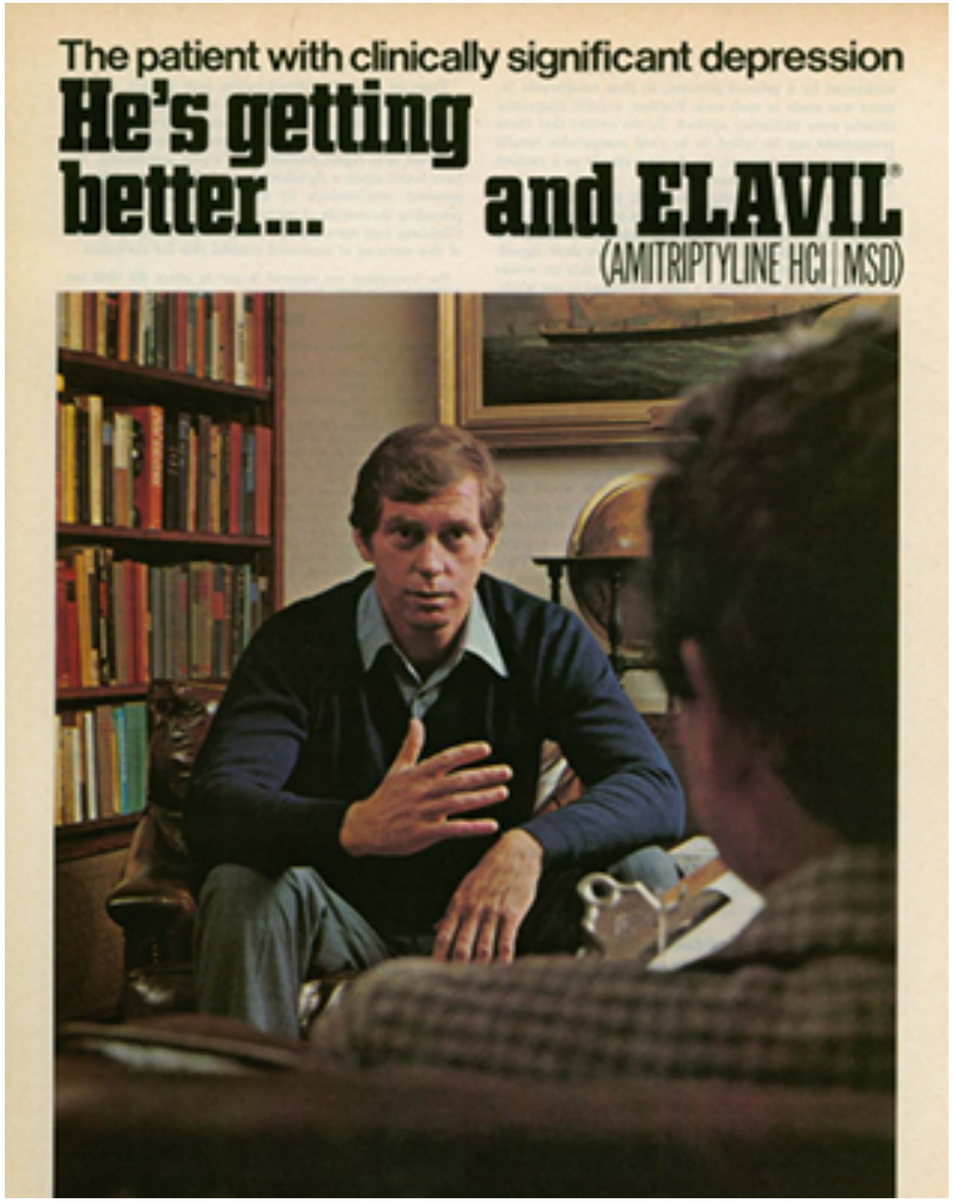
TCA	5	*1959-2006*
Other	12	*1970-2019*
SRI	9	*1991-2002*
SNRI	5	*1993-2013*

ANTIDEPRESSANTS

SRI	Prozac, Zoloft, Paxil, Celexa, Lexapro, Luvox, Sarafem
SNRI	Effexor/Pristiq/Khedezla, Cymbalta, Fetzima
TCA	Elavil (AMI), Norpramin (DMI), Anafranil (CMI), Tofranil (IMI), Pamelor (NTI)
MAO	Marplan, Parnate, Nardil, Emsam
Other	Zulresso, Wellbutrin, Spravato/Ketalar (ketamine), Remeron, Serzone, Desyrel (trazodone), Viibryd, Trintellix

CHOOSING

- Effective with low side effects
  - SRI or Wellbutrin
- Wellbutrin
  - No sexual effects, weight gain, sedation
  - Attention boost
  - Helps the non-specific anxiety that accompanies depression
  - SE: Insomnia, possible seizures with high doses
- SRI
  - Lexapro or Zoloft
  - Best SE and drug interactions



CO-MORBIDITY

- “Two-fers”
- Anxiety: TCAs, SRIs
- Bulimia: Prozac
- Smoking: Wellbutrin
- ADHD: Wellbutrin
- Fibromyalgia: Cymbalta
- DM neuropathic pain: Cymbalta
- PMDD: SRIs
- Depressed + underweight + insomnia: Remeron (no sexual effects)

TRD

- Treatment resistant depressior
- Failed 2 prior trials of ADs
- Adequate doses and duration?
- STAR*D trial
  - Switch vs augment
  - No clear statistical leader

INTERPRETING KEY TRIALS

BRADLEY N. GAYNES, MD, MPH*
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Massachusetts General Hospital, Boston; Professor of Psychiatry; Investigator, STAR*D study

The STAR*D study: Treating depression in the real world

ABSTRACT

The Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study evaluated feasible treatment strategies to improve clinical outcomes for real-world patients with treatment-resistant depression. Although the study found no clear-cut "winner," it does provide guidance on how to start therapy and how to proceed if initial treatment fails.

KEY POINTS

Remission (ie, complete relief from a depressive episode) rather than response (merely substantial improvement) should be the goal of treatment, as it is associated with a better prognosis and better function.

Should the first treatment fail, either switching treatment or augmenting the current treatment is reasonable.

For most patients, remission will require repeated trials of sufficiently sustained, vigorously dosed antidepressant medication. Physicians should give maximal but tolerable doses for at least 8 weeks before deciding that an intervention has failed.

DEPRESSION can be treated successfully by primary care physicians under "real-world" conditions.

Furthermore, the particular drug or drugs used are not as important as following a rational plan: giving antidepressant medications in adequate doses, monitoring the patient's symptoms and side effects and adjusting the regimen accordingly, and switching drugs or adding new drugs to the regimen only after an adequate trial.

These are among the lessons learned from the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study, the largest prospective clinical trial of treatment of major depressive disorder ever conducted. It was funded by the National Institutes of Health and directed by A. John Rush, MD.

WHAT WERE THE AIMS OF STAR*D?

Depression, a common and debilitating condition, affects approximately one in eight people in the United States.[1] It is expected[2] to be the second-leading cause of disability in the world by the year 2020; today, it is the second-lead-

APPROACH TO TRD

- Switch ADs
  - AD of a different class
- Alternatively, augment after first failure, perhaps this order
  - Wellbutrin or Remeron
  - SNRI
  - MAO or TCA
- Next, combo, perhaps this order
  - SRI or SNRI plus
  - Wellbutrin
  - Atypical AP
  - Lithium or thyroid
- Devices

SUICIDE

- Increased risk of ideation in children and adolescents 2004 FDA
  - 2007 + up to age 24.
- Very light rise in S/Ideation
- Controversial
- Depression's risk of suicide
- Closer follow up early in treatment or after stop treatment
- Warning on all ADs

OTHER CLASS WARNINGS

- Mania switch
  - History of mania, hypomania, or family h/o bipolar
- Serotonin syndrome
  - Agitation, hallucinations, other MS changes, hyperthermia, tachycardia, labile BP, cyclones, hyperreflexia, incoordination, N, V, D)
  - Rare, life-threatening
  - Combo of serotonin agents
    - SRI, SNRI, BuSpar, lithium, MAOI

ANTIDEPRESSANT WITHDRAWAL

- “Discontinuation syndrome”
- Within days of stopping AD
- Not medically dangerous
- Usually self-limiting
- Uncomfortable
- Dizzy, N, HA, irritability, diarrhea, agitation, sensory disturbance (electric shock), lethargy, abnormal dreams
- Higher dose and longer term
- Highest risk: Paxil, Effexor (short-acting)
- Lowest risk: Wellbutrin, Remeron, Prozac
- 25% weekly taper x 4 weeks, may slow to several month taper. Or Prozac switch

BLEEDING

- Serotonin
- GI bleed, bruising, nosebleed
- ASA, NSAIDS, anticoagulants, antiplatelet drugs

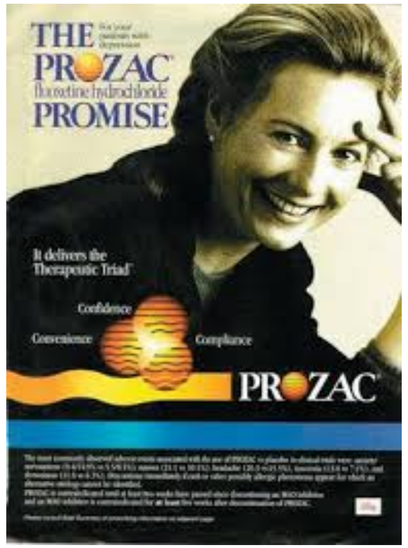
THE ANTIDEPRESSANTS...

SRI

- First line for depression and anxiety
- All = efficacy
- Worst side effects in…
  - Nausea (Zoloft)
  - Insomnia & anxiety (Prozac)
  - Constipation & sedation (Paxil)
  - Sexual (all, especially Paxil)
  - Weight gain (worst with Paxil), apathy, HA
- Serious but rare: Hyponatremia (elderly), GI bleed (especially with NSAIDs)
- Drug interactions worst with Prozac, Luvox, Paxil

SRI

- Prozac: more activating, more anxiety, insomnia, low appetite, drug interactions
- Paxil: sexual, weight, sedation, constipation, drug interaction
- Anxiety: Start low
- OCD: need hi SRI doses



EFFEXOR, PRISTIQ

- Effexor XR
  - May be more effective than SRI but HBP, withdrawal make it 2nd line
- Pristiq, Khedezla
  - Higher than 50 mg causes SE, no benefit
  - No clear advantage over Effexor XR or others
  - Europe application withdrawn after regulator called Pristiq less effective than Effexor, and no advantages

CYMBALTA

- Depression + comorbid pain syndromes
- HBP
- Possibly serious liver SE. Avoid in heavily alcohol or liver dz patients
- Europe: stress urinary incontinence

FETZIMA

- For patients who need NE effects of SNRi
- Cons: $, N, titration, urinary retention
- Enantiomer (mirror-image) of Savella
  - Fibromyalgia
  - Savella approved for depression in US

If you've been unsuccessful treating your depression, maybe you don't need an additional medicine. Maybe you just need a different one. Fetzima is thought to work by increasing the levels of 2 chemicals in the brain: serotonin and norepinephrine. If depression has you feeling sad and lonely AND is disrupting your ability to be productive, talk to your doctor about Fetzima.

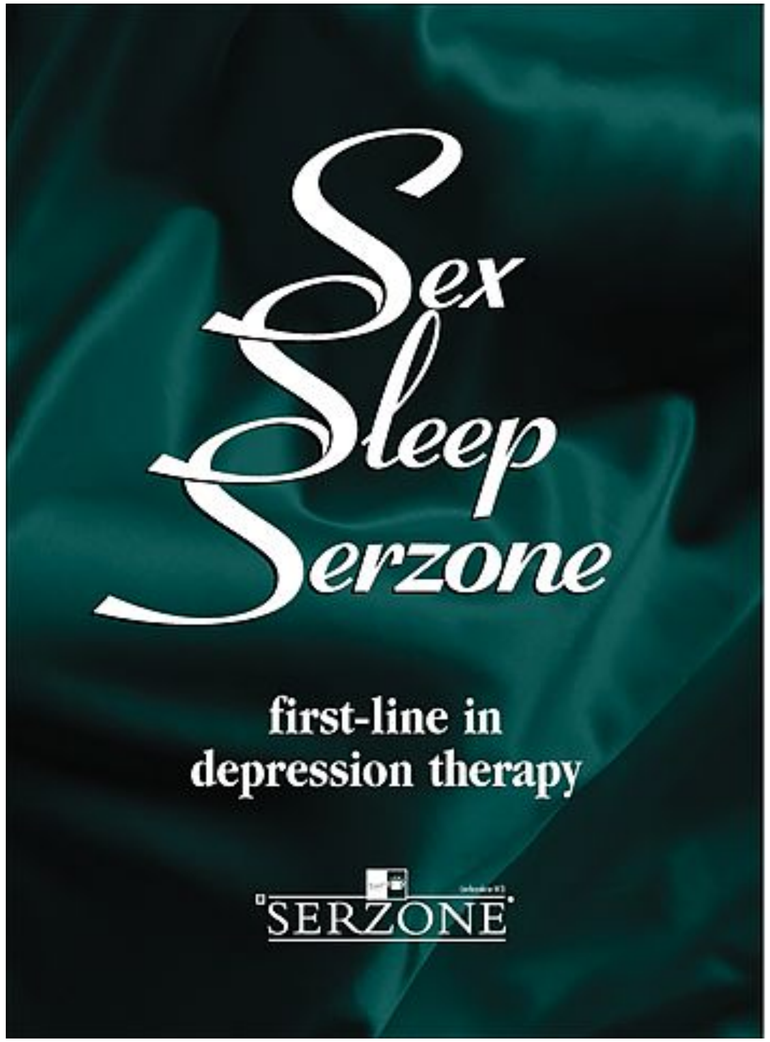
Fetzima
levomilnacipran ER capsules
20 mg • 40 mg • 80 mg • 120 mg

REMERON

- Underprescribed
- Weight gain (elderly, cancer)
- Sedation
- No sexual effects
- Faster onset?
- Higher dose may improve sedation

SERZONE

- No sexual side effects
- Was popular
- Not now
- Hepatic (rare) 1/200,000 risk, or 3-4 times
- Similar to trazodone structure, less sedating
- Still generic (nefazodone)



TRICYCLIC ANTIDEPRESSANTS

- Depression, OCD, chronic pain, insomnia
- Secondary: less sedating, better tolerated
  - DMI, NTI
- Tertiary: more sedating
  - AMI, IMI
- SE: sleepy, dry mouth, constipation, weight, sexual, urinary, vision, cardiac, OD risk
- Action: SNRI
- Discovery: IMI tweaked from Thorazine, but didn't work for psychosis

TRAZODONE

- Desyrel
- Pros: Less sexual, weight
- Cons: sleepy & dizzy days
- Insomnia. Rarely used for depression
- Priapism, orthostatic hypotension
- Action: SRI, others

TRINTELLIX

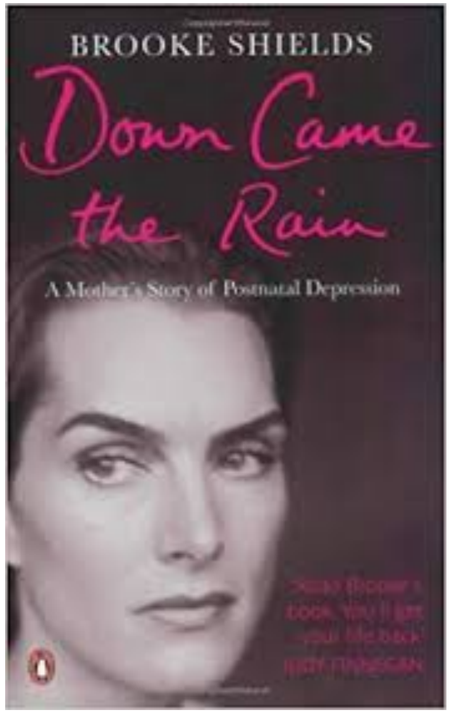
- Was Brintellix. “Bring intelligence”. Confused with Brilinta
- Pros: Pro-cognitive? Lower sexual effects
- Cons: N, $
- Action: multimotor AD; serotonin modulator and stimulator

VIIBRYD

- SRI + BuSpar
- Probably not better sexually
- Slow titration, must take with food, drug interactions
- Naming
  - Rhymes with hybrid (SSRI and 5-HT1A)
  - Virile, implying “no” sexual SE

ZULRESSO

- brexanolone
- Postpartum depression
- Given a long infusion at a clinic with close monitoring
- Possible severe reactions
- $34,000 + provider + facility
- No f/u data after 30 days
- Action: GABA-A
  - A neurosteroid like the allopregnanolone hormone, which rises during pregnancy and falls abruptly after delivery



MONOAMINE OXIDASE INHIBITORS (MAOI)

- Marplan, Nardil, Parnate. Emsam patch
- 1959. First AD
- TB: INH, a mild MAOI, elevated mood
- Foods (little risk with *low* Emsam dose)
  - Tyramine, tryptophan, tyrosine, phenylalanine
  - Aged cheese, dried or cured meats, fava/broad beans, draft beers, Marmite, sauerkraut, soy sauce, spoiled food
- More effective than TCAs for atypical depression
  - 1970s and 1980s studies
  - = overreact, oversleep, rejection sensitivity, mood reactivity
- Waiting period when switching from other/to ADs.

THYROID

- Cytomel, Synthroid
- Off-label
- T3 preferred to T4 for psych
- Mixed efficacy
- Modestly better remission, and better SE, than lithium augmentation

KETAMINE

- 1960s, anesthetic that didn’t lower respiration or BP.
- Vietnam War “buddy drug” carried by soldiers
- Modestly effective for TRD
- Appealing alternative vs ECT
- Ultra-rapid AD; 24 hours
- Ketalar (ketamine) IV, use 25% of anesthetic dose
- Spravato (esketamine) nasal spray
  - No food or water before
  - 2 hours of observation in clinic or office
  - Week 1-4 induction phase, twice a week
  - Maintenance phase every 2 weeks after
  - Action: NDMA antagonist
  - Schedule III

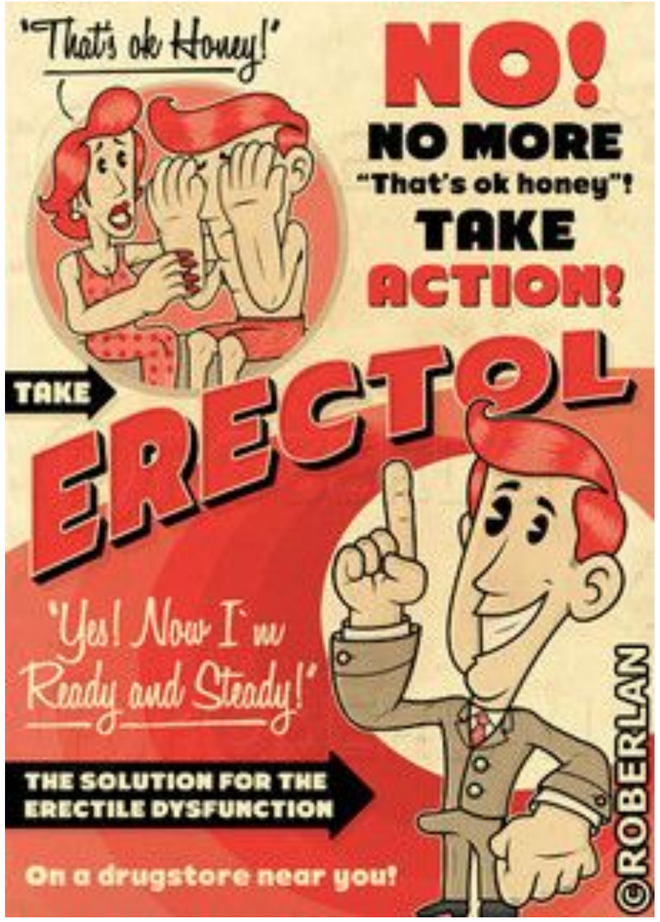
CLINICAL TRIALS

- Psilocybin
- Magnetic seizure therapy
- Stem cell treatment

SEXUAL DYSFUNCTION

CAUSES

- Most antidepressants
- Not Wellbutrin, Remeron
- Low libido, anorgasmia, erectile dysfunction
- Antipsychotics
  - Lower libido
  - Sometimes due to prolactin
- Fixing the (medication) cause
  - Decrease dose, switch, antidote, 2-3 day holiday
  - Prescribe another med



PDE-5 INHIBITORS

- Erectile dysfunction
- Avoid with any nitrates, including poppers

Drug	How soon? (min)	How long? (hr)	Food delay?
Viagra	30	2	Y
Levitra Staxyn	30	2	Fatty
Cialis	60	36	N

TESTOSTERONE

- Men with low testosterone
- Won’t work if normal T levels
- N, HA, insomnia, anxiety, acne, water & e’lyre retention, irritation of gel/gum, injection pain,
  DVT, PE, MI, stroke, BPH worse, prostate cancer

LOW SEXUAL DESIRE IN WOMEN

- No miracles
- 2 approved
- Libido, not orgasm
- Premenopausal women

LOW SEXUAL DESIRE IN WOMEN

- Addyl
  - Every night. Try for 8 wks. No alcohol (2 hours before or after)
- Vyleesi
  - Take when needed; auto-injection under skin; max 8 doses/month, 1/d
  - 4-8% over placebo, 40% dropout, hyperpigmentation, N 40%
  - Melanocortin
  - unblush.com

SRI SEXUAL EFFECTS

- SRI sexual effects
- Periactin (cyproheptadine)
  - Off label, sedating
  - For anorgasmia
  - Appetite stimulant for cats
  - Serotonin blocker
- Wellbutrin
- Remeron

MEDICATION SEXUAL EFFECTS

- Great opportunity to talk to patients about sex and how to improve theirs

DEVICES

AGENDA

1. Light boxes
2. ECT
3. Magnets
4. Vagal nerve
5. Other

SOMATIC TREATMENTS

- Light, electricity, magnets, surgery

- BLT bright light therapy
- ECT electroconvulsive therapy
- TMS transcranial magnetic stimulation
- VNS vagal nerve stimulation

BRIGHT LIGHT THERAPY

- Works on seasonal affective disorder SAD
  - Mood worse in F/W, improves Sp/Su
  - Especially oversleep and overeating sx
- Seasonal Pattern Assessment Questionnaire
- Light stimulates optic n., thus pineal gland suppresses melatonin
- Patient sits in front of box x 30 min after awaken each morning, best if same time. May read, computer, treadmill

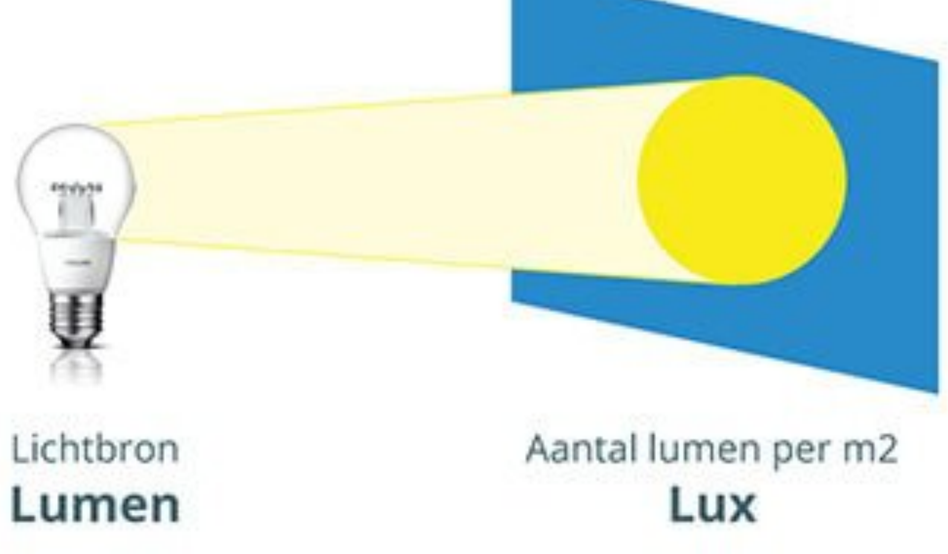
Wirecutter Pick

2020

c|net

"Best overall sunrise alarm clock"
July 2020

BRIGHT LIGHT THERAPY



- Full spectrum. At least 10k lux
- Like 30 min outside after sunrise
- Choose: 10k lux intensity at 24 inches. Smaller = glare
- Checkup 1st if glaucoma or cataracts
- Medication OK
- Some need evening light Automated Morningness-Eveningness Questionnaire
- Dawn simulator lamps may work as well.
  - Fit in standard lamp. Light slowly increases over an hour to mimic sunrise
  - 250 lux
  - No need to sit

ECT

- 1938
- One of most effective treatments. Depression 70-90% remission
- Severe TRD or psychosis, catatonia
- Cognitive effects, worse with bilateral lead
  - 30 min acute confusion
  - Memory loss x weeks
  - HA
  - Longer memory problem in 25%
- Safe in pregnancy
- Better response in elderly patients

ECT PROCEDURE

- Monitor leads
- Electrodes (bilat, R unilat, bifront)
- IV hypnotic + muscle relaxant
- Seizure x 30-60 sec induced by electrical stimulus
- 3x a week, response after 1-2 w, average 7-10 treatments done
- Weekly x 2-4 w, then monthly x 6+ months

TMS

- Transcranial magnetic stimulation
- Daily clinic visit x 6 w, 30-40 min
- Response by 20 x. Then taper, maintenance
- Reasonable tx for TRD; OCD; migraine pain
- Magnetic coils, controller, comfy seat
- Frequency, intensity, train (duration), interval, # trains/session
- Magnetic field modulates cortex neurons, which is under-active in depression
- ECT better for suicidal or psychotic depression
- TMS needs no anesthesia, fewer SE

VNS

- Vagus nerve stimulation
- Very controversial
- TRD, seizure d/o
- Surgery, device placed under skin of chest, wires to vagus nn in chest.
- Pulses x 30 sec q 5 min
- SE: 50% voice changes or horseness. Infections, nerve damage
- Vagus N sends fibers to serotonin and NE areas

COMING SOON

- CES cranial electric stimulation
  - Fisher Wallace Stimulator
  - Alpha-Stim
  - Depression and anxiety
  - Weak evidence
- eTNS external trigeminal nerve stimulator
  - ADHD age 7-12, not on meds
- DBS deep brain stimulation
  - Surgery
  - Parkinson’s dz, tremor
  - Approved for humanitarian use for tx-resistant OCD

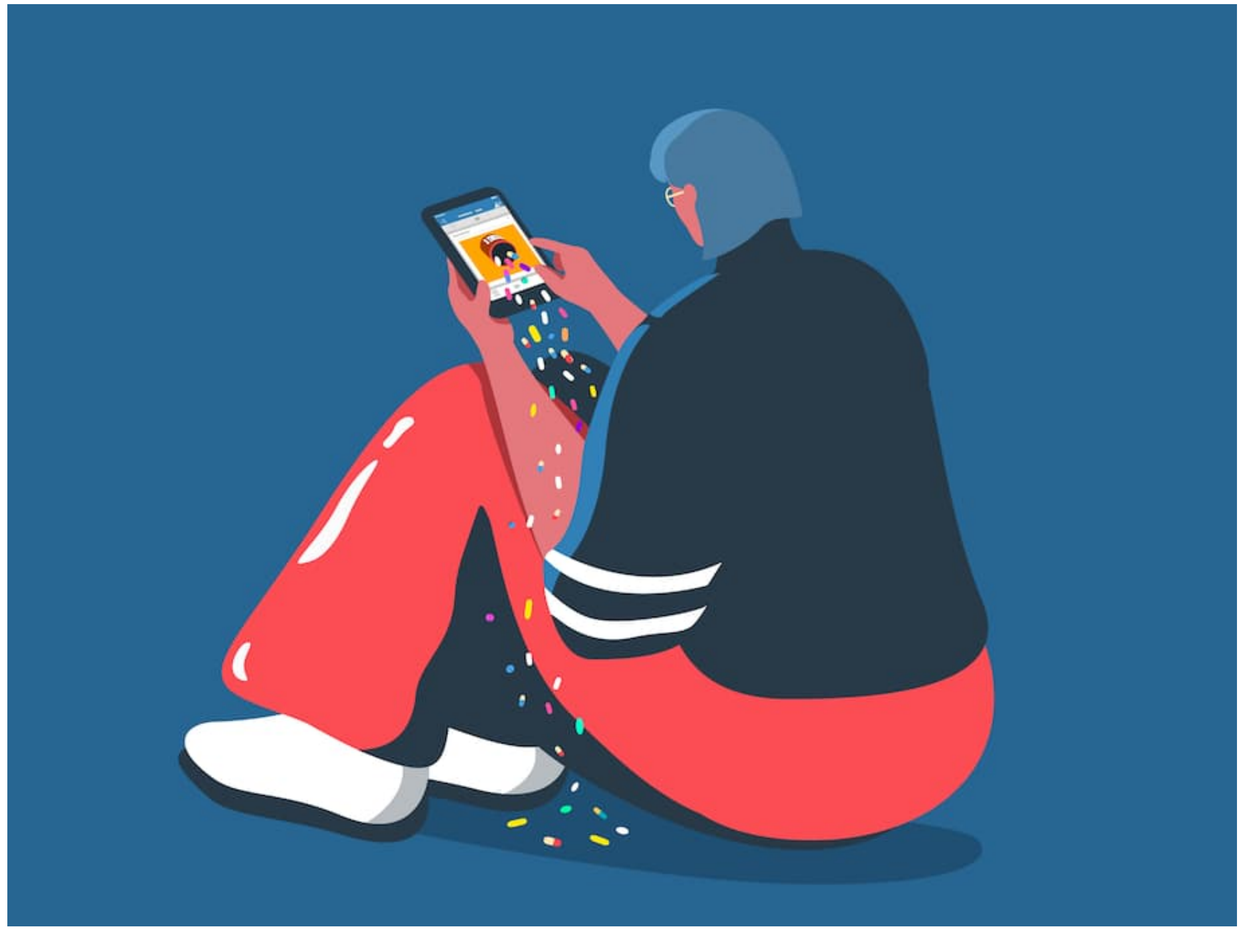
ANTIPSYCHOTICS

AGENDA

1. Choosing
2. Side effects
3. Best & newest

CHOOSING

- Efficacy
- Side effects
- Cost



EFFICACY

- Most effective: Clozaril>Zyprexa>
  - SE, including weight
- SGAs
  - Broader spectrum? Psychosis + mood
  - Better for negative symptoms
    - Or because the SE (especially EPS)of FGAs mimic negative sx
- Prices improving for SGAs

SIDE EFFECTS

- Weight, lipids, diabetes
  - Worst: Clozapine, Zyprexa
  - Best: Abilify, Latuda, Geodon
- Sedation
  - Worst: Clozaril, Zyprexa, Seroquel
  - Best: Abilify, Risperdal, Latuda, Rexulti, Saphris/Secuado
- EPS
  - EPS: Haldol, Invega, Risperdal
  - Akathisia: Abilify, Rexulti
  - Least: Thorazine, Clozaril, Fanapt, Zypreza, Seroquel, Geodone

RISKS

- Discontinuation
  - Supersensitivity psychosis
    - AP exposure increases DA receptors
  - Warn patients, slow taper
- Withdrawal dyskinesia
  - TD sx when lower or stop. Lips, tongue, hand, foot.
- Cholinergic rebound
  - SLUD: Salivation, lacrimation, urination, defecation
    - N, V, D, HA, sweat, insomnia.
  - Very anticholinergic drugs like Clozaril, Zyprexa
  - Cholinergic super-sensitivity when stop or switched

SWITCHING

- Switching between Ads
- Immediate or cross-taper
- Immediate may be just as effective

COST

- Generics vs $1k-3k/month.

CLASS WARNINGS

- Weight gain, hyperglycemia, DM new or worse, hyperlipidemia
- Worst: Clozaril, Zyprexa > Seroquel, Risperdal
- Weight and metabolic worse in pediatric
- After initial checks, monitor weight (q3m), waist (yearly) BP, glc, lipids (annual)
- Black box: higher mortality in geriatric pts with dementia-related psychosis (< double)
- Stroke, TIA in geriatric
- Neuroleptic malignant syndrome
  - Fever, muscle rigidity, autonomic instability
- Tardive dyskinesia
- Newborn EPS and withdrawal

TREATMENT ALGORITHM

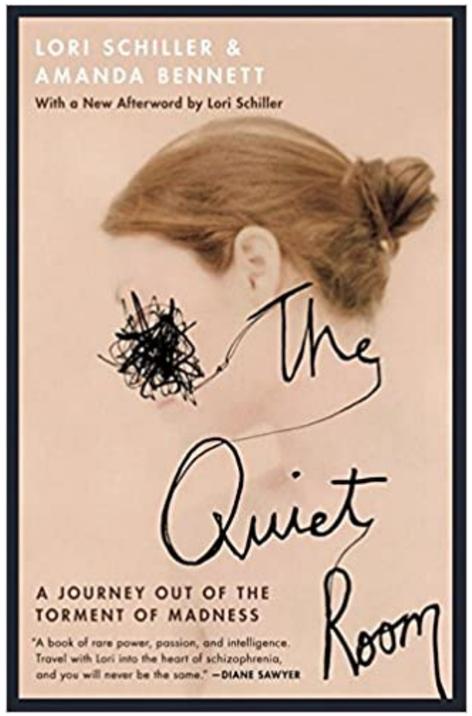
- Not agitated
  - Abilify, Risperdal, Latuda
- Agitate, accepts meds
  - Zyprexa ODT, Seroquel
- Agitated, acute, refuses meds
  - Haldol, lorazepam, benztropine/diphenhydramine
  - Zyprexa
  - geodone
- Negative sx: Vraylar, Clozaril, +Remeron
- Treatment resistant: Clozaril, Zyprexa, +VPA, combos

ABILIFY

- Minimal weight, metabolic SE
- Akathisia
- Generic
- D2 and serotonin
- MyCite (contains ingestible sensor)

CLOZARIL

- Probably most effective AP. Anti-suicide
- Rarely used
- One of worst SE profiles of any psych drug
  - Weight: 1/2 of patients gain >20% body weight
  - After 1 year, 15-30 lb avg. gain
  - Sedation, drooling
  - Life-threatening neutropenia, monthly blood draws
- Use after 2 failed APs
- Lori Schiller. The Quiet Room



FANAPT

- Second line
- Less effective than other APs?
- Twice-daily
- Titrate to start, again if interrupted
- QT, dizzy, weight gain, glucose
- 2002 FDA approval delayed to 2009 (corporate, more data requested)

GEODON

- “Down to earth” geo-down
- Weight, metabolic
- QT prolong (overblown?)
- Twice-daily, with meals (2x absorption)

INVEGA

- Like Risperdal
- No drug interactions
- Same prolactin
- More QT, tachycardia, maybe EPS
- Easy transition to LAI without oral overlap
- Ghost pills (like Concerta, Wellbutrin SR) in stool
- First schizoaffective approval

LATUDA

- Decent metabolic, QT
- No titration
- Must take with >350 cals food
- Drug interactions, sedation, akathisia, EPS
- Competitive with Abilify and Geodon
- Serotonin affinity (depression, anxiety pain, cognition, memory) but unproven superiority

NUPLAZID

- Hallucinations and delusions in Parkinson’s disease
- Don’t know yet about schizophrenia
- No weight gain
- Safety concerns
- No DA effect so doesn’t worsen Parkinson’s

RISPERDAL

- First choice for many new psychosis
- Use for irritability in autism
- SE
  - EPS over 4 mg/day
  - Sleepiness in kids
  - Orthostatis, prolactin (sex, milk, periods)

SEROQUEL

- Broad spectrum:

  Schizophrenia, bipolar, MDD adjunct
- Don’t crush, chew or break XR
- Sedation, weight, orthostasis
- Low EPS
- Cataracts in beagles

VRAYLAR

- Close to Abilify
- Claims to help negative symptoms
- Too early to tell
- SE: EPS, akathisia

ZYPREXA

- Weight: 30% of patients gained 7%

LAI

- Long-acting injectable APs
- Depot APs
- Why?
  - Keep up serum levels in non-adherent pts…if they accept the shot
  - Keep families and clinicians from arguing with pts
  - Lower OD risk
- Mixed studies
  - No difference in relapse from oral?

LAI: USE

- Try oral first (effective, tolerable?)
- Full benefits take longer than oral
- Oral overlap
- Avoid LAI if NMS history

- Deep IM injection speeds absorption, often ventro-gluteal mm of hip
- Don’t massage injection site (goes to fatty tissue, slows absorption)

LAI: TYPES

- Prolixin D: q2w, ¢, EPS, TD, oral overlap
- Haldol D: q4w, ¢, EPS, TD, oral overlap
- Zyprexa Relprevv: q2-4w depending on dose. Worst LAI SE?
- $, better SE, most require oral overlap
  - Abilify Maintena: q4w
  - Aristada: Abilify pro-drug, q6-8w
  - Aristada Initio: same, but no oral overlap
  - Invega Sustenna q4w; Invega Trinza q3m
  - Invega Trinze: q3m
  - Risperdal Consta: q2w
  - Perseris: q4w Risperdal

TD

- Tardive dyskinesia
- Risk: FGA 3-5%/yr, higher potency, duration, dose, elderly, Black, Reglan, Compazine
- Involuntary movements, usually after months-years of APs.
- Mouth-lips-tongue: chew, lip smack, tongue protrusion
- Fingers, toes
- D2 blockade causes DA receptor super-sensitivity
- Ingrezza
- Austedo
- Xenazine

MOOD STABILIZERS

AGENDA

1. Choosing
2. Side effects
3. Best & newest

MOOD STABILIZERS

- Lithium
- Depakote
- Lamictal
- Tegretol
- Trileptal
- Antipsychotics
- Novel anticonvulsants

GENERAL

- Manic episodes
  - APs are most effect for fast control of acute mania
  - Adding mood stabilizers helps
  - Three most popular for agitated, psychotic patients also give worst side effects
    - Zyprexa, Seroquel, Haldol
    - Risperdal + lithium or Depakote, + prn Ativan
- Bipolar depression
  - Prozac + Zyprexa; Seroquel; Latuda; Vraylar
  - Lithium, Lamictal, Abilify
  - + Wellbutrin least likely to cause manic switch

BIPOLAR MAINTENANCE

- Reduce cycling and delay acute episodes
- Lithium (better for mania than depression)
- Lamictal (better for depression than mania)
- Depakote or Tegretol

WARNINGS

- Suicide thoughts or behavior 0.4? vs 0.2% placebo
- DRESS: drug rash with eosinophilia and systemic symptoms, a fatal, multi-organ hypersensitivity reaction
  - Fever, rash, lymphadenopathy, organ damage

SWITCHING OR STOPPING

- High risk of manic or depression relapse
- Stopping maintenance lithium: 60-90% risk of relapse within a year
- Risk worse if lithium stopped (over < 2 wk vs <4 wk)
- Cross-taper between drugs over 2 weeks

NOVEL ANTICONVULSANTS

- Epilepsy drugs
- Weak results
  - Neurontin, Lyrica, Topamax
  - Other uses (anxiety, alcohol dependence, weight loss)

- Side effects
  - Compared to older seizure meds, less toxic, no drug monitoring, fewer interactions
  - Suicide thoughts, behavior warning (0.4 vs 0.2% placebo)
- Lyrica schedule V

TREATMENT OF BIPOLAR-MANIA

- Euphoria
  - Lithium, lithium + AP, or VPA +/- AP
- Mixed mania
  - AP or AP + VPA or Li
- Acute agitation
  - IM Haldol + lorazepam, Zyprexa, Geodon
- Treatment resistant
  - Lithium + VPA + AP, Tegretol, Clozaril
- Nothing working
  - Allopurinol, tamoxifen
- Unlikely to help: Lamictal, Neurontin, Trileptal

MOOD STABILIZIER: LITHIUM

- Gold standard, under prescribed
- Acute & euphoric mania, not mixed or rapid cycling
- Bipolar depression
- TRD augmentation
- Patients tolerate SE better than expected
- N, D, tremor, thirst, polyuria, memory, weight, thyroid (8%; especially women), acne, kidney (DI), cardiac
- Blood tests
- Li removed from 7-Up in 1950

MOOD STABILIZERS

- Lamictal
  - Maintenance of bipolar, especially depressive. Not acute mania
  - Slow titration up. SJS
- Depakote
  - Acute mania, faster than lithium with lower SE, fewer interactions than Tegretol, tx rapid cycling
  - SE: lower platelets (reversible), liver toxic
  - 1882 from valeric acid (valerian)
- Tegretol: blood and liver effects, rash, SJS
    - Trileptal: probably not as good, but easier (labs, interactions)

NOVEL ANTICONVULSANTS

- Neurontin (gabapentin)
  - No help for bipolar
  - Antianxiety but abusable
  - Neuropathy and restless leg syndrome
  - Alcohol or BZD withdrawal
  - Schedule V in Kentucky
- Lyrica (pregabalin): GAD, BZD withdrawal, schedule V, abuse
- Topamax
  - For seizures, migraines, (alcohol dependence, bipolar, obesity).
  - Cognitive SE (Dopamax) dose-related

ANXIOLYTICS

BENZODIAZEPINES (BZD)

- Antidepressants are most effective anxiolytics?
- BZD work fast, reliably
- Dependance, addiction
- SUD means monitor closely, not a rule-out
- Limit refills, ask about SU
- Long-acting (Klonopin): slower on/off, less likely addiction?
- Short-acting (Xanax, Ativan): for prn or occasional need
- Often add BZD when start SRI, stop in 2 weeks
- Equivalencies mg
  - Xanax 0.5, Klonopin 0.25-0.5, Valium 5, Ativan 1, Restoril 15

WARNINGS

- Don’t mix BZD and opioids
- Long term use of BZD affects sleep architecture
- Elderly
  - Falls 1.5x, worst in week 1-2
  - Dementia 1.5-1.8x
- Cognition

NON-BZD

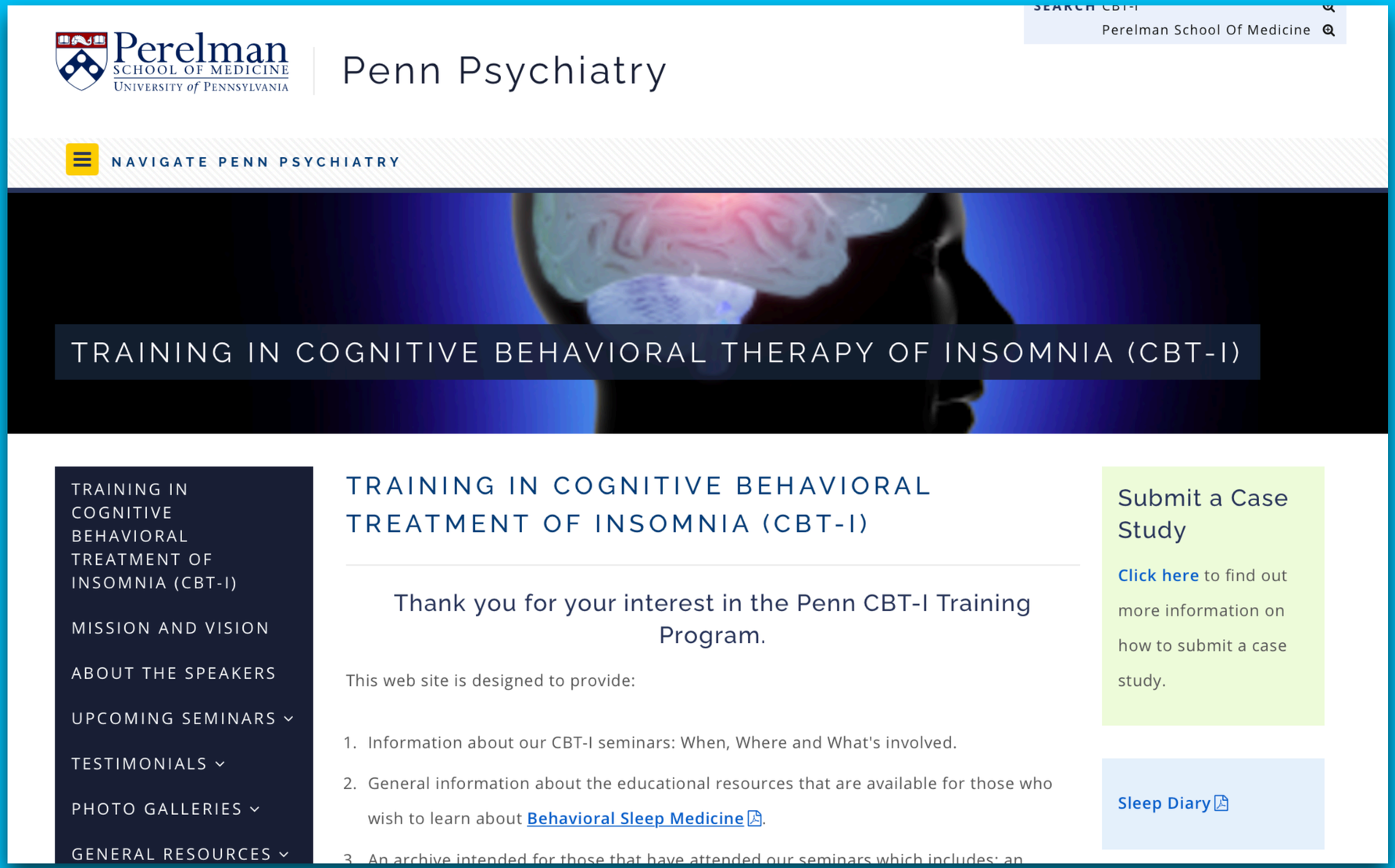
- BuSpar for GAD. A non-BZD. Weaker. 1-2 w onset
  - Abilify, Geodon, Viibryd also serotonin 5-HT1A partial agonist
- Propranolol (beta blocker) for somatic sx of anxiety (palpitations, SOB), stage fright
- Clonidine (alpha-2 agonist) or Prazosin (alpha-1 antagonist) for anxiety and insomnia
- Prazosin for PTSD?
- SRI or SNRI for comorbid depression
- Neurontin, pregabalin for neuropathic pain
- Seroquel for bipolar depression
- Clonidine or Prazosin for PTSD, nightmares, severe insomnia
- Hydroxyzine if SUD or risk

HYPNOTICS

INSOMNIA

- Underlying causes addressed? Anxiety, depression, stress, med SE
- Sleep hygiene
  - Nicotine, caffeine, alcohol, exercise, bedroom environment, sleep restriction, relaxation
  - CBT-I reduces insomnia by 50% and majority keep their gains when done
  - CBTI at U Penn

MED.UPENN.EDU/CBTI



SLEEPING PILLS

- AD alone, or add hypnotic (for depression + insomnia)
- Z-drugs (Sonata, Ambien, Lunesta)
  - Bind GABA receptors, less relaxing or addicting than BZD
- Antihistamines OTC; confusion in elderly
- BZD
- Rozerem
- Suvorexant, a dual orexin blocker (DORA)
- trazodone, doxepin (vs Silenor), Remeron
  - Silenor (doxepin)
- Seroquel
- melatonin (early evening)

SIDE EFFECTS

- Daytime groggy, hangover (antihistamines, some BZD, Ambien CR)
- Anterograde amnesia (antihistamines, Z drugs)
- CNS depression, alertness, driving
- Respiratory depression (avoid with opiates, COPD, sleep apnea)
- Paradoxical reactions
- Tolerance
- Withdrawal
- Abuse
- Sleep driving, eating, texting, sex. With no recollection

BELSOMRA

- suvorexant
- Blocks orexin receptors
  - DORA (dual orexin receptor antagonist)
- Orexins promote wakefulness
- Other hypnotics stimulate GABA or melatonin or block histamine
- Not better but same abuse risk

ROZEREM

- Different than BZD or Z-drugs
- Melatonin agonist
- Less respiratory or hangover SE
- Patients say doesn’t work for a few days
- Rare hormonal effects

ADHD

AGENDA

1. Choosing
2. Side effects
3. Best & newest

DECIDING

- Stimulants work better
- Non-stimulants
  - Drug abusers
  - Strattera, Wellbutrin, clonidine, guanfacine
- Short vs. long-acting stimulants
  - Appetite, timing, exposure, sleep, convenience
- Amphetamines vs methylphenidate
  - AMP better for adults?
  - MPH safer for kids, adolescents?
- Broad spectrum
    - Depression, sleep, tobacco

DECIDING

- Expensive new products
- Chews, longer acting, liquids,
  - Methylphenidates MPH
    - Quillichew ER (chewable)
    - Cotempla XR-ODT (oral dissolving)
    - Journay PM (take night before, acts next morning)
  - Amphetamines AMP
    - Adzenys XR-ODT (oral dissolving)
    - Dynavel XR (liquid)

STIMULANTS

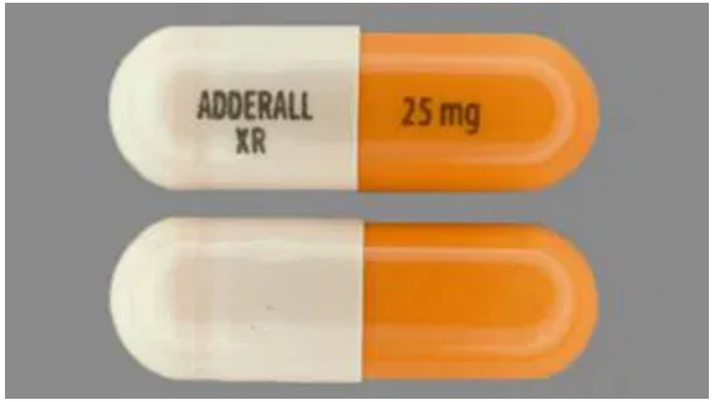
- Side effects
  - Psychosis, aggression
  - Rare, dose-related, more likely if predisposed to psychosis?
- Tourette’s or tics, unmasking (MPH or guanfacine preferred)
- Seizures, lower threshold?
- Growth or weight, with long term use? Drug holidays
- CV safety
  - FDH class warning 2006

STIMULANTS

- Schedule II
  - Electronic only (1/2021); monthly script; now can post-date
- Start with amphetamine or methylphenidate
- Avoid with antacids

AMPHETAMINES

- Adderall
  - Twice as potent as MPH
  - More of a kick than MPH?
  - 2005 Canada held, cardia concerns
- dextroamphetamine (Dexedrine, Zenzedi, ProCentra)
  - D-isomer, the more potent isomer of AMP.



AMPHETAMINES, NEW

- Vyvanse 2007
  - Smooth, “less abuse”
  - DextroAMP + lysine
  - Binge ED
- Adzenys XR-ODT
- Dynavel XR
- Evekeo
- New formulations, expensive
- Allow liquid or dissolving tablet

SIDE EFFECTS

- Psychosis or aggression
  - Dose-related; predisposition?
- Tourette’s or tic
  - Worsening or new
  - Less risk with MPH or guanfacine
- Seizures
- Growth or weight
  - Drug holidays
- Cardiovscular
  - 2006 FDA class warning; newer date reassuring. Ask patient first
- Schedule II (refills, electronic)

AMPHETAMINES

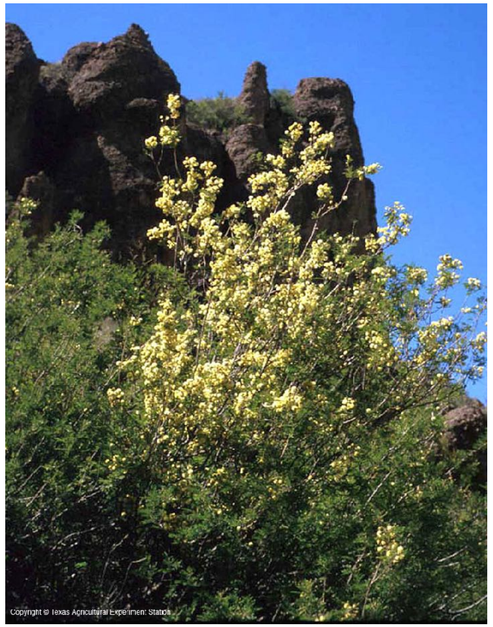
- Indication: ADHD. Off: Depression
- History: SK&F “Benzedrine” inhaler
- Dose: 10-30 BID (adults)
- SE
  - Abdominal pain, appetite, weight, sleep, headache, anxiety
- Action: Inhibits reuptake of DA, NE

METHYLPHENIDATES

- dexmethylphenidate (Focalin)
  - Dextro isomer of MPH. Like Ritalin, 2x potent, so often use 1/2 the dose
  - XR capsules: Beads, 1/2 IR, 1/2 delayed, okay to open and sprinkle
- MPH (Ritalin, Methylin)
  - Named after Rita, the nickname of the chemist's wife, taken as a stimulant before a tennis game
  - Concerta, Ritalin SR or LA
    - Concerta, like Invega, uses osmotic delivery system (immed/delayed)
  - Aptenso or Adhansia: mix of IR and ER beads
  - Daytrana patch

METHAMPHETAMINE

- Desoxyn
  - Pharmaceutical-grade meth
  - More addictive
  - Acacia trees in West Texas



NON-STIMULANTS

- Strattera
- clonidine (Kapvay, Catapres)
  - Use: Hypertension, ADHD, (conduct disorder, pervasive DD, tics, migraines prevention, opioid withdrawal).
  - Action: alpha-2 agonist
- guanfacine (Intuniv, Tenex)
- Wellbutrin

WAKEFULNESS

- Provigil (modafinil) & Nuvigil
  - Nuvigil lasts longer
  - DRI
- Sunosi (DNRI)
- Excessive daytime sleepiness due to narcolepsy or apnea
- Shift-work disorder
- Jet lag
- Sleepiness from ADs
- ADHD
- Fatigue
- TRD

DEMENTIA

THESE MEDS CAN MIMIC DEMENTIA

- BZDs
- Z-drugs
- Anticholinergics
  - TCAs, Paxil
  - Compazine, Phenergan
  - Antihistamines G1
  - Incontinence
  - Antiparkinsonian (Cogentin, Artane)
  - APs (G1, Zyprexa, Clozaril)
  - MM relaxants (Flexeril, Robaxin, Norflex)

CI'S TO TREAT COGNITIVE IMPAIRMENT

- Cholinesterase inhibitors (CI)
- Do not improve memory
- Stop decline x 6-12 months, then decline resumes
- Stopping med drops memory by 6-12 months
- Restarting won't bring it back

COGNITIVE IMPAIRMENT

- CI's
- Mild-moderate cognitive impairment
  - Start with Aricept (best data, but others equally effective)
  - Aricept (donazepil), Razadyne/Reminyl (galantamine), Namenda (memantine)
  - GI, vivid dreams
- Combo of Aricept & Namenda (or Namzaric)
- Exelon (revastigmine) is BID, expensive, N, V

OTHER DEMENTIA SYMPTOMS

- 90% of dementia patients have secondary sx
- BPSD = “Behavioral and psychological symptoms of dementia”
- Agitation, aggression, wandering, psychosis, depression, anxiety
- Recreational, art, music, and habilitation therapy
- Cholinesterase inhibitors
- SSRIs
- Remeron
- BZD (avoid, but choose short acting)
- APs (vs black box on mortality, stroke), so restrict to psychosis and severe aggression
- Mood stabilizers (Neurontin 100 mg prn)
- Acetaminophen, low-dose opiates, trazodone, Prazosin, clonidine, Marinol

NATURAL TREATMENTS

AGENDA

1. Deplin
2. L-tryptophan
3. Melatonin
4. NAC
5. Fish oil
6. SAMe
7. SJW

NATURAL TREATMENTS

- CAM: complementary & alternative medicine
- Exercise, light therapy, massage, meditation
- Not regulated by FDA
  - Quality control
    - Brand to brand, batch to batch
    - Adulterations with herbs, chemicals, drugs, toxins
- NIH National Center for Complimentary and Integrative Health

DEPLIN

- L-methylfolate $$
- Half of the population has impaired function of the enzyme needed to change folic acid to l-methylfolate. Need LMF to make monoamine (5-HT, NE, DA).
- Try folic acid $ first
- FDA
  - A “medical food,” not a drug
  - Prescription only
- SE: May hide B12 deficiencies neurologic signs
- Action: Increase monoamines?

L-TRYTOPHAN

- “Serotonin boost” alternative to SRI and SNRIs?
- An essential amino acid.
- 300-500 mg/day with antidepressants. From 500 to my 6000 mg used
- SE abdominal pain, N, V, D, gas, HA; eosinophilia-myalgia in 1990
- Thanksgiving turkey coma probably comes from the carbs.
- Dietary: milk and cookies to sleep
- Very limited evidence.

MELATONIN

- Shortens time to fall asleep by 12 min
- Try in older patients
- No reliable long-term safety data
- Dosing
  - Sleep: 0.5-20 mg in early evenings (not bedtime). Varies by age and health
  - Jet lag: 1-3 mg on departure day, at a time that matches anticipated bedtime at destination. Then 1-3 mg HS for next 3-5 days
- Action: melatonin receptor agonist
- Pineal gland secretes M'. Increases at sunset, peaks at middle of the night.
- OTC in US since 1990s. Rx or banned in many countries
- Cherries, bananas, grapes, rice, cereals, herbs, olive oil, wine, beer.

NAC

- N-acetylcysteine
- Comes from cysteine, an amino acid used to make glutathione, an antioxidant. Moderates glutamate
- Used for Tylenol OD
- Add-on to SRIs for: OCD, Trichotillomania, nail biting, skin picking
- 1200-2400 mg/d, divide by BID to reduce GI SE (which go away in a few weeks).
- Study bias by an Australian researcher?

FISH OIL

- Omega-3 fatty acids. Fish better than flax
- Adjunct for depression (uni, bip).
- Dose
  - Start with 500 mg, target 1-2 gm
  - Don’t exceed 3g/d
  - May divide by BID-TID
  - 300-6000 mg used in studies.
- SE; especially over 4g/d. Fishy aftertaste, N, loose stools, bleeding. Avoid if seafood allergy.
- Mercury and PCBs? Manufacturing process.
- SMASH (salmon, mackeral, anchovies, sardines, herring)

SAMe

- SAMe: s-adenosyl-l-methionine
- May be as effective as TCAs.
- Use: Mild to moderate depression where alternate therapy requested, or partial responders.
- Other use: arthritis, cirrhosis, fatty liver disease
- Dose: 1600 mg/d (start with 400)
- Action: methyl group helps synthesis of neurotransmitters.
- US: dietary supplement since 1999. Rx: Italy 1979, Spain 1985, Germany 1989

ST. JOHN'S WORT

- More effective than placebo, similar to SRIs for mild depression.
- Short-term treatment of mild depression
- Many drug interactions
  - Serotonin syndrome
  - Lowers OCP by 15% (bleeding, pregnancy)
- Dose: 300 mg TID, depending on product
- Withdrawal
- Action: Modulates monoamines
- John the Baptist, born June 24. The plant (wort) blooms 6/24.
- Invasive weed to Australia, now 20% of world's crop grown there.

VITAMIN D

- Depression
- For patients with low D levels
- 1000-5000 IU/d
- Monitor 25(OH)D levels, a breakdown product of vitamin D
- Sunlight, diet, supplements
- Difficult to get enough D3 through diet alone
  - D2 plants: mushrooms, soy
  - D3 animal: raw fish, mackerel, smoked salmon

PREGNANCY

PREGNANCY & LACTATION

- Pregnancy does not protect a women from psychiatric episodes, recurrence, or worsening
- Generally not recommended to stop meds
- All psych meds cross placenta; weigh mom vs fetus risks
- Same with breastfeeding
- US: major malformations 1-4%
- Older meds usually preferred
- mothertobaby.org
- MGH Center for Women’s Mental Health

SPECIFIC MEDS

- BZD
  - Cleft lip, palate, floppy infant, withdrawal, lower Apgar
  - Avoid early and late in pregnancy?
- Benadryl
  - Safest hypnotic for pregnancy, breastfeeding
- Z-drugs
  - Weak data
- Trazodone
  - Safe?

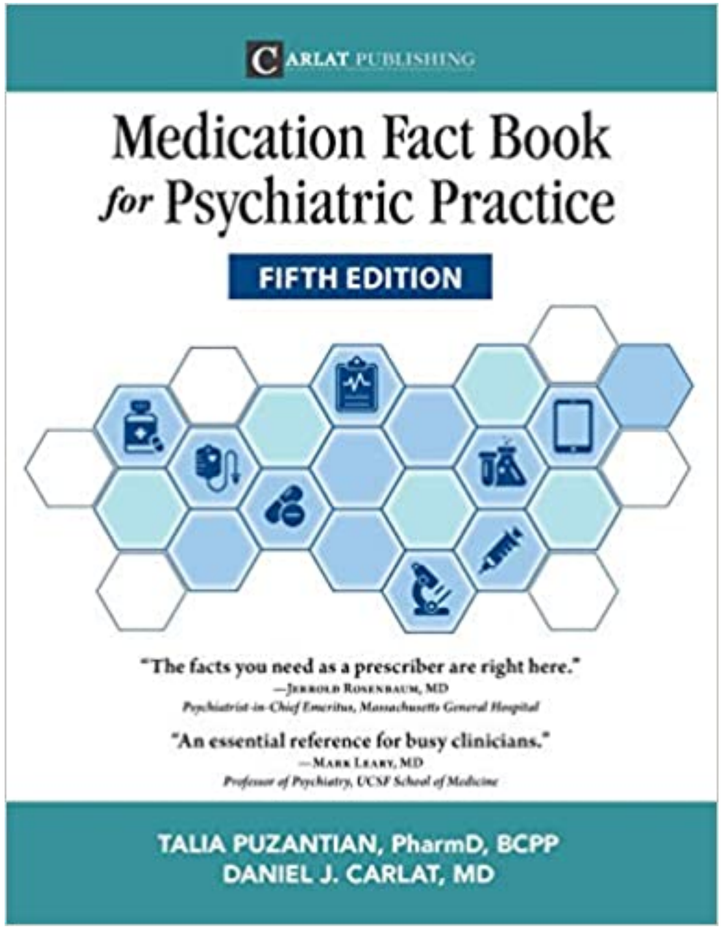
- Tegretol & Depakote, avoid
- Lamictal
  - Safest anticonvulsant?, limited data
- Lithium
  - Avoid esp. 1st trimester
- Atypicals, Wellbutrin, Remeron, SRIs
  - Relatively safe
- Stimulants, avoid
  - Vasoconstriction blocks blood to fetus. Probably safe breastfeeding

PHARMACO-GENETIC TESTING

PHARMACOGENETIC TESTING

- Genes effect seem levels
- Liver CYP450 polymorphisms
- Affect how patients respond to meds: normal, slower, poor, ultra rapid
- Clinical importance not clear yet
- Genesight, Genecept, CNSDose
- Some FDA drug labels specify lowering startting doses
- Most? docs skip the testing, but start low, increase slowly

READING



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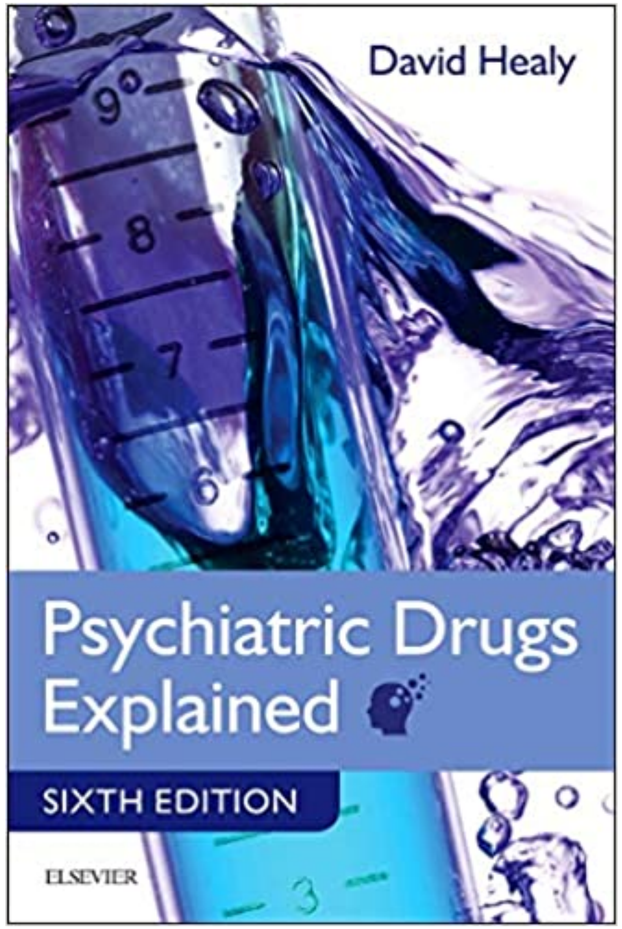

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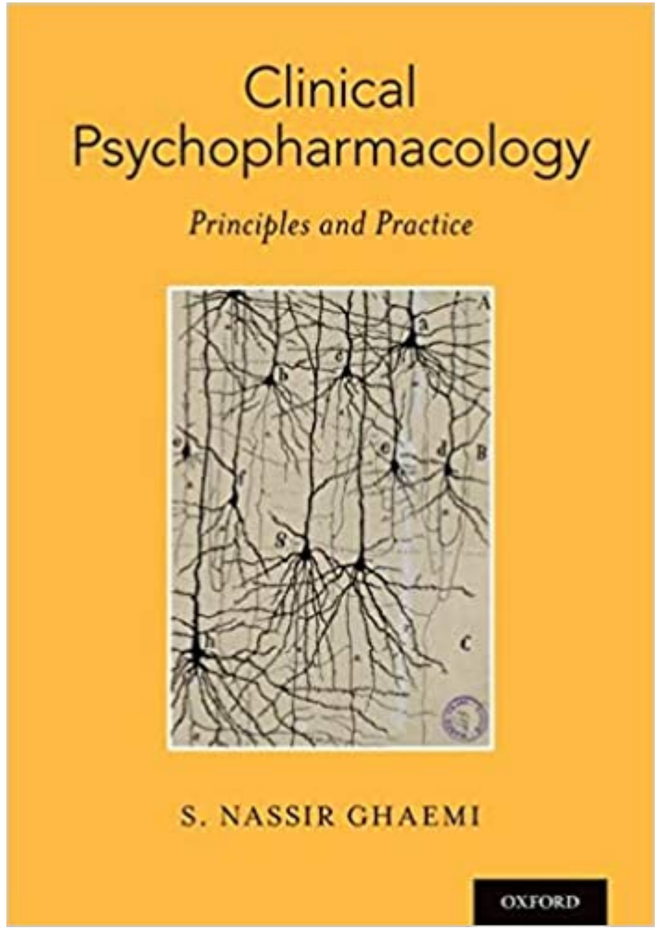

Ghaemi

SUMMARY