

The Much Too Medicated Patient

Chris Aiken, MD

Editor-in-Chief, *Carlat Report*

Assistant Prof Psychiatry,
NYU and WFU Medical Schools





Disclosure

In compliance with the ACCME Standards for Commercial Support of CME, as the speaker I do not have any relevant financial relationships to disclose in relation to this presentation.

★ Polypharmacy USA ★



RI

DC

WV

KY

AL

Polypharmacy more common in...



Women



**Disabilities
Foster care
(children)**

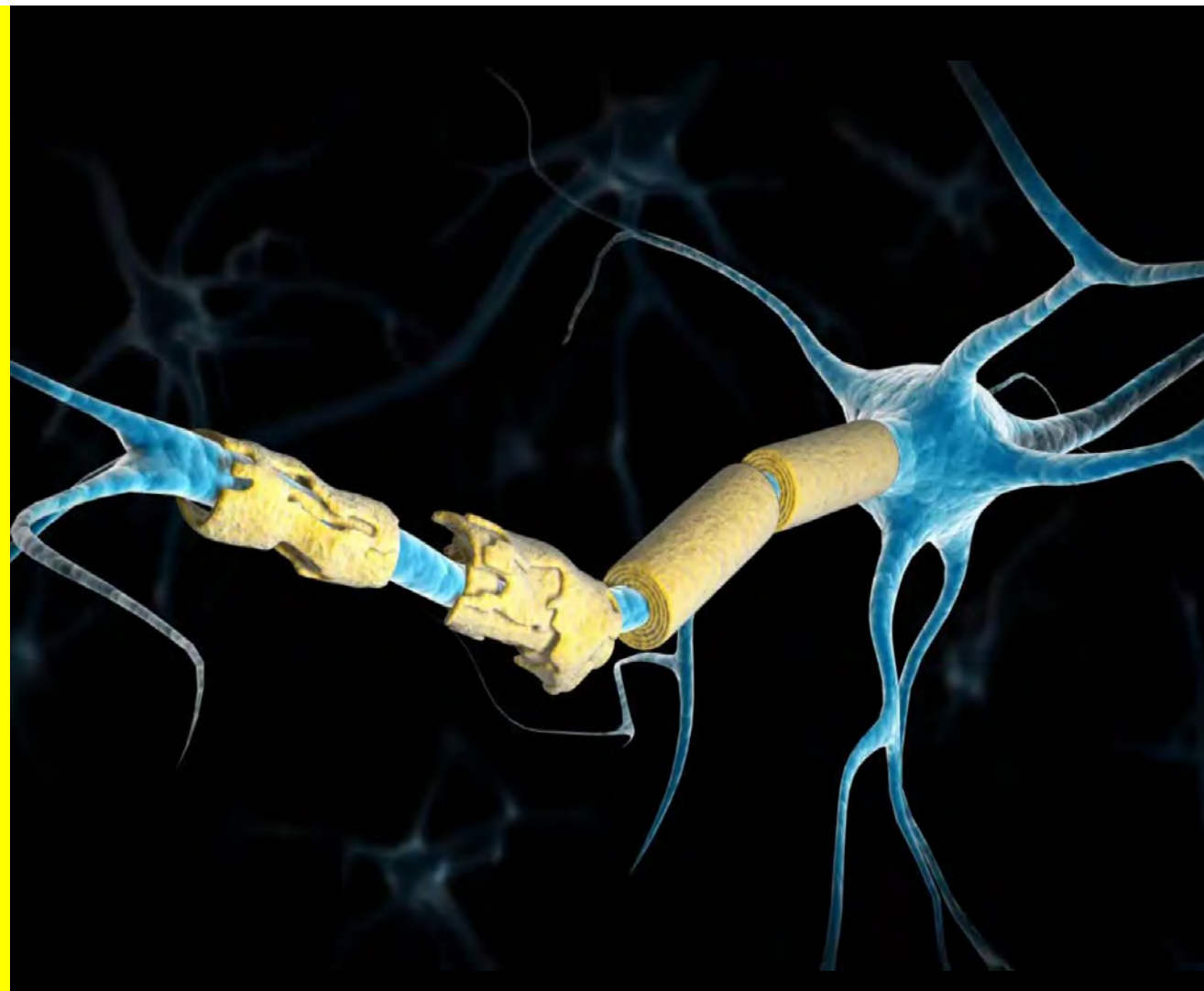


Medicaid

CAM Therapy

Is it natural to the
body or common in
the diet?

Phytochemicals
vs
Nutraceuticals





Polypharmacy Prevention



Set an end date for short-term treatments

Rapid anti-depressants:

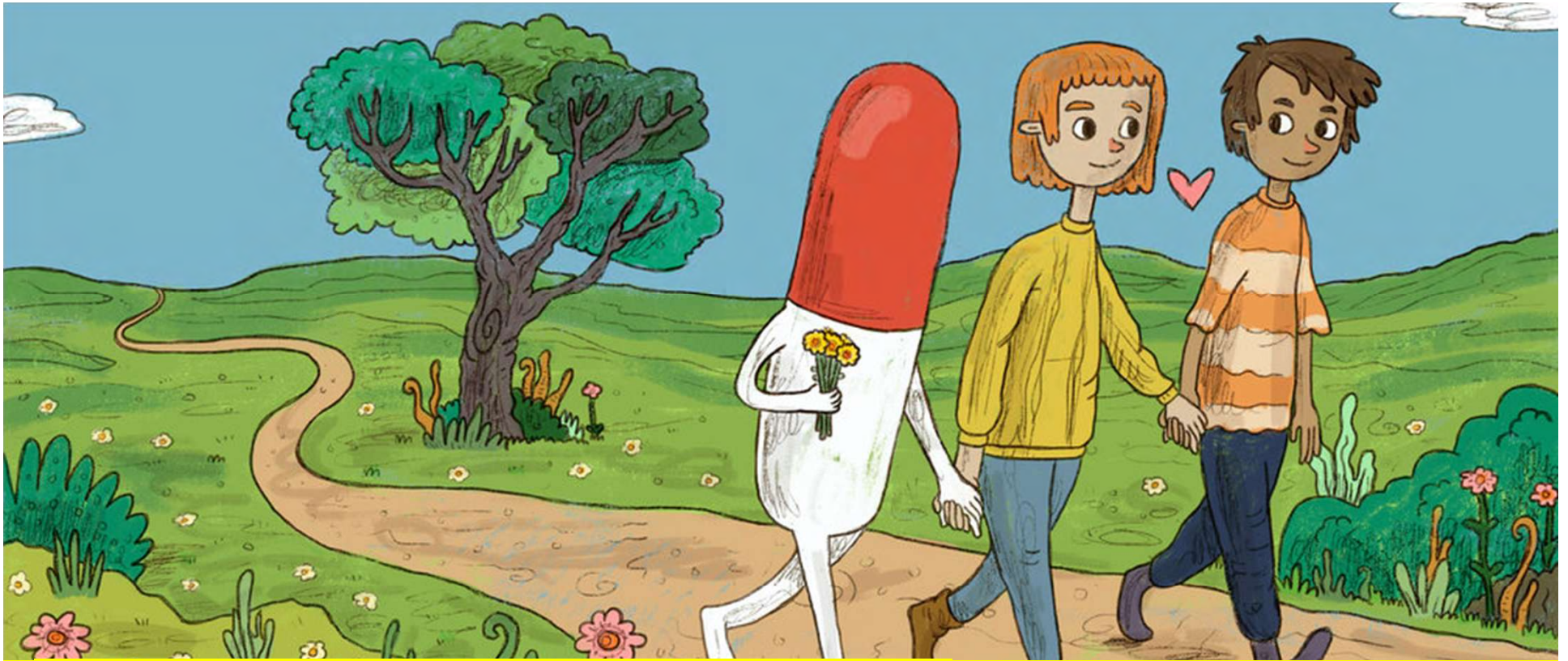
Consider short-term (2-6 weeks)

OLD

- Benzodiazepines (alprazolam)
- Eszopiclone
- Pindolol
- Thyroid (T3)

NEW

- Bupropion-Dextromethorphan (Auvelity)
- Ketamine and Esketamine
- Zuranolone (for postpartum)
- *Future? Psychedelics*



Short-term Antidepressants

Taper after 6-12 mth remission in single episode depression, or when used as adjunct in recurrent MDD or bipolar depression

Short-term Antipsychotic Augmentation

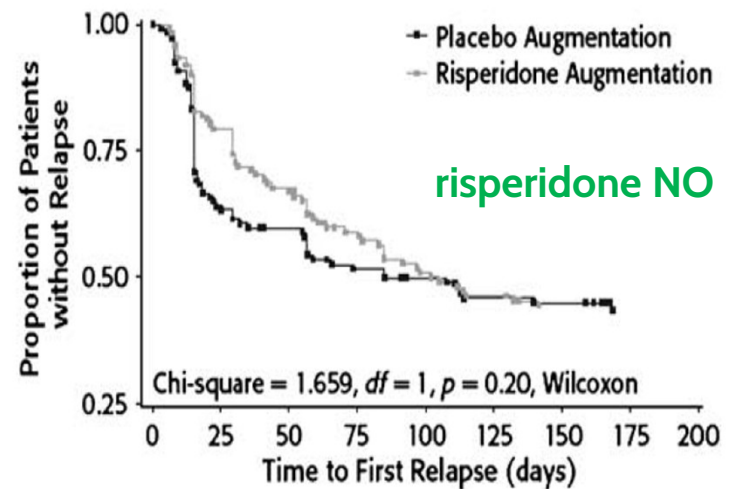
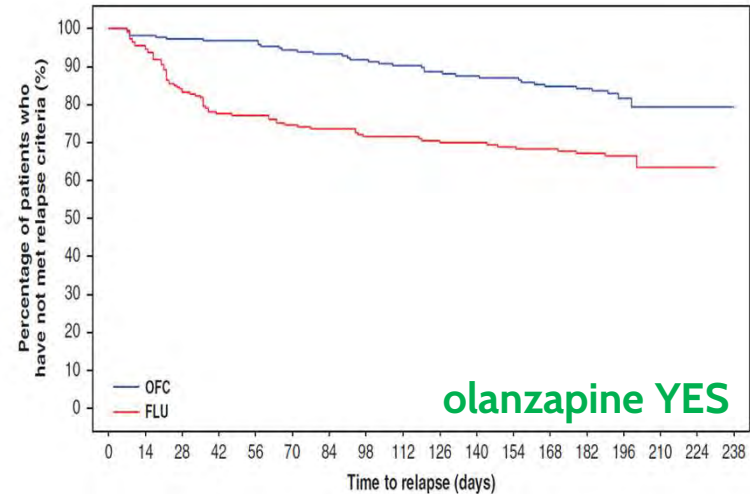
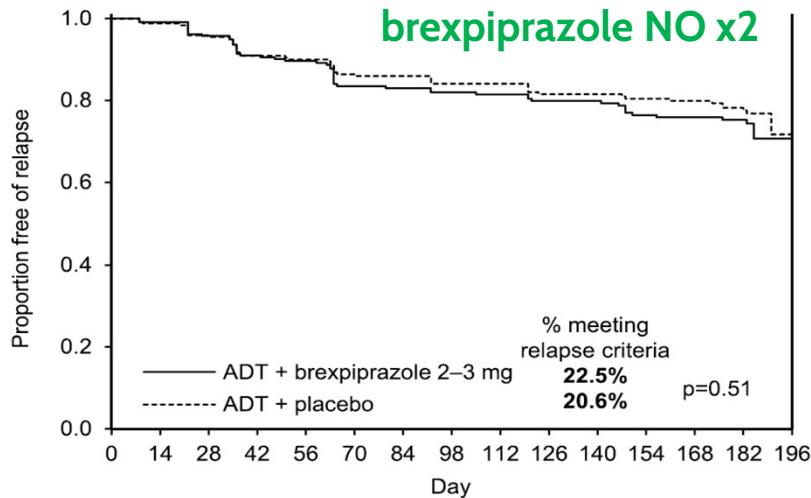
Taper after at least 6 months of remission in mood disorders



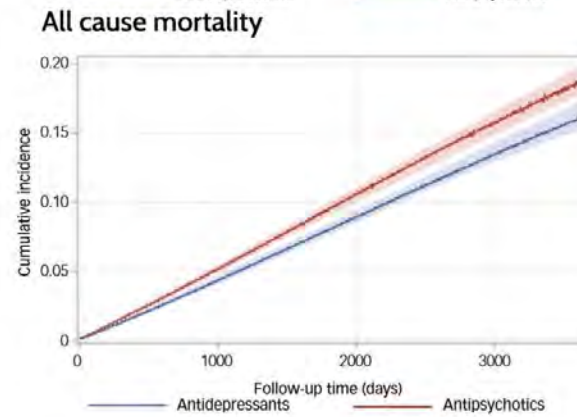
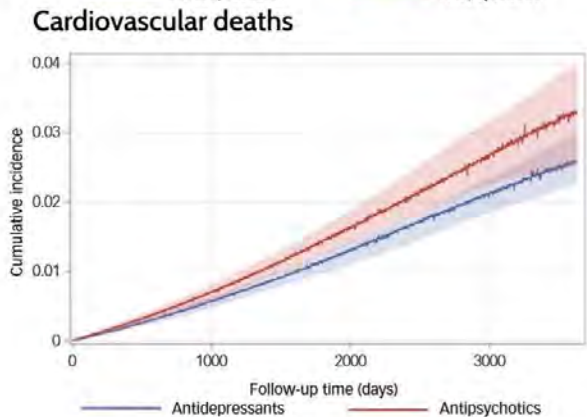
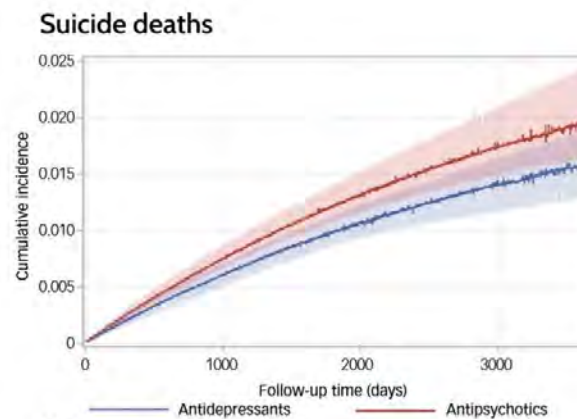
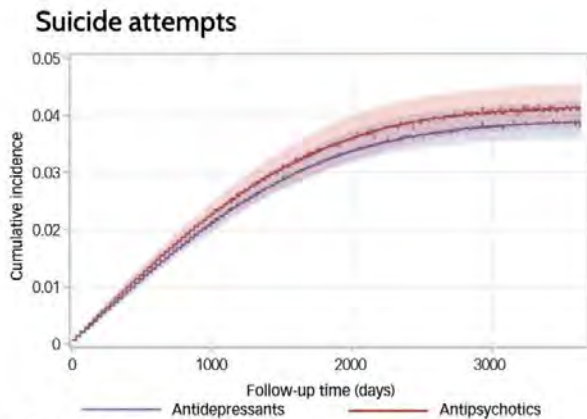
Yatham LN et al, Mol
Psychiatry 2016;21(8):1050-6

Do antipsychotics prevent unipolar depression?

Not in 3/4 trials (6 months, n=2,308)



Antipsychotics don't prevent suicide, may raise mortality



Comparative cohort study of 79,898 patients with TRD.

Antipsychotic augmentation vs. matched controls who received third-line antidepressants

Psychotic Depression

May require long-term antipsychotic augmentation

Relapse
20% vs 55%

Flint AJ et al, JAMA
2019;322(7):622-31





Time-limited stimulants

- Subthreshold ADHD
- ADHD that resolves in adulthood



Short-term Anxiolytics

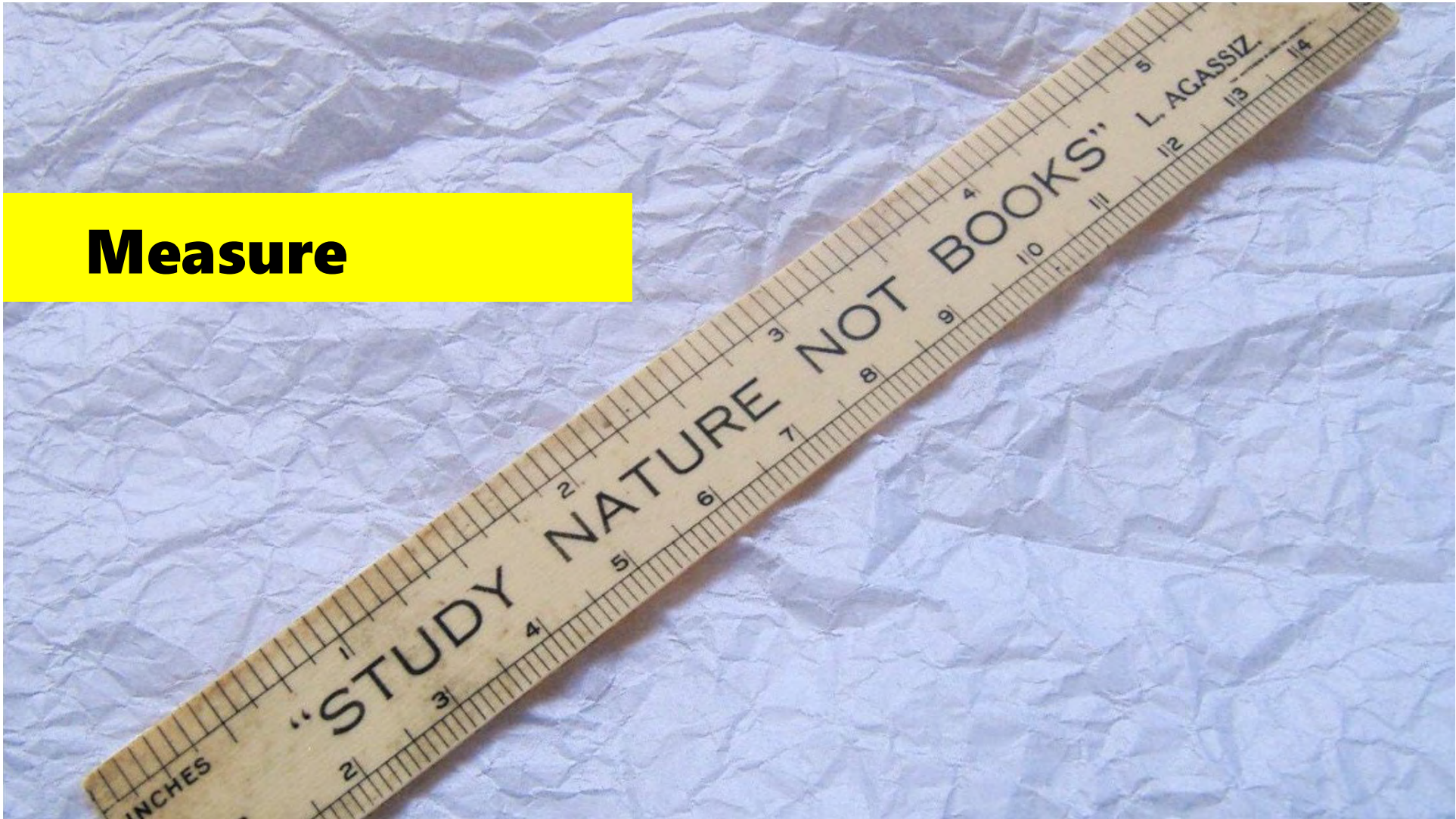
2-6 weeks ideal for benzodiazepines in acute anxiety

Hypnotics: 1-3 mth

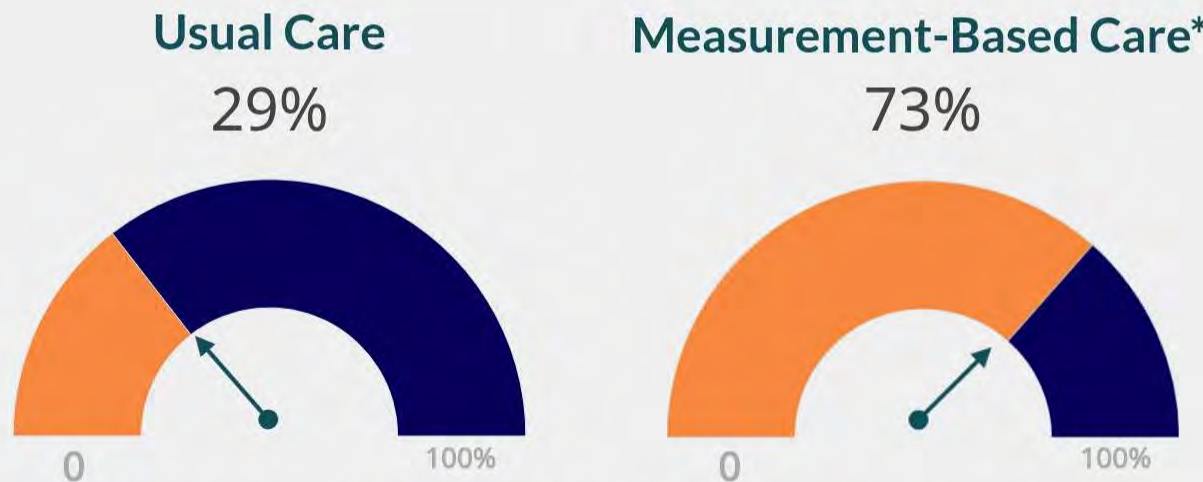
Replace with CBT-insomnia
(Sleep Coach app)



Measure



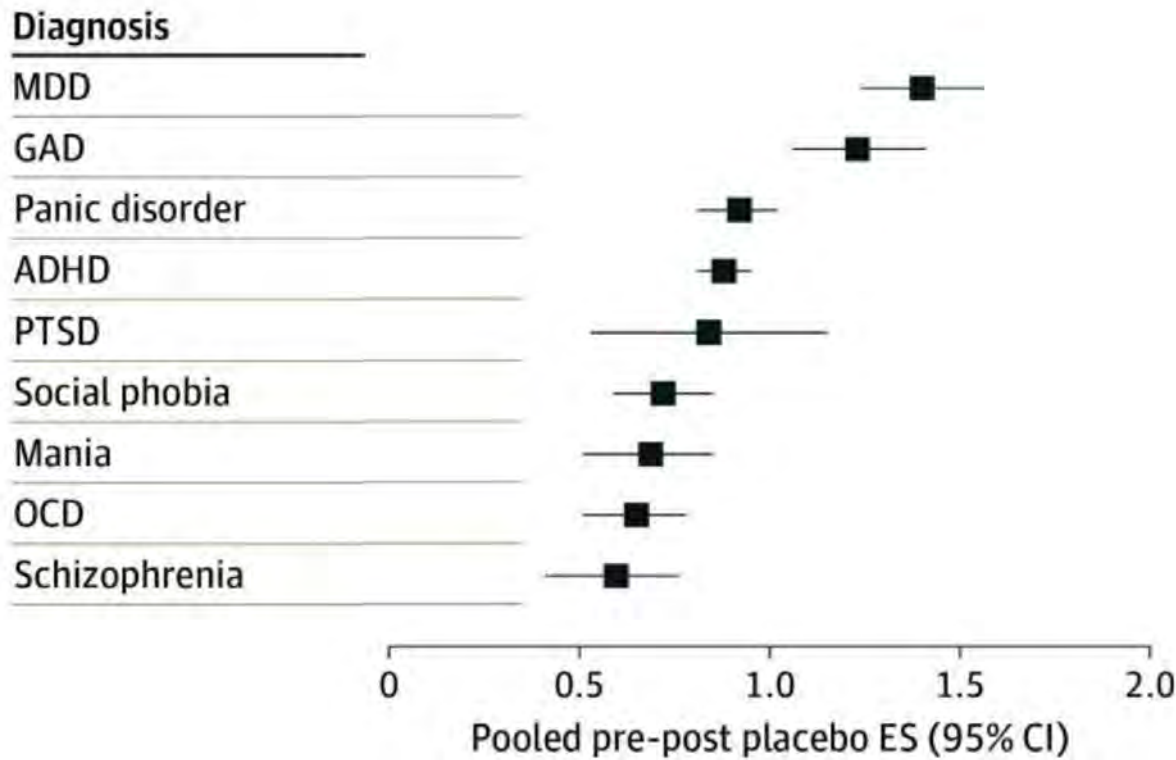
Regular Measurement Raises Remission in Depression



Guo T et al, *Am J Psych*,
2015;172:1004-13

*Self-rated QIDS with algorithm-guided care based on QIDS level.
Both groups only allowed paroxetine and mirtazapine (n=120).

Placebo response by diagnosis



Bschor T et al, JAMA Psychiatry
2024;81(8):757-768.

Huneke NTM et al, Mol
Psychiatry 2024;29(12):3915-
3925.



Polypharmacy Reduction

Before tapering

Secure alliance

Explain rationale

Understand hopes and fears

Get collateral input on response

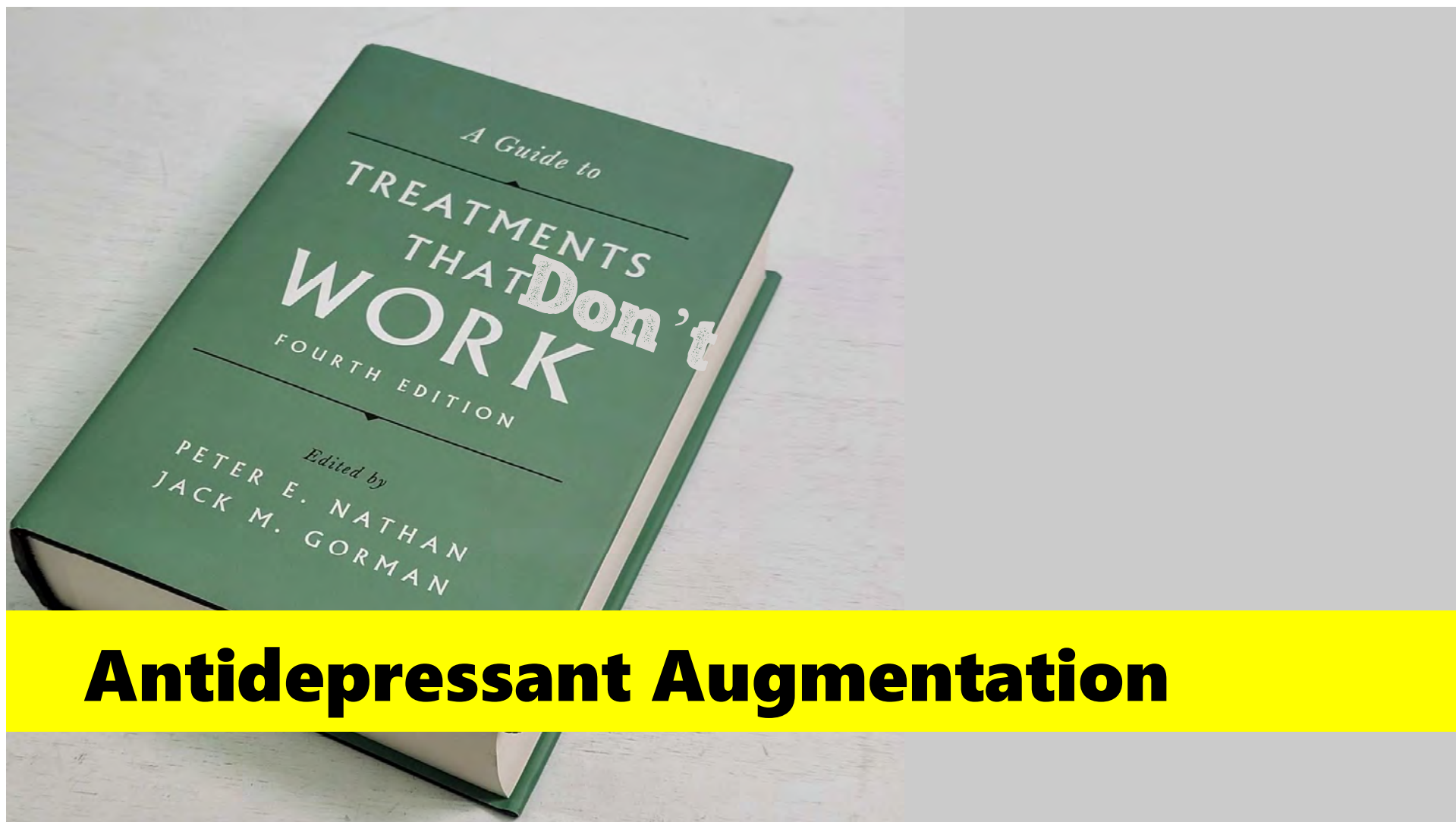
If med was effective, wait at least 6 months of full remission

Wait for stress to stabilize

Add behavioral change

What to taper

1. Dangerous medications
2. Irrational combinations
3. High doses
 - Exceptions in depression: Tricyclics, MAOIs
 - Exceptions in schizophrenia: Olanzapine
4. Meds without controlled-trial or patient-level evidence to work



Antidepressant Augmentation

1

3

2

Bupropion

Mirtazapine

Buspirone

5

8_{small}

Above each medication is the number of large, negative RCTs for antidepressant augmentation in MDD

Stimulants

Lamotrigine

<p>Obesity (BMI > 30) Inflammation (CRP ≥ 3) Nicotine cessation</p>	<p>Anxious Depression</p>	<p>Anxious Depression (as first-line monotherapy)</p>
<p>Bupropion</p>	<p>Mirtazapine</p>	<p>Buspirone</p>
<p>Methylphenidate: Elderly w/apathy, medical d/o</p> <p>Lisdexamfetamine Depression w/ executive dysf</p>	<p>Chronic Depression (over 8 years)</p>	<p>Above each medication are populations where the augmentation strategy worked in secondary analyses</p>
<p>Stimulants</p>	<p>Lamotrigine</p>	

MDD Augmentation References

Bupropion: Unpublished, cited in Zhou X et al, J Clin Psychiatry 2015;76(4):e487-98

Buspirone: Appelberg BG et al, J Clin Psychiatry 2001;62(6):448-52; Landén M et al, J Clin Psychiatry 1998;59(12):664-8.

Mirtazapine: Kessler D et al, Health Technol Assess 2018;22(63):1-136

Stimulants: Richards C, et al. J Affect Disord 2016;206:151-160; Ravindran AV et al, J Clin Psychiatry 2008;69(1):87-94; Patkar AA et al, J Clin Psychopharmacol. 2006;26(6):653-656; Trivedi MH et al, J Clin Psychiatry. 2013;74(8):802-809

Lamotrigine: Goh KK et al, J Psychopharmacol 2019;33(6):700-713

Antipsychotics: Brunner E et al, Neuropsychopharmacology 2014;39(11):2549–2559; Rapaport MH et al, Neuropsychopharmacology 2006;31(11):2505–2513; Bauer M et al, Acta Neuropsychiatr 2019;31(1):27–35; McIntyre RS et al, Acta Neuropsychiatr 2024;17:1–12

Treatments that probably don't work

**Off-label
anticonvulsants**

Bipolar Mania (levetiracetam possible;
oxcarbamazepine unlikely)

Brexpiprazole

Bipolar Mania

Antidepressants

Bipolar I Disorder (except OFC-combo)

Vortioxetine

ADHD

**Bupropion,
Viloxazone,
Vortioxetine**

Anxiety disorders (unless anxious MDD)

Valproate

Schizophrenia

Modafinil

Sedation on antipsychotics

Stimulants

Cognition in schizophrenia

Antipsychotics

Delirium (symptoms or mortality)

Disorders where meds usually fail

POSSIBLE EXCEPTIONS

Pediatric MDD

Fluoxetine

Anorexia

Zinc

Autism

Aripiprazole and risperidone for behavioral aggression, some CAMs (folinic acid, omega-3, NAC, probiotics)

Trichotillomania

Memantine, NAC

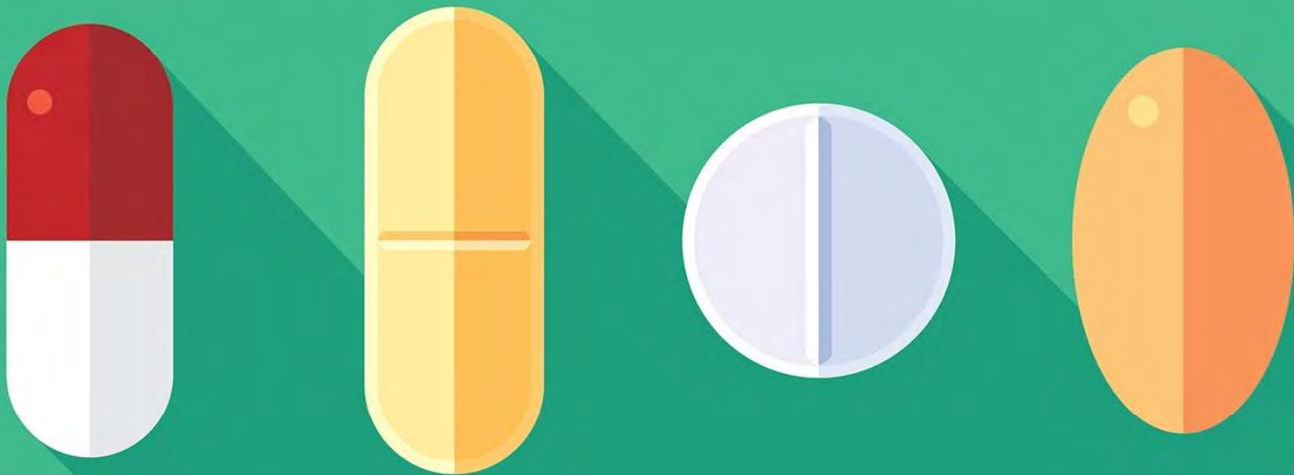
Cognition in chronic psych disorders

Agitation in dementia

Brexpiprazole

Psychosis in dementia

Small effect with antipsychotics



Risky and Irrational Combinations



Anticholinergics

TABLE 17-2. The Human Cost of Anticholinergic Drugs

Anticholinergic Effect	Why it Matters
Dry mouth	Tooth decay, gum inflammation and ulceration, halitosis; poor dental hygiene is a risk factor for depression and dementia
Constipation	Bowel obstruction with potentially fatal paralytic ileus and sepsis
Urinary retention	Urinary tract infections, renal or bladder damage
Dilated pupils	Acute narrow-angle glaucoma, traffic accidents, falls
Impaired papillary accommodation	Inability to read fine print
Increased heart rate	Increased risk of cardiac arrest
Decreased sweating	Hyperthermia
Decreased bronchial secretions	Mucous plugging of small airways, which worsens respiratory illnesses like asthma and bronchitis
Cognitive impairment	Poor memory and concentration; delirium; increased risk of dementia

acbcalc.com

Anticholinergic Burden				
	Very Low (0)	Low (1)	Medium (2)	High (3)
Antidepressants		Bupropion Citalopram Fluoxetine Fluvoxamine Selegiline Trazodone Venlafaxine	Desipramine Sertraline Trimipramine	Amitriptyline Clomipramine Doxepin Imipramine Nortriptyline Paroxetine
Antipsychotics	Brexipiprazole Lumateperone Lurasidone Thiothixene Ziprasidone	Aripiprazole Asenapine Haloperidol Iloperidone Paliperidone Quetiapine Risperidone	Loxapine Pimozide Prochlorperazine	Amoxapine Chlorpromazine Clozapine Fluphenazine Olanzapine Perphenazine Thioridazine
Other		Alprazolam Clorazepate Diazepam Pramipexole	Amantadine Carbamazepine Oxcarbazepine	Benzotropine Diphenhydramine Doxylamine (Unisom) Hydroxyzine

Taper slowly (2-4 weeks)

Avoid anticholinergic
rebound:

Anxiety, insomnia,
confusion, EPS,
sweat, salivation,
diarrhea



A black and white photograph of a tunnel with a heart-shaped opening at the end. The tunnel is formed by a series of concentric, curved structures that create a sense of depth and perspective. The light trails and the bright light source on the left suggest motion and energy. The overall composition is dynamic and visually striking.

QTc

crediblemeds.org

Risk of Torsades de Pointes With Psychiatric Medications

	Conditional (Low) Torsades Risk	Possible Torsades Risk	Known Torsades Risk	Only Dangerous in Congenital Long QT
Antidepressants	Amitriptyline Clomipramine Doxepin Fluoxetine Fluvoxamine Paroxetine Sertraline Trazodone	Desipramine Imipramine Maprotiline Mirtazapine Nortriptyline Trimipramine Venlafaxine	Citalopram Escitalopram	
Antipsychotics	Olanzapine Quetiapine Risperidone Ziprasidone	Aripiprazole Asenapine Clozapine Iloperidone Lumateperone Lurasidone Perphenazine Paliperidone Pimavanserin Promethazine	Chlorpromazine Haloperidol Pimozide Thioridazine	
ADHD		Atomoxetine		Psychostimulants
Other	Amantadine Chloral hydrate Diphenhydramine Galantamine Hydroxyzine	Lithium Buprenorphine Deutetrabenazine Valbenazine Tetrabenazine Dextromethorphan/ Quinidine Memantine Pitolisant Vardenafil	Donepezil Ondansetron Methadone	

When to Worry

Electrolyte imbalance, heart disease, older age, cocaine/stim misuse



Falls

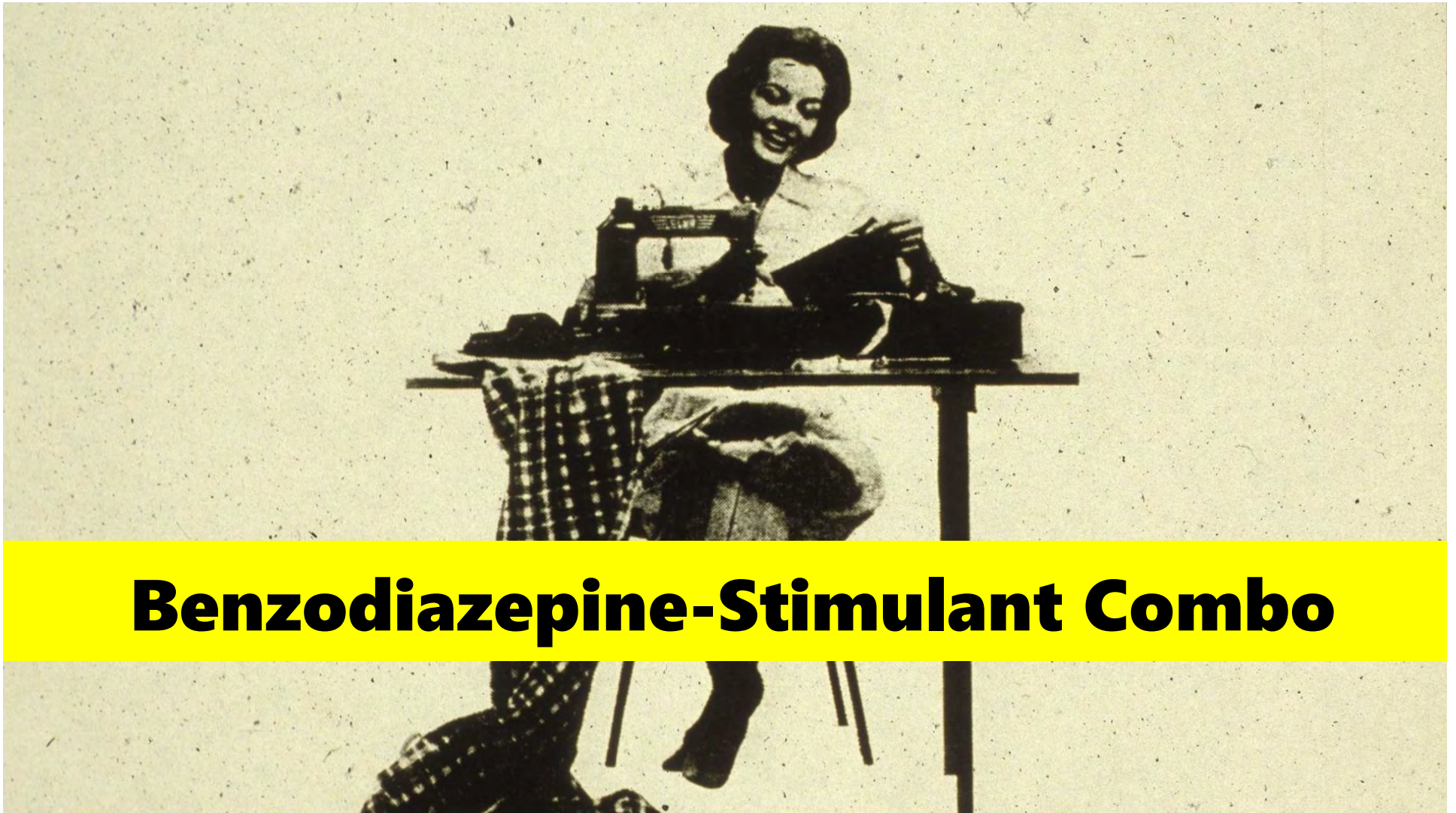


STOPPFall

■ Strongly agree ■ Agree ■ Neutral

- Benzodiazepines
- Antipsychotics
- Benzodiazepine-related drugs
- Opioids
- Antidepressants
- Anticholinergics
- Antiepileptics





Benzodiazepine-Stimulant Combo

*to help you transform a tense, irritable, depressed
patient into a woman who is receptive to your counsel
and adjusted to her environment*



DEXAMYL® SPANSULE®

brand of sustained release capsules

FORMULA: Each 'Spancule' capsule No. 1 contains Dexedrine® (brand of dextro amphetamine sulfate), 10 mg.; amobarbital (Warning, may be habit-forming), 1 gr. Each 'Spancule' capsule No. 2 contains 'Dexedrine' (brand of dextro amphetamine sulfate), 15 mg.; amobarbital (Warning, may be habit-forming), 1½ gr. The active ingredients of the 'Spancule' capsule are distributed among hundreds of minute pellets with varying disintegration times. A therapeutic dose is released immediately and the remaining medication, released slowly and without interruption, sustains the effect for 10 to 12 hours.

sive states; (2) for control of appetite in overweight.

USUAL DOSAGE: One 'Dexamyl' 'Spancule' capsule taken in the morning.

SIDE EFFECTS: Insomnia, excitability and increased motor activity are infrequent and ordinarily mild.

CAUTIONS: Use with caution in patients hypersensitive to sympathomimetic compounds or barbiturates and in cases of coronary or cardiovascular disease or severe hypertension.

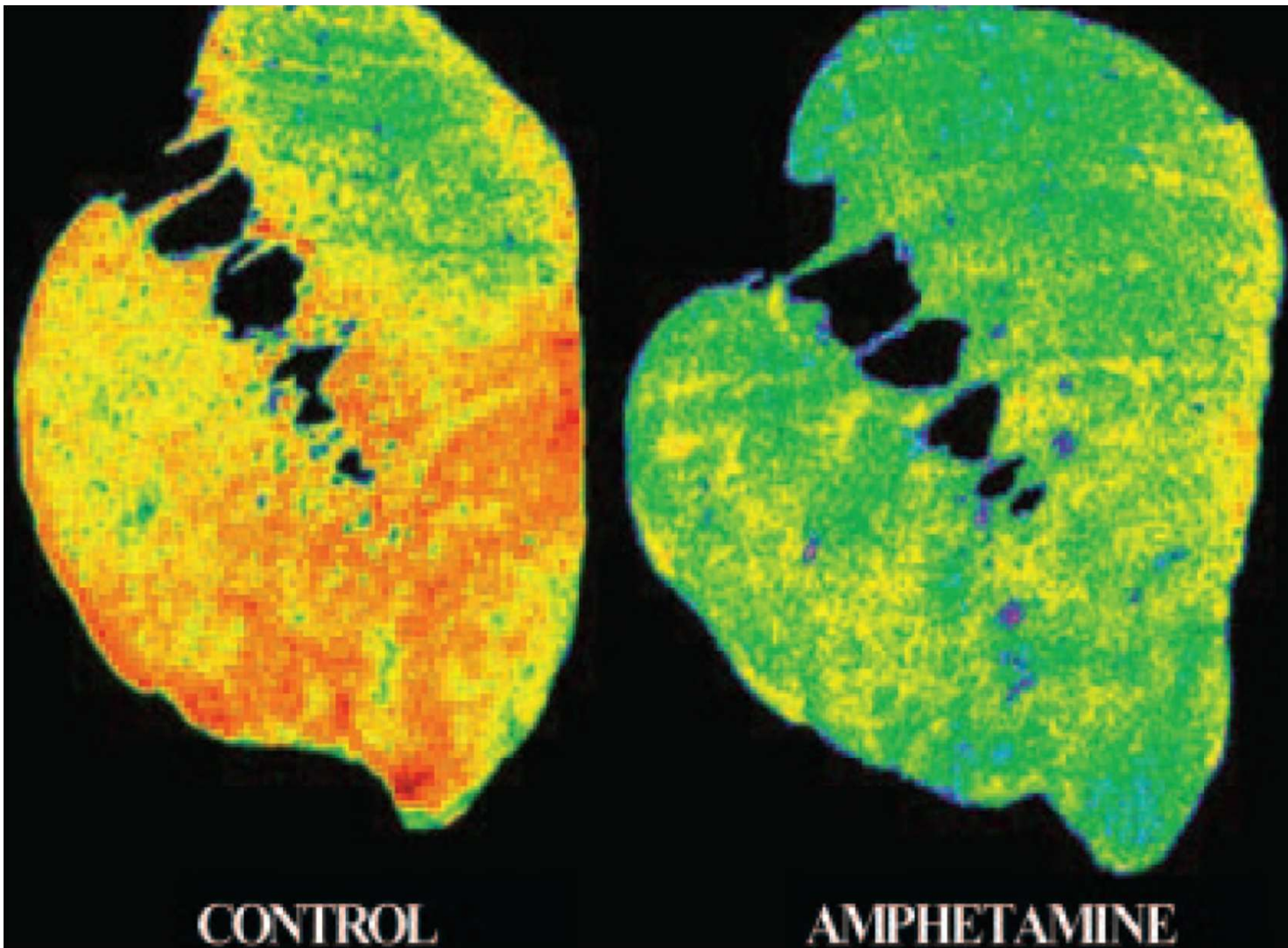
PRESCRIPTION SIZE: Bottles of 30 capsules.

1950-1970: Dextroamphetamine-Amobarbital

1 in 15 on benzo also on stimulant...



...in 2018, 40% higher than 2013



**A decade
of benzos
impairs
cognition,
attention,
processing
speed
with large
effect size**

Crowe SF and Stranks EK,
Arch Clin Neuropsychol 2018;
33(7):901-911

Highest link to car accidents?



Amphetamine-Benzo

Zarkowski PA, Int J Psychiatry
Med 2020;55(2):82-104



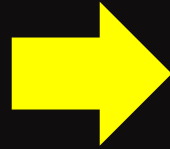
1. MISUSE: Taper off now

Oxazepam = Lower misuse liability

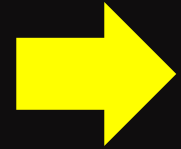
2. LIFESTYLE USE: Taper gradually



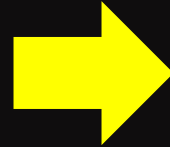
Work Stress



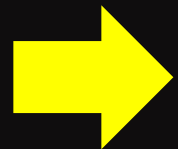
Insomnia



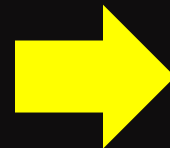
ADD Symptoms



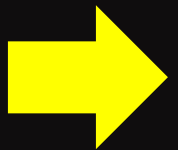
Amphetamine



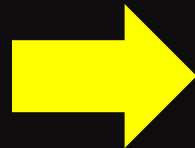
Insomnia



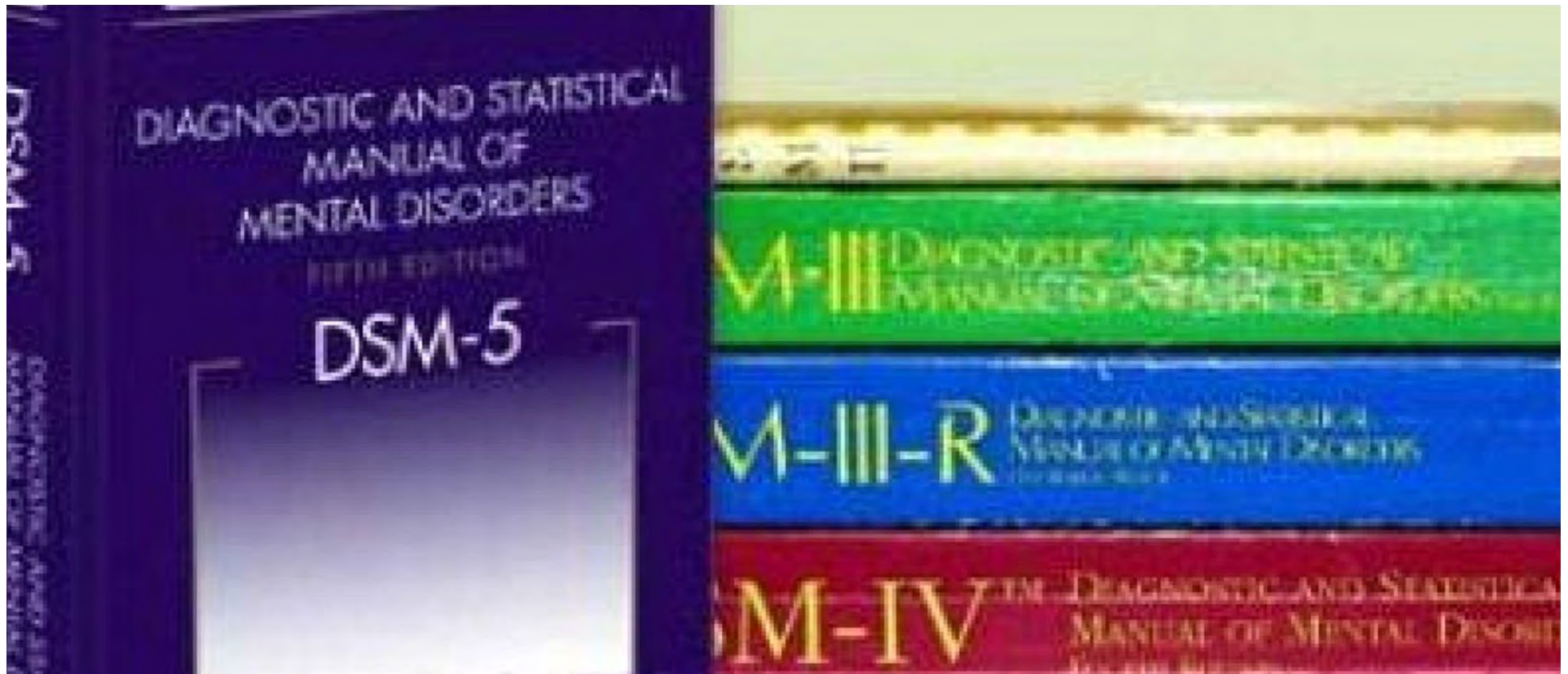
ADD Sympt.



Benzo



Cognitive Impair



3. COMPLEX COMORBIDITY: Taper gradually

4. Rational use

Stimulant for ADHD

Rare benzo for panic/phobia

Questions?

caiken@thecarlatreport.com

