NATIONAL REGISTER

OF HEALTH SERVICE PSYCHOLOGISTS

Introduction to Psychopharmacology for the BHC

MORGAN T. SAMMONS, PhD, ABPP

National Register of Health Service Psychologists

Psychopharmacology for the BHC: Drugs for Depression

MORGAN T. SAMMONS, PhD, ABPP

National Register of Health Service Psychologists

Psychopharmacology for the BHC: Drugs for ADHD

MORGAN T. SAMMONS, PhD, ABPP

National Register of Health Service Psychologists

Psychopharmacology for the BHC:
Drugs for Insomnia

MORGAN T. SAMMONS, PhD, ABPP

National Register of Health Service Psychologists

Improvement and side effects as a function of dose increases

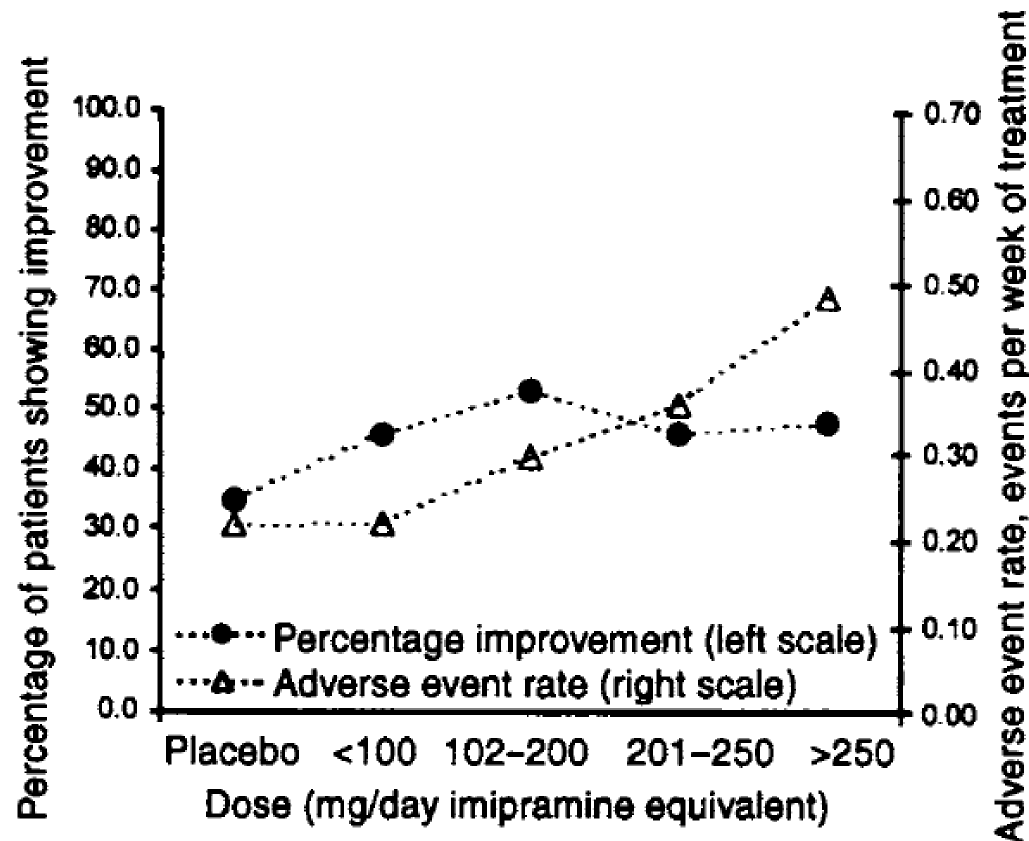


Fig. 1 Estimated percentage improvement and adverse event rate from the final regression models.

Source: Bollini et al., British Journal of Psychiatry, 1999

Use of Antidepressants more common, psychotherapy less

- Olfson and Marcus (2009) data abstracted from Medical Expenditure Panel Survey
- **20% of US population** has sought MH tx (2003), compared to **12% in early-1990's**. Rate of use of ADPs doubled from 13-23M people yearly.
- **Most got Rx**, not psychotherapy. **Less than 20%** of those getting an ADP for depression got psychotherapy, **compared to 30% a decade ago**, but length of psychotherapy remained the same (~8 visits)
- **Rate of use of antipsychotics** among depressed pts also increased significantly.
  - Olfson M, Marcus, S (2009) National Patterns in Antidepressant Medication Treatment Arch Gen Psychiatry. 2009;66(8):848-856

General considerations for patients taking psychotropics

- **General state of health, comorbidities:**
  - Hypertension, diabetes, heart conditions
  - Pregnancy or breastfeeding
- **Substance use:**
  - Alcohol
  - Sedatives
  - Marijuana or stimulants
- **Recent labs/physical exam**
- **Informed consent dynamic, not static**
  - Address throughout treatment

ANTIDEPRESSANT AGENTS

General precautions with ADPs (mostly SRIs and SNRIs)

- **Increased risk of bleeding due to inhibition of platelet aggregation.**
- Serotonin syndrome and Neuroleptic Malignant Syndrome (NMS).
- **Lowering of seizure threshold.**
- General contraindication in pregnancy and nursing mothers.
- **Concerns regarding activation of suicidal behavior or ideation.**
- Activation of mania/hypomania.
- Increasingly, drug drug interactions (3A4, 2D6) or metabolic concerns.
- **Coadministration with MAOIs.**
- Initiation and discontinuation syndromes.
- **Angle closure glaucoma.**

SRI (Trade)	Generic	Indications	Dose	Concerns, Cautions, Pearls
Brintillex (2013)	Vortioxetine	MDD	5 mg/d then 10-20 mg/d	5HT1a agonist 5HT3 antagonist Caution with 2D6 poor metabolisers & coadministration with CYP inducers; Name confusion with Brilinta (ticagelor; platelet inhibitor).
Celexa	Citalopram	Depression	10-40 mg/d	Max dose reduced from 50 to 40 mg due to ECG change (long QT)
Lexapro	Escitalopram	MDD GAD	5-30 mg/d, also as oral solution	5-20 mg/d, age 12 and up 5-10 mg/d
Luvox	Fluvoxamine	OCD	50-300 (adults) 25-200 (peds)	Indicated for OCD only 8-17 years
Paxil Paxil CR Pexeva Brisdelle (2014)	Paroxetine	MDD GAD PTSD OCD PD PMDD	20-50 mg/d 20 mg target dose 20-40 mg 40 mg target 40 mg target 7.5 mg only	Very sedating, best given at night, note 1st trimester cardiac defect risk, unusual discontinuation symptoms. Max dose 60 mg/d. Equivocal approval process Menopausal hot flashes only
Viibryd (2011)	Vilazodone	MDD	10-40 mg/d titrated up weekly; max 20 mg with 3A4 inhibitors	5HT1a partial agonist Monitor 3rd trimester exposed neonates for PPHN, discontinuation syndrome, 3A4 interactions

SRIs

SRIs: Drug (trade)	Generic	Indication	Dose	Concerns, Cautions, Pearls
Prozac Prozac weekly Sarafem	Fluoxetine	MDD, Bipolar I, Bulimia, PD, TRD Children: MDD OCD MDD, continuation PMDD	10-80 mg/d 10-20 mg/d 10-60 mg/d 90 mg 20 mg/d	Very long half life (may help avoid discontinuation sx) Weekly enteric coated capsule Continuous or intermittent dose schedule
Viibryd (2011)	Vilazodone	MDD	10-40 mg/d titrated up weekly; max 20 mg with 3A4 inhibitors	5HT1a partial agonist Monitor 3rd trimester exposed neonates for PPHN, discontinuation syndrome, 3A4 interactions
Zoloft		Social anxiety, PD OCD MDD, PMDD, PTSD	25-200 mg/d 25-200 mg/d 25-200 mg/d	Adolescents and adults Adults 6 and up Adults

SNDRI, SARIs

Drug (Trade)	Drug (Generic)	Indication	Dose	Action	Concerns, cautions, pearls
Serzone* *unavailable; only as generic	Nefazodone	Depression	100-300 mg twice daily Max 600 mg/d Contraindicated with: Carbamazepine Pimozide Terfenadine Cisapride Astemizole	SNDRI: 5HT, NE, DA, reuptake inhibitor Weak reuptake inhibitor, Agonist at: 5HT1A, 5HT2A, Alpha-1 receptors	Serzone sales in US halted in 2004 due to fatalities associated with acute hepatic failure Generic available Sedation and orthostasis common Potent 3A4 inhibitor
Desyrel	Trazodone	MDD	50-400 mg daily	5HT antagonist and reuptake inhibitor (SARI)	Strongly sedating; mostly used as sleep aid (50-100 mg/d) priapism
Oleptro (2010; withdrawn?)	Trazodone	MDD	Start 75 x2/d, then 150, up to 375 mg/d.		Somnolence, Priapism, prolonged QT interval, orthostasis.

Tetracyclic/Noradrenergic and Specific Serotonin Antagonist (NaSSA)

Drug (Trade)	Generic	Indications	Dose	Actions	Concerns, Cautions, Pearls
Remeron Remeron SolTabs (rapid disintegrating sublingual tablets)	Mirtazapine	MDD (18 +)	15-45 mg/day Soltabs: Same Better at bedtime	Tetracyclic 5HT1, 5HT2 antagonist Histamine antagonist	Highly sedating (5HT1 antagonism?) MIR may be sexually activating. fMRI studies show enhanced sexual response vs. SRIs.
					SolTabs: Use immediately after removing from blister pack

Serotonin and Norepinephrine reuptake inhibitors (SNRIs)

SNRI: Drug (Trade)	Generic	Indications	Dose	Cautions, Concerns, Pearls
Cymbalta (2004)	Duloxetine	MDD, GAD diabetic neuropathy, fibromyalgia, chronic musculoskeletal pain	40-60 mg/d, max 120 (7 yrs & up) 30-60 mg/d	Lower dose for pain conditions
Effexor Effexor ER Khedezla Pristiq	Venlafaxine	MDD MDD, GAD, PD, Soc. Anx. MDD MDD	75-225 mg/d Max 225 mg/d 50-100 mg/d 50/100 mg/d	Nausea, BP elev. BP caution Khedezla: “No benefit > 50 mg/d” Pristiq: “No benefit > 50 mg/d”
Fetzima (2013)	Levomilnacipran	MDD	40-120 mg/d	3A4 interactions (Note: related molecule, milnacipran (Savella) indicated only for fibromyalgia.

Aminoketone

Drug (trade)	Drug (generic)	Indication	Dose	Cautions, Concerns, Pearls
Wellbutrin Forfivo XL Zyban	Bupropion	MDD Smoking Cessation	200-450 mg/d 150-300 mg/d	Insomnia, CX seizure disorders; morning dosing
Aplenzin (2008)	Bupropion ER	MDD; SAD	174 mg to 348 daily;	Dose = 150-300 mg bupropion; CX seizure disorders

ACOG practice guidelines for pharmacotherapy in depression (2008/2012)

Antidepressants

- **Paroxetine: AVOID. Fetal ECG for women exposed in 1st trimester.**
- Multidisciplinary management (inc. MH provider) during pregnancy
- **Use single med at higher doses v. multiple meds**
- 'Individualize' doses of SRIs.
- **Close monitoring of lithium levels.**

– Source: ACOG (2008/2012) Use of psychiatric medications during pregnancy and lactation; ACOG practice bull. #92

Mood Stabilizers

- **Lithium – small increase in cardiac defects (1.2-7.7 RR)**
- Valproate: AVOID, esp in 1st trimester:
  - risk neural tube defects, neurocog defects, etc.
- Carbamazepine: AVOID, esp. in 1st trimester:
  - Fetal carbamazepine syndrome
- **Benzodiazepines:**
  - ↑ risk of cleft palate (RR 0.01%) Antenatal use associated with floppy infant syndrome.
- LAMOTRIGINE: potential maintenance during pregnancy for women with bipolar disorder.

Treatment of depression in pregnancy:
Summary slide

- **Careful evaluation** of chronicity & severity of prior depression essential.
- **Not all women** respond to drugs in pregnancy, and drugs not necessarily proof against relapse.
- Use **non pharmacological treatments** when possible.
- No dose-response curve for ADPs vis-à-vis fetal defects.
- **1st trimester use low** but present association with cardiac, cephalic, GI defects, esp with paroxetine, fluoxetine.
- 3rd trimester use associated with Poor Neonatal Adaptation Syndrome.
- For mania, Lamotrigine least risky.

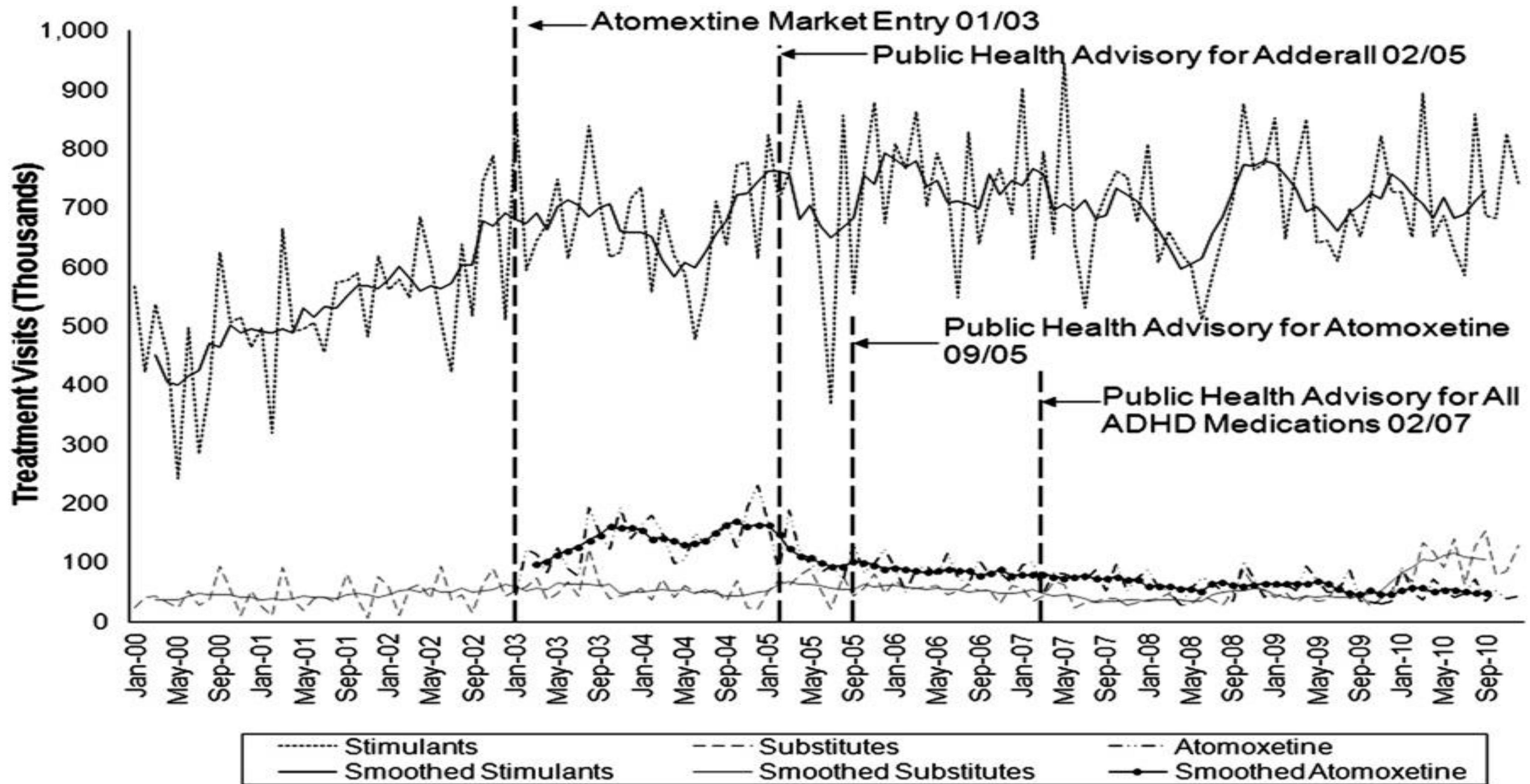
- **My conclusion: Use only if non-drug treatment doesn't work, careful informed consent; consider referral.**

General guidance regarding antidepressants
(mostly newer ones)

I. In general, all are equal in terms of efficacy and tolerability **(except Paxil)**
II. Side effects, past experience, and patient preference drive the train
III. Suicidal behavior, aggression, akathisia, irritability must be monitored during start and stop
    I. No TCAs for suicidal patients
IV. Initiate gradually to lowest effective dose, discontinue gradually
V. General cautions in pregnancy, esp. paxil, fluoxetine
VI. Noradrenergic agents (bupropion, levomilnacipran) may be better for patients with anergia, cognitive slowing

DRUGS FOR ADHD

ADHD diagnosis and treatment 2000-2010



"Substitutes"= guanfacine, bupropion, clonidine. Graph: Garfield, C. F., et al. (2012). Trends in Attention Deficit Hyperactivity Disorder Ambulatory Diagnosis and Medical Treatment in the United States, 2000–2010. Acad. Pediatrics, 12, 110-116.

General considerations - ADHD

- **13.3% boys** and **5.6% girls** aged 4-17 have dx ADHD
- In general, **10% of children** have dx ADHD
- **Boys 2x more likely than girls**
- Largest increase in dx in the **6-12 age** range in **past 7 years**.
- Highest rate of dx in **Caucasian children (11.5%)**
  - **African American (8.9%)**
  - **Hispanic (6.3)**
- More commonly diagnosed in children with **public or private insurance**.
- More commonly diagnosed in relatively **low income children**

— Pastor, et al., (2015). Association between diagnosed ADHD and selected characteristics in children…NCHS data brief #201

Stimulants - general considerations

- Largest effect size for ADHD of any medication or treatment.
- Issues of dependence make all DEA schedule II drugs (no phone Rx, no refills)
- Are sympathomimetics - may lower seizure threshold, cx in hypertension
- Weight loss, insomnia, headache, irritability common side effects; may worsen anxiety, tics (but not associated with irreversible tic)
- Cannot be used with MAOIs

Stimulants strength of evidence

- Well conducted meta-analysis suggests that methylphenidate use results in
- **VERY MODEST improvements in**
  - Teacher reported symptoms
  - Teacher reported general behavior
  - Parent reported quality of life
  - Some mild adverse effects (physiological, appetite)
  - No serious adverse effects.

— Storebo, O., et al. (2015). Methylphenidate for ADHD in children and adolescents….British Medical Journal, 351:h5203/doi:10.1136/bmj.h5203

Amphetamine salts

Drug (Trade)	Drug (generic)	Age range	Dose	Indication
Adderal and others Mixed salt amphetamines	Adderal and others; Amphetamine + dextroamphetamine	3-5 6 and older	2.5 mg – 40 mg 5-40 mg/d (up to 60 in narcolepsy)	ADHD Pediatric narcolepsy (6 and older)
Adderal ER	Mixed salt amphetamines ER	6-12	10-30 mg/d	ADHD
Dexedrine, Dexedrine Spansules (LA) Zenzedi		6 and up	5- 40 mg (5-60 mg/d for narcolepsy) 2.5-40 mg	ADHD Pediatric narcolepsy
Desoxyn	methamphetamine	6 and older 12 and older	5-25 mg/d 5 mg before meals	ADHD Exogenous obesity
Dynavel XR	Amphetamine CR oral	6 and older	2.5-20 mg	ADHD
Regimex	Benzphetamine	12 and older	25-150 mg/d	Exogenous obesity
Vyvanse	Lisdexamphetamine	6 and older	30-70 mg/d	ADHD

Methylphenidate preparations (partial)

Drug (trade)	Drug (generic)	Ages	Doses	Indication
Focalin Focalin ER	dexmethylphenidate	6-17	2.5 mg x2 daily, to 10 mg x2 daily	ADHD
Quillichew	dexMPH ER	6 and up	20-60 mg/d	ADHD
Aptensio XR	MPH ER	6 and up	10-60 mg/d	ADHD
Metadate CD	MPH ER	6-15	18-72 mg daily	ADHD
Concerta	MPH ER	13-17	18-72 mg daily	ADHD
Methylin CT	MPH IR (chewable)	6 and up	5, 10, 20 mg	ADHD, narcolepsy
Daytrana	MPH transdermal patch	6 and up	10 mg patch daily	ADHD

Other agents

Drug (trade)	Drug (generic)	Ages	Doses	Indications	Concerns, cautions, pearls
Strattera	Atomoxetine	6-17; up to 70 kg	0.5 mg/kg/d up to 1.2 mg/kg/d; max 100 mg/d	ADHD	Black box (suicide); 2D6 poor metabolizers; BP concerns
Kapvay	Clonidine ER	6-17	0.1 mg at bed up to 0.4 mg in divided dose	ADHD	Very sedating; BP change, orthostasis
Intuniv	Guanfacine ER	6-17	1-7 mg/d	ADHD	Very sedating; BP change, orthostasis

DRUGS FOR INSOMNIA

FDA approved sedative hypnotics

Alcohols:
Placidyl (ethchlorvynol)

Barbiturates:
Butisol sodium (butabarbital sodium)
Carbtrital (pentobarbital and carbromal)
Seconal (secobarbital sodium)

Benzodiazepines:
Dalmane (flurazepam hydrochloride)
Doral (quazepam)
Halcion (triazolam)
Prosom (estazolam)
Restoril (temazepam)

GABA receptor agonists:
Ambien, Ambien CR (zolpidem tartrate)
Edluar (zolpidem tartrate)
Intermezzo (zolpidem)
Lunesta (eszopiclone)
Sonata (zaleplon)
Zolpimist (zolpidem tartrate)

Melatonin receptor agonists:
Rozerem (ramelteon)

Orexin receptor agonists:
Belsomra

Tricyclics:
Silenor (doxepin hydrochloride)

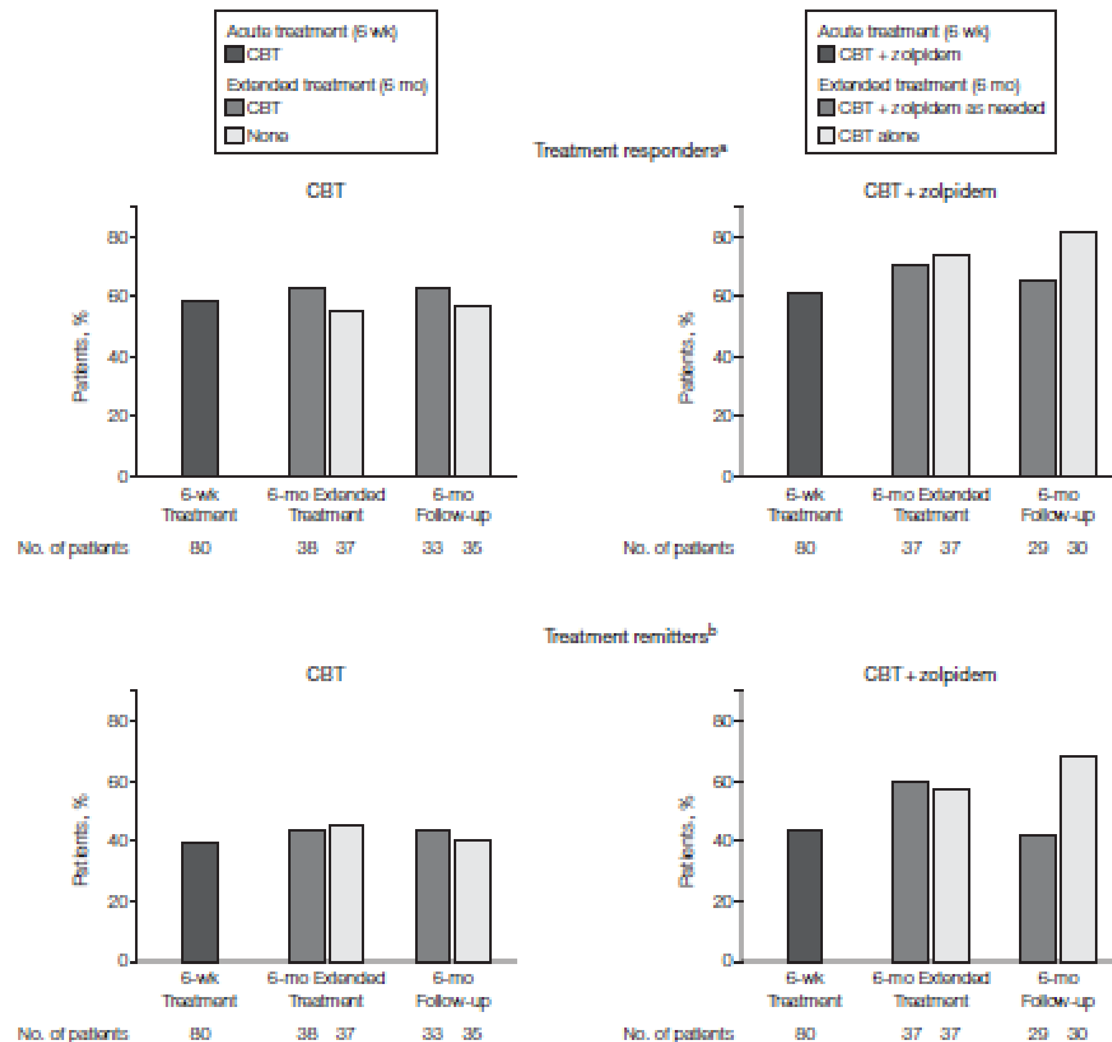
Insomnia and the “Z” drugs – Zaleplon, Zolpidem, Zopiclone

- Selective BDZ 1 receptor drugs are effective for insomnia
- But tolerance, dependence have been observed.
- Should not be used for long term use
- Behavioral treatments (sleep hygiene) more efficacious in the long run

Asleep at the wheel: Emerging problems with GRAs

- **Many reports of anterograde amnesia**
- Dyscoordination
- **Impaired reflexes**
- Hallucinations (visual) other unusual behavior rare but well documented in literature
- **Medicolegal file growing –**
- Excellent review is:
  - Gurja Clinical and Forensic Toxicology of Z drugs (2013). J. Med. Toxicol. (2013) 9:155–162

Morin, et al. (2009) CBT, singly and combined with RX, for persistent insomnia. *JAMA, 301,* 2005-2015



GABA RECEPTOR AGONIST TYPE DRUGS

Class	Drug	FDA Schedule	Dose Range
Z-drugs	Zolpidem (Ambien; Intermezzo SL)	IV	5-10 mg or 1.75-3.5
	Eszopliclone (Lunesta)	IV	1-3 mg, maybe lower?
	Zaleplon (Sonata)	IV	5-20? Recommend lower, “middle” insomnia
	Zopiclone (Imovane*)	N/A	
Melatonin Agonist	Ramelteon (Rozerem) MT1 agonist	Not scheduled	8 mg
Orexin Agonist	Suvorexant (Belsomra)	IV	5-20 mg
GABA agonist	Zyrem (sodium oxybate)	III narcolepsy only	4.5-9 *grams* nightly in 2 doses

Recall – low doses always better

NATIONAL REGISTER
OF HEALTH SERVICE PSYCHOLOGISTS