

# **Generalized Anxiety Disorder**

**R. Bruce Lydiard PhD, MD**

**Director, Southeast Health Consultants**

**Charleston SC**

**And**

**Medical University of South Carolina**

# **Generalized Anxiety Disorder (GAD) Pharmacotherapy Lecture Outline**

- **Questions and Learning Points**
- **Diagnosis and Epidemiology**
- **Course of Illness**
- **Neurobiology**
- **Morbidity and Comorbidity**
- **Assessment**
- **Treatment**
- **Summary**
- **Questions and Answers**
- **Future Treatments (Optional)**

# Question #1

True or False

**Women have a HIGHER Lifetime Prevalence of GAD as compared to Men.**

## Question #2

Which Psychiatric Illness has the  
**HIGHEST LIFETIME  
PREVALENCE of COMORBIDITY**  
with GAD?

# Question #3

What **Anxiety Assessment Scale** is commonly used to Assess Outcomes in GAD? and...

A decrease of \_\_\_% or greater on this scale defines **RESPONSE** while a score of \_\_\_ or less on this scale defines **REMISSION**.

# Question #4

What **PHARMACOLOGIC TREATMENTS** are Effective in Treating GAD?

## Question #5

What **percentage** of patients with **GAD relapse** within the first year after discontinuation of effective pharmacotherapy?

# Teaching Point #1

GAD...

- Is More Likely to Occur in **Women**
- Has a Modal Age of Onset in the **Early 20s**
- Is **Usually Comorbid** with Another Psychiatric Illness



# Teaching Point #2

- **Somatic symptoms** are prevalent in GAD
- **Concurrent medications and medical conditions** should be Included in the differential diagnosis for GAD

# Teaching Point #3

- **SSRIs, SNRIs and benzodiazepines** are effective for GAD
- **Azapirones** are effective, but
  - evidence suggests that their relative efficacy ( vs. antidepressants and benzodiazepines) may be less robust
  - No long-term controlled studies to date
- **Long term treatment** often necessary

# DSM-IV GAD Diagnostic Criteria

- Excessive or difficult to control worry and anxiety
- More days than not for  $\geq 6$  months\*
  - 6-month duration affects prevalence but not course or disability.\* Increasingly controversial
- Symptoms impair social, occupational, family role functioning and/or cause significant distress

# DSM-IV Diagnostic Criteria for GAD, cont

- **Associated with  $\geq 3$  of the following**
  - **restlessness/keyed-up**
  - **easily fatigued**
  - **difficulty concentrating**
  - **irritability**
  - **muscle tension**
  - **sleep disturbance**
- **Does not occur only when another Axis 1 disorder is present ( such as MDD) or be due a substance or medical condition**

# GAD Symptoms

- **Psychic symptoms**
  - worry
  - “on edge”/unable to relax
  - Impaired concentration-memory
  - \*Concern over health\*
- **Somatic symptoms**
  - muscle tension
  - Insomnia
  - Fatigue
  - irritability
  - nausea or diarrhea\*
  - Sweating\*
  - urinary frequency\*
  - Palpitations\*
  - Pain\*

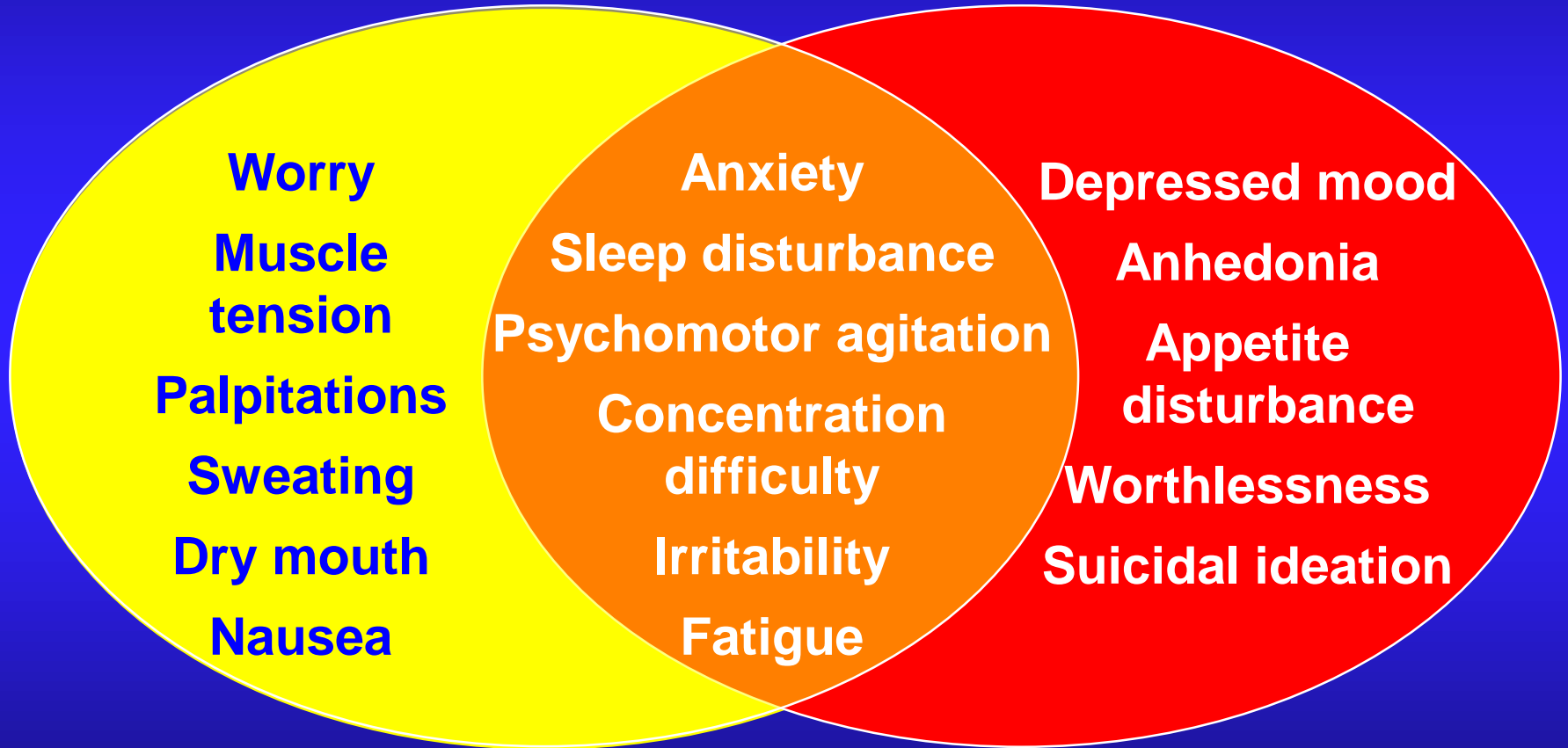
DSM IV-TR. Washington, DC: American Psychiatric Association. 2000.

Symptoms not diagnostic but often present (Schweizer E et al. J Clin Psychiatry. 1997;58(suppl 3):27-31.)

# Overlapping Symptoms of MDD and GAD

Generalized Anxiety Disorder

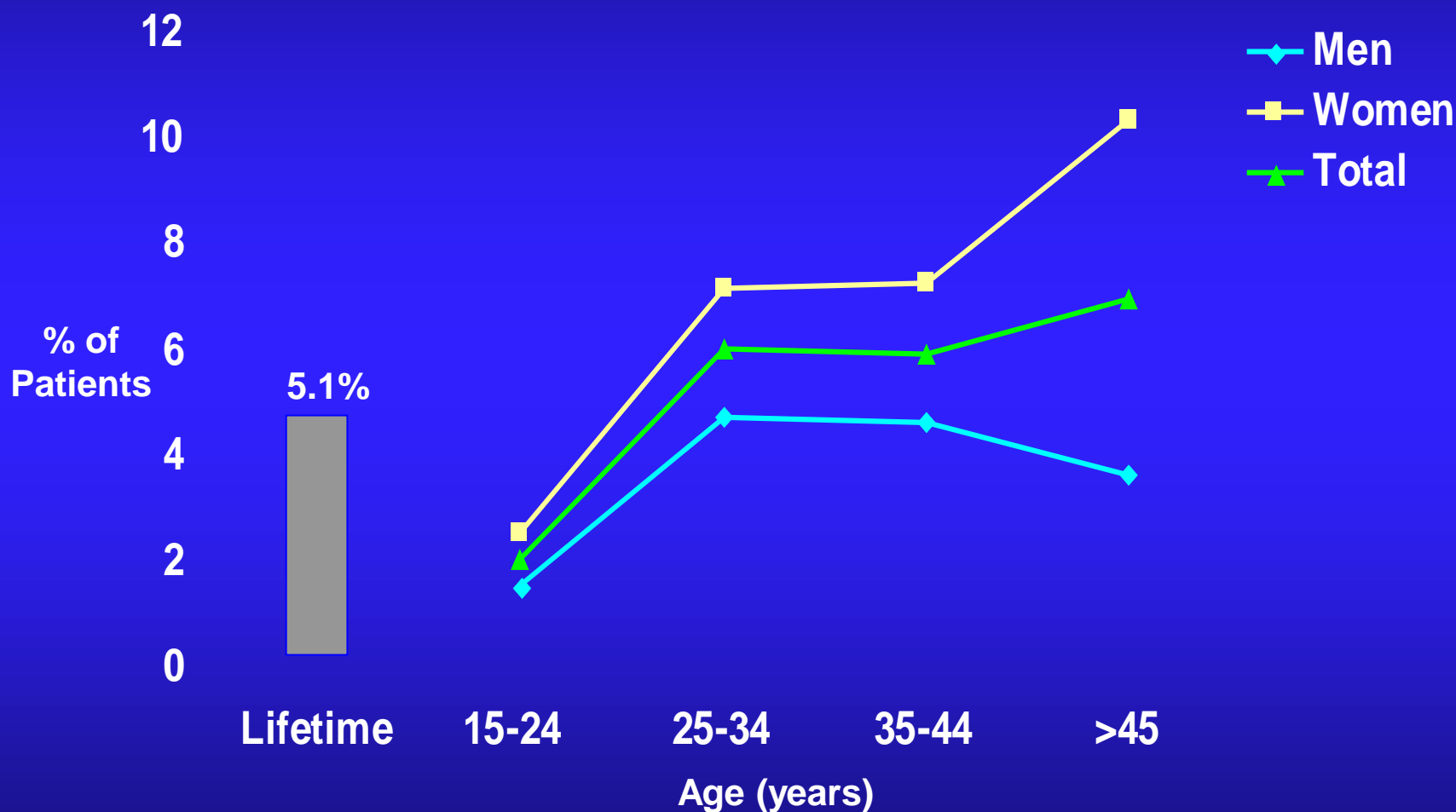
Major Depressive Disorder



# Epidemiology of GAD

- Lifetime prevalence ~ 5.1 %
- 12-month prevalence ~ 3
- Women > men 2:1
- Modal age of onset is early 20s
- High comorbidity in clinical and community samples. : “Pure” GAD is rare.

# Lifetime Prevalence of GAD: National Comorbidity Survey





# GAD Longitudinal Course

Chronic course -- > Chronic Treatment Indicated

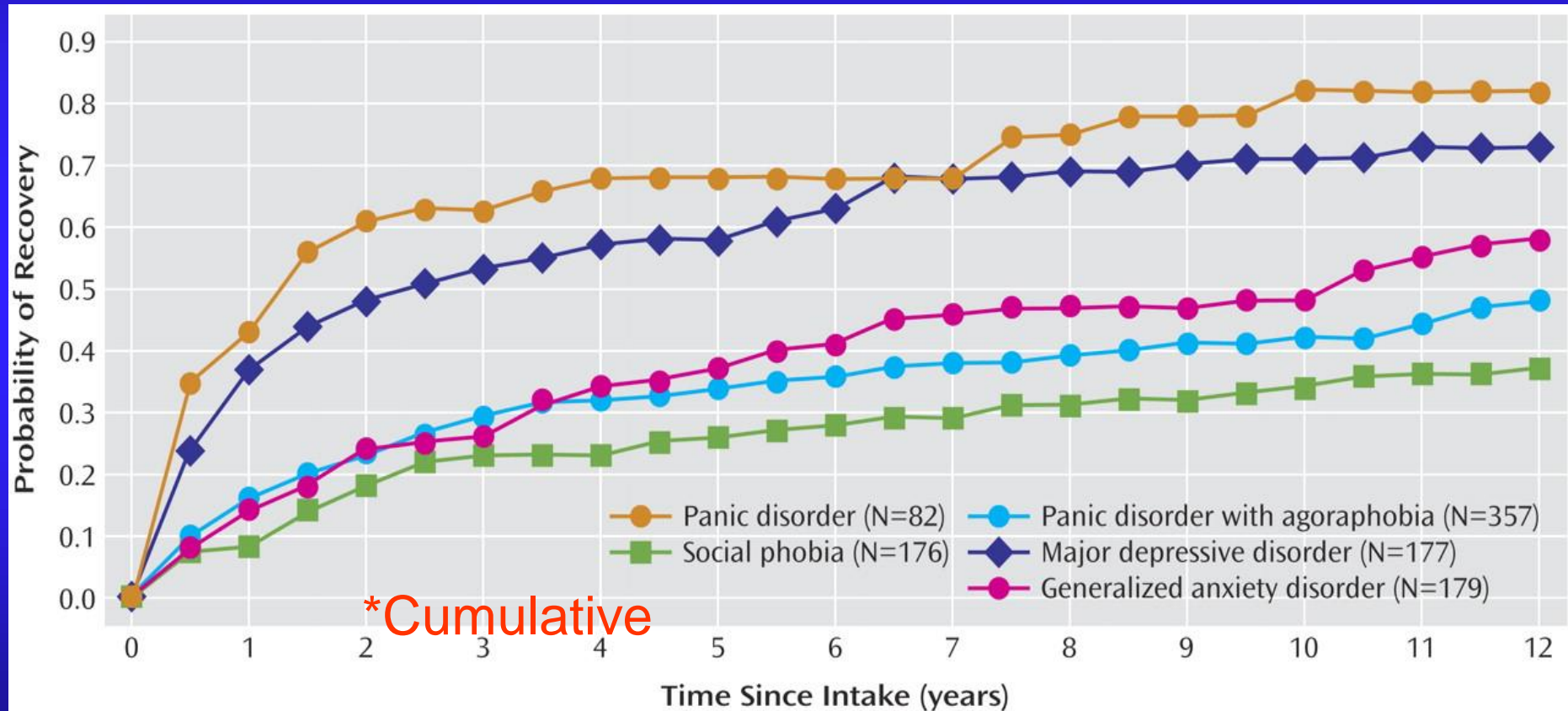
- **Overlap with MDD**
  - Both increase risk for the other
  - Literature differs on timing of onset
- **Low rate of remission (25% at 2 yrs) in both psychiatric and primary care settings**
- **Remission further reduced ( additive):**
  - with each add'l Axis I disorder
    - (50% less likely)
  - with each add'l Axis III disorder
    - (19% less likely)

Sartorius N et al. Br J Psychiatry. 1996;168(suppl 30):38-43; Maier W et al. Acta Psychiatr Scand. 2000;101:29-36; Keller, J Cin Psych 2002; 63 (suppl) :11-16;Yonkers KA et al. Br J Psychiatry. 2000;176:544-549 Yonkers et al, Depress Anxiety 2003 17:173-9. Rodriguez et al J Nerv Ment Dis 2006; 194:91-7; Keller and Lydiard , Psych CME Reports 2005; 1:1-7; Moffit et al, Arch Gen Psych 2007;64: 651-60



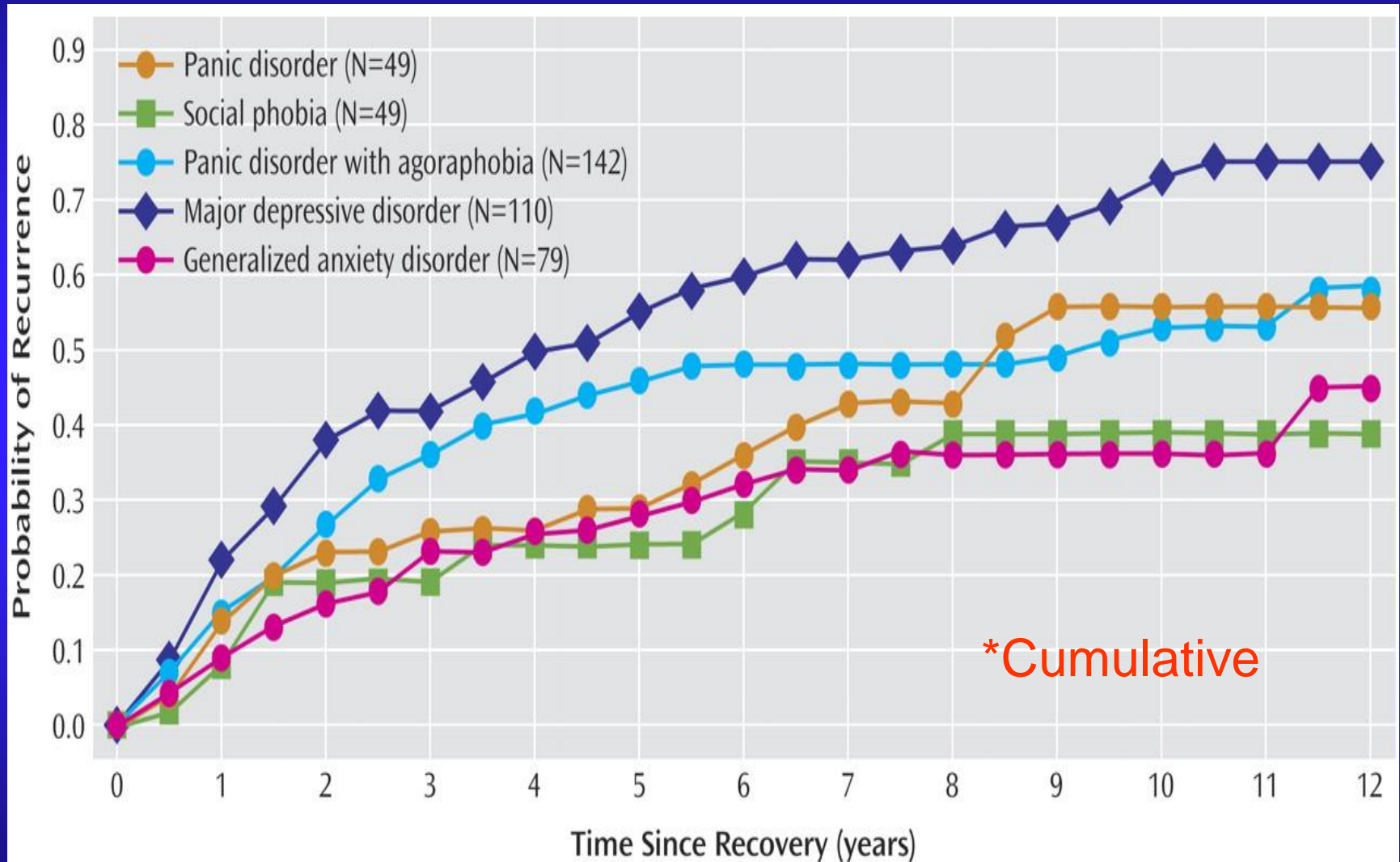
## •12-Yr Probability of Remission in GAD

Low rate of recovery and recurrence (See notes)



# 12-Yr Probability for Recurrence

Relatively low rate of recurrence



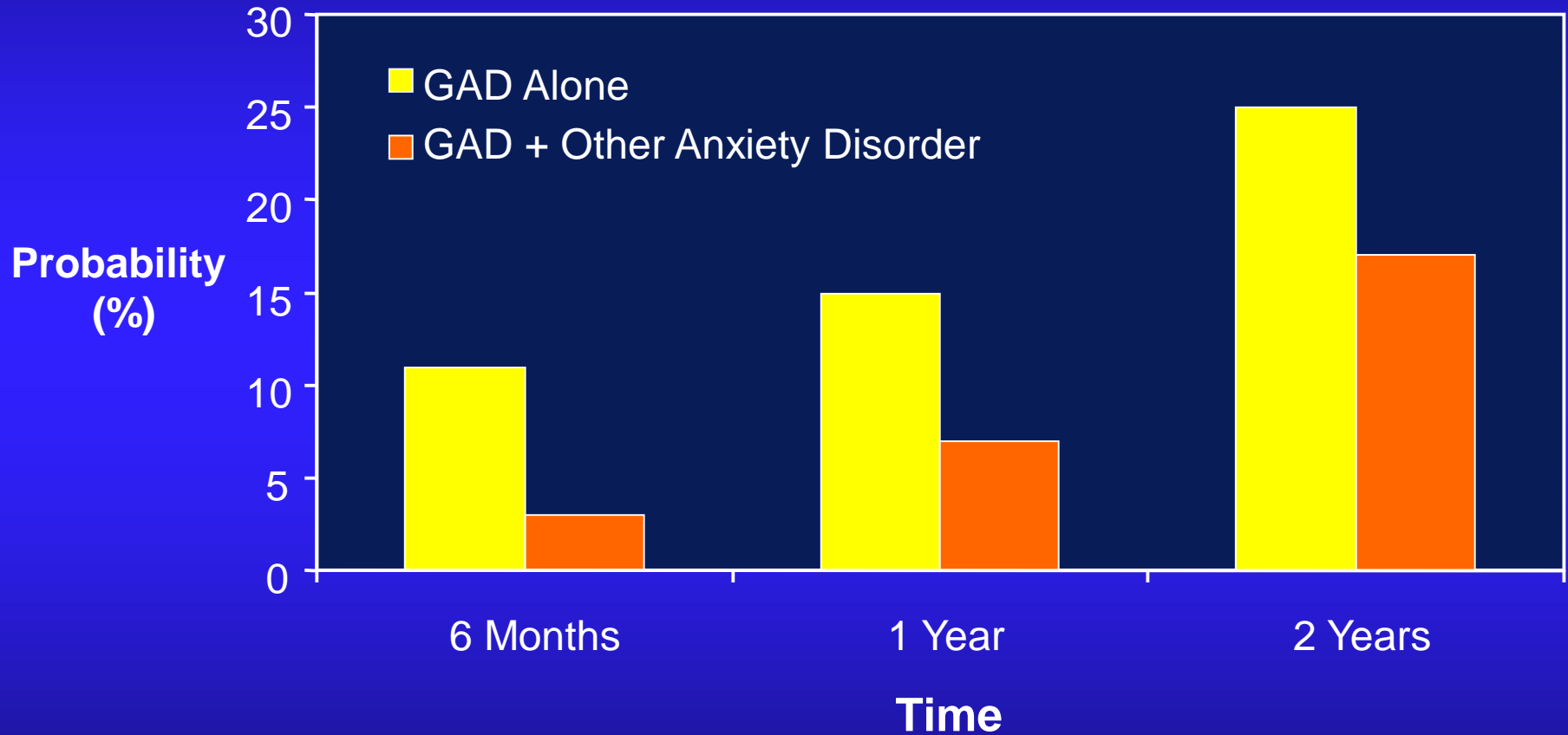
\*Cumulative

Bruce et al, AJP 2005 162:1179-87;Harvard Anxiety Research Program



# Low Probability of Remission in GAD\*

## Patients in treatment (HARP)



Yonkers KA et al. *Br J Psychiatry*. 1996;168:308-313.

# GAD Patients: Comorbidity

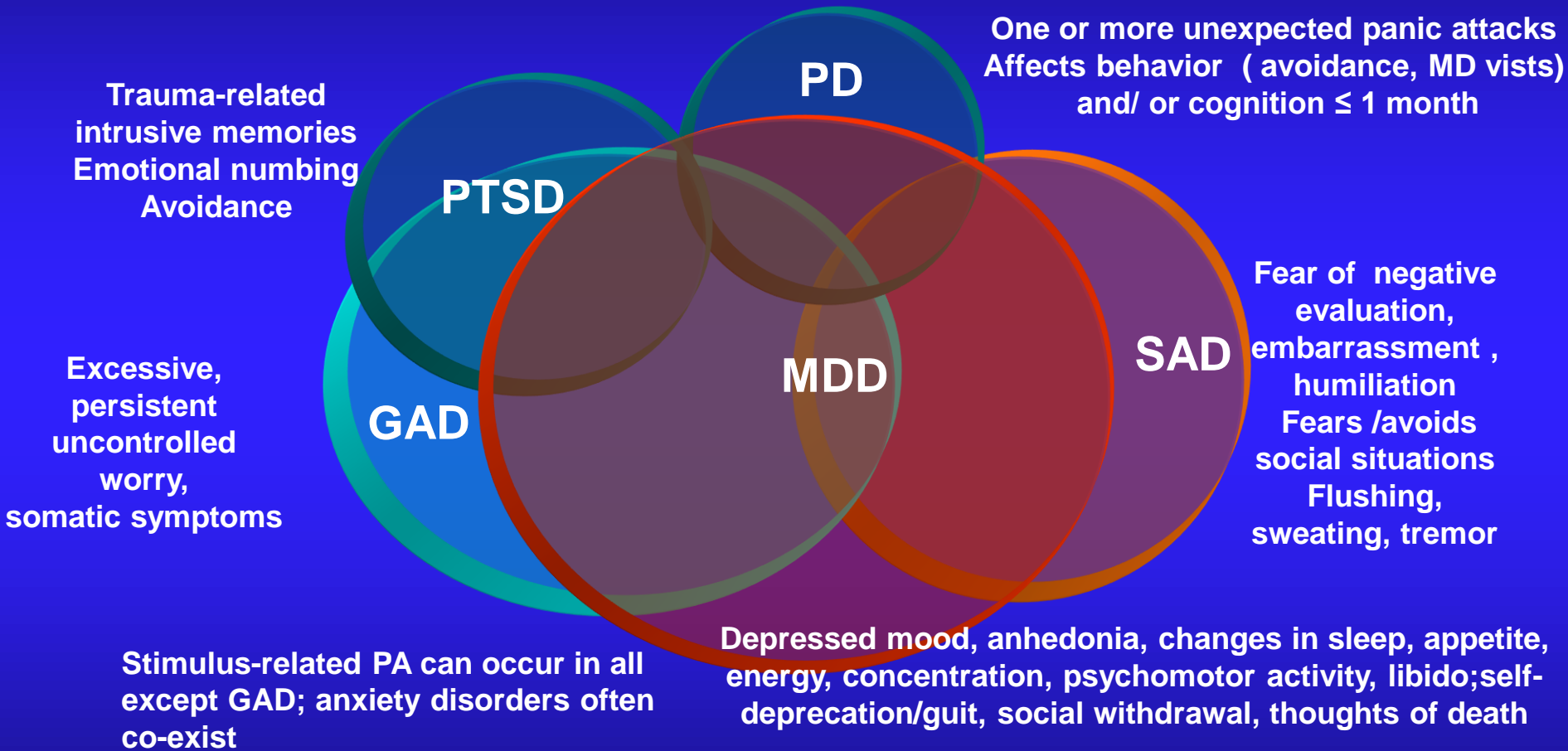
- **90% have another psychiatric disorder**
- **In patients with GAD**
  - **62% have lifetime major depression**
  - **40% have dysthymia**
- **Anxiety disorders predict greatest risk of secondary MDD**
- **58% of patients with lifetime MDD have an anxiety disorder**

Kessler RC et al. Br J Psychiatry. 1996;168(suppl 30):17

Wittchen H-U et al. Arch Gen Psychiatry. 1994;51:355

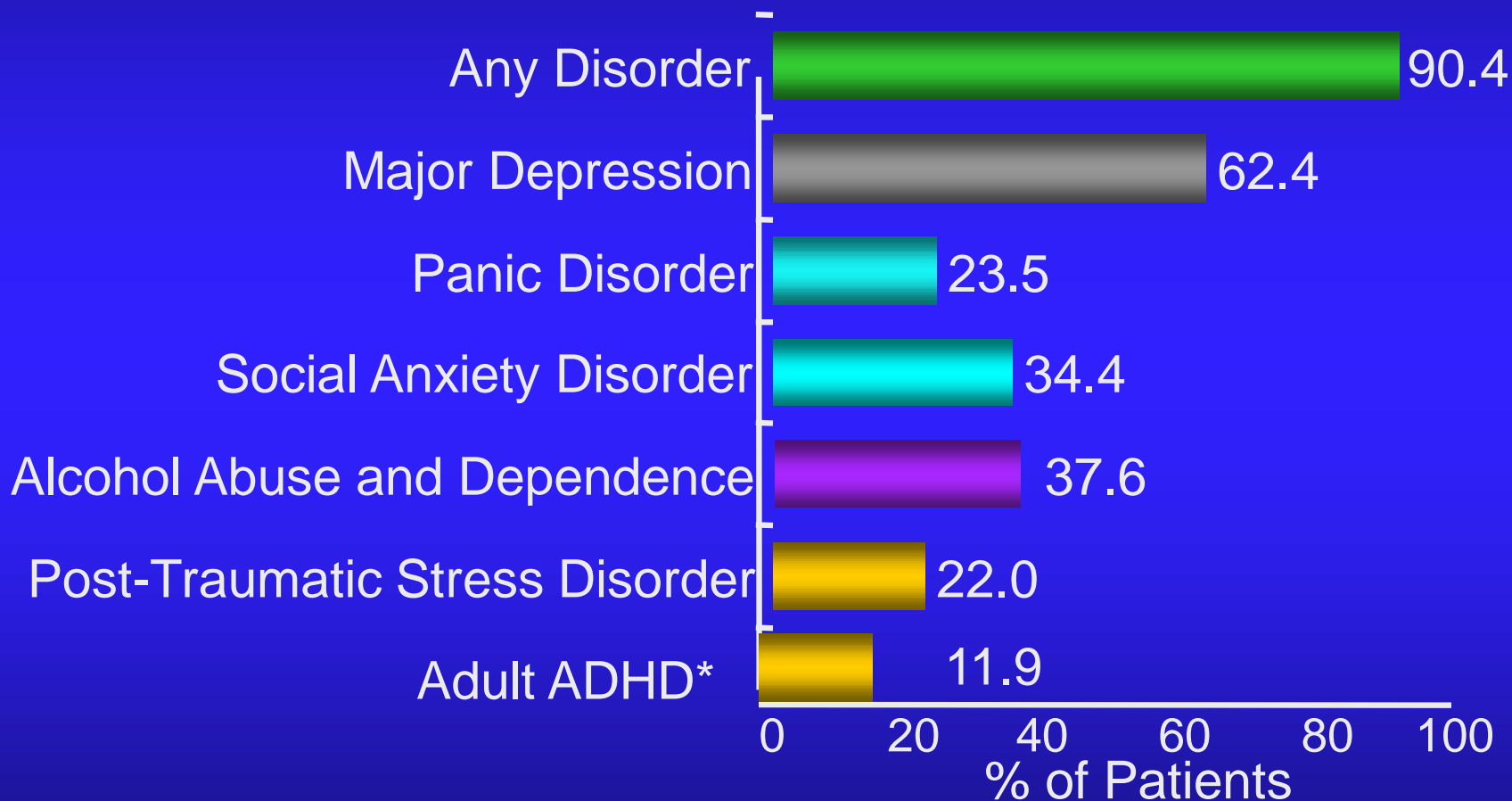


# Anxiety and Depression: Pure DSM-IV Disorders are Rare



Not intended to be accurate; estimates vary widely

# Lifetime Prevalence of Comorbid Disorders in Patients with GAD



Wittchen HU, et al. *Arch Gen Psychiatry*. 1994;51:355-364; Kessler et al, *Arch Gen Psychiatry*, 2000; Kessler et al, *Am J Psychiatry* 2006;163:716-23\*.



# GAD+MDD: Implications

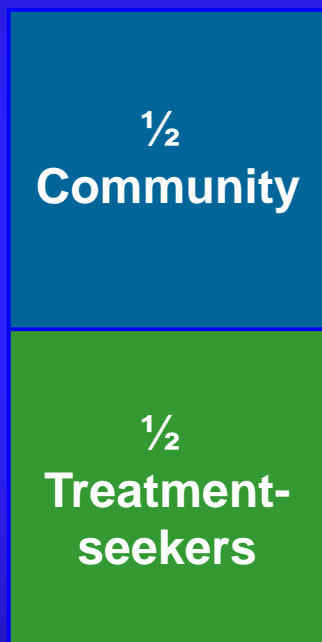
- **Treatment resistance or delayed response**
- **Increased suicidal behavior**
- **Antidepressants indicated**
  - **One open-label clinical practice reports effectiveness of venlafaxine in comorbid state**
  - **CBT efficacy for comorbid states less clear, needs study**
  - **Much written, little known**
- **Brown et al AJP 1996; 153: 1293-1300; Gaynes et al, Gen Hosp Psych 1999; 21:158-67; Goodnick et al, JCP199; 60: 446-48; Silverstone et al JCP 1999; 60: 22-8; Perugi et al, Neuropsychobiology, 2002**



# Anxiety: Worse Long-term Health

## German Health Survey (n=4181)

~300 Individuals with GAD or Panic Disorder



2 to 6 times as many medical disorders vs. controls\*

- Cardiovascular disorders
- Respiratory disorders
- Endocrine-metabolic disorders
- Autoimmune disorders
- Allergic disorders

\*Controlled for gender, depression, substance abuse.

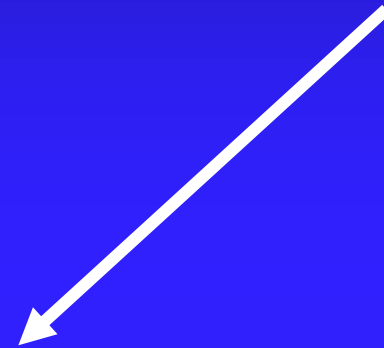
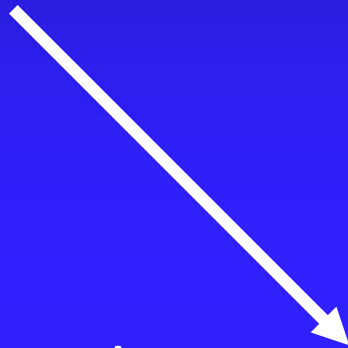
# **GAD Often Presents as a Physical Complaint**

- Gastrointestinal distress**
- Insomnia**
- Fatigue**
- Musculoskeletal complaints**
- Headache**
- Cardiovascular complaints**

# Generalized Anxiety Disorder (GAD)

Under-recognized

Under-treated



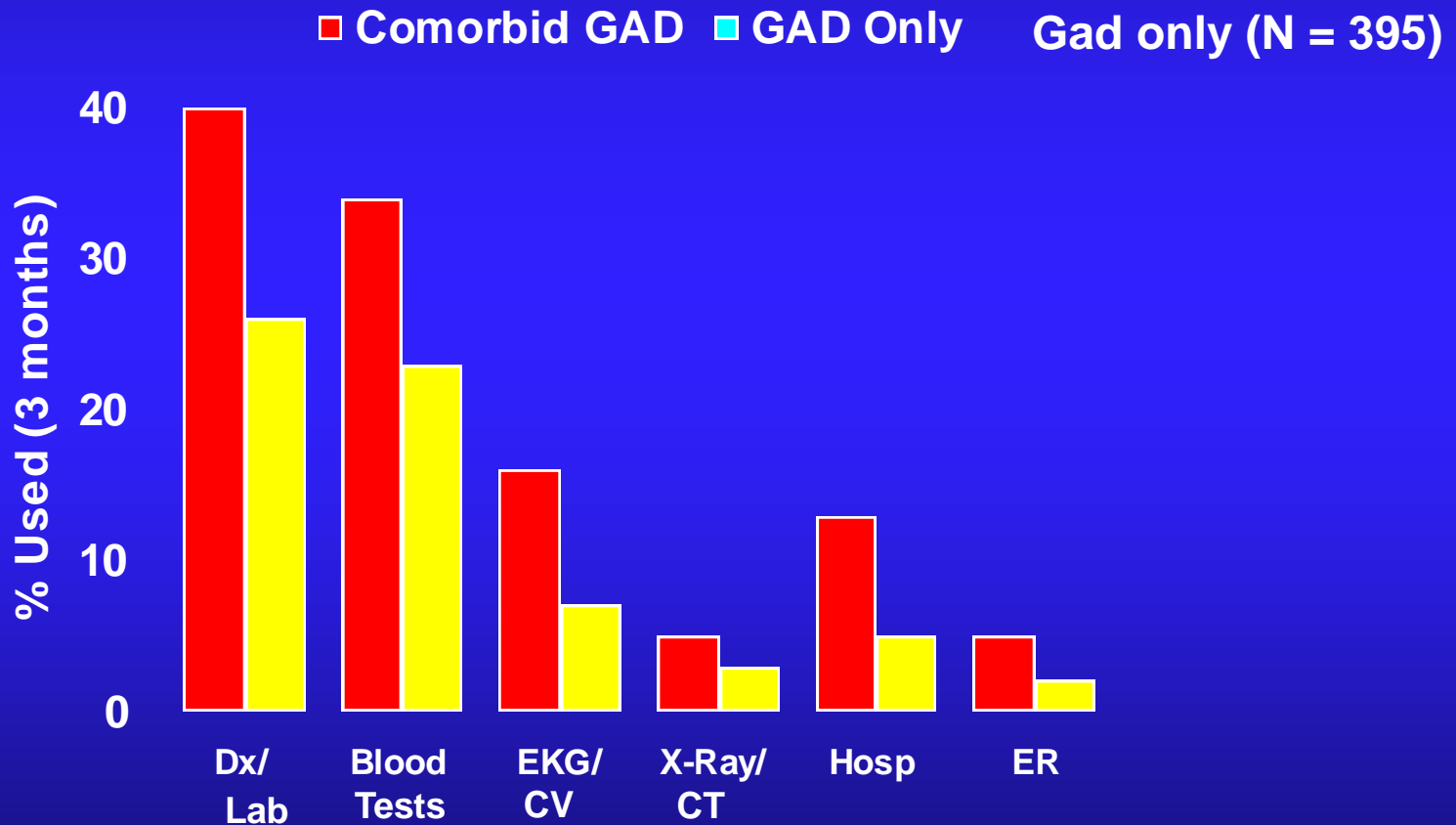
↑ Health-care utilization

↑ Disability/impairment

↑ Risk for new psychiatric disorders

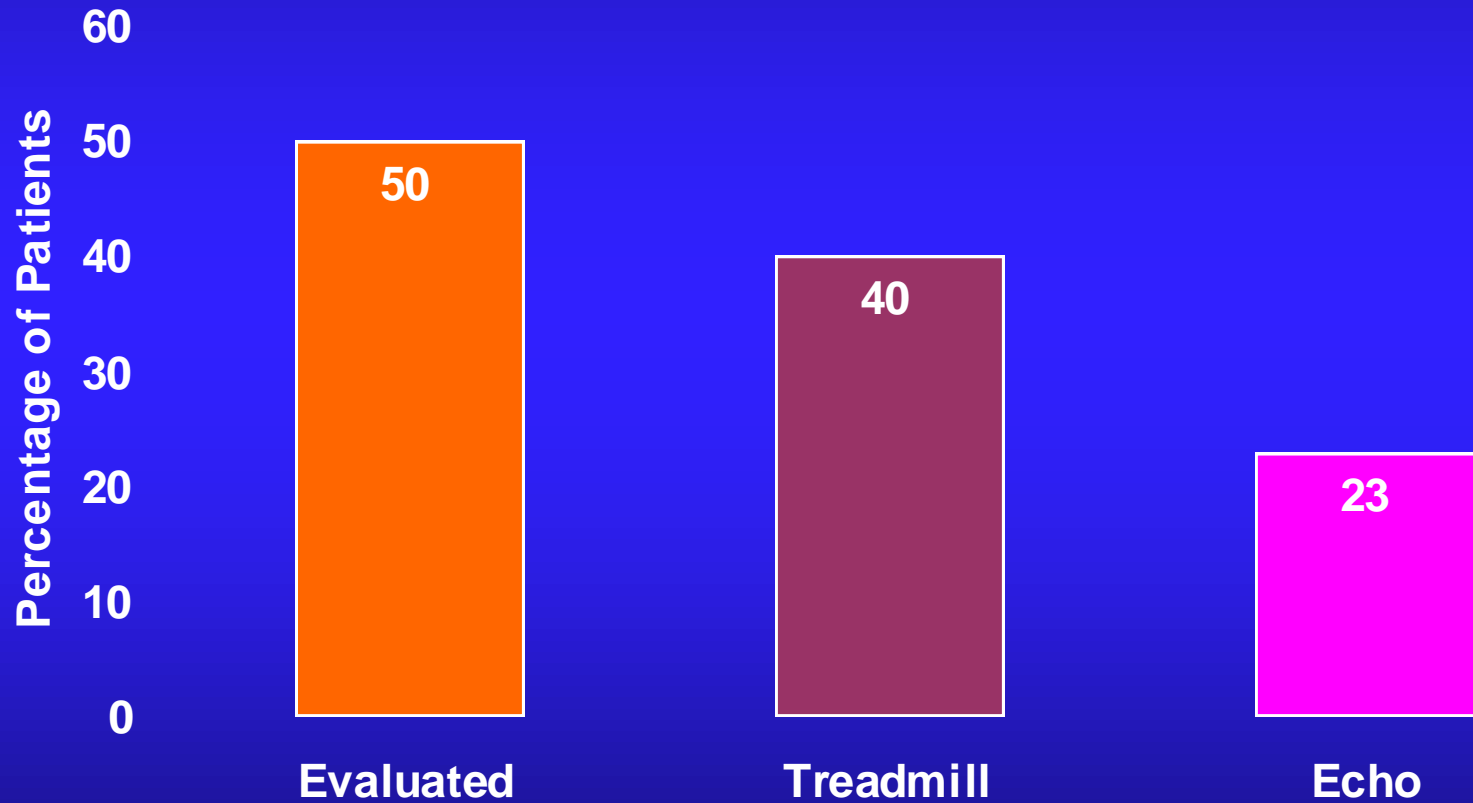
# Generalized Anxiety Disorder

## Services Utilization and Comorbidity



# GAD in Cardiology

## Cardiovascular Evaluation Sought by GAD Patients



# GAD Neurobiology

## Partial List

- Stress reactivity
- Genetic
  - Gender differences: risk for women 2x men
  - Familial inheritance pattern
  - Same gene, different environments?
  - Polymorphism
- Neurotransmitter differences
  - NE overactivity
  - BZ receptor differences
- Immune Dysfunction
  - Immunosuppression
  - Worry --> pro-inflammatory cytokine release
- Imaging
  - Lower BZ receptor density
  - Increase cCBF following worry



# **GAD: Increased rCBF in Response to Fear Cues and Worry: Reduced after Citalopram Rx**

QuickTime™ and a  
TIFF (Uncompressed) decompressor  
are needed to see this picture.

**Abnormally increased activation :PFC, striatum,  
insula and paralimbic regions after citalopram treatment**

**Hoehn-Saric et al J Psych Res, 2004; 131: 11-21**



# Reduced L Temporal BZ Receptor Density in GAD (A) vs Normals (B) via SPECT

QuickTime™ and a  
TIFF (Uncompressed) decompressor  
are needed to see this picture.

Tilhonen et al, Mol Psych 1997;2:463-71





# **GAD**

## **Differential Diagnosis**

### **–Adjustment disorders**

- **With anxiety**
- **With depression**
- **With mixed symptoms**

### **–Anxiety disorders**

- **Generalized anxiety disorder (GAD)**
- **Panic disorder**
- **Phobias**
- **Post-traumatic stress disorder (PTSD)**
- **Obsessive-compulsive disorder (OCD)**

# Patient Assessment

- Establish Diagnosis
- Comorbid diagnosis present?
  - Current or past depression
- Natural History of Illness
- Treatment History
- Family History
- Medical History and exam
  - Review medications, *including herbal medicine*

# Differential Diagnosis

## Medications Which Can Cause Anxiety Symptoms

- Stimulants (caffeine)
- Thyroid supplementation
- Antidepressants
- Corticosteroids
- Oral contraceptives
- Bronchodilators
- Decongestants
- Abrupt withdrawal of CNS depressants
  - Alcohol
  - Barbiturates
  - Benzodiazepines

Fernandez et al. J Clin Psychiatry. 1995;56(suppl 2):20–29.

Kirkwood et al. Anxiety disorders. In: DiPiro et al, eds. Pharmacotherapy: A Pathophysiologic Approach. 3rd ed. 1997:1443–1462.

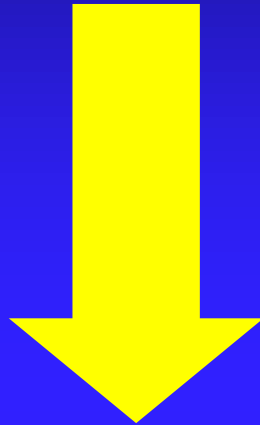
# *Differential Diagnosis*

## **Medical Conditions with Secondary Anxiety Symptoms**

- **Endocrine disorders**
  - Thyroid disease
  - Parathyroid diseases
  - Hypoglycemia
  - Cushings Disease
- **Cardio-respiratory disorders**
  - Angina
  - Pulmonary embolism
- **Autoimmune disorders**
- **Neurological**
  - Seizure disorder
- **Substance-related  
dependence/ withdrawal**
  - Nicotine
  - Alcohol
  - Benzodiazepines
  - Opioids

# Assessing GAD Treatment Effects

Response



≥ 50% decrease from baseline  
in HAM-A scores or  
CGI score of 1 or 2

Remission\*



HAM-A score ≤ 7  
Patient asymptomatic  
Psychosocial/occupational  
functioning restored

Allgulander C et al. *Br J Psychiatry*. 2001;179:15-22.  
Pollack MH et al. *J Clin Psychiatry*. 2001;62:350-357.



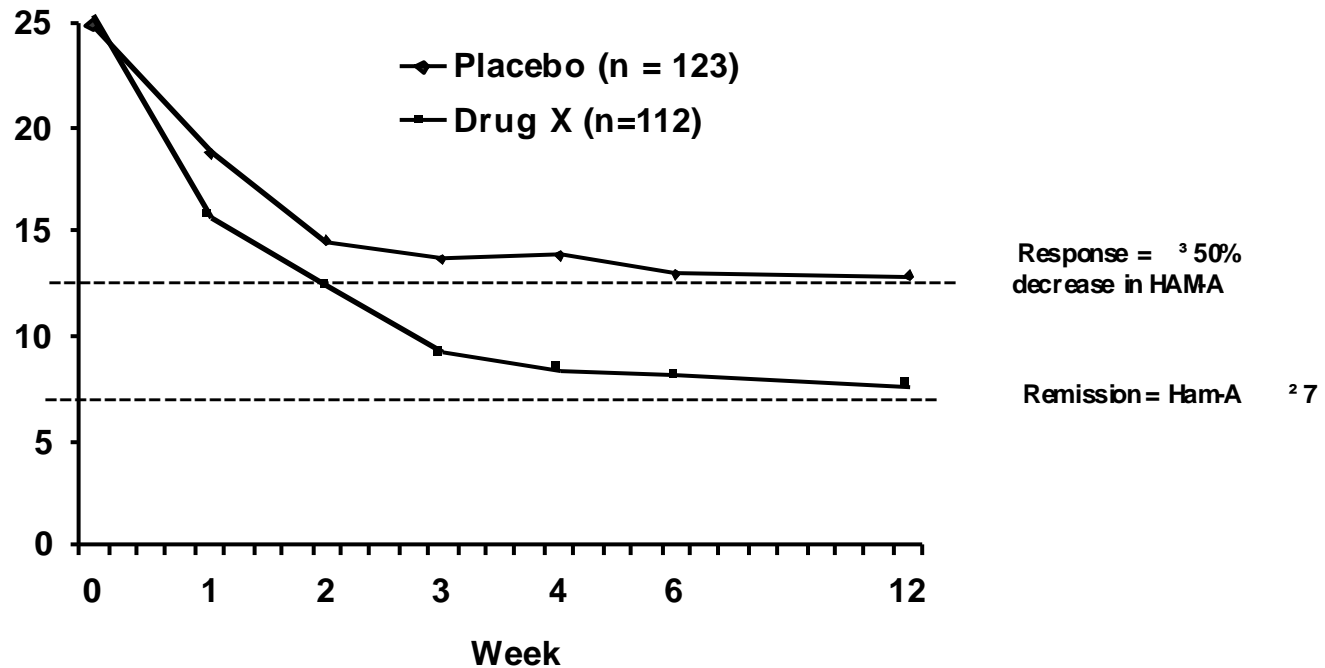
# Interpreting the Literature

- **Efficacy ≠ Effectiveness**
- **Loss of impairment most important**
- **Short-term studies can't really examine this**
  - **Acute GAD-look for  $\geq 10$  point HAM-A decrease**
  - **Superior to placebo by  $\geq 5$  points HAM-A**
  - **Guideline only**



# Response vs Remission

## HAM-A Total Score Change During Treatment



# Outcomes Assessment in GAD

- **Hamilton Anxiety Rating Scale**
  - Traditionally used in clinical trials
- **Hospital and Anxiety Rating Scale**
  - Patient rated 14 items
    - 7 items for anxiety
    - 7 items for depression
    - Sensitive to change
    - Equivalence to Hamilton Anxiety Scale shown in large patient sample



# Treating Anxiety Disorder May Reduce Risk of MDD

- National Comorbidity Survey
  - Sept. 1990 - Feb. 1992 (interview and re-interview 2y later)
- Respondents with GAD w/o prior MDE
- $\geq 4$  doses psychotropic medication for GAD
  - Lower risk of depression
    - » 5.73% vs. 18.9%,  $p < 0.0001$
  - Receiving any medication for GAD or consulting mental health specialist was not.

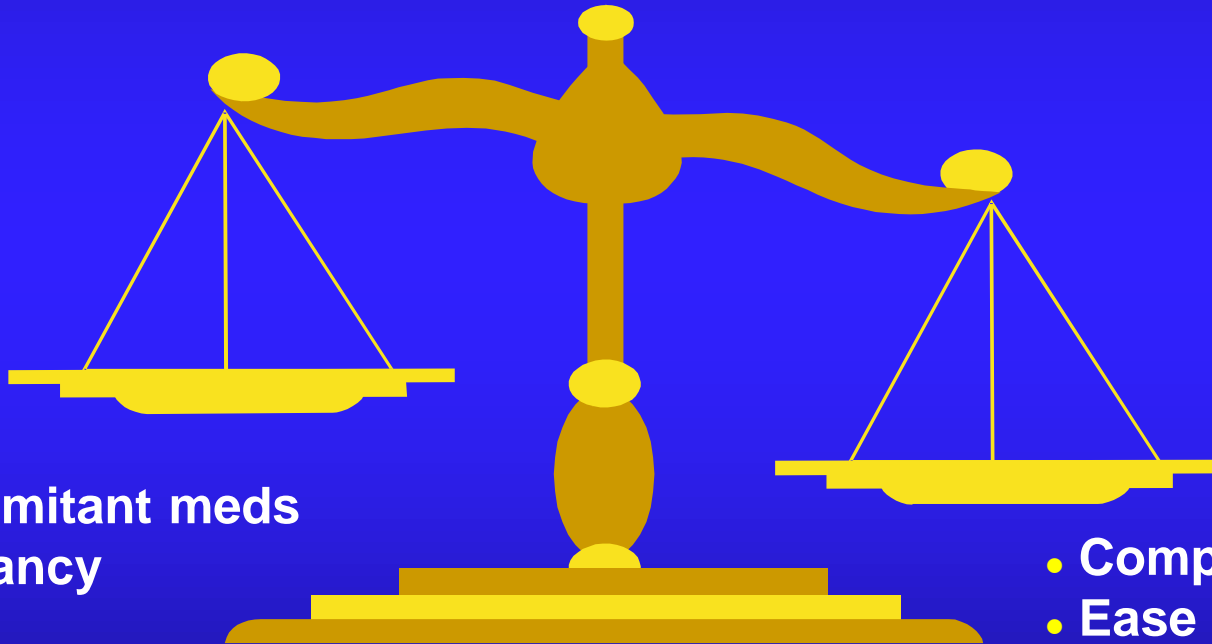
Goodwin RD and Gorman JM, Am J Psychiatry 2002;159(11):1935-37



# Initiating therapy: treatment considerations

---

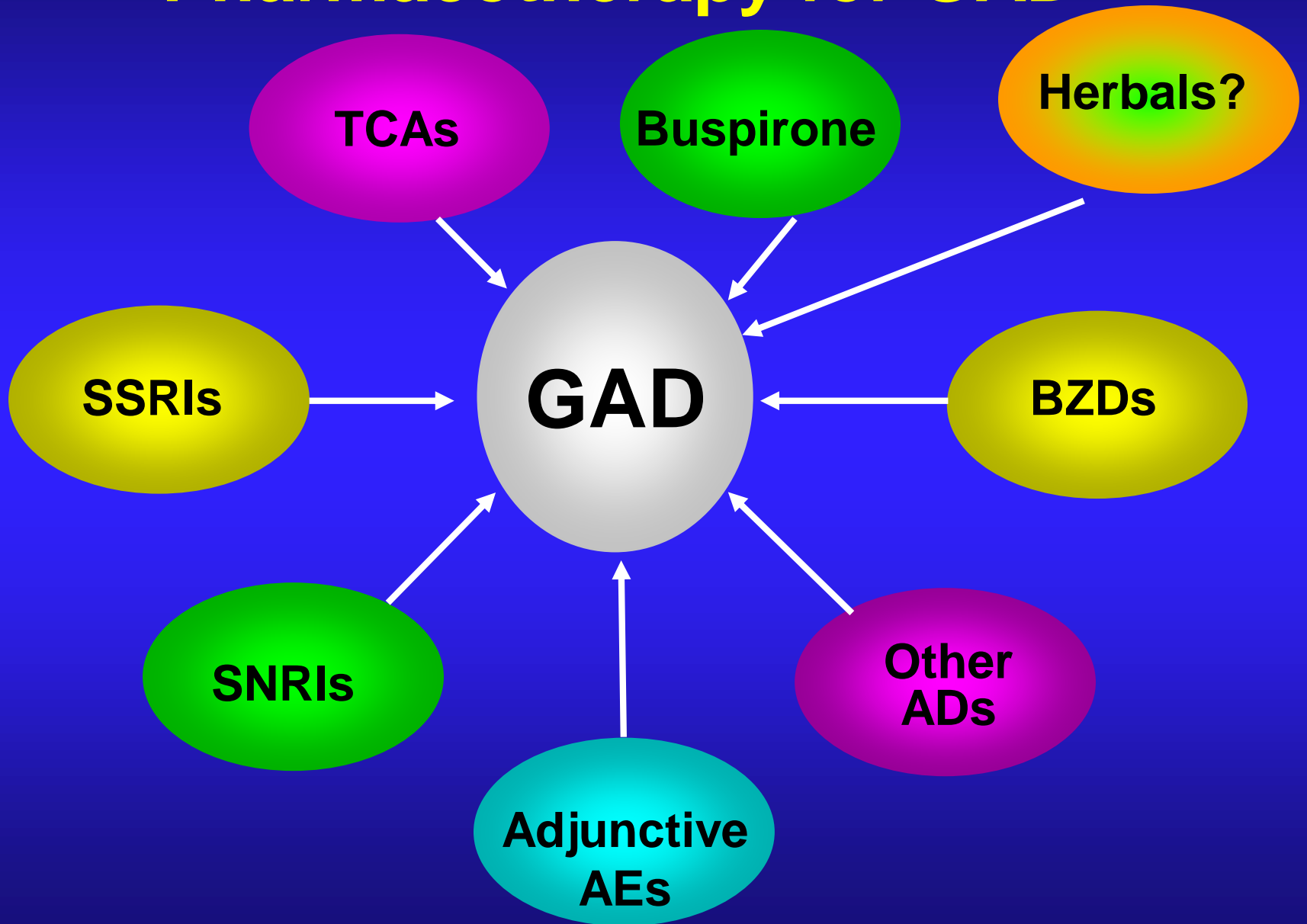
Ease of management



- Safety
- Concomitant meds
- Pregnancy
- Age
- Washout

- Compliance
  - Ease of switching
  - Ease of discontinuation
-

# Pharmacotherapy for GAD



# Traditional Anxiolytics

## *Limitations*

- **Poor tolerability (TCAs, MAOIs)**
  - *SSRIs & SNRIs-Less than ideal*
  - *Tolerance*
  - *“Poopout”*
- **Limited breadth of efficacy**
  - TCAs, BZDs, azapirones
- **Lack of antidepressant efficacy**
  - (buspirone, BZDs)
- **Safety (TCAs, MAOIs)**



# **GAD Treatments**

## **SSRIs and SNRIs**

---

### Advantages

- **Effective**
- **Safety**
- **Tolerability**
- **No dependence**
- **Once-daily dosing**

### Disadvantages

- **Delayed onset of action**
- **Early anxiogenic effects**
- **Sexual side-effects**
- **Dose titration (often)**
- **Discontinuation Sx**



## Antidepressants in Anxiety and Mood Disorders

FDA-Approved -X    Effective  $\geq$  1 RCT -X

SSRIs	MDD	PD	SAD	PTSD	GAD	OCD	PMDD
Citalopram	X	X	X	X	X	X	X
Escitalopram	X	X	X	X	X	X	X
Fluoxetine	X	X	X	X	X	X	X
Fluvoxamine	X	X	X	X	X	X	X
Paroxetine	X	X	X	X	X	X	X
Sertraline	X	X	X	X		X	X
SNRIs							
Venlafaxine	X	X	X	X	X	?	X
Duloxetine	X	?	?	?	X	?	



# Summary: GAD Antidepressant Dosing

## Category

## Usual Dosage Range (mg/d)

### SSRIS

Fluoxetine	20-60
Sertraline	100-200
Paroxetine	20-40
Fluvoxamine	100-300
Citalopram	20-40
Escitalopram	10-20

### SNRIs

Venlafaxine	75-225
Duloxetine	60-120

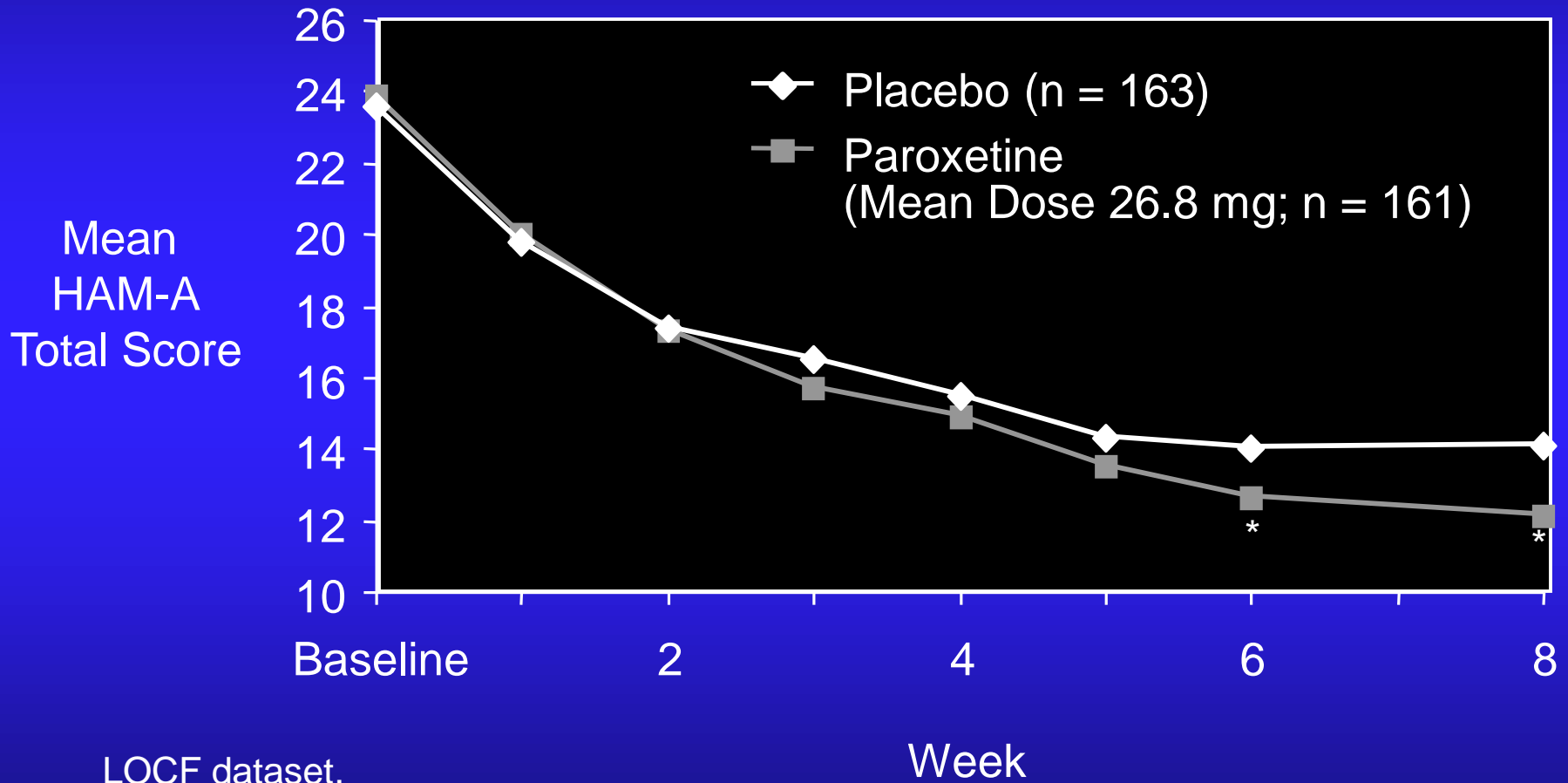
### Tricyclic Antidepressants

Imipramine*	100-300
Clomipramine	50-100



# SSRIs: Paroxetine for GAD

## Flexible Dosing



LOCF dataset.

\* $P < .05$  vs placebo.

Pollack MH et al. *J Clin Psychiatry*. 2001;62:350-357.





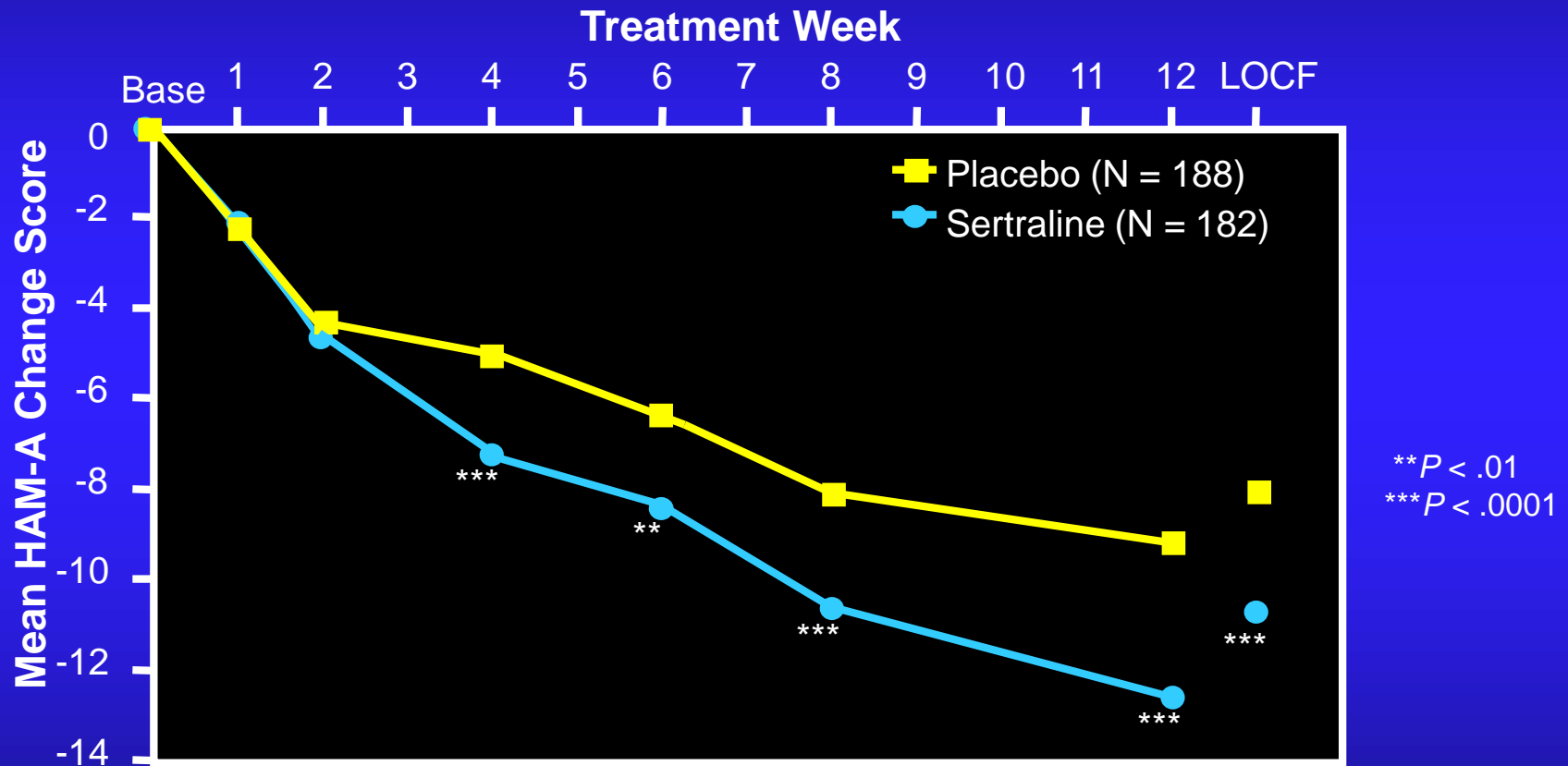
# Paroxetine: The Best or the Most?

- **1800 outpatients with DSM-IV GAD**
  - **Placebo-controlled RCTs**
    - 3 eight-week studies
    - 6-month relapse prevention
    - Solid design and sample size
- **BUT the majority of comparative studies indicate no significant differences among SSRIs in GAD**
- **Most studied but not superior to other SSRIs or the SNRIs**



# SSRIs for GAD: Sertraline vs Placebo

ITT sample

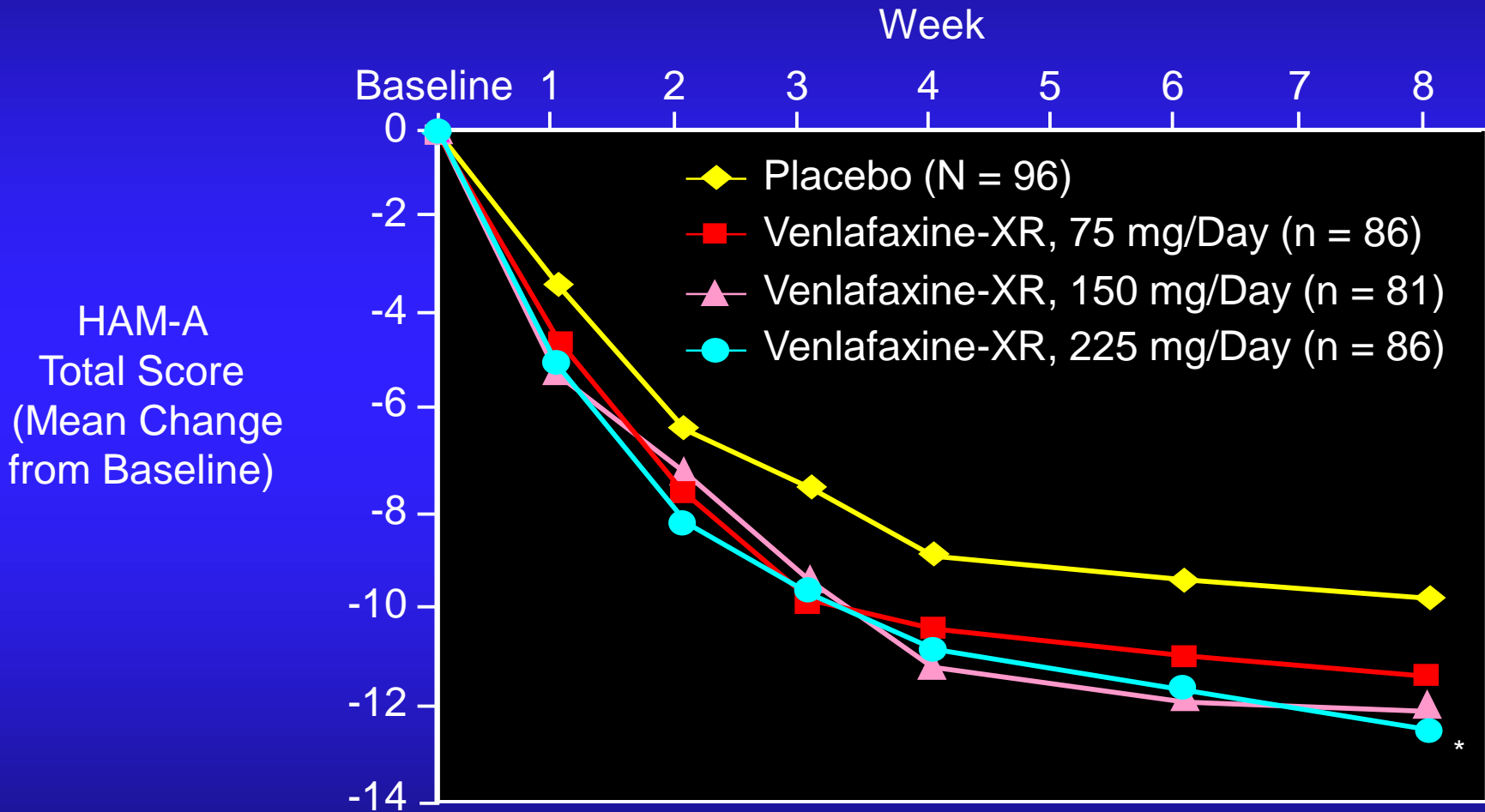


Adapted from Dahl AA et al. Acta Psychiatrica Scand 2005; 111:429-35



# Venlafaxine Treatment of GAD

## Fixed-dose Study



\* $P = .03$ .

Rickels K et al. *Am J Psychiatry*. 2000;157:968-974.



# Venlafaxine in Childhood GAD

- 2 RCTs, placebo controlled
- DSM-IV GAD, ages 6 - 17
  - 59 sites in 2000-2001
- Flexible dosage of extended-release venlafaxine
  - (N=157) or placebo (N=163) for 8 wks
- Study 1 Significant on primary & some secondary outcome measures
- Study 2 Significant on some secondary, not primary
- Pooled sample-Significant primary outcome overall
  - See notes



# Duloxetine

- **SNRI: binds with high affinity to serotonin and norepinephrine transporters**
  - More potent than fluoxetine as inhibitor of serotonin reuptake
- **3 RCTs with placebo completed, 9-10 weeks (see notes)**
  - 60-120 mg daily
  - one fixed dose 60 and 120 vs PbO
  - 2 flexible dosing 60-120 vs PbO
  - Improved anxiety, reduced disability and increased quality of life
- **Effective in preventing relapse of GAD**
- **FDA-approved for MDD, GAD and fibromyalgia**



# **GAD Treatment**

## **Benzodiazepines**

---

### Advantages

- **Rapid onset**
- **Effective**
- **Well-tolerated**
- **General anti-anxiety effects**
- **Safe in overdose**
- **Generics available**

### Disadvantages

- **Withdrawal reactions**
- **Sedation**
- **Multiple daily dosing often required except clonazepam**
- **Abuse potential in patients w/ Hx drug abuse**
- **Antidepressant effect unreliable**

**\* Long-term GAD treatment with BZs has not been systematically studied; far more opinion than fact is reported in the literature**

# GAD Treatment

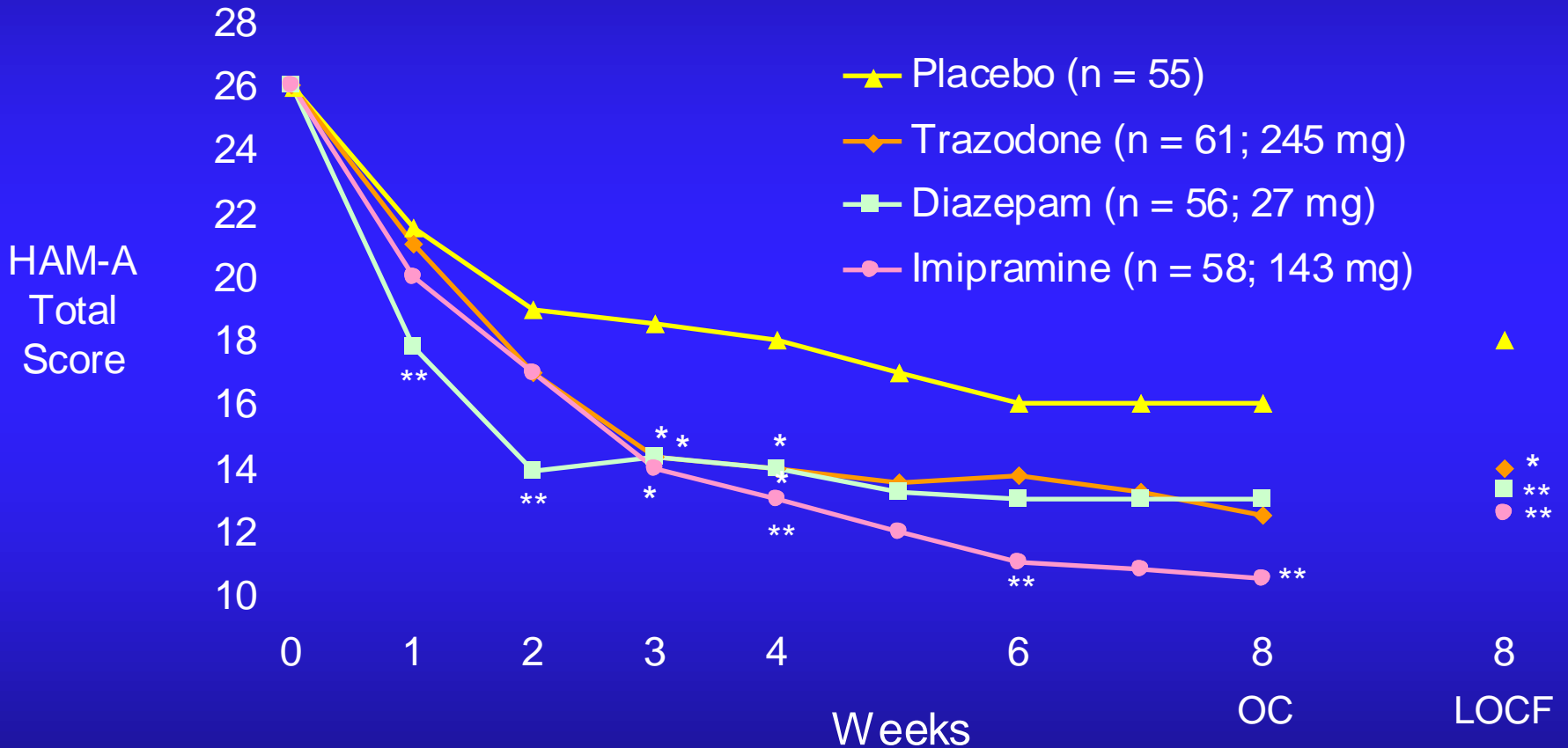
## Benzodiazepines

Agent	Daily Dosage
Benzodiazepines	Range (mg)
Alprazolam	2-6
Clonazepam*	1-3
Lorazepam	4-10
Diazepam*	15-20

\*Slow elimination, longer to steady-state



# Imipramine, Diazepam, and Trazodone Treatment of GAD



OC = observed cases; OC dataset.

\* $P < .05$ . \*\* $P < .01$ .

Rickels K et al. *Arch Gen Psychiatry*. 1993;50:884-895.





# BZ for GAD-Considerations

- No long-term studies with BZ monotherapy
- GAD
  - Highly comorbid with depression
  - Often requires long-term therapy
- Benzodiazepines
  - Not effective for depression
  - Not considered ideal as *monotherapy* treatment
    - This is based on zero data
  - Useful as adjunctive medication for many patients



# Buspirone

- **Buspirone-Partial 5HT<sub>1a</sub> agonist**
  - **Early studies showed efficacy at 15 mg comparable to diazepam 15 mg**
  - **Limited breadth of efficacy in comorbid patients limits enthusiasm**
  - **Outcomes of various studies are uneven**
  - **Higher dose ( at least 30 mg daily) probably necessary**



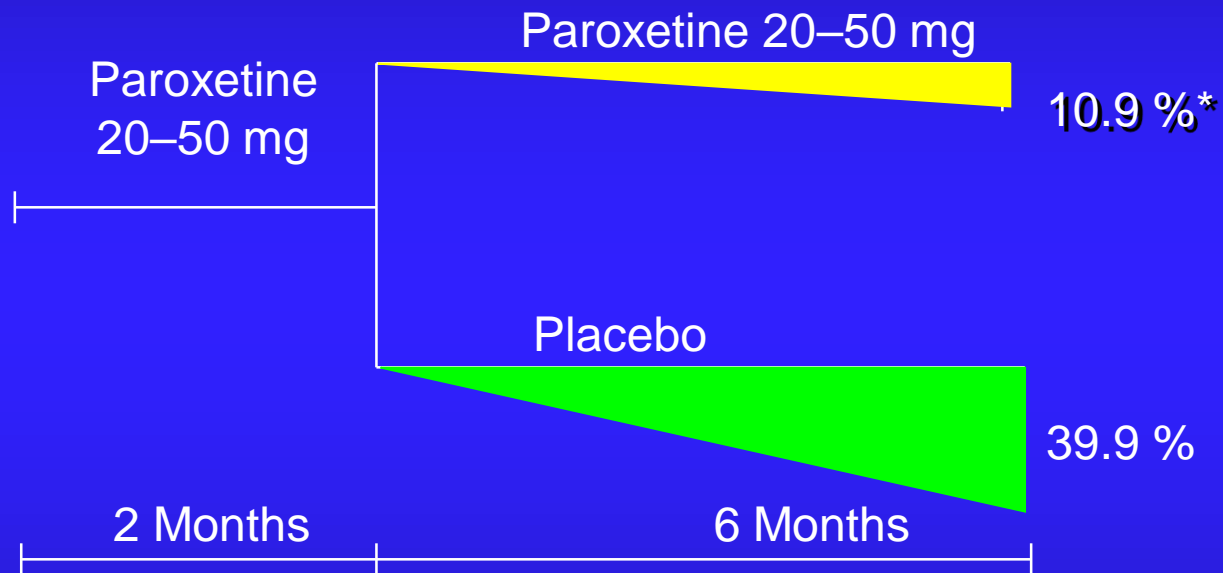
# Long-Term Treatment of GAD

- Need to treat for long term
- Full relapse in approximately 25% of patients 1 month after stopping treatment
- 60%-80% relapse within 1st year after stopping treatment

\*

Hales RE et al. *J Clin Psychiatry*. 1997;58(suppl 3):76-80.  
Rickels K, Schweizer E. *J Clin Psychopharmacol*. 1990;10(3 suppl):101S-110S.

# Paroxetine Long-Term GAD Treatment Relapse Prevention



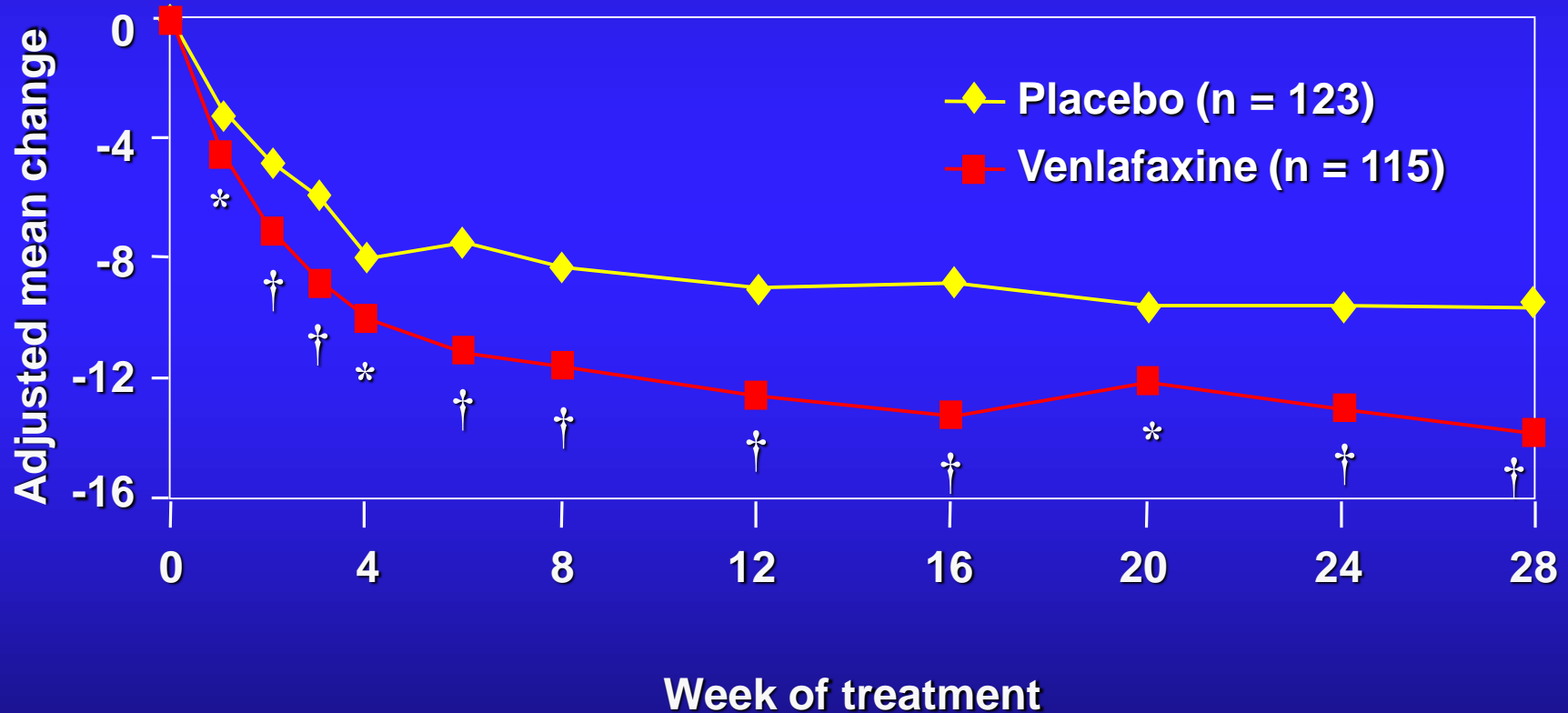
\* $P < .001$ ; N = 286/274; LOCF

Stocchi et al J Clin Psychiatry 2003; 64: 250-58.



# 6-Month, Placebo-Controlled Trial of Venlafaxine XR in GAD

HAM-A Total—Observed Cases Analysis  
(Mean Baseline HAM-A Total Score 25.0, Mean Daily Dose 176 mg)

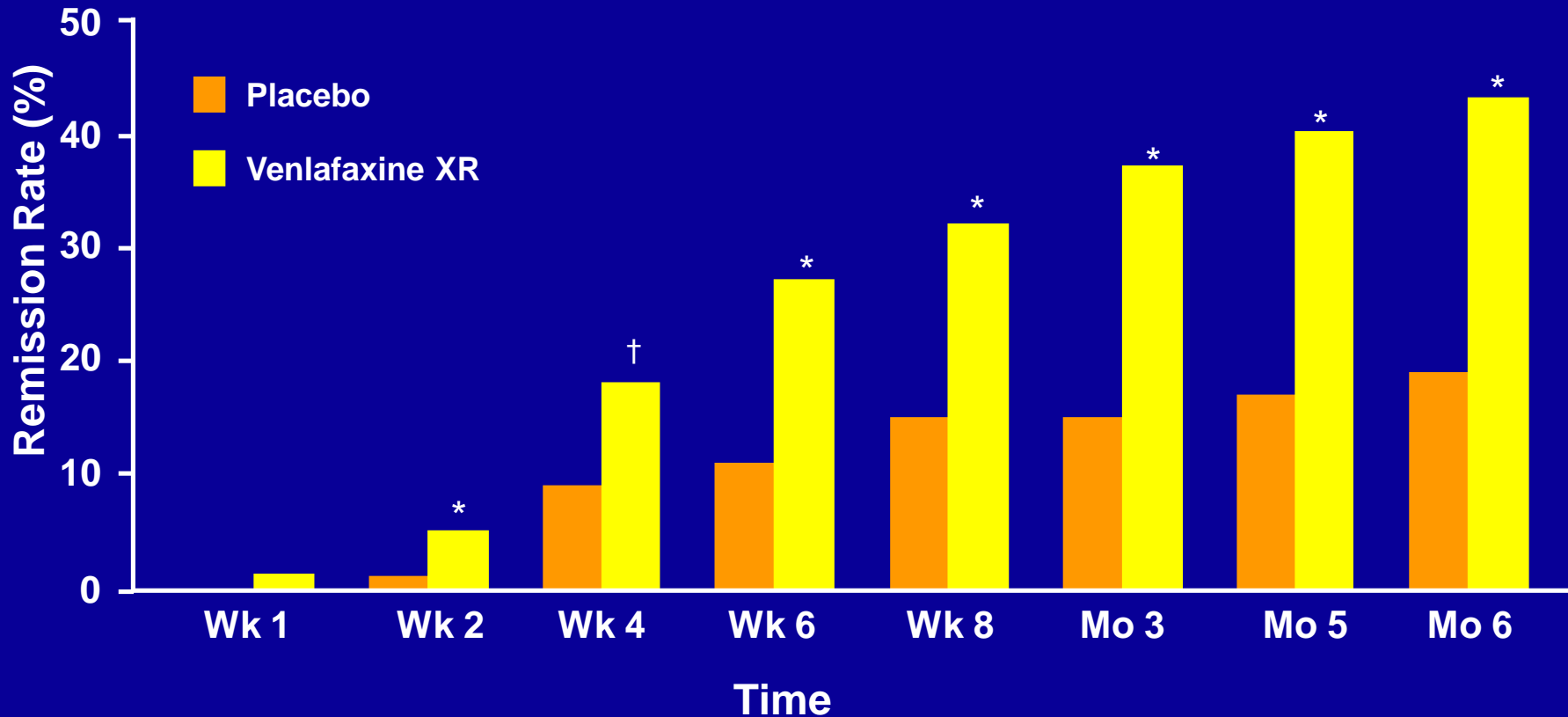


\*  $P < 0.05$  vs. placebo †;  $P < 0.001$  vs. placebo Gelenberg AJ et al. *JAMA*. 2000;283:3082-3088.

# Remission Takes Time

## GAD Pooled Analysis (N=767)

Remission HAM-A  $\leq 7$



\* $P < 0.001$  vs. placebo. † $P < 0.01$  vs. placebo.

Montgomery SA, et al. *J Psychiatr Res.* 2002;36:209-217 .



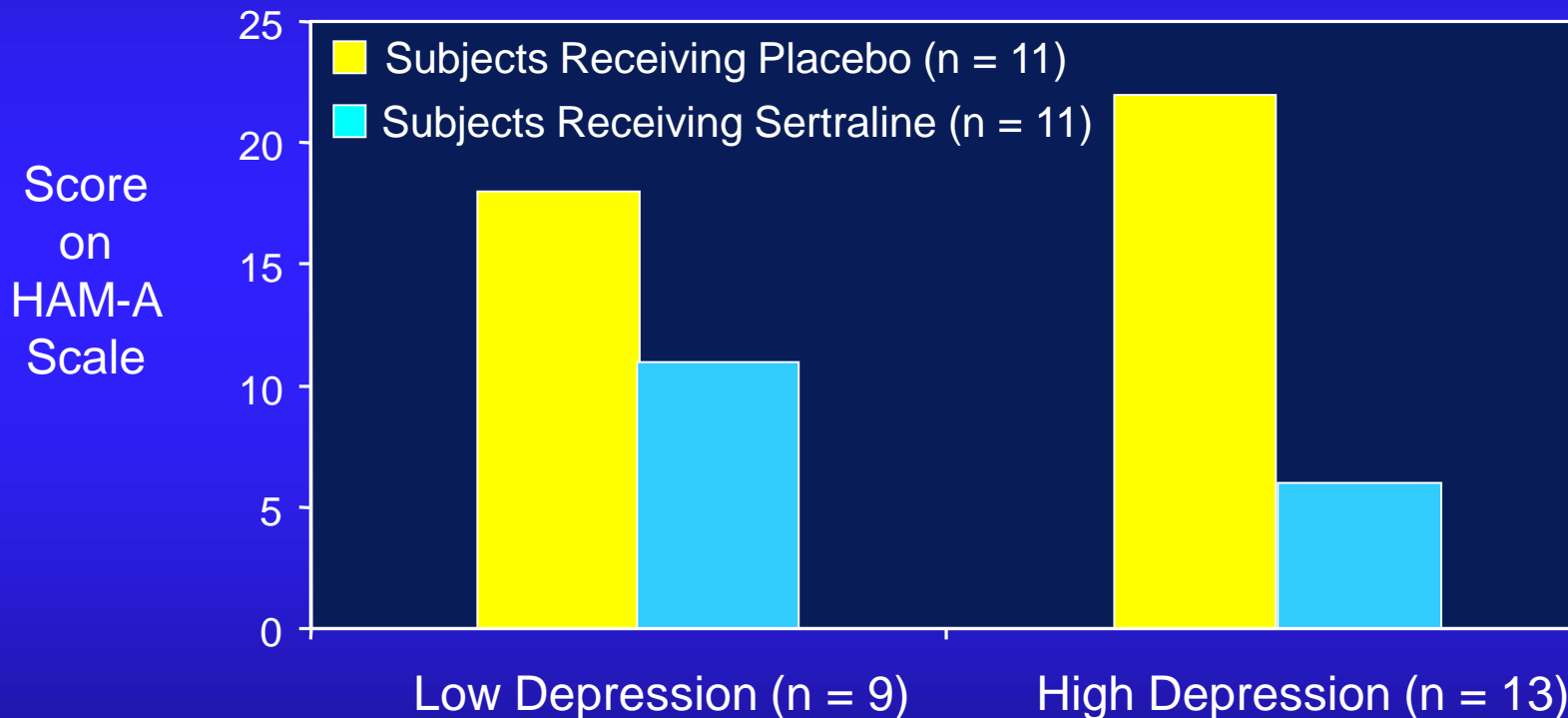
# Placebo-Controlled Trial of Sertraline in the Treatment of Children with GAD

- N = 22
- 2-3 week run-in, 9 weeks of double-blind treatment with sertraline or placebo
- Primary diagnosis of GAD; excluded MDD, OCD, MR, ADD
- Ages 5-17 years (mean  $11.7 \pm 3.9$  years)
- Sertraline dose: 25 mg/d for week 1; 50 mg/day weeks 2-9



# Placebo-Controlled Trial of Sertraline in the Treatment of Children with GAD

Mean Total Scores on Hamilton Anxiety Rating Scale at 9 Weeks\*



\*LOCF. Low and high depression severity indicated by Hamilton Depression Rating Scale scores  $\leq 10$  and  $> 10$ , respectively.

Rynn MA et al. *Am J Psychiatry*. 2001;158:2008-2014.

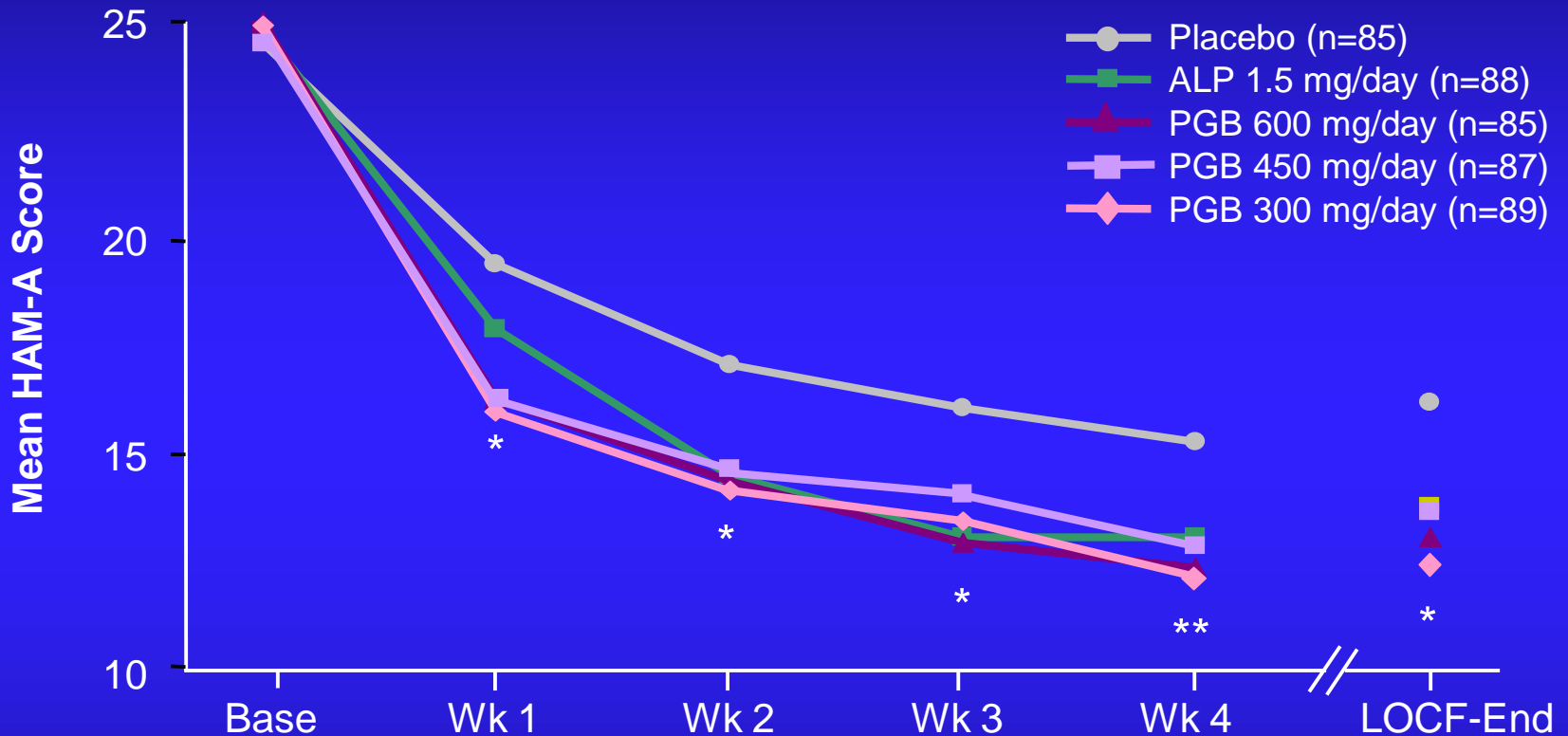




# Pregabalin

- **PGB target**
  - Binds to  $\alpha_2\delta$  subunit of widely distributed voltage-dependent calcium channels
  - Reduces calcium influx through transmembrane ion channel
- **Downstream effect**
  - Inhibition (especially under excitatory conditions) of release of rapid excitatory neurotransmitters
    - glutamate, aspartate, NE, DPN, 5-HT, substance P, others

# Efficacy of Three Doses of Pregabalin vs Alprazolam in Reducing the HAM-A Total Score



All medications dosed tid.

\*  $P \leq .05$  vs placebo (ANCOVA) for all medications.

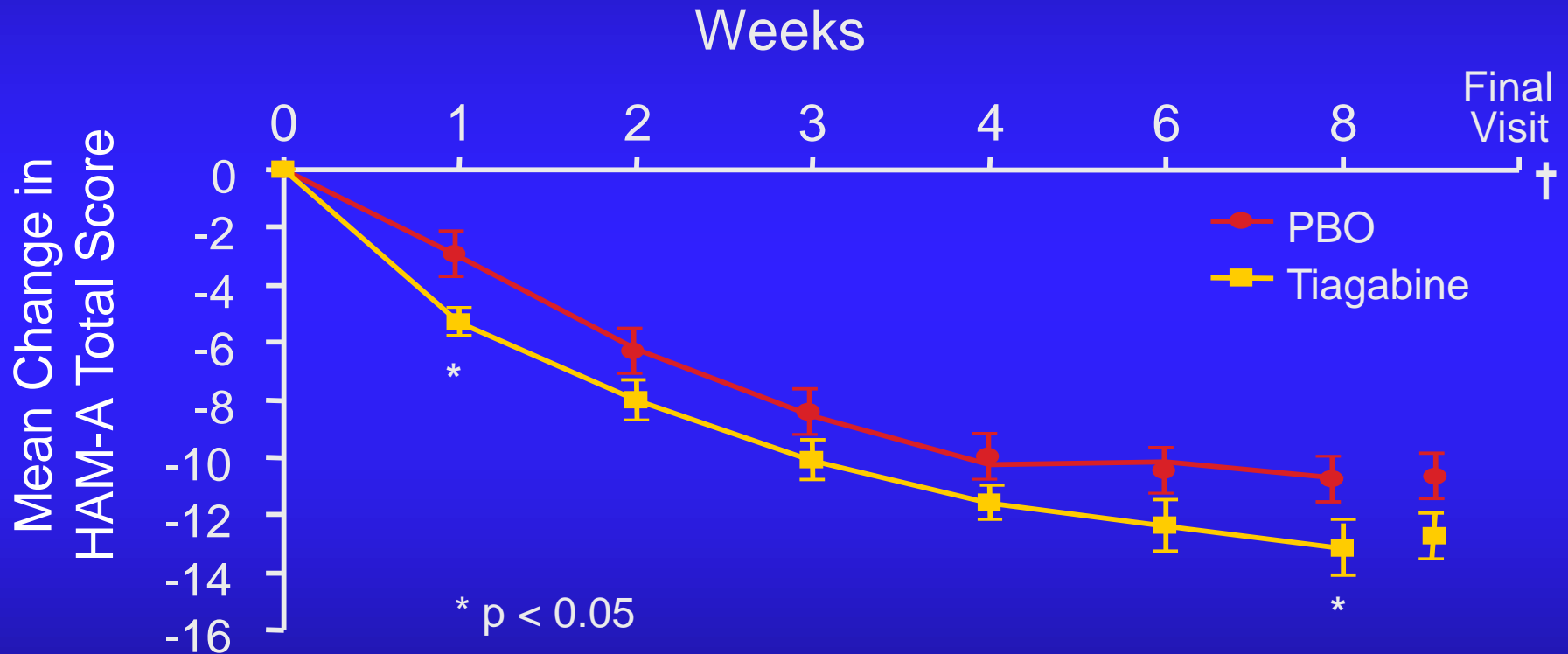
\*\*  $P \leq .05$  vs placebo (ANCOVA) for PGB 300 mg/day and PGB 600 mg/day only (OC).

# Pregabalin vs. Venlafaxine in GAD

- DSM-IV GAD outpatients(n = 421), 6 wks
- Primary care and psychiatry settings (Europe)
  - PGB 400 or 600 mg/d
  - Venlafaxine 75 mg/day
  - placebo
- Both PGB dosages > PbO by wk 1
- Venlafaxine > PbO by week 2
- 75 mg venlafaxine approved for GAD in Europe
  - Lower doses venlafaxine may be sufficient
  - Discontinuation for side effects ven -20.4%,PGB 400 - 6.2%; PGB 600 - 13.6%; placebo- 9.9%.

# Selective GABA Reuptake Inhibitor Tiagabine for GAD :

HAM-A Total Scores--marginal effect possibly due to design--  
Followup Study-NS; abandoned development



† Final visit was calculated using last post-baseline observation for each patient.

# Kava (*Piper methysticum*) Ineffective for GAD

- 3 placebo-controlled RCTs
  - One with active comparator
- DSM-IV GAD ages  $\geq 18$ 
  - Pooled sample: kava-28; placebo-30; venlafaxine-6
- No evidence for efficacy of kava
- Placebo >kava in patients with higher initial anxiety
- Safe, well-tolerated
- Very small sample sizes--Type II error possible
  - See notes



# Ginkgo Biloba (Egb 761) in GAD

- DSM-III-R GAD (n=82) or DSM-III-R adjustment disorder with anxious mood (n=25)
- 4 wk placebo controlled RCT ( Germany)
- Both 480 mg-Egb(14.3), 240 mg Egb(12.1) > PbO-7.8 on HAM-A
- High dose superior all measures
  - Possible dose-response effect
- May be effective in elderly with cognitive decline
- Well-tolerated
  - Comparable to SSRIs, SNRIs, BZs even with small samples
  - May not have been as ill as pts in US RCTs
  - **Downside-formulation may be unreliable at usual sources**
  - See notes



# Strategies for Refractory GAD

- Evaluate treatment intensity
  - Dose and duration of antidepressant Rx?
- Switch to a second SSRI/antidepressant
- Add
  - benzodiazepine
  - buspirone
  - Anticonvulsants
    - Gabapentin, tiagabine, vigabatrin, topiramate,
  - low dose atypical neuroleptic
    - (olanzapine, quetiapine, ziprasodone others)
- Review psychosocial variables for stress management
  - Add CBT

\* Most suggestions from clinical experience and Coplan et al JCP 154 (supp) 63-74,1993; Pollack et al, Biol Psychiatry 2006;59:211-215; Stein DJ CNS Spectrums, 2005 (Dec); Snyderman et al J Clin Psychopharmacol 2005; 25:497-499

# CBT for GAD

- **Cochrane Review, 2007**
  - 25 studies, total n =1305
- **CBT vs.**
  - Treatment as usual (TAU) /waiting list (WL) (13 studies)
  - Other psychological therapy (12 studies)
- **CBT superior to TAU or waitlist**
  - CBT “very effective” in for secondary symptoms
  - Group CBT Rx , elderly : higher dropout rate
- **CBT vs. other psychological treatments -unclear**
- **None were long-term**
- **Comparative studies with medication not yet done**
  - See notes

Hunot et al, Cochrane Reviews 2007, Issue 1.  
Art. No.: CD001848. DOI: 10.1002/14651858.CD001848.pub4





# Summary

- **GAD is common**
- **Remission is the goal**
  - Identification of target symptoms, including physical symptoms
- **Careful evaluation, patient education key aspects of treatment**
- **Medication: start low and go slow**
  - Adequate dosages for adequate lengths of time
  - May require long-term treatment



# Question #1

## True or False

**Women have a HIGHER Lifetime Prevalence of GAD as compared to Men.**

## Question #2

Which Psychiatric Illness has the  
**HIGHEST LIFETIME  
PREVALENCE of COMORBIDITY**  
with GAD?

# Question #3

What **Anxiety Assessment Scale** is commonly used to Assess Outcomes in GAD? and...

A decrease of \_\_\_% or greater on this scale defines **RESPONSE** while a score of \_\_\_ or less on this scale defines **REMISSION**.

# Question #4

What **PHARMACOLOGIC TREATMENTS** are Effective in Treating GAD?

## **Question #5**

**What Percentage of Patients with  
GAD Relapse Within the First  
Year After Stopping  
Pharmacotherapy?**

**Answer #1**

**TRUE!**

# **Answer #2**

**Major Depressive Disorder**



# Answer #3

## Hamilton Anxiety Rating Scale

A decrease of 50% or greater on this scale defines **RESPONSE** while a score of 7 or less on this scale defines **REMISSION**.

# Answer #4

- **Benzodiazepines**
- **Buspirone**
- **Tricyclic Antidepressants**
- **Selective Serotonin Reuptake Inhibitors**
- **Serotonin Norepinephrine Reuptake Inhibitors**
- **Pregabalin**

# Answer #5

60-80%