Detecting and treating anxiety disorders in the elderly: clinical applications of new research findings

Eric Lenze, M.D.
Associate Professor of Psychiatry
Washington University School of Medicine

October 2007, Updated September 2009

Goals of this lecture

- Describe research in pharmacologic and psychotherapeutic treatment of late-life anxiety disorders and anxious depression.
- Describe detection and management strategies for these disorders.

Self-Assessment Question 1

Which of the following should be considered in the differential diagnosis of anxiety symptoms in elderly patients?

A. Cardiopulmonary and other medical conditions
B. Medication side effects
C. Sedative hypnotic withdrawal
D. All of the above
E. None of the above

Self-Assessment Question 2

What risks are associated with chronic benzodiazepine use in elderly?

A. Delirium
B. Cognitive impairment
C. Falls
D. Fractures
E. All of the above

Self-Assessment Question 3

Which of the following may contribute to the low estimate of prevalence of anxiety disorders in the elderly?

A. Age-related brain changes

B. Selective increase in mortality among anxiety disorder patients

C. Epidemiologic studies do not necessarily capture anxiety as it presents in older adults

D. All of the above

E. None of the above

Self-Assessment Question 4
Which of the following contribute to the importance of identifying and treating Generalized Anxiety Disorder in the elderly?

A. Its prevalence may be as high as 7%

B. It is unlikely to remit without treatment

C. Effective pharmacotherapeutic treatment has been demonstrated.

D. All of the above

E. None of the above

Self-Assessment Question 5

Which of the following is true of late-life depression with comorbid anxiety as compared to “pure” depression?

A. Severity of the illness is no different.

B. Antidepressant treatment response is better when comorbid anxiety is present.

C. Comorbid anxiety is associated with greater long-term cognitive decline.

D. All of the above

E. None of the above

Self-Assessment Question 6

Which of the following treatments has been demonstrated efficacious for older adults with anxiety disorders?

A. Cognitive Behavioral Therapy.
B. Selective Serotonin Reuptake Inhibitors.
C. Benzodiazepines.
D. All of the above
E. None of the above

How fear works

Amygdala

Arousal
Acute anxiety
Panic attack

Larson et al, 2006

How fear works

Arousal
Acute anxiety
Panic attack

Amygdala

Frontal cortex

Worry
Escape
Avoidance

Larson et al, 2006

How fear works

Arousal
Acute anxiety
Panic attack

Amygdala

Control

Frontal cortex

Worry
Escape
Avoidance

Larson et al, 2006

Worry

“What if…?”

Hoehn-Saric et al, 2004

Worry

Frontal cortex

Worry
+/- Avoidance
Control

Hoehn-Saric et al, 2004

Anxiety disorders have distinct clinical features

	Fear	**Avoidance**	Autonomic Arousal	Anticipatory worry	**Panic attacks**
Panic disorder	x	x	x	**x**	x
Social , specifc phobia	x	x	x	**x**	x
OCD	x	+/-			
GAD		+/-		x	
PTSD	x	x	x		

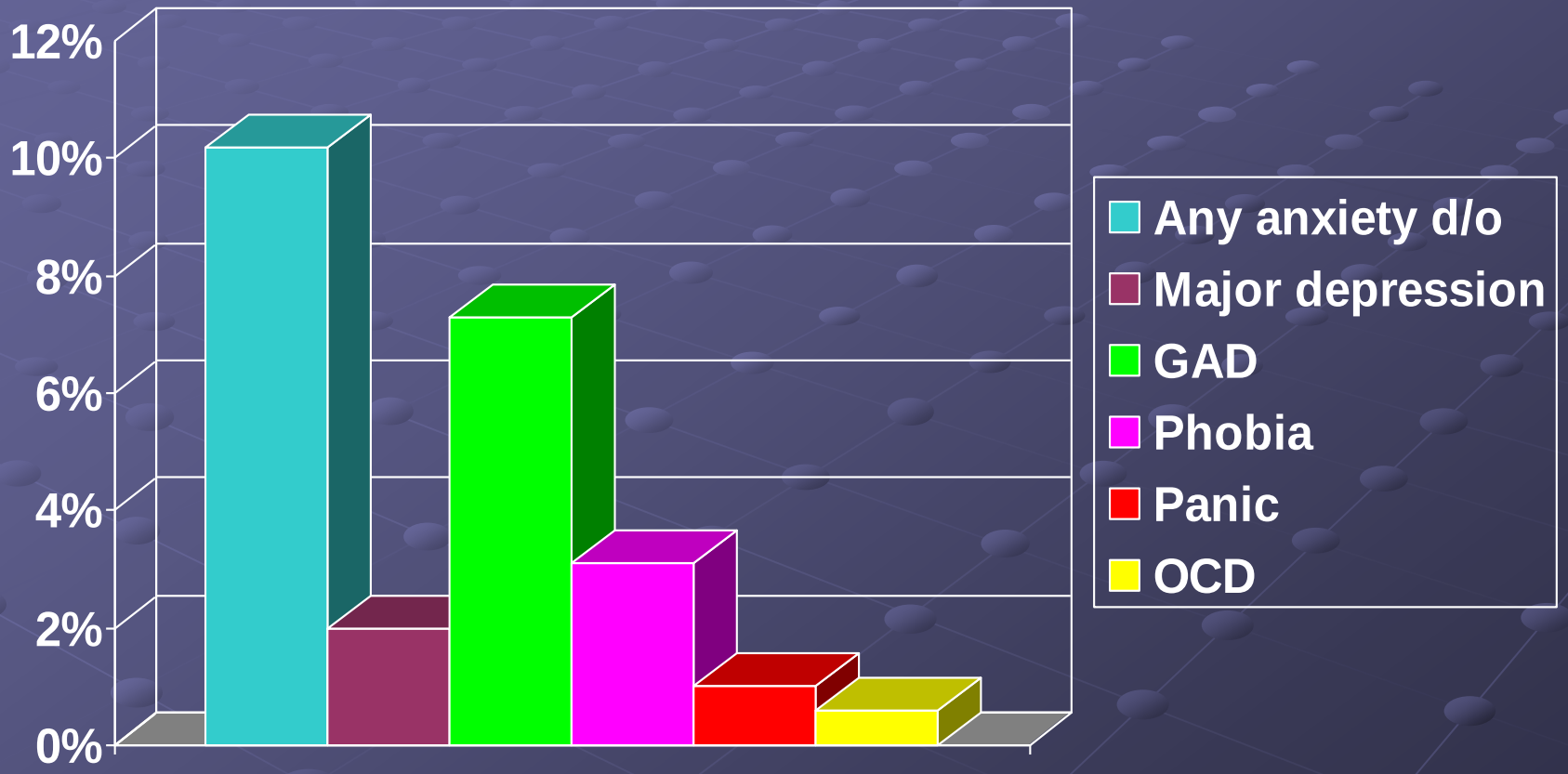
Anxiety disorders have distinct clinical features

	Fear	Avoidance	Autonomic Arousal	**Anticipatory worry**	Panic attacks
Panic disorder	x	x	x	x	x
Social , specifc phobia	x	x	x	x	x
OCD	x	+/-			
GAD		**+/-**		**x**	
PTSD	x	x	x		

What do psychiatrists ask about late-life anxiety?

- How important is it?
- Who sees these cases?
- Is there something unique about treating this?

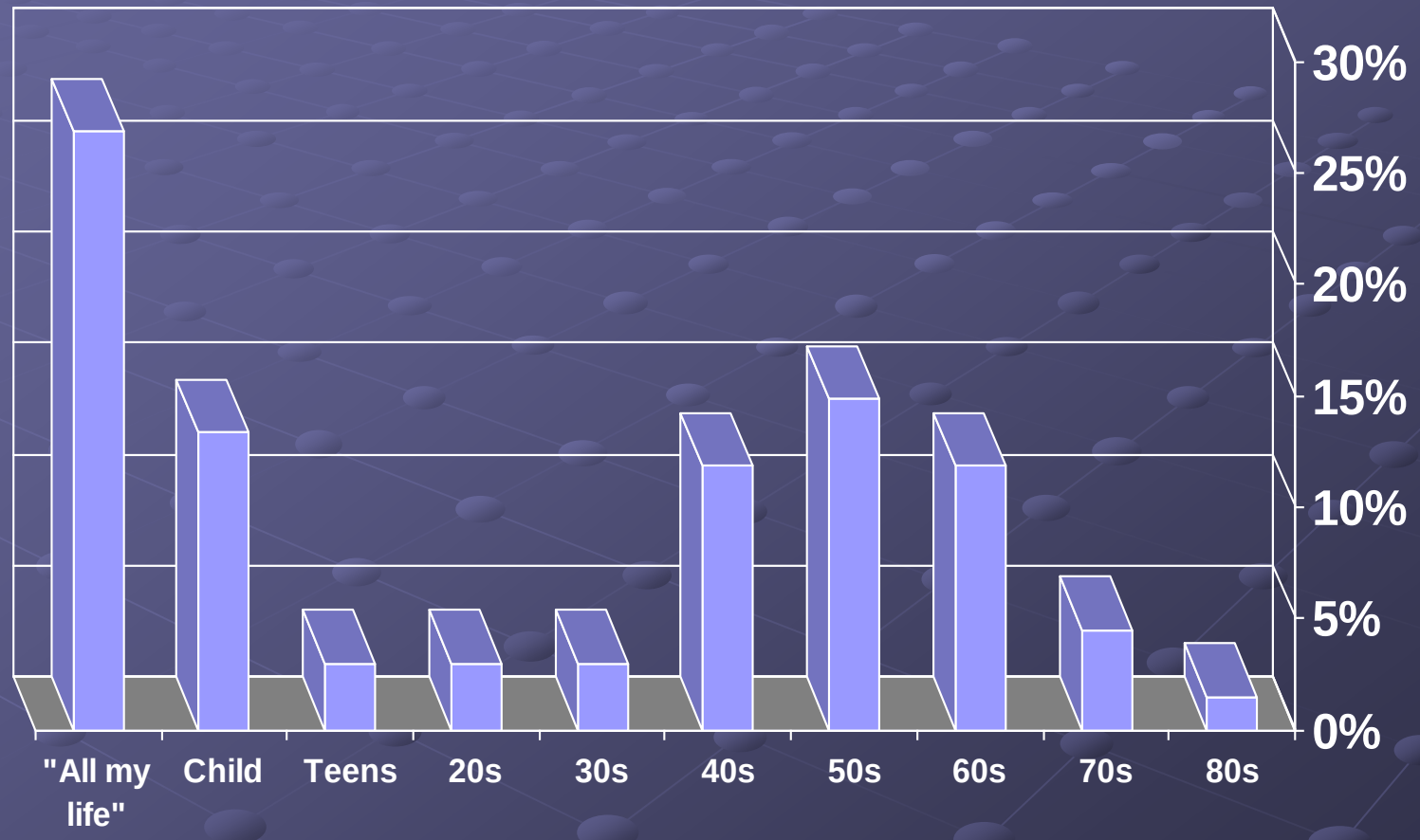
Prevalence of anxiety disorders in older adults



Beekman et al., 1995, 1998

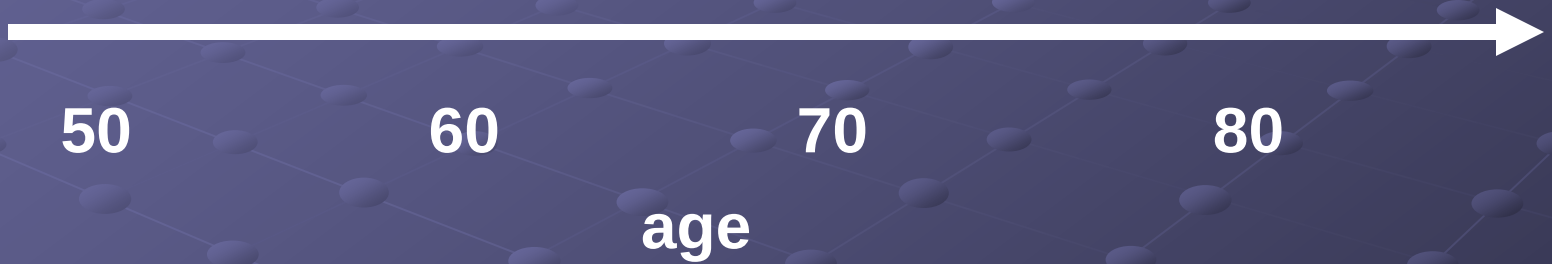
- GAD: chronic, difficult-to-control worry
  - “I can’t turn my mind off”
  - “I’m a worrier”
- Associated symptoms of GAD
  - Sleep disturbance
  - Fatigue
  - Irritability
  - Keyed up/on edge
  - Muscle tension
  - Difficulty concentrating (elderly may describe as memory)

Early vs. late-onset GAD



Le Roux, Gatz, & Wetherell, 2005

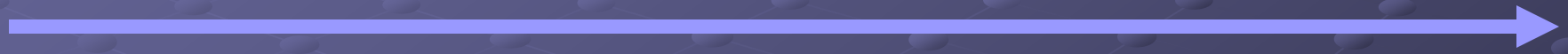
Aging: increased vulnerability to sequelae of anxiety



Aging: increased vulnerability to sequelae of anxiety

Aging: increased vulnerability to sequelae of anxiety

Declining homeostasis/reserve



childhood **adulthood** **late life** **very-late life**

1. HPA axis functioning

Aging: increased vulnerability to sequelae of anxiety

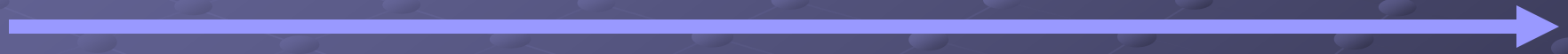
1. HPA axis functioning
2. Cognitive reserve, brain volumes

Aging: increased vulnerability to sequelae of anxiety

1. HPA axis functioning
2. Cognitive reserve, brain volumes
3. Functional ability, physical performance

Aging: increased vulnerability to sequelae of anxiety

Declining homeostasis/reserve



childhood **adulthood** **late life** **very-late life**

1. HPA axis functioning

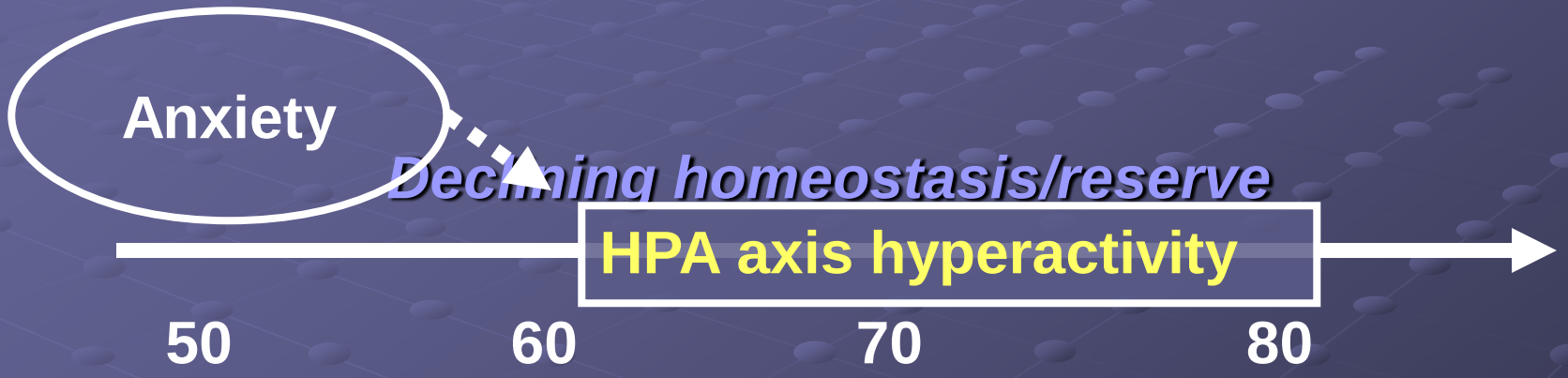
2. Cognitive reserve, brain volumes

3. Functional ability, physical performance

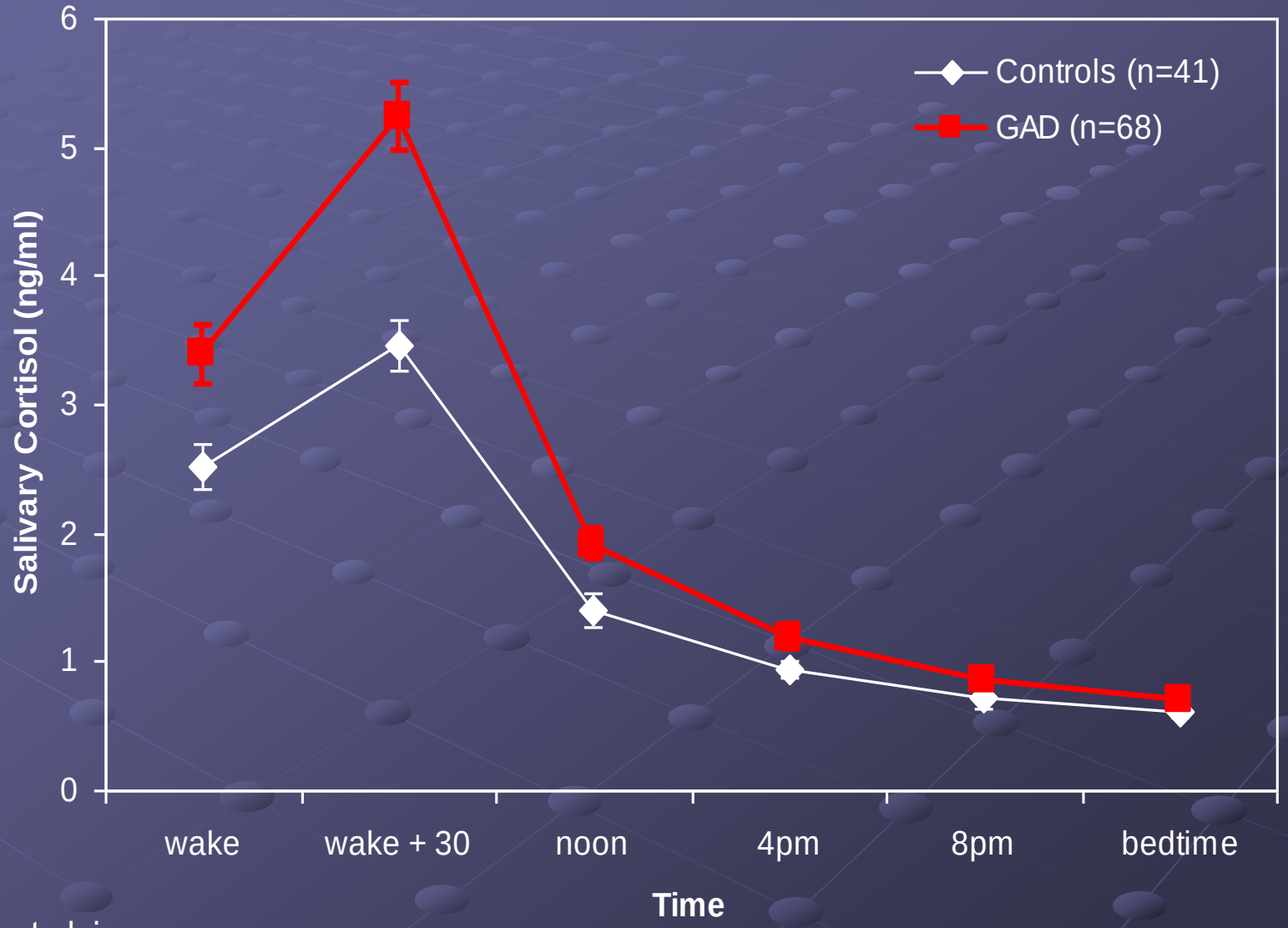
4. Systemic functions (cardiac, renal, etc)

Aging: increased vulnerability to sequelae of anxiety

Aging: increased vulnerability to sequelae of anxiety

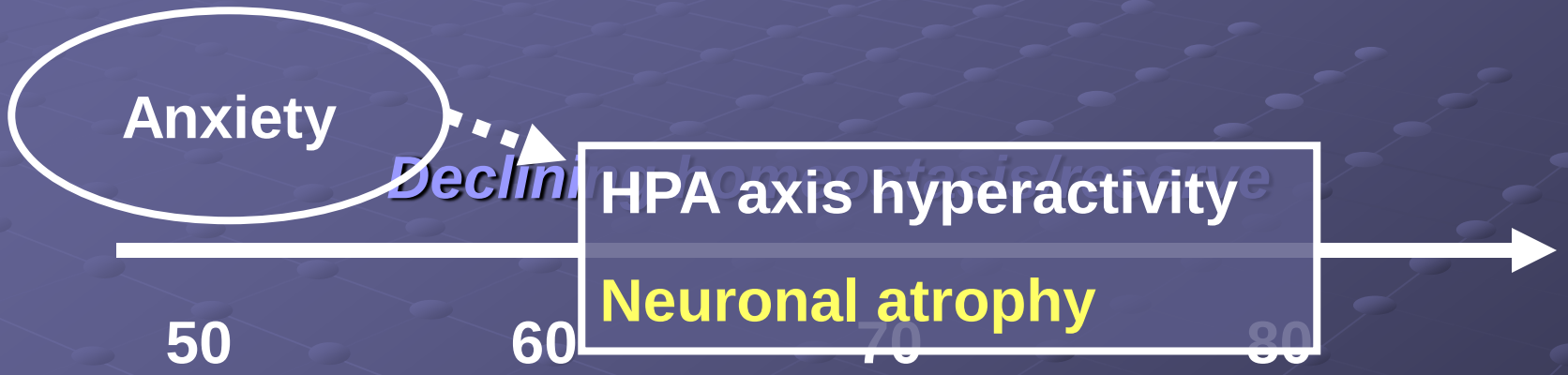


HPA Axis in Late-Life GAD

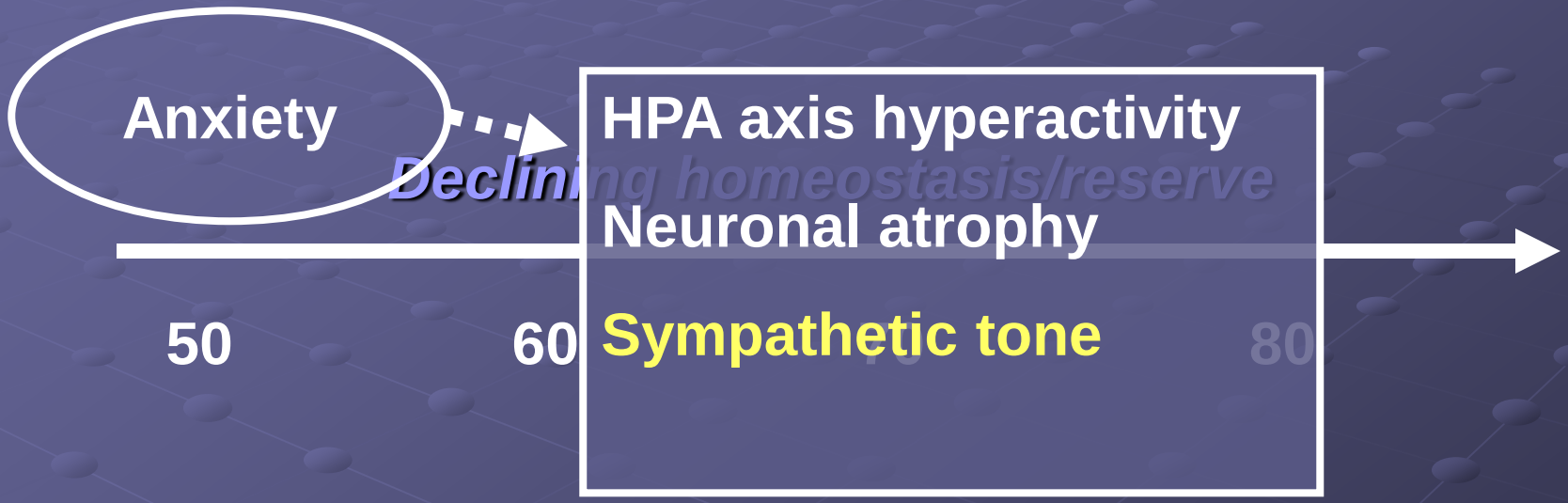


Mantella et al, in press

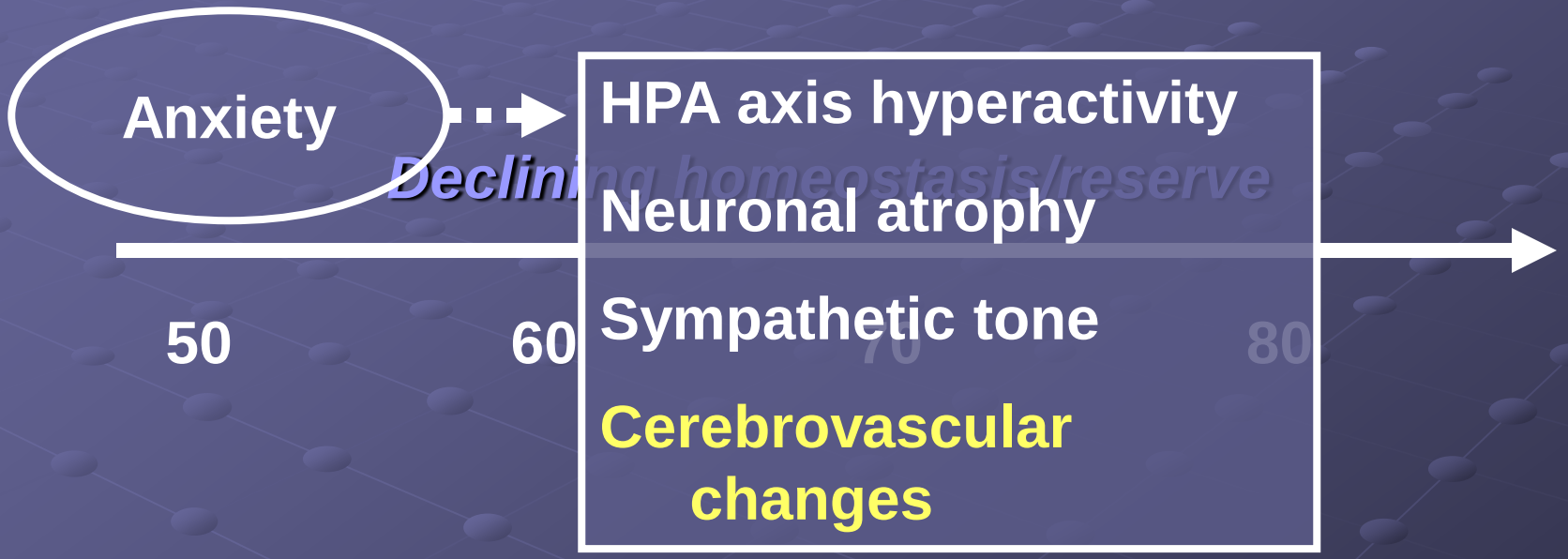
Aging: increased vulnerability to sequelae of anxiety



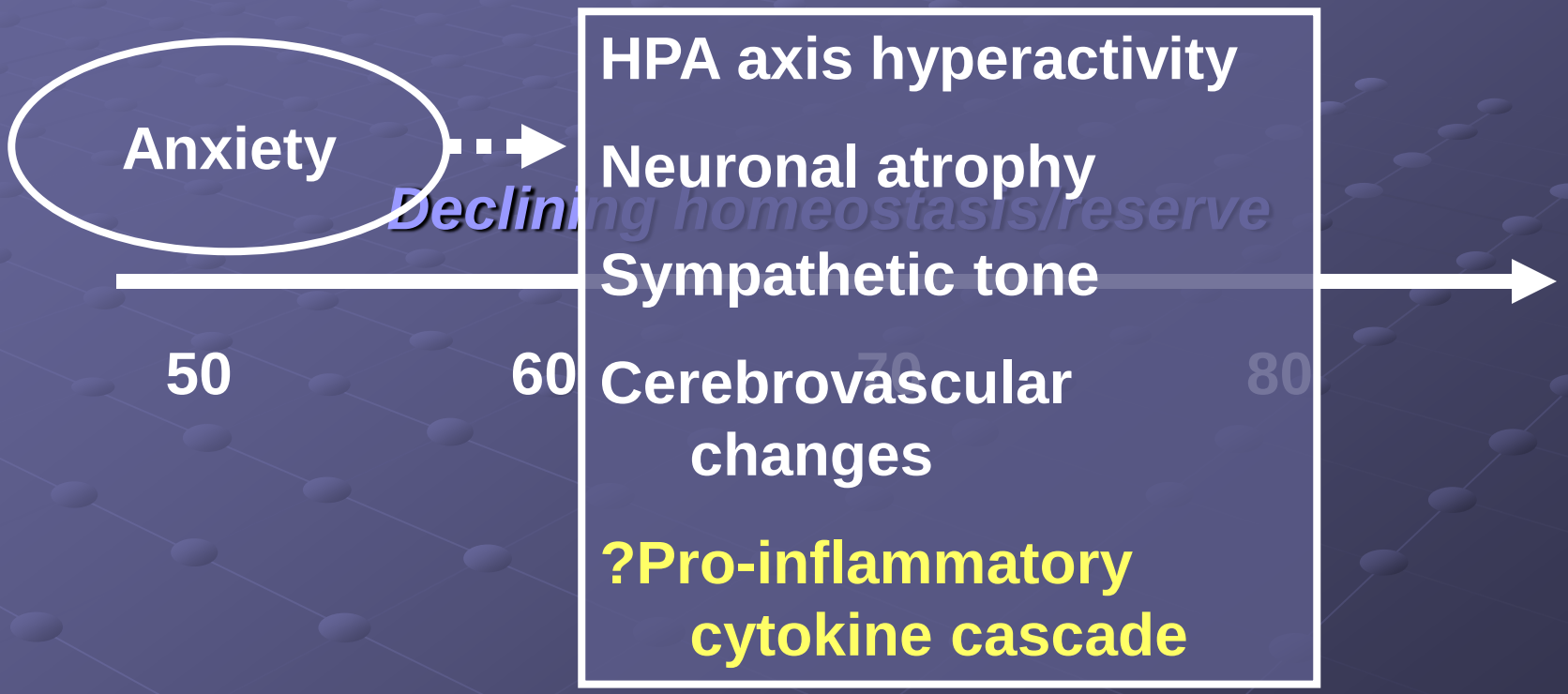
Aging: increased vulnerability to sequelae of anxiety



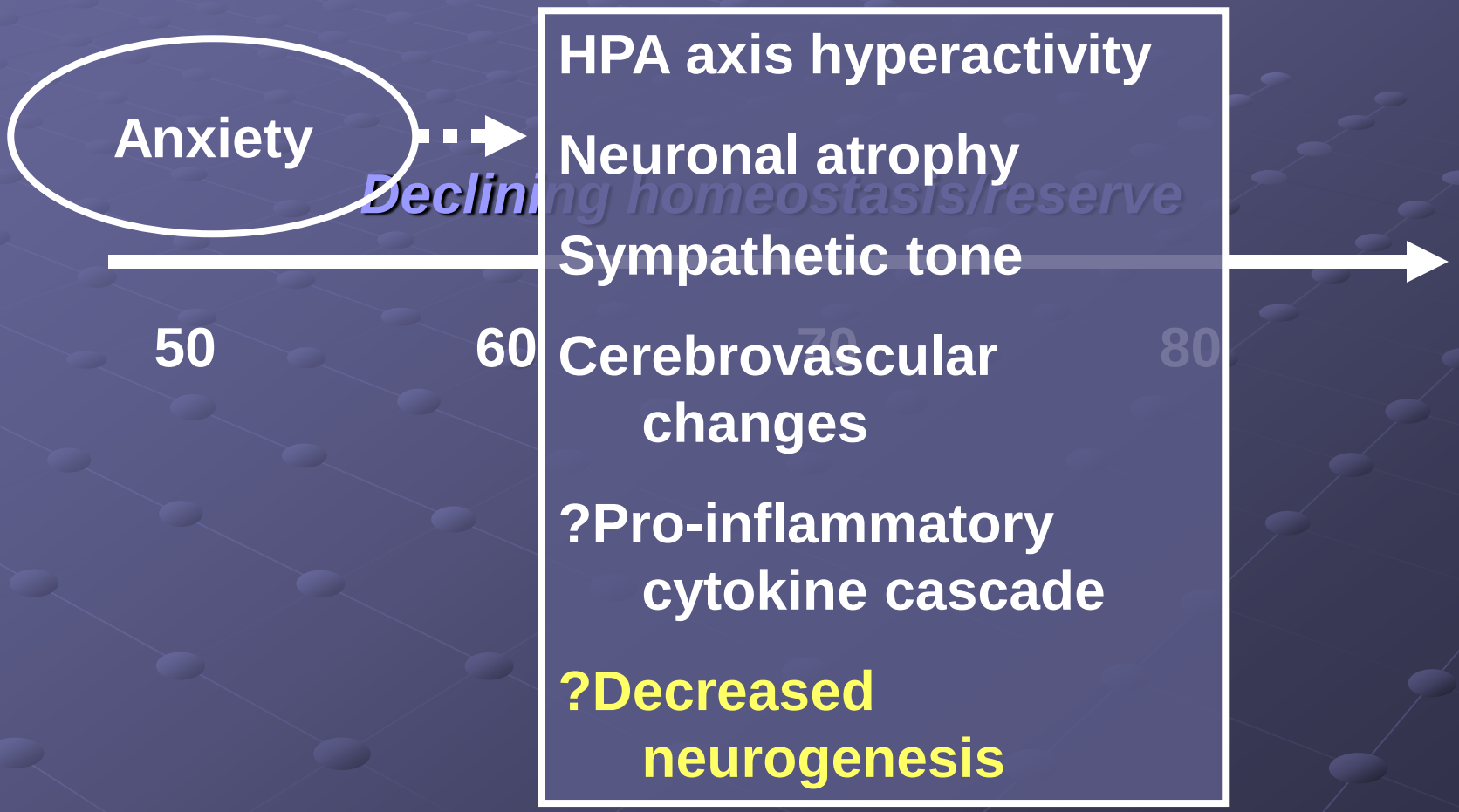
Aging: increased vulnerability to sequelae of anxiety



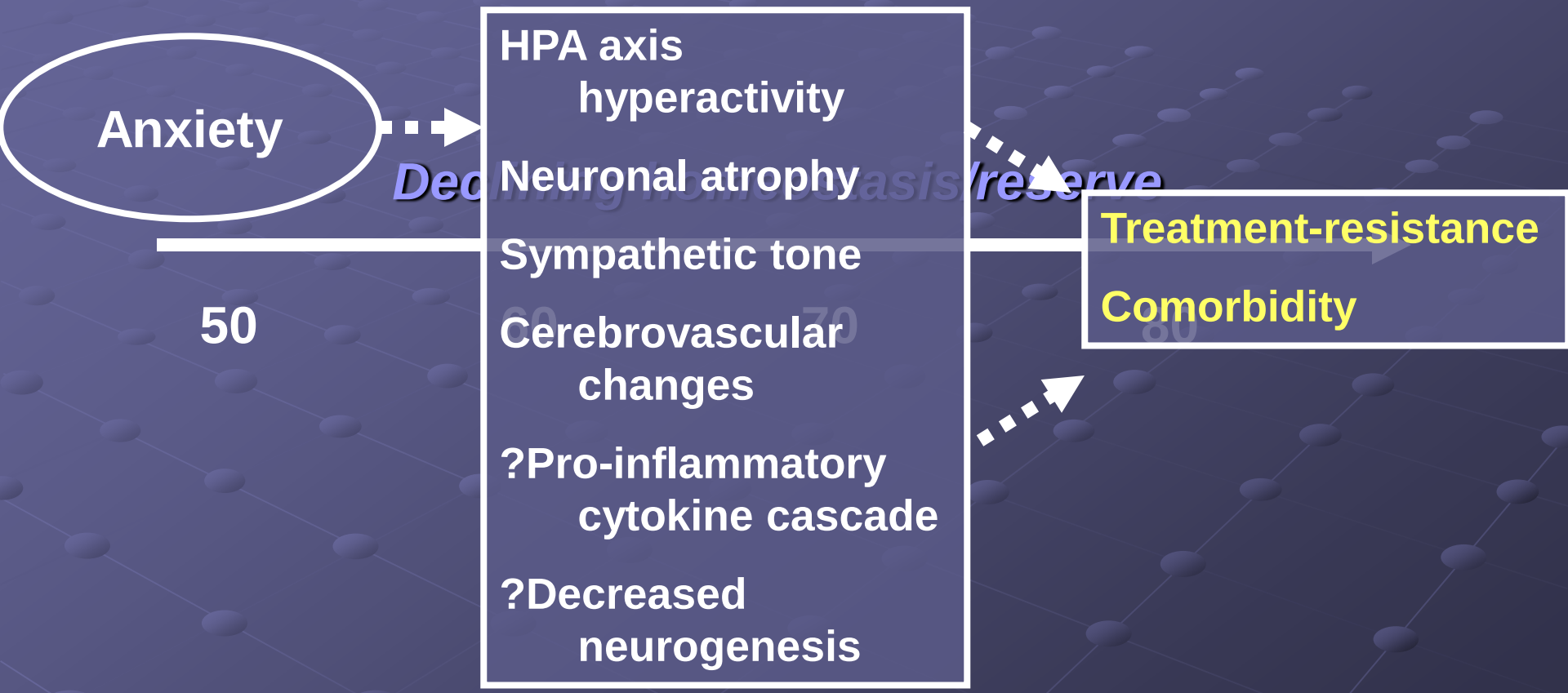
Aging: increased vulnerability to sequelae of anxiety



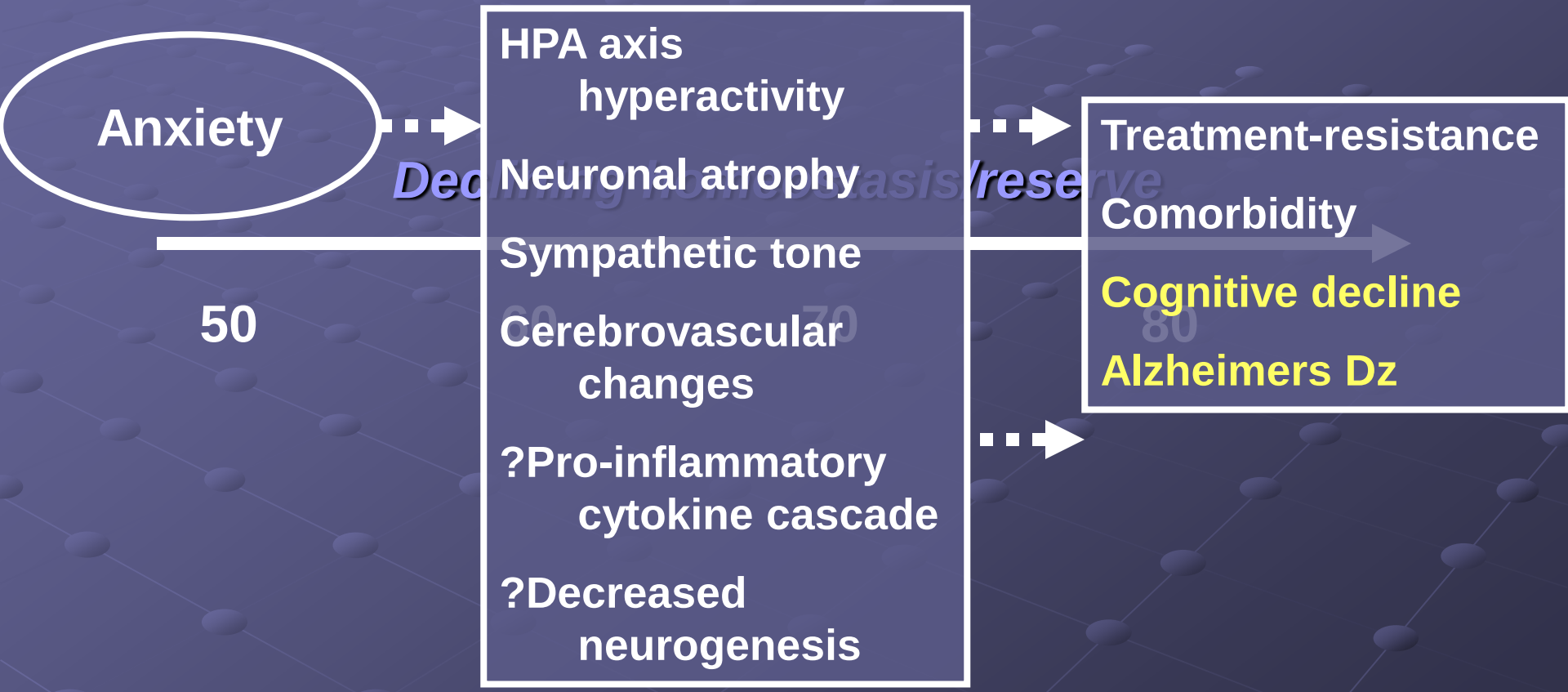
Aging: increased vulnerability to sequelae of anxiety



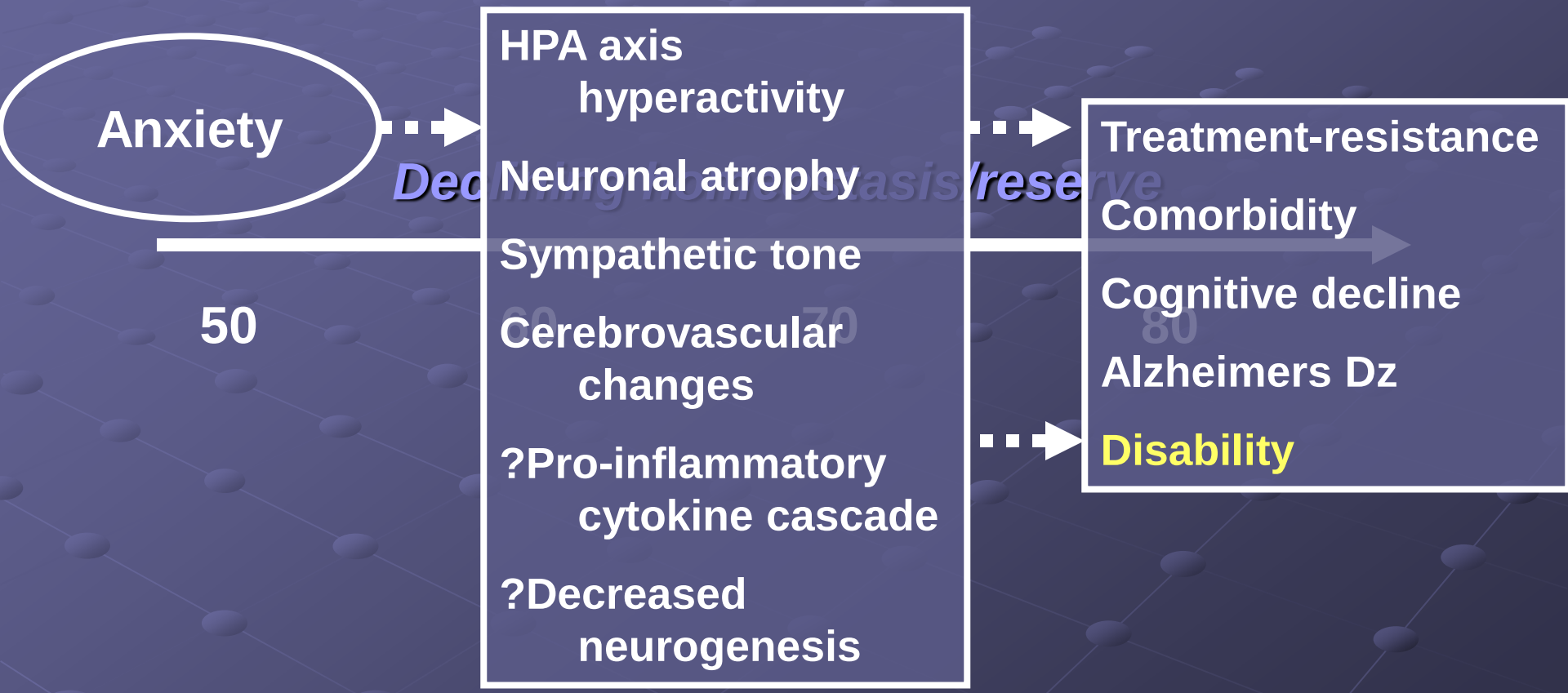
Aging: increased vulnerability to sequelae of anxiety



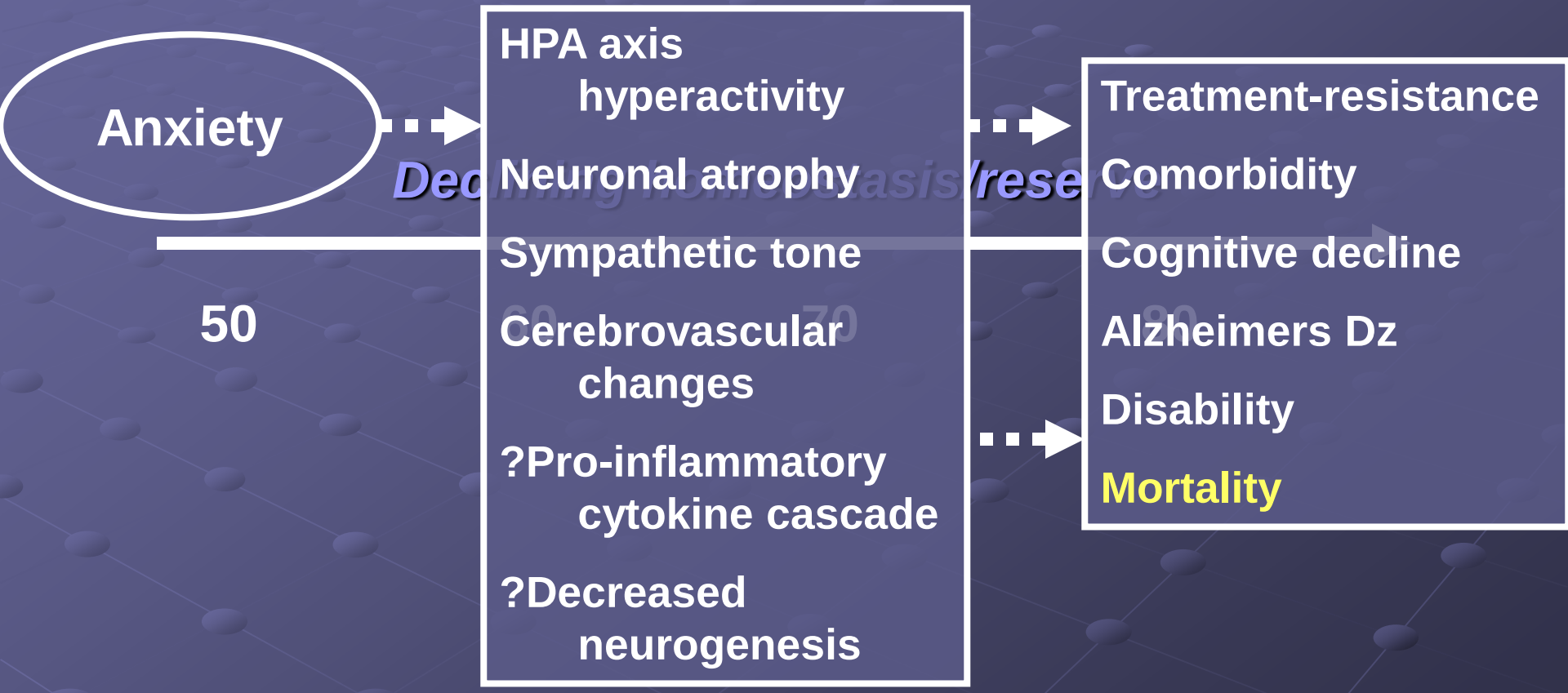
Aging: increased vulnerability to sequelae of anxiety



Aging: increased vulnerability to sequelae of anxiety

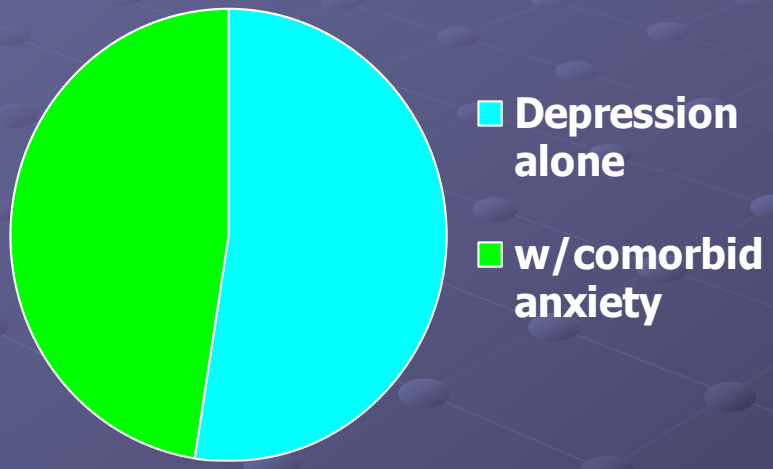


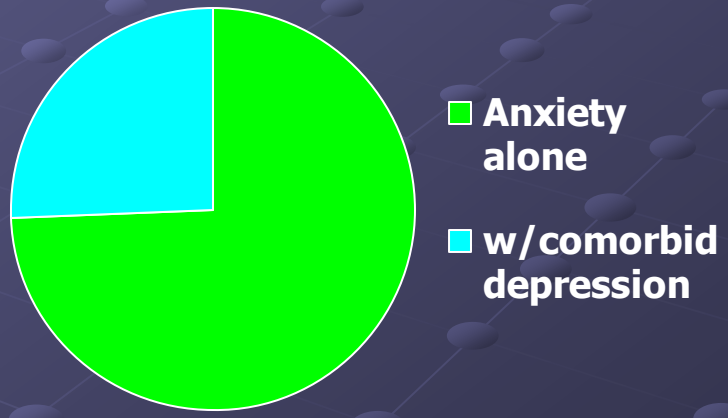
Aging: increased vulnerability to sequelae of anxiety



This highlights the need to treat anxiety in older adults!

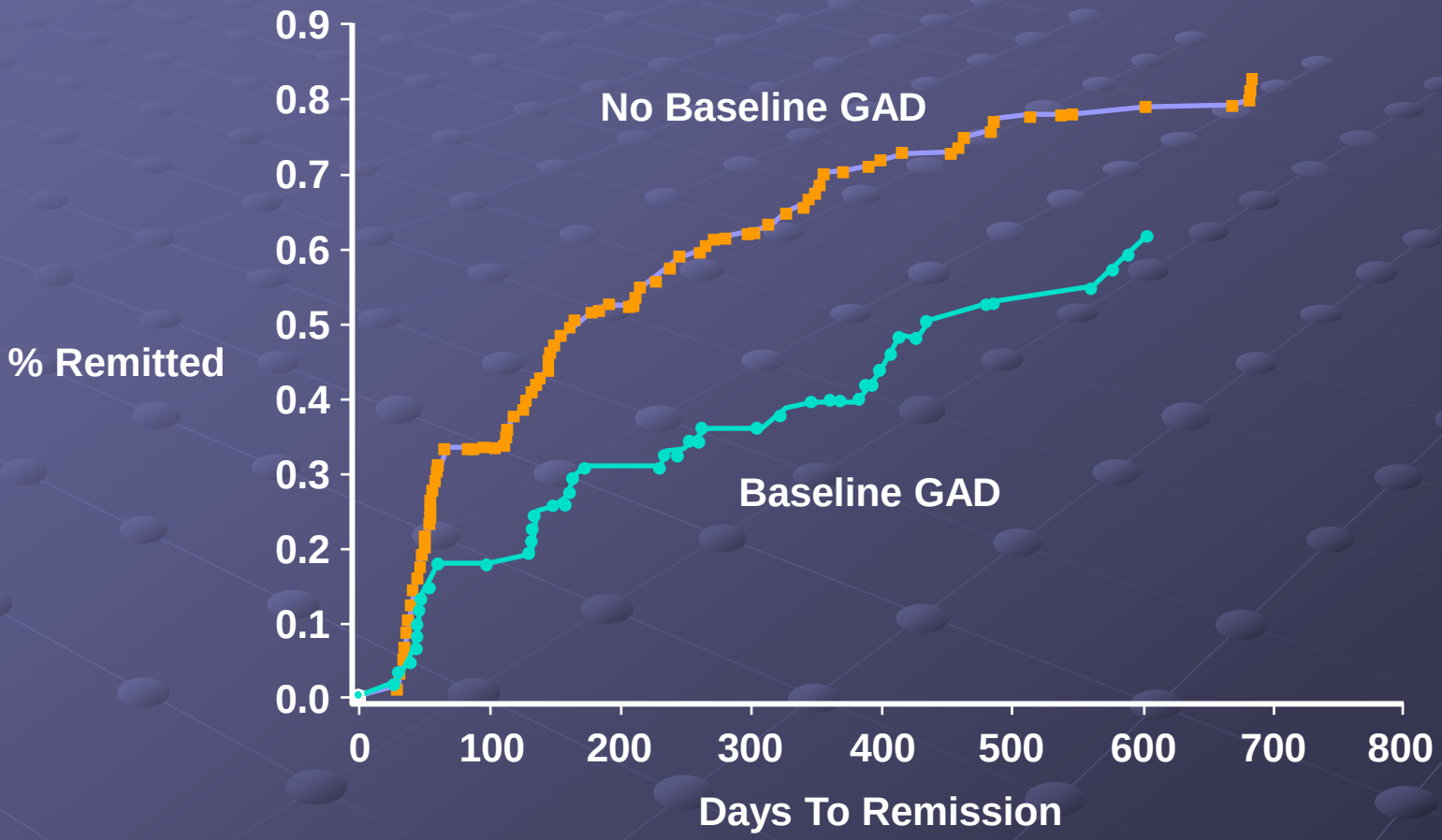
Comorbidity in late-life depression and anxiety





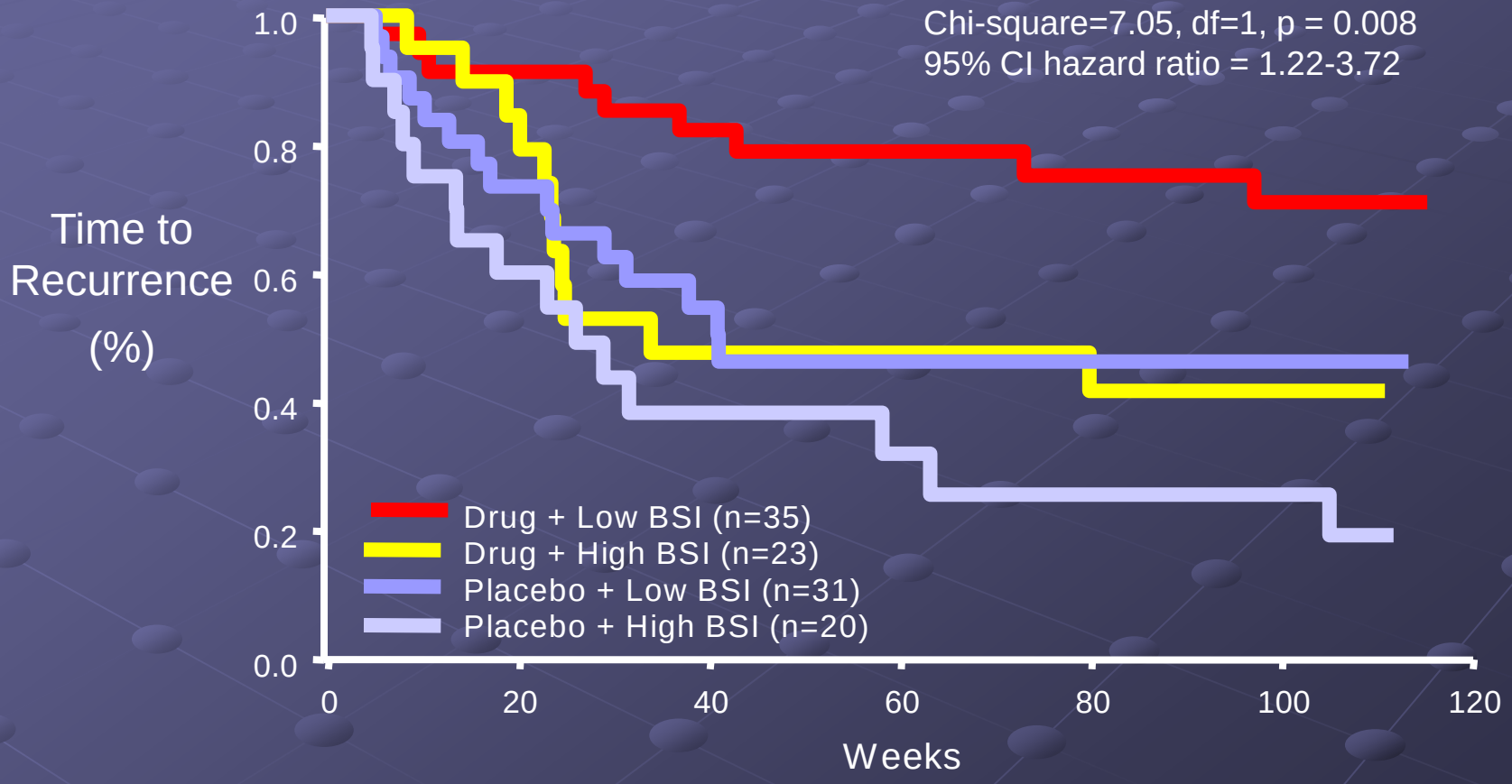
Beekman et al., 2000 (LASA)

Anxiety comorbidity and acute treatment response in LLD



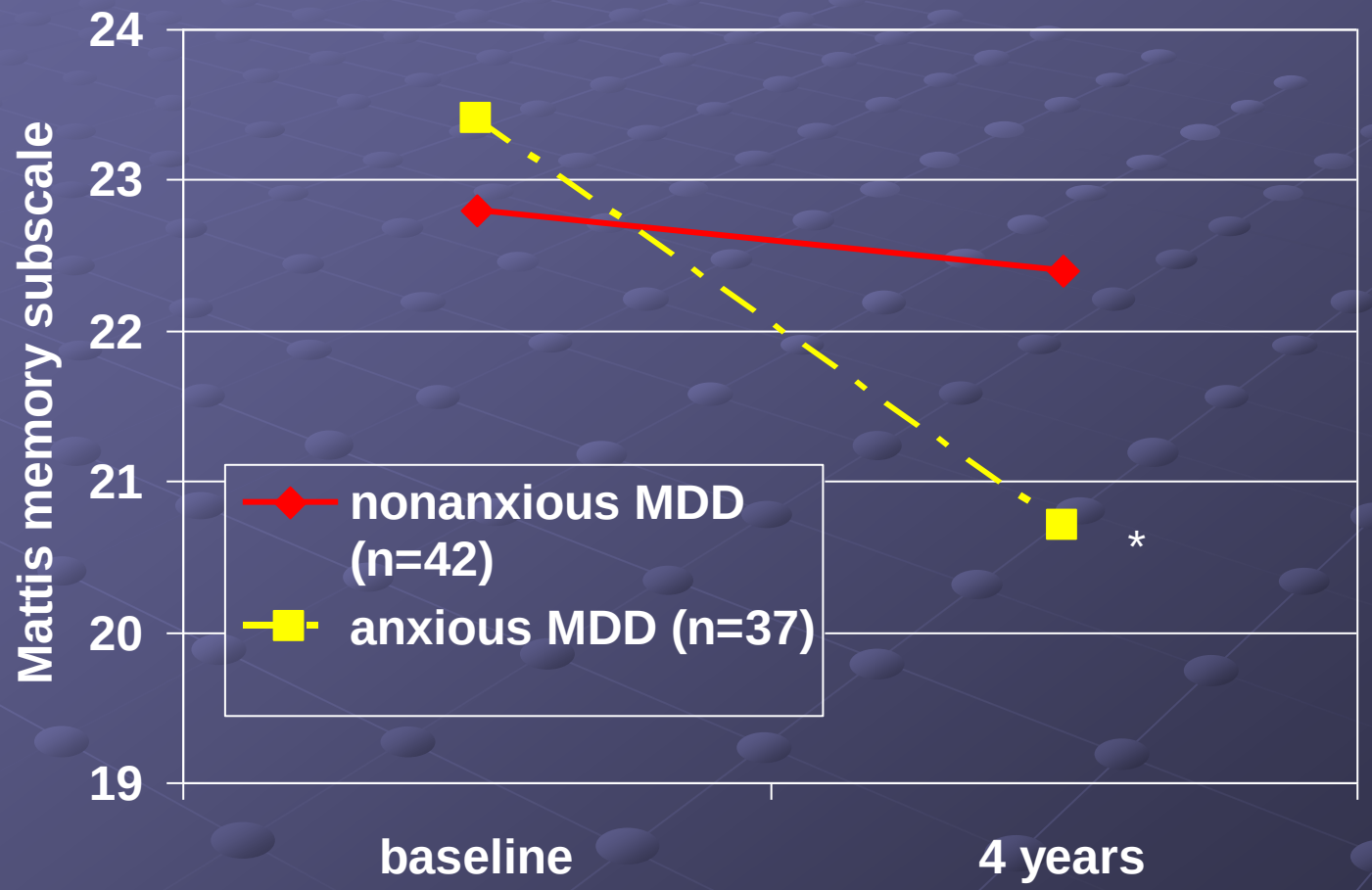
Steffens and McQuoid, Am J Geriatr Psychiatry. 2005; 13:40-47.

Effect of Baseline Anxiety on Time to Recurrence in MDD



Andreescu et al, 2007

MDD with comorbid GAD/panic: memory decline over 4 years f/u



*p=0.05 for group x time comparison
DeLuca et al, 2005

Medications efficacious for GAD

From clinical trials in young adults:

- FDA-approved: escitalopram, paroxetine, venlafaxine XR, duloxetine, buspirone.
- Also efficacious: other SSRIs, benzodiazepines, pregabalin, antihistamines

Prospective controlled studies in late-life GAD prior to 2005

Agent	study	Length	N	Age	Efficacy Results
oxazepam	Koepke 1982	4 wk	220	60+	oxazepam > placebo
ketazolam	Bresolin 1988	30 dy	63	66+	ketazolam > placebo
alpidem	Frattola 1992	3 wk	40	65+	alpidem > placebo
abecarnil	Small 1997	6 wk	182	60+	abecarnil > placebo

Koepke HH, et al. *Psychosomatics.* 1982;23:641-645.
Bresolin N, et al. *Clin Ther.* 1988;10:536-546.
Frattola L, et al. *Clin Neuropharmacol.* 1992;15:477-487.
Small GW, Bystritsky A. *J Clin Psychiatry.* 1997;58(suppl):24-29.

Problems With Benzodiazepines

- Benzodiazepines efficacious BUT
- Already heavily prescribed in elderly

Problems With Benzodiazepines

- Benzodiazepines efficacious BUT
- Already heavily prescribed in elderly
- Associated with falls

Psychotropic	Odds Ratio of Fall
Benzodiazepine	1.4*
Antidepressant	0.9
Antipsychotic	1.5*
Sedative/hypnotic	1.1

***P*<.05.**

Landi F, et al. *J Gerontol A Biol Sci Med Sci.* 2005;60:622-626.

Problems With Benzodiazepines

- Benzodiazepines efficacious BUT
- Already heavily prescribed in elderly
- Associated with falls
- Associated with cognitive impairment and decline

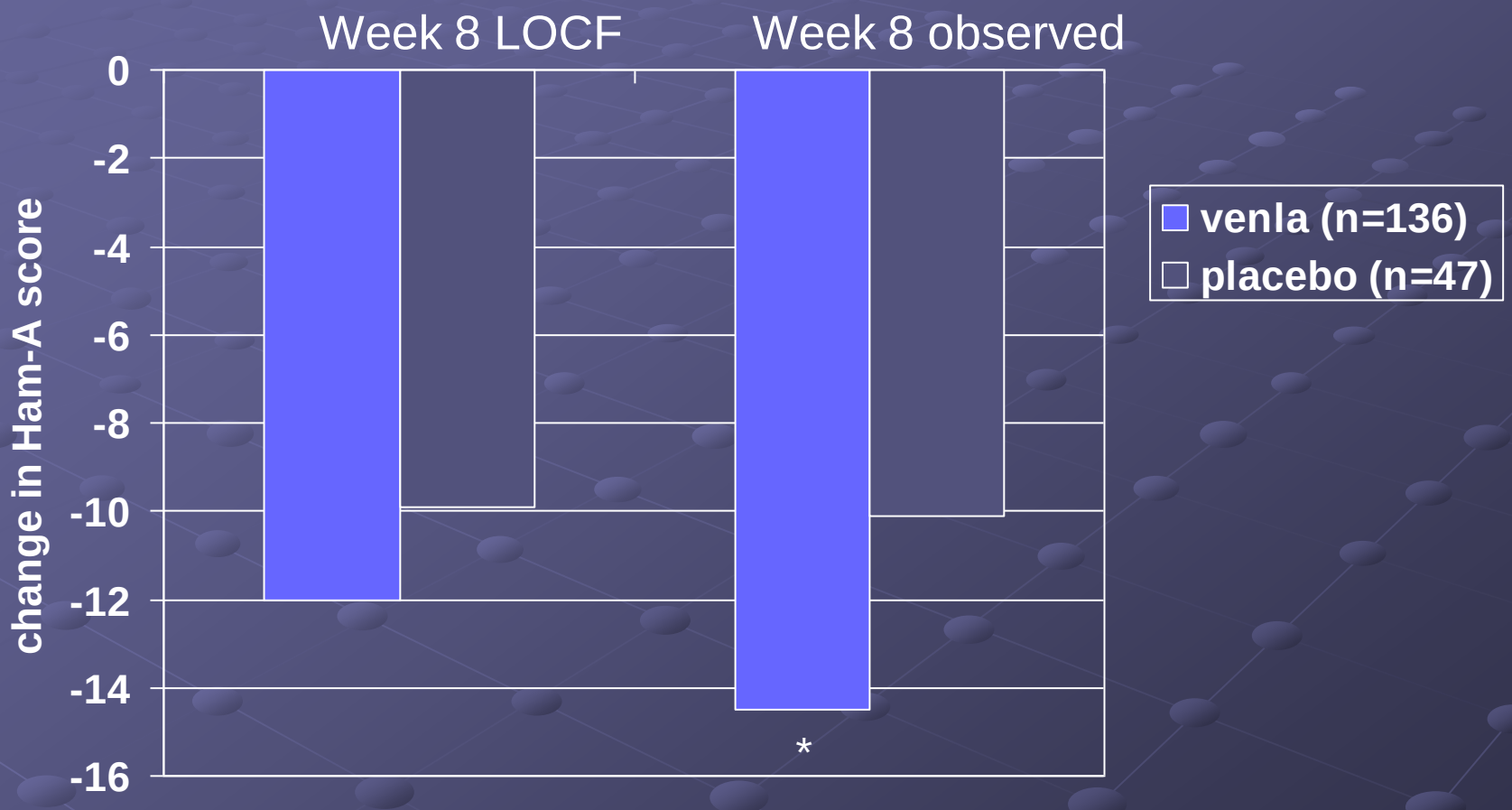
Cognitive decline	Nonusers (N = 126) *n* (%)	Chronic users (n = 63) *n* (%)	OR (95% CI)
Mini-Mental State Examination	19 (15.3)	14 (22.2)	2.0 (0.9–4.4)
Wechsler Digit Symbol Substitution Test	31 (25.0)	23 (36.5)	2.2 (1.1–4.5)
Trail Making Test	35 (29.7)	26 (43.3)	2.2 (1.1–4.6)
Finger Tapping Test	19 (15.5)	8 (12.7)	0.9 (0.3–2.2)
Auditory Verbal Learning Test	9 (8.0)	7 (12.3)	1.7 (0.5–5.1)

*ORs computed from logistic regression adjusting on baseline cognitive score.

†CI, confidence interval; OR, odds ratio.

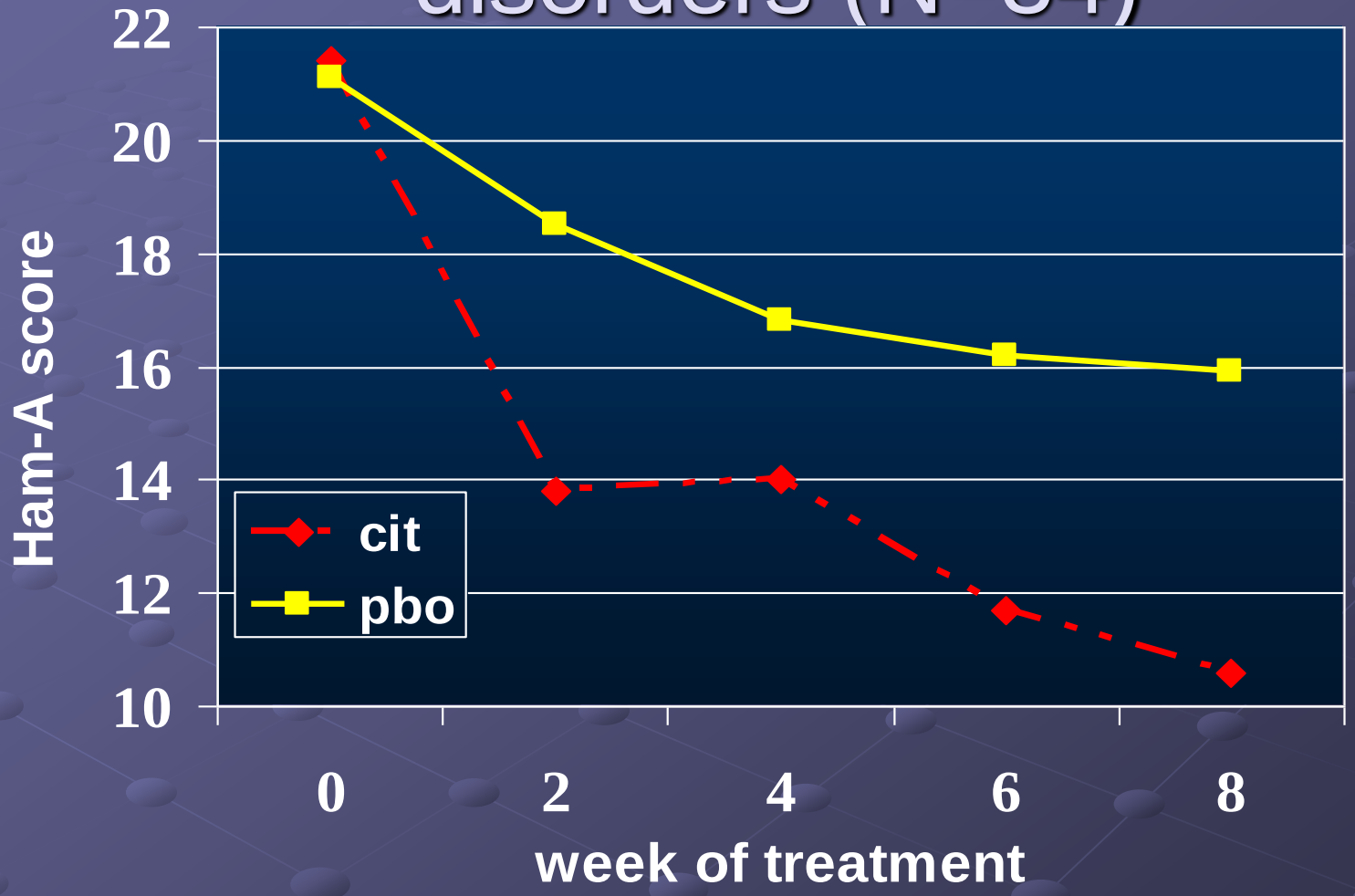
Paterniti S, et al. J Clin Psychopharmacol, 2002.

Venlafaxine ER in older GAD pts



*p < 0.01 for change compared to placebo
Katz et al, 2002

Citalopram in geriatric anxiety disorders (N=34)



Citalopram was significantly better than placebo in response rate and Improved anxiety symptoms, Lenze et al, Am J Psychiatry, 2005

Citalopram for Geriatric Anxiety Disorders

- 30 subjects received citalopram for up to 32 weeks
- Significant improvements in 4 of the 6 most common somatic symptoms:
  - Fatigue/asthenia
  - Headache
  - Gastrointestinal distress
  - Palpitations

Blank S, et al. *J Clin Psychiatry.* 2006;67:468-472.
Lenze EJ, et al. *Am J Psychiatry.* 2005;162:146-150.

Relief from anxiety in older adults

12 weeks escitalopram or placebo (n=177)

12 weeks open escitalopram

Does escitalopram help?

Time to response

Anxiety symptoms

Lenze et al, JAMA, 2009

JAMA®

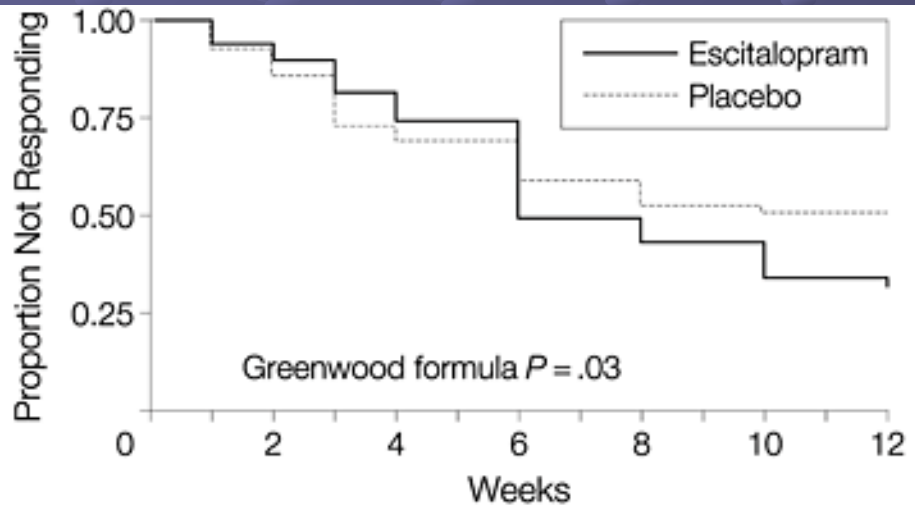
Online article and related content current as of April 16, 2009.

Escitalopram for Older Adults With Generalized Anxiety Disorder: A Randomized Controlled Trial

Eric J. Lenze; Bruce L. Rollman; M. Katherine Shear; et al.

JAMA. 2009;301(3):295-303 (doi:10.1001/jama.2008.977)

http://jama.ama-assn.org/cgi/content/full/301/3/295



No. at risk

Escitalopram	85	73	67	59	51	33	28	22	21
Placebo	92	84	75	61	56	46	39	36	34

Cumulative response: 69% escitalopram vs. 51% placebo (p= 0.03)

Escitalopram in late life GAD: Side effects

	No (%)	
	Active	**Placebo**
Total No. of participants	**85**	**92**
≥1 side effect	65 (76.5)*	59 (64)
Withdrew due to side effects	3 (3.5)	4 (4.3)
Most common side effects		
Fatigue or somnolence	35 (41.1)***	10 (10.9)
GI upset	22 (25.9)	26 (28.3)
Headache	13 (15.3)	7 (7.6)
Sleep disturbance	12 (14.1)**	2 (2.2)
Sweating	11 (12.9)	5 (5.4)
Sexual	9 (10.6)*	3 (3.3)
Urinary	8 (9.4)***	0 (0)
Increased anxiety or depression	7 (8.2)	9 (9.8)
Light-headed	7 (8.2)	7 (7.6)

Lenze et al, JAMA 2009

Limitations of medications

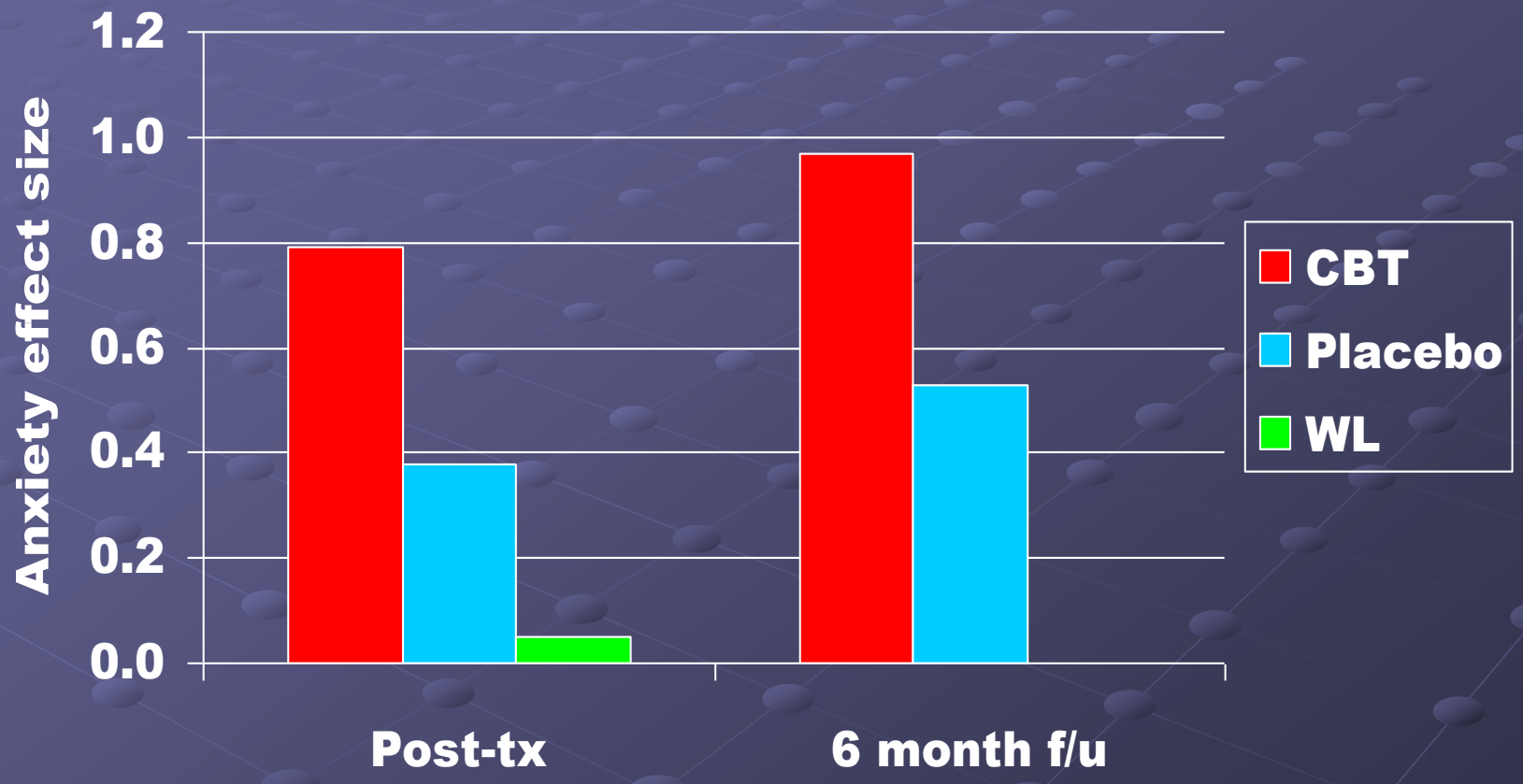
- Many respond, few remit
  - Construct of “I’m a worrier” does not seem to change
  - Many will not accept medication
  - In our current study, many refuse to start
- Uncertain long-term benefits
  - Not thought to have “durable” benefits (i.e., maintenance after med discontinuation)
- Phobias unlikely to respond to medication
  - Medication could even impair response to therapy

Psychotherapy in late-life anxiety

- Many elderly persons will prefer psychotherapy to medication
  - Cognitive Behavioral Therapy (CBT) can be as efficacious as medication
  - Cognitive impairment can interfere; a motivated patient is best

Wetherell, Hopko et al., 2005; Mohlman & Gorman, 2005

Comparison of CBT and attention placebo for late-life GAD



Wetherell et al., 2003

JAMA®

Online article and related content current as of April 16, 2009.

Cognitive Behavior Therapy for Generalized Anxiety Disorder Among Older Adults in Primary Care: A Randomized Clinical Trial

Melinda A. Stanley; Nancy L. Wilson; Diane M. Novy; et al.

JAMA. 2009;301(14):1460-1467 (doi:10.1001/jama.2009.458)

http://jama.ama-assn.org/cgi/content/full/301/14/1460

Table 3. Mean Percentages of Patients Classified as Treatment Responders According to Meaningful Change Scores on the PSWQ (8.5) and the GADSS (2.0) at 3 and 15 Months

	No. (%)			
Measure	CBT (n = 70)	EUC (n = 64)	χ^2	*P* Value
PSWQ				
3 mo	28 (40.0)	14 (21.9)	5.10	.02
15 mo	29 (41.4)	17 (26.6)	3.28	.07
GADSS				
3 mo	38 (54.3)	31 (48.4)	.46	.50
15 mo	29 (41.4)	24 (37.5)	.22	.64

Abbreviations: CBT, cognitive behavior therapy; EUC, enhanced usual care; GADSS, Generalized Anxiety Disorder Severity Scale; PSWQ, Penn State Worry Questionnaire.

- Many elderly persons will prefer psychotherapy to medication.

- Motivated, cognitively intact, verbal patients are best candidates

CBT in older adults with anxiety

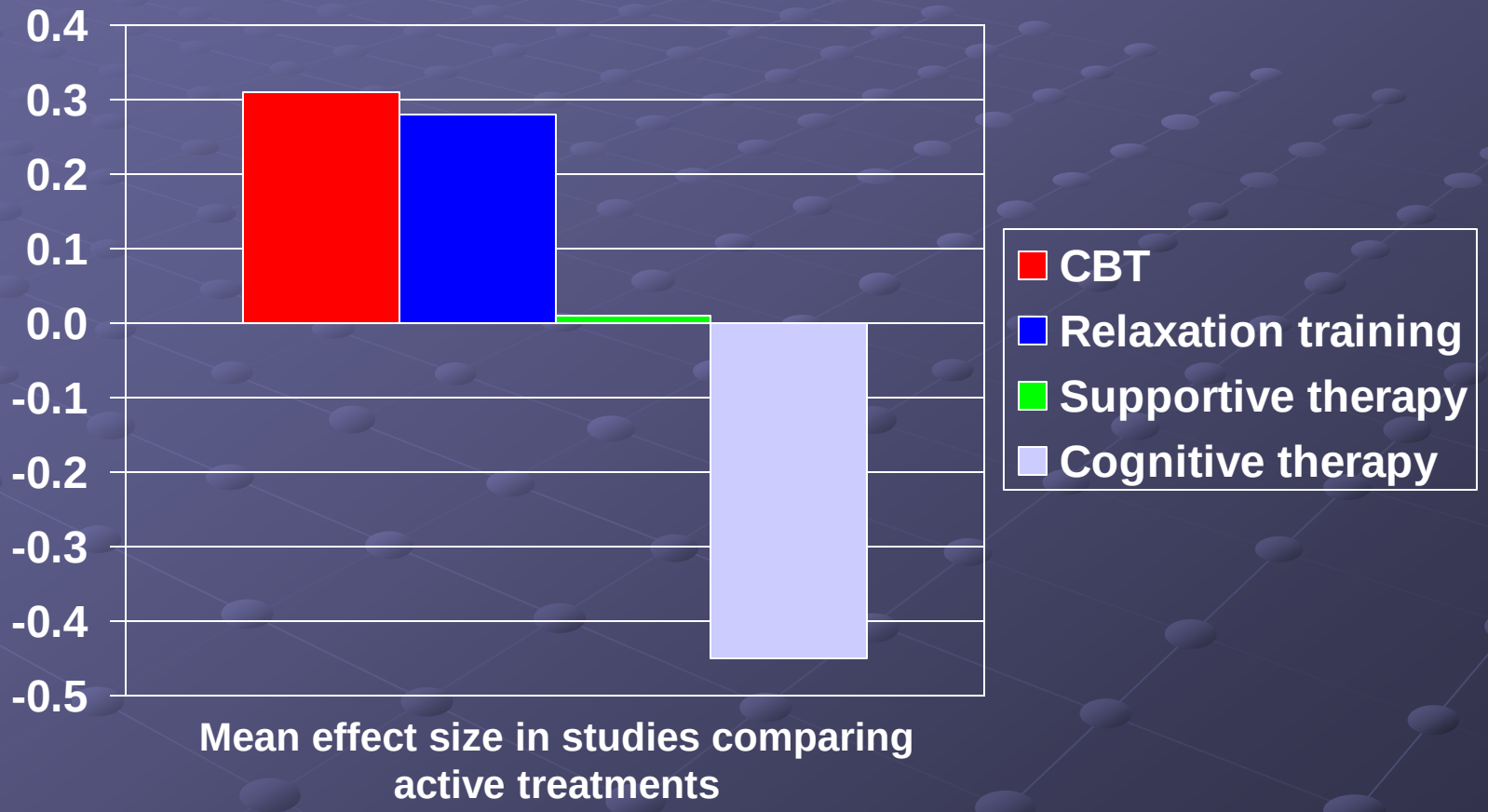
- Relaxation training
  - Slow, deep breathing
  - Progressive muscle relaxation
  - Imagery
- Changing negative automatic thoughts
  - Overestimation of risk
  - Catastrophization
- Exposure to anxiety-provoking situations
  - e.g., systematic desensitization

Psychotherapy in late-life GAD

- Many elderly persons will prefer psychotherapy to medication
  - CBT most efficacious in those who can be adherent to homework
  - Cognitive impairment can interfere

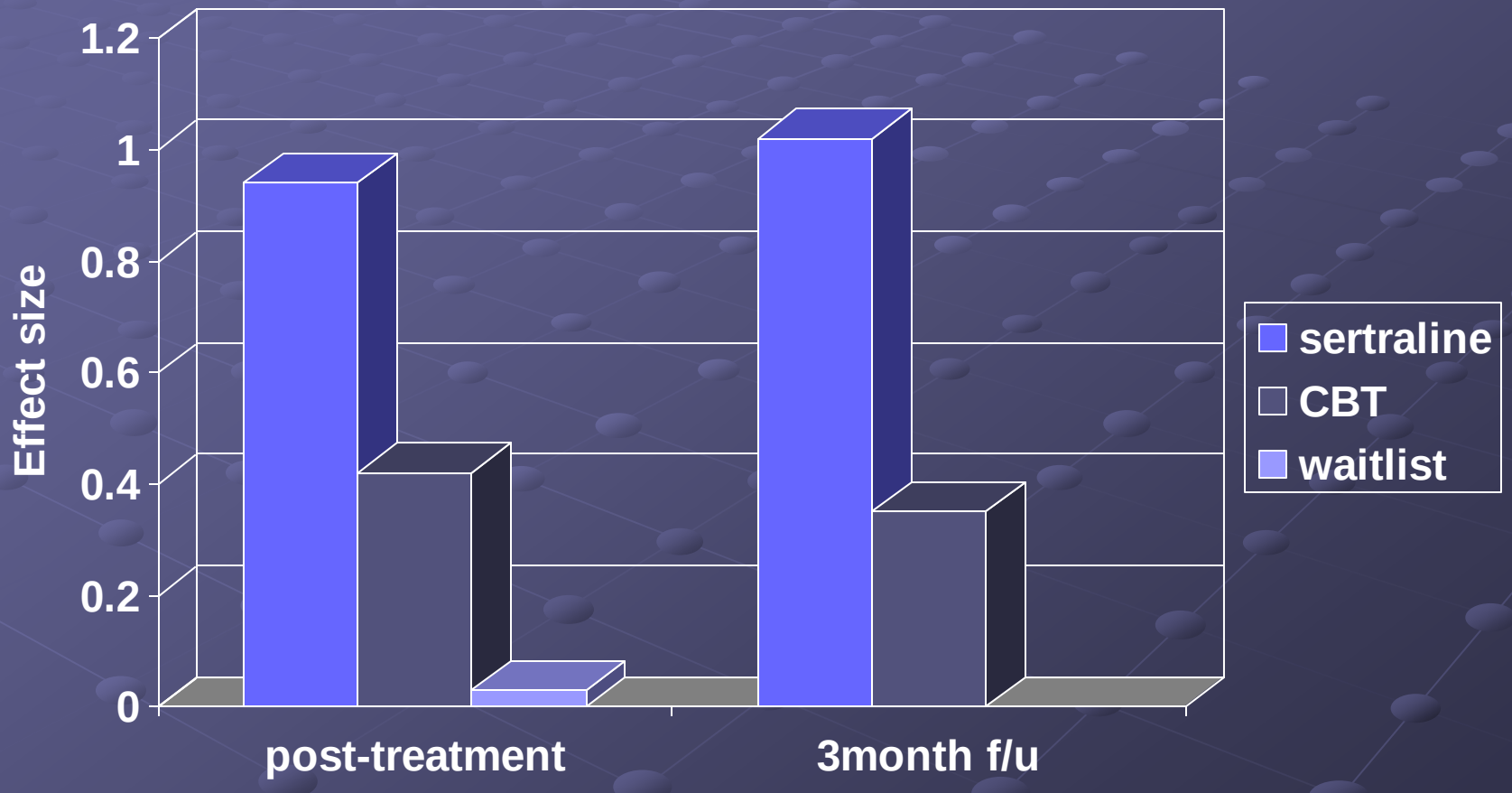
Wetherell, Hopko et al., 2005; Mohlman & Gorman, 2005

Relaxation training appears to be the most effective ingredient



Ayers, Sorrell, Thorp, & Wetherell, AJGP 2009

Comparison of SSRI and CBT for late-life GAD and panic disorder

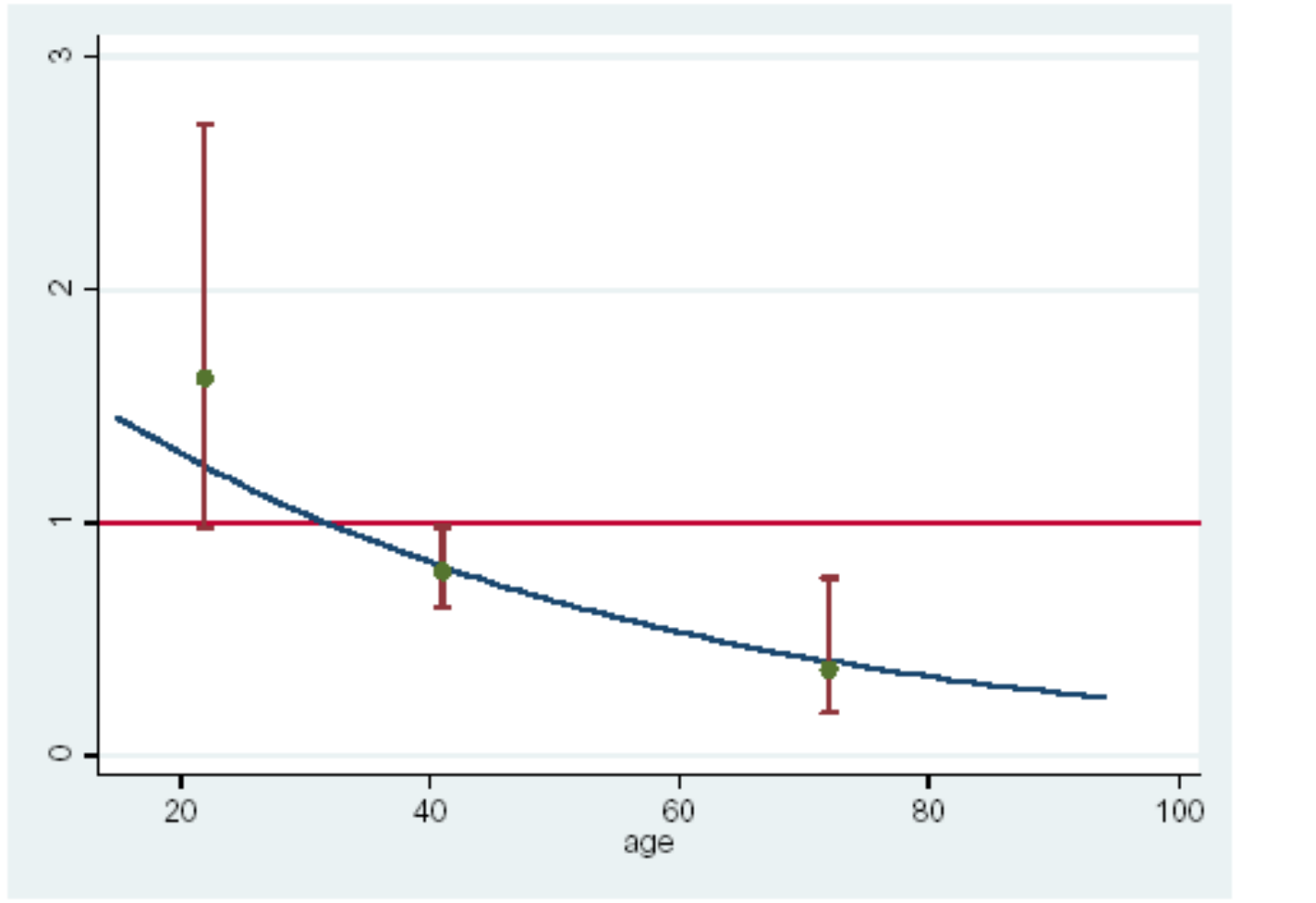


Schuurmans et al, 2006

Possible Risks of SSRIs in Elderly

- Suicide?
  - FDA meta-analysis = protective in age >65
- Falls
  - Association studies, some experimental
- Bleeding
  - Particularly in “old-old”, h/o GI bleed
- Hyponatremia
  - Tends to occur within 2 wk of initiation
  - Risk factors: baseline low Na^+, on diuretics

Suicidality and SSRIs: effects of age



Possible Risks of SSRIs in Elderly

- Suicide?
  - FDA meta-analysis = protective in age >65
- Falls
  - Association studies, some experimental
- Bleeding
  - Particularly in “old-old”, h/o GI bleed
- Hyponatremia
  - Tends to occur within 2 wk of initiation
  - Risk factors: baseline low Na^+, on diuretics

Possible Risks of SSRIs in Elderly

- Suicide?
  - FDA meta-analysis = protective in age >65
- Falls
  - Association studies, some experimental
- Bleeding
  - Particularly in “old-old”, h/o GI bleed
- Hyponatremia
  - Tends to occur within 2 wk of initiation
  - Risk factors: baseline low Na^+, on diuretics
- NEW FOR 2007: BONE LOSS!

Pharm management of late-life anxiety disorders

- SSRI seems to be a good first-line choice
  - Lexapro, Paroxetine, Effexor XR approved by FDA
  - Mgmt more important than specific med used
- High risk of “side effects” leading to dropout
  - Anxiety symptoms misperceived as due to medication: increased anxiety, GI symptoms, fatigue/sedation, restlessness
  - “Medication phobia”
- Start low, go slow – but not too slow

Detecting anxiety in elderly persons

- Elders less up-front about anxiety Sx
  - Asking about anxiety in several ways may help (e.g., “anxious”, “worried”, “concerned”)
    - “How do you feel in times of stress?”
    - “What sorts of things do you worry about?”
    - “How often do you feel that way?”
    - “When you start worrying, what do you do to try to stop it?”

Managing anxiety about medication

- Combination of:
  - Anticipatory dread
  - Vigilance to interoceptive stimuli
  - Catastrophization
- Frequent visits and support, immediate availability
- Counsel in advance about side effects
  - Likely to be temporary, unlikely to be toxic or incapacitating

When they do get side effects…

- Stay calm
- Remember the attribution error
  - But: don't argue about their validity
- Manage the catastrophization
  - "How is it today?" "Is it tolerable right now?" "Are you mainly worried that it will get worse?"
- Be persistent
  - Hear them out, then: "let's keep going"

When to choose psychotherapy

- Motivated, cognitively intact patient
- Phobias
  - Consider delaying medication until after Tx
- Will not accept medication
- Partial response to medication
- Availability of high-quality psychotherapy

Summary

- Late-life anxiety disorders are important.
  - Common
  - Different risk factors
  - Probably more vulnerable to harmful effects
  - Anxious depression is a particularly severe, treatment-resistant illness.
- Detection: ask, gently.
- Management: be pleasantly persistent.

Self-Assessment Question 1

Which of the following should be considered in the differential diagnosis of anxiety symptoms in elderly patients?

A. Cardiopulmonary and other medical conditions
B. Medication side effects
C. Sedative hypnotic withdrawal
D. All of the above
E. None of the above

Self-Assessment Question 2

What risks are associated with chronic benzodiazepine use in elderly?

A. Delirium
B. Cognitive impairment
C. Falls
D. Fractures
E. All of the above

Self-Assessment Question 3

Which of the following may contribute to the low estimate of prevalence of anxiety disorders in the elderly?

A. Age-related brain changes

B. Selective increase in mortality among anxiety disorder patients

C. Epidemiologic studies do not necessarily capture anxiety as it presents in older adults

D. All of the above

E. None of the above

Self-Assessment Question 4
Which of the following contribute to the importance of identifying and treating Generalized Anxiety Disorder in the elderly?

A. Its prevalence may be as high as 7%

B. It is unlikely to remit without treatment

C. Effective pharmacotherapeutic treatment has been demonstrated.

D. All of the above

E. None of the above

Self-Assessment Question 5
Which of the following is true of late-life depression with comorbid anxiety as compared to “pure” depression?

A. Severity of the illness is no different.

B. Antidepressant treatment response is better when comorbid anxiety is present.

C. Comorbid anxiety is associated with greater long-term cognitive decline.

D. All of the above

E. None of the above

Self-Assessment Question 6

Which of the following treatments has been demonstrated efficacious for older adults with anxiety disorders?

A. Cognitive Behavioral Therapy.
B. Selective Serotonin Reuptake Inhibitors.
C. Benzodiazepines.
D. All of the above
E. None of the above

Self-Assessment Question Answers

1. D
2. E
3. D
4. D
5. C
6. D