HIDDEN IN PLAIN SIGHT — (LATE-LIFE) ANXIETY IN THE COMMUNITY

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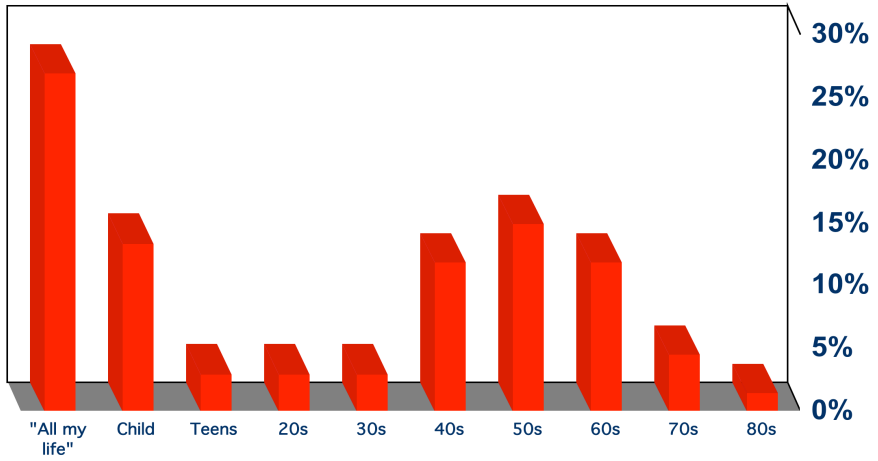
HOW FREQUENT IS ANXIETY LATER IN LIFE?

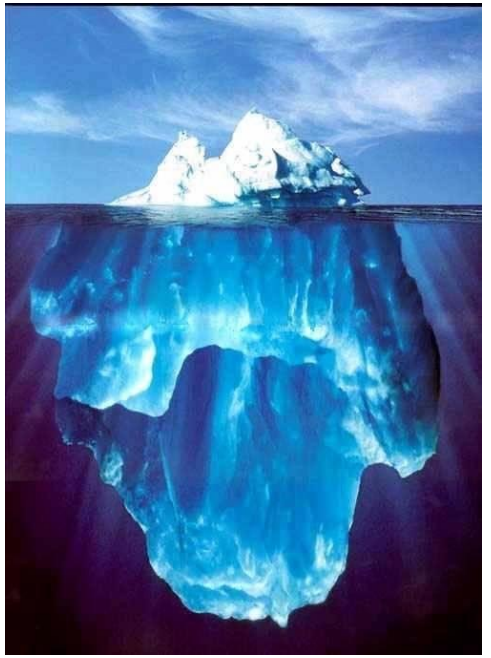
- One in four adults in the United States will have at least one episode of an anxiety disorder in their lifetime[1]
- Most anxiety disorders are carried over from adolescence and midlife[2]
  - Panic disorder
  - OCD
  - Phobias (specific/social)
- Anxiety disorders with frequent onset late in life[3]:
  - Generalized Anxiety Disorder
  - Agoraphobia



1. Kessler RC, McGonagle KA, Zhao S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. Results from the National Comorbidity Survey. *Arch Gen Psychiatry.* Jan 1994;51(1):8-19.
2. Flint AJ. Epidemiology and comorbidity of anxiety disorders in later life: implications for treatment. *Clin Neurosci.* 1997;4(1):31-36.
3. Le Roux H, Gatz M, Wetherell JL. Age at onset of generalized anxiety disorder in older adults. *Am J Geriatr Psychiatry.* Jan 2005;13(1):23-30.

PREVALENCE OF ANXIETY IN LATE LIFE

- Anxiety disorders and symptoms – prevalence in late-life:
  - 17.2 (Any anxiety disorder) vs. 14.5 (Any depressive disorder) (12 month prevalence)[1]
  - Generalized Anxiety disorder – only ONE THIRD receive treatment



- Most cases hide in the community:
  - 20% of older adults report anxiety symptoms [2] or severe worry [3]

- A categorical diagnosis excludes the majority of cases:
  - Only 20% of older adults with severe worry qualify for a GAD diagnosis [4]

1. Sylke, Schultz et al.: Prevalence of mental disorders in elderly people: The European mentDis_ICF65+ Study, *British J Psych,* Feb 2017
2. Forlani, Morri et al.: Anxiety symptoms in 74+ community-dwelling elderly. *PLoS One*, 2014.
3. Golden, Conroy et al.: The spectrum of worry in the community-dwelling elderly. *Aging Ment Health,* Nov 2011
4. Kertz, Bigda-Peyton et al.: The important of worry across diagnostic presentations. *J Anxiety Disord,* Jan 2012.

BARRIERS IN DIAGNOSING ANXIETY IN LATE-LIFE

- Older adults and clinicians view anxiety/fear/avoidance as normal in aging

- Older adults tend to[1]:
  - Minimize symptoms
  - Use different language (e.g. "concern" or "stress" instead of "worry")
  - Attribute symptoms to physical illnesses
  - May experience anxiety differently/disconnection between somatic and psychological symptoms
  - Discount complex assessment questions (e.g. "In the past 12 months have you had a period of a month or more when for most the time you felt worried, tense, or anxious about everyday problems such as work or family?")

1. Wolitzky-Taylor et al.: *Depression and Anxiety*, 2010

ATYPICAL ANXIETY SYNDROMES OFTEN ENCOUNTERED IN LATE-LIFE

- Fear of falling
- Hoarding syndrome
- PTSD in the older adults – prevalence of re-experiencing symptoms decreases
- Frequent somatic symptoms (e.g. dizziness/shakiness)
- ”Agitation” in Dementia
- Anxiety associated with common medical conditions:
  - COPD [18-50% of older adults with COPD]
  - Heart disease
  - Parkinson’s disease [~40% of PD]
  - Irritable Bowel Syndrome
  - Vestibular symptoms [37-42%]

ANXIETY AND COGNITIVE DECLINE

- Anxiety in late-life increases the risk of cognitive decline [1]
- Bidirectional association: Anxiety↔Cognitive Decline
- Increased risk of developing MCI 20 years later for midlife adults with severe anxiety [2]
- Anxiety symptoms double the risk of conversion from MCI to AD [3]
- Diagnostic challenges:
  - Patients with AD may have difficulties relaying information
  - Anxiety symptoms often present as agitation/aggression/hoarding symptoms/increasing clinging behaviors
  - May have to rely on caregiver report – no info re: internal symptoms (i.e. worry).

1. Sinoff et al.: IJGP, 2003
2. Gallacher et al.: Psychosom Med, 2009
3. Palmer et al.: Neurology, 2007

NORMAL VS. PATHOLOGICAL ANXIETY/WORRY

- Advantages of anxiety & worry
  - Anxiety is an even better teacher than reality, for one can temporarily evade reality by avoiding the distasteful situation; but anxiety is a source of education that is always present because one carries it within (Rollo May, *The Meaning of Anxiety,* 1950).
  - Worry: Modifies threat-related decision-making (evolutionary advantage)[1]

1. Miloyan B et al.: Episodic foresight and anxiety: proximate and ultimate perspectives. The British J of Clin Psychology, 2016.

PATHOLOGICAL WORRY – FEATURES

- Excessive = out of proportion with both the likelihood and the potential impact of the anticipated event
- Distressing = marked disturbance in functioning
- Pervasive = frequent, prolonged + ample range of worry topics
- No clear precipitant of worries
- Discomforting associated symptoms (restlessness, impaired sleep and concentration)

TYPES OF ANXIETY

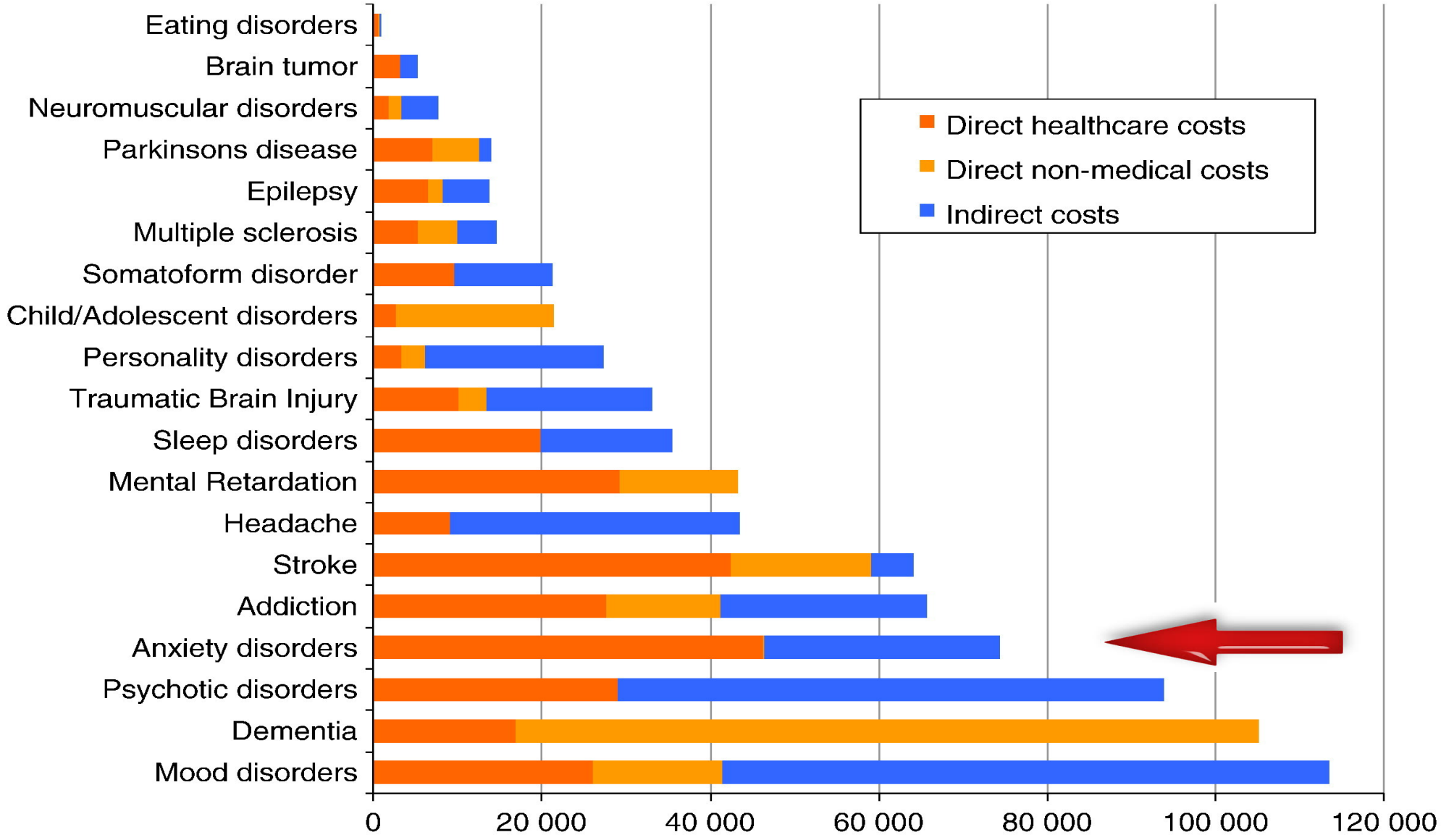
Fear – core of phobias

Arousal/Somatic anxiety – core of Panic/Somatization

Worry – core of GAD

	Fear	Avoidance	Arousal	Anticipatory worry	Panic attacks
Panic Disorder	x	x	x	x	x
Social and other phobias	x	x		x	x
OCD	x	+/-			
GAD		+/-		x	
PTSD	x	x	x		

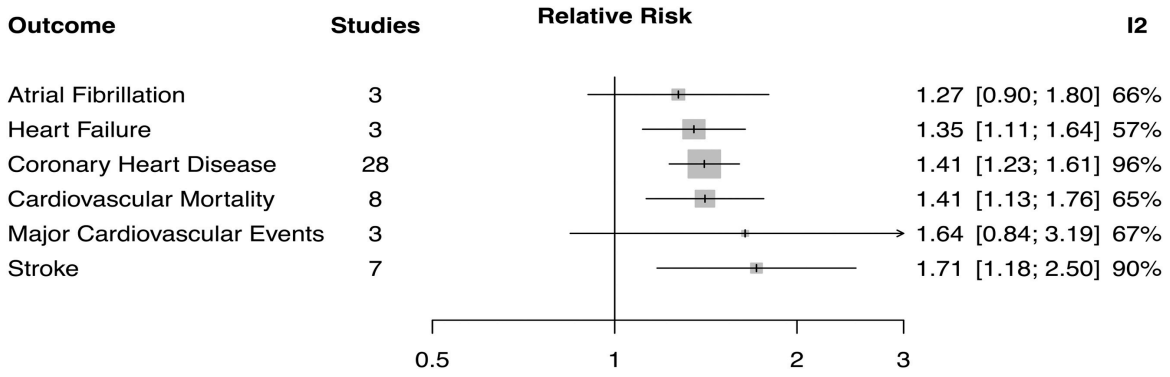
Anxiety Disorders are costly



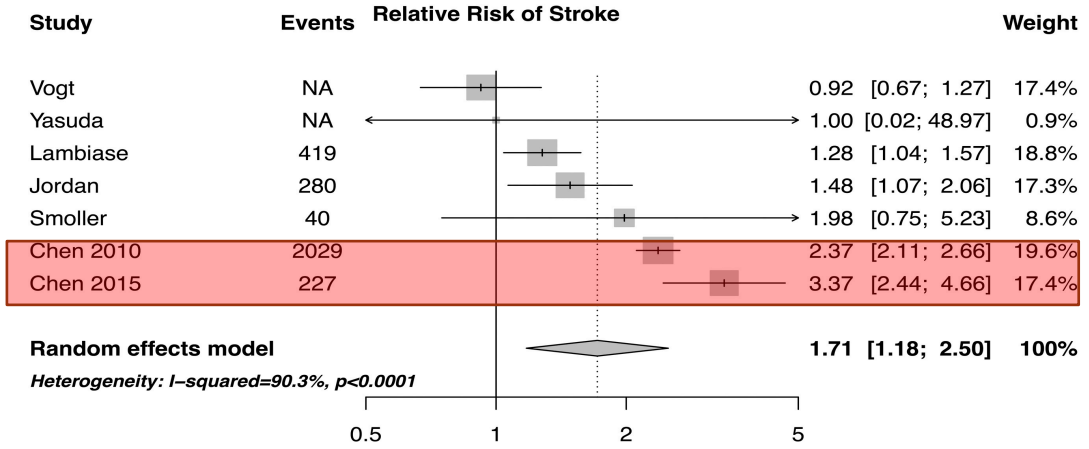
Gustavsson et al: Cost of disorders of the brain in Europe 2010. *Eur Neuropsychopharmacol*, 2011.

Anxiety disorders are deadly

Association of anxiety with cardiovascular disease



Association of anxiety with stroke

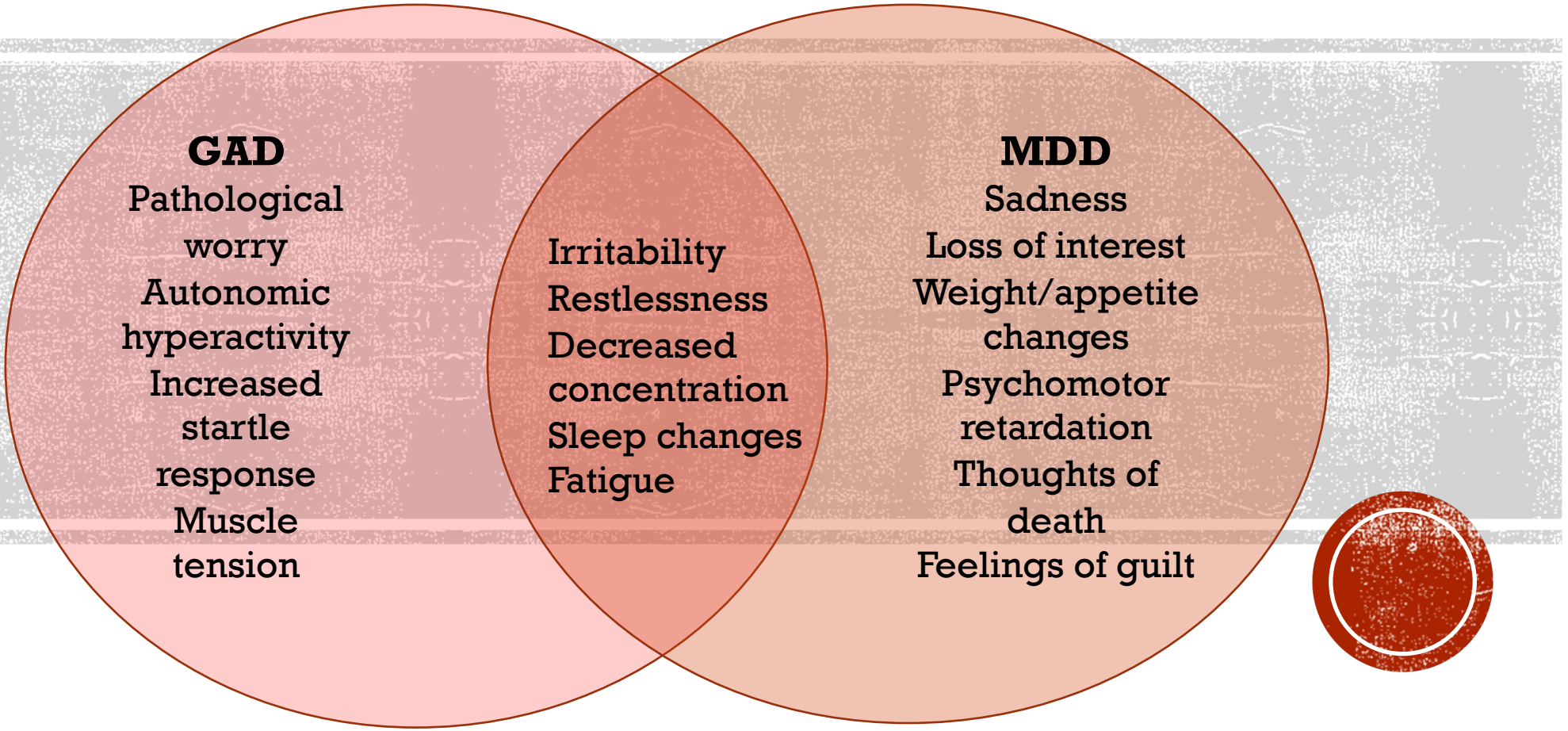


Anxiety was associated with:

- 41% higher risk of cardiovascular mortality
- 41% higher risk of coronary heart disease
- 71% higher risk of stroke
- 35% higher risk of heart failure

Emdin et al., *The American Journal of Cardiology,* August 2016.

COMORBIDITY OF ANXIETY AND MOOD DISORDERS



Overlapping and distinct symptoms of GAD and MDD [Ressler, Pine, Rothbaum – *Primer on Anxiety Disorders*, 2015]

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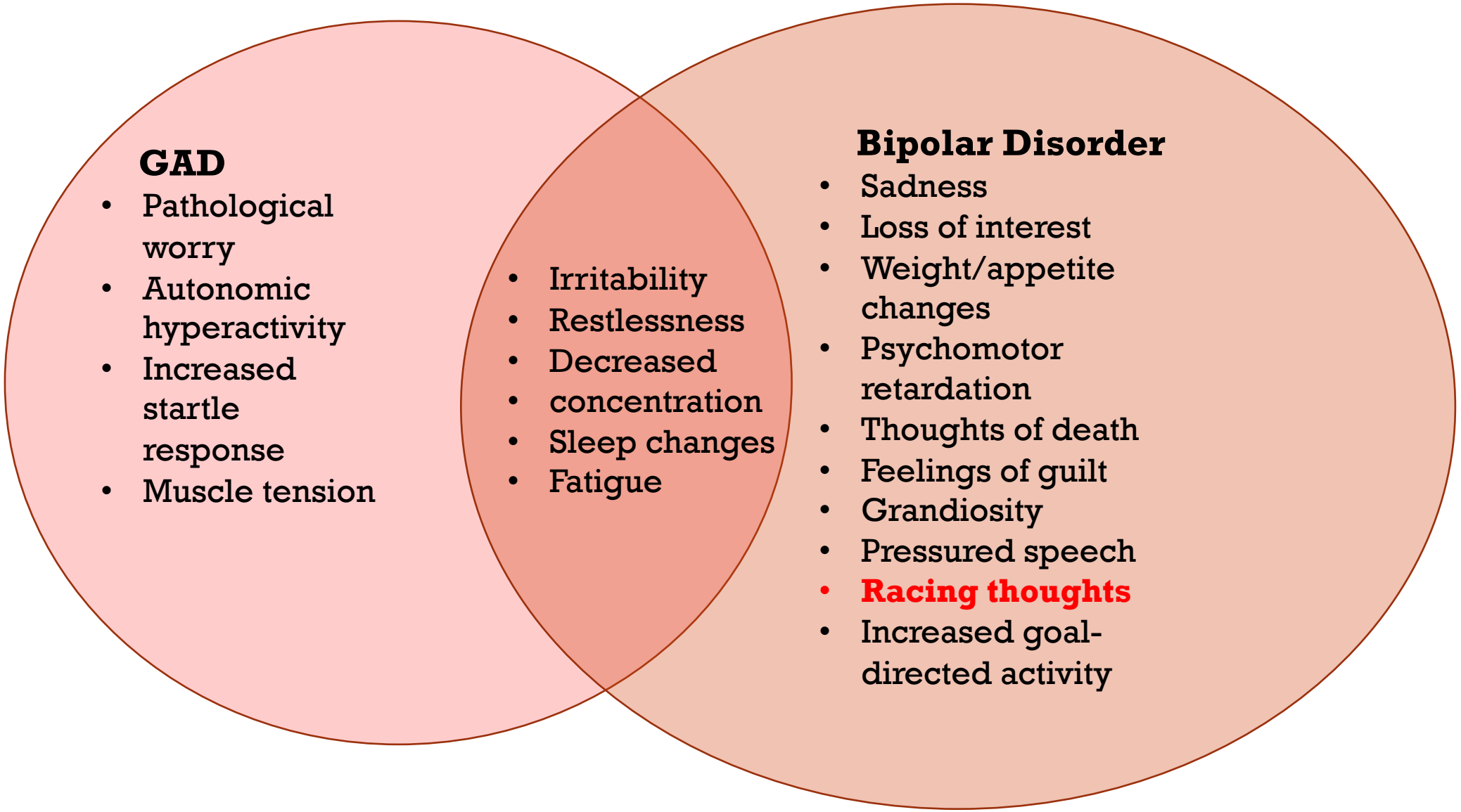


Overlapping and distinct symptoms of GAD and Bipolar Disorder[Ressler, Pine, Rothbaum – Primer on Anxiety Disorders, 2015]

SUBSTANCE ABUSE AND COMORBIDITY WITH ANXIETY

- One in five Substance Use Disorder (SUD) meet criteria for an Anxiety Disorder (National Comorbidity Survey Replication, 2005)

- Theories of AD/SUD comorbidity:
  - Self-medication hypothesis
  - Substance-induced anxiety
  - Common factors theory (shared personality/neurobiological vulnerabilities)

GENERAL TREATMENT APPROACHES IN SUD-ANXIETY DISORDERS COMORBIDITY

Approach	Description	Advantages	Disadvantages
Sequential treatment	SUD treated first	Consistent with the structure of most treatment facilities	Costly for patients
	Delay tx of AD until SUD is solved	Consistent with the disorder-specific training model	Attrition of patients
			Relapse of SUD triggered by untreated AD
Parallel treatment	SUD and AD are treated simultaneously by different doctors	Enhances treatment outcome and reduces risk of relapse	Costly for patients
		Addresses both disorders at the same time	Requires coordination between doctors
Integrated treatment	Both are treated simultaneously by a single doctor	Reduces cost (time/money)	Few evidence-based approaches available
		Promotes pt understanding of connection between symptoms	Fewer doctors trained in delivery of integrated treatments

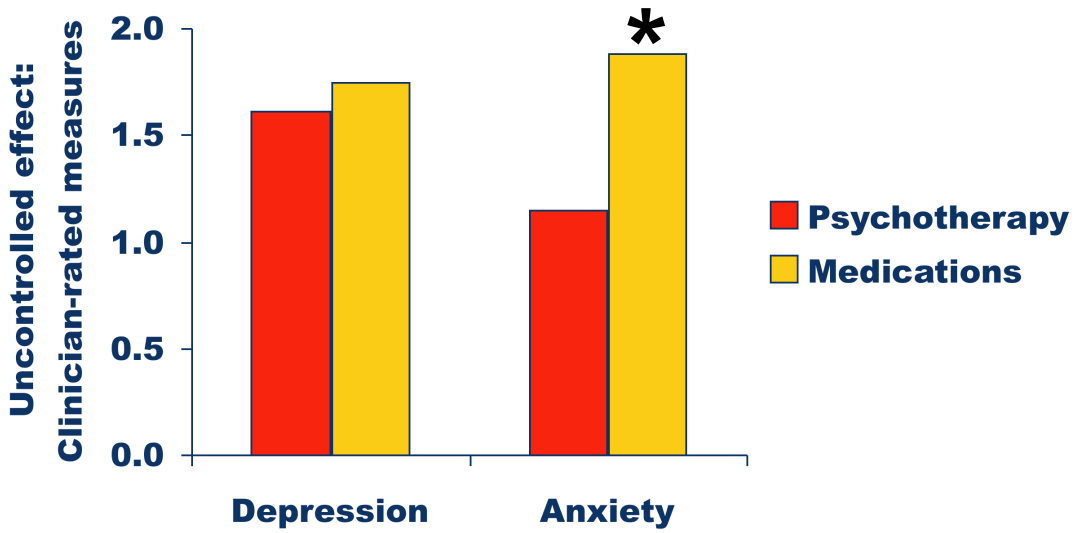
REASONS TO WORRY ABOUT GAD

- GAD is the most common anxiety disorder among people aged 55-85
- GAD is the most frequently seen anxiety disorder in primary care settings (US & World)
- GAD is associated with significantly increased health care utilization & costs
- GAD patients have the highest rate of marital dissatisfaction among psychiatric disorders (Ontario Health Survey)
- Rates of spontaneous remission are very low

GAD TREATMENT OPTIONS

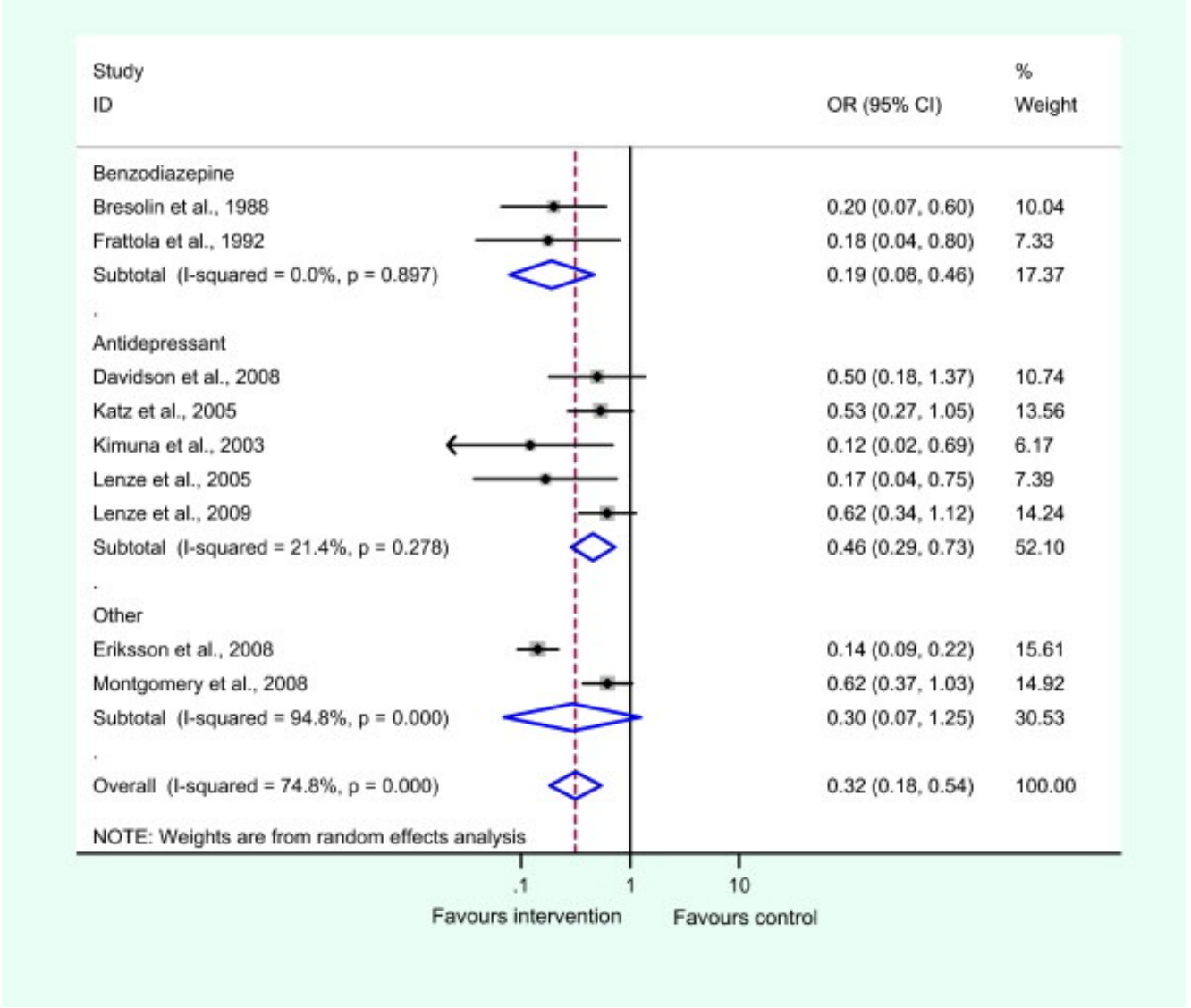
- Some respond, but few remit
- Many patients fear medications/will discontinue treatment
- Relapse is very common

MEDICATIONS ARE MORE EFFECTIVE THAN PSYCHOTHERAPY FOR GERIATRIC ANXIETY



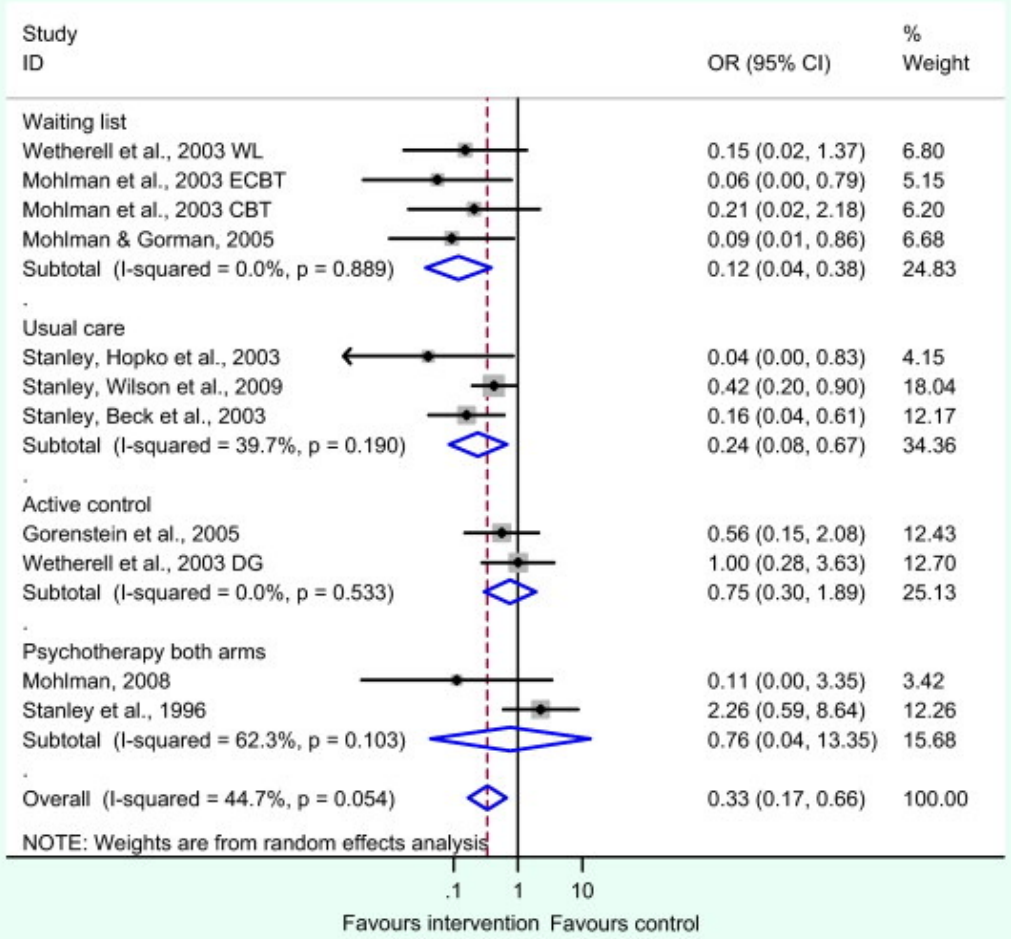
* p < .05; Pinquart et al., 2006; Pinquart & Duberstein, 2007

PHARMACOLOGICAL TRIALS IN LATE-LIFE GAD



Goncalves & Byrne: *Journal of Anxiety Disorders*, 2012

PSYCHOTHERAPY TRIALS IN LATE-LIFE GAD



Goncalves & Byrne, *Journal of Anxiety Disorders*, 2012

PHARMACOTHERAPY AND PSYCHOTHERAPY IN LATE-LIFE GAD

- Pharmacological trials favor treatment with an active substance when compared with a placebo condition. [1]
- When drug classes were considered separately, both benzodiazepines and antidepressants exhibited statistically significant treatment effects. [1]
- Psychotherapeutic trials also favor active interventions (compared with waiting list/care as usual/minimal contact)[1]
- The comparison between psychotherapy and another active control condition (e.g. discussion group) was not significant.[1]
- There was no difference between different types of psychotherapy.[1]
- Furthermore, CBT failed to prove to be more effective than both an active control condition or another type of psychotherapy for the treatment of late-life anxiety, whereas relaxation training obtained superior results [2]

1. Goncalves & Byrne: *Journal of Anxiety Disorders*, 2012
2. Thorp et al: *AJGP*, 2009

PARTICULARITIES OF OLDER ADULTS ENGAGED IN TREATMENT

- Older adults are more reluctant to seek help from mental health professionals[1]
- They are more likely to drop out of treatment due to perceived stigma[2]
- Older adults were reluctant about participating in group therapy, but were willing to attend psychoeducational classes[3]
- Psychotherapy was selected as the preferred treatment by the majority of older adults who answered a survey about anxiety treatment[4]

1. de Beurs et al: *Psychological Med*, 1999
2. Sirey et al: *Psychiatr Serv*, 2001
3. Arean et al: *Biol Psychiatry*, 2002
4. Mohlman et al: *Psychol Aging*, 2012

PHARMACOLOGICAL OPTIONS

- SSRIs (please avoid Paroxetine) – Sertraline and Citalopram proven efficacy
- SNRIs (venlafaxine XR, duloxetine) – dose dependent increase in BP (venlafaxine)
- Atypical antipsychotics
  - Some 2nd-line augmentation data (Risperidone)
  - Quetiapine XR efficacious for late life GAD (N=450) – SE (somnolence, dizziness, dry mouth)
- Pregabalin – one positive large study (N-273)

Wolitzky-Taylor et al: *Depress Anxiety*, 2010
Andreescu & Varon: *Curr Psychiatry Rep*, 2015

PHARMACOLOGICAL OPTIONS

- Mirtazapine
- Buspirone: similar efficacy when compared with sertraline (N=46)
- Not recommended: antihistamines, anticholinergics, sedatives.
- Benzos
  - Best as short-term adjunct.
  - PRN use should be discouraged.
  - The most commonly used pharmacological treatment of anxiety in late-life
  - Prescribed more often in the absence of an antidepressant in older adults (43% vs. 32%)

Wolitzky-Taylor et al: *Depress Anxiety*, 2010
Andreescu & Varon: *Curr Psychiatry Rep*, 2015

POSSIBLE RISKS OF SSRIS IN OLDER ADULTS

- Suicide?
- Falls
  - Association studies, some experimental
- Bleeding
  - Particularly in “old-old”, h/o GI bleed
- Hyponatremia
  - Particularly in those with low Na^+, on diuretics
- Bone loss
  - Association with osteopenia in both lumbar spine and hip
- Cognitive impairment?
  - No evidence (unlike benzodiazepines)

PROBLEMS WITH BENZODIAZEPINES

- Benzodiazepines efficacious BUT
  - Already heavily prescribed in older adults
  - Associated with falls
  - Also associated with cognitive impairment

Psychotropic	Odds ratio of fall
Benzodiazepine	1.4*
Antidepressant	0.9
Antipsychotic	1.5*
Sedative/ hypnotic	1.1

Limitations of Medications

- Many respond, few remit
  - Construct of "I'm a worrier" does not seem to change
  - Many will not accept medication
  - Many will discontinue
- 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

COGNITIVE BEHAVIORAL THERAPY FOR LATE-LIFE GAD

- Relaxation training
- Cognitive restructuring
- Some protocols include worry exposure, problem-solving, sleep hygiene, behavioral activation/pleasant activities
- Modified to fit the needs of older subjects:
  - Between-session reminder phone calls
  - Weekly review of concepts
  - In-home assignments
  - Simplify approach

Relaxation Training is the Most Effective Component of CBT

Meta-analysis of intervention vs active control condition	Mean Effect Size (95% CI)
CBT without Relaxation Training	0.00 (-0.46, 0.46)
CBT with Relaxation Training	0.33 (-0.07, 0.74)
Relaxation Training alone	**0.90 (0.44, 1.44)**

CBT, cognitive-behavioral therapy; CI, confidence interval.

Thorp SR et al: *Am J Geriatr Psychiatry* 2009;17:105-15

ADJUSTING PSYCHOTHERAPEUTIC INTERVENTIONS FOR OLDER ADULTS

- Incorporate religion and/or spirituality for older African American subjects [1]
- Telephone-delivered CBT (for rural populations) - was superior to telephone-delivered NST in reducing worry, additional GAD symptoms, and depressive symptoms in older adults with GAD [2]
- CBT in primary care: improvement in worry severity, depressive symptoms, and general mental health for older patients with GAD [3]
- Internet delivered CBT: older patients more likely to complete iCBT than younger patients, but younger adults responded more robustly [4]

1. Stanley et al, *AJGP*, 2016
2. Brenes et al, *JAMA Psychiatry*, 2015
3. Stanley et al, *JAMA*, 2009
4. Hobbs et al, J *Affective Disorders*, 2017

TREATMENT OPTIONS - CONCLUSIONS

- GAD is is one of the least likely mental disorders to remit and most likely to relapse [1]
- Current treatment choices reduce overall burden of anxiety but are less effective in reducing worry severity [2, 3]
- Sequential pharmacotherapy→psychotherapy [4]
- Treatment modified to fit the needs of older subjects

1. Lenze et al, 2011
2. Lenze et al, *JAMA*, 2009
3. Weisberg, RB, *J Clin Psychiatry*, 2009
4. Wetherell et al, *Am J Psychiatry*, 2013

WELCOME TO THE ARGO LAB

At the ARGO Neuroscience of Aging Research Lab, our focus is on what happens to our brain as we age. Our studies focus on late-life anxiety, depression, and Alzheimer's Disease.

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