Evidence Based Review of Generalized Anxiety Disorders

Utilizing the Oregon Psychiatric Access Line (OPAL) for Support

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Disclosure

Dr. Betlinski and Dr. Ames have no relevant financial disclosures

This presentation includes discussion of off label medications

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Learning Objectives

- Develop an evidence-based treatment plan for a patient newly presenting with an anxiety disorder
- Identify at least one non-pharmacologic treatment modality that can be used to improve anxiety symptoms
- Describe the Oregon Psychiatric Access Line and what resources it provides to clinicians

Pre - Test Questions

1. What percentage of adults in Oregon had anxiety and/or depression in 2023?

a. 17% b. 25% c . 33% d. 42%

2. Which Comorbid Medical Condition may predict a diminished response to treatment for anxiety?

a. Asthma b. Cardiovascular Disease c. Diabetes d. Migraines

3. Which of the following suggests a primary anxiety disorder rather than anxiety secondary to organic causes?

a. Onset of anxiety symptoms before age 35 years
b. Lack of personal or family history of anxiety disorder
c. Lack of childhood history of significant anxiety
e. Poor response to psychiatric treatment

Pre - Test Questions

4. In a recent meta-analysis, which SSRI demonstrated the greatest efficacy as measured by the mean change in HAM-A scores?

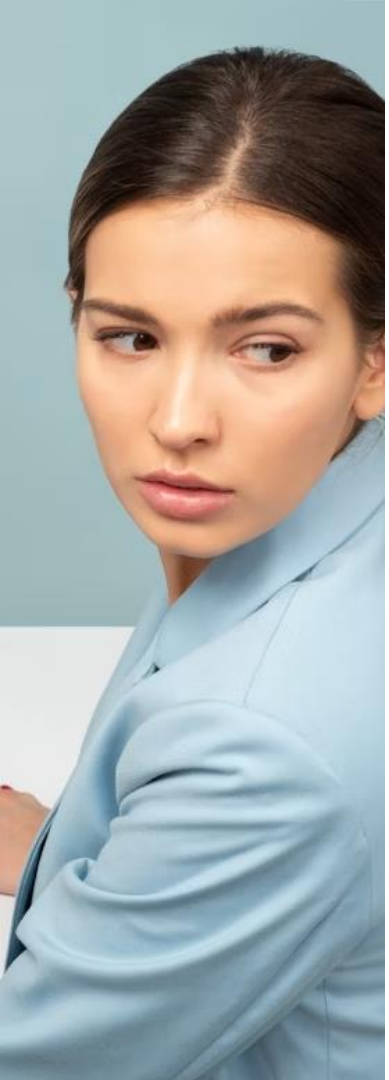
   a. Fluoxetine b. Citalopram c. Escitalopram d. Fluvoxamine

5. Which second-line adjunctive agent does NOT have sedation/somnolence as a major side effect?

   a. Quetiapine XR b. Buspirone c. Pregabalin d. Benzos

Agenda

- Review the epidemiology of anxiety
- Review medical comorbidities
- Review criteria for GAD, PD, and SAD
- Introduce and explain the GAD-7, PDSR, Mini-SPIN, GAS, GAI
- Review nonpharmacologic treatments for anxiety
- Review pharmacologic treatments for anxiety
- Review additional resources available in Oregon



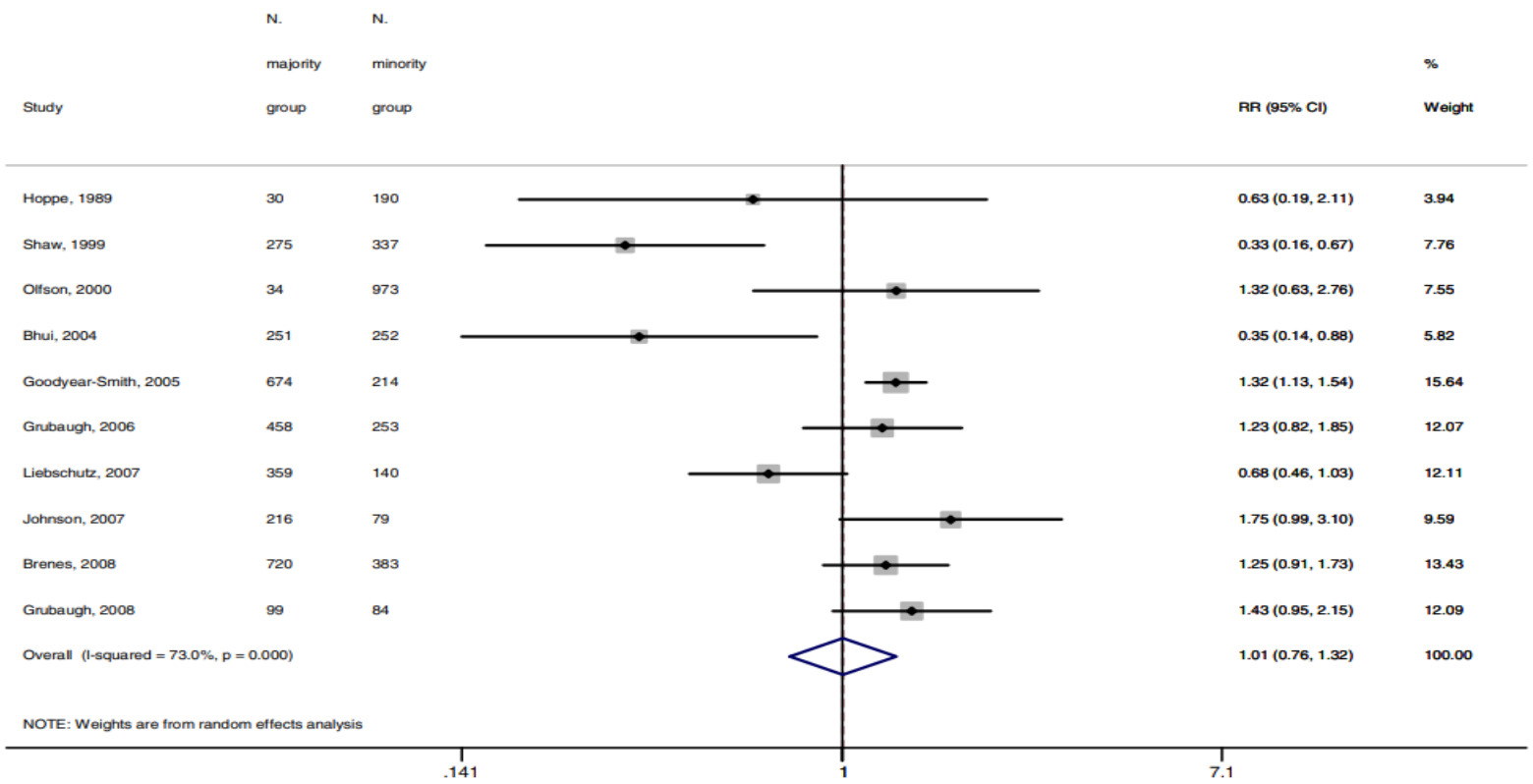
Jenny is a 49-year-old woman in upper-level management. Even though she has worked for the same, thriving company for over 20 years, she has always been worried about losing her job and being unable to provide for herself. This worry has been troubling her more so for the past several years, gradually getting worse (though with a tendency to ebb and flow). Despite her best efforts, she hasn't been able to shake the negative thoughts.

Jenny feels restless, tired, and tense. She often paces in her office when she's there alone. She's had several embarrassing moments in meetings where she has lost track of what she was trying to say. When she goes to bed at night, it's as if her brain won't shut off. She finds herself mentally rehearsing all the "worst-case" scenarios regarding losing her job, including ending up homeless.

On further assessment, Jenny admits to worrying about more than just her job and finances. She has also worried about her health and relationships since childhood.

Epidemiology

No Ethnic Variations in Anxiety?



https://pubmed.ncbi.nlm.nih.gov/21705094/

Fig. 3. Forest plot of RR for the effect of MI group compared with MA group on the prevalence of anxiety.

Anxiety in a Primary Care Office

A 2007 study of patients from 15 clinics

- 19.5% had at least 1 anxiety disorder
- 8.6% PTSD
- 7.6% Generalized Anxiety Disorder
- 6.8% Panic Disorder
- 6.2% Social Anxiety Disorder
- 41% of those with Anxiety Disorders had no current treatment

http://www.ncbi.nlm.nih.gov/pubmed/17339617

Anxiety in the USA

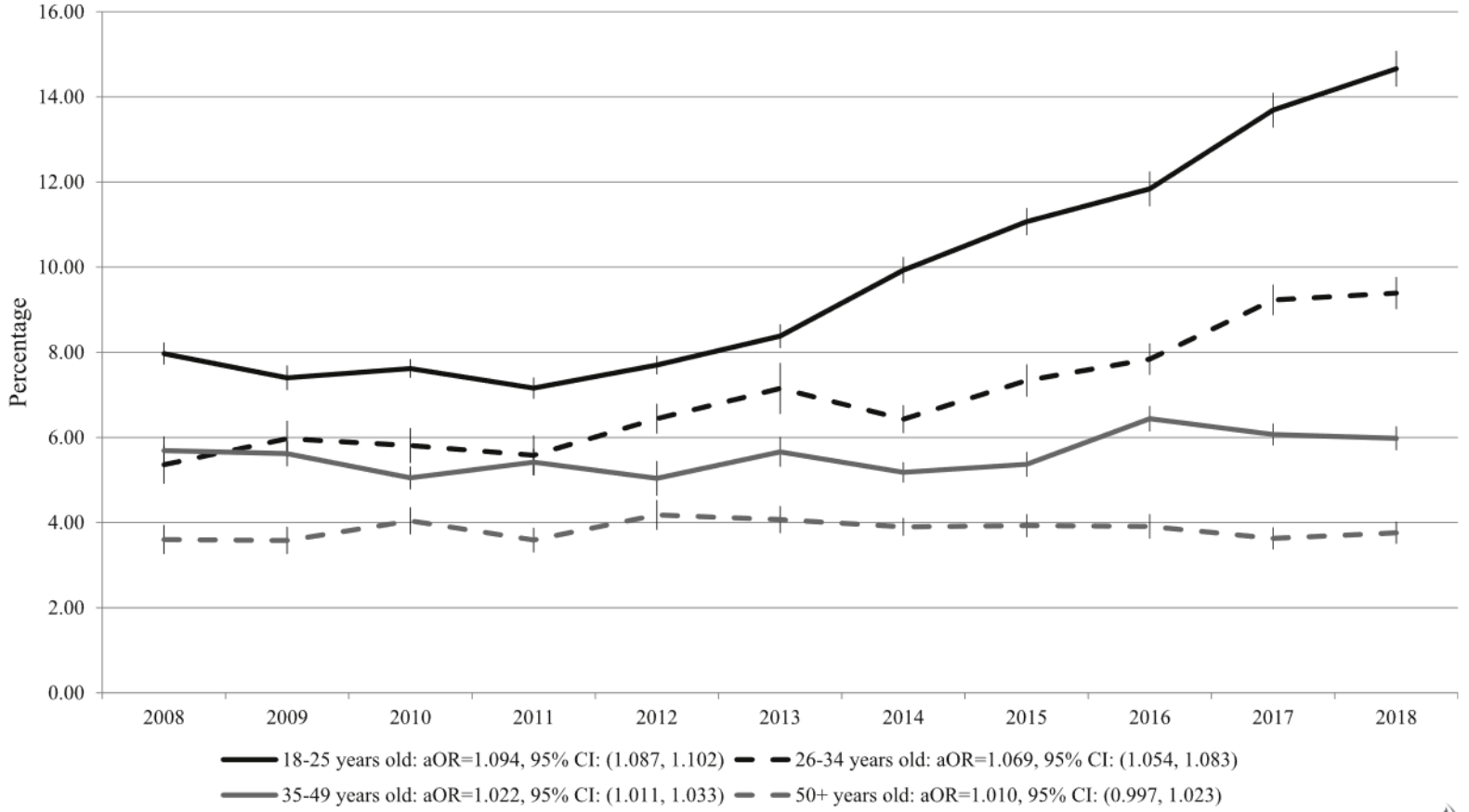
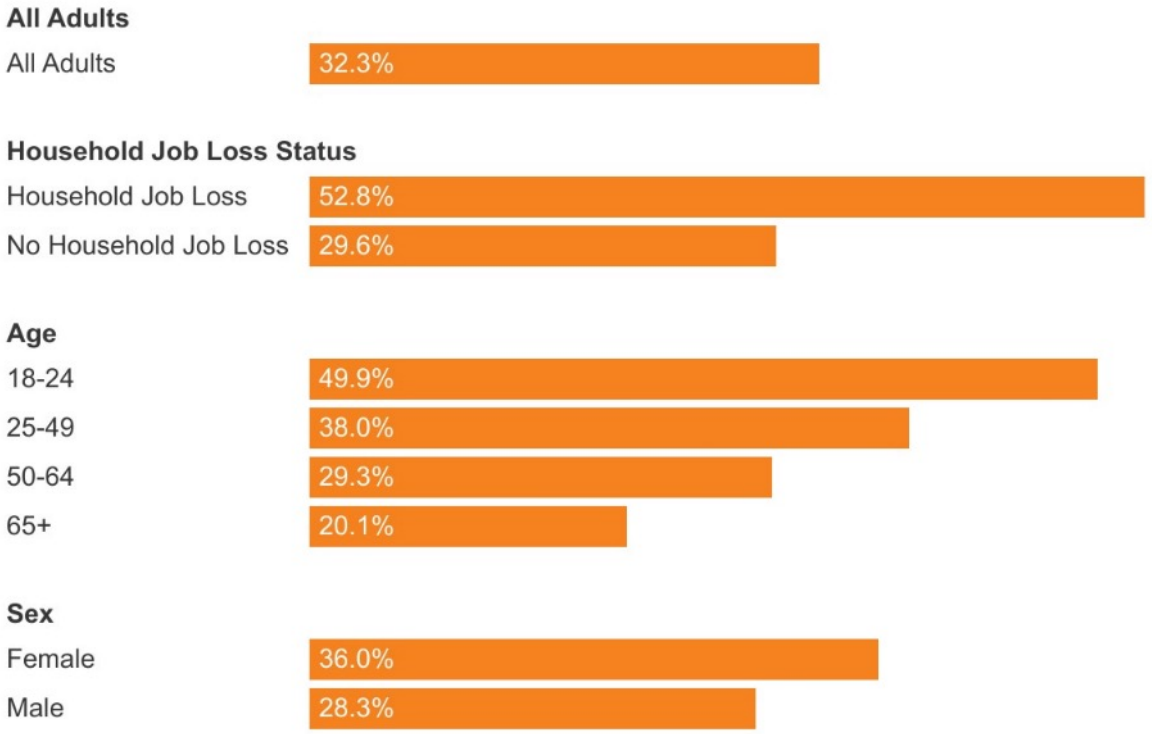


Fig. 2. Prevalence of past-month anxiety by age from 2008 to 2018 (NSDUH, US adults ages 18 years and older)[a].
Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; NSDUH, National Survey on Drug Use and Health.
[a]Anxiety was operationalized as self-reported nervousness in the past month most of the time or all of the time.
Note: Odds ratio for calendar yearly linear trend was adjusted for gender, race/ethnicity, income, marital status, and educational attainment.

https://pubmed.ncbi.nlm.nih.gov/21705094/

OHSU

Share of Adults Reporting Symptoms of Anxiety and/or Depressive Disorder, February 2023

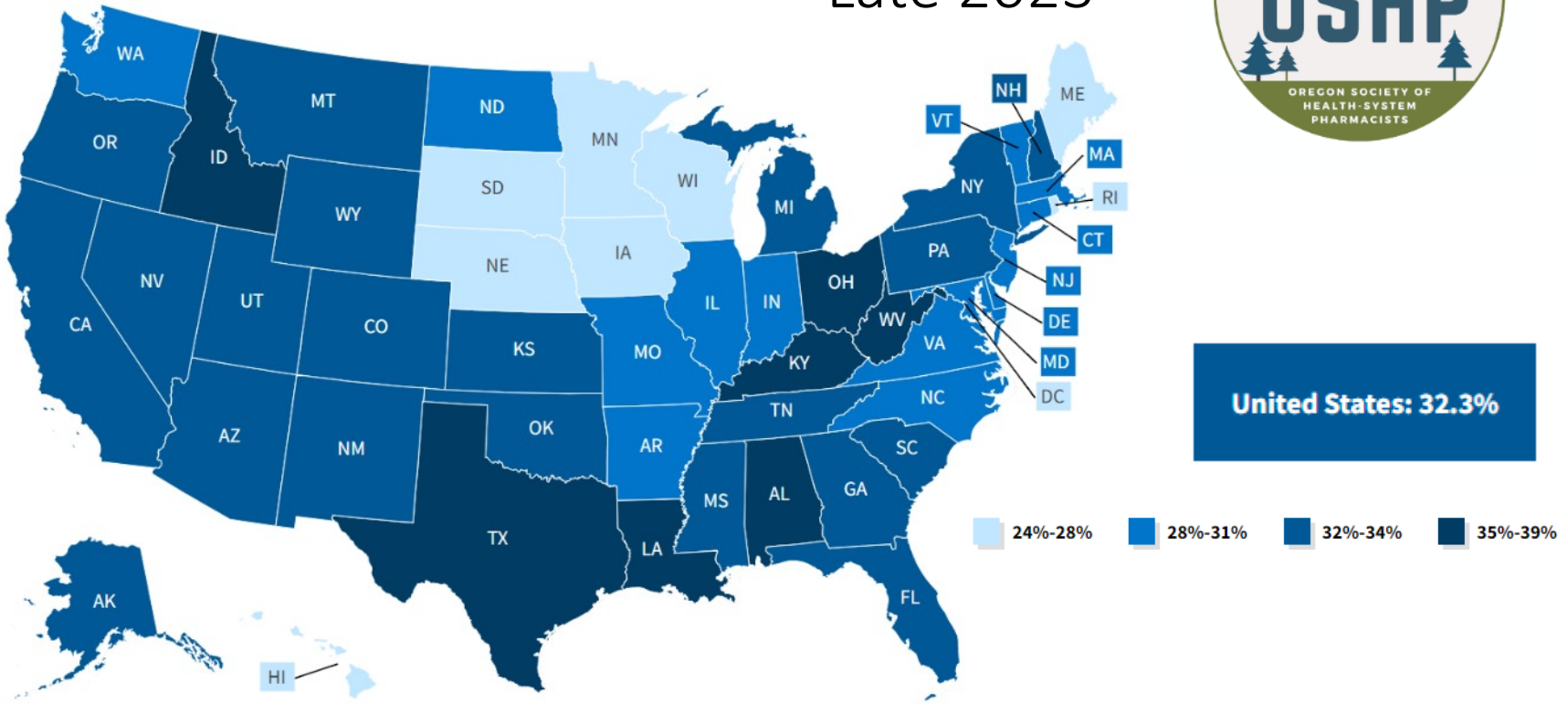


NOTE: Adults having symptoms of depressive or anxiety disorder were determined based on having a score of 3 or more on the Patient Health Questionnaire (PHQ-2) and/or Generalized Anxiety Disorder (GAD-2) scale. Household job loss status refers to whether anyone in the respondent's household experienced loss of employment income in the past four weeks.

SOURCE: KFF analysis of U.S. Census Bureau, Household Pulse Survey, 2023

https://www.kff.org/coronavirus-covid-19/issue-brief/the-implications-of-covid-19-for-mental-health-and-substance-use/

Adults with Anxiety and/or Depression Late 2023



https://www.kff.org/statedata/mental-health-and-substance-use-state-fact-sheets/

The Impact of Anxiety

The Impact of Anxiety

- Increased hospitalization
- Increased use and cost of healthcare
- Increased chronic illness and physical disability
- Increase in medically unexplained symptoms
- Increased memory impairment
- Increased loneliness
- Decreased independence and life satisfaction
- Decreased compliance with medical treatment

https://cdn.mdedge.com/files/s3fs-public/Document/September-2017/1003CP_Article3.pdf

Anxiety and Physical Health

- Increased prevalence of Anxiety Disorders
  - Cardiovascular Disease
  - Gastro-intestinal Disease
  - Respiratory Disease
  - Migraines
  - Chronic Pain
  - Cancer
- Odds of an Anxiety Disorder increase with increasing number of CMC's

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3797868/pdf/nihms500343.pdf

Anxiety and Physical Health

Those with Anxiety Disorders have

- Higher frequencies of some CMC's
  - Irritable Bowel Syndrome
  - Asthma
- Worse Symptom Severity and Impairment
  - Asthma
  - Cardiovascular Disease
  - Diabetes
- Increased risk for disease progression

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3797868/pdf/nihms500343.pdf

Anxiety and Physical Health

Patients with
multiple Comorbid Medical Conditions
can benefit from anxiety treatment
as much as
those with low medical comorbidity*

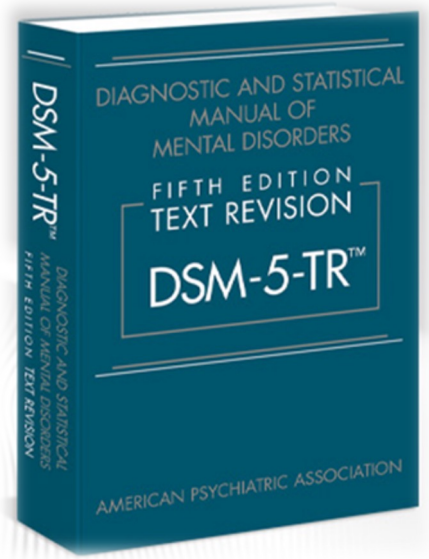
**(except maybe migraines)*

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3797868/pdf/nihms500343.pdf

Diagnostic Criteria

Generalized Anxiety Disorder

- Excessive anxiety or worry for >6m about a number of events or activities
- Individual finds it difficult to control the worry
- Three or more of the following are present
  - Restlessness or feeling keyed up or on edge
  - Being easily fatigued
  - Difficulty concentrating or mind going blank
  - Irritability
  - Muscle Tension
  - Sleep Disturbance



https://www.psychiatry.org/psychiatrists/practice/dsm

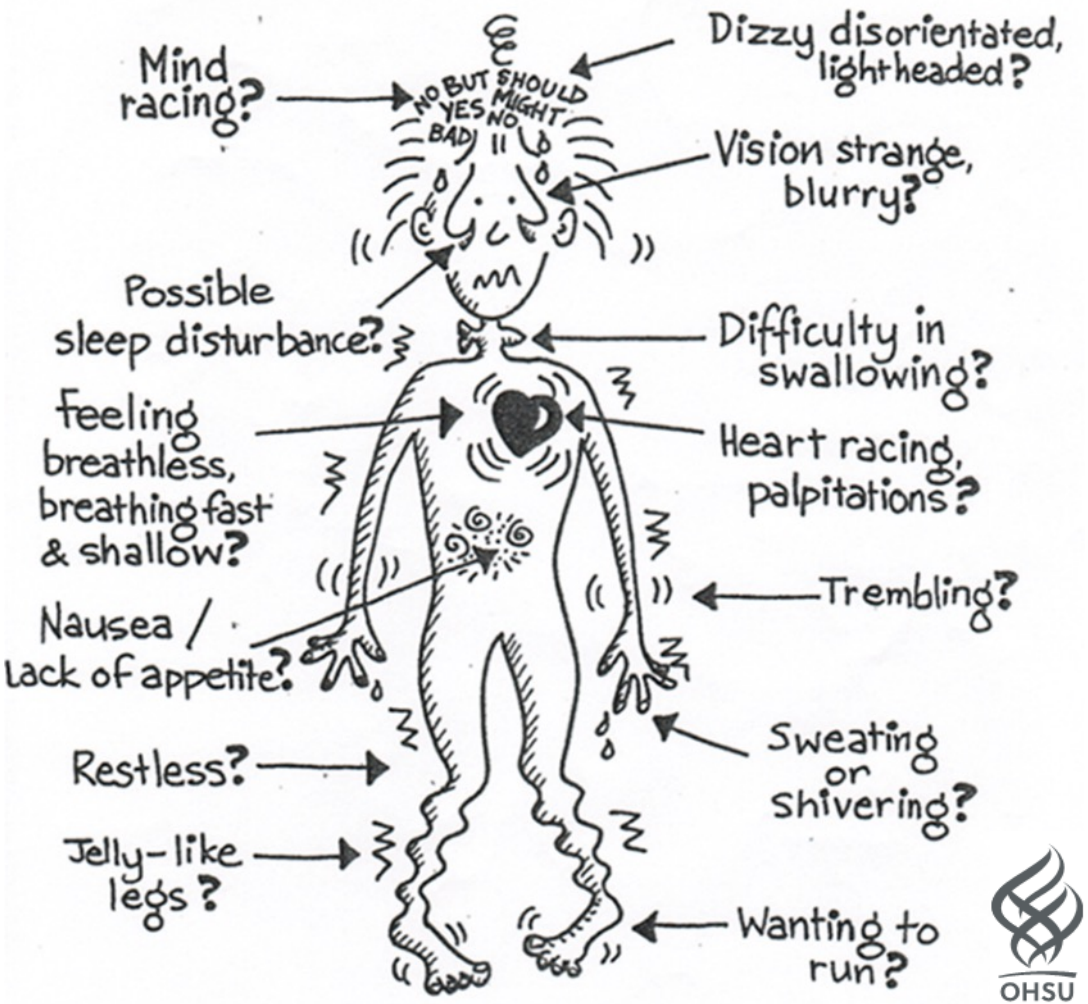
Panic Attack

Intense fear or discomfort that starts abruptly, peaks in 10 minutes and includes four or more of the following

- Palpitations, pounding heart or accelerated heart rate
- Sweating
- Trembling or Shaking
- Sensations of shortness of breath or smothering
- Feeling of choking
- Chest pain or discomfort
- Paresthesias
- Nausea or abdominal distress
- Feeling dizzy, unsteady, lightheaded or faint
- Derealization or depersonalization
- Fear of losing control or going crazy
- Chills or hot flashes
- Fear of dying

https://www.psychiatry.org/psychiatrists/practice/dsm

Panic Attack!!!



"Living With IT"

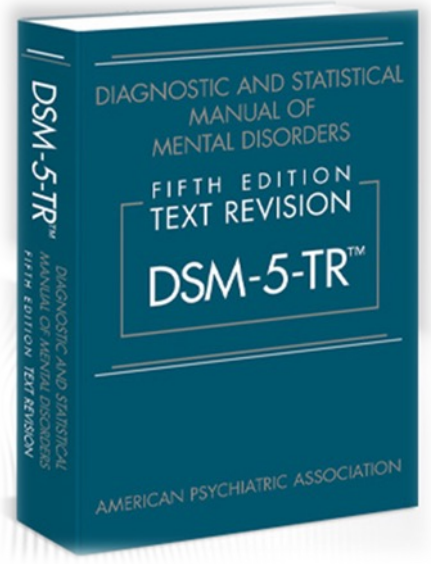
Beth Aisbett

http://www.bevaisbettartofanxiety.com/books.html

OHSU

Panic Disorder

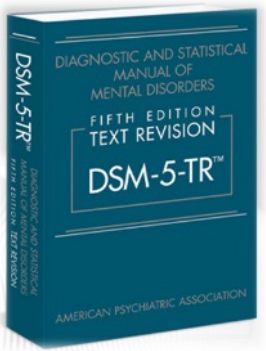
- Recurrent unexpected Panic Attacks
- At least one of the attacks has been followed by 1 month (or more) of one (or more):
  - Persistent concern about having additional attacks
  - Worry about the implications of the attack or its consequences
  - Significant change in behavior related to the attacks



https://www.psychiatry.org/psychiatrists/practice/dsm

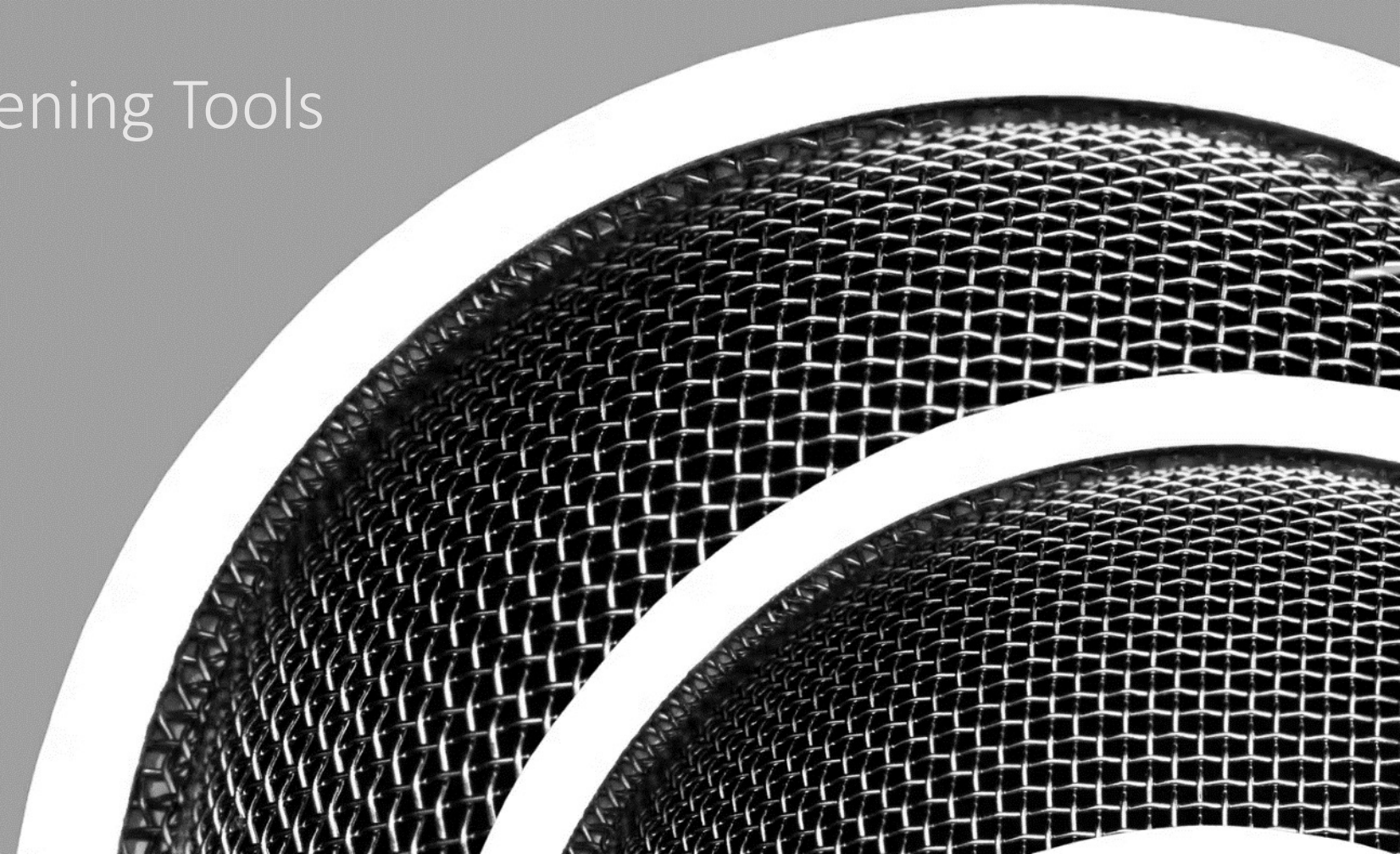
Social Anxiety Disorder

- A persistent fear of one or more social or performance situations in which the person is exposed to unfamiliar people or to possible scrutiny by others. The individual fears that he or she will act in a way that will be embarrassing and humiliating
- Exposure to the feared situation almost invariably provokes anxiety, which may take the form of a situationally bound or situationally pre-disposed Panic Attack
- The person recognizes that this fear is unreasonable or excessive
- The feared situations are avoided or else are endured with intense anxiety and distress
- The avoidance, anxious anticipation or distress in the feared social or performance situation(s) interferes significantly with the person's normal routine, occupational functioning, or social activities or relationships, or there is marked distress about having the phobia



https://socialanxietyinstitute.org/dsm-definition-social-anxiety-disorder
https://www.psychiatry.org/psychiatrists/practice/dsm

Screening Tools



Screening for Anxiety

Tool	Cutoff Score	Sensitivity	Specificity	Reference
GAD-7	10	89	82	http://www.ncbi.nlm.nih.gov/books/NBK126694/
	Scores of 5, 10, and 15 indicate mild, moderate and severe anxiety			
PDSR	8.75	89	100	https://www.ncbi.nlm.nih.gov/pubmed/16594812
Mini-SPIN	6	89	90	http://www.aafp.org/afp/2008/0815/p501.html
GAS	9	60	75	https://www.ncbi.nlm.nih.gov/pubmed/25271176
GAI	10	69.5	100	https://www.ncbi.nlm.nih.gov/pubmed/16805925

GAD-7

Over the last 2 weeks, how often have you been bothered by the following problems? *(Use "✔" to indicate your answer)*	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3

(For office coding: Total Score T____ = ____ + ____ + ____)

https://www.phqscreeners.com

GAD-7

GAD-7: Interpretation

GAD (10): 89% sensitivity, 82% specificity
PD (7): 74% sensitivity, 82% specificity
SAD: 72% sensitivity, 80% specificity
PTSD: 66% sensitivity, 81% specificity

Score of 5, 10 and 15 are the cut-offs for mild, moderate and severe anxiety

https://www.hiv.uw.edu/page/mental-health-screening/gad-7

PDSR

Panic Disorder Self-Report (PDSR)

		No	Yes
1	During the last six months, have you had a panic attack or a sudden rush of intense fear or anxiety?	☐	☐
If **YES**, please continue			
If **NO** (you have not experienced a panic attack), please leave the rest of this form blank			
When was the most recent time this occurred? (please record date)			
2	Was at least one panic attack unexpected, as if it came out of the blue?	☐	☐
3	Did it happen more than once?	☐	☐
4	If **YES** to 3, approximately how many panic attacks have you had in your lifetime?		
	If **NO** to 1, 2, and 3, please leave the rest of this form blank, otherwise continue		
5	Have you ever worried a lot (for at least one month) about having another panic attack?	☐	☐
6	Have you ever worried a lot (for at least one month) that having the attacks meant you were losing control, going crazy, having a heart attack, seriously ill, etc?	☐	☐
7	Did you ever change your behaviour or do something different (for at least one month) because of the attacks?	☐	☐
If **YES** to 5, 6 or 7 please answer the following questions:			
Think back to your most severe panic attack. Did you experience any of the following symptoms?			
8	Shortness of breath or smothering sensations?	☐	☐
9	Feeling dizzy, unsteady, lightheaded, or faint?	☐	☐
10	Palpitations, pounding heart, or rapid heart rate?	☐	☐
11	Trembling or shaking?	☐	☐
12	Sweating?	☐	☐
13	Feelings of choking?	☐	☐
14	Nausea or abdominal distress?	☐	☐
15	Numbness or tingling sensations?	☐	☐
16	Flushes (hot flashes) or chills	☐	☐
17	Chest pain or discomfort?	☐	☐
18	Fear of dying?	☐	☐
19	Fear of going crazy or doing something uncontrolled?	☐	☐

20. How much do these symptoms interfere with your daily functioning? (Please circle one)

0	1	2	3	4
Not at all	Mildly	Moderately	Severely	Very severely / disabling

21. How distressing do you find these symptoms? (Please circle one)

0	1	2	3	4
No distress	Mild distress	Moderate distress	Severe distress	Very severe

22	When you have bad panic attacks, does it often take less than ten minutes from the point at which the attack begins, to the point at which it reaches a peak or becomes most intense?	☐	☐
23	Just before you began having panic attacks, were you taking any drugs or excessive amounts (more than 4 cups daily) of stimulants (e.g. coffee, tea, or cola with caffeine)?	☐	☐
23a	If **YES**, what was it that you were taking?		
23b	How much of it were you taking (in cups, etc.)?		
24	Have you ever been diagnosed with a medical problem (e.g. hyperthyroidism, a seizure or cardiac condition, etc.) that could have caused your panic symptoms?	☐	☐

https://www.uspreventiveservicestaskforce.org/Home/GetFileByID/1899
https://cmit.cms.gov/CMIT_public/ListMeasures?q=suicide
https://callhelpline.org.uk/Download/Panic%20Disorder%20Self-Report%20(PDSR)%20Feb16.pdf

Panic Disorder Self Report - Scoring

- 24 questions related to panic disorder
- Items 1-3 must all be Yes
- Items 1-3, 5-19, and 22 are 1 point each
- Items 20 and 21 are each divided by 2
- Items 4, 23 and 24 are not scored

Cut off score is 8.75

89% Sensitivity, 100% Specificity

https://pubmed.ncbi.nlm.nih.gov/16594812/
https://pubmed.ncbi.nlm.nih.gov/1760593

Mini-SPIN

The Mini-SPIN Screening Tool for Social Phobia

RATE EACH OF THE FOLLOWING ITEMS FROM 0 TO 4:	*NOT AT ALL*	*A LITTLE BIT*	*SOMEWHAT*	*VERY MUCH*	*EXTREMELY*
Fear of embarrassment causes me to avoid doing things or speaking to people.	0	1	2	3	4
I avoid activities in which I am the center of attention.	0	1	2	3	4
Being embarrassed or looking stupid are among my worst fears.	0	1	2	3	4

NOTE: *A total score of 6 points or more is a positive screen.*

SPIN = Social Phobia Inventory.

Adapted with permission from Connor KM, Kobak KA, Churchill LE, et al. Mini-SPIN: a brief screening assessment for generalized social anxiety disorder. Depress Anxiety. 2001;14(2):139.

OSHP
OREGON SOCIETY OF HEALTH-SYSTEM PHARMACISTS

Sensitivity 89%

Specificity 90%

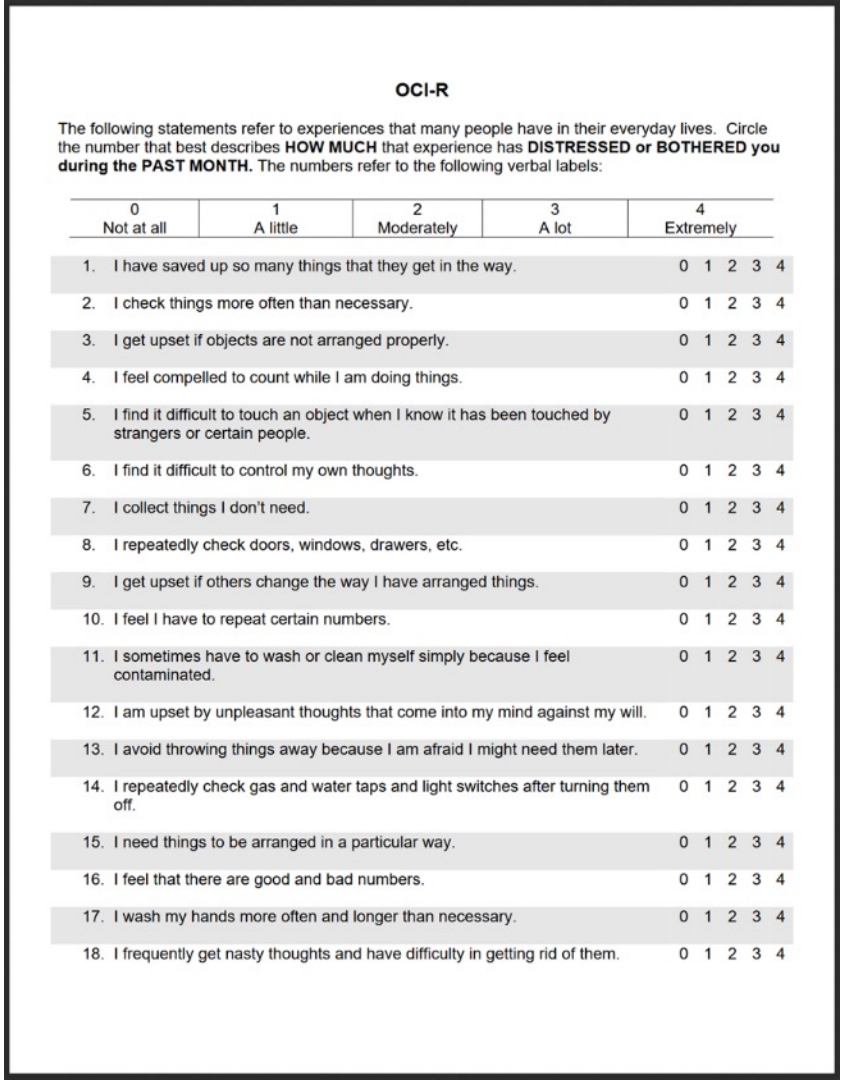
PPV 53%

NPV 98%

https://pubmed.ncbi.nlm.nih.gov/12958087/
https://pubmed.ncbi.nlm.nih.gov/18756659/

Shorter version of the 17-item SPIN

https://psychology-tools.com/test/spin



OCI-R

The following statements refer to experiences that many people have in their everyday lives. Circle the number that best describes **HOW MUCH** that experience has **DISTRESSED or BOTHERED you during the PAST MONTH.** The numbers refer to the following verbal labels:

0 Not at all	1 A little	2 Moderately	3 A lot	4 Extremely

1.	I have saved up so many things that they get in the way.	0 1 2 3 4
2.	I check things more often than necessary.	0 1 2 3 4
3.	I get upset if objects are not arranged properly.	0 1 2 3 4
4.	I feel compelled to count while I am doing things.	0 1 2 3 4
5.	I find it difficult to touch an object when I know it has been touched by strangers or certain people.	0 1 2 3 4
6.	I find it difficult to control my own thoughts.	0 1 2 3 4
7.	I collect things I don't need.	0 1 2 3 4
8.	I repeatedly check doors, windows, drawers, etc.	0 1 2 3 4
9.	I get upset if others change the way I have arranged things.	0 1 2 3 4
10.	I feel I have to repeat certain numbers.	0 1 2 3 4
11.	I sometimes have to wash or clean myself simply because I feel contaminated.	0 1 2 3 4
12.	I am upset by unpleasant thoughts that come into my mind against my will.	0 1 2 3 4
13.	I avoid throwing things away because I am afraid I might need them later.	0 1 2 3 4
14.	I repeatedly check gas and water taps and light switches after turning them off.	0 1 2 3 4
15.	I need things to be arranged in a particular way.	0 1 2 3 4
16.	I feel that there are good and bad numbers.	0 1 2 3 4
17.	I wash my hands more often and longer than necessary.	0 1 2 3 4
18.	I frequently get nasty thoughts and have difficulty in getting rid of them.	0 1 2 3 4

Obsessive Compulsive Inventory - Revised

Cutoff Score: 21

http://www.caleblack.com/psy5960_files/OCI-R.pdf
https://link.springer.com/content/pdf/10.1007/s10862-005-2411-y.pdf
https://www.sciencedirect.com/science/article/pii/S2211364920300786

Screening for Anxiety

- Most screening tools were developed for younger adults
- Several screening tools work well
  - Geriatric Anxiety Inventory
  - Geriatric Anxiety Scale
  - Worry Scale
  - STAI, BAI, PSWQ, STICSA

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5896683/pdf/cia-13-573.pdf

Geriatric Anxiety Presents Differently

- High medical comorbidities
  - Anxiety often expressed somatically
  - Sleep difficulties are rather common
- High psychiatric comorbidities
  - Depression (1/4 cases of MDD)
  - Dementia
- Aging process

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5896683/pdf/cia-13-573.pdf
https://cdn.mdedge.com/files/s3fs-public/Document/September-2017/1003CP_Article3.pdf

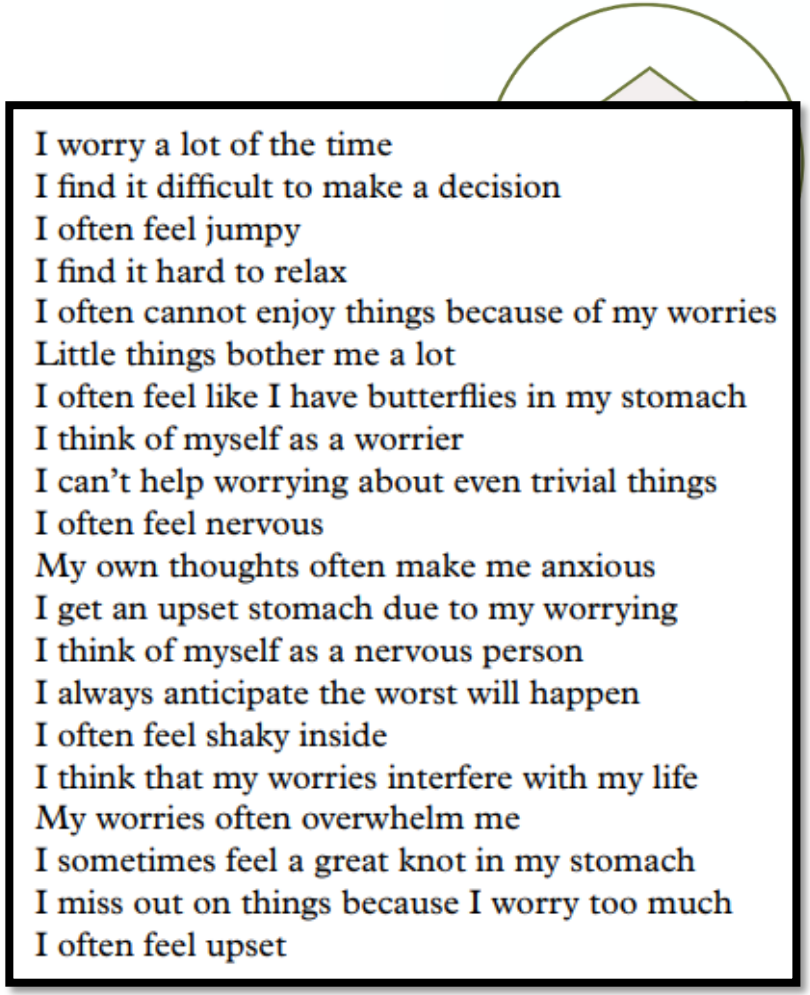
Geriatric Anxiety Presents Differently

- More concerns about health
- Less concerns about finance and family
- More likely to minimize symptoms
- More likely to be direct (vs. shame or guilt)
- More likely to report things not on surveys
- Less likely to endorse absolutes
- Less commonly report negative affect

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5896683/pdf/cia-13-573.pdf

Geriatric Anxiety Inventory

- Self-report
- 20 agree/disagree items
- Cutoff score >8
- 69.5% sensitivity, 100% specificity
- Less useful for severity
- Available as GAI-SF
  - 1, 6, 8, 10, 11
  - >2, 78%, 98.3%



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5896683/pdf/cia-13-573.pdf
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4501012/pdf/S1041610214001586a.pdf
https://www.ncbi.nlm.nih.gov/pubmed/16805925

Geriatric Anxiety Scale

- Self-report
- 30 scaled items
  - Somatic
  - Cognitive
  - Affective
- Cutoff score >9
- 60% sensitivity
- 75% specificity
- Available as GAS-10

	Not at all (0)	Sometimes (1)	Most of the time (2)	All of the time (3)
1. My heart raced or beat strongly.				
2. My breath was short.				
3. I had an upset stomach.				
4. I felt like things were not real or like I was outside of myself.				
5. I felt like I was losing control.				
6. I was afraid of being judged by others.				
7. I was afraid of being humiliated or embarrassed.				
8. I had difficulty falling asleep.				
9. I had difficulty staying asleep.				
10. I was irritable.				
11. I had outbursts of anger.				
12. I had difficulty concentrating.				
13. I was easily startled or upset.				
14. I was less interested in doing something I typically enjoy.				
15. I felt detached or isolated from others.				
16. I felt like I was in a daze.				
17. I had a hard time sitting still.				
18. I worried too much.				
19. I could not control my worry.				
20. I felt restless, keyed up, or on edge.				
21. I felt tired.				
22. My muscles were tense.				
23. I had back pain, neck pain, or muscle cramps.				
24. I felt like I had no control over my life.				
25. I felt like something terrible was going to happen to me.				
26. I was concerned about my finances.				
27. I was concerned about my health.				
28. I was concerned about my children.				
29. I was afraid of dying.				
30. I was afraid of becoming a burden to my family or children.				

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5896683/pdf/cia-13-573.pdf
https://www.ncbi.nlm.nih.gov/pubmed/25271176
https://gerocentral.org/wp-content/uploads/2013/03/Geriatric-Anxiety-Scale-v2.0_FINAL.pdf

Treating Anxiety Disorders

Thorough medical workup

Education and Lifestyle Modification

Behavioral and Cognitive Approaches

Thorough Medical Workup

Anxiety and Physical Health

- Start with a thorough medical work up
  - Neurologic
  - Endocrine (thyroid, pheo, carcinoid)
  - Mitral valve prolapse
- Evaluate for Substance Abuse
  - Both intoxication and withdrawal
  - Don't forget alcohol, caffeine and nicotine
- Evaluate for other psychiatric disorders

http://www.aafp.org/afp/2000/1001/p1591.html
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC427612/

Organic Anxiety

Anxiety Secondary to Organic Causes

- Onset of anxiety symptoms after age 35 years
- Lack of personal or family history of an anxiety disorder
- Lack of childhood history of significant anxiety
- Absence of significant life events generating anxiety symptoms
- Lack of avoidance behavior
- Poor response to psychiatric treatment

Differential Diagnosis: Anxiety Secondary to Organic Factors

- Medical Illness
  - Brucellosis
  - Carcinoid syndrome
  - Cerebral arteriosclerosis
  - Chronic obstructive pulmonary disease
  - Coronary insufficiency
  - Diabetes mellitus
  - Drug withdrawal: anxiolytic agents, caffeine, alcohol, sedatives, opiates
  - Pancreatic tumor
  - Pheochromocytoma
  - Psychomotor epilepsy, complex partial seizures
  - Pulmonary emboli
  - Thyroid disease (hypo- and hyperthyroidism, thyroiditis)
- Medications
  - Analgesics
  - Anticholinergics
  - Antihistamines
  - Antihypertensives
  - Antimicrobials
  - Calcium channel blockers
  - Estrogen
  - Insulin
  - Muscle relaxants
  - Non-steroid anti-inflammatory drugs
  - Sedatives
  - Sympathomimetics
  - Theophylline

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC427612/

Education and Lifestyle Modification

Education and Lifestyle Modification

- Educate about the cycle of anxiety

  http://www.jabfm.org/content/22/2/175.full.pdf+html
- Regular exercise counteracts anxiety

  http://ajp.psychiatryonline.org/doi/full/10.1176/appi.ajp.162.12.2376
- Avoid alcohol, caffeine, and cannabis

  http://www.jabfm.org/content/22/2/175.full.pdf+html

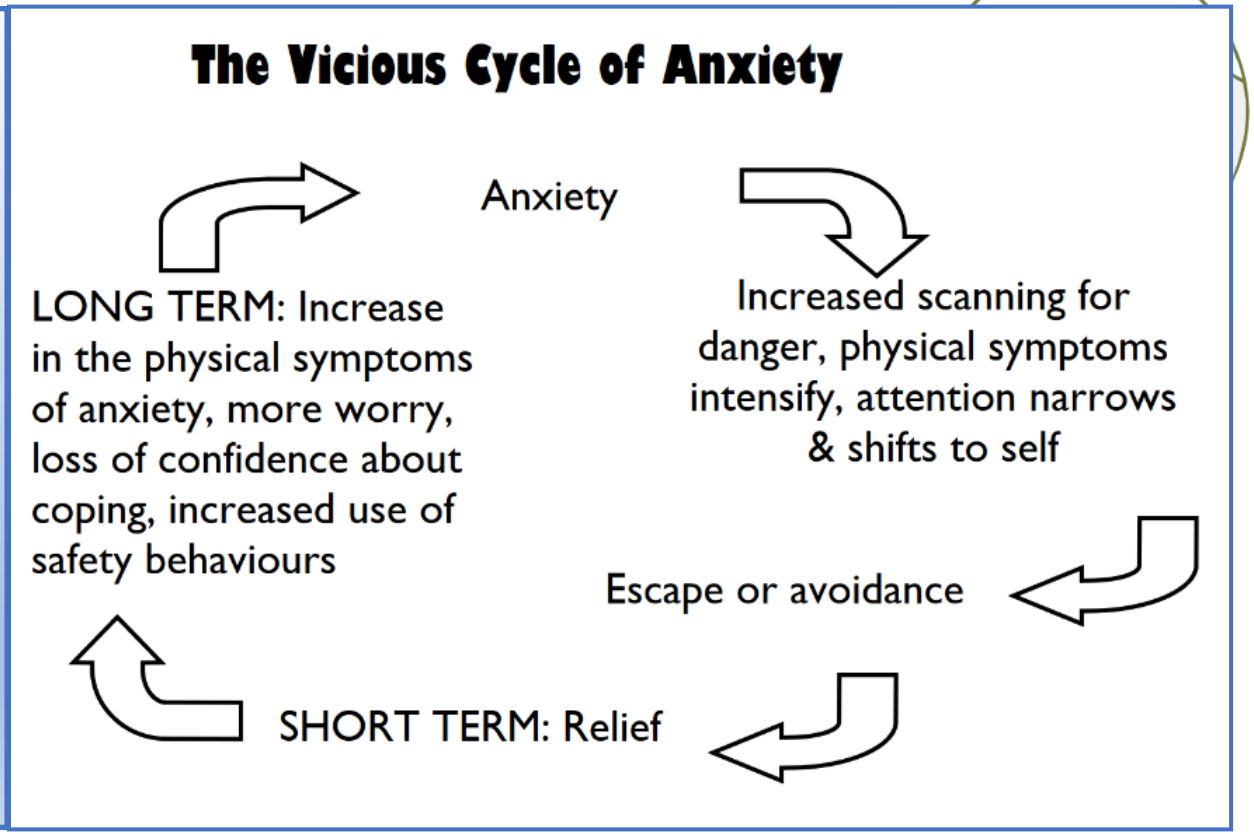
  https://www.med.upenn.edu/cbti/assets/user-content/documents/s11920-017-0775-9.pdf
- Practice good sleep hygiene

  http://www.jabfm.org/content/22/2/175.full.pdf+html

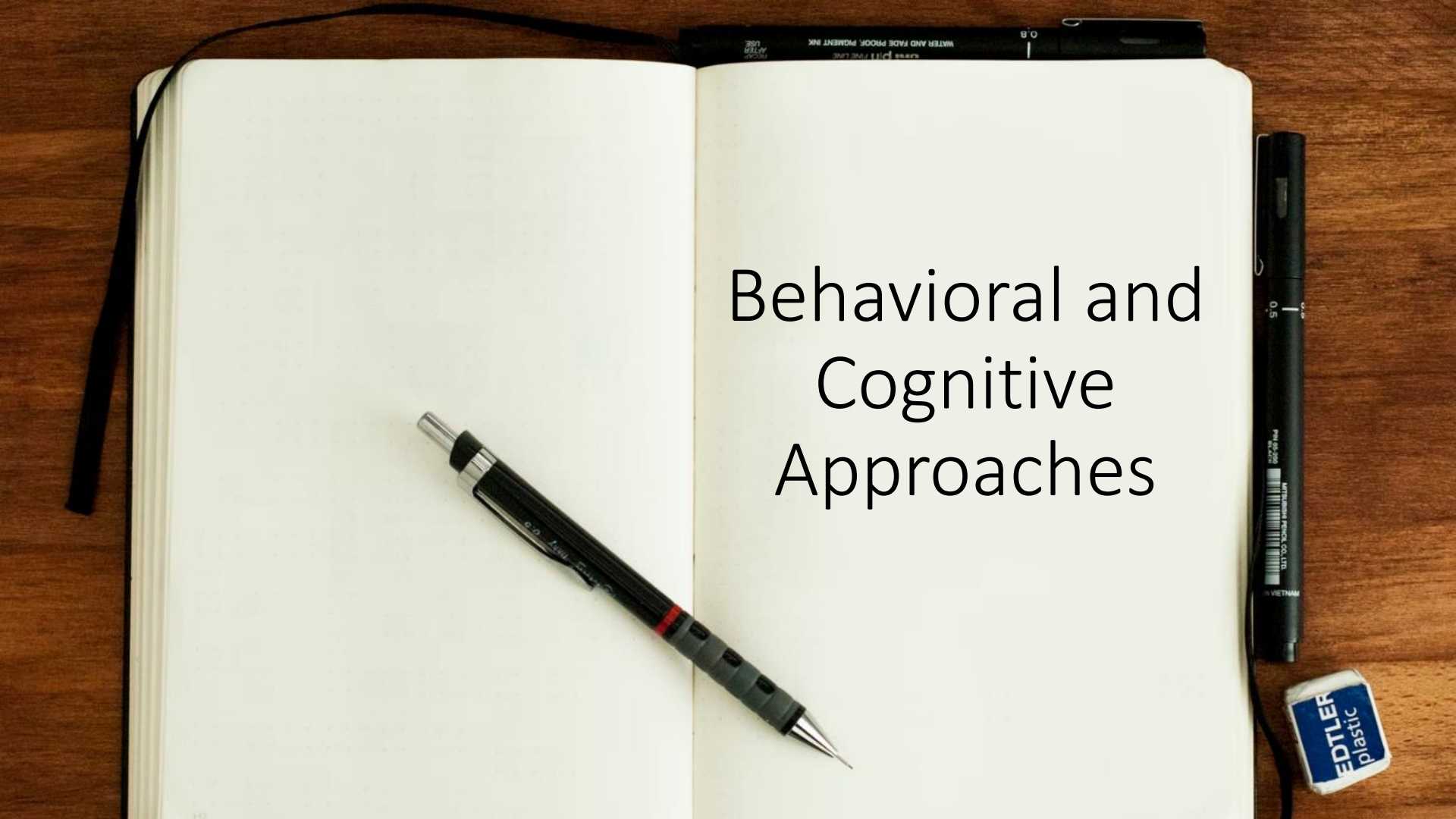
  https://www.cci.health.wa.gov.au/~/media/CCI/Mental%20Health%20Professionals/Sleep/Sleep%20%20Information%20Sheets/Sleep%20Information%20Sheet%20-%2004%20-%20Sleep%20Hygiene.pdf

Our goal is *managing* anxiety, rather than erasing it

Educate About The Cycle of Anxiety



https://www.cci.health.wa.gov.au/-/media/CCI/Mental-Health-Professionals/Panic/Panic---Information-Sheets/Panic-Information-Sheet---03---The-Vicious-Cycle-of-Anxiety.pdf

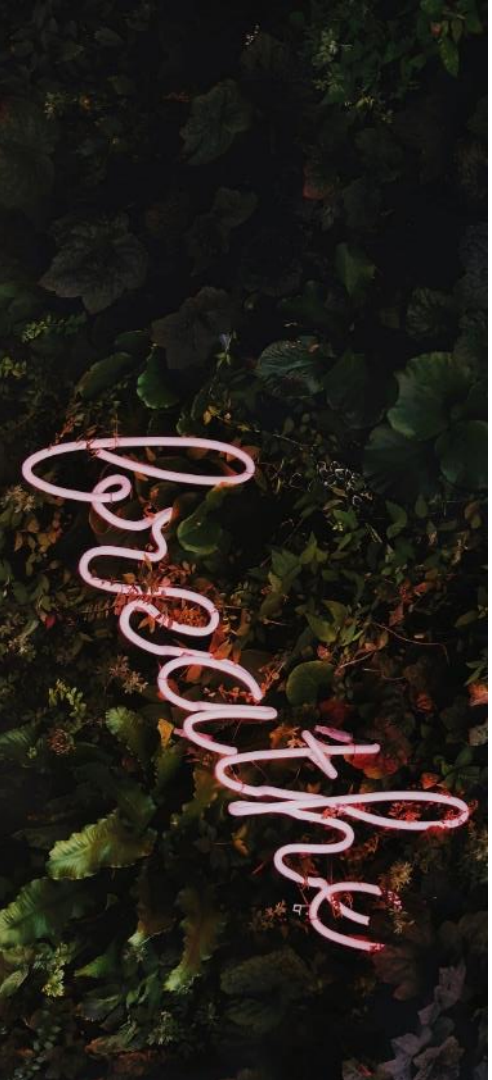


Behavioral and Cognitive Approaches

Behavioral & Cognitive Approaches

- Address behavioral avoidance with gradual exposure
- Address cognitive distortions with evidence
- Address physical symptoms with DB and PMR
- Consider Cognitive Behavioral Therapy

http://www.jabfm.org/content/22/2/175.full.pdf+html



Diaphragmatic Breathing

- Increases parasympathetic tone
  - Slows heartrate
  - Decreases blood pressure
  - Increases oxygen
  - Decreases carbon dioxide
- Practice for five minutes twice daily
- Use as needed

http://www.anxietybc.com/sites/default/files/CalmBreathing.pdf
https://www.psychology.uga.edu/sites/default/files/CVs/Clinic_Diaphragmatic_Breathing.pdf
https://www.cci.health.wa.gov.au/~/media/CCI/Mental-Health-Professionals/Anxiety/Anxiety---Information-Sheets/Anxiety-Information-Sheet---08---Breathing-Retraining.pdf

Progressive Muscle Relaxation

- Deliberately ordered tensing and relaxation of muscle groups
- 65% Panic-free at 12 weeks, 82% at 1 year
  - vs. 74% and 89% with CBT
- Keys for use
  - Often helpful for bedtime relaxation
  - Practice the same system
  - Use a tape or video to help

http://www.ncbi.nlm.nih.gov/pubmed/7887873?dopt=Abstract
https://www.youtube.com/watch?v=86HUcX8ZtAk
https://www.cci.health.wa.gov.au/~/media/CCI/Mental-Health-Professionals/Anxiety/Anxiety---Information-Sheets/Anxiety-Information-Sheet---08---Breathing-Retraining.pdf

Cognitive Behavioral Therapy

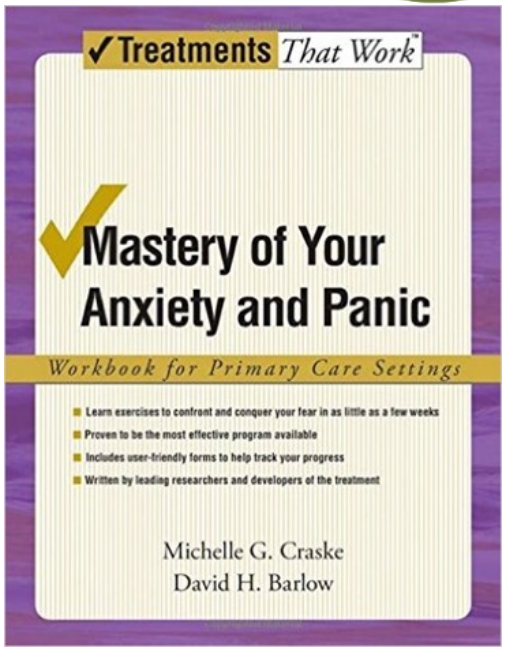
- Effects persist at least 6-12 months
- Cognitive component may be more effective
- More effective than either Supportive Therapy or Psychodynamic Therapy
- May outperform pharmacotherapy*
  - Response rates of 56%
  - Highly motivated problem solvers
  - Cost-effective

http://www.aafp.org/afp/2000/1001/p1591.html
https://www.uptodate.com/contents/generalized-anxiety-disorder-in-adults-cognitive-behavioral-therapy-and-other-psychotherapies
*https://pubmed.ncbi.nlm.nih.gov/26422604/

Cognitive Behavioral Therapy

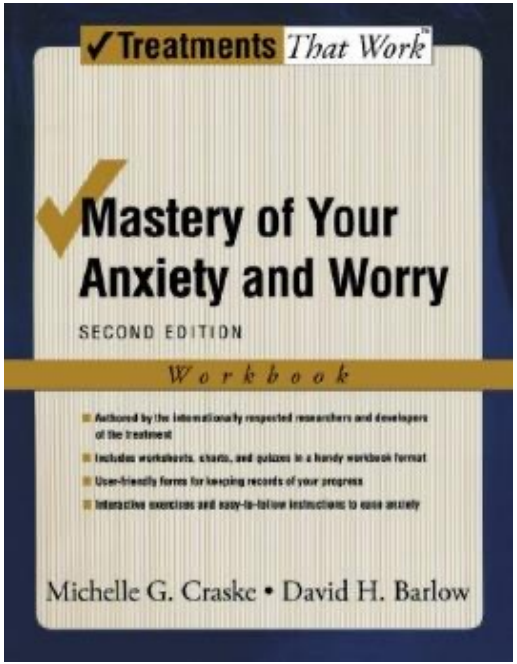
- Usually lasts 6-15 sessions
- Addresses the **cognitive**, **physical** and **behavioral** symptoms of anxiety
  - Education
  - Self-monitoring
  - Relaxation training
  - Cognitive Restructuring
  - Imagery Exposure
  - Situational Exposure
  - Relapse Prevention

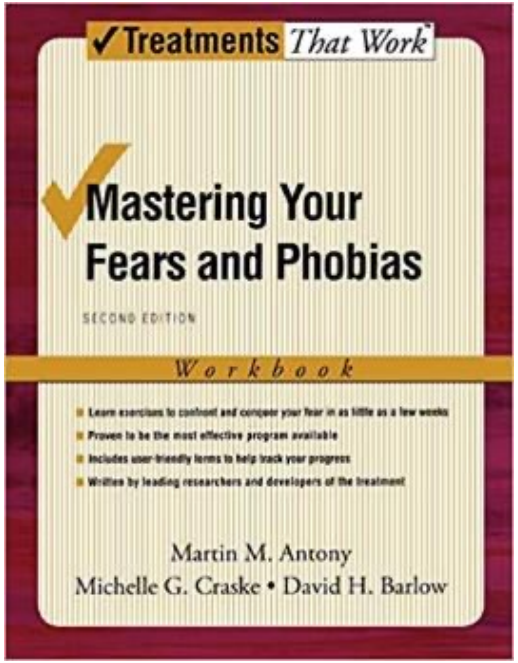
https://www.uptodate.com/contents/generalized-anxiety-disorder-in-adults-cognitive-behavioral-therapy-and-other-psychotherapies

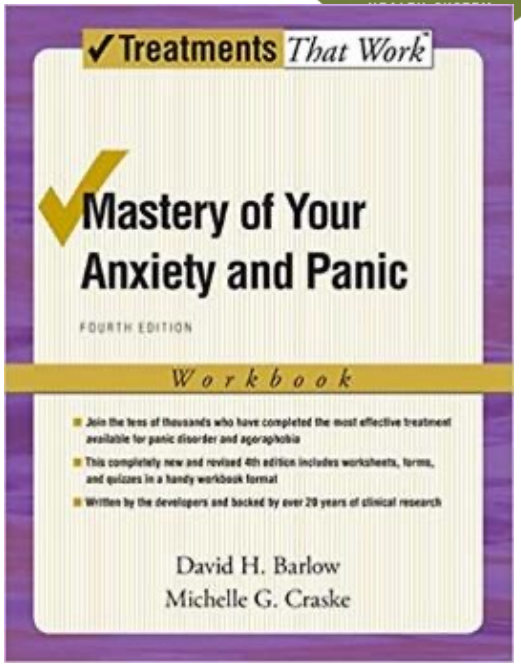


https://www.powells.com/book/-9780195311341

But Everyone's Full!







Additional Self-Help Resources

https://www.keltyskey.com

GOVERNMENT OF WESTERN AUSTRALIA

Centre for Clinical Interventions

https://www.cci.health.wa.gov.au/Resources/Looking-After-Yourself

Pharmacologic Treatment of Anxiety Disorders

Treatment Recommendations

Canadian Practice Guidelines for Anxiety Disorders (2014)
https://bmcpsychiatry.biomedcentral.com/track/pdf/10.1186/1471-244X-14-S1-S1

American Psychiatry Association (2009-2013)
https://www.psychiatry.org/psychiatrists/practice/clinical-practice-guidelines

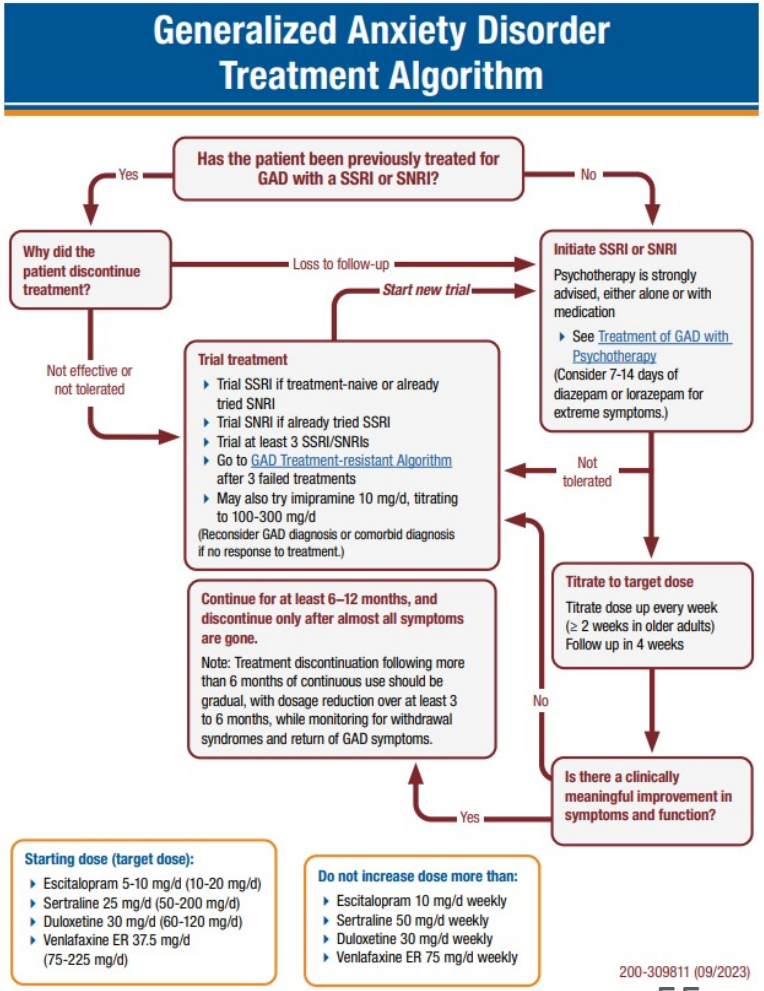
World Federation of Biological Psychiatry (2022)
https://doi.org/10.1080/15622975.2022.2086295

National Institute for Health and Clinical Excellence (2011)
https://www.nice.org.uk/guidance/cg113

Oregon Health Authority Mental Health Clinical Advisory Group (MHCAG)

Recommendations and Resources

https://www.oregon.gov/oha/hpa/dsi-pharmacy/pages/mhcag-recommendations.aspx



Neurochemical Theories of Anxiety

Noradrenergic Model

- Autonomic nervous system is hypersensitive and overreactive to various stimuli
- Drugs that modulate noradrenergic activity in the locus ceruleus or raphe nucleus are anxiolytic

GABA Receptor Model

- GABA is the major inhibitory neurotransmitter in the CNS and modulates NE, 5HT and dopamine
- Drugs that enhance the inhibitory effects of GABA reduce neuronal excitability and are anxiolytic

Treatment Considerations

- Educate, shared decision making
- Anxiety disorders have a waxing and waning course, treatment should continue for 6-12 months after response/remission
- Anxiety disorders are often chronic, **goal is to improve functionality** not necessarily to “cure” anxiety
- Useful to monitor clinical improvement using a validated grading scale (HAM-A, GAD-7)

Drug Classes Studied in Anxiety Disorders

Drug Class	Panic	GAD	SAD
SSRIs	X	X	X
SNRIs	X	X	X
TCAs	X	X	
Pregabalin		X	X
Benzodiazepines	X	X	X
Buspirone		X	
Hydroxyzine		X	
Atypical antipsychotics		X	
Misc (bupropion, mirtazapine)	X	X	

SSRIs/SNRIs in Treatment of Anxiety

- First line treatment
- Acute  symptoms (restlessness, jitteriness, insomnia) can occur in the first days to weeks; minimized by using low starting doses
- Anxiolytic effect can take 2-4 weeks (up to 6-8 weeks in some patients)
- Ideal in the setting of co-morbid depression

Is there a preferred agent?

	Slee, A. et.al. Lancet 2019	Kong, W. et.al. Front. Pharmacol 2020
Number of studies	89	32
Efficacy measurement	Mean difference in change of HAM-A score	Proportion with final score <7 on HAM-A
Tolerability measurement	Study discontinuation for any cause	Study discontinuation for adverse effects
Study duration 4-26 weeks, (average 8-10 weeks), primarily vs. placebo (small proportion vs. active drug but no direct SSRI-SNRI comparisons)		

Is there a preferred agent?

Most evidence for efficacy & tolerability

- Escitalopram, venlafaxine, duloxetine

Effective, less tolerable

- Paroxetine

Tolerable, slightly less effective

- Sertraline, fluoxetine (smaller sample sizes)

Common Adverse Effects

SSRIs	SNRIs
• Nausea • Vomiting • Dizziness • Insomnia • Agitation • Headache • Sexual dysfunction • Sweating • Urinary retention	• Nausea • Vomiting • Dizziness • Insomnia • Anxiety • Headache • Somnolence • Decreased appetite • Sexual dysfunction

Comparative Adverse Effects

- **Nausea and vomiting**: Venlafaxine has the highest incidence of nausea
- **Weight gain**: Mirtazapine > paroxetine > citalopram, fluoxetine, sertraline, bupropion causes weight loss
- **Diarrhea**: Sertraline > bupropion, citalopram, fluoxetine, fluvoxamine, mirtazapine, paroxetine, venlafaxine
- **Hypertension**: Duloxetine & venlafaxine
- **Withdrawal**: Paroxetine & venlafaxine > other SSRIs; Lowest with fluoxetine
- **Sexual Dysfunction**: Bupropion < SSRIs; Paroxetine > other SSRIs

SSRIs/SNRIs in Treatment of Anxiety

- Highest estimates of response ranges 60-75%
- Ensure adequate trial duration (AT LEAST 4 weeks)
- Push the dose
- Address substance abuse, medication adherence, psychoeducation
- Non-pharm modalities (CBT etc)

Adjunctive/Second Line Therapies

Pregabalin

Quetiapine XR

Buspirone

Hydroxyzine

Anti-Adrenergics

Benzos

Pregabalin

First line adjunct or monotherapy, 150-600 mg/day

Pros	Cons
High quality evidence for efficacy	Cost, lack of FDA approval
Faster onset (1-3 weeks)	Side effect profile (dizziness, sedation, impaired cognition)
Appears effective for somatic sx	Controlled substance, potential for misuse, avoid with SUD
Lower dropout rate vs. benzos	Withdrawal symptoms

Quetiapine XR

Second line, primarily studied as monotherapy

50 – 150 mg/day

Pros	Cons
Moderate evidence for use in GAD	2016 meta-analysis (Maneeton et al.) found benefit with 50 mg & 150 mg doses only
Potentially faster onset	Significant side effect profile
Helpful with sleep	Evidence only with XR product

Buspirone

Second line adjunct or monotherapy

10 – 30 mg/day

Pros	Cons
Evidence for use in GAD	Several studies showed no benefit
Different mechanism, may be helpful in SSRI/SNRI failure	Frequent dosing, slow onset

Hydroxyzine

Second line adjunct or monotherapy

25 – 100 mg/day

Pros	Cons
Effective for GAD vs. placebo	Older data, smaller studies, lack of standardized diagnostic criteria
Similar dropout rate vs. other agents	Frequent dosing, less safe in elderly patients
Helpful with sleep	Sedation, anticholinergic effects

Anti-Adrenergics

- May help with hypervigilance, sleep disturbance (nightmares) and activation
- Propranolol 10 – 40 mg po 3-4x/day
  - Best evidence with treating somatic sx (tachycardia, sweating) in PTSD and situational anxiety (giving a speech)
- Clonidine 0.1 - 0.3 mg po bedtime and PRN
- Prazosin 1 – 3 mg po bedtime (up to 15 mg studied)

Central alpha-adrenergic agonists (e.g. clonidine) ↓ sympathetic outflow from the alpha-2 receptor sites in the brain, ↓ peripheral vascular resistance and slows surge of catecholamines. Prazosin is a central and peripheral alpha-adrenergic antagonist.

Propranolol competitively blocks response to B1/B2 activation resulting in ↓HR and BP

Benzos!!!

Benzodiazepines in Treatment of Anxiety Disorders

Effective

- Potentiate the effects of GABA, main inhibitory neurotransmitter
- Limited by sedation, dizziness, cognitive impairment, abuse potential
- 2020 FDA Black Box warning for physical dependence, abuse, withdrawal

Long Term Use

BZRA = Benzodiazepine Receptor Agonists

	Rosenqvist, et. al. Am J Psychiatry 2024 Danish Cohort Study (20 years)
Use of BZRA >1 year	Overall risk 15%, highest with Z drugs
Use of BZRA > 7 years	Overall risk 3%, highest with Z drugs
Dose escalation	7% of continuous users escalated in doses > recommended max Psychiatric comorbidity & substance use highly associated
Utilization	46% single fill 22% > 5 fills

Benzodiazepine Discontinuation

	Maust, et.al. JAMA Network Open 2023 Retrospective review
Non-opioid exposed	Adj cumulative incidence of death after 1 year = **5.5%** (Discontinued) Adj cumulative incidence of death after 1 year = **3.5%** (Continued)
Opioid exposed	Adj cumulative incidence of death after 1 year = **6.3 %** (Discontinued) Adj cumulative incidence of death after 1 year = **3.9 %** (Continued)
	Optum claims data over 4 year period (2013 – 2017) Excluded cancer, hospice patients, liquid fills

Known Risks

- Elderly
  - Cognitive Impairment/Falls
  - Delirium (especially inpatient)
  - No association between use and development of dementia
- Substance abuse
  - Higher in younger population
- Tolerance
  - Sedation effect more than anxiolytic effect
- Withdrawal syndromes

Role in Treatment

Greatest benefit with short term use (2 - 4 weeks)

- Anxiolytic effect starts in minutes
- Somatic symptoms (Panic Disorder)
- Initiating SSRI/SNRI
- Alternative agents and/or non-pharmacologic modalities should be used long-term
- Preferred agents: Lorazepam, Diazepam

Benzodiazepine Taper Schedules

- Abrupt discontinuation can result in withdrawal
  - Tremors, anxiety, psychosis, seizures, perceptual disturbances
- Different taper schedules, must be individualized
  - 25% reduction per week until 50% of original dosage is reached, then 1/8th dose reduction every 4-7 days
  - Therapy > 8 weeks, slow taper over 2-3 weeks
  - Therapy > 6 months, taper over 4-8 weeks
- Short half life drugs more likely to cause withdrawal
  - Avoid alprazolam

SSRI/SNRI taper schedules

- Abruptly stopping SSRI/SNRIs can result in withdrawal
  - Dizziness, fatigue, headache, nausea, insomnia, anxiety
  - Increased risk: higher dose, longer treatment duration, short half life, previous discontinuation syndrome

- Taper schedules vary in the medical literature and will need to be individualized per patient
  - SSRIs – 2-4 week taper is generally sufficient (EXCEPT for paroxetine which can require 3-5 week taper)
  - SNRIs – 2-4 week taper; venlafaxine associated with highest withdrawal symptoms and can require 4-6 week taper

Welcome to the Oregon Psychiatric Access Line (OPAL)

OPAL-K about Kids

OPAL-A about Adults

Phone

Toll-Free: 1-855-966-7255

Portland Metro: 503-346-1000

OPAL call center hours

9 a.m. – 5 p.m.

Monday through Friday, excluding major holidays

OPAL is not a walk-in clinic or in-person referral site

www.ohsu.edu/opal

How OPAL Works

Open
9 - 5
Excluding most national holidays

Call OPAL

OSHP
OREGON SOCIETY OF HEALTH-SYSTEM PHARMACISTS

Call is transferred to OPAL consultant

Consultant writes summary

Office staff send summary

Oregon ECHO Network

https://www.oregonechonetwork.org

Home About Project ECHO Programs Addiction Med HEAL-OR Accessibility and Technology About Oregon ECHO Network

Partners Contact Us Log In to CONNECT

WELCOME TO THE OREGON ECHO NETWORK

Connect and Learn

ECHO is an interactive educational and community-building experience that allows healthcare professionals throughout the state of Oregon to create a case-based learning environment through the convenience of video connection.

- Adult Mental Health II
- Child Psychiatry
- Deprescribing for Older Adults
- Foundations of SUD Care II
- Hepatitis C: Treatment and Elimination
- Implementing Pharmacologic Weight Management in Primary Care
- Leading Employee Well-being
- Nursing Facility Behavioral Health: SUDs
- Pain and SUDs in Dental Settings
- Rheumatic & Musculoskeletal Disease
- SUDs in Emergency Departments
- Suicide Prevention ECHO

- 7 Communities of Practice

MHCAG Recommendations & Resources

Pharmacy Policy and Programs Home

Contact Us

Oregon Prescription Drug Program (OPDP)

Northwest Prescription Drug Consortium

COMMITTEES AND WORKGROUPS

CCO Pharmacy Directors

Mental Health Clinical Advisory Group (MHCAG)

Pharmacy & Therapeutics Committee (P&T)

Community Pharmacy Partners Workgroup

MHCAG Recommendations

The MHCAG continues to work on developing treatment algorithms and other clinical practice recommendations and resources for clinicians, patients, families, friends and others.
Recommendations will be posted within 30 days of approval to this page and are based on scientific research and MHCAG member professional expertise.*

OPAL

Oregon Psychiatric Access Line (OPAL) is a clinical consultation service for prescribing providers only.

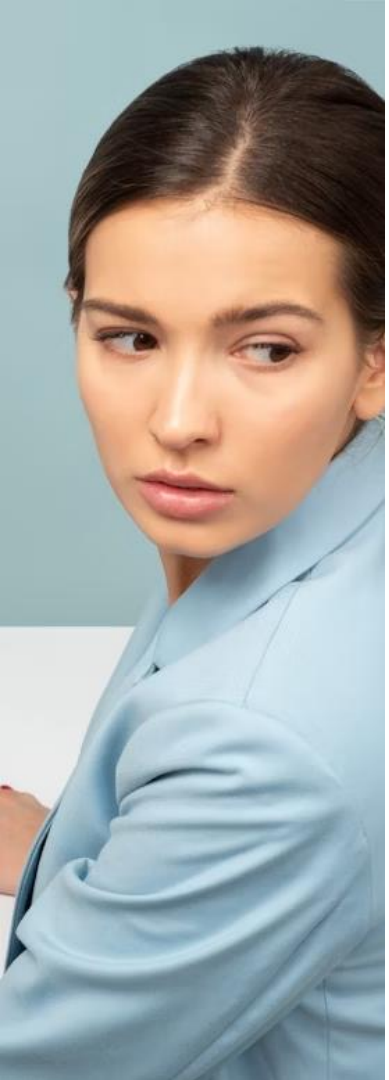
OPAL is available Monday – Friday (excluding major holidays) from 9am-5pm by calling 503-346-1000.

Clinical Practice Recommendations by Disorder

Anxiety Disorders

Bipolar Disorder

https://www.oregon.gov/oha/HPA/DSI-Pharmacy/Pages/MHCAG-Recommendations.aspx

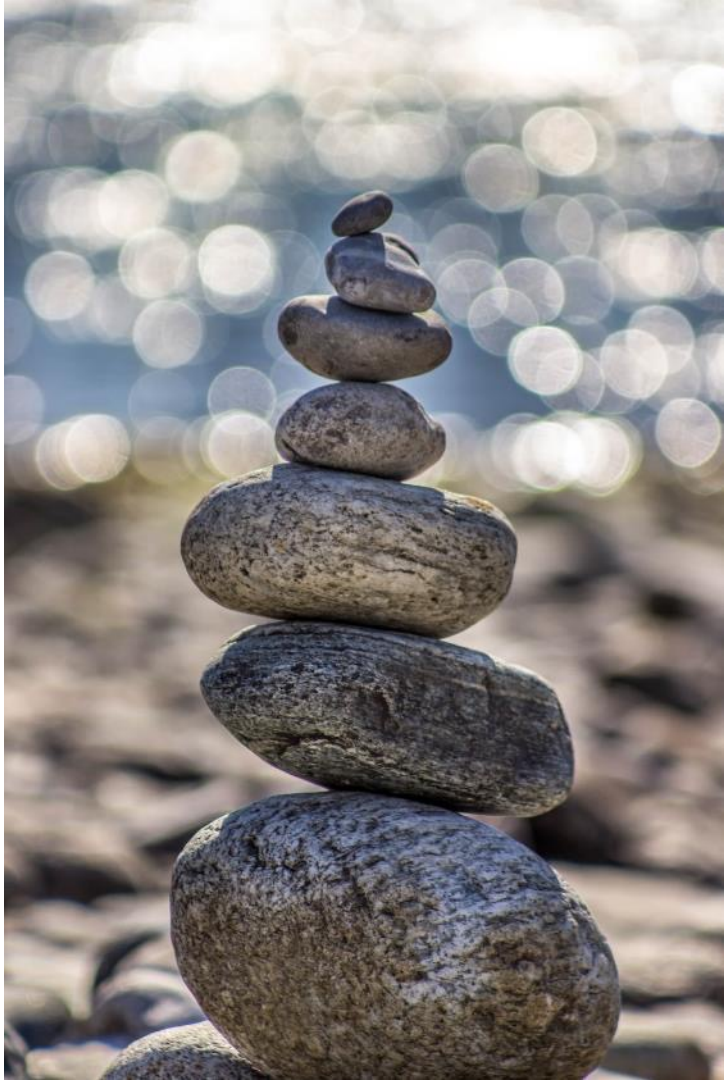


49-year-old woman with a long history of difficult-to-control worries in a variety of settings accompanied by fatigue, restlessness, sleep disturbance, and impaired concentration

- Screen and track with GAD-7
- Thorough medical work-up
- Cognitive and Behavioral Approaches
  - Educate about the cycle of anxiety
  - Regular exercise
  - Avoid alcohol, caffeine, and cannabis
  - Practice good sleep hygiene
  - Belly Breathing and Progressive Muscle Relaxation
- Refer for Cognitive Behavioral Therapy
- Consider an SSRI, SNRI, or Buspirone (if desired and not contraindicated)

Summary

- Anxiety Disorders are very common
- Anxiety Disorders commonly improve
- Efficient screening increases recognition
- Treatment begins with
  - A thorough medical work-up
  - Cognitive and Behavioral approaches
  - An SSRI or SNRI



Post- Test Questions

1. What percentage of adults in Oregon had anxiety and/or depression in 2023?

a. 17% b. 25% c . 33% d. 42%

2. Which Comorbid Medical Condition may predict a diminished response to treatment for anxiety?

a. Asthma b. Cardiovascular Disease c. Diabetes d. Migraines

3. Which of the following suggests a primary anxiety disorder rather than anxiety secondary to organic causes?

a. Onset of anxiety symptoms before age 35 years
b. Lack of personal or family history of anxiety disorder
c. Lack of childhood history of significant anxiety
e. Poor response to psychiatric treatment

Post Test Questions

4. In a recent meta-analysis which SSRI demonstrated the greatest efficacy as measured by the mean change in HAM-A scores?

a. Fluoxetine b. Citalopram c. Escitalopram d. Fluvoxamine

5. Which second line adjunctive agent does NOT have sedation/somnolence as a major side effect?

a. Quetiapine XR b. Buspirone c. Pregabalin d. Benzos

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