

Common Things Are Common: Generalized Anxiety, Panic, Adjustment Disorder and Subclinical Worries in the Busy Office Practice

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Disclosures

- No financial relationships to disclose
- Off label use of medications
- Adult psychopathology
- EBM.....as much as possible



Learning Objectives

1. Describe diagnostic criteria for major Anxiety Disorders along with their etiology, epidemiology, and differentials.
2. Perform an evidence based assessment of patients presenting with the symptom of anxiety.
3. Choose among therapeutic options for patients who meet criteria for select Anxiety Disorders and those with subclinical symptoms of anxiety and worry.



DSM-5 Anxiety & Related Disorders

- **Anxiety Disorders**
 - Separation Anxiety Disorder
 - Selective Mutism
 - Specific Phobia
 - Social Anxiety Disorder (Social Phobia)
 - Panic Disorder
 - Agoraphobia
 - Generalized Anxiety Disorder
 - Substance/Medication-Induced Anxiety Disorder
 - Anxiety Disorder Due to....
 - Other Specified Anxiety Disorder
 - Unspecified Anxiety Disorder
- **Obsessive-Compulsive and Related Disorders**
 - Obsessive-Compulsive Disorder
 - Reactive Attachment Disorder
 - Body Dysmorphic Disorder
 - Hoarding Disorder
 - Trichotillomania
 - Excoriation Disorder
 - ⋮
- **Trauma and Stressor-Related Disorders**
 - Reactive Attachment Disorder
 - Disinhibited Social Engagement Disorder
 - Posttraumatic Stress Disorder
 - Acute Stress Disorder
 - Adjustment Disorders
 - ⋮



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 - **Adjustment Disorders**
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Epidemiology

- 7.3% (5.3% – 10.4%) Global 12-month prevalence
- 28% lifetime prevalence (> than Depressive Disorders)
- Primary and comorbid anxiety - 75% of all psychiatric disorders
- 3 fold increase in use of medical services by pts with Anxiety Disorders
- On average 10 health care visits before correct Dx made
- Mean time to tx 10 years
- Of those with anxiety disorder and depressive symptoms in last 12 mos
 - 25.4% reported work loss in last 30 days
 - 48% reported they cut back on work in last 30 days
 - 4.5 “impaired” work days in last 30 days

Baxter, A. J., et al. (2014). *Psych Med*, 44(11), 2363-2374.

Janssen, E. H., et al. (2012). *General Hosp Psych*, 34(5), 460-467.

Kessler, R. C., et. al. (2005). *Arch Gen Psychiat*, 62(6), 593-602.

Roy-Byrne, P. (2015). *Dialogues Clin Neurosci*, 17(2), 191.



The Problem of Anxiety in Primary Care

- 19.5% had ≥ 1 Anxiety Disorder
 - 7.6% GAD
 - 6.8% Panic Disorder
 - 3.0% Adjustment Disorders
-
- 14-36% w/ Anxiety Disorders are recognized
 - 42% received Rx only
 - 25% receive an adequate trial of Rx
 - 4% receive counseling/therapy only
 - 13% combined Rx and counseling/therapy
 - 41% reported no current treatment



Differentials and Comorbidities

ARDS	Body Dysmorphic Disorder
Addison's Disease	Brief Psychotic Disorder
Adjustment Disorder	Bulimia
Adrenal Crisis	Caffeine-Related Disorders
Alcohol Related Psychosis	Cannabis abuse
Alcoholism	Cardiogenic Shock
Amphetamine- Related Disorders	Delirium
Anaphylaxis	DTs
Androgen Excess	Delusional Disorder
Anorexia Nervosa	Depression
Asthma	DM I
A-Fib	Diabetic Ketoacidosis
Atrial Tach	Dig toxicity
	Dissociative Disorders



Differentials and Comorbidities

Dysthymic Disorder	Hyperaldosteronism
Encephalopathy	Hypercalcemia
Epilepsy	Hyperparathyroidism
Esophageal Motility Disorders	Hyperprolactinemia
Esophageal Spasm	Hypersensitivity Reactions
Euthyroid Hyperthyroxinemia	Inhalant-Related Disorders
Factitious Disorder	Injectable Drug Use
Fibromyalgia	Insomnia
Folic Acid Deficiency	IBS
Food Poisoning	Lyme Disease
Gastritis	Malingering
Goiter	Meningitis
Hallucinogens	Multifocal atrial tach



Differentials and Comorbidities

Personality Disorders
PMDD
Prescription drug reaction
Primary Hypersomnia
Primary Insomnia
Schizoaffective Disorder
Schizophrenia
Schizophreniform Disorder
Sleep Apnea
Somatoform Disorders
Stimulants
SIADH
Thyroiditis

Tourettes
Undifferentiated Connective
Tissue Disease
Unstable Angina
More.....

YIKES!!!



DIVINE MD TEST

Table 2 – The mnemonic DIVINE MD TEST

General categories	Medical conditions
Drugs	Illicit drugs and alcohol, prescribed and over-the-counter medications, herbal preparations, caffeine, nicotine
Infectious/ Inflammatory (local, systemic, CNS)	Syphilis, HIV infection, encephalitis, tuberculosis, brain abscess, influenza, pneumonia, any prolonged infection, pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS)
Vascular	Myocardial infarction, congestive heart failure, cerebral arteriosclerosis, thrombosis
Immunological	<i>Autoimmune diseases:</i> multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus <i>Immunosuppression:</i> AIDS, cancer, chemotherapy
Nutritional	Nutritional and vitamin B ₁ (thiamine), B ₃ (niacin), B ₆ (pyridoxine), and B ₁₂ (cobalamin) deficiencies
Endocrine	Hypopituitarism, acromegaly, hypothyroidism, hypoparathyroidism, hyperparathyroidism, diabetes mellitus, hypogonadism, postmenopausal status, Cushing syndrome, adrenal insufficiency
Metabolic	Wilson disease, porphyria, hyponatremia, hypokalemia, hypercalcemia, hypocalcemia, hypoglycemia
Degenerative/ Demyelinating	Parkinson disease, Alzheimer disease, dementia, multiple sclerosis, muscular dystrophy, Friedreich ataxia, myotonic dystrophy
Trauma	Traumatic head injury, blast injuries, postconcussion syndrome
Epilepsy	Convulsive and nonconvulsive seizures
Structural	<i>Space-occupying lesions:</i> cerebral tumors, tumors of the endocrine glands, neoplasms with CNS or endocrine gland metastasis, pancreatic carcinoma, insulinoma
Toxins	<i>Heavy metals:</i> lead, mercury, iron, bromium, and manganese; carbon monoxide poisoning; toxins caused by hypovolemia, uremia, anoxia, and corticosteroid therapy

Khouzam, H.R. (2009). *Consultant*. 49(3), 169-169.

Adapted from Brewerton TD. *Resident and Staff Physician*. 1985°; Khouzam HR et al. *Handbook of Emergency Psychiatry*. 2007.¹⁸



Differential Diagnosis

- **Medical**
 - Cardiovascular
 - Endocrine
 - Metabolic
 - Neurologic
 - Respiratory
 - Others
- **Psychiatric**
 - Other Anxiety Disorders
 - Major Depressive Disorder
 - Psychotic Disorders
- **Substances**
 - Iatrogenic
 - Recreational drugs



Common Rx used in Primary Care

- **Asthma**
 - beta-2 agonists
 - theophylline
- **Hormonals**
 - OCPs
- **Amphetamines**
- **Steroids**
- **Thyroid medications**
 - levothyroxine
 - liothyronine
- **Others**
 - Antidepressants
 - bupropion
 - SNRIs
 - fluoxetine
 - Metoclopramide
 - Decongestants
 - Caffeine additives
 - Cafergot/Ergotamine
 - Excedrin Migraine
 - Nicotine Replacement



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Etiology

- Neurotransmitter hypothesis
- Genetic hypothesis
- Cognitive explanation
 - Faulty beliefs, expectations, assumptions
 - Misattribution of internal sensations
- Behavioral explanation
 - Anxiety leads to altered behaviors (avoidance)
 - Reinforcement
 - Spiraling symptoms
- Biopsychosocial interaction (genetic vulnerability, environmental situations, stress, trauma)



Panic Disorder

DSM-5 Criteria

- Recurrent, unexpected Panic Attacks
 - Discrete period of intense fear or discomfort
 - Abrupt surge of intense fear or discomfort reaching a peak w/in minutes
 - $\geq 4/13$ clinical symptoms (STUDENTS FEAR THE 3Cs)
- At least one attack followed by ≥ 1 month
 - persistent concern about recurrence, and/or
 - significant maladaptive change in behavior (avoidance)
- Not attributable to substances, a general medical condition, or another mental disorder



Panic Attack Mnemonic

STUDENTS FEAR THE 3Cs

- **S** weating
- **T** rembling
- **U** nsteadiness/dizziness
- **D** erealization/depersonalization
- **E** levated heart rate (tachycardia, palpitations)
- **N** ausea, numbness
- **T** ingling
- **S** hortness of breath
- **Fear**: of death, loss of control, going crazy
- **3Cs**: choking, chest pain, chills



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“Other Specified Anxiety Disorder”



Panic Attack

- **Epidemiology**
 - 11.2% 1-year prevalence
 - 22.7% lifetime prevalence of an isolated panic attack
 - Lower rates from European countries (2.7-3.3%)
 - Females>Males although more so w/ the Disorder
 - Age of onset (22-23 years)
 - Likely influenced by a co-occurring mental disorder or stressful life event
 - Rare in children until puberty
 - Declines in older individuals



Panic Disorder

- **Epidemiology**
 - 2-3% 1-year prevalence
 - 3-4% lifetime prevalence
 - Lower among US Latinos, African Americans, Caribbean blacks & Asian Americans
 - Higher rates among American Indians
 - 10% of pts referred for mental health evaluation
 - 20-25% of pts presenting to the ED
 - Up to 60% of pts in general med settings
 - 1-6% point prevalence in primary care
 - Variable age of onset (late adolesc - mid 30s)
 - 2:1 Female:Male



Panic Disorder

- **Epidemiology**
 - 8x more likely in first degree relatives
 - 90% will have ≥ 1 other lifetime psychiatric disorder
 - Childhood abuse common (relative to other anx disorders)
 - Smoking is a risk factor
 - Identifiable stressors linked to first attack
 - Asthma association
 - Increased suicide (ideation, attempt, rates)



Generalized Anxiety Disorder

DSM-5 Criteria

- >6 months of excessive anxiety and worry, more days than not, about a number of events or activities
- Difficulty controlling the worry
- 3/6 clinical symptoms (AND IC REST)
- Clinically significant distress or impairment....
- Not attributable to substances, a general medical condition, or another mental disorder



Generalized Anxiety Disorder

AND IC REST

- **A**nxious, constantly worried
- **N**o control over the worry
- **D**uration of 6 months
- **I**rritability
- **C**oncentration impairment
- **R**estlessness
- **E**nergy decreases
- **S**leep impairment
- **T**ension in muscles



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“Other Specified Anxiety Disorder”



Generalized Anxiety Disorder

- **Epidemiology**
 - 9% lifetime prevalence
 - 2.9% (adults) 1-year prevalence, 0.9% (adolescents)
 - Roughly identical rate in other countries
 - Higher lifetime prevalence in those living in the Northeast US
 - 2:1 Females:Males
 - Age of onset: 30 years (earlier onset = more comorbidity and impairment)
 - Peaks in middle age and declines thereafter
 - > in those of European descent, those from developed countries
 - Psychiatric comorbidities common



Adjustment Disorder with Anxiety

DSM-5 Criteria

- Emotional symptoms w/ onset within 3 months of identifiable stressor
- Clinically significant symptoms/behaviors with either:
 - Marked distress that is out of proportion
 - Significant impact on social, occupational or other.....
- Not normal bereavement
- Once stressor is terminated, symptoms do not persist for more than an additional 6 months.

“Other Specified Anxiety Disorder”



Adjustment Disorders

- **Epidemiology**
 - 5-20% point prevalence in o/p mental health
 - Prevalence varies widely by setting (up to 19% in onc/hemat)
 - Estimates up to 18% in Primary Care
 - Up to 35% in Consultation Liaison Psychiatry
 - Younger
 - Life events in relation to work, most frequent cause (43%)
 - Unstable family environ, divorce, military service, natural disasters
 - Psychiatric comorbidities
 - Low perceived QOL

American Psychiatric Association. (2013). Diagnostic and Statistical Manual of Mental Disorders (DSM-5®). American Psychiatric Pub.
Casey, P. (2009). CNS Drugs, 23(11), 927-938.
Fernández, A., et al. (2012). Brit J Psychiat. 201(2), 137-142.



Subclinical Worries/Subsyndromal Anxiety

- No formal DSM-5 diagnosis(es)
- Estimates 3.6% (12-mo), 8% (lifetime) overall
- 6-11% in Primary Care
- Worsens course of concurrent somatic disease(s)
- High functional impairment
- Low QOL
- Higher number of disability days
- Greater healthcare utilization

Somatic Symptom and Related Disorders

- Somatic Symptom Disorder
- Illness Anxiety Disorder
- Conversion Disorder
- Psychological Factors Affecting other Medical Conditions
- Factitious Disorder



Assessment Strategies

- **Common and Practical Assessment Approach**
 - DSM-5 clinical criteria
 - Screening questions: GAD-2 (Sen. 86% Sp. 83%)
 - Rating Scales (Zung, Hamilton-A, Beck AI, Fear Questionnaire, GAD-7, OASIS)
 - R/O differentials and comorbidities (labs, imaging, etc. PRN)
 - Safety evaluation



GAD-2

Over the <u>last 2 weeks</u> , 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

Hallgren, J. D., & Morton, J. R. (2007). *J Fam Pract*, 56(7), 579-580.

Plummer, F., Manea, L., Trepel, D., & McMillan, D. (2016). *Gen Hosp Psychiat*, 39, 24-31.



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 - Safety evaluation



GAD-7

Generalized Anxiety Disorder Screener (GAD-7)

Over the <i>last 2 weeks</i> , how often have you been bothered by the following problems?	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 irritated	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3
	Add columns			
	Total Score			
8. If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?	Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult

Plummer, F., Manea, L., Trepel, D., & McMillan, D. (2016). *Gen Hosp Psychiat*, 39, 24-31.



Overall Anxiety Severity and Impairment Scale (OASIS)

- **In the past week:**
 - how often have you felt anxious?
 - when you felt anxious, how intense or severe was your anxiety?
 - how often did you avoid situations, places, objects, or activities because of anxiety or fear?
 - how much did your anxiety interfere with your ability to do the things you needed to do at work, at school, or at home?
 - how much has anxiety interfered with your social life and relationships?



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Anxiety Treatment

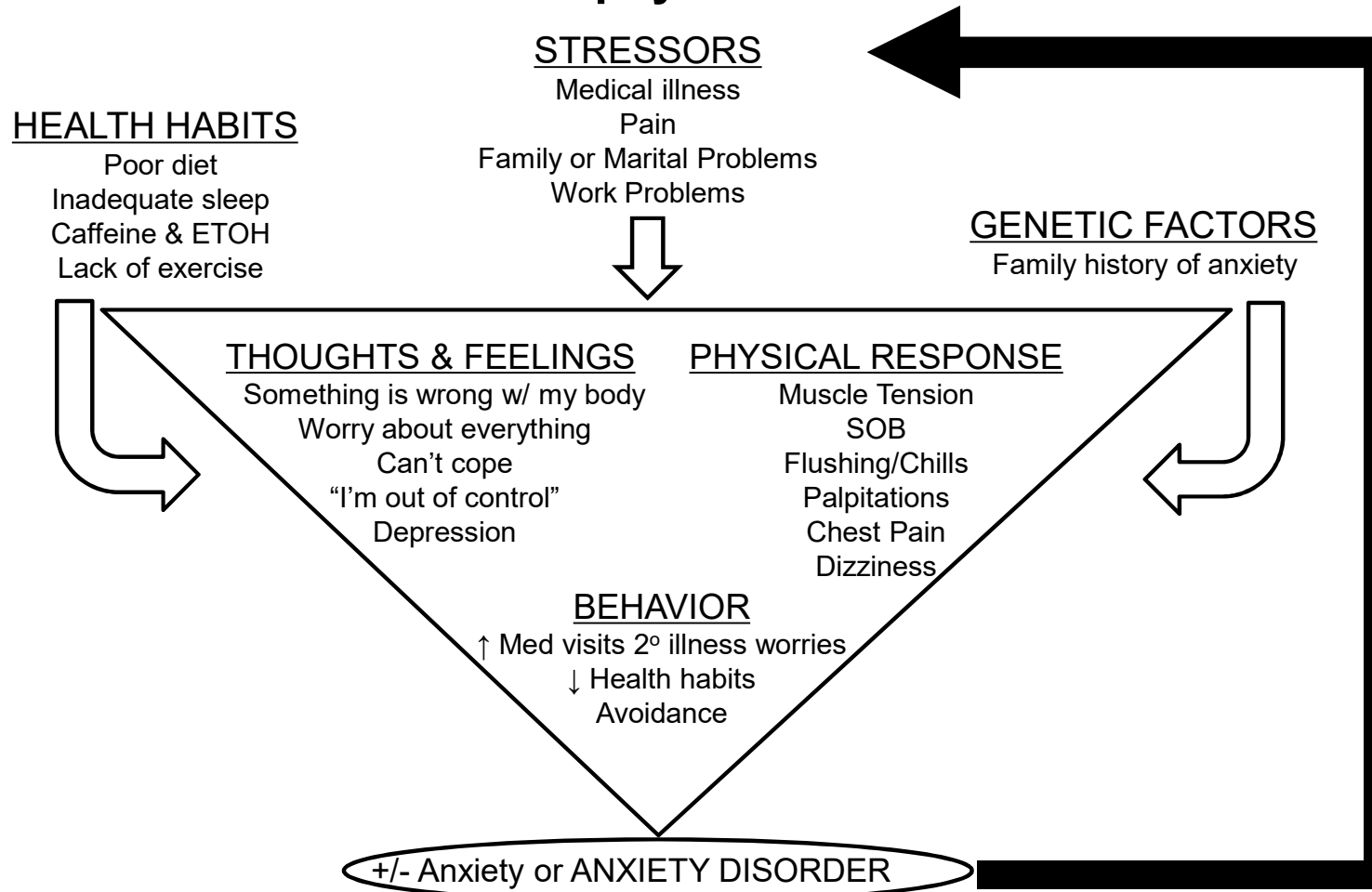


Treating Mental Health Problems in Primary Care (Integrated Care)

- Availability, access
- Affordability
- Patients prefer it
- Patients more likely to receive MH care when identified and treated in primary care
- Better integration of care
- Reduce the stigma of mental illness



ANXIETY – The Biopsychosocial Model



Adapted from: Roy-Byrne, P., et al. (2009). *J Am Board Fam Med*, 22(2), 175-186.



Therapeutic Options

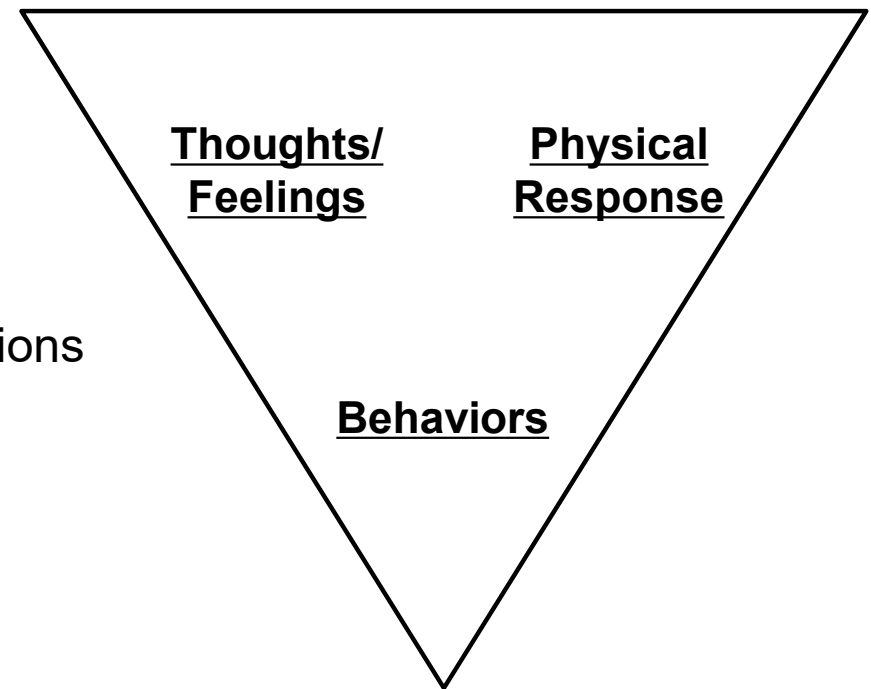
- Treat comorbidities
- Nonpharmacological
 - Cognitive Behavioral Interventions
- Pharmacological
- Combination treatment
- Referral



Cognitive-Behavioral Intervention

Anxiety Disorders & esp. Subsyndromal Anxiety

- Psychoeducation
- Physical symptom management
 - relaxation techniques, biofeedback
- Social skills training
- Cognitive restructuring (ABCs)
- Gradual exposure to feared situations (systematic desensitization)
- Telemedicine

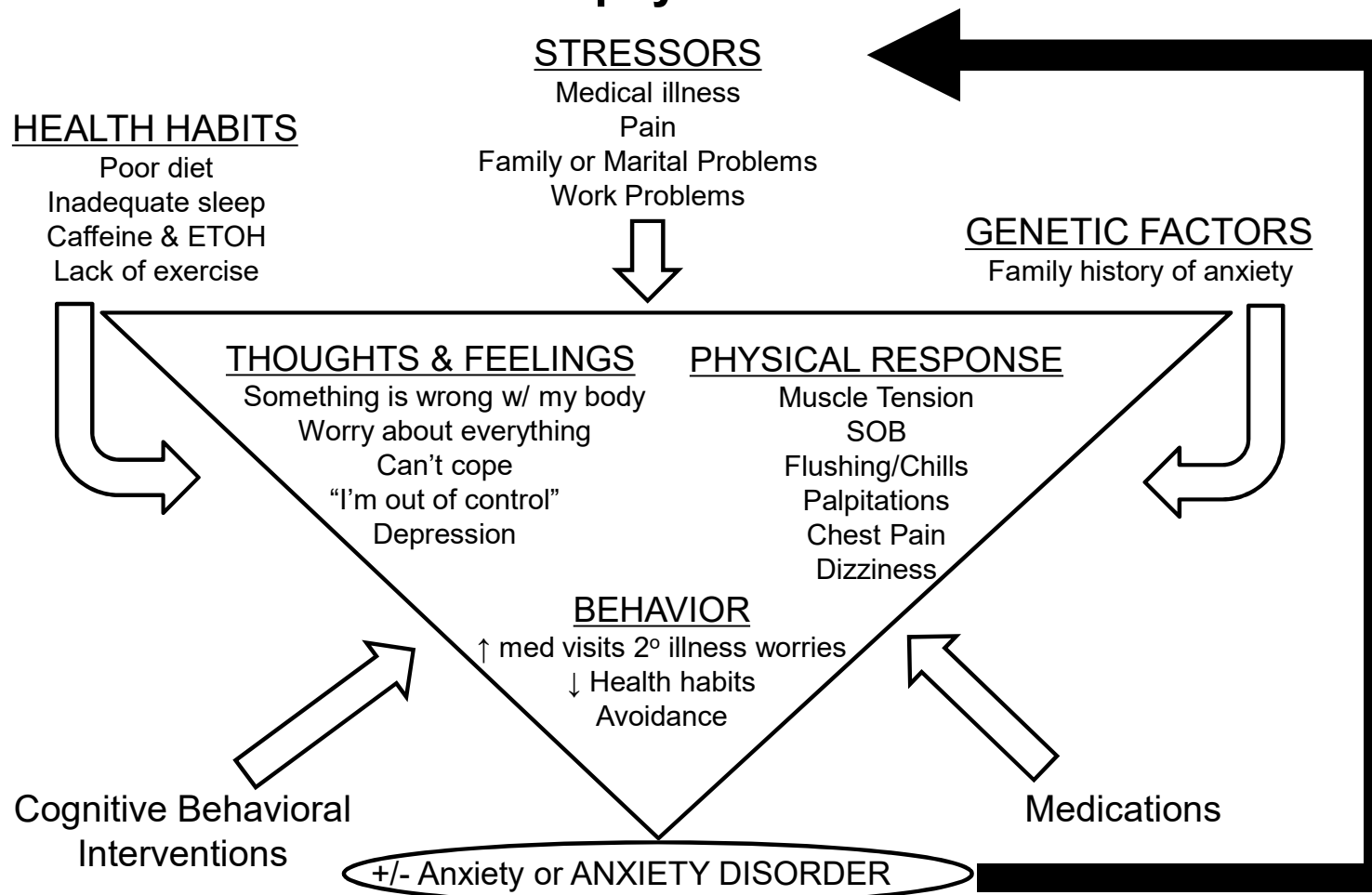


Coffey, S. F., Banducci, A. N., & Vinci, C. (2015). *Am Fam Physician*, 92(9), 807-812.

Olthuis, J. V., et. al. (2016). Therapist-supported Internet cognitive behavioural therapy for anxiety disorders in adults. *Cochrane Database of Systematic Reviews*, (3).



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Psychopharmacology

	Panic	GAD	Adjustment Disorder	“Anxiety”
SSRI	FDA	FDA		
SNRI	FDA	FDA		
TCA (<i>Anafranil</i>) - OCD		Used*		FDA/Used*
Benzodiazepine	FDA	Used*		FDA
β -Blocker (<i>Inderal</i>)				
buspirone		Used*		FDA
hydroxyzine (<i>Vistaril</i>)	Used*	Used*		FDA
quetiapine (<i>Seroquel</i>)		Used*		
Anticonvulsant	Used*	Used*		
meprobamate				FDA
prochlorperazine maleate				FDA
pregabalin (<i>Lyrica</i>)		Used*		

* Used but not FDA approved



Benzodiazepines

	Dose (mg/d)	Equivalent Dose (mg)	
HIGH POTENCY			
Alprazolam (Xanax)	0.75-4 (4-10)*	0.5	SHORT
Lorazepam (Ativan)	0.5-10	1.0	
Clonazepam (Klonopin)	1-4*	0.25	LONG
LOW POTENCY			
Oxazepam (Serax)	30-120	15	SHORT
Diazepam (Valium)	2-40	5	
Clorazepate (Tranxene)	7.5-60	7.5	LONG
Chlordiazepoxide (Librium)	25-100	10	

*Panic dosing



Benzodiazepines

- **Cautions**
 - Elderly (AGS Beers Criteria)
 - Sedation, confusion, accidents
 - Impairment of memory and recall
 - Depression/emotional blunting
 - Rebound anxiety and withdrawal
 - Abuse
 - Dependence (physical & psychological)



Benzodiazepines – Avoiding Dependence

- Patient education
- Treat comorbid depression and/or alcoholism
- Patient education
- Use other medication options (alone or in combination with benzodiazepines) – titrate one while you taper the other
- Patient education
- Use BZDs with less reinforcing properties



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Benzodiazepines – Tapering

- **When to taper**
 - Continuous use >3-4 weeks
 - Older patients (>65 yo)
 - Supratherapeutic doses
 - Concomitant controlled substances or recreational drugs
 - Active alcoholism
 - Comorbid cognitive disorder (dementia, TBI)



Benzodiazepines – Tapering

- **Tapering strategies**
 - Use same drug and taper
 - Switch to a long half-life agent and taper
 - Use adjunctive medications
 - ↓ 10-25% current dose/week
 - Slow, over extended time if necessary
- **Discontinuation Withdrawal symptoms**
 - Within 1-2 days with short half-life BZs
 - Within 3-8 days with long half-life BZs

Ashton, H. (2005). *Curr Opin Psychiatry*, 18(3), 249-255. Lader, M., Tylee, A., & Donoghue, J. (2009). *CNS drugs*, 23(1), 19-34. National Center for PTSD (2013). https://www.va.gov/painmanagement/docs/osi_6_toolkit_taper_benzodiazepines_clinicians.pdf



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National Center for PTSD (2013). https://www.va.gov/painmanagement/docs/osi_6_toolkit_taper_benzodiazepines_clinicians.pdf



Benzodiazepines – Tapering

- **Predictive factors for difficult tapers**
 - Previous failed attempts
 - Comorbid psychiatric or physical illness
 - Personality Disorders
 - Hx of alcohol or drug use
 - Lack of family or social support
 - Older age
 - Poor or conflictual rapport w/ prescriber



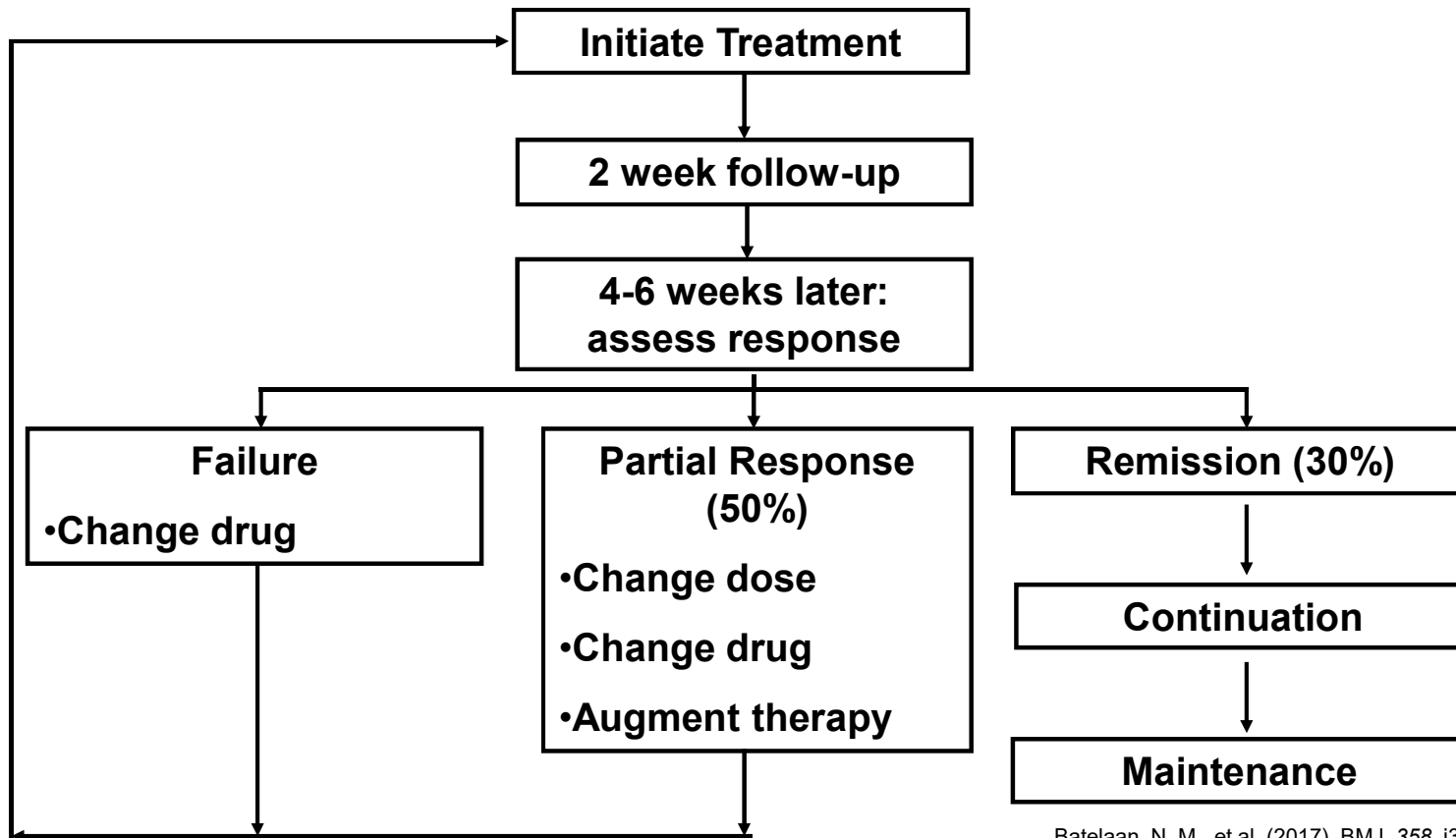
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hydroxyzine (<i>Vistaril</i>)	Used*	Used*		FDA
quetiapine (<i>Seroquel</i>)		Used*		
Anticonvulsant	Used*	Used*		
meprobamate				FDA
prochlorperazine maleate				FDA
pregabalin (<i>Lyrica</i>)		Used*		

* Used but not FDA approved



Treatment Algorithm



Batelaan, N. M., et al. (2017). BMJ, 358, j3927.



Rx Augmentation Strategies

- Buspirone
- Antipsychotics*
- Lithium*
- Pregabalin, gabapentin*
- Hydroxyzine pamoate
- Beta Blocker
- Long term BZD use
- 2 SSRIs/SNRIs
- Antiepileptics*
- Meprobamate
- Prochlorperazine maleate

Other Novel Strategies

- THC?
- CBD & other herbals?
- Ketamine?
- rTMS, VNS, DBS?

* Used but not FDA approved for "anxiety" or Anxiety Disorders
Patterson, B. & Van Ameringen, M. (2016). *Depress Anxiety*, 33(8), 728-736.



Therapeutic Options

- Treat comorbidities
- Nonpharmacological
 - Cognitive Behavioral Interventions
- Pharmacological
- Combination treatment
- Referral



Treatment Resistant Anxiety (Pseudo and True Resistance)

- Pseudo-resistance (insufficient treatment)
 - Type of treatment is wrong
 - Dose is wrong
 - Manner of treatment delivery is wrong
 - Non-adherence
- True resistance

Anxiety Recurrence

- Initial remission: 25-35% with treatment
- Relapse after remission
 - 10% at 1 year
 - 20% at 5 years
 - 30% at 10 years



Treatment Resistance or Recurrence

- **Risk Factors**

- Incorrect diagnosis
- Comorbid disorders (medical & psychiatric)
- Medications (sub therapeutic 20%, adequate trial, nonadherence)
- Severe intensity of anxiety symptoms, avoidance
- Suicidal thoughts or behavior
- New or recurring stressors (environ. factors)
- CBI (nonadherence, recalcitrant, clinician factors)
- Uninformed/unrealistic/unmotivated patients
- Enzyme inducers, rapid metabolizers?

- **Responses & Options**

- Reassess for alternate dx
- Reassess, tx or refer
- Identify reason(s) and address
- Refer to psychiatric provider
- Assess and treat/refer appropriately
- Reassess, Pt education, CBI
- Identify reason(s), address, refer
- Pt education, motivational interviewing tech.
- Pharmacogenetic testing
- THC?
- CBD & other herbals?
- Ketamine?
- rTMS, VNS, DBS?

Bystritsky, A. (2006). *Mol Psychiatr*, 11(9), 805.

Lorenz, R. A., Jackson, C. W., & Saitz, M. (2010). *J Hum Pharm and Drug Ther*, 30(9), 942-951.



Therapeutic Options

- Treat comorbidities
- Nonpharmacological
 - Cognitive Behavioral Interventions
- Pharmacological
- Combination treatment
- Referral



Referral

- **Seek More Urgent Mental Health Consultation**
 - Serious risk of suicide
 - Diagnosis is uncertain
 - Psychotic symptoms are present
 - Comorbid illicit drug or alcohol use is present
 - Anxiety symptoms are chronic, severe, and disabling
 - Patient is elderly or is a child or adolescent
 - Patient refuses to adhere to the recommended treatment
 - Difficult Rx taper
 - No improvement is evident after a period of initial treatment and follow-up





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Brief intervention for anxiety in primary care patients

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Thanks for Listening!
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Selected References

1. American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders (DSM-5®)*. American Psychiatric Pub.
2. Anxiety Disorders Association of America. <http://www.adaa.org/>.
3. Archer, J., et al. (2012). Collaborative care for depression and anxiety problems. *Cochrane Database of Systematic Reviews*, 10.
4. Ashton, H. (2005). The diagnosis and management of benzodiazepine dependence. *Curr Opin Psychiatr*, 18(3), 249-255.
5. Batelaan, N. M., et al. (2017). Risk of relapse after antidepressant discontinuation in anxiety disorders, obsessive-compulsive disorder, and post-traumatic stress disorder: systematic review and meta-analysis of relapse prevention trials. *Brit Med J*, 358, j3927.
6. Baxter, A. J., Vos, T., Scott, K. M., Ferrari, A. J., & Whiteford, H. A. (2014). The global burden of anxiety disorders in 2010. *Psychol Med*, 44(11), 2363-2374.
7. Bystritsky, A. (2006). Treatment-resistant anxiety disorders. *Mol Psychiatr*, 11(9), 805.
8. Campbell-Sills, L. & Stein, M.B. (2006). *Guideline watch: practice guideline for the treatment of patients with panic disorder*. Arlington, VA: American Psychiatric Association.
9. Canadian Psychiatric Association. (2006). Clinical practice guidelines. Management of anxiety disorders. *Can J Psychiatr*, 51(8 Suppl 2), 9S.
10. Casey, P. (2009). Adjustment disorder. *CNS Drugs*, 23(11), 927-938.
11. Coffey, S. F., Banducci, A. N., & Vinci, C. (2015). Common Questions About Cognitive Behavior Therapy for Psychiatric Disorders. *Am Fam Physician*, 92(9), 807-812.
12. College of Physicians and Surgeons of Alberta (2016). Benzodiazepines: Use and Taper (Clinical Toolkit). Retrieved from http://www.cpsa.ca/wp-content/uploads/2016/08/Clinical-Toolkit_BDZ_Nov_2016.pdf
13. Ebell, M.H. (2008). Diagnosis of anxiety disorders in primary care. *Am Fam Physician*, 78(4), 501-2.
14. Fernández, Anna, et al. (2012). Adjustment disorders in primary care: prevalence, recognition and use of services. *Brit J Psychiatr*, 201(2), 137-142.
15. Fricchione, G. (2004). Generalized anxiety disorder. *New Engl J Med*, 351(7), 675-682.
16. Gliatto, M.F. (2000). Generalized anxiety disorder. *Am Fam Physician*, 62(7), 1591-1600.
17. Goodwin, R. D., et al. (2005). The epidemiology of panic disorder and agoraphobia in Europe. *Eur Neuropsychopharm*, 15(4), 435-443.
18. Haller, H., Cramer, H., Lauche, R., Gass, F., & Dobos, G. J. (2014). The prevalence and burden of subthreshold generalized anxiety disorder: a systematic review. *BMC Psychiatr*, 14(1), 128.

Selected References

19. Hallgren, J. D., & Morton, J. R. (2007). What's the best way to screen for anxiety and panic disorders? *J Fam Pract*, July, 56(7), 579-580.
20. Ham, P., Waters, D. B., & Oliver, M. N. (2005). Treatment of panic disorder. *Am Fam Physician*, 71(4): p. 733-739.
21. Janssen, E. H., et al. (2012). Recognition of anxiety disorders by family physicians after rigorous medical record case extraction: results of the Netherlands Study of Depression and Anxiety. *Gen Hosp Psychiat*, 34(5), 460-467.
22. Kessler, R. C., et al. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiat*, 62(6), 593-602.
23. Khouzam, H.R., Anxiety Disorders: Guidelines for Effective Primary Care, Part 1, Diagnosis. *Consultant*, 2009. 49(3): p. 1-3.
24. Kroenke, K., Spitzer, R. L., Williams, J. B., Monahan, P. O., & Löwe, B. (2007). Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. *Ann Intern Med*, 146(5), 317-325.
25. Lader, M., Tylee, A., & Donoghue, J. (2009). Withdrawing benzodiazepines in primary care. *CNS drugs*, 23(1), 19- 34.
26. Lorenz, R. A., Jackson, C. W., & Saitz, M. (2010). Adjunctive use of atypical antipsychotics for treatment-resistant generalized anxiety disorder. *Pharmacotherapy: J Hum Pharm and Drug Ther*, 30(9), 942-951.
27. National Center for PTSD (2013). Retrieved from https://www.va.gov/painmanagement/docs/osi_6_toolkit_taper_benzodiazepines_clinicians.pdf
28. National Institute for Health and Care Excellence. (2011). *Generalised anxiety disorder and panic disorder in adults: management* (NICE Clinical Guideline CG113). Retrieved from <https://www.nice.org.uk/guidance/cg113?unlid=25209853520162212188>
29. National Institute for Health and Care Excellence. (2013). *Social anxiety disorder: recognition, assessment and treatment* (NICE Clinical Guideline CG159). Retrieved from <https://www.nice.org.uk/guidance/cg159>
30. National Institute of Mental Health. *Anxiety Disorders*. Retrieved from <http://www.nimh.nih.gov/health/topics/anxiety-disorders/index.shtml>
31. Norman, S. B., Campbell-Sills, L., Hitchcock, C. A., Sullivan, S., Rochlin, A., Wilkins, K. C., & Stein, M. B. (2011). Psychometrics of a brief measure of anxiety to detect severity and impairment: the Overall Anxiety Severity and Impairment Scale (OASIS). *J Psychiat Res*, 45(2), 262-268.
32. Ogbonna, C. I., & Lembke, A. (2017). Tapering patients off of benzodiazepines. *Am Fam Physician*, 96(9), 606-610.
33. Olthuis, J. V., Watt, M. C., Bailey, K., Hayden, J. A., & Stewart, S. H. (2016). Therapist-supported Internet cognitive behavioural therapy for anxiety disorders in adults. *Cochrane Database of Systematic Reviews*, (3).

Selected References

34. Patterson, B., & Van Ameringen, M. (2016). Augmentation strategies for treatment-resistant anxiety disorders: A systematic review and meta-analysis. *Depress Anxiety*, 33(8), 728-736.
35. Plummer, F., Manea, L., Trepel, D., & McMillan, D. (2016). Screening for anxiety disorders with the GAD-7 and GAD-2: a systematic review and diagnostic meta analysis. *Gen Hosp Psychiat*, 39, 24-31.
36. Practice Guidelines for the Treatment of Patients With Panic Disorder (2010) American Psychiatric Association. Retrieved from https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/panicdisorder.pdf
37. Richlie D. (2011) Anxiety Disorders in the Primary Care Setting. Retrieved from http://www.ucdenver.edu/academics/colleges/medicalschoo/departments/medicine/GIM/education/ContinuingEducation/Documents/TMC%202011-2012/11-1-2011_RichlieD.pdf
34. Roy-Byrne, P., et al. (2005). A randomized effectiveness trial of cognitive-behavioral therapy and medication for primary care panic disorder. *Arch Gen Psychiat*, 62(3), 290-298.
35. Roy-Byrne, P., et al. (2009). Brief intervention for anxiety in primary care patients. *J Am Board Fam Med*, 22(2), 175-186.
36. Roy-Byrne, P. (2015). Treatment-refractory anxiety; definition, risk factors, and treatment challenges. *Dialogues Clin Neurosci*, 17(2), 191.
37. Servant, D., et al. (2013). Adjustment disorders with anxiety. Clinical and psychometric characteristics in patients consulting a general practitioner. *L'Encephale*, 39(5), 347-351.
38. Yates, W. R. (2011). *Anxiety Disorders*. <http://emedicine.medscape.com/article/286227-overview>.