Generalized Anxiety Disorder (GAD) in Adults: Information for Primary Care

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Summary: Generalized anxiety disorder (GAD) is one of the most common anxiety disorders encountered by primary care physicians. Key features are significant worries accompanied by somatic symptoms and impaired function. Management in primary care can include education about self-management strategies and recommendations for specialized mental health supports and other local supports.

Case

G. is a 25-yo college student who has "always been a worrier." Since leaving her hometown and moving to college however, things have been quite stressful. Her room mates call her a worry wort, and she realizes that perhaps her anxiety really does seem to get in the way of her life. She wonders if it might be possible for her to be more confident just like her roommates, or if she will always be a worrier...

Epidemiology

- Anxiety disorders are the most prevalent of psychiatric disorders and GAD is the most common to be seen in the primary care setting (Davidson et al)
- Up to 18% of primary care patients suffer from any anxiety disorder
- Nearly 8% of patients consulting a primary care physician have GAD (WHO)
- Females are twice as likely as males to experience GAD (DSM-5)
- Prevalence peaks in middle age and declines across later years

Risk Factors

- Consider screening patients with risk factors such as
    - Family history of anxiety
    - Substance use problems
    - Medical conditions
    - Socioeconomic risk factors such as low SES
    - Depression
    - Stressful life events

History/Interviewing Questions

- Normalizing statement
    - Everyone has worries. What kinds of things do you worry about?
- Insight
    - Would you say that you're a worrier? Do you think you worry too much about everyday things such as your family, health, work, or finances?
- Impairment
    - Do friends or loved ones tell you that you worry too much?
    - Do you have difficulty controlling your worry, such that the worry keeps you from sleeping or makes you feel physically ill with headaches, stomach troubles or fatigue?
    - Does this worry get in the way of your life?

Screening Tools

Consider using screening tools such as the GAD-2 or GAD-7, or simply asking the screening questions as part of your interview.

- GAD-2
    - Over the last 2-weeks, how often have you been bothered by the family problems?
        - Feeling nervous, anxious or on edge?
        - Not being able to stop or control worrying?
- GAD-7
    - Over the last 2-weeks, how often have you been bothered by the family problems?
        - Feeling nervous, anxious or on edge?
        - Not being able to stop or control worrying?
        - Worry too much about different things?
        - Having trouble relaxing?
        - Being so restless that it is hard to sit still?
        - Becoming easily annoyed or irritable?
        - Feeling afraid, as if something awful might happen?

Diagnosis

Essential features of generalized anxiety disorder are

- Excessive anxiety / worry and
- Somatic symptoms (e.g. restlessness, fatigue, problems with concentration), and
- Distress/impairment

DSM-5 Criteria

A. Excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least 6 months, about a number of events or activities (such as work or school performance)
B. The individual finds it difficult to control the worry
C. The anxiety and worry are associated with ≥3 of the following 6 symptoms (with at least some symptoms having been present for more days than not for the past 6 months):

    1. Restlessness or feeling keyed up or on edge
    2. Fatigue
    3. Difficulty concentrating
    4. Irritability

5. Muscle tension
6. Sleep disturbance

A. The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning
B. The disturbance is not attributable to the physiological effects of a substance (drug of abuse, a medication) or another medical condition (hyperthyroidism)
C. The disturbance is not better explained by another mental disorder (anxiety or worry about having panic attacks in panic disorder, negative evaluation in social anxiety disorder, contamination or obsessions in OCD, etc)

Differential Diagnosis

- Anxiety disorder due to another medical condition
  - Hyperthyroidism
  - Cushing Disease
  - Pheochromocytoma
  - Congestive heart failure, arrhythmia, mitral valve prolapse
  - Asthma, COPD, pneumonia

- Substance/medication induced anxiety disorder
  - Alcohol, caffeine, nicotine
  - Steroids
  - SSRIs
  - Digoxin
  - Thyroxine
  - Theophylline
  - Opiate and benzodiazepine abuse

- Other anxiety disorders
  - Social anxiety disorder: Are there significant problems with shyness? Discomfort in social situations?
  - Obsessive-compulsive disorder: Are there obsessions, i.e. intrusive thoughts that come over and over again? Are there compulsions, i.e. repetitive rituals that the person must do over and over again?

- Other psychiatric disorders
  - Posttraumatic stress disorder and adjustment disorders
  - Depressive, bipolar, and psychotic disorders

Physical Exam

- Anxiety often manifests with a number of physical symptoms; examine the areas of physical complaint to rule out medical conditions
- Physical signs may include:
  - Tremor
  - Tachycardia
  - Tachypnea
  - Sweaty palms
  - Agitation

Investigations

- Generalized anxiety disorder is a clinical diagnosis; there are no pathognomonic diagnostic tests

- Investigations to rule out medical causes include:
    - CBC for anemia
    - Fasting blood glucose for hypoglycaemia
    - Electrolytes
    - Liver enzymes, serum bilirubin for alcohol use problems
    - Urinanalysis for infection
    - Urine toxicology for substance use
    - TSH level for hyperthyroidism
    - If episodic anxiety symptoms, consider 24-hour urine test (metanephrines and vanillylmandelic acid) for pheochromocytoma

Management

- Overall goals of treatment (Davidson et al):
    - Reduce core symptoms of GAD
    - Improve patient function and quality of life
    - Treat co-morbid disorders
    - Treat for long enough to attain remission and, if possible, prevent relapseFor mild to moderate symptoms
- Consider starting with non-medication interventions such as
    - Cognitive behaviour therapy (CBT)
    - Lifestyle modifications
        - For moderate to severe symptoms, or with symptoms that do not respond to CBT, consider medication treatment

Management: Psychological Interventions

- Consider referral to mental health professional for CBT / psychotherapy, or providing CBT
    - Typically 10-15 individual and/or group sessions
    - Educate about their symptoms, their anxiety and fear, and the treatment plan
    - Self-monitoring of worrying or related symptoms to help identify triggers and targets for therapy
    - Relaxation training including deep breathing, muscle relaxation, and exercise
    - Cognitive restructuring reassesses unwarranted worrying and unrealistic interpretations and replaces the thoughts with problem-solving strategies. It also helps patients learn to deal with uncertainty and perfectionism and focuses on catastrophizing and overestimating.
    - Exposure therapy to both internal (physical, emotional, cognitive) cues and external (situational) cues that would trigger worry in patient and helps patient shift their appraisals of the triggers and lessen their reactivity
    - Rehearsal of coping skills and preparation for periods of increased anxiety or lapses in treatment. Prepare patients to repeat certain modules of CBT and to learn to regain progress
- Lifestyle Interventions
    - Incorporate exercise (regular aerobic exercise >20 min)
    - Incorporate good sleep habits
    - Decrease or discontinue stimulant use such as caffeine
    - Decrease or discontinue alcohol and other sedative or hypnotic use
    - Spend quality time with family and friends

Management: Medication

- If non-medication strategies have been insufficient, or if psychotherapy is not possible, then consider medications
    - Start medications at low dosage, and ideally follow-up at 1-2 weeks to monitor
    - Once the first line medication is optimized
        - If inadequate response or side effect, switch to another first line agent
        - If partial response, consider adding another agent rather than switching
    - Duration of treatment
        - Treat generalized anxiety disorder for at least 1 year after a good response is achieved

Medications for Anxiety

First Line

Medication	Starting / Initial target	Maximum daily dosage
Escitalopram (Cipralex)*	Start 5-10 mg daily, titrate up to 10-20 mg daily	20 mg
Paroxetine (Paxil)*	Start 20 mg daily Usual dosage range 20-50 mg daily	60 mg
Sertraline (Zoloft)*	Start 50 mg daily Usual dosage range 50-200 mg daily	200 mg
Venlafaxine XR (Effexor XR)*	Start 37.5-75 mg daily	225 mg
Pregabalin	Start 75 mg two times daily, titrate up to 450 mg daily	600 mg

Second line

Name of Medication	Starting / Initial target	Maximum daily dosage
Benzodiazepines*		
Alprazolam	Start 0.25-0.5 mg three times daily	4 mg
Bromazepam	Start 6 mg daily	30 mg
Lorazepam	Start 0.5-1 mg two to three times daily, titrate up to 0.5-2 mg two to three times daily	10 mg
Diazepam	Start 2-5 mg twice daily, titrate up to 2-10 mg daily	10 mg
Others		
Bupropion XL (Wellbutrin NDRI)	Start 150 mg daily, titrate up to 300 mg daily	450 mg
Buspirone (Buspar)*	Start 7.5 mg two times daily	60 mg
Imipramine	Start 25 mg daily	150 mg
Quetiapine XR	Start 50 mg daily	300 mg
Vortioxetine	Start 10 mg daily, titrate up to 5-20 mg daily	20 mg
Hydroxyzine	Start 50 mg four times daily	400 mg

* Indicates approval by Health Canada for anxiety disorder such as Generalized Anxiety Disorder, Obsessive Compulsive, Panic Disorder, Social Anxiety Disorder, etc.

Reference for Medications: Katzman, CANMAT Guidelines for Anxiety Disorders 2014

When to refer

- Consider referral to mental health services if:
    - Complicated presentation with significant co-morbid psychiatric or medical illness
    - Inadequate response to treatment
    - Unclear diagnosis
    - Significant safety concerns with risk of harm to self or others

1. Which of the following statements is correct regarding generalized anxiety disorder (GAD)

- ○ Men suffer from GAD more frequently than women
- ○ GAD is the least common anxiety disorder to be seen in primary care
- ○ Prevalence of GAD peaks in childhood, then slowly tapers off
- ○ GAD symptoms last at least 6 months (DSM-5 criteria)
- ○ Family history of anxiety is not a risk factor for GAD

2. Which of the following medications is considered first line for generalized anxiety disorder (GAD)?

- ○ Imipramine
- ○ Vortioxetine
- ○ Fluoxetine
- ○ Buspirone
- ○ Quetiapine XR

Resources for patients

Anxiety Disorders Association of Canada
http://anxietycanada.ca

Anxiety Disorders Association of Ontario
http://www.anxietydisordersontario.ca

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