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

CARMEN ANDREESCU, MD
ASSOCIATE PROFESSOR OF PSYCHIATRY
DIRECTOR – ARGO NEUROBIOLOGY OF AGING LAB
UNIVERSITY OF PITTSBURGH
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 life³:
  - Generalized Anxiety Disorder
  - Agoraphobia

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**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 \(^4\)

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

Older adults tend to¹:
- 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

- Bidirectional association: Anxiety ↔ Cognitive Decline

- Increased risk of developing MCI 20 years later for midlife adults with severe anxiety

- Anxiety symptoms double the risk of conversion from MCI to AD

- 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).
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)\(^1\)

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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

<table>
<thead>
<tr>
<th></th>
<th>Fear</th>
<th>Avoidance</th>
<th>Arousal</th>
<th>Anticipatory worry</th>
<th>Panic attacks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panic Disorder</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Social and other phobias</td>
<td>x</td>
<td>x</td>
<td></td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>OCD</td>
<td>x</td>
<td>+/-</td>
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<td></td>
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<tr>
<td>GAD</td>
<td>+/-</td>
<td></td>
<td></td>
<td>x</td>
<td></td>
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<tr>
<td>PTSD</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
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</tbody>
</table>
Anxiety Disorders are costly

Association of anxiety with cardiovascular disease

- 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

GAD
- Pathological worry
- Autonomic hyperactivity
- Increased startle response
- Muscle tension

Irritability
Restlessness
Decreased concentration
Sleep changes
Fatigue

MDD
- Sadness
- Loss of interest
- Weight/appetite changes
- Psychomotor retardation
- Thoughts of death
- Feelings of guilt

Overlapping and distinct symptoms of GAD and MDD [Ressler, Pine, Rothbaum – Primer on Anxiety Disorders, 2015]
COMORBIDITY OF ANXIETY AND MOOD DISORDERS

GAD
- Pathological worry
- Autonomic hyperactivity
- Increased startle response
- Muscle tension

- Irritability
- Restlessness
- Decreased concentration
- Sleep changes
- Fatigue

Bipolar Disorder
- Sadness
- Loss of interest
- Weight/appetite changes
- Psychomotor retardation
- Thoughts of death
- Feelings of guilt
- Grandiosity
- Pressured speech
  - Racing thoughts
- Increased goal-directed activity

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

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

<table>
<thead>
<tr>
<th>Study</th>
<th>ID</th>
<th>OR (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bresolin et al., 1988</td>
<td></td>
<td>0.23 (0.07, 0.60)</td>
<td>10.04</td>
</tr>
<tr>
<td>Fratola et al., 1992</td>
<td></td>
<td>0.18 (0.04, 0.80)</td>
<td>7.33</td>
</tr>
<tr>
<td>Subtotal (I-squared = 0.0%, p = 0.897)</td>
<td></td>
<td>0.19 (0.08, 0.46)</td>
<td>17.37</td>
</tr>
<tr>
<td>Antidepressant</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Davidson et al., 2008</td>
<td></td>
<td>0.50 (0.18, 1.37)</td>
<td>10.74</td>
</tr>
<tr>
<td>Katz et al., 2005</td>
<td></td>
<td>0.63 (0.27, 1.65)</td>
<td>13.56</td>
</tr>
<tr>
<td>Kimura et al., 2003</td>
<td></td>
<td>0.12 (0.02, 0.69)</td>
<td>6.17</td>
</tr>
<tr>
<td>Lenze et al., 2005</td>
<td></td>
<td>0.17 (0.04, 0.75)</td>
<td>7.39</td>
</tr>
<tr>
<td>Lenze et al., 2009</td>
<td></td>
<td>0.62 (0.34, 1.12)</td>
<td>14.24</td>
</tr>
<tr>
<td>Subtotal (I-squared = 21.4%, p = 0.278)</td>
<td></td>
<td>0.46 (0.29, 0.73)</td>
<td>52.10</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eriksson et al., 2008</td>
<td></td>
<td>0.14 (0.09, 0.22)</td>
<td>15.61</td>
</tr>
<tr>
<td>Montgomery et al., 2008</td>
<td></td>
<td>0.62 (0.37, 1.03)</td>
<td>14.92</td>
</tr>
<tr>
<td>Subtotal (I-squared = 94.8%, p = 0.000)</td>
<td></td>
<td>0.30 (0.07, 1.25)</td>
<td>30.63</td>
</tr>
<tr>
<td>Overall (I-squared = 74.8%, p = 0.006)</td>
<td></td>
<td>0.32 (0.18, 0.64)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

*NOTE: Weights are from random effects analysis*
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\(^2\).

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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\(^4\)

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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
Andreeascu & 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
Andreeascu & 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

<table>
<thead>
<tr>
<th>Psychotropic</th>
<th>Odds ratio of fall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepine</td>
<td>1.4*</td>
</tr>
<tr>
<td>Antidepressant</td>
<td>0.9</td>
</tr>
<tr>
<td>Antipsychotic</td>
<td>1.5*</td>
</tr>
<tr>
<td>Sedative/hypnotic</td>
<td>1.1</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Meta-analysis of intervention vs active control condition</th>
<th>Mean Effect Size (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBT without Relaxation Training</td>
<td>0.00 (-0.46, 0.46)</td>
</tr>
<tr>
<td>CBT with Relaxation Training</td>
<td>0.33 (-0.07, 0.74)</td>
</tr>
<tr>
<td>Relaxation Training alone</td>
<td>0.90 (0.44, 1.44)</td>
</tr>
</tbody>
</table>

CBT, cognitive-behavioral therapy; CI, confidence interval.
ADJUSTING PSYCHOTHERAPEUTIC INTERVENTIONS FOR OLDER ADULTS

- Incorporate religion and/or spirituality for older African American subjects
  
- 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

- CBT in primary care: improvement in worry severity, depressive symptoms, and general mental health for older patients with GAD

- Internet delivered CBT: older patients more likely to complete iCBT than younger patients, but younger adults responded more robustly

\section*{TREATMENT OPTIONS - CONCLUSIONS}

- GAD is one of the least likely mental disorders to remit and most likely to relapse \textsuperscript{1}

- Current treatment choices reduce overall burden of anxiety but are less effective in reducing worry severity \textsuperscript{2,3}

- Sequential pharmacotherapy \rightarrow psychotherapy \textsuperscript{4}

- Treatment modified to fit the needs of older subjects

1. Lenze et al, 2011
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.

Learn More