Anxiety Disorders in the Elderly

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Objectives:

- Understand the characteristics of anxiety disorders in old age
- Recognize the diagnostic challenges
- Gain more awareness of treatment options and challenges in the management of such disorders
Outline:

- Epidemiological Considerations
- Clinical Presentation
- Treatment
Epidemiological considerations:
Prevalence:

History:

- Murphy et al. (1984): Generalized Anxiety 2.9% in all ages. <1% in men >45, 2% in women >45.
- Warheit et al. (1980): Blacks, females, the elderly had highest self-reported scores of anxiety.
Methodological issues:

- Some argue that anxiety disorders in this population are qualitatively different.
- Current diagnostic criteria do not capture such disorders in this population.
- They also argue that most of these disorders occur in the context of depression (Flint, 2005).
- Co-morbidity with physical problems poses diagnostic challenges.
- Study of anxiety in cognitive disorders remains largely neglected (Bryant et al., 2008).
Contemporary studies:

NCS-R (2005): Anxiety disorders are commonest problem (1-yr prevalence 18.1% vs. 9.5% for mood disorders). Lifetime prevalence = 15.3%

- 2% for Panic Disorder
- 1% for Agoraphobia
- 7.5% for Specific phobia
- 6.6% for Social phobia
- 3.6% for GAD
- 2.5 for PTSD
- 0.7% for OCD
ECA (1990): GAD 1-yr prevalence 2.2% in >65

Cumulative prevalence of GAD
<table>
<thead>
<tr>
<th>Age</th>
<th>Outpatient use%</th>
<th>Inpatient use%</th>
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<tbody>
<tr>
<td>45-64</td>
<td>37</td>
<td>10.3</td>
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<tr>
<td>65+</td>
<td>53.5</td>
<td>38.4</td>
</tr>
</tbody>
</table>

Use of inpatient & outpatient general health services by age & diagnosis of GAD (ECA)
Many have onset of GAD in childhood/adolescence. About half develop the disorder in late life (Le Roux et al., 2005)

There is a widely held belief that these disorders tend to be less common in older adults than their younger counterparts
24% of medically ill older adults have an anxiety disorder (Tolin et al., 2005)
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Homebound & those in NH have higher rates (Juninger et al., 1993)
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Homebound & those in NH have higher rates (Juninger et al., 1993)

Up to 20% have significant anxiety symptoms but do not meet criteria (Himmelfarb & Murrell, 1984)
Late-life anxiety is associated with disability, impairment in QoL, and \( \uparrow \) MR (De Beurs et al. 1999; van Hout et al., 2004; Wetherell et al., 2004)
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It is also associated with ↑ visits to primary care & ↑ length of visits (van Hout et al., 2004)
Fear of falling:

- Poor balance
- Reduced activity levels
Research in this field is scanty vs in late-life depression despite the higher prevalence and associated doubling of Medicare claims (Ayers et al., 2009)
Clinical presentation:

- Risk factors
- Medical disorders that could masquerade as anxiety
- Specific presentations of various anxiety disorders
- Co-morbidity
- Assessment instruments
<table>
<thead>
<tr>
<th>Biological</th>
<th>Psychological</th>
<th>Social</th>
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<tbody>
<tr>
<td>• Number of chronic health conditions</td>
<td>• Personality traits (Cluster C)</td>
<td>• Attachment status</td>
</tr>
<tr>
<td>• Cardiovascular &amp; cerebrovascular factors</td>
<td>• Locus of control</td>
<td>• Relationship problems</td>
</tr>
<tr>
<td>• General poor health status</td>
<td>• Neuroticism</td>
<td>• Childhood adversity</td>
</tr>
<tr>
<td>• Polypharmacy especially if there is abuse</td>
<td>• Lower level of extraversion</td>
<td>• Recent negative life events</td>
</tr>
<tr>
<td>• Poor self-perceived health &amp; pain</td>
<td>• Impulsivity</td>
<td>• Spousal depressive symptoms</td>
</tr>
<tr>
<td>• Functional limitations &amp; sensory impairment</td>
<td>• Dysfunctional coping</td>
<td>• Recent traumatic events incl. crime</td>
</tr>
<tr>
<td>• Alcohol, smoking, obesity</td>
<td>• Low self-esteem/ego-strength</td>
<td>• Being older</td>
</tr>
<tr>
<td></td>
<td>• Past psychiatric hx</td>
<td>• Lower educational attainment</td>
</tr>
</tbody>
</table>

(Vink et al., 2008)
Clinical Presentation:
Medical disorders that could mimic anxiety

(Beyer & Krishnan, 2002)
Clinical Presentation:

- Worry is different in this population group. Work & interpersonal matters vs illness/injury/health (Roemer et al., 1997; Hunt et al., 2003)
- OCD:
  - Symmetry/need to know/counting vs hand washing/fear of having sinned (Kohn et al., 1997).
  - Higher levels of hoarding (Teachman, 2007)
Panic Disorder:
- Lower levels of arousal
- Less avoidance
- Fewer symptoms
- Less depression (Sheikh et al., 2004)

SAD:
- No systematic studies.
- Eating & writing in public can be exceedingly difficult

Phobia:
- Fear of crime is particularly prevalent (Cassidy et al., 2002)
GAD: Those with early onset have a more severe course.

- Breakdown in coping skills vs. inherent vulnerability
- Role disability may be a risk factor (Le Roux et al., 2005)

PTSD: Evidence supporting onset may be delayed until later life or symptoms might re-emerge (Port et al., 2001)

- Cognitive impairment (attention, WM, EM)
- Social isolation & worsening of health (Floyd et al., 2002)
- Failure of suppression of symptoms due to ↓ levels of activity (Lipton & Shaffer, 1988)
Medical Co-morbidity:

Anxiety

- GAD
- Panic
- PTSD
- Sub-threshold symptoms

Medical Problems

- CVS
- Respiratory
- Endocrine
- GIT

- Headaches
- Muscle aches
- Diarrhea
- Sleep disturbance
Primary Care Physicians

(Ayers et al., 2009)
Psychiatric Co-morbidity:

Depression:

- 35% of those with depression have $\geq 1$ lifetime anxiety-problem & 23% have a current diagnosis (Lenze et al., 2000)
- Anxiety often leads to depression (Lenze et al., 2005)
- 10% of a community sample suffered from $\geq 2$ anxiety diagnoses (van Belkom et al., 2000)
- There is under-recognition by clinicians and under-reporting by patients of anxiety in this situation (Lindesay, 2000)
- Best perceived dimensionally
Substance Misuse:

- Little research has been done in this field.
- It is suggested that hypnotics, alcohol & anti-anxiety medication are misused in an attempt to self-medicate (van Belkom et al., 2000).
Cognitive Impairment:

- Few studies
- Linear relationship:
  - ↑anxiety $\rightarrow$ ↓poorer reasoning, learning, executive functions, STM & attention (Mantella et al., 2007)
  - ↑cognitive impairment $\rightarrow$ ↑anxiety symptoms (Beaudreau & O’Hara, 2008)
- Higher rates of anxiety in MCI (Apostolova & Cummings, 2008)
Those with MDD & a co-morbid anxiety disorder exhibited greater memory decline than those without an anxiety disorder (DeLuca et al., 2005).

Comorbid anxiety in MCI may be a strong indicator of an underlying neurodegenerative process (Beaudreau & O’Hara, 2008).

Executive dysfunction negatively impacts treatment outcome in late-life anxiety disorders (Mohlman, 2005).
Dementia:

158 subjects from a memory clinic:

- 22% subjective anxiety
- 11% autonomic anxiety
- 38% tension
- 13% situational anxiety
- 29% had one or more anxiety symptom (Ballard et al., 1996)

May be higher in VaD than AD and decreases as illness progresses (Seignourel et al., 2008)
Assessment instruments:

- Studies usually use instruments that have not been validated in this population.
- Older patients may have problems with accurate identification of their own anxiety symptoms.
- There is a need to use cohort-appropriate language (Wetherell et al., 2003).
Clinician Rating Scales:

- Hamilton Anxiety Rating Scale (HARS)
- Anxiety Disorders Interview Schedule (ADIS-R)
- Structured Clinical Interview for the DSM (SCID DSM-III version) (Spitzer et al., 1987; Beck et al., 1999)
- Clinician-Administered PTSD Scale (CAPS) (Hyers et al., 1996)
Self-report Measures:
- Beck Anxiety Inventory (BAI)
- State-trait Anxiety Inventory (STAI)
- Penn State Worry Questionnaire (PSWQ)

Other self-report measures:
- Adult Manifest Anxiety Scale-elderly (AMAS-E)
- Short Anxiety Screening Test (SAST)

(Ayers et al., 2009)
Treatment & Prognosis:

- Talking therapies
- Herbal remedies
- Pharmacological treatments
CBT:

- Education
- Self-monitoring
- Relaxation training
- Exposure & Response Prevention
- Cognitive restructuring

- Problem solving skills training
- Sleep hygiene
- Other therapies: Psychodynamic, CAT, IPT, Systemic family therapy, supportive therapy
Most widely researched therapy with strong evidence base (Thorp et al., 2009)

CBT more effective than MCC or WL (Stanley et al., 2003)

Memory aides & between-session calls led to better compliance & ↑ effect size (Mohlman et al., 2003)

Studies in PD & PTSD in this population are sparse

RT produced mixed results. Evidence points to necessity of practice.

Imagined relaxation = standard progressive muscle relaxation (De Berry, 1981)
CALM study: (controlling anxiety in later-life medical patients)

- Recognizing anxiety
- Learning to relax
- Getting to sleep
- Solving problems
- Accepting the inevitable
Controlling worry
Increasing your pleasure
Challenging your thoughts
Facing your fears
Coping with pain
Asserting yourself
Managing your time
Maintaining your progress

(Wetherell et al., 2005)
Some procedural modifications:

- **Tackling cognitive changes**
  - Repeat & summarize information
  - Present information in multiple modalities
  - Use folders & notebooks
  - Consider offering memory training

- **Tackling sensory impairment**
  - Help correct if possible
  - Prepare written material in large bold fonts
  - Use tape recorders
Physical health:
- Agree realistic goals
- Tackle dysfunctional beliefs that limit activity
- Input from geriatric medicine

Therapy setting & format:
- Be flexible
- Consider using an outreach approach
- Consider merits of group vs individual CBT

(Evans, 2007)
Sleep hygiene:

- Maintain a regular sleep-wake cycle & restrict naps
- Avoid caffeine after 12:00 pm
- Daily exercise during morning hours
- Move evening meal to an earlier time
- Hot bath before bedtime
- Small bedtime snack (eg. Hot milk)
- Meditation or relaxation exercises at bedtime
- Keep bedroom quiet & dark
- Quit smoking, limit liquids in the evening and/or bladder re-training
Herbal Remedies:

- Readily available
- 34% of users of complimentary medicine take these remedies
- 18.9% of adult Americans have used natural products in the previous year (Barnes et al., 2004)
- Depression & anxiety are prominent indications
- 41 million websites offering information (Ernst, 2007)
- Interaction with prescribed drugs
- Side effects
<table>
<thead>
<tr>
<th>Herbal medicines</th>
<th>Synthetic drugs</th>
</tr>
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<tbody>
<tr>
<td>Active ingredient unknown</td>
<td>Active ingredient known</td>
</tr>
<tr>
<td>Pure compound not available</td>
<td>Pure compound available</td>
</tr>
<tr>
<td>Quality variable</td>
<td>Quality controlled</td>
</tr>
<tr>
<td>Mechanism often unknown</td>
<td>Mechanism usually known</td>
</tr>
<tr>
<td>Toxicology often unknown</td>
<td>Toxicology known</td>
</tr>
<tr>
<td>Wide therapeutic window</td>
<td>Narrow therapeutic window</td>
</tr>
<tr>
<td>Adverse effects rare</td>
<td>Adverse effects frequent</td>
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</tbody>
</table>

(Ernest, 2007)
<table>
<thead>
<tr>
<th>Condition</th>
<th>Not effective</th>
<th>Promising</th>
<th>Effective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>Gingko Biloba (maiden hair tree)</td>
<td>Lavandula angustifolia (common lavender)</td>
<td>Hypericum perforatum (St John’s Wort)</td>
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<td></td>
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<td>Crocus sativus (saffron crocus)</td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>Valeriana officinalis (valerian)</td>
<td>Matricaria recutita (German chamomile)</td>
<td>Piper methysticum (kava)</td>
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<tr>
<td></td>
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<td>Melissa officinalis (lemon balm)</td>
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</table>

(Ernest, 2007)

• **Passiflora (passion flower): equivocal results**

(Miyasaka et al., 2009)
Pharmacological treatment:
Polypharmacy:

- Over 30 new medications are introduced each year
- Recognizing drug interactions is a daily challenge and is becoming increasingly more difficult
- Multiple drug regimes carry the risk of adverse interactions
- Precipitant drugs modify the object drugs absorption, distribution, metabolism, excretion or clinical effect
Average use for persons 65 years or older:

- 2 to 6 prescription drugs and 1 to 3.4 over-the-counter medicines

The most consistent risk factor for adverse drug reactions (ADRs) is the number of drugs being taken

- Risk rises exponentially as the number of drugs increases
Drug reactions in the elderly often produce effects that simulate the conventional image of growing old:

- Unsteadiness
- Dizziness
- Confusion
- Nervousness
- Fatigue
- Insomnia
- Drowsiness
- Falls
- Depression
- Incontinence
- Malaise
Pharmacokinetics:

Oral ingestion

Absorption
(stomach, small intestine)

First pass through liver

Systemic circulation and distribution

Brain
Other target organs
Peripheral storage sites (fat or muscle)

Metabolism
(liver)

Elimination
(kidneys)

Adipose tissue

Muscle

Intramuscular/
Subcutaneous

Intravenous

(Jacobson et al., 2007)
Pharmacodynamics:

- Little studied in aging populations
- Increased pharmacodynamic response is only postulated
- Reduced receptor density is proven in aging
- The ability to up- or down-regulate postsynaptic receptors may decrease with aging
Benzodiazepines (BZ):

- Most common treatment
- 33% of NS women are currently prescribed BZ’s
- Help with short-term symptoms
- Limited & short-term use is recommended (Sheikh & Cassidy, 2000)
Serious AE: Falls, cognitive impairment, ataxia, poor coordination, MVA

Medical use vs recreational use (Jacobson et al., 2007)

Absorption: ↑ by alcohol ↓ antacids

Level ↑ by CYP3A4 inh. (antifungals, antibiotics, fluvoxamine & grapefruit juice)

Level ↓ CYP3A4 ind. (CBZ, St. John’s Wort, smoking, ch. Alcohol use)
Relative risk and falling in current users of benzodiazepines (Ensrud et al., 2002)
<table>
<thead>
<tr>
<th>Benzodiazepines</th>
<th>Main characteristics</th>
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<tbody>
<tr>
<td></td>
<td>Anxiolytic</td>
<td>Hypnotic</td>
<td>Protein binding (%)</td>
<td>Rate of absorption</td>
<td>Hepatic Insufficiency (affected by)</td>
<td>T1/2 (average; hours)</td>
<td>Sedation</td>
<td>Hypoexcitability phenomenon</td>
<td>Memory impairment</td>
<td>Sleep architecture impairment</td>
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<tr>
<td>Chloridiazepoxide</td>
<td>96</td>
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<tr>
<td>Diazepam</td>
<td>98</td>
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<tr>
<td>Flurazepam</td>
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<tr>
<td>Halazepam</td>
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<tr>
<td>Prazepam</td>
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<td>2-Keto</td>
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<tr>
<td>Lorazepam</td>
<td>85</td>
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<td>15</td>
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<td>Temazepam</td>
<td>96</td>
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<td>12</td>
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<td>Oxazepam</td>
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<td>Triazolo</td>
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<td>Triazolam</td>
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<td>Clonazepam</td>
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<td>Nitrazepam</td>
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<td>30</td>
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<td>Non-benzodiazepines</td>
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<td>The ‘Z’ drugs</td>
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<td>Zaleplon</td>
<td>??</td>
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<td>1.5</td>
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<tr>
<td>Zolpidem</td>
<td>92</td>
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<td>3</td>
<td></td>
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<tr>
<td>Zopiclone</td>
<td>60</td>
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<td></td>
<td>5</td>
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**Legend**

- **More characteristic**
- **Less characteristic**
- **Rarely causes side-effect or data is not well-established**
- **Most effective as**
Benzodiazepine withdrawal:

- Interruption or D/C of therapeutic doses → rebound symptoms of anxiety
- D/C of high doses → withdrawal symptoms
- Withdrawal peaks @ 2 days for short-acting agents & 4-7 days for longer ones
- Most patients tolerate a tapering of 10-25%/week (Jacobson et al., 2007)
### Hypnotics:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Onset of effect</th>
<th>Peak level (hours)</th>
<th>Major active metabolite</th>
<th>Parent half-life (hours)</th>
<th>Metabolite half-life (hours)</th>
</tr>
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<tbody>
<tr>
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<td></td>
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<tr>
<td>eszopiclone</td>
<td>Intermediate</td>
<td>1</td>
<td>No</td>
<td>9</td>
<td>—</td>
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<tr>
<td>ramelteon</td>
<td>Intermediate</td>
<td>0.5–1.5</td>
<td>No</td>
<td>1–2.6</td>
<td>—</td>
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<tr>
<td>zaleplon</td>
<td>Intermediate</td>
<td>1</td>
<td>No</td>
<td>1–2</td>
<td>—</td>
</tr>
<tr>
<td>zolpidem</td>
<td>Intermediate</td>
<td>2.2</td>
<td>No</td>
<td>2–2.6</td>
<td>(longer in elderly)</td>
</tr>
</tbody>
</table>

(Jacobson et al., 2007)
Antidepressants:

- **Fluvoxamine**: Good response in a sample with mixed anxiety disorders (Wylie et al., 2000)
- **Venlafaxine**: Effective in GAD (Katz et al., 2000)
- **Citalopram**: Superior to PL in the only prospective study of an SSRI (Lenz et al., 2005)

All antidepressants are superior to placebo in GAD with an NNT of 5.15 (Kapczinski et al., 2003)
Other agents:

- **Prazosin**: 50% reduction in nightmares in PTSD
  
  (Peskind et al., 2003)

- **Buspirone**:
  - 5-HT1A presynaptic receptor agonist & partial 5-HT1A postsynaptic agonist
  - Causes downregulation of 5-HT2 receptors (similar to antidepressants)
  - Long latency to effect, short T ½
  - May not be effective in those recently exposed to BZ’s (DeMartinis et al., 2000)
  - “Azapirones may be less effective than benzodiazepines and we were unable to conclude if azapirones were superior to antidepressants, kava kava or psychotherapy” (Chessick et al., 2009)

- **Cognitive enhancers in dementia** (donepezil & galantamine)
Best avoided:

**Antihistaminics:**
- Readily available over the counter (diphenhydramine, doxylamine)
- Anticholinergic side effects
- Daytime sedation
- Impairment of driving skills

**Antipsychotics:**
- Not recommended for the treatment of anxiety &/or insomnia in non-psychotic elderly patients
Prognosis:

Panic Disorder:

- No systematic studies
- Rarely resolves without intervention
- If untreated 50% develop depression & 43% have attempted suicide
- May lead to alcohol abuse, higher CV mortality in males (Coreyll, 1988)
GAD:

- Presence of a co-morbid diagnosis is associated with worse prognosis
- Women are especially vulnerable (Yonkers et al., 1996)
Thank you