Late-Life Depression and Anxiety

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What do these older adults have in common?

- Mr. A: Irritable and socially withdrawn, says “I am not depressed”
- Ms. B: Convinced she has cancer despite negative workup, mood is anxious
- Mr. C: High blood pressure, atrial fibrillation, sedentary and apathetic
- Mr. D: After his stroke, poor participation in rehab and hopeless about the future
- Ms. E: Moderately demented, refuses food and moans all night

Prevalence of Depressive Syndromes in Later Life

	Clinically Significant Depressive Symptoms[1]	**Major Depressive Disorder[1]**
Community	**8-15%** 9.7-26.1% for 75+[3]	**1-3%** 4.4-10.6% for 75+[2]
Primary Care		6-9%[3]
Long Term Care	30-50%	6-25%

Bipolar Disorder, in comparison, affects 0.1-0.4%[4] older adults.

1. Ellison JM, Gottlieb G: Recognition and management of late life mood disorders. In: Sirven JI, Malamut BL (eds): Clinical Neurology of the Older Adult, 2nd Edition. Philadelphia, Lippincott Williams & Wilkins, 2008; 2. Luppa et al. J Aff Dis 2012;136:212-221; 3. National Health and Nutrition Survey 2013-2016; 4. Unutzer et al. Milbank Q 1999;77:225-6

Adverse Outcomes of Untreated LLD[1-7]

- Increased use of non-mental health services
  - 2x medical appointments, 2x polypharmacy
- Reduced medical treatment adherence
- Functional Decline / Increased disability
- Increased morbidity/mortality:
  - CVA/MI/Hypertension/Diabetes/Dementia/SUD/Suicide
- Increased health care costs[7]
- And yet – more than ½ of depressed elders go untreated.[8]

1. Beekman et al. Psychol Med 1997;27:1397-409; 2. Bruce and Leaf. Am J Public Health. 1989;79:727-30; 3. Romanelli et al. J Am Geriatr Soc 2002;50:817-22; 4. Alexopoulos GS. *Lancet* 2005; 365): 1961–70; 5. Katon et al. Arch Gen Psychiatry 2003;60:897-903; 6. Hall and Reynolds. Maturitas 2014;79:147-52; 7. Beyer and Johnson Current Psychiatry Reports 2018;20:34-;8. Barry et al. J Affect Dis 2012;136:789-96.

Some Risk Factors for LLD

- Demographic Risk Factors
  - Older age
  - Female sex
  - Race/Ethnicity (Black, Hispanic)
  - Educational level
  - Lower income
  - Transitioning to retirement
- Health
  - Physical disability
  - Diabetes mellitus
  - HTN/OH
  - Vascular disease
  - Sensory deficits
  - Cognitive impairment
  - Pain
  - Sleep disturbance
- Low Social Support
  - Marital status/Conflict/Divorce
  - Caregiver burden
  - *Bereavement/Loss
  - Limited network/ *Loneliness/Social conflict
  - Less Spirituality support
- Habits
  - Alcohol use
  - Smoking
  - Diet (non inflammatory diet)
  - Low physical activity
  - Obesity

Vyas CM, Okereke. Harvard Review of Psychiatry, 2020;28(2):72–99. doi:10.1097/HRP.0000000000000240 : PMID 31977599.

Diagnosis:
The Definitions

DSM-5-TR MDD = DSM-4-TR Minus Bereavement Exclusion

- **5 required sx (present at least 2 wk), depressed mood OR loss of interest (I) /pleasure must be present. At least 4 additional symptoms present most or all days:**
  - weight loss or appetite decrease/weight gain (A)
  - insomnia/hypersomnia (S)
  - psychomotor agitation/retardation (P)
  - fatigue/loss of energy (E)
  - worthlessness/guilt (G)
  - diminished concentration/decision-making (C)
  - thoughts of death/suicide/attempt (S)
- Distress or functional impairment
- Medical/Substance/Psychiatric exclusions
- There has not been a manic/hypomanic episode

SIG: E CAPS

Sleep
Interest
Guilt/worthlessness
Energy
Concentration
Appetite/weight
Psychomotor
Suicidal

MDD = "Major Depressive Disorder"

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Text Revision. Washington DC, American Psychiatric Association, 2022.

New for DSM 5/5-TR: Persistent Depressive Disorder

- Incorporates 2 DSM IV disorders: **Chronic Major Depressive Disorder** and **Dysthymic Disorder**
  - Depressed mood more days than not, for at least **2 years**
  - **Two or more** of these sx: appetite, sleep, energy, self-esteem, concentration, hopelessness
  - No remission more than 2 months at a time in 2 yr period
  - Major Depressive Disorder criteria may also be met.
  - Symptoms are not explained by manic, hypomanic, cyclothymic, other psychiatric, substances, medical
  - Significant distress (social, occupational, other)

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Text Revision. Washington DC, American Psychiatric Association, 2022.

What Is Exceptional About LLD?

- 1. Etiologies can differ
  - Recurrence of early onset mood disorder
  - Unique psychosocial stressors of late life (including loneliness)
  - Affective consequences of medical burden:
    - Medical sx can mimic depressive sx
    - Vascular depression hypothesis[1]
    - Inflammation hypothesis[2]
- 2. Locus of Care: Help sought in Primary Care
  - Higher medical burden (illnesses, symptoms)
  - Comfort/relationship with Primary Care setting
  - Untreated/undertreated patients are common[3]

1. Alexopoulos et al. Dialogues Clin Neurosci 1999;1:68-80; 2. Maes et al. Metab Brain Dis 2009;24:27-53;
3. Mitchell et al. Psychother Psychosom 2010;79:285-94.

3. Presentations Can Obscure Diagnosis

A. Subthreshold: Beneath "Major Depression"

B. Different symptoms:

- **"Depression without sadness"[1]**
- **Somatic (sometimes cognitive) focus**
- **Depression with psychotic features**

C. Medical etiology of symptoms:

- **Depression with cerebrovascular disease (vascular and post-CVA depression)**
- **Depression with cognitive impairment[2,3]**

1,Gallo and Rabins. Am Fam Physician 1999;60:820-6; 2. Butters et al. Am J Psychiatry 2000;157:1949-54;
3. Sáez-Fonseca et al. J Affect Disord 2007;101:123-9

D. More About Depression with Psychotic Features

- Delusions (mood-congruent)/hallucinations (auditory) with MDD symptoms.
- Higher prevalence in older depressives.[1]
  - 20-45% of hospitalized older depressed adults
  - 15% of community older depressed adults
- Associated with:[2,3]
  - Later onset
  - Poorer response to monotherapy/maintenance
  - Higher recurrence rate/suicide risk
- ECT or combination ADD/APD are best treatments.[4]

1. Reinhardt and Cohen. Curr Psychiatry Rep 2015;17:1; 2. Gournellis et al. Int J Geriatr Psychiatry 2001;16:1085-91;
3. Flint and Rifat Am J Psychiatr 1998;155:178-83; 4. Meyers et al. Arch Gen Psychiatry. 2009;66:838–47.

Assessment Approach

1. Screening Tools for LLD

- CES-D, HAM-D, MADRS, BDI
- ***Geriatric Depression Scale (GDS)**
- ***PHQ-2, PHQ-9**
- ***Cornell Scale for Depression in Dementia (CSDD)**

1. Diagnosing, Screening, and Monitoring Depression in the Elderly: A Review of Guidelines. Canadian Agency for Drugs and Technologies in Health. Accessed 12/27/15; https://www.cadth.ca/sites/default/files/pdf/htis/sep-2015/RC0691_Diagnosing%20depression%20in%20elderly_Final.pdf; 2. Phelan et al. BMC Fam Pract. 2010;11:63.

A. Assessment: GDS 15

1. **Are you basically satisfied with your life ?**
2. **Have you dropped many of your activities and interests ?**
3. **Do you feel that your life is empty ?**
4. **Do you often get bored ?**
5. **Are you in good spirits most of the time ?**
6. **Are you afraid that something bad is going to happen to you ?**
7. **Do you feel happy most of the time ?**
8. **Do you often feel helpless ?**
9. **Do you prefer to stay at home, rather than going out and doing new things ?**
10. **Do you feel you have more problems with memory than most?**
11. **Do you think it is wonderful to be alive now ?**
12. **Do you feel pretty worthless the way you are now?**
13. **Do you feel full of energy ?**
14. **Do you feel that your situation is hopeless ?**
15. **Do you think that most people are better off than you are ?**

GDS is in the Public Domain, can be freely reproduced and used. Score 1 pt for each "Yes" on 2,3,4,6,8,9,10,12,14,15 or "No" on 1,5,7,11,13. A score of 6 or higher suggests need for definitive diagnostic evaluation. (http://www.stanford.edu/~yesavage/GDS.html)

D. Cornell Scale for Depression in Dementia

Scoring System

A = unable to evaluate 0 = absent 1 = mild or intermittent 2 = severe

Ratings should be based on symptoms and signs occurring during the week prior to interview.

No score should be given in symptoms result from physical disability or illness.

A. Mood-Related Signs	
1. Anxiety: anxious expression, ruminations, worrying	0 1 2
2. Sadness: sad expression, sad voice, tearfulness	0 1 2
3. Lack of reactivity to pleasant events	0 1 2
4. Irritability: easily annoyed, short-tempered	0 1 2
B. Behavioral Disturbance	
5. Agitation: restlessness, handwringing, hairpulling	0 1 2
6. Retardation: slow movement, slow speech, slow reactions	0 1 2
7. Multiple physical complaints (score 0 if GI symptoms only)	0 1 2
8. Loss of interest: less involved in usual activities	0 1 2
(score only if change occurred acutely, i.e. in less than 1 month)	

Alexopoulos et al. Biol Psych 1988;23:271-284.

C. Physical Signs

9. Appetite loss: eating less than usual	0 1 2
10. Weight loss (score 2 if greater than 5 lb. in 1 month)	0 1 2
11. Lack of energy: fatigues easily, unable to sustain activities (score only if change occurred acutely, i.e., in less than 1 month)	0 1 2

D. Cyclic Functions

12. Diurnal variation of mood: symptoms worse in the morning	0 1 2
13. Difficulty falling asleep: later than usual for this individual	0 1 2
14. Multiple awakenings during sleep	0 1 2
15. Early morning awakening: earlier than usual for this individual	0 1 2

E. Ideational Disturbance

16. Suicide: feels life is not worth living, has suicidal wishes, or makes suicide attempt	0 1 2
17. Poor self esteem: self-blame, self-depreciation, feelings of failure	0 1 2
18. Pessimism: anticipation of the worst	0 1 2
19. Mood congruent delusions: delusions of poverty, illness, or loss	0 1 2

Alexopoulos et al. Biol Psych 1988;23:271-284.

2. Medical Burden: Assess Contribution

- Medications, Alcohol, Drugs
- Endocrinopathy
- Malignancy
- Infection
- Metabolic disorders
- Nutritional deficiencies
- Sleep disorders
- Vascular disease
- Neurological disorders

- Depressive episode should be treated while independently managing medical condition

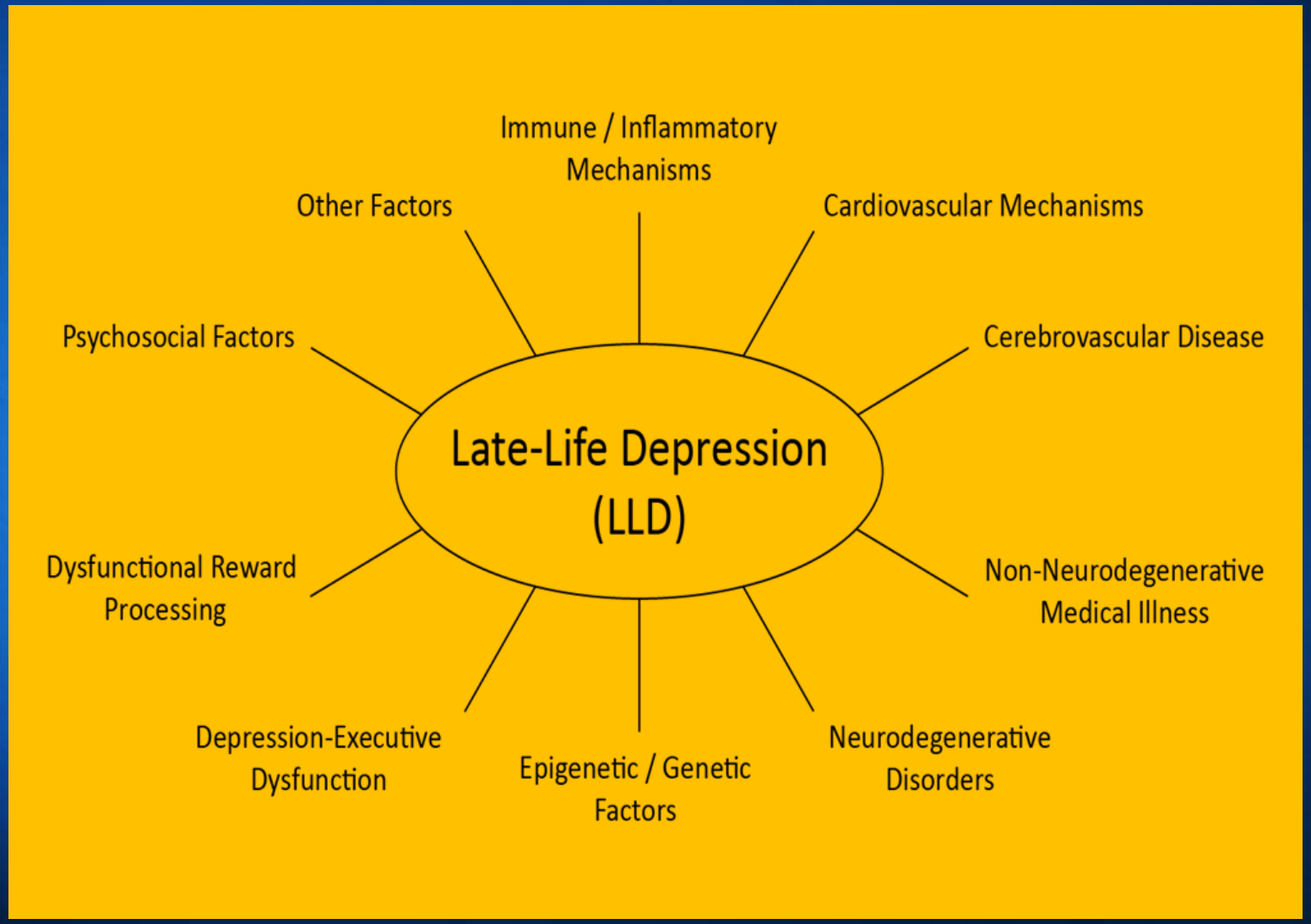
3. Laboratory Results: Identify and Manage Remediable Medical Contributors

- **Hematology**
  - CBC with indices/differential
  - ESR
- **Chemistry**
  - Lytes, BUN, Creatinine
  - Liver function tests
  - Thyroid function tests
  - Fasting glucose level
  - Folate, B12[1]
- **Urine**
  - Urinalysis
  - Culture and sensitivity
- **Additional tests, e.g.**
  - Electrocardiogram
  - Chest X-Ray
  - Neuroimaging (?)

1. Petridou et al. Aging Ment Health 2016;20(9):965-73. doi: 10.1080/13607863.2015.1049115.

Treatment Approach

1. Assess Contributing Factors



Husain-Krautter and Ellison. Focus 2021;19:282-93.

2. Address Substance Use

- Benzodiazepines:
  - Chronic use (daily>3 months): 12% of elderly [1]
  - 9.5% of users are dependent[1]
- Alcohol (>7 drinks/wk is considered excessive)
  - 25% of elderly are daily drinkers
  - 10% of elderly alcohol users "binge drink"[2]
- Other drugs of concern: analgesics, hypnotics
- Illicit and nonmedical prescription drug use much greater among 50-64 year olds.[1]

1. Wu and Blazer. J Aging and Health 2011;23:481-504; 2. Culberson. Geriatrics 2006;61:23-27.

3. Address Pain

- Pain often accompanies MDD[1]
  - Chronic painful physical conditions are increased fourfold in MDD patients.
  - Headache, neck and back, abdominal, and musculoskeletal pain are common.
- Chronic painful physical conditions are an independent risk factor for MDD and poor treatment response.[1]
  - Pain affects other depressive symptoms adversely (exacerbates sleep, energy, anxiety symptoms).
  - MDD+pain is associated with worse outcome to SSRI treatment proportional to pain severity.
- The presence of pain is associated with increased help-seeking[2]

1. Brannan et al. J Psychiatr Research 2005;39:43-53; 2. Bonnewyn et al. J Aff Dis 2009;117:193-6.

Depression and Medical Illness

- Medical burden in the elderly is great, and illnesses complicate the diagnosis of depression because of overlapping symptoms.
- Many illnesses are linked with increased depression risk: e.g. Coronary Artery Disease (15-23%), Diabetes Mellitus (17-25%), ESRD with dialysis (25%), Cancer (25%)
- Disease mechanisms can be synergistic; treatment requires attention to adverse effects / interactions.
- In general, the medical disorder and depression are both treated.

see Harnett and Pies, in Ellison et al (eds). Mood Disorders in Later Life (2nd Ed). Taylor & Francis 2008.

4. Consider Non-Pharmacological Treatments

- Non-pharmacological strategies, alone or with antidepressants, are effective in treating Late Life Depression and should be strongly considered when planning treatment.

Reynolds CF 3rd, Dew MA, Martire LM, *et al*. Treating depression to remission in older adults: a controlled evaluation of combined escitalopram with interpersonal psychotherapy versus escitalopram with depression care management. Int J Geriatr Psychiatry 2010; 25:1134–1141.

A. Several Evidence-Based Psychosocial Interventions Treat Late Life Depression

- Spirituality[1]:
  - Spirituality attenuates the link between depressive symptom severity and feelings of meaningless in life.
- Psychotherapy with RCT support:[2]
  - Supportive Therapy
  - Cognitive Behavioral Therapy (CBT)
  - Interpersonal Therapy (IPT)
  - Problem Solving Therapy (PST)
  - ENGAGE

1. Bamonti et al. Aging Ment Health 2016;20:494-9; 2. See Antognini and Liptzin in Ellison et al. Mood Disorders in Later Life. Informa 2008.

B. Physical Activity

- Greater midlife physical activity is associated with lower depressive sx in later life.[1]
- Physical inactivity in older adults is associated with both depression and cognitive deficits.[2]
- Meta-analysis supports LLD benefit for Physical Exercise, more evidence needed to support use over 80 years old or with MMSE < 23/30.[3]
- Higher and faster remission in LLD linked with exercise augmentation of sertraline (24 wk of PAE).[4]

1. Chang et al. J Gerontol A Biol Sci Med Sci. 2016;71(4):502-7. doi: 10.1093/gerona/glv196; 2. Gallagher et al. J Affect Disord 2016;190:235-240. doi: 10.1016/j.jad.2015.09.046; 3. Klil-Drori et al. J Clin Psychiatry 2020;21;81(1):19r12877. doi: 10.4088/JCP.19r12877; 4. Belvederi Murri et al. Br J Psychiatry 2015;207:235-42.

5. Pharmacologic Treatment

Antidepressant Efficacy

- All FDA-indicated antidepressants treat LLD[1]
- Response rate (50% symptom decrease)[2]
  - 50 – 65% in ITT* trials, 25 – 30% respond to placebo
  - Number Needed to Treat (NNT*): 2.5 to 5
- Remission (≥90% symptom decrease)[2]
  - Typically 30 – 40% with medication vs 15% for placebo, NNT: 4 to 7
- Most important barrier = undertreatment![3,4]

ITT: Intention to Treat, NNT: Number Needed to Treat

1. See Ellison et al. Mood Disorders in Later Life. Taylor & Francis 2008; 2. Shanmugham et al. Psychiatr Clin North Am. 2005;28:821-35;3.Wang et al. J Clin Psychopharmacol 2005;25:118-26; 4. Barry et al. J Affect Disord 2012;136:789-96.

Geriatric Side Effects: SRIs

- Discontinuation is less common with SSRI treatment than with TCA treatment. But significant side effects with SRIs include:
  - Sedation
  - Weight gain
  - GI symptoms
  - Hyponatremia
  - Risk for bruising
  - Risk for GI bleeding
  - Sexual dysfunction
  - Falls?

Antidepressant Drug/Drug Interactions

- Age exacerbates potential for adverse effects and interactions
  - Hepatic inactivation of drugs ↓
  - Renal elimination of drugs ↓
  - Anticholinergic vulnerability ↑
- Average adult > 65 years old is on 4 or more prescribed medications daily, 39% on 5 or more/d[1]
- Many interactions are possible
  - Pharmacodynamic
  - Pharmacokinetic

1. Sollitto M. https://www.agingcare.com/articles/polypharmacy-dangerous-drug-interactions-119947.htm

Antidepressant Cost

- Adherence can depend upon affordability
- Limitations of Medicare Part D
- Range of generically available antidepressants
- Avoid **first line** use of brand name drugs:
  - Trintellix (vortioxetine)
  - Fetzima (levomilnacipran)
  - Spravato (intranasal ketamine isomer)
  - Auvelity (dextromethorphan/bupropion)
  - Exxua (gepirone)

SSRIs – Still 1st Choice in LLD

- Several are well-tested, generic, well-tolerated, with limited drug interactions, appropriate elimination half-lives.
  - A Danish registry study tracking 96,737 antidepressant-naïve older adults found lowest d/c rate with **sertraline**. Venlafaxine, mirtazapine, escitalopram had higher d/c rates in this, but not in a different study.[1]
  - Avoid:[2]
    - Citalopram/escitalopram with high baseline QTc
    - Amitriptyline and paroxetine (high anticholinergic burden)
  - Favor bupropion and mirtazapine with past/current low Na^+.[2,3]

1 Ishtiak-Ahmed et al. Am J Psychiatry 2024;181:47-56; 2. Walaszek A. Am J Psychiatry 2024;181:7-10; 3. Holland and Bhogle. Psychiatr Danub. 2013;25 Suppl 2:S286-90.

Additional Considerations

- Bupropion
  - Less sedation and sexual side effects
  - Less help with anxiety/psychosis
  - Special contraindications
- Mirtazapine
  - More anxiolytic, less sexual side effects, less nausea
  - More weight gain and sedation
  - Could exacerbate REM sleep behavior in those with Parkinsonism[1]
  - Associated with small/significant risk for neutropenia, agranulocytosis; minimal interaction with warfarin

Don’t forget TCAs, MAOIs!

1. Onofrj M, Luciano AL, Thomas A, Iacono D, D’Andreamatteo G. Mirtazapine induces REM sleep behavior disorder (RBD) in parkinsonism. Neurology 2003;60:113–5.

SNRIs

- SNRIs share potential adverse effects of:
  - Hypertension
  - Anxiety
  - Insomnia
  - Share with SSRIs the potential for discontinuation symptoms
- Duloxetine – Analgesic effects are a bonus.[1]

1. Brannan et al. J Psychiatr Research 2005;39:43-53.

Treatment of Depression in Patients with Dementia

- Multiple antidepressants studied, including
  - Citalopram[1]
  - Sertraline[2,5]
  - Clomipramine[3]
  - Moclobemide[4]
  - Mirtazapine[5]
- RCT (DIADS) failed to show superiority of sertraline over placebo for cognition, some benefit for mood and behavior symptoms.[6] DIADS-2 failed to show sertraline > placebo.[7]
- Side effect assessment - more difficult in dementia
- Clinical approach – try, but discontinue if ineffective

1. Nyth et al. Acta Psychiatr Scand 1992;86:138-45; 2. Lyketsos et al. Am J Psychiatry. 2000;157:1686-9; 3. Petracca et al. J Neuropsychiatry Clin Neurosci.1996;8:270-5;4. Roth et al. Br J Psychiatry 1996;168:149-57; 5. Banerjee et al. Health Technology Assessment 2013;17(7):1-166; 6. Lyketsos et al. Arch Gen Psych 2003;60;737-46; 7. Rosenberg et al. AJGP 2010;18:136-45.

Approaching Treatment Resistant Depression: Has Attention Been **PAID** To Both Psychopharmacologic and Nonpharmacologic Factors?

- **Prescriptions:**
  - Choice, Dose, Duration
  - Address through optimization of type, dose, augmenters
- **Adherence:**
  - Side effects, Cost
  - Address through inquiry
- **Interfering Factors:**
  - Psychiatric or medical diagnosis
  - Medications, substances
  - Stressors, Supports
  - Address through new “HPI”
- **Dynamics of Resistance**

Dynamics of Antidepressant Resistance

- Resistance TO Medications
  - Ambivalence about
    - Treatment, medication
    - Illness
    - Treaters
  - Manifests in
    - Nonresponse
    - Nonadherence
    - Side effects
  - Countertransference
    - Frustration
    - Helplessness
- Resistance FROM Medications
  - Meds are reportedly effective
  - Meds are used in service of countertherapeutic ends
- Manifests in
  - Patient reports helpfulness of meds
  - Desire for more meds
  - Functioning doesn't improve
  - "Chronification"
- Countertransference
  - Prescriber feels guilt/shame

Mintz D. Psychodynamic Psychopharmacology. American Psychiatric Association Publishing, 2022, p. 59.

ADVANCED PHARMACOTHERAPY FOR TREATMENT RESISTANT DEPRESSION

Is Antipsychotic **Monotherapy** for LLD "For Real"?

- Quetiapine XR monotherapy (9 wk RCT in adults > 65)
  - Dx: MDD
  - Dose: 50-300 mg/d (mean dose 159 mg/d) vs placebo
  - Outcome: Improvement on MADRS + AE = sleepiness[1]
- Aripiprazole 7.5-10 mg/d in retrospective review of 54 older patients with LLD achieved a remission rate of nearly 60% (33 actually were "augmentation" rather than monotherapy).[2]

1. Katila et al. Am J Geriatr Psychiatry 2013;21:769-84;2. Sonal and Srivastava. J Clin Psychopharmacology 2022;42:280-283.

The Newer Antidepressants

- Viibryd (Vilazodone) - generic is available
  - SSRI and partial agonist at 5HT1a
- Trintellix (Vortioxetine)
  - SSRI, agonist 5HT1a, partial agonist at 5HT1b antagonist 5HT3a/5HT7
- Fetzima (Levomilnacipran)
  - Balanced SNRI
- Spravato (esketamine)
  - Different mechanism and effects
- Auvelity (bupropion/dextromethorphan) – not studied in adults over 64
- Exxua (gepirone) – 5HT1A partial agonist, QTc prolongation, only 12/1639 subjects in RCT were 65+
- [Brexanolone and zuranolone – only for PPD]

Rational Use of Augmentors[1]

- Augmenters:
  - Lithium carbonate+*
  - Triiodothyronine+*
  - Atypical antipsychotic+
    - Aripiprazole[2+]
    - Brexiprazole[3+]
    - Cariprazine[4+]
    - Lumateperone[+]
  - Methylphenidate[5*]
  - Not lamotrigine[6*] (predominantly negative evidence)
  - Co-Prescribed Antidepressants*

+ signifies presence of credible evidence base for use/ *signifies “off label” in this use

1. See Ellison et al, in Ellison et al (eds): Mood Disorders in Later Life. New York, Taylor & Francis 2008; 2. Lenze et al. Lancet 2015;Sep 24. pii: S0141-6736(15)00308-6. doi: 10.1016/SO140-6736(15)00308-6; 3. Lenze EJ et al. Lancet. 2015 Dec 12;386(10011):2404-12; 4. Earley et al. Psychopharm Bull 2018;48:62-80; 5. Lavretsky et al. Am J Psychiatry 2015;172(6):561-9;6. Goldberg J. J Clin Psychiatry 2024;85:23ac15219.

New Antipsychotic Comparison for MDD: 4 Adjunctive Tx Choices (ABCL)[1-4]

	Mechanism	Prominent AE	Antidepressant Dosing in Later Life	
Aripiprazole	**D2 Partial Agonist** **5HT2A Antagonist** **5HT1A Partial Agonist**	**Akathisia** **Insomnia**	**Start at 2 mg/d** **Target 5 mg/d** **Maximum 10 mg/d**	**Approved for adjunctive tx of MDD /** **Mania Monotherapy**
Brexpiprazole	**D2 Partial Agonist** **5HT2A Antagonist*** **5HT1A Partial Agonist**	**Weight gain**	**Start at 0.5 mg/d** **Target 1-2 mg/d** **Maximum 2 mg/d**	**Approved for adjunctive tx in MDD**
Lurasidone	D2 Antagonist 5HT2A Antagonist 5HT1A Partial Agonist 5HT7 Antagonist*	Sedation EPS QTc prolongation	Start at 20 mg/d Target 20-40 mg/d Maximum 40 mg/d	Approved as monotherapy/adjunctive therapy for bipolar depression
Cariprazine	**D2&D3* Partial Agonist** **5HT2A/2B Antagonist** **5HT1A Partial Agonist**	**Akathisia** **EPS** **Insomnia**	**Start at 1.5 mg/d** **Target 3 mg/d** **Maximum 4.5 mg/d**	Approved for monotherapy BP Depression, **adj tx in MDD**
Lumateperone	D2 Partial Agonist 5HT2A Antagonist 5HT2C Partial Agonist* 5HT transporter inhibitor	Sedation	Start at 42 mg/d Target 42 mg/d Maximum 42 mg/d	Approved as monotherapy/adjunctive therapy for bipolar depression and **adjunctive for MDD**

1. Lenze et al. The Lancet 2015;386:2404-12; 2. Al Shirawi et al. Clin Med Insights: Therapeutics 2017;9:1-10;3. Earley et al. Psychopharmacol Bull. 2018 Jun 20;48: 62–80; 4. Durgam et al. J Clin Psychiatry 2025;86(4):25m15848.

The "OPTIMUM" Trial: Switch vs Augmentation in Geriatric TRD

- Landmark multicenter comparative study treated 619 adults ≥yr old, TRD, in 2 steps, **trials ONLY 10 wk**:
  - STEP 1: Augment with aripiprazole (2.5-15 mg/d) or bupropion (150-450 mg/d) VS switch to bupropion
    - Augmentation more effective, safer; switch was less effective and associated with increased falls.
    - **Remission about 28% with augment**, about 19% switch
- STEP 2: Augment with lithium carbonate (0.6 mmol/l) vs switch to nortriptyline (80-120 ng/ml)
  - Remission similar (18.9% li, 21.5% nortriptyline)

Lenze et al. NEJM 2023;388(12):1067-1079.

Stimulants*

- Limited data on use in LLD
- Case study describes benefit for apathy distinct from (low) benefit for depression in 1 patient.[1]
- MPH (mean 16 mg) + citalopram (mean 32 mg) associated with faster and greater improvement in RTC of LLD with anxiety.[2]
- Bottom line - MPH with citalopram may speed antidepressant response; stimulant monotherapy has minimal support; stimulants not shown to imiprove TRD response.

*stimulants are used off label in treatment of depression

1. Padala et al. Methylphenidate may treat apathy independent of depression, Ann Pharmacother 2005;39:1947–1949. 2. Lavretsky et al. Am J Psychiatry 2015;172:561-9;3. Nelson JC. Am J Psychiatry 2015;172:505-7.

Esketamine (intranasal)?

- IN Esketamine is FDA indicated for treatment of depression resistant to prior antidepressant treatment. TRD is defined as 2 failed adequate trials
- The core RCT in older adults, TRANSFORM-3, co-administered IN esketamine with a “new oral antidepressant” to TRD adults > 64 and found a nonsignificant positive trend with flexible dosing up to 84 mg twice weekly for 4 wk. The response was **significant in subgroup 65-74**.[1]
- Side effects (principally dizziness, nausea, slowed reaction time) are mild.
- Delivery of this treatment is challenging because of requirement for post-use observation and enrollment in “Spravato REMS”.
- UK’s National Institute for Health and Care Excellence has chosen not to recommend its use.

1. Ochs-Ross et al. Am J Geriatric Psychiatry 2020;28:121-141; 2. Sukhdeo et al. Am J Geriatr Psychiatry 2026;34:84-102.

Electroconvulsive Therapy

- Underused modality, especially suitable with:
  - Antidepressant intolerance or non-response
  - Prior positive response to ECT
  - Delusions
  - Catatonia
  - Mania
  - Emergency

Flint and Rifat. Int J Geriatr Psychiatry 1998;13:23-8; Manly et al. Electroconvulsive therapy in old-old patients Am J Geriatr Psychiatry. 2000 Summer;8(3):232-6.

.

ECT Efficacy

- Of 240 patients in PRIDE Phase 1, 61.7% remitted, 70% met response criteria, 28.3% dropped from tx with 3x/wk ultrabrief pulse RUL ECT plus venlafaxine. Mean number of treatments to remission was 7.3.[1]
- A review found LLD response to ECT was not predicted by salivary cortisol, baseline white matter hyperintensities, total amyloid load, global cortical atrophy. Higher response was associated with retardation and psychotic features.[2]
- Current data finds limited adverse cognitive effects. MMSE scores were followed in a LLD ECT cohort at baseline, during treatment, and 6 months later and found significant improvement when baseline score <24, stability for baseline score ≥24.[3]
- Mixed cognitivei findings in earlier studies attributed to technique and/or underlying disease.[4]

1. Kellner et al. Am J Psychiatry 2016;173(11):1101-1109; 2. Moyano et al. Swiss Med Wkly. 2024;154:3684; 3. Obbels et al. Am J Geriatr Psychiatry 2019;27(9):934-944; 4.Galvez et al. Curr Psychiatry Rep 2015;17:59-74.

Transcranial Magnetic Stimulation[1]

- TMS (rTMS) is considered safe and well-tolerated in LLD.[2]
  - 20-50% response rate open label, older adults
  - Poorer response associated with cortical atrophy
  - Better response with higher intensity stimulation?
- May be suitable for individuals unable to accept ECT.
- Modifications:
  - Adjusted treatment schedule
  - Deep rTMS achieved efficacy in LLD of 40% vs 14.8% in control group.
  - There is interest in assessing for TR LLD

1. Galvez et al. Curr Psychiatry Rep 2015;17:59-74; 2. Kaster et al. Neuropsychopharmacology 2018;43(11):2231-8.

The Importance of Maintenance

- Even with maintenance, there is a high recurrence rate.
- Maintenance pharmacotherapy reduces recurrence risk. RCTs support:
  - Nortriptyline + IPT[1]
  - Citalopram[2]
  - Paroxetine[3]
- After remission, sustaining an effective dose for at least 1 year, with longer durations for recurrent or severe episodes.[4]
- Slower initial responders may do better with combined therapy in maintenance[5]

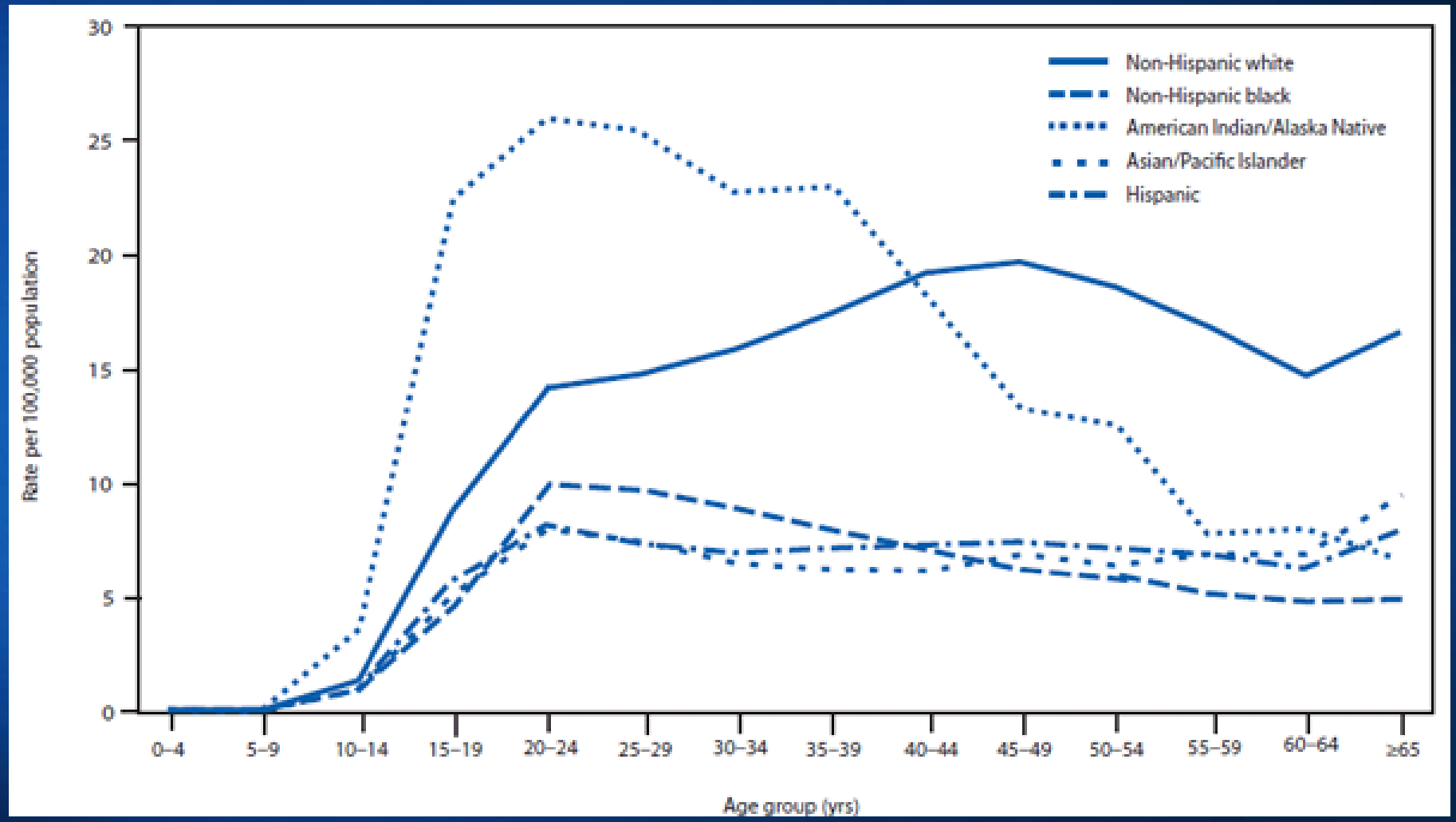
1. Reynolds et al. JAMA 1999;281:39-45; 2. Klysner et al. Br J Psychiatry 2002 Jul;181:29-35. ;
3. Reynolds et al. N Engl J Med. 2006;354:1130-8;4. Srifuengfung et al. Ther Adv Psychopharmacol 2023;13:20451253231212327;
5. Dew et al. J Affect Disord 2001;65:155-66.

Depression Preceding Suicide is Often Missed

In a 2004 study of U.S. depressed elderly adults seen in primary care during the 12 months preceding a suicide attempt, fewer than 1/10 had received an appropriate depression diagnosis.

1. Suominen et al. Int J Geriatr Psychiatry 2004;19:35-40.

Suicides in US 1999-2007 by Age/Ethnicity



Crosby et al. Suicides — United States, 1999–2007. CDC. Morbidity and Mortality Weekly Report (MMWR), January 14, 2011 / 60(01);56-59

Firearms and Older Adult Safety

- Among males 55 and older, firearms are the suicide method of choice.[1]
- 92% of older adult firearm deaths in 2018 were suicides.[1]
- Firearms suicides in older adults were 12x more common than firearm homicides and 99x more common than firearm unintentional deaths.[1]
- Firearms owners with a history or suicidal thoughts were 45% likelier to store firearms loaded and unlocked.[2]

1. Price and Payton. J Community Health 2025;50:464-71;2. Anestis and Bond. Suicide and Life-Threatening Behavior 2025;55:e70026.

How Can Late Life Depression Be Detected and Treated More Effectively in Primary Care Settings?

- Primary Care settings are optimal site for detecting and initiating treatment of late life depression.
- Several model programs have demonstrated efficacy:
  - IMPACT
  - PROSPECT
  - PRISM-E
  - TIDES

Conclusions

- Depression: Not a normal part of aging
- Age affects LLD:
  - Risk
  - Etiology
  - Presentation
  - Assessment
  - Treatment
  - Prognosis
- Remember to look for LLD and to treat actively!

Anxiety Disorders and Older Adults

What do these older adults have in common?

- Mr. A: worried, restless, trouble sleeping, not sad
- Ms. B: convinced she has Alzheimer's despite normal function
- Mr. C: injured in a fall, now house-bound
- Mr. D: tripped over his 1954 collection of Life Magazine, one pile he can't part with in a very cluttered tiny living space
- Ms. E: picked with fingernails through her scalp into her skull
- Mr. F: breathing better yet more anxious on new COPD meds

Epidemiology of Late Life Anxiety Disorders

- 5.5-10.2% of older adults have an Anxiety Disorder
- **Most important: GAD**
  - prevalence: similar to that in younger adults (1.2-7.3%)
- Other anxiety disorders are less prevalent in older adults.
  - Phobic disorders 0.6-4.8% (simple > generalized)
  - Panic disorder 0.1-0.8%
  - OCD 0.1-0.8%
  - PTSD 0.4-1%
- Symptoms can differ in older adults, so actual prevalence might be greater.

Lenze et al. Anxiety, Obsessive-Compulsive, and Trauma-Related Disorders. In Steffens et al (eds). The American Psychiatric Publishing Textbook of Geriatric Psychiatry. Fifth Edition. American Psychiatric Publishing 2015. Washington, DC.

How Does Anxiety Present in Older Adults?

- Often as in younger adults, but…
  - Aging diminishes panic symptoms and increases somatization.
  - Older adults are more likely to report or manifest:
    - Fear of falling, memory loss, or incontinence
    - Hoarding
    - Anxious thoughts of death (self or partner)
  - Medically-related anxiety
    - Medicine or substance or illness-related
    - Prodromal to cognitive decline

Lenze et al. Anxiety, Obsessive-Compulsive, and Trauma-Related Disorders. In Steffens et al (eds). The American Psychiatric Publishing Textbook of Geriatric Psychiatry. Fifth Edition. American Psychiatric Publishing 2015. Washington, DC.

Aging Alters Vulnerability to Anxiety Symptoms

Decreased Vulnerability

- Negative affect decreases with age (though increases in the mid-70's)[1]
- Life experience offers "stress inoculation"[2]
- The aging locus coeruleus becomes less responsive[3]

Increased Vulnerability

- Accumulated losses
- Greater medical burden
- Functional disability
- Degeneration of dorsolateral prefrontal cortex (DLPFC) may impair cognitive control[4]

1. Teachman. Psychol Aging 2006;21:201-7; 2. Jarvik and Russell. J Gerontol 1979; 37:197-200; 3. Flint. Am J Psychiatry 1994;151:640-9; 4. Lenze et al. Anxiety, Obsessive-Compulsive, and Trauma-Related Disorders. In Steffens et al (eds). The American Psychiatric Publishing Textbook of Geriatric Psychiatry. Fifth Edition. American Psychiatric Publishing 2015. Washington, DC.

A Dire Consequence of Anxiety: Increased Suicide Risk

- **Even the subsyndromal presence of anxiety increases suicidal thoughts in older adults.**
  - In a large community study of older adults, the prevalence of suicidal ideation was tripled by the presence of anxiety[1]
- Presence of anxiety **disorder*** boosted mixed age annual rates of suicide attempts and suicides many times.[2]
  - Suicide attempts: 1350/100,000
  - Completed suicides: 193/100,000

*Disorders included: PD,GAD,PTSD,OCD,SAD

1. Almeida et al. *Br J Psychiatry*. 2012;201:466-72;2. Khan et al. *J Affect Disord*. 2002;68:183-90.

And Yet, Anxiety is Overlooked in Older Adults

- Clinicians may attribute anxiety symptoms to normal aging or illness.
- Patients may minimize or forget to report symptoms.
- Self-labeling may mislead, e.g., “concern” rather than “anxiety.”
- Age-specific anxiety disorders (fear of falling, hoarding) are less familiar and may go unrecognized.
- Patients may fear/avoid treatment.

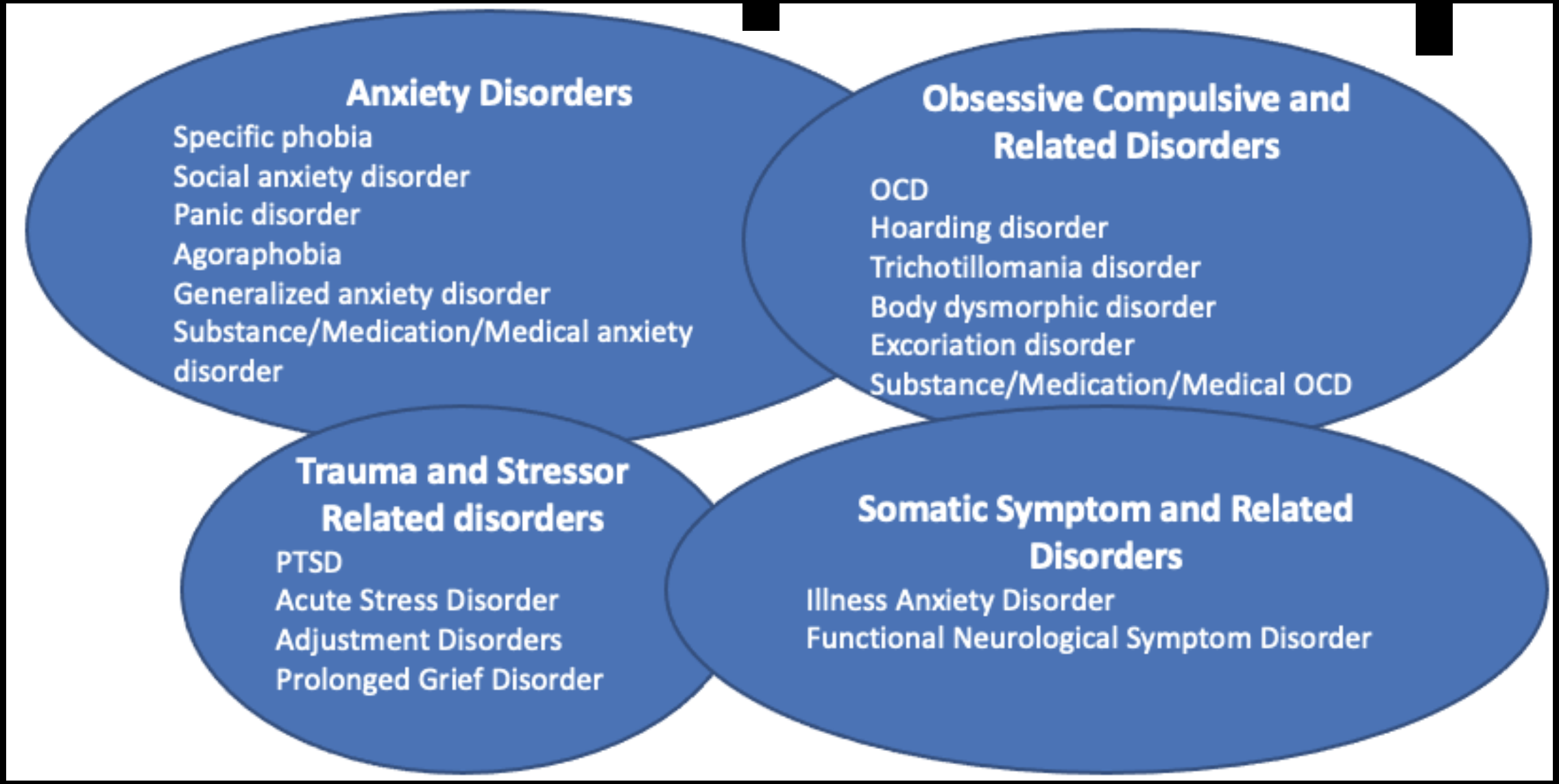
Wolitzky-Taylor et al. Depression and Anxiety. 2010;27:190-211

Anxiety Assessment

- Psychiatric Interview
  - Include collateral reports
  - Include cognitive screening
  - Hx, triggers, variation through time
- Medical evaluation – can be essential
  - Laboratory Assessment
  - ECG
  - When indicated:
    - Neuropsychological Assessment
    - Neuroimaging Assessment
- Next, let’s review the disorder classification:

DSM-5-TR Anxiety Disorders

The New Landscape of DSM-5-TR Anxiety



Anxiety Disorder Due to General Medical Condition (GMC) in DSM-5-TR

Diagnosis (summarized)

A. **Prominent anxiety or panic attacks**

B. Evidence that anxiety is a direct physiological consequence of GMC

C. Not another mental disorder

D. Not delirium

E. Significant distress/impairment

American Psychiatric Association (Ed.). (2022). Diagnostic and statistical manual of mental disorders: DSM-5-TR (Fifth edition, text revision). American Psychiatric Association Publishing.

Medical Conditions Can Present with Anxiety

- 80-86% of adults ≥ 65 years have at least one chronic medical condition. One study reported:
  - Comorbidity increased with increasing age.
  - Anxiety disorders were present in:
    - 18-50% of COPD patients
    - 42% of patients with vestibular sx (fear of falling common)
    - 40-43% of PD patients
    - 36% of cardiac patients
    - 5-21% of patients with dementia showed anxiety symptoms.
- Medical mortality was increased with anxiety.

Wolitzky-Taylor et al. Depression and Anxiety 2010;27:190-211

Some Additional Anxiety-Associated Medical Conditions

- Endocrine: hyper and hypothyroidism, pheochromocytoma, Cushing's Syndrome, hypoglycemia
- Cardiac: congestive heart failure, arrhythmia, MI
- Respiratory: COVID19, COPD, hyperventilation, asthma, pulmonary embolism
- Metabolic: electrolyte imbalance, B12 deficiency, porphyria
- Neuro: encephalitis, tumors, complex partial seizures

Drugs and Medications: Substance-Induced Anxiety Disorder (DSM-5-TR)

Diagnosis (summarized)

A. Prominent anxiety or panic attacks

B. Evidence that:

1. anxiety developed during or soon after substance/medication intoxication or withdrawal, or medication exposure/withdrawal, and
2. Involved substance/medication is capable of producing anxiety

C,D,E. Not another anxiety disorder, delirium, causes significant distress/impairment

American Psychiatric Association (Ed.). (2022). Diagnostic and statistical manual of mental disorders: DSM-5-TR (Fifth edition, text revision). American Psychiatric Association Publishing.

Some Anxiogenic Drugs

- Stimulants/modafinil
- **Antidepressants**: bupropion, fluoxetine, venlafaxine, tranylcypromine
- Anticholinergics: ditropan, benztropine
- Bronchodilators: isoproterenol, albuterol
- Steroids
- Hallucinogens

Non-Medications/Meds Used Non-Medicinally/ Discontinuation/Withdrawal

- Intoxication
  - Stimulants, caffeine, cocaine, PCP, marijuana, nicotine, hallucinogens, organophosphates, heavy metal poisoning (lead, mercury, arsenic)
- Withdrawal
  - Alcohol
  - Opiates
  - Barbiturates/other sedative-hypnotics
  - Serotonergic antidepressants

General Treatment Principles for Medical/Medication/Substance-Related Anxiety

- Treat the underlying medical condition
- Remove the offending agent
- Avoid abruption withdrawal of medications/substances with discontinuation syndromes.
- Provide Symptomatic Treatment
  - If anxiety does not resolve quickly consider short term anxiolytic therapy

Specific Phobia in DSM-5-TR

Diagnosis (summarized)

A. Marked fear or anxiety about **specific object or situation**
B. Feared object/situation almost always provokes anxiety
C. Avoidance or endurance with anxiety
D. Anxiety out of proportion to danger
E. Lasts 6 months or more
F. Clinically significant distress/impairment
G. Exclusion: not another mental disorder

- Specifier: animal/environment/blood/situation/other

American Psychiatric Association (Ed.). (2022). Diagnostic and statistical manual of mental disorders: DSM-5-TR (Fifth edition, text revision). American Psychiatric Association Publishing.

Specific Phobia: Common in Elderly

- Estimated prevalence in older adults up to 4.8%
- Important phobias in older adults:
  - Fear of **memory loss**: In one study, fear of developing Alzheimer's was independently associated with subjective memory symptoms (but not objective performance findings).
  - Fear of **falling**: Common and disabling…
  - **Incontinence** fears
- Detection complicated by:
  - Lifestyle accommodations
  - "Reasonableness" of fears (e.g. fear of falling)

Wolitzky-Taylor et al. *Depression and Anxiety* .2010;27:190-211; Andria et al. *Aging & Mental Health*. 2020;24:308-314

Fear of Falling: More Common Than You Knew!

- Falls often lead to subsequent **restriction of activities**.
- In a study of 640 adults ≥ 75 years old, 41.5% feared falling.
- Fear of falling was associated with history of falls, female gender, depressive symptoms, disability
- Fear of falling predicted greater fall risk!
  - 41.7% of those who reported fear of falling suffered at least one fall in the subsequent 24 months.

Laveda et al. *PLoS ONE.* 2018;13(3): e0194967. https://doi.org/10.1371/journal. pone.0194967

Psychotherapy Is First-Line Approach to Phobias – and Older Adults Often Prefer Psychotherapy

- Ideal older psychotherapy patient is:
  - Motivated
  - Cognitively intact
- Prefers talking or wishes to avoid medications
- Responded previously to talking or has failed with medications
- Psychosocial goals exceed scope of medication effects.
- But…appropriate psychotherapy may be difficult to access!

CBT for Fear of Falling in Elderly

- Of 389 adults ≥ 70 years old with concerns about falling and restricted activities, 194 were offered a CBT program consisting of 3 home visits and 4 telephone contacts.
- After 12 months,
  - Cognitive restructuring instilled adaptive and realistic views.
  - Concerns about falls and activity avoidance were reduced.
  - Anxiety symptoms, but not number of falls, were reduced.

Dorresteijn et al. *BMC Geriatr*. 2016;16:2.

Medications May Help Some Anxiety Disorders – But They Have Limitations

- Many older patients fear medications.
- Some conditions (e.g., phobias) respond better to psychotherapy.
- Medication “response” is more common than “remission”.
- Long-term benefits may require prolonged vs episodic treatment.
- Aging/Medical conditions may increase the risk for adverse reactions
- Polypharmacy is common in elderly and can predispose to drug-drug interactions

FDA Indicated Medications for Anxiety Disorders

	GAD	Panic	OCD	Social Anxiety	PTSD	Agoraphobia	Phobia	BDD	Excoriation	Trichotillomania
Anafranil			X							
Fluoxetine		X	X			(X)				
Fluvoxamine			X							
Paroxetine	X	X	X	X	X					
Sertraline		X	X	X	X					
Escitalopram	X									
Venlafaxine XR	X	X		X						
Duloxetine	X	X								
Buspirone	X									
Alprazolam	X	X				(X) With panic				
Clonazepam	anxiety	X								
Isocarboxazid Phenelzine		X X								
rTMS			adjunct							

Citalopram? No anxiety indication; Lorazepam? “anxiety disorders” or short term relief of anxiety

Social Anxiety Disorder: DSM-5-TR

Diagnosis (summarized)

A. Marked fear/anxiety of 1 or more **social situations, possible scrutiny**

B. Fear of negative evaluation

C. Feared social situations almost always provoke fear/anxiety

D. Avoidance or anxious endurance

E. Out of proportion to actual threat

F. 6 months or more

G. Clinically significant stress/impairment

H, I, J. Not substance, mental, medical

- Specify if "**performance only**"

American Psychiatric Association (Ed.). (2022). Diagnostic and statistical manual of mental disorders: DSM-5-TR (Fifth edition, text revision). American Psychiatric Association Publishing.

Social Anxiety: Psychosocial Tx

Based on results with younger patients,[1]

- Psychotherapy is first line treatment
  - Cognitive Behavioral Therapy
    - Cognitive restructuring, exposure with response prevention
    - Individual or group format
  - Social Rehabilitation
    - Social skills training, communication and assertiveness training
    - Role playing, joining clubs
- Medications can be helpful – data support SSRIs, SNRIs; research has explored use of D-cycloserine with psychotherapy (exposure therapy).[2]

1. Aggarwal et al. Focus 2017;5(2):157-161. doi: 10.1176/appi.focus.20160045; 2. Guastella et al. Biol Psychiatry 2008; 63:544–549.

Panic Disorder in DSM-5-TR

Diagnosis (summarized)

A. Recurrent **attacks** (abrupt surge of anxiety with 4 or more of symptoms:
(4 or more of: palpitations, sweating, trembling, SOB, choking, chest pain, nausea, dizzy, chills, paresthesias, derealization, fear lose control, fear of dying)

B. At least 1 attack followed by 1 month of concern or behavior change

C/D: Not substance, medication, medical, or other mental disorder

American Psychiatric Association (Ed.). (2022). Diagnostic and statistical manual of mental disorders: DSM-5-TR (Fifth edition, text revision). American Psychiatric Association Publishing.

Panic Disorder (PD) Treatment

- In a small RCT, CBT results were better than paroxetine results for Panic Disorder patients older than 60 years.[1]
- Rarity of late onset PD necessitates medical assessment.
- Medications – suggested by analogy with younger patients because of limited info on older PD patients:[2]
  - First line: SSRI or SNRI
  - May need initial or short-term augmentation (BZD, e.g. lorazepam, has been used[3])
  - Resistant cases may respond to adjunctive (off label) non-serotonergic antidepressant such as mirtazapine or to gabapentin.[3]

1. Hendriks et al. Int J Geriatr Psychiatry 2012; 27:146–150; 2. Aggarwal et al. Focus 2017;5(2):157-161. doi: 10.1176/appi.focus.20160045;
3. Flint and Gagnon. Drugs Aging 2003;20:881-91.

Agoraphobia: A Separate Dx in DSM-5-TR

Diagnosis (summarized)

A. Marked fear/anxiety about 2 or more of: public transportation, open spaces, closed places, crowds/lines, outside home or alone

B. Fear/avoidance because escape might be difficult or help unavailable

C. Agoraphobic situations almost always provoke fear/anxiety

D. Active avoidance or endurance with fear

E. Out of proportion

F. At least 6 months

G. Clinically significant distress/impairment

H/I. Not medical or other mental disorder

- Can be co-diagnosed with or without Panic Disorder

American Psychiatric Association (Ed.). (2022). Diagnostic and statistical manual of mental disorders: DSM-5-TR (Fifth edition, text revision). American Psychiatric Association Publishing.

Generalized Anxiety Disorder in DSM-5-TR

Diagnosis (summarized)

A. Excessive **worry** on more days than not for at least 6 months about several events
B. Difficult to control worry
C. 3 or more of these 6 sx: Restlessness or keyed-up, easily fatigued, difficulty concentrating, irritability, muscle tension, sleep disturbance
D. Significant distress/impairment
E,F. Not substance, medical, other mental disorder

American Psychiatric Association (Ed.). (2022). Diagnostic and statistical manual of mental disorders: DSM-5-TR (Fifth edition, text revision). American Psychiatric Association Publishing.

GAD in Older Adults

- One of the most common psychiatric disorders in elderly –
  - Prevalence 1.2 to 7.3%[1,2]
  - High rate in medical settings
- Onset: 2/3 in childhood/adolescence but ¼ ≥ 50 years of age[3]
- Course:
  - Often chronic, can present with 20-30 yr history[2]
  - Remission is rare
- Diagnostic pitfalls: Theme of worry may seem "reasonable"
  - Health, relationships, money
  - Patients seek medical, not mental health, specialists
  - Attend to intensity and functional impairment

1. Grant et al. Psychol Med 2005;35:1747-59; 2. Schuurmans et al. Am J Geriatr Psych 2006;14:255-263; 3. Mackenzie et al. Am J Geriatr Psychiatry 2014; 22:854–865

GAD Treatment

- Psychotherapy:
  - CBT (Cognitive Restructuring/ Relaxation Training)
  - Psychodynamic (Resolve conflict, master anxiety)
  - Supportive Therapy (Reduce stress, improve coping skills, psychoeducation)
  - In mixed-age meta-analysis, larger effect with psychotherapy than meds[1]
  - Lower mean age of subjects predicted larger treatment effect size for psychotherapy, not for pharmacotherapy.[1]
  - Meta-analysis of studies in **older adults** found similar effect size in psychotherapy vs pharmacotherapy.[2]
- Pharmacotherapy: SRI, SNRI are first line medications for GAD in later life.[3]
- Only 1 buspirone/GAD (single-blind) study in older adults[4]
- Additional (off-label) treatment: exercise![5]

1. Carl et al. Cogn Behav Ther 2020;49: 1–21; 2. Gonçalves and Byrne. Anxiety Disorders 2021;26:1-11; 3. Aggarwal et al. Focus 2017;5(2):157-161. doi: 10.1176/appi.focus.20160045;4. Mokhber et al. Psychiatry and Clinical Neurosciences 2010;64:128-133; 5. 5. Kazeminia et al. Health Qual Life Outcomes 2020;18:363.

Benzodiazepine Use?

- **Not first line GAD treatment for older adults**
- Acute, time-limited use may be of help.
- Consider antidepressants first.
- Older adults have increased sensitivity to side effects/adverse events and lowered metabolism.
  - Dizziness, weakness, sedation (interfering with driving, operating machinery), falls and fractures are hazards of benzodiazepines in older adults.
  - Long-acting vs short-acting have pros/cons.

American Geriatrics Society 2015 Beers Criteria Update Expert Panel JAGS 2015; 63:2227-2246.

OCD AND RELATED DISORDERS

New in DSM-5-TR: Obsessive-Compulsive and Related Disorders

- Obsessive-Compulsive Disorder
- Body Dysmorphic Disorder
- Hoarding Disorder
- Trichotillomania Disorder
- Excoriation Disorder
- Substance/Medication-Induced Disorder
- Medical/Other/Unspecified

American Psychiatric Association (Ed.). (2022). Diagnostic and statistical manual of mental disorders: DSM-5-TR (Fifth edition, text revision). American Psychiatric Association Publishing.

OCD in DSM-5-TR

Diagnosis (summarized)

A. **Obsessions, compulsions, or both**
B. Time-consuming or distress/impairment
C. Not substance/medical disorder
D. Not caused by another mental disorder

Specifier: Good/fair vs poor vs absent/delusional insight

- OCD with delusions NOT called a “psychotic disorder”.
- Sensory experiences can precede compulsions (up to 60%).
- Suicide risk is significant (OR = 9.8).

American Psychiatric Association (Ed.). (2022). Diagnostic and statistical manual of mental disorders: DSM-5-TR (Fifth edition, text revision). American Psychiatric Association Publishing.

OCD in Later Life[1]

- Less prevalent in older than younger adults/warrants further study
- A small percentage of cases begin in later life, persist years without treatment.[1]
- Course of Illness is often chronic. Pathologic doubt may predominate.
- Treatment is by analogy with trial results from younger patients:
  - Psychotherapy: CBT is first-line
  - Medications: SRI recommended, and by analogy with younger patients, resistant OCD in older adults is treated with buspirone or (cautiously) clomipramine augmentation; presence of delusional ideation can justify risperidone augmentation.
  - **FDA-indicated since 2018** - rTMS[4]

1. Jenike M. J Geriatr Psychiatry Neurol 1991;4:34-9. 2. Jazi and Asghar-Ali. J Psychiatr Pract 2020;26:175-184;
3. Mar-Barrutia et al. World J Psychiatry 2021;11:659-80;4. Carmi et al. Am J Psychiatry 2019;176:931-8.

Hoarding Disorder in DSM-5-TR

Definition (summarized):

A. Persistent **difficulty discarding or parting with** possessions regardless of actual value
B. Sense of perceived need to save, distress with discarding
C. Results in accumulation that clutters active living areas and compromises use
D. Clinically significant distress/impairment
E. Not another medical disorder or mental disorder

- Specify if with excessive acquisition
- Specify good/fair vs poor vs absent/delusional insight

American Psychiatric Association (Ed.). (2022). Diagnostic and statistical manual of mental disorders: DSM-5-TR (Fifth edition, text revision). American Psychiatric Association Publishing.

Hoarding in Elderly

- Prevalence estimated at 6.2% in 55 to 94 year old population.
- More common in older than young and more in women.
- Onset typically before age 40, increases after middle age.
- Linked with
  - **Childhood adversity, self-neglect, social isolation, never married**
  - **Depression (14-54%), OCD (13.3-16%), GAD (23.3%), PTSD (3.5-18%), increased alcohol dependence (HR 2.7), dementia (26%)**
  - Linked with arthritis, Sleep apnea, diabetes, hypertension
  - Linked with deficits in memory, attention, executive function

Roane et al. *Int Psychogeteriatrics.* 2017;29:1077-84.

“Hoarding” with Dementia[1]

- Note: “Hoarding disorder is not diagnosed if the accumulation of objects is judged to be a direct consequence of a degenerative disorder”.[2]
- Seems to represent **failure to discard**
- Can be associated with squalor
- Often fills all rooms, interferes with personal care, food preparation, safety, 17% show self-neglect to point of filth.
- Paper, containers, clothing, food books trash, less commonly purchases

1. Kim et al. Health Soc Work 2001;26:176-84. doi: 10.1093/hsw/26.3.176; 2. American Psychiatric Association (Ed.). (2022). Diagnostic and statistical manual of mental disorders: DSM-5-TR (Fifth edition, text revision). American Psychiatric Association Publishing.

Interventions

- Treating comorbid psychiatric disorder?
- Partial or complete cleaning with assistance of family, agency was not associated with sustained improvement.[1]
- Counseling **(CBT),** individual or group, with at-home decluttering sessions and accountability has shown preliminary promise.[2]
- With severe cognitive impairment, external intervention may be a necessity.

1. Kim et al. *Health Soc Work.* 2001;26:176-84. doi: 10.1093/hsw/26.3.176; 2. Linkovski et al. *J Psychiatr Res.* 2018;107:145-150. doi: 10.1016/j.jpsychires.2018.10.001.

Trichotillomania Disorder in DSM-5-TR

Diagnosis (Summarized)

A. Recurrent pulling out of one's hair resulting in hair loss

B. Repeated attempts to decrease or stop

C. Significant distress/impairment in functioning

D. Not another medical condition or mental disorder

(1-2% in general population - Often comorbid with excoriation disorder, depression, nail-biting, OCD but differs from OCD)

American Psychiatric Association (Ed.). (2022). Diagnostic and statistical manual of mental disorders: DSM-5-TR (Fifth edition, text revision). American Psychiatric Association Publishing.

Trichotillomania in Elderly

- Onset typically in adolescence, can begin at any age.
- Habit reversal therapy (HRT) and other behavioral therapies better supported than pharmacologic approaches.
- Medications – limited benefit overall – with equivocal results for off-label trials of SSRI, naltrexone, TCA, some support for clomipramine, NAC, olanzapine in small nongeriatric samples.
- With dementia: case reports support use of risperidone with naltrexone, mirtazapine with various SSRI's, citalopram.

Bartley et al. Int Psychogeriatrics 2017;29:691-4.

Excoriations (Skin-Picking) Disorder in DSM-5-TR

- **Diagnosis (summarized)**
  A. Recurrent skin picking resulting in lesions
  B. Repeated attempts to decrease
  C. Clinically significant distress/ impairment in functioning
  D. Not or medical disorder

American Psychiatric Association (Ed.). (2022). Diagnostic and statistical manual of mental disorders: DSM-5-TR (Fifth edition, text revision). American Psychiatric Association Publishing.

Excoriation Disorder

- General population prevalence: 1.4-5.4%
- Common in adolescence, adulthood
- Female predominance, may be comorbid with OCD, mood, BDD, GAD, depression, yet presents to dermatologist
- Relieves “negative affective states”
- No specific or recommended treatment option
- **Differential diagnosis in older adults must include dry skin, CKDAP, other dermatologic conditions.**

Jafferany and Patel. CNS Drugs 2019;33:337-46.

Treatment of Excoriation Disorder

- Case reports, not meta-analysis, support off-label use of SSRIs, SNRIs, antipsychotics, glutamine-modulating agents (NAC 1200-3000 mg/d, lamotrigine, topiramate), naltrexone augmentation, inositol.
- Psychotherapies – support for “Habit Reversal Therapy”
  - Awareness training (self monitoring)
  - Competing-response training (stress ball)
  - Stimulus control (e.g., wearing gloves
  - Relaxation training (e.g., deep breathing, PM, imagery)
  - Social Support (reminders, rewards)

Jafferany and Patel. CNS Drugs 2019;33:337-46.

Trauma and Stressor Related Disorders

PTSD: Diagnosis in DSM-5-TR (summarized)

A. **Exposure** (1 or more):

- Direct experience
- Witnessing
- Learning of event with close person
- Experiencing repeated or extreme exposure to aversive details

B. Presence of **intrusive** sx associated with traumatic events (1 or more):

- Recurrent involuntary and intrusive distressing memories
- Dreams
- Dissociative reactions (flashbacks)
- Intense/prolonged psychological distress at cue exposure
- Marked physiological reactions to internal/external cues

C. Persistent **avoidance (1 or more)**

- Avoid distressing memories, thoughts, feelings
- Avoid external reminders

D. **Cognition and mood** – negative alterations with 2 or more:

- Inability to remember important aspect of events
- Negative beliefs/expectations
- Distorted cognitions
- Negative emotional state
- Diminished interest in participation
- Detachment or estrangement from others
- Inability to experience positive emotions

E. Altered **arousal/reactivity** assoc with traumatic events, 2 or more of:

- Irritable without provocation
- Reckless
- Hypervigilant
- Startle
- Concentration
- Sleep disturbance

F. **More than 1 month**, G. **Impairment/distress,** H. **Exclusions**

***Specify** – with dissociative sx (depersonalization, derealization)

***Specify** – with delayed expression (6 mo)

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PTSD: Epidemiology

- Lifetime prevalence in mixed-age community sample is 8%.[1]
  - In high-risk groups, prevalence 5-75%
  - Worse trauma associated with higher PTSD risk
- In elderly,
  - Traumatic exposure in 70-90%, PTSD in up to 4%[1]
  - War trauma
  - Medical trauma
- Chronic course

1. Kaiser et al. Posttraumatic Stress Symptoms among Older Adults: A Review.Accessed September 11, 2022: https://www.ptsd.va.gov/professional/treat/specific/symptoms_older_adults.asp#:~:text=The%20prevalence%20of%20current%20PTSD,several%20community%20studies%20(5); 2. Acierno et al. J Interpersonal Violence 2007;22:250-8.

PTSD Psychotherapy

- Dearth of data in elderly: controlled research investigating psychotherapeutic and psychopharmacologic interventions specifically in this population is lacking
- Psychotherapy Treatment
  - Some psychotherapy studies with CBT, Exposure/Response Prevention, Eye Movement Desensitization & Reprocessing therapy (EMDR);
  - Contraindicated: Debriefing

Dinnen et al. Aging Ment Health 2015;19:144-50.

PTSD Pharmacotherapy

- Pharmacotherapy (with cautious dosing)
  - First line
    - FDA indicated: sertraline and paroxetine
    - Evidence in combat veterans: citalopram[1] , mirtazapine[2]

English et al. *J Clin Psychopharm*. 2006;26:84-8; 2. Chung et al. *Hum Psychopharm*. 2004;19:489-94.

PTSD: Additional Off-Label Pharmacotherapies

- Second line
  - Anticonvulsants[1] (target re-experiencing)
  - Atypical antipsychotics (risperidone, quetiapine, olanzapine)[2,3] as augmentation–weigh risks vs benefits
- Third line
  - TCAs (doxepin often used), MAOIs
  - Buspirone, benzodiazepines
  - Beta blockers or Alpha 2 blockers (prazosin[3])
  - Off-label – psychedelics[4]

1. Marco M et al. *Journal of Clinical Psychopharmacology.* 2007; 263-272; Hamner et al. 2003; 3. Stein et al. 2002; 3. Raskin et al. *Biol psychiatry.* 2007;61:928-34; 4. Nutt D. Diaglogues Clin Neurosci 2019;21:139-47.

Prolonged Grief Disorder in DSM-5-TR

Diagnosis (summarized)

A. Death of close relationship **at least 12 months ago.**

B. For more days than not, nearly every day in past month, clinically significant, intense yearning for deceased and/or preoccupation with thoughts/memories

C. At least 3 of these symptoms most days, nearly every day for last month:

- Identity disruption, disbelief, avoidance of reminders, emotional pain, difficulty reintegrating, emotional numbness, feeling life is meaningless, intense loneliness

D. Significant functional impairment/distress

E. Duration of grief too long for cultural/religious/age-appropriate norms

F. Not substance, medical condition, or other mental disorder

American Psychiatric Association (Ed.). (2022). Diagnostic and statistical manual of mental disorders: DSM-5-TR (Fifth edition, text revision). American Psychiatric Association Publishing.

Contrast: Healing of Normal Grief[1]

- 4 stages: Predeath, Acute, Adaptation, Integration[1]
- 4 major tasks for integration: Accepting reality of the loss; Processing the emotional pain; Adjusting to life without the deceased; Establishing an enduring connection with deceased while moving forward.
- Peer support groups: efficacy not shown except in participants with “low interpersonal and emotional competencies”.
- Symptom and self-care improvement has been shown with **structured groups, specialist leaders, mindfulness techniques/spirituality**.

1. Meichsner et al. AJGP 2020;28:560-9; 2. Davidow et al. AJGP 2022;30(3):404-18

Complicated Grief's Complications

- Complicated Grief develops in about 7% of bereaved people.[1]
- Negative Health Consequences of complicated grief include increased risk for [2]
  - Impaired self-care
  - Disturbed sleep
  - Substance use
  - Increased suicidality
  - Worse executive function
  - Increased brain atrophy
  - Increased cognitive decline

1. Zisook and Shear. World Psychiatry. 2009;8:67-74; 2. Meichsner et al. AJGP. 2020;28:560-9.

Complicated Grief: Risk Factors

- Pre-loss factors:
  - Dysfunctional attachment
  - History of anxiety or depression
  - Female sex, older age, lower educational level, lower socioeconomic status, lower social support
- Loss-related factors:
  - Type of loss (e.g. spouse/child, stigma)
  - Suddenness
  - Immediate response
- Post-loss factors:
  - Negative coping strategies (e.g. avoidance, alcohol)
  - Lack of social support, Negative consequences

Shear et al. Curr Psychiatry Rep. 2013;15:406; Bui et al. Bereavement, grief, and depression: clinical update and implications. Psychiatric Times. 2017;34:31-3.

Interventions for Complicated Grief

- Prolonged grief disorder symptoms can be “prevented” or diminished in high-risk individuals by internet-based, therapist-assisted CBT intervention addressing education, stress management, behavioral activation, accommodation of loss, relapse prevention.[1]
- In established Complicated Grief, Complex Grief Therapy (CGT) does better than CBT, focusing on history, grief experience, situation revisiting, and personal goals e.g. coping strategies and social connections. Exposure, IPT and motivational interviewing are included in CGT.[2]

1. Litz et al. Behav Res Ther 2014;61:23-34; 2. Shear et al. JAMA Psychiatry 2014;71:1287-95.

Somatic Symptom and Related Disorders

Illness Anxiety Disorder in DSM-5-TR

Diagnosis (summarized)

A. **Preoccupation with having or acquiring a serious disease**
B. Somatic symptoms not present or mild
C. High level of health anxiety, easily alarmed
D. Excessive health-related behaviors, checking or avoidance
E. At least 6 months
F. Not another mental disorder

*Specify - Care-seeking vs care-avoidant

American Psychiatric Association (Ed.). (2022). Diagnostic and statistical manual of mental disorders: DSM-5-TR (Fifth edition, text revision). American Psychiatric Association Publishing.

Illness Anxiety Disorder

- Replaces DSMIV “hypochondriasis” to reduce stigmatization, to focus on anxiety, and this reduces number affected.
- Prevalence 0.1% in general population, worsens with age
- Differential diagnosis – medical illness, OCD, depression
- Treatment:
  - Alliance, acknowledgement, referral management, behavioral referral
  - CBT: address excessive health related checking/interpretation of sx
  - Meds: SSRIs, SNRIs can be adjunctive to therapy

Scarella T, et al. Illness Anxiety Disorder: Psychopathology, Epidemiology, Clinical Characteristics, and Treatment Psychosom Med. 2019 Jun;81(5):398-407. doi: 10.1097/PSY.0000000000000691. Accessed 9/13/2022: https://www.ncbi.nlm.nih.gov/books/NBK554399/?report=printable

Functional Neurological Symptom Disorder

1. One or more symptoms of altered voluntary motor or sensory function.
2. Clinical findings provide evidence of incompatibility between the symptom and recognized neurological or medical conditions.
3. The symptom or deficit is not better explained by another medical or mental disorder.
4. The symptom or deficit causes clinically significant distress or impairment in social, occupational, or other important areas of functioning or warrants medical evaluation.
5. The symptom or deficit is not intentionally produced or feigned (as in Factitious Disorder or Malingering).

Treatment of FNSD

1. Education and Reassurance
2. Cognitive Behavioral Therapy (CBT)
3. Physical Therapy
4. Medication
5. Occupational Therapy
6. Speech Therapy
7. Support Groups

Parting Considerations

Anxiety Disorders in Later Life

- Common but can present disguised
- Phobias most common (including specific age-related)
- GAD next most common
- Medical assessment is critical
- Don’t neglect psychotherapy
- Pharmacotherapy may be appropriate, with caution
- Anxiety in dementia – a separate topic

Questions/Discussion