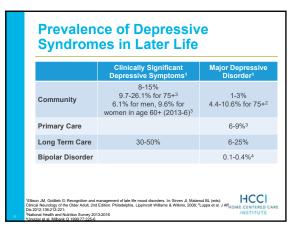


Describe the varied presentations and assessment approach for different types of depressive disorders in complex, frail, elderly patients in the home setting.

Explore effective strategies for the treatment of depression in homebound patients.

Provide timely guidance to caregivers of homebound patients with depressive disorders.

3



Some Risk Factors for LLD **Coping/Social Support Demographics** Older age · Recent negative life Female events Lower income · Lack of social support Small social network Health Unmarried New/chronic medical Bereaved illness Loneliness · Vascular disease **Habits** Psychiatric illness history Alcohol problem Cognitive impairment • Smoking Sleep disturbance · Low exercise level Pain HCCI Functional limitations

Adverse Outcomes of Untreated LLD1-6

- · Increased use of non-mental health services
 - · Twice as many doctor appointments
 - Twice as likely to received 5 or more medication
- Reduced adherence to medical treatment
 - · Functional decline/Increased disability
- Increased medical morbidity/mortality
 - CVA/MI/Dementia
- · Increased risk for suicide

And yet - more than 1/2 of depressed elders go untreated.7

et al. J Am Geriatr Soc 2002;50:817-22; "Alexopoulos GS. Lancet 2005; 365; 1961-70; "Katon et al. sychiatry 2003;60:897-903; "Hall and Reynolds. Maturitas 2014;79:147-52; "Barry et al. J Affect Dis

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DSM 5 MDD = DMS14TR Minus Bereavement Exclusion

- · Depressed mood OR loss of interest/pleasure, plus
- At least 4 other SIGECAPS
- Present at least during the same 2 week
- · Distress or functional impairment
- · Medical/Substance/Psychiatric exclusions • There has not been a manic/hypomanic
- NO BEREAVEMENT EXCLUSION (differs from DSMIVTR: Depression resembles but

differs from "responses to a significant loss")

SIG E CAPS

Sleep Interest

Guilt/worthlessness

Energy

Concentration

Appetite/weight **P**sychomotor

Suicidal

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DSM 5 CMDD+DD = Persistent Depressive Disorder (Dysthymia)" 300.4

Consolidates 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 symptoms: appetite, sleep, energy, selfesteem, concentration, hopelessness
- No remission more than 2 months at a time in 2 year period
- · Major Depressive Disorder criteria may also be met
- Symptoms not explained by manic, hypomanic, cyclothymic, other psychiatric, substance, medical
- · Significant distress (social, occupational, other)

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What is Special About LLD?

Etiologies

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- · Recurrence of early onset mood disorder
- · Psychosocial stressors of late life
- Physiologic effects of aging/illness
 - · Disease sx can mimic depressive sx
 - Vascular depression hypothesis¹ · Inflammation hypothesis2

Elders seek help in Primary Care

- Higher medical burden (illnesses, symptoms)
- · Fewer than half of cases are recognized3
- · Disguised/Limited symptoms

os et al. Dialogues Clin Neurosci 1999;1:68-80 ; Maes et al. Metab Brain Dis 2009;24:27-53;

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Special Symptomatic Presentations of LLD

Beneath the "Major Depression" threshold "Depression without sadness"1 Somatic (sometimes cognitive) focus **Depression with psychotic features** Depression with cognitive impairment 2,3

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Vascular Depression: Neuropsychological Correlations¹

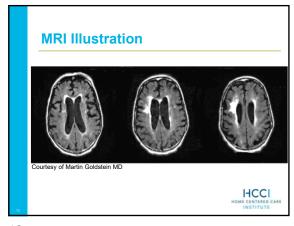
Presence of moderate to severe white matter hyperintensities in depressed patients has been linked with decreased agitation/guilt, increased psychomotor retardation and disability, and:

- Poorer Executive Functioning
- · Slower response to citalopram treatment²
- · Greater relapse risk

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HCCIntelligence™ Webinar/Virtual Office Hours



Depression with Psychotic Features · Psychotic symptoms (delusions or hallucinations) with major depression More prevalent among older vs younger depressives **Associated with:** Later onset

- · Hypochondriacal and nihilistic delusions
- Poorer response to monotherapy/maintenance
- Higher recurrence rate
- · Higher suicide risk

et al. Int J Geriatr Psychiatry 2001;16:1085-91; lifet Am J Psychiatr 1998:155:178-83

with Dementia

14

16



13

Depression in Alzheimer's Dementia: Provisional Diagnostic Criteria

3 or more of following in 2 week period

- Depressed mood
- · Decreased positive affect/pleasure in usual activities/contacts
- Social isolation or withdrawal Meets criteria for DAT
- Disruption in appetite
- Disruption in sleep
- Psychomotor changes Irritability
- · Fatigue/loss of energy
- · Worthlessness, hopelessness, guilt • Thoughts of death, SI or behavior

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Distress or disruption

medication, or better

• Not delirium, drug,

accounted for by

other conditions

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Likelihood that depression is present is increased in the presence of:

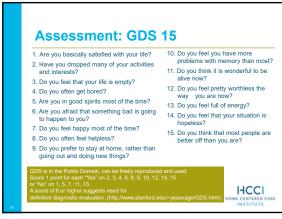
"Masked Depression" Associated

- Delusions1
- Verbal/physical aggressive behaviors²
- · Suicidal or self-destructive behaviors
- Disruptive vocalizations3
- Weight loss4

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PHQ-2 Over the past 2 weeks, how often have you been bothered by any of the following problems? 1. Little interest or pleasure in doing things 2. Feeling down, depressed or hopeless 82.1 3 82.9 90.0 38.4 62.3 95.4 75.0 93.3 45.5 50.9 53.7 56.4 26.8 99.4 78.6 99.8 92.9



Psychometrics of GDS

Appears to be most widely used screen In public domain, multiple translations 4 versions range from 4 to 30 questions GDS15 with cut-off of 5/6:

• Sensitivity overall 84.3%

• Specificity 73.8%

• Figures are lower in in outpatient and nursing home settings

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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 a 0 1 2 2. Sadness: sad expression, sad voice, tearfulness a 0 1 2 3. Lack of reactivity to pleasant events a 0 1 2 4. Irritability: easily annoyed, short-tempered a 0 1 2 5. Agitation: restlessness, handwringling, hairpulling a 0 1 2 6. Retardation: slow movement, slow speech, slow reactions a 0 1 2 7. Multiple physical complaints (score 0 if 61 symptoms only) a 0 1 2 8. Loss of interest: tess involved in susual activities a 0 1 2 9 (score only if change occurred acutely, i.e. in less than 1 month)

Cornell Scale for Depression in Dementia

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

D. Oycle Functions
12. Diurnal variation of mood: symptoms worse in the morning
13. Difficulty falling asleep: later than usual for this individual
14. Multiple awakenings during sleep
15. Early morning awakening: earlier than usual for this individual
20. Lideational Disturbance
16. Suicide: feels life is not worth living, has suicidal wishes, or makes suicide attempt
17. Poor self esteem: self-blame, self-depreciation, feelings of failure
18. Pessimism: anticipation of the worst
19. Mood congruent delusions: delusions of poverty, illness, or loss

21 22

2. Assessing Effect of Medical Burden • Medications, Alcohol, Drugs • Endocrinopathy • Malignancy • Infection Depressive episode should be treated while managing the comorbid medical condition

Assessing Laboratory Results Hematology Urine · CBC with · Urinalysis indices/differential · Culture and sensitivity • ESR Additional tests, e.g. Chemistry Electrocardiogram • Lytes, BUN, · Chest X-Ray Creatinine • Neuroimaging (?) · Liver function tests · Thyroid function tests Fasting glucose level Folate, B12¹ HCCI





1. Psychotherapy

Several are evidence-based treatments for Late Life Depression

RCTs support¹

• Cognitive Behavioral Therapy (CBT)
• Interpersonal Therapy (IPT)
• Problem Solving Therapy (PST)
• ENGAGE

2. Physical Activity

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- Greater midlife physical activity is associated with lower depressive symptomatology in later life¹
- Physical inactivity in older adults is associated with both depression and cognitive deficits²
- Higher and faster remission in LLD linked with exercise augmentation of sertraline (24 wk of PAE).³

*Chang et al. J Gerontol A Biol Sci Med Sci 2015 Nov 2.pii: glv 196 (epub)
*Paulo et al. J Aging Phys Act 2015 (epub)
*Belvederi Murri et al. Br J Psychiatry 2015:207:235-42.

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Pharmacologic Treatment Antidepressant Efficacy

All FDA-indicated antidepressants treat LLD¹ Response rate (50% symptom decrease)²

- 50 65% in trials with ITT analyses
- 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

ITT: Intention to Treat NNT: Number Needed to Treat



See Ellison et al. Mood Disorders in Later Life. Informa Health Care 20 Shanmugham et al. Psychiatr Clin North Am. 2005:28:821-35. **Antidepressant Side Effects: SRIs**

- Discontinuation is less common with SSRI treatment (17%) than with TCA treatment (24%)
- · Significant side effects with SSRs:
 - Sedation
- Risk for bruising
- Weight Gain
- · Risk for GI bleeding
- GI Symptoms Hyponatremia
- Sexual dysfunctionFalls?

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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 5 prescribed medications
- Many interactions are possible
 - Pharmacodynamic
 - Pharmacokinetic



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)
 - · Viibryd (vilazodone)
 - Emsam (transdermal selegiline)



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SSRs - Still 1st Choice in LLD

Several well-tested, generic, well-tolerated, with limited drug interactions, appropriate elimination half-lives:

- Sertraline
- · Citalopram (Note FDA dosage warning)
- Escitalopram



SNRIs

SNRIs share potential adverse effects of:

- Hypertension
- Anxiety
- · Insomnia
- · Share with SSRIs the potential for discontinuation symptoms

Duloxetine – analgesic effects are a bonus



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Other Antidepressants to Consider

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 PD¹
- · Associated with small/significant risk for neutropenia, agranulocytosis; minimal interaction with warfarin



On The Horizon: Ketamine*?

Limited data in elderly

- Early open trial with 4 subjects reported limited benefit and severe dissociative adverse effects in 3 nonresponders.1
- Pilot RTC showed subq ketamine up to 0.5 mg/kg to midazolam in 16 older TRD adults superior to midazolam, with only 50% remitting 7 or more days.2
- Case report remission induced after 4 infusions.³
- Case series poor maintenance of remission in the older adults treated.4

*ketamine is still investigational or off label in the treatment of depression



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

ECT Efficacy

Greater in older adults1

- RUL: for ≥60 yr old, 70.4% remission vs 46% in <60
 BT: for ≥60 yr old, 75% remission vs 58.3% in <60

Better than meds in recent comparison:*

- 3.1 +/- 1.1 wk to ECT remission vs 4.0 +/- 1 wk with meds 2
- Remission rate: 63.8% at 6 wk vs 33.3% at 12 wk in med

Cognitive effects: stable or improved in recent study³, mixed findings in earlier studies attributed to technique and/or underlying disease.4

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Additional Neurotherapies¹

Repetitive Transcranial Magnetic Stimulation²

- 20-50% response rate open label, older adults
- · Poorer response associated with cortical atrophy
- · Better response with higher intensity stimulation?

VNS - limited data in elderly

- *Transcranial Direct Current Stimulation
- *Magnetic Seizure Therapy
- *Deep Brain Stimulation

these neurotherapies are used investigationally or off label in treatment of depression



ulos GS, Kelly Jr RE. Research advances in geriatric depression. World Psychiatry. 2009; 8(3): 140–149 tt al. Curr Psychiatry Rep 2015;17:59-74

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Treatment of Depression in Dementia

- Multiple antidepressants studied, including
 - Citalopram¹
 - Sertraline^{2,5}
 - Clomipramine³ Moclobemide⁴
 - Mirtazapine⁵
- Large controlled trial (DIADS) failed to show superiority of sertraline over placebo
- Side effect assessment more difficult in dementia
- Clinical approach try, but discontinue if ineffective

Nyth et al. Acta Psychiatr Scand 1992;88:138-45; *Lyketsos et al. Am J Psychiatry. 2000;157:1686-9; *Petracca et al. J Neuropsychiatry Clin Neurosci.1996;8:270-5; *Roth et al. Br J Psychiatry 1996;168:149-57

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Treatment Resistant Depression and the "ABCD" Review

Adequacy of prior treatment

- Duration of treatment
- · Dosage of medication

Behavioral/Environmental factors

- Personality disorder
- · Psychosocial stressors

Compliance/Adherence

- · Patient education
- · Treatment intolerance

Diagnosis

- · Missed medical diagnosis or adverse medication effect
- · Missed psychiatric

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DSM 5: Persistent Complex Bereavement Disorder

- · Death of close relationship
- · For more days than not, clinically significant, persistent for at least 12 months (6 for bereaved children):
 - · At least 1 of following:
 - Yearning/longing
 - Sorrow/emotional pain · Preoccupation with deceased
 - · Preoccupation with circumstances of the death
 - And at least 6 symptoms from a group describing reactive distress and social/identity disruption
- · Significant functional impairment/distress
- · Out of proportion to cultural/religious/age-appropriate norms

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Complicated Grief: Risk Factors

Pre-loss factors:

- · Prior personal or family psychiatric illness
- Female sex
- · Cognitive decline

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



Benzodiazepines:

- Chronic use (daily>3 months): 12% of elderly 1
- 9.5% of users are dependent1

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



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• Pain often accompanies MDD1

Spotlight on Pain

- · 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 incr HCCI help-seeking²

Next Step in Treatment Resistant Depression

Optimize

Switch

Augment/Co-prescribe

ECT

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Importance of Maintenance

Even with maintenance, there is a high recurrence rate

Maintenance pharmacotherapy reduces recurrence risk

- Nortriptyline + IPT1
- Citalopram²
- Paroxetine³

Slower initial responders may do better with combined therapy in maintenance4



Epidemiology of Suicide in Later Life

In older adults, one of 4 suicide attempts is fatal.1

Increased risk with2:

- · Older, white, male
- · Widower, living alone, isolated, loss of social support, financial stress
- Pain, Perceived poor health
- · Greater functional impairment
- Acute stressful event bereavement
- · Access to lethal means
- · DEPRESSION!

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Illness Risk Factors

Major depression¹:

 Among depressed elderly seen in primary care during 12 months prior to suicide attempt, fewer than 1/10 received appropriate depression dx before attempt.

Medical illnesses2:

- Cancer, neurological diseases and cardiovascular diseases are the most frequently reported disorders associated with suicide.
- The relative risk for suicide is 1.5 to 4 times higher if an individual has one of these illnesses.



¹Suominen et al. Int J Geriatr Psychiatry 2004;19:35-40 ²Juurlink et al. Arch Intern Med 2004;164;1179-1184.

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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.

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see Harnett and Pies, in Ellison et al (eds). Mood Disorders in Later Life...Informa Health Care 2008.

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Detecting and Treating LLD More Effectively

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!

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HCCIntelligence™ Virtual Office Hours: Ask the Experts An open forum for questions and answers HCCI HCCI

Introductions



Thomas Cornwell, MD
CEO, Home Centered Care Institute
Founder, Northwestern Medicine HomeCare Physicians



Paul Chiang, MD
Senior Medical and Practice Advisor, Home Centered Care
Institute

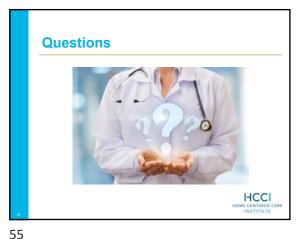
Medical Director, Northwestern Medicine HomeCare Physicians



Brianna Plencner, CPC, CPMA
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