Depression and Dementia in the Elderly

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March 22, 2019

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Disclosures

- Dr. Nguyen and Dr. Zdanys have no conflicts of interest to disclose.
- Non-FDA approved indications will be discussed.

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Outline

- Epidemiology of late-life depression
- Forms of depression in older adults
- Suicide risk in the elderly
- Relationship of depression and dementia
- Identifying depression vs. dementia
- Treatment approaches

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Late-Life Depression (LLD)

- “Depression” may fall into one of many categories
- Symptoms may vary even within a single diagnostic category
- Biological, Psychological, and Social components

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Biological Factors

- Female Gender
- Neurotransmitter Dysfunction
  - serotonergic neurotransmission
- Endocrine Changes
  - Sustained increases in cortisol associated with chronic stress
  - Lower testosterone
- Genetics
  - Multi-factorial, inconclusive
  - Twin studies more robust in earlier life
- Vascular Changes
- Medical Illness
- Co-morbid psychiatric disorders

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Psychological and Social Factors

- Psychological
  - Personality attributes / coping skills
  - Cognitive distortions
- Social
  - Stressful life events / loss
  - Chronic stress
  - Low socioeconomic status

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Epidemiology

- Community survey of 1300 adults > age 60
  - 27% reported depressive symptoms
  - 19% mild dysphoria
  - 4% symptomatic depression
  - 0.8% major depressive episode
  - 1.2% mixed depression / anxiety

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Epidemiology

- Major depression prevalence ~1%-3%
- Prevalence major depression higher in long-term care facilities ~6-14.4%
- Anxiety disorders ≥ depression, ~5.5%
- For both depression and anxiety, prevalence is higher in females
- Prevalence of *symptoms* is much higher than prevalence of *disorders*

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Types of LLD

- Major Depressive Disorder
- Grief
- Bipolar Disorder
- Psychotic Depression
- Dysthymia
- Adjustment Disorder with Depressed Mood
- Depression Associated with Medical Illness
- Dementia-related

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Major Depressive Disorder (MDD)

- 5+ of the following:
  - Depressed mood—either subjective or observed by others
  - Markedly diminished interests / pleasure
  - Change in more than 5% body weight in a month or change in appetite
  - Insomnia or hypersomnia
  - Psychomotor agitation or retardation
  - Fatigue / loss of energy
  - Feelings of worthlessness / inappropriate guilt
  - Poor concentration / indecisiveness

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SIGECAPS

- Sleep
- Interests
- Guilt
- Energy
- Concentration
- Appetite
- Psychomotor
- Suicidal thoughts

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Depression vs. Grief

- DEPRESSION
  - Persistent depressed mood
  - Inability to anticipate pleasure / happiness
  - Pervasive unhappiness
  - Self-critical, guilty feelings, pessimistic
  - Worthlessness
  - Suicidal thoughts
- GRIEF
  - Predominant emptiness / loss
  - Decreases in intensity days to weeks
  - Occurs in waves
  - May experience positive emotions / humor
  - Self-esteem preserved
  - Morbid thoughts about “joining” deceased

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Psychotic Depression

- Delusions
  - Incurable illness, focus on abdomen
  - Persecution
- Guilt
  - Trivial episode from past
- Worthlessness
- Psychomotor retardation
- Increased suicidal ideation
- May stop eating

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Dysthymia

- Also called “Persistent Depressive Disorder”
- Unremitting depressive symptoms
  - 2+ symptoms
  - More days than not
  - At least 2 years
  - Never more than 2 months without symptoms
- Associated with psychosocial stressors
- Can co-exist with major depressive disorder

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Adjustment Disorder

- Maladaptive reaction to an identifiable stressor
  - Family / relationship stress
  - Loss of social role
  - Change in housing
- Results in impairment of functioning (social, occupational)
- In addition to depressed mood, may have:
  - Anxiety
  - Mixed Anxiety / Depressed Mood
  - Mixed Disturbance of Emotions / Conduct

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Bipolar Disorder

- Also called “manic-depressive disorder”
- May start in childhood, adolescence, early adulthood, or later adulthood
- Characterized by major swings in highs and lows

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Bipolar Disorder

- Mania:
  - Grandiosity / increased self esteem
  - Decreased need for sleep
  - Flight of Ideas
  - Talkativeness
  - Psychomotor Agitation
  - Distractability
  - Spending sprees

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Depression Associated with Medical Illness

- Depressive disorders associated with:
  - Cancer
  - Cardiovascular disease
  - Stroke
  - Parkinson's disease
- Physiological effects in brain
- Psychological reaction to disability
- Associated life changes

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Depression in Cancer

- Not all cancer patients get depressed
- “Desire for hastened death” more common in depressed / hopeless cancer patients (Breitbart et al. 2000)
- Depression in cancer known to increase mortality (Brown et al. 2003)

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Depression in Heart Disease

- Cardiovascular mortality is increased in depressed patients (Glassman and Shapiro 1998)
- Myocardial Infarction (Schleifer et al. 1989)
  - 45% patients met dx criteria for major or minor depression within 10 days of MI, 18% MDD
  - 3-4 months post-MI 33% still met criteria for depression including 77% of those who previously met criteria for MDD

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Depression in Stroke

- MDD up to 25%, minor depression another 30%
- Peak 3-6 months post-stroke, may persist several years
- May have had pre-existing vascular depression
- More common in women

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Depression in Parkinson's

- Up to 60% PD patients have depression
- Associated with decreased time to medication for motor symptoms
- Treating depressive symptoms may improve motor symptoms

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Suicide Risk

- Suicide rate among all age groups is highest for older men (50/100k vs. 22/100k younger men)
  - Caucasian
  - >75 y.o.

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Suicide Risk

- Older women worldwide are >3x as likely to die from suicide than young women (15.8/100k vs. 4.9/100k)
  - In US, 30% more likely

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Depression vs. Dementia

- Can be difficult to distinguish!

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Depression-Related Dementia

- Someone who is very depressed “looks” demented
  - Slow
  - Confused
  - Disoriented
  - Apathetic
  - Non-communicative

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Depression-Related Dementia

- Theoretically, treating depression improves cognitive symptoms
- Even if improved, 40% will develop dementia within 3 years
- Is depression an early sign of dementia?

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Work-Up

- History
- Screening
- Physical Examination
- Laboratory tests
- Polysomnography
- MRI

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History

- Duration of current episode
- Current symptoms / severity
- Impact on functioning
- History of previous episodes
- Substance abuse
- Response to previous treatments
- Family history
- Recent stressors
- Collateral from family / caregiver

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Functioning

- Activities of Daily Living
  - Ambulation, Eating, Dressing, Toileting, Bathing
- Instrumental Activities of Daily Living
  - Telephone, Medications, Finances, Driving, Shopping, Cooking, Housework

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Screening

Are you basically satisfied with your life?
Have you dropped many of your activities or interests?
Do you feel that your life is empty?
Do you often get bored?
Are you in good spirits most of the time?
Are you afraid that something bad is going to happen to you?
Do you feel happy most of the time?
Do you feel helpless?
Do you prefer to stay at home, rather than go out and do things?
Do you feel that you have more problems with memory than most?
Do you think it is wonderful to be alive now?
Do you feel pretty worthless the way you are now?
Do you feel full of energy?
Do you feel that your situation is hopeless?
Do you think that most people are better off then you are?

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	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

FOR OFFICE CODING 0 + _____ + _____ + _____

=Total Score: _____

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Suicide Risk Assessment

- Do you ever think about dying?
- Do you ever think about killing yourself, or wish you were dead?
- If yes:
  - When you think about dying, do you have a plan about how to do it?
  - Do you have the means to carry out your plan?
  - Is there a history of previous suicide attempts? How many?

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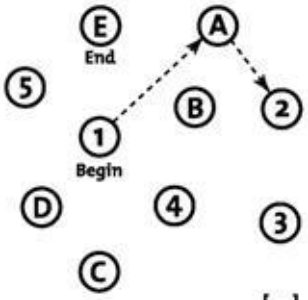
MONTREAL COGNITIVE ASSESSMENT (MOCA)

NAME :
Education : Date of birth :
Sex : DATE :

VISUOSPATIAL / EXECUTIVE



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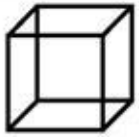


[ ] [ ]

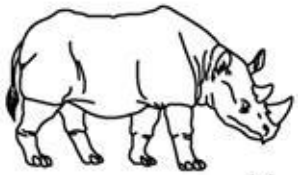
Draw CLOCK (Ten past eleven) (3 points)

[ ] Contour [ ] Numbers [ ] Hands

POINTS __/5

NAMING

[ ]



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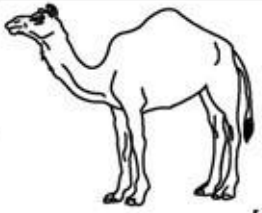

[ ] __/3

MEMORY

Read list of words, subject must repeat them. Do 2 trials. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION

Read list of digits (1 digit/ sec.). Subject has to repeat them in the forward order [ ] 2 1 8 5 4

Subject has to repeat them in the backward order [ ] 7 4 2 __/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B __/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt** __/3

LANGUAGE

Repeat : I only know that John is the one to help today. [ ]

The cat always hid under the couch when dogs were in the room. [ ] __/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] ____ (N ≥ 11 words) __/1

ABSTRACTION

Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler __/2

DELAYED RECALL

	Has to recall words	FACE	VELVET	CHURCH	DAISY	RED	Points for UNCUED recall only
	WITH NO CUE	[ ]	[ ]	[ ]	[ ]	[ ]	
Optional	Category cue						
	Multiple choice cue						

__/5

ORIENTATION

[ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City __/6

 Version 7.0 www.mocatest.org

Normal ≥ 26 / 30

TOTAL __/30

Add 1 point if ≤ 12 yr edu

Administered by: _____

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Physical Exam

- Weight loss
- Pulmonary (sleep study?)
- Cardiac
- Neurologic
  - Laterality (vascular)
  - Rigidity or gait changes (Parkinson's)

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Lab Work

- Thyroid panel
- Complete blood count
- B12
- Folate
- Consider D3

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For Possible Dementia…

- MRI of the brain
- Neuropsychological testing referral

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Take-Home Point

- If you are thinking depression, look for dementia.

- If you are thinking dementia, look for depression.

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Treatment Approaches

Sarah A. Nguyen, MD

Successful Aging: The Intersection of Physical and Behavioral Health Conference sponsored by DMHAS/DORS

March 22, 2019 – Masonicare at Ashlar Village

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What is “Successful” Aging?

- “…key ideas such as life satisfaction, longevity, freedom from disability, mastery and growth, active engagement with life, and independence.”

- Age related life stressors
  - Impending and/or chronic illness
  - Social losses
  - “lack of person-environment fit”

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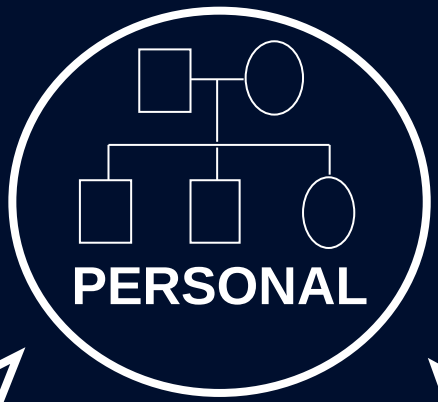
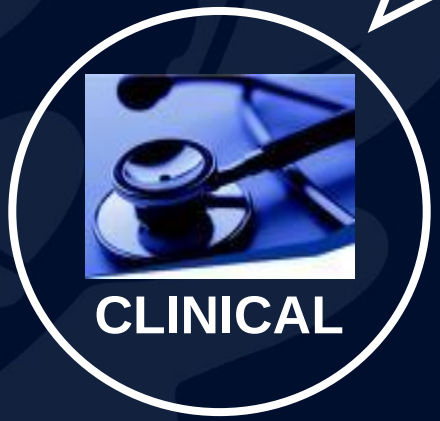
Martin et al. The Gerontologist, 2015. 55 (1): 14–25

Later Life Challenges

PERSONAL: retirement and financial issues, grandparenthood, bereavement and widowhood, loss of loved ones, caregiver issues



SYSTEMS: fearful, pessimistic view of aging stereotyped as old fashioned, rigid, boring, demented, burdensome; institutionalized view of aging



CLINICAL: chronic illness, progressive cognitive and physical decline, end of life care

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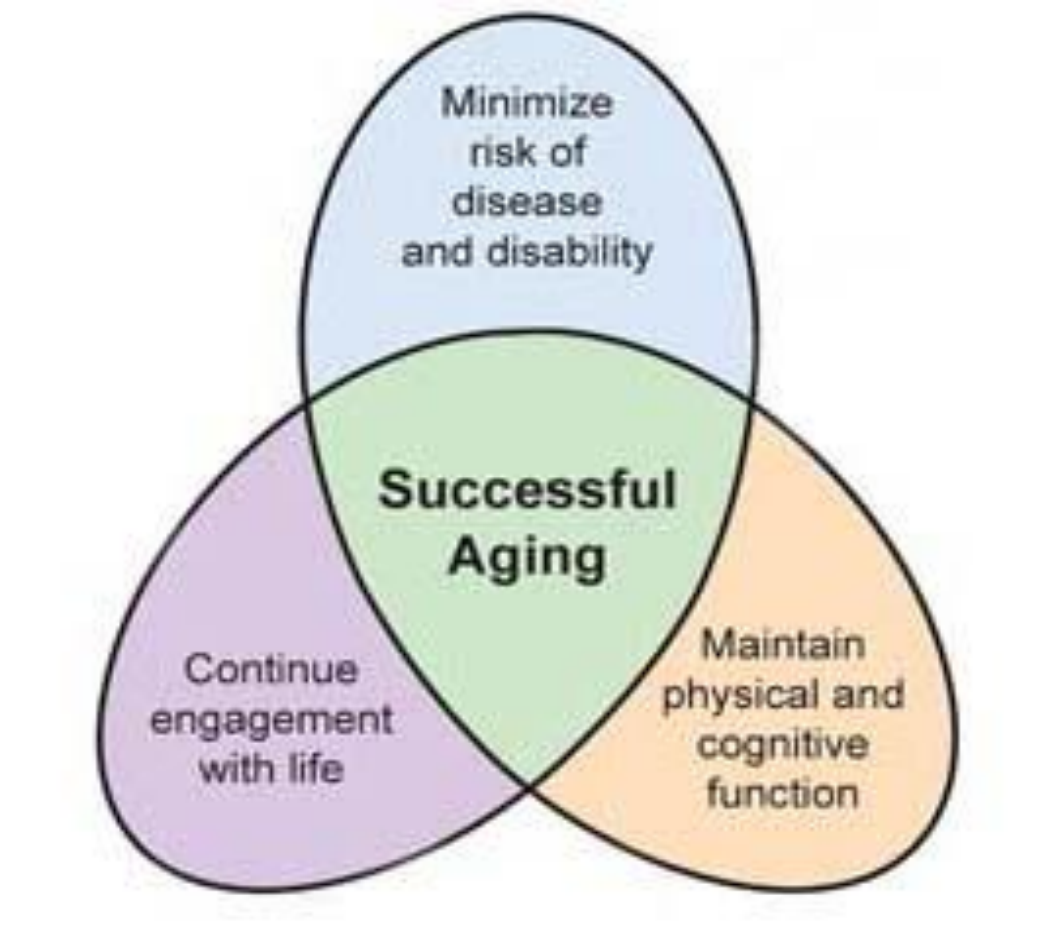
Goals



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http://rogena.com/2015/03/15/what-is-successful-aging/

Non-Pharmacological Approaches

- Senior day programs
  - Structured group activities
- Skills training
  - Social skills
  - Occupational skills
  - Vocational skills
  - Stress management skills
  - Life skills
  - All of above: psychosocial rehabilitation

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Lifestyle Changes

- Moderate intensity physical activity
- Improving nutrition
- Increasing engagement in pleasurable activities and social interactions

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D'Onofrio G. et al. 2016. Non Pharmacological Approaches to Dementia.

Evidence-Based Psychotherapies

- Cognitive behavioral therapy (CBT)
- Interpersonal therapy (IPT)
  - Grief
  - Role transition
  - Interpersonal deficits
  - Interpersonal conflict
- Problem solving therapy (PST)
  - Insufficient problem solving skill
  - Abandonment of skill
  - Perceived complexity of problems

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Atognini and Liptzin in Ellison et al. Mood Disorders in Later Life. Informa 2008.

Bright Light Therapy

- Indications
  - Seasonal affective disorder
  - Aberrant sleep/wake cycles
- 10,000 lux at 18 inches away
- 20-30 min/day, preferably AM

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Pharmacology in Later Life

- Pharmacokinetics: action of the body on the drug
- Pharmacodynamics: mechanism of action
- Polypharmacy and drug-drug interactions
- Safety and adherence
- Less than 1/3 of package inserts have specific dosing recs for elderly patients

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Geriatric Pharmacokinetics

1. **Absorption:** gastric pH can increase, gastric and colonic motility can decrease
2. **Distribution:** higher body fat by 50-100%, less total body water by 10-15%, lower albumin
3. **Metabolism in liver:** lower blood flow (40%) leads to lower clearance and decline occurs in certain metabolic enzymes
4. **Elimination:** renal function decreased

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Treatment: Consensus Guidelines

- Nonpsychotic MDD → SSRI/SNRI + psychotherapy
- Psychotic MDD → (SSRI/SNRI + antipsychotic) or ECT
- MDD + medical d/o → treat both from outset
- Dysthymia → SSRI + psychotherapy
- MDD with insomnia → sedating antidepressant (trazodone or mirtazapine) or add zolpidem or zaleplon

Alexpooulos GS, Katz IR, Reynolds CF III, et al. The Expert Consensus Guideline Series: Pharmacotherapy of Depressive Disorders in Older Patients. Postgrad Med Special Report. 2001 (October): 1-86.

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Choosing a Medication

- Safety profile (eg orthostasis, overdose)
- Pharmacodynamic profile (eg renal, hepatic effects)
- Drug-drug interaction profile
- Pharmacokinetic profile (eg dosing schedule, evenness of plasma levels)
- Tolerability (eg anticholinergic effects)
- Beneficial added effects (eg sedation)
- Previous response

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Other Considerations

- Depression with:
  - Insomnia
  - Poor appetite
  - Pain
  - Hypertension
  - Heart disease
  - Renal disease
  - Liver disease
  - Diabetes Mellitus
  - Alzheimer's Disease
  - Cerebrovascular disease

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Pharmacotherapy Approach

- All antidepressants equally effective
- Adequate trial: 8 weeks at therapeutic dose
- Dosing: start ½ adult dose
- Response: 50-65% to first trial / 30% to placebo
- Remission: 30-40% to first trial / 15% to placebo

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Predictors of Delayed or Poor Treatment Response

- Older age
- Longer duration of episode
- Presence of cognitive impairment
  - "Impaired response inhibition"
  - Longer symptom duration and more chronic episodes
- Higher anxiety levels

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SSRIs

- Still 1st choice in LLD
- Several well-tested, generic, well-tolerated, with limited DDI, appropriate elimination half-lives:
  - Sertraline
  - Citalopram (note FDA dosage warning)
  - Escitalopram

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SSRIs Geriatric Safety

- May reduce platelet aggregation
- Fewer myocardial infarctions than non-SSRI treated patients
- Fluoxetine and sertraline
  - benign in ischemic heart disease (IHD)

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FDA warning on citalopram, 2011

- 20 mg/day for patients > 60 years of age
- Dose-dependent QT interval prolongation
  - Torsades de Pointes
  - Ventricular tachycardia
  - Sudden death

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SNRIs

- FDA approved, but not first line:
  - Desvenlafaxine (Pristiq)
  - Duloxetine (Cymbalta): neuropathic pain and fibromyalgia
  - Venlafaxine (Effexor): panic disorder and social anxiety
  - Caution with renal or liver disease, alcohol use

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SNRI Adverse Effects

- Hypertension or orthostatic hypotension
- EKG changes and arrhythmias
- Anxiety
- Insomnia
- Adrenergic SE: dry mouth, constipation, urinary retention, IOP, transient agitation

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Other Antidepressants

- Buproprion (Wellbutrin)
  - Less sedation and sexual SE
  - Less helpful with anxiety/psychosis
  - Special contraindications: seizure, case reports for psychosis
- Mirtazapine (Remeron)
  - More anxiolytic, less sexual SE, less nausea
  - More weight gain and sedation
  - Exacerbates REM sleep behavior in PD
  - Associated with small risk for neutropenia, agranulocytosis, minimal interaction with warfarin

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Newer Antidepressants

- Viibryd (vilazodone)
  - SSRI and partial agonist at 5HT1a
- Brintellix (vortioxetine)
  - SSRI, agonist 5HT1a, partial agonist 5HT1b, antagonist 5HT3a/5HT7
- Fetzima (levomilnacipran)
  - SNRI

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Switching Medications

- SSRI non-responsiveness, consider SWITCH to:
  - Venlafaxine: anxiety prominent
  - Bupropion: apathy prominent
  - Mirtazapine: insomnia/anxiety prominent
  - Nortriptyline: melancholic depression

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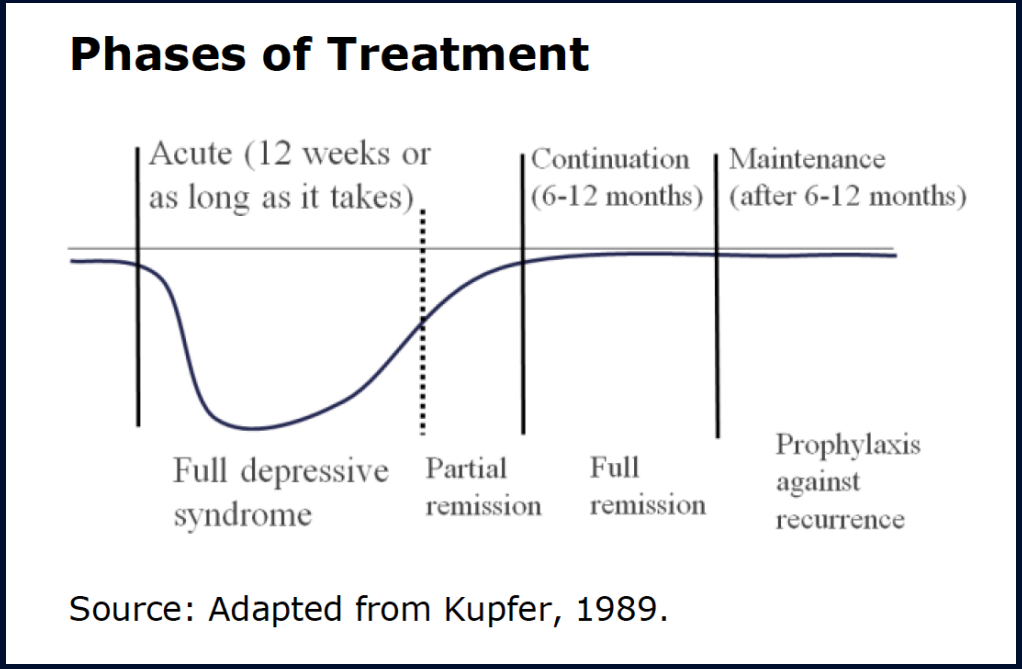
Duration of Treatment

- Single severe episode of MDD
  - Continue AD at least 1 year
- Two episodes of MDD
  - Continue AD for 1-3 years
- Three or more episodes of MDD
  - Continue AD for longer than 3 years



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TCAs

- Secondary TCAs: nortriptyline, desipramine
  - preferred, selective for NE, less SE
- Tertiary TCAs: imipramine, amitriptyline, clomipramine, doxepine
- Obtain EKG before and after therapeutic level achieved
- Drawbacks in LLD:
  - Anticholinergic effects
  - Postural hypotension
  - Cardiac effects
    - Type 1 antiarrhythmic
    - 2:1 AV block with BBB

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MAOIs

- MAOIs – efficacious but rarely used unless failed SSRI, SNRI, TCA
  - Significant hypotension
  - Life-threatening hypertensive or serotonergic crisis
  - Avoid tyramine rich foods
  - DDI with sympathomimetic drugs
- Phenelzine preferred to tranylcypromine
- Selegeline transdermal patch: avoids GI tract and reduces risk of hypertensive crisis

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Augmentation Strategies

- Stimulants: methylphenidate
- Lithium
- T3
- Antipsychotics: aripiprazole, quetiapine
- Combination therapy
  - Buproprion, mirtazapine, stimulants

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Electroconvulsive Therapy (ECT)

- Elderly have better response to ECT than younger patients
- In the old-old, may be more efficacious and cause less s/e than medications
- 86% response in depressed patients with dementia
- Indications: moderate-severe depression, psychotic features, intolerance to medications, fast response needed, etc

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Tew 1999, Manly 2000, APA Practice Guidelines

Other Therapies

- Repetitive Transcranial Magnetic Stimulation (rTMS)
  - More efficacious than sham treatment in older adults, age >50, with vascular depression (n=92)

- Bibliotherapy > waitlist and education for mild-moderate depression
  - Gains maintained at 2 years

Jorge 2008, Scotin 1989

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Treatment Resistant Depression: ABCD Review

- **A**dequacy of prior treatment
  - Duration and dosage
- **B**ehavioral/environmental factors
  - Personality disorders, psychosocial stressors
- **C**ompliance/adherence
  - Treatment intolerance, psychoeducation
- **D**iagnosis
  - Missed medical or psychiatric diagnosis, adverse SE

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Depression with Dementia

- MDD confounded by deficits in verbal expression and cognitive symptoms
- AD + MDD
  - Presence of 3+ symptoms, not including difficulty concentrating, and nonsomatic symptoms
  - Irritability and social withdrawal
- VaD + MDD
  - More vegetative symptoms
  - Fatigue, muscular weakness, weight loss

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Olin et al. 2002. Provisional diagnostic criteria for depression of Alzheimer disease. Am. J. Geriatr. Psychiatry. 10:125–8.
Park et al. 2007. Depression in vascular dementia is quantitatively and qualitatively different from depression in Alzheimer's disease. Dement. Geriatr. Cogn. Disord. 23:67–73.

Treatment of MDD + Dementia

- Assess severity and “masked” depression
- Consider psychosocial interventions
- Choose medication and target symptoms
- Monitor improvement and adverse effects
- Modify approach based on outcome
- Consider discontinuation

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Late Life Delusional Depression

- Expert consensus: antipsychotic + antidepressant
- ECT produces more rapid response than meds
- Compared to younger adults, RCTs guiding treatment choice in LLD with psychotic features much more limited

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Alexpooulos et al J. Clin Psychiatry 2004; 65 Suppl 2:5-99
Flint and Rifat. Int J Geriatr Psychiatry 1998; 13:23-8.

Medication-Induced Depression

- Acyclovir
- Anabolic steroids
- **ACE inhibitors**
- **Anticonvulsants**
- Baclofen
- Barbiturates
- Benzodiazepines
- **B-blockers**
- Bromocriptine
- **Calcium channel blockers**
- Ciprofloxacin
- Clonidine
- Corticosteroids
- Digitalis
- Disulfiram
- Estrogen
- Guanethidine
- **H2 receptor blockers**
- Interferon alpha
- Interleukin-2
- Isotretinoin
- **Levodopa**
- Methyldopa
- Metoclopramide
- Metrizamide
- Metronidazole
- **NSAIDS (indomethacin)**
- **Opioids**
- Pergolide
- Reserpine
- **Sulfonamides**
- **Thiazide diuretics**
- Topiramate
- Vinblastine
- Vincristine

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Ko et al, Jama, 2002

Take Home Points

- Age-related physiological changes and DDI are important considerations for pharmacological interventions
- Depression in late life is treatable, even among older adults with dementia
- Consider psychotherapies in treatment of LLD – strong evidence but not as frequently used!

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