DEPRESSION IN THE ELDERLY

Synergize
March 3, 2016

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Presenter disclosures

Faculty: Dallas Seitz

Relationships with commercial interests:

- NONE

Potential for conflict(s) of interest:

- NONE

Objectives

1. Review the epidemiology of depression in older adults.
2. Describe the presentation of depression in older adults.
3. Develop an approach to the management of depression in older adults and review recent developments in treatment options.

OBJECTIVE 1: EPIDEMIOLOGY OF DEPRESSION IN OLDER ADULTS

Case presentation

- Mrs. A presents to your clinic today with her daughter, who is worried her mother might be depressed:
  - Mrs. A is 75 years old
  - Retired Nurse
  - Lives independently at home
  - More details to come…

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How common is depression?

- Prevalence:
  - Depressive symptoms in community up to 28.7%
  - Lifetime prevalence MDD in age >60 10.3%
  - 5-10% in primary care settings
  - 12-45% within hospitals
  - Up to 37% after hospitalization for critical illness
  - Up to 40% in LTC

Kessler 2005 Glasmaer 2011
Taylor 2014 Lyness 1999
Jackosn 2014 CCSMH 2006

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Prevalence

- Depression is under reported
  - Considered a "normal" consequence of ageing
  - Stigma
  - Race
- Depression is under diagnosed
  - Co-morbid medical illness: symptom overlap
  - Not reported
- Depression is under treated

Conner 2010
Lyness 1995

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Risk factors

- Female gender
- Sleep disturbance
- Prior depression
- Cognitive impairment
- New medical Illness
- Poor self-rated health
- Disability
- Stressful life events
- Bereavement
- Alcohol use

Cole 2003
Chang-Quan 2010
CCSMH guidelines

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Medical comorbidity and depression

Medical conditions associated with MDD

- Ischemic Heart Disease
- Diabetes
- Arthritis/pain
- Stroke
- Parkinson's disease
- Dementia
- Hip fractures
- Respiratory disorders

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Patten 2001

Impact of depression

- Health related consequences:
  - Increased perceived poor health
  - Poor function
  - Non-adherence to medical treatments
  - Cognitive decine
  - Increased mortality
- Health economic consequences:
  - Utilization of Medical Services
  - Increased health care costs

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Beekman 2002

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OBJECTIVE 2: PRESENTATION OF DEPRESSION IN OLDER ADULTS

More on Mrs. A

- Her daughter tells you Mrs. A is:
  - Withdrawn and has stopped going to church
  - Spends much time in bed
  - Has lost weight
  - Has been more forgetful
  - Has been self-deprecating, and at times saying the "world would be a better place without me"
- Her past medical history is significant for DM II, HTN, and she was recently diagnosed with CHF and moderately severe CKD
- She also suffers from neuropathic pain

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Differential?

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Differential

- Delirium (especially hypoactive)
- Pain or discomfort
- Other medical causes
- Environmental causes
- Apathy associated with dementia

Sink, JAMA, 2005

Differential

Medication use potentially related to depression:

- Methyldopa
- Benzodiazepines
- Propranolol
- Reserpine
- Steroids
- Anti-Parkinsonian drugs
- β blockers
- Cimetidine
- Clonidine
- Hydralazine
- Oestrogens
- Progesterone
- Tamoxifen
- Vinblastine
- Vincristine
- Dextropropoxyphene

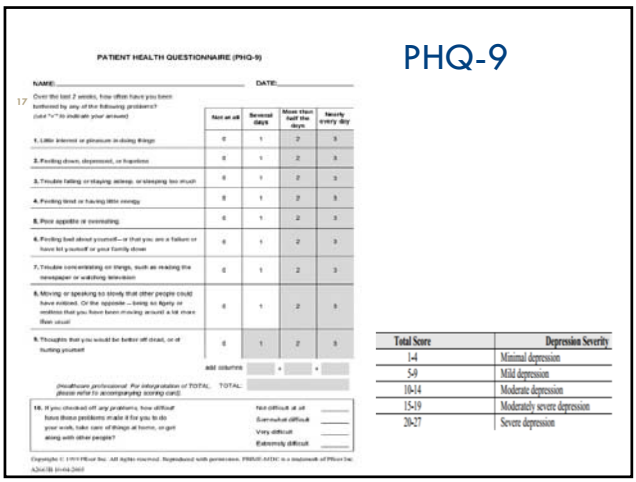
Medical conditions potentially related to depression:

- Endocrinopathy—hypothyroidism, hyperthyroidism, hypoparathyroidism, hyperparathyroidism, hypoadrenocorticism, hyperadrenocorticism, Cushing's disease
- Malignant disease—leukaemia, lymphoma, pancreatic cancer
- Cerebrovascular disease—lacunar infarcts, stroke, vascular dementia
- Myocardial infarction
- Metabolic disorder—B12 deficiency, malnutrition

Alexopoulos, Lancet, 2005

Screening tools

PHQ-9



PATIENT HEALTH QUESTIONNAIRE (PHQ-9)

NAME:_____ DATE:_____

17 Over the last 2 weeks, how often have you been bothered by any of the following problems? (use "✓" to indicate your answer)

	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 figety 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	0	1	2	3
	add columns	+	+	+
(Healthcare professional: For interpretation of TOTAL, please refer to accompanying scoring card).	TOTAL:			

10. If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all _____
Somewhat difficult _____
Very difficult _____
Extremely difficult _____

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A29-0B 10/04/2005

Total Score	Depression Severity
1-4	Minimal depression
5-9	Mild depression
10-14	Moderate depression
15-19	Moderately severe depression
20-27	Severe depression

GDS (SF)

GERIATRIC DEPRESSION SCALE (GDS, SHORT FORM)

Choose the best answer for how you felt over the past week.

1. Are you basically satisfied with your life?	yes/**no**
2. Have you dropped many of your activities and interests?	**yes**/no
3. Do you feel that your life is empty?	**yes**/no
4. Do you often get bored?	**yes**/no
5. Are you in good spirits most of the time?	yes/**no**
6. Are you afraid that something bad is going to happen to you?	**yes**/no
7. Do you feel happy most of the time?	yes/**no**
8. Do you often feel helpless?	**yes**/no
9. Do you prefer to stay at home, rather than going out and doing new things?	**yes**/no
10. Do you feel you have more problems with memory than most?	**yes**/no
11. Do you think it is wonderful to be alive now?	yes/**no**
12. Do you feel pretty worthless the way you are now?	**yes**/no
13. Do you feel full of energy?	yes/**no**
14. Do you feel that your situation is hopeless?	**yes**/no
15. Do you think that most people are better off than you are?	**yes**/no

Score 1 point for each bolded answer. Cut-off: normal 0–5; above 5 suggests depression.

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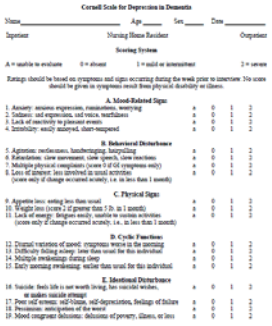
Cornell Scale for Depression in Dementia



Cornell Scale for Depression in Dementia

Name_____ Age_____ Sex_____ Date_____

Inpatient Nursing Home Resident Outpatient

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 to 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

B. Behavioral Disturbance

5. Agitation: restlessness, handwringing, hairpulling A 0 1 2
6. Retardation: slow movement, slow speech, slow reactions A 0 1 2
7. Multiple physical complaints (score 0 if GI symptoms only) A 0 1 2
8. Loss of interest: less involved in usual activities A 0 1 2
(score only if change occurred acutely, i.e. in less than 1 month)

C. Physical Signs

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

D. Cyclic Functions

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

E. Ideational Disturbance

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

DSM-5 criteria for MDD

- **≥ 5** of the following symptoms; same 2-week period; represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.
  - Depressed mood
  - Markedly diminished interest or pleasure
  - Significant weight loss or decrease or increase in appetite
  - Insomnia or hypersomnia
  - Psychomotor agitation or retardation
  - Fatigue or loss of energy
  - Feelings of worthlessness or excessive or inappropriate guilt
  - Decreased concentration, or indecisiveness
  - Recurrent thoughts of death (not just fear of dying) or suicidal ideation

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Features of late life depression

- "Depressed mood" may be less prominent
- More anxiety
- More likely to express somatic complaints
  - 65% have hypochondriacal symptoms
- Cognitive impairment
- Psychosis more common
- Less likely to have family history of depression

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Alexopoulos, 2005

Depression and cognition

- Relationship to dementia: each increases risk of the other
- Concept of "vascular depression"
  - Greater disability
  - More cognitive impairment
- Brain imaging:
  - lateral ventricles more enlarged
  - More white matter intensities
  - Temporal lobe atrophy
- Effect of depression on cognition
  - Memory, verbal learning
  - Especially on tasks involving focused attention, verbal learning, working memory

Beekman 2013
Saczynski 2010
Bayer 2011
Olesen 2010

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OBJECTIVE 3: DEVELOP AN APPROACH TO MANAGEMENT

Mrs. A?

- Anything else you want to know?
- Any tests you would order?

Assessment

- Past psychiatric history
  - Depression, bipolar disorder (or history of manic type episodes), anxiety, suicide attempts
    - History of treatment response
- Past Medical History:
  - Screen for diseases that may increase risk of depression (e.g. Parkinson's disease, stroke) or that may be affected by treatment
  - Review medications for potential contributing causes and potential drug interactions if treatment is initiated
- Screen for cognitive impairment
  - What type of problems, if any?
  - Clarify timeline
  - In theory, cognitive changes associated with depression are reversible but…
- Obtain collateral

Assessment

- Labs
  - Routine, especially:
  - TSH, B12: rule out contributing causes
  - Consider ECG, lytes
- Nutritional status
- BP

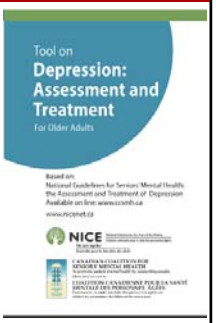
Blazer, 2003

Management

- Guidelines
- Nonpharmacological
- Pharmacological

Management: what do guidelines say?

- Non-pharmacological
  - Supportive care should be offered to all
  - Psychotherapy is a first line option alone or in combination
    - Based on type of depression (and severity), coping style, cognition
- Pharmacological
  - Mild-moderate: antidepressants, psychotherapy or combo
  - Severe: combination; consider ECT



CCSMH, 2006

Non-pharmacological treatments

Psychotherapy

- Strongest evidence for Cognitive Behavioural Therapy (CBT) and Problem Solving Therapy (PST)
- Interpersonal Therapy (IPT)
- Usually weekly visits for 8-12 weeks
- Access, presence of cognitive impairment, patient motivation all potential barriers

Evidence for PST

- PATH (problem solving approach + caregiver participation) in older adults with cognitive impairment ranging from mild deficits to moderate dementia
  - **37.8% vs. 13.5%** remission rate compared to supportive therapy in a RCT
  - **66.7% vs. 32.3%** response rate
  - Dementia or depression severity at baseline not significant moderators

Kiosses, JAMA Psychiatry, 2015

Non-pharmacological Treatments

- Electroconvulsive Therapy (ECT)
- Consider if:
  - Medical refractory/resistant/intolerant
  - Severe suicidal risk
  - Food/fluid refusal
  - Psychotic depression
  - Depression with motor symptoms (e.g. catatonia)
- Good response rates in older adults, as well tolerated as in younger adults
- Transcranial Magnetic Stimulation
  - Conflicting evidence re: age influence on response

Pharmacological treatments

General principles:

- Start lower (usually half of dose used in younger adults)
- Go slower (but go!)
- Aim to reach target dose in one month
- Use lower max dose in most cases
- Monitor treatment response and do not continue ineffective medications

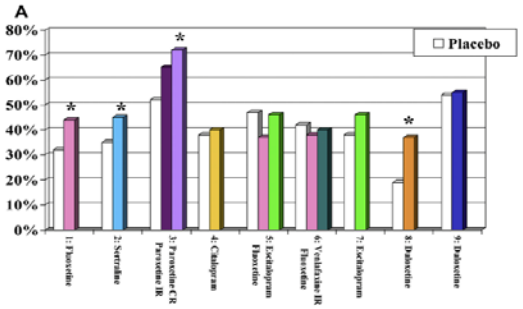
CCSMH, 2006

Pharmacological Treatments

- First line: SSRIs
  - Effective in some but not all trials
  - Generally effective in larger trials
    - Response rates 35-60% vs. 26-40% with placebo
  - Paroxetine effective in trials but usually avoided due to increased anticholinergic side effects
  - Citalopram, escitalopram, sertraline generally used first due to tolerability
  - Check sodium
- Second line: SNRIs
  - Venlafaxine and duloxetine

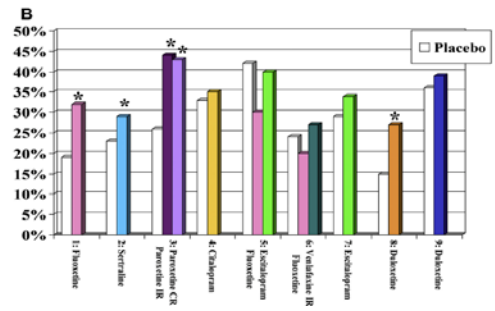
NEJM, 2014

Response rates



Mulsant et al. Clin Geriatr Med, 2014

Remission rates



Mulsant et al. Clin Geriatr Med, 2014

Pharmacological treatments

- Other options (3rd line, or augmentation)
- Bupropion XL
- Mirtazapine
- TCAs
  - As effective as SSRIs, but more side effects
  - Nortriptyline

NEJM 2014
Mulsant, Am J Geriatr Psychiatr, 2001

Pharmacological treatments

Other

- Atypical antipsychotics
  - Augmentation not monotherapy
  - Aripiprazole and quetiapine
- Stimulants
  - Few high quality or large controlled trials
- Lithium
  - Supported by evidence in older adults but can be difficult to initiate due to side effects and need for monitoring

Commonly Used Anti-Depressant Medications - National Guidelines for Seniors Mental Health: Part 5.

Generic Name SSRI	Trade Name	Starting Dose (mg/day)	Average Dose	Maximum recommended dose (CPS)	Comments/Caution
Citalopram	Celexa	10	20-40	40 mg	
Escitalopram	Cipralex	5	10-20	20 mg	
Sertraline	Zoloft	25	50-150	200 mg	
Other agents					
Bupropion	Wellbutrin	100	100 mg BID	150 mg BID	May cause seizures
Mirtazapine	Remeron	15	30-45	45 mg	
Moclobemide	Manerix	150	150-300 BID	300 mg BID	Do not combine with MAO-B inhibitors or Tricyclics
Venlafaxine	Effexor	37.5	75-225	*375 mg	*For severe depression, may increase blood pressure
Tricyclic antidepressants					
desipramine	Norpramin	10-25	50-150	300 mg	Anticholinergic properties; cardio-vascular side effects; monitor blood levels
Nortriptyline	Aventyl	10-25	40-100	200 mg	Anticholinergic properties; cardio-vascular side effects; monitor blood levels

Treatment: how long?

- Guidelines:
  - In remission after first episode: treat minimum 1 and up to 2 years from time of improvement
  - Recurrent episodes: indefinite maintenance treatment
  - LTC: ?, evaluate regularly
- Psychotherapy
  - Not clear
  - Some evidence to support decreased risk of relapse (check for PST)

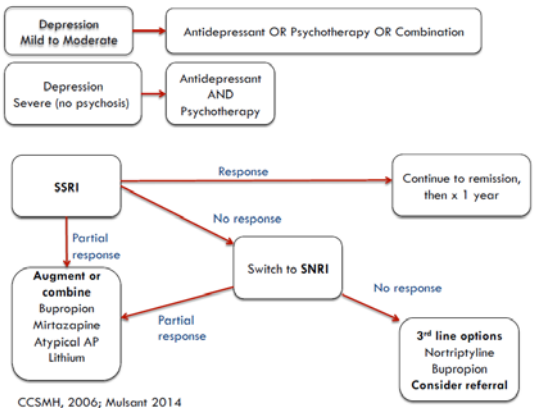
Treatment: partial or no response?

Guidelines

- If no improvement after 2 weeks at average dose, increase further until there is some improvement, max dose reached, or limited by side effects

Controversial

- Change if, at max tolerated or recommended dose:
  - No improvement at 4 weeks
  - OR insufficient improvement at 8 weeks
- In general: optimize, augment or switch, augment or switch



CCSMH, 2006; Mulsant 2014

Summary

- Treatment often guided by practices in younger populations
  - Limited data on efficacy and safety in older adults
  - Little data on long-term treatment or maintenance strategies
- Little evidence to support practice of individualizing treatment/matching side effect profile to symptoms
- Comparable efficacy of all antidepressants across the lifespan

"Approach with therapeutic optimism"

Blazer, 2004
CCSMH, 2006
Mulsant, 2014

Update on recent evidence

Stepped care approach vs. usual care

IMPACT

- Antidepressant or PST→switch→combine antidepressant and PST

PROSPECT

- Optimize dose→switch to citalopram→augment with buproprion→switch to venlafaxine→augment with mirtazapine, nortriptyline,
- *same eligibility criteria in study and usual care groups

1. Goldwasser, Int J Aging Hum Dev, 1987
2. Buettner L, Am J Alz Dis Other Dement, 2002
3. Buettner L, Am J Alz Dis, 1999

Combined citalopram and methylphenidate improved treatment response compared to either drug alone in geriatric depression: a randomized double-blind, placebo-controlled trial

Helen Lavretsky, M.D.[1], Michelle Reinlieb, Ph.D.[1], Natalie St. Cyr, M.A.[1], Prabha Siddarth, Ph.D.[1], Linda M. Ercoli, Ph.D.[1], and Damla Senturk, Ph.D.[2]

- 16 week RCT in 143 geriatric outpatients with major depression (N = 143)
- 3 treatment groups:
  - Citalopram 20-60mg
  - Methylphenidate 5-40mg
  - Methylphenidate + citalopram
- Depression significantly improved in all groups
  - Greater and faster improvement in combination group
  - No differences in cognitive outcomes

Am J Psychiatry, 2015

Efficacy, safety, and tolerability of augmentation pharmacotherapy with aripiprazole for treatment-resistant depression in late life: a randomised, double-blind, placebo-controlled trial

Eric J Lenze, Benoit H Mulsant, Daniel M Blumberger, Jordan F Karp, John W Newcomer, Stewart J Anderson, Mary Amanda Dew, Meryl A Butters, Jacqueline A Stack, Amy E Begley, Charles F Reynolds III

- 12- week RCT of aripiprazole augmentation of venlafaxine in depressed adults >60 years old (N = 181)
- Pre-trial treatment (N = 468) with at least 12 weeks of venlafaxine (150-300mg/day)
- Patients who did not achieve remission randomized to aripiprazole (10-15mg/day) or placebo
- Greater proportion achieved remission in aripiprazole group
  - 44% vs. 29% (p=0.03)
  - Akathisia (26%) and Parkinsonism (17%) most common side effects

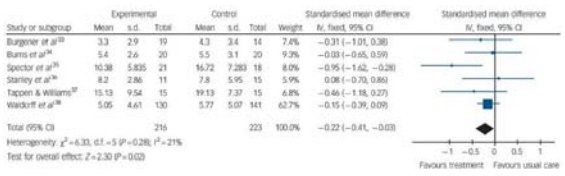
Lancet, September 2015 (online)

Depression in Dementia (DpD)

- NIMH provisional criteria
- Two week period of ***three* or more symptoms:**
  - **Depressed mood**
  - **Decreased positive affect or pleasure in response to social contacts and usual activities**
  - Disruption of sleep and/or appetite
  - Psychomotor changes
  - Irritability
  - Fatigue or loss of energy
  - Feelings of worthlessness, hopelessness, or excessive guilt
  - Recurrent thoughts of death, suicidal ideation or plan

Psychological Treatments for DpD

- 6 randomized controlled trials[1]
  - Based on various models (CBT, IPT, counseling)
  - No effect on secondary outcomes, such as ADLs, quality of life, cognition, or caregiver depression



1. Ortega, B J Psych, 2015

Antidepressants for DpD

- 2 meta-analyses of antidepressants for depression in dementia failed to find statistically significant benefits over placebo:
  - Nelson et al (N=7 studies):
    - Response OR: 2.12 (0.95 – 4.70)
    - Remission OR: 1.97 (0.85 – 4.55)
    - Adverse event rates relatively low: 9% vs. 6% with placebo
  - Bains et al[2] (N=4 studies)
    - Weak support for efficacy of antidepressants
- 11RCTs
  - 5 positive, 6 negative studies

Nelson, J Am Geriatr Soc, 2011
Bains et al., Cochrane Syst Rev, 2002
Enach, Curr Op in Psych, 2011

Challenges: DpD

- Can be difficult to assess and diagnose
- Overlap between symptoms of dementia and depression
- Limited role for psychological therapies in individuals with cognitive impairment
- Inconsistent evidence for pharmacological treatments

Thanks

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