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Ontario CLRI

Update: Management of Depression in Older Adults

Rob Madan MD FRCPC, Geriatric Psychiatrist
Baycrest
University of Toronto
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Learning Objectives

- By the end of the session, participants will be able to:
  - List various disorders that present with depressed mood
  - Describe the workup for late life depression
  - List 2 evidence –based treatment for depression in older adults

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Outline

1. Assessment
2. Pharmacological treatments
3. Other treatments for geriatric depression

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Differential Diagnosis "I feel down…"

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Differential Diagnosis "I feel down…"

- Major Depressive Disorder – Major Depressive Episode
- Bipolar Disorder – Major Depressive Episode
- Persistent Depressive Disorder- pure dysthymic type
- "Minor/subthreshold depression"
- Adjustment Disorder
- Bereavement
- Personality Disorder
- Mood disorder due to a medical condition
- Substances/meds

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MDE Symptoms

- *Depressed/empty
- *Anhedonia
- Sleep (less or more)
- Appetite (less or more)
- Reduced energy
- Poor concentration
- Guilt or worthlessness
- Psychomotor slowing or restlessness
- Thoughts of death or suicide
- Distress or impairment in functioning X 2 weeks

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Question: What are the Challenges in Diagnosing Depression in Dementia?

- Unable to recall
- Unable to articulate/describe
- Loss if interest vs inability
- Sleep and appetite
- Psychomotor changes

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Depression of Dementia (dAD) NIMH

DSM
- At least 5 symptoms
- Almost every day

dAD
- At least 3 symptoms
- Not every day
- Added irritability
- Added social isolation or withdrawal

Olin et al., Am J of Ger Psych 2002, 10: 125-128, 129-141

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Assessment

- Interview
- Collateral History
- Safety
- Cognitive Assessment
- Physical exam
- Bloodwork
  - CBC, Lytes, Thyroid, B12, Calcium, glucose
- Imaging
- Driving

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Rating Scales

- Geriatric Depression Scale
  - 15 item
- PHQ -9 - Patient Health Questionnaire
- MADRS – Montgomery Asperg Depression Scale
- Beck Depression Inventory
- Cornell Scale for depression in dementia

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Treatment

- Pharmacotherapy
- Psychotherapy
- Other somatic treatments

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	Biological	Psychological	Social
predisposing			
precipitating			
perpetuating			
protective			

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Antidepressants

- Serotonin re-uptake inhibitors (SSRI)
  - E.g. sertraline, escitalopram, citalopram, paroxetine)
- Serotonin norepinephrine re-uptake inhibitors
  - Venlafaxine, duloxetine
- Bupropion, mirtazapine
- Tricyclic antidepressants
- Monoamine oxidase inhibitors

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Randomized Placebo-Controlled Trials

Antidepressant	Positive Study	Negative Study	Equivocal
agomelatine	+		
Bupropion			+
citalopram		+	
duloxetine	+++		+
escitalopram	+	++	
fluoxetine	+	++	
paroxetine	++		
Quetiapine XR	+		
sertraline	+		
tianeptine	+		
venlafaxine		+	
vortioxetine	+		

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Meta-Analyses

- 2nd generation – effective
  - 44.4% vs 34.7%
- TCA's, SSRIs and other antidepressants were superior to placebo
  - NNT were 14.4 and 6.7 for remission and response
- sertraline, paroxetine, and duloxetine were significantly better than placebo in achieving a partial response
- duloxetine > placebo in achieving remission and response. SSRIs in 3 studies were not significantly better than placebo

Nelson et al. Am J Geriatr Psychiatry 2008; 16:558 –56
Kok et al., Journal of Affective Disorders 141 (2012) 103–115
Thorlund et al., ; J Am Geriatr Soc 63:1002–1009, 2015
Tham et al., Journal of Affective Disorders 205 (2016) 1–12

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Prevention of Relapse Studies

- Escitalopram 10-20 (24 weeks)
  - risk of relapse was 4.4 times higher for the placebo group
- Citalopram X 48 weeks -positive
- A systematic reviews/meta-analysis
  - ongoing treatment with antidepressants is efficacious in preventing relapse as compared to placebo
  - maintenance treatment with SSRIs was better than placebo in preventing relapse with NNT = 5

Gorwood et al., Am J Geriatr Psychiatry 2007; 15:581–593
Klysner et al., JOURNAL OF PSYCHIATRY (2002), 181, 29-35
Kok et al., Am J Geriatr Psychiatry 19:3, March 2011
Tham et al., Journal of Affective Disorders 205 (2016) 1–12

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Recommendations

- 1st line
  - Duloxetine or sertraline
  - May consider escitalopram but be wary of the Qtc

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How Long to Stay on Antidepressant?

- Minimum of 1 year, even in the case of a single episode (Diniz 2014).
- A Cochrane review in 2016
  - quality of evidence was low with only 3 RCTs
  - NNT = 5
  - The authors suggest that "Continuing antidepressant medication for 12 months appears to be helpful with no increased harms.." Recurrent geriatric depression
- 3 years and for up to 2 years in older patients with a single episode (Rajji 2008).

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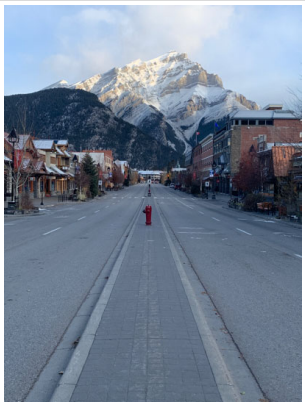

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MDE with Psychotic Features

- ECT first-line
- STOP-PD study
  - higher remission rates after 12 weeks of treatment with olanzapine combined with sertraline as compared to olanzapine with placebo

Meyers et al., Arch Gen Psychiatry. 2009; 66(8):838– 847. [PubMed: 19652123]

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MDE with Anxious Distress

- Poor response to treatment
- Longer time to response
- Early withdrawal from medications
- More severe presentation of depression
- Poorer social functioning
- Higher suicidal ideation and somatic symptoms
- Shorter time to relapse if residual anxiety present

Flint at el., Am J Geriatr Psychiatry 1997; .5:107-115
Lenze et al., BRITISH JOURNAL OF PSYCHIATRY (2007), 190, 344^349. doi: 10.1192/bjp.bp.106.027169

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Approach: Anxious Distress

- Rule out medical conditions
  - mitral valve prolapse, arrhythmias, chronic obstructive pulmonary disease, coronary insufficiency , substance withdrawal, hypoglycemia, various malignancies and autoimmune conditions, Parkinson's disease, dementia, multiple sclerosis, and metabolic and gastrointestinal disorder

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"aim high (dosage) and treat long".
(Lenze and Mulsant, 2001)

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MDE with Anxious Distress

- Post-hoc analysis of an RCT involving patients ≥65
  - duloxetine 60 mg over 8 weeks produced significant reductions ins anxiety compared to the placebo group (Russell 2007)
- Kitchen sink

Russell et al., Psychiatry. 2007; 4(6):33–45

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Treatment Resistance

- Only 50% of elderly patients respond to first-line treatment and less than 40% reach remission

Bennabi et al., J Affect Disord 171:137–141

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Approach

- Assess medication adherence
- ?alcohol, substances, and medications
- The diagnosis should be reviewed
- Drug-drug interactions
- Medical conditions should be reviewed, hyponatremia.

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Mulsant et al., 2014

	Majority consensus and minority alternative
Step 1	Escitalopram;[1,3] SSRI Alternatives: sertraline, duloxetine
Step 2 for minimal or non-response	Switch to duloxetine;[1] SSRI Alternatives: venlafaxine, desvenlafaxine
Step 3 for minimal or non-response	Switch to nortriptyline Alternative: bupropion
Step 2-3 for partial response	Augment antidepressant with lithium or an atypical antipsychotic. Alternatives: combine SSRI or SNRI with mirtazapine or bupropion
Duration of each step	6 weeks;[1,3] SSRI Alternatives: 4 weeks; 8 weeks

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Non-Major Depression

- "Minor" Depression, subsyndromal, subthreshold
- Dysthymia
- Depressive Episode with Insufficient Symptoms
  - depressed affect and 1 other symptom along with impairment/ distress for at least 2 weeks
- Common

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- **The only placebo controlled RCT with fluoxetine compared to placebo was negative (Devanand et al., 2005).**
- **Recommendation?????**

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Depression in Dementia

Trial	Medication	Scale	Outcome
Riefler 1989	imipramine	HAM-D	+
Nyth 1992	citalopram	HAM-D	+
Petracca 1996	clomipramine	HAM-D	+
Roth 1996	moclobemide	HAM-D	+
Magai 2000	sertraline	CSDD	-
Petracca 2001	fluoxetine	HAM-D	-
DIADS 2003	sertraline	HAM-D, CSDD	+
De Vasconcelos Cunha 2007	Venlafaxine IR	MADRS	-
DIADS -2 and 24 extension 2010	sertraline	mADCS-CGIC, CSDD	-
HTA-SADD 2011, 2013	Sertraline/mirtazapine	CSDD	-
An 2017	escitalopram	CSDD	-

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Other Treatments

- Electroconvulsive Therapy
- Transcranial Magnetic Stimulation
  - NNT= 4 (40%rTMS vs 14.% sham remission)
  - Kaster et al., Neuropsychopharmacology (2018) 43:2231–2238;
- Psychotherapy
  - Cognitive behavioural therapy
  - Problem solving therapy
  - ?interpersonal psychotherapy
  - ?group, dynamic, family therapy, other….?
- Exercise

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Exercise Meta-Analyses

- Guidelines from the National Institute for Health and Clinical Excellence for exercise as a management strategy for depression
- Structured, supervised exercise programs, three times a week (45–60 min) over 10–14 weeks, at low-intensity for mild to moderate depression

Catalan-Matamoros, Psychiatry Research. 244:202-9, 2016 10 30
Rhyner et al., Journal of Aging & Physical Activity. 24(2):234-46, 2016 Apr

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Case JH

- 79 y.o married man with 2 children, retired teacher
- Depression after retirement
- History of 2 MDEs in 1960s and 1970s with admission and ECT, no suicide attempts
- Hx of alcohol use disorder, now drinks 2 beers/day
- Hx of benzodiazepine dependence
- Hearing impairment, sciatica

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Meds - JH

Sertraline 200 mg p.o. daily.
Methotrimeprazine 7.5 mg at night.
Oxazepam 15 mg at night.
Clonazepam 0.25 mg daily.
Atorvastatin 40 mg daily.
Docusate Sodium.
ASA 81 mg.
Pregabalin 25 mg h.s.
Tolterodine 4 mg daily.

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- Family Hx of depression (parent)
- Grew up very poor, little money, squalor and infestation, put down by father
- Low self-esteem
- Great relationship with wife, children, family
- MOCA 26/30
- GDS 9/15

- Oh yes…and he owns a rifle (heirloom)

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	Biological	Psychological	Social
predisposing			
precipitating			
perpetuating			
protective			

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	Biological	Psychological	Social
predisposing	Family history of depression Past depression	Low self-esteem	Poverty Verbal abuse
precipitating	Pain Hearing impairment Alcohol use?	Low self-esteem	retirement
perpetuating	Alcohol use benzodiazepines	Low-self esteem	No meaningful activities No friends
protective	No major medical illnesses	Good insight, help seeking	Supportive family

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Canadian Coalition for Seniors Mental Health Guideline Update

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Discussion

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