Chapter 7: Assessment and Management of Depression in Old Age

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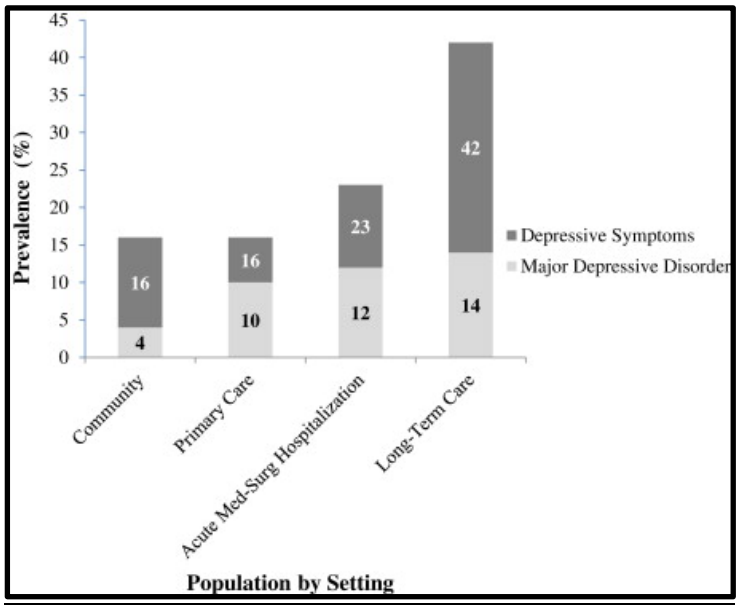
Introduction

1. Depression occurs commonly in persons as they age:

- Approximately 14% of persons older than 55 develop some symptoms, with 2% developing major depression; while in persons older than 75 years of age, major depression occurs in about 7% (Kok & Reynolds, 2017) (Luppa et al., 2012)
- The diagnosis of depression in older persons is made more commonly in women (about 30-50% higher rates).
- Most studies report depression being more common in care settings, increasing from old age homes through to acute care and hospital settings. See Figure 1 below.
- Depression is more common in persons with physical conditions and morbidity, and it is also more common in persons with cognitive impairment.

Figure 1: Prevalence of MDD and Depression Symptoms by setting



2. Course and trajectory

- Depression in older persons may follow several trajectories including: a no/low grade symptom group; an emergent depression group; a relapsing/remitting group; and a persistent/severe group
- These trajectories are predicted by co-morbidity burden, social isolation, inactivity, living arrangement and the presence/absence of neurologic disease.

3. A model of late-life depression (adapted from (Alexopoulos, 2019)

- The depressive syndrome is comprised of cognitive components (negative thoughts including suicidality), impaired reward response (anhedonia), and impaired salience (inability to attribute positive elements to the environment and experience).
- The underlying neurobiology is related to the dysregulation of cortical and limbic (emotional) centres.
- These brain regions may be impacted on by structural changes (e.g., vascular), altered neurogenesis / accelerated apoptosis, and increased neuro-inflammatory states.
- Driving these processes are a complex array of GENETIC factors, PSYCHO-SOCIAL stress factors, and AGING factors (including degeneration / neuronal loss, and amyloid deposition).

<u>Pathophysiological considerations:</u>

- The above model of depression in older persons has led to the hypotheses of 4 main 2linic-pathological types:

(1) *A depression-dysexecutive syndrome:* this type is clinically correlated with features of frontal-subcortical cognitive impairment (e.g., cognitive inflexibility, impaired behavioural inhibition and novelty problem solving), and the depressive features of apathy and anhedonia. The underlying neurobiology includes dysfunction of the anterior cingulate and/or dorsolateral prefrontal cortex and connecting sub-cortical circuits. These findings have been demonstrated on structural imaging (and therefore there may be considerable overlap with the vascular depressive type- vascular lesions, loss of volume changes), white matter tractography, and functional imaging (hypometabolic neocortical structures, and hypermetabolic ventral limbic structures). This type is associated with poor response to anti-depressants.

(2) *A vascular depression type*: this type has been associated with the presence of vascular risk factors, demonstrated vascular brain pathology and the post-stroke depression syndrome. These factors are required to entertain the diagnosis. Clinical correlates include anhedonia and cognitive impairment- notably dysexecutive syndrome, hence considerable

overlap with the DED above. The onset or worsening of depression is related in time to the development of vascular risk factors and/or cerebrovascular disease. These patients may also respond poorly to anti-depressants.

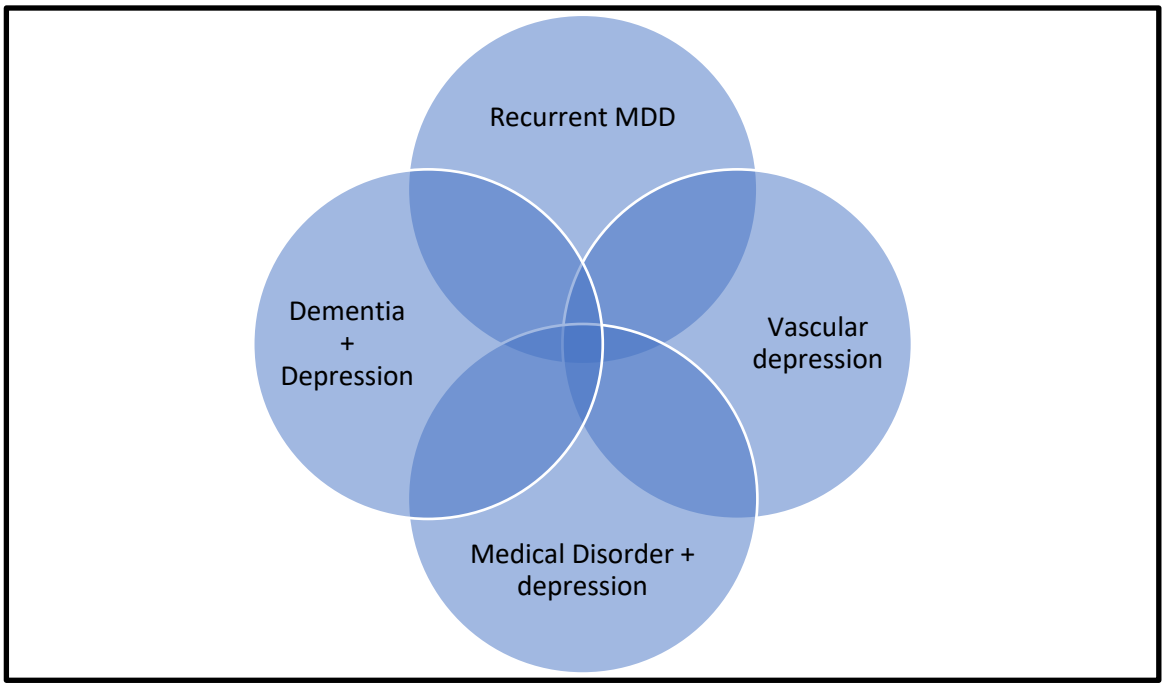
(3) *An inflammatory depressive type*: in ageing, enhanced CNS inflammation is seen with increases in cytokines (TNF-a, IL-6, and IL1b), and the consequent activation of microglia. These markers have been measured in the periphery and correlated with depressive features. Nuclear imaging studies may confirm microglial activation. The inflammatory cascade may also be activated by stress. Some antidepressants reduce the inflammatory markers but whether these antidepressants are more efficacious is not yet clear. Also, anti-inflammatory agents can reduce depressive symptoms in these patients but cannot be solely used to treat depression.

(4) The amyloid-Tau accumulation type: The development of depression in older persons may be accompanied by accumulation of amyloid-b. Similarly, patients with MCI and depression are more likely to develop Alzheimer's disease. The use of anti-depressants in these patients may result in lower amyloid, and the adequate treatment of depression in MCI may delay the onset of AD (Bartels et al., 2018; Cirrito et al., 2011). There remains no clarity though, on the relationship between Alzheimer's pathology and depression in older persons: for instance, in non-demented patients, with and without prior depression, there is no difference in the amyloid burden.

Clinical Types

- Patients in practice will not present with the above "models" or "types", so it can then be useful to consider the broad clinical history and presentation in the assessment. Again, significant overlap between these "clinical types" is common:

Figure 2. Conceptual Models of Clinical Types in Old Age Depression



- The clinical history will reveal whether there has been a history of previous MDE, psycho-social stress, medical co-morbidity and medication use
- The clinical assessment will reveal the presence of neurologic abnormalities (such as focal signs or extra-pyramidal features); cognitive impairment (and whether it is dysexecutive or not); and functional ability.
- In older persons, there can be considerable overlap between depressive symptoms and those of normal ageing: for instance sleep and appetite changes, fatigue and slowing, thoughts of death (may be appropriate). Depression may present with marked somatic complaints, including pain, disability, and general physical complaints.
- The use of scales or instruments which are sensitive to these differences may be useful- see for example the Geriatric Depression Scale (Yesavage et al., 1982). See Appendix 1. Others include the Cornell Scale for Depression.
- The DSM 5 and ICD11 remain the diagnostic systems commonly used to formally diagnose depression, but the above variability must be considered. Don't forget depressive syndromes other than MDD, including minor depression, bipolar depression, adjustment disorder, and depression secondary to another medical condition. Older persons who abuse alcohol and other CNS depressants may also develop depressive syndromes, but many will resolve or improve on cessation of the offending molecule.
- The medical work-up must include appropriate special investigations with regard to conditions that may occur more commonly in older persons, including vitamin deficiencies, thyroid disorders and neurologic conditions.

Table 1: Clinical Features of Types in Late Life Depression

	Depression + Dementia	Recurrent MDD	Vascular depression	Medical Disorder + Depression
History	History of MDD may predispose to dementia.	+ history MDE and/or family history	Vascular risk factors; onset > 50 years	Medical co-morbidities: IHD, Parkinson's, Cancer
Clinical		Lower co-morbidity burden	Post-troke (neurologic), apathy, anhedonia, psychomotor features	Recent and active history of medical conditions. Polypharmacy
Neurocognitive	Must rule out pseudo-dementia. (See Appendix 2). For dementia + depression: cognitive testing minimally impacted by mood	Lower rates of cognitive impairment. Mood features far outweigh cognitive picture	Dysexecutive picture / sub-cortical picture or in keeping with stroke	Varied picture, may be similar to dysexecutive syndrome
Imaging	Global atrophy, hippocampal atrophy, with/without evidence of PVWMD	Non-specific atrophy on structural imaging	See chapter on Alzheimer's and Vascular dementia for types- must have evidence for CVD	Non-specific
Treatment implications	For pseudo-dementia, cognition may improve but 40% dement by 2 years. For Dementia + depression, may respond and improved quality of life	Use previously successful treatments, consider longer treatment	Poor or delayed treatment response. May respond better to SNRI's rather than SSRI's. May benefit from problem-solving and / or case management approaches	Select agent with best safety and side-effect profile

Suicide in the Elderly

No discussion of late life depression without a mention of suicide.

- Suicide in elderly 2x general population.
- Rates of suicide in elderly individuals are raised almost exclusively in white men
- Among those who attempt suicide, elderly people are most likely to die.
- Depressive syndromes are present in 80% of people aged >74 years who commit suicide
- Disruption of social ties is associated with late-life suicide independently of depression, especially in individuals with a rigid, anxious, and obsessive personality.
- The availability of firearms doubles the risk of suicide in elderly people
- Suicidal ideation decreases with ageing, but if older people have suicidal thoughts they are at a higher risk of committing suicide than younger people…Suicidal ideation is closely associated with the severity of depression.

Table 2: Risk and Protective Factors for Suicide in the Elderly

Increased risk
Age ≥75 years
Male
White
Widowed or divorced
Living alone, isolated, or recently moved
Retired or unemployed
Poor physical health, terminal illness, multiple or debilitating illnesses, or pain
Depression, substance abuse or dependence, hopelessness
History of suicide, depression, or other mental illness in close family members
Compensatory or protective
Able to learn from experience and accept help; sense of meaning in life; sense of humor and capacity for loving; able to reminisce about positive life experiences
History of successful transitions and coping with life challenges
Caring and available family member or supportive community network; accessible and caring health care provider
Membership in a religious community, especially Catholic or Jewish
Source. Adapted from Holkup 2003.

(Holkup, 2003)

Treatment of Depression in Older Persons

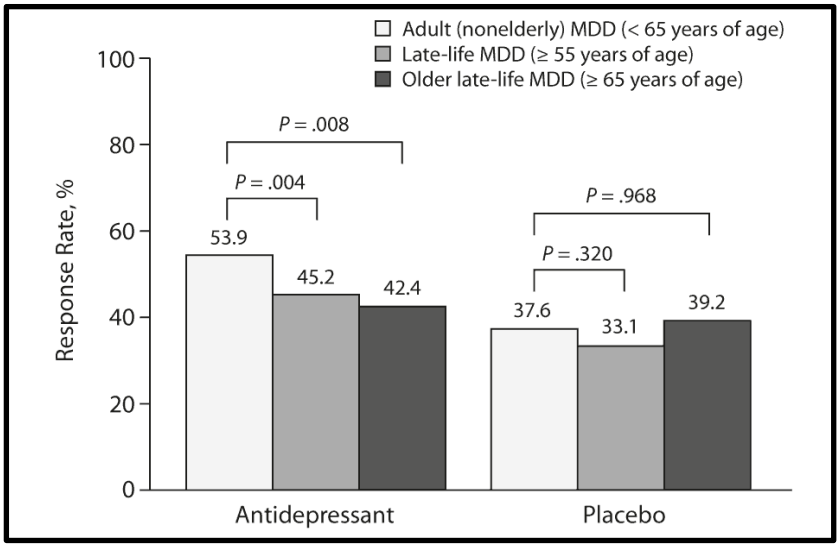
1. General considerations

- Older persons with depression often go untreated, under-treated, and then not for long enough. This may lead to excess morbidity and mortality. Treatment response rates might be slower than adults of younger age.
- Depression in an older person may: relapse more readily, be harder to treat, and exacerbate co-morbid medical conditions.
- Older adults with depression may not adhere to treatment due to cognitive effects or pill burden and need clarity on the treatment administration plan.
- Older persons with dementia may NOT respond to anti-depressant treatment (see (Nelson & Devanand, 2011))
- ECT is not contra-indicated and may be effective in 70% of cases, including in persons with dementia (Kerner & Prudic, 2014)
- Psycho-therapy in older persons with depression is effective, including problem-solving therapy, cognitive-behavioural therapy, and interpersonal therapy. In older, frail patients, these therapies have not been well tested. Case management and supported problem-solving may be useful in primary care.
- The management of offending medical conditions (where possible) and medications is key. Many medications aggravate depression.

2. Principles of anti-depressant treatment and selection

- Anti-depressants for older adults with depression are effective. Response rates decline with older age (see Figure 3 below). (Tedeschini et al., 2011)

Figure 3: Treatment Response in Older Adults vs Non-Elderly



- SSRIs are often proposed as first-line treatment. Doses used are the same as for younger adults but might need to be commenced more slowly. The risk of bleeding and hyponatraemia must be noted.
- SNRIs are also used, with due caution for side-effects.
- Other agents such as vortioxetine, mirtazapine, bupropion, and agomelatine are also used at similar doses.
- When inadequate treatment response is noted, augmentation with (i) lithium or aripiprazole has been proposed, (ii) the use of methylphenidate for apathy, and (iii) donepezil for cognitive impairment. Pramipexole has been used in patients with Parkinson's disease plus depression, and in those with a dysexecutive syndrome but RCTs are lacking (see for instance (Barone et al., 2010)
- In patients with vascular depression, there are studies supporting the addition of calcium-channel antagonists, such as nimodipine and verapamil; and also angiotensin receptor blockers. (see (Alexopoulos, 2019) for a description).

- Appendix 1:

The Geriatric Depression Scale (GDS)

Choose the best answer for how you felt this past week ***CIRCLE ONE***

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 hopeful about the future?	Yes	**No**
6. Are you bothered by thoughts you can't get out of your head?	**Yes**	No
7. Are you in good spirits most of the time?	Yes	**No**
8. Are you afraid that something bad is going to happen to you?	**Yes**	No
9. Do you feel happy most of the time?	Yes	**No**
10. Do you often feel helpless?	**Yes**	No
11. Do you often get restless and fidgety?	**Yes**	No
12. Do you prefer to stay at home, rather than going out and doing new things?	**Yes**	No
13. Do you frequently worry about the future?	**Yes**	No
14. Do you feel you have more problems with memory than most?	**Yes**	No
15. Do you think it is wonderful to be alive now?	Yes	**No**
16. Do you often feel downhearted and blue?	**Yes**	No
17. Do you feel pretty worthless the way you are now?	**Yes**	No
18. Do you worry a lot about the past?	**Yes**	No
19. Do you find life very exciting?	Yes	**No**
20. Is it hard for you to get started on new projects?	**Yes**	No
21. Do you feel full of energy?	Yes	**No**
22. Do you feel that your situation is hopeless?	**Yes**	No
23. Do you think that most people are better off than you are?	**Yes**	No
24. Do you frequently get upset over little things?	**Yes**	No
25. Do you frequently feel like crying?	**Yes**	No
26. Do you have trouble concentrating?	**Yes**	No
27. Do you enjoy getting up in the morning?	Yes	**No**
28. Do you prefer to avoid social gatherings?	**Yes**	No
29. Is it easy for you to make decisions?	Yes	**No**
30. Is your mind as clear as it used to be	Yes	**No**
Total **bold (depressed)** answers		
Total score (No. of depressed answers)		

Normative scores:
Normal 5 +/- 4 Mildly depressed 15 +/- 6 Very depressed 23 +/- 5

Original article
Yesavage JA, Brink TL, Rose TL, et al. Development and validation of a geriatric depression rating scale: a preliminary report. J Psych Res. 1983; 17:27.

Appendix 2:

Table 3–5. Differences between depression with cognitive impairment and dementia

Depression with cognitive impairment	Dementia
Clinical course and history	
Onset fairly well demarcated	Onset indistinct
History short	History quite long before consultation
Course rapidly progressive	Early deficits often go unnoticed
History of psychiatric difficulty or recent life crisis	History of psychiatric problem or emotional crisis uncommon
Clinical behavior	
Detailed complaints of cognitive loss	Few complaints of cognitive loss
Distress caused by cognitive problems	Varied reaction to cognitive loss
Behavior does not reflect cognitive loss	Behavior compatible with cognitive loss
Persistent mood disorder	Mood apathetic or environmentally responsive
Nocturnal exacerbation rare	Nocturnal exacerbation common
Mood-congruent delusions	Mood-incongruent delusions
Examination findings	
Patients expend little effort during examination	Patients commonly struggle to perform cognitive tasks
Patients frequently answer, "I don't know"	Patients usually make an effort to answer questions
Memory loss is inconsistent for recent and remote events	Memory impairments are greater for recent than for remote events
Patients may have specific memory gaps	Patients do not have specific memory gaps
Inconsistent performance across similar types of tasks	Consistently impaired performance on tasks of a particular ability
Prompting and semantic organization are helpful in improving recall	Prompting and semantic organization have limited benefit
Recognition memory is relatively intact	Recognition memory is impaired; there may be false-positive errors

Source. Adapted from Strub and Black 1988; Kaszniak and Christenson 1994.

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