Management and Treatment of Dementia

Charles T Nevels, MD

Incidence of Neurocognitive disorders

- 1 in 9 individuals over 65 years of age have dementia
- 1 person develops dementia every 67 seconds in the United States
- Incidence of dementia almost doubles with every 5 year increase in age of a cohort.
- Per 2019 CDC/CMS data 58.9% of all (long term) SNF patients have dementia
- More recent data shows the percentage increasing to near 60%.
- 2019 CDC/CMS data shows 53% of all SNF patients have depression
- Researchers examined data on more than 3.7 million admissions to 15,600 facilities nationwide from 2012 to 2014. Even after excluding dementia and Alzheimer's disease, which are a common causes of nursing home admissions, people with behavioral health issues account for about half of all residents, researchers note in the *American Journal of Geriatric Psychiatry, 2018*. With behavioral health problems, patients were also more likely to be sent to one-star homes, the lowest quality facilities, the study also found.

Prevalence of Alzheimer's Dementia in USA

- Ages 40-65 1 in 1000
- Ages 65-74 3%
- Ages 75-84 17%
- Age 85+ 32%

Prevalence of Dementia, NOS Ages 71 Y/O and up approx. 14%

With similar increase with age…

Risk Factors for Dementia

- Gender: male
- Age: 60-70 years
- Prior stroke
- Hardening of the arteries
- Heart disease
- High blood pressure
- Diabetes
- Cholesterol problems
- Atrial fibrillation
- Smoking
- Education
- Race
- Family history

FIG. 4. In the laboratory of the neurology clinic, Munich: *1*, F. Lotmar; *2*, Frau Grombach; *3*, St. Rosenthal; *4*, Ugo Cerletti; *5*, Allers(?); *6*, F. Bonfiglio; *7*, A. Alzheimer; *8*, N. Achucarro; *9*, G. Perusini; *10*, F. H. Lewy.

A picture of Alois Alzheimer and his co-workers in which Friedrich Lewy is standing to the very right side of the picture

In 1906, the German psychiatrist and neurologist Dr Alois **Alzheimer first** identified the illness that would become known as **Alzheimer's disease**. His discovery was based on the case of a 51-year-old woman, Auguste Deter, who had suddenly begun to exhibit irrational behaviour and memory loss.

Etiologic Diagnosis of Progressive Dementias in Adults

- **Neurodegenerative Diseases**
  - Alzheimer's disease
  - Parkinson's disease
  - Diffuse Lewy body disease
  - Progressive supranuclear palsy
  - Multisystem atrophy
  - Huntington's disease
  - Frontotemporal dementias – e.g. Pick's disease

Etiology *contd.*

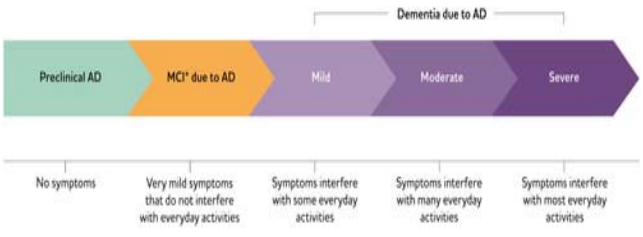
- **Structural Disease or Trauma**
  - Normal pressure hydrocephalus
  - Neoplasms
  - Dementia pugilistica
- **Vascular Disease**
  - Vascular dementia
  - Vasculitis
- **Heredometabolic Disease**
  - Wilson's disease
  - Other late-onset lysosomal storage diseases

Etiology *contd.*

- **Demyelinating or Dysmyelinating Disease**
  - Multiple sclerosis
- **Infectious Disease**
  - Human immunodeficiency virus, type 1
  - Tertiary syphilis
  - Creutzfeldt-Jakob disease
  - Progressive multifocal leukoencephalopathy
  - Whipple's disease
  - Chronic meningitis – e.g. Cryptococcal

Memory in typical aging

- Myth: "Forgetfulness" is an inevitable consequence of aging.
- Typical aging per se does not degrade memory - - - disease does.
- Everyday forgetfulness occurs in most
  - Easy to overlook genuine memory lapses in dementia
  - Misleads people with normal brain function who fear development of AD



Alzheimer's disease (AD) continuum. *MCI is the acronym for mild cognitive impairment.

Signs and Symptoms of AD

Mild AD	Moderate AD	Severe AD
• Forgetfulness	• Disorientation	• Agnosia } More pronounced
• Word finding difficulty	• ↑ memory loss	• Apraxia } More pronounced
• Apathy	• Confusion	• Aggression
• Poor attention	• Insomnia	• Agitation
• Difficulty with complex tasks	• Wandering	• Incontinence
• Depression	• Speech difficulty	• Poor basic ADLs
• Work trouble	• Restlessness	• Gait disturbance
	• Difficulty with IADLs	

IADLs=instrumental activities of daily living
ADLs=activities of daily living

Diagnostic Criteria for Dementia

- Presence of at least 2 of the following impairments.
  - Impaired learning and impaired retention of new or recently acquired information **(short-term memory)**
  - Impaired handling of complex tasks
  - Impaired reasoning ability **(Abstract thinking)**
  - Impaired spatial ability and orientation **(constructional difficulty and agnosia)**
- The impairments interfere with work or usual social activities or relationships with others
- The impairments represent a notable decline from a previous level of functioning
- The impairments do not occur exclusively during the course of delirium
- The impairments are not better explained by a major psychiatric diagnosis

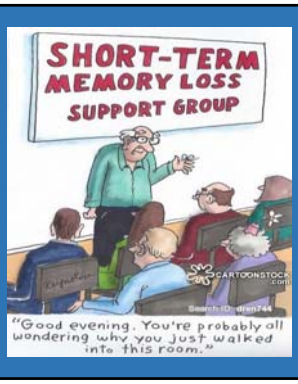


Table 1. Identifying Cognitive Behavioral Syndromes for the Differential Diagnosis of AD

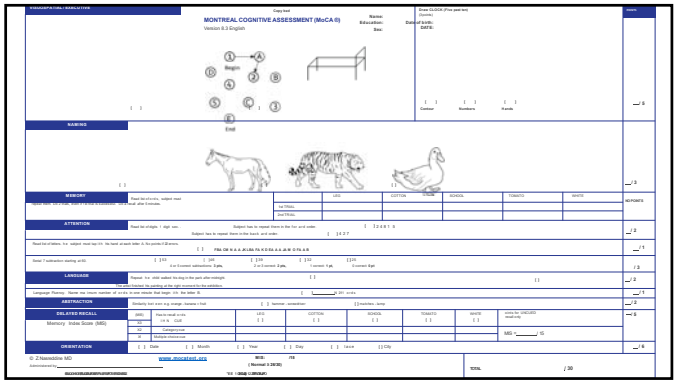
Syndrome	Cogni◆ve-Behavioral Major Characteris◆cs	Differen◆al Diagnosis of Neuropathological Cause(s)
Progressive amnes◆c syndrome (single- or mul◆-domain)	Difficulty learning and remembering new information; often accompanied by executive dysfunction, depression, or anxiety	Usually due to AD or AD with co-pathologies (eg, AD+VBI, AD+LBD, AD+VBI+LBD); sometimes hippocampal sclerosis
Progressive aphasic syndrome/primary progressive aphasia	Speech and language impairments, eg, word-finding difficulty (anomia), speech sound errors, impaired repetition (often due to impaired auditory-verbal working memory), alexia, agraphia	Logopenic variant PPA and related forms of multi-domain aphasic dementias are often due to AD; semantic dementia variant PPA (mostly TDP-43) and progressive non-fluent variant PPA (mostly TDP-tau) are usually due to FTLD-related pathologies but can be due to AD
Progressive visuospa◆al dysfunc◆on/posterior cor◆cal atrophy	Difficulty with visual/spatial perception/cognition, often with limb apraxia, alexia, agraphia, acalculia, and related cognitive dysfunction localizable to posterior cortical regions	Usually due to AD; sometimes due to DLB or AD+DLB; occasionally due to CBD; very rarely due to FTLD or CJD
Progressive behavioral/frontal/dysexecu◆ve syndrome	Changes in comportment, personality, and social/interpersonal/emotional behavior; often includes early difficulty with executive function (judgment, problem solving, reasoning) and attention	Usually due to FTLD-related pathology (FTLD-tau or FTLD-TDP-43); not uncommonly a presentation of young-onset AD, or due to VBI, mixed AD+VBI; sometimes due to DLB, PSP, CBD
Primary Parkinsonian syndrome with cogni◆ve features/primary somatosensorimotor cor◆cobasal syndrome	Elements of Parkinsonism (asymmetric rigidity, motor dysfunction), REM sleep behavioral disorder, autonomic and/or cortical sensorimotor dysfunction (eg, limb apraxia in CBS), progressive cognitive difficulties (eg, fluctuating attention, executive/visuospatial functions)	LBD (manifest as DLB or PDD) or mixed LBD with AD and/or VBI; sometimes PSP, FTLD, CBD, MSA; rarely AD (sometimes AD in CBS)

Based on Ari 2019.x
Abbreviations: AD = Alzheimer's disease; CBD = corticobasal degeneration; CBS = corticobasal syndrome; CJD = Creutzfeldt-Jakob disease; DLB = dementia with Lewy bodies; FTLD = frontotemporal lobar degeneration; HS = hippocampal sclerosis; LBD = Lewy body disease; MSA = multiple systems atrophy; PDD = Parkinson disease dementia; PPA = primary progressive aphasia; PSP = progressive supranuclear palsy; TDP = TAR DNA-binding protein; VBI = vascular brain injury.

Table 2. Comparative Summary of Selected Validated and Standardized Brief Cognitive Assessment Tools to Detect Cognitive Impairment and Dementia (CID)

Name	MoCA[16]	MMSE[17]	Mini-Cog[18,19]	SLUMS[20]	GPCOG[21]
Time to administer (minutes)	10–15	7–10	2–4	7	2–5 patient 1–3 informant
Cut-off for CID	< 26/30	< 26/30	≤ 3/5	< 27/30	< 5 patient ≤ 3 informant[ ]
Sensitivity for cognitive impairment	90%	81%	76%	96%	85%
Specificity for cognitive impairment	87%	82%	89%	61%	86%
Cognitive domains[22] assessed					
Complex attention	✓	✓		✓	
Executive function	✓		✓	✓	✓
Learning and memory	✓	✓	✓	✓	✓
Language	✓	✓		✓	
Visuoconstruction	✓	✓	✓	✓	✓
Orientation	✓	✓		✓	✓
Available in multiple languages	Yes	No	Yes	No	Yes
Considerations	• Mixed findings in patients with low education	• Well-known among clinicians • Purchase required • Limited evidence for sensitivity to detect mild changes	• Simple scoring algorithm • Limited evidence for sensitivity to detect mild changes	• Evidence for sensitivity to detect mild changes • Largely studied in veteran populations	• Validated in primary care settings • Limited evidence for sensitivity to detect mild changes

Abbreviations: GPCOG = General Practitioner Assessment of Cognition, MMSE = Mini-Mental State Examination, MoCA = Montreal Cognitive Assessment, SLUMS = St. Louis University Mental Status examination



Mini-Mental State Examination (MMSE)

- Cognitive measurement
- Brief, structured mental status examination
- 10-15 minutes to administer
- Adjustments need to be made for age, gender, education, and culture
- Copyright issues

Scores Range From 0-30

28-30=Normal
25-27=Mild cognitive impairment
19-24=Mild dementia
10-18=Moderate dementia
0-9=Severe dementia

Typical deterioration of 3-4 points per year

Folstein MF, et al. *J Psychiatr Res.* 1975;12(3):189-198.

Mini-Mental State Examination (MMSE)

Patient's Name _____ Date _____

Instructions: Score one point for each correct response within each question or activity.

Maximum Score	Patient's Score	Questions
5		"What is the (year) (season) (date) (day) (month)?"
5		"Where are we now? (state) (county) (township) (hospital) (floor)?"
3		The examiner names three unrelated objects clearly and slowly, then the instructor asks the patient to name all three of them. The patient's response is used for scoring. The examiner repeats them until patient learns all of them, if possible.
5		"I would like you to count backward from 100 by sevens." (93, 86, 79, 72, 65, ...) Alternative: "Spell WORLD backwards." (D-L-R-O-W)
3		"Earlier I told you the names of three things. Can you tell me what those were?"
2		Show the patient two simple objects, such as a wristwatch and a pencil, and ask the patient to name them.
1		"Repeat the phrase: 'No ifs, ands, or buts.'"
3		"Take the paper in your right hand, fold it in half, and put it on the floor." (The examiner gives the patient a piece of blank paper.)
1		"Please read this and do what it says." (Written instruction is "Close your eyes.")
1		"Make up and write a sentence about anything." (This sentence must contain a noun and a verb.)
1		"Please copy this picture." (The examiner gives the patient a blank piece of paper and asks him/her to draw the symbol below. All 10 angles must be present and two must intersect.)
30		TOTAL

Interpretation of the MMSE:

Method	Score	Interpretation
Single Cutoff	<24	Abnormal
Range	<21	Increased odds of dementia
	>25	Decreased odds of dementia
Education	21	Abnormal for 8th grade education
	<23	Abnormal for high school education
	<24	Abnormal for college education
Severity	24-30	No cognitive impairment
	18-23	Mild cognitive impairment
	0-17	Severe cognitive impairment

Interpretation of MMSE Scores:

Score	Degree of Impairment	Formal Psychometric Assessment	Day-to-Day Functioning
26-30	Questionably significant	If clinical signs of cognitive impairment are present, formal assessment of cognition may be valuable.	May have clinically significant but mild deficits likely to affect only most demanding activities of daily living.
20-25	Mild	Formal assessment may be helpful to better determine pattern and extent of deficits.	Significant effect. May require some supervision, support and assistance.
10-20	Moderate	Formal assessment may be helpful if there are specific clinical indications.	Clear impairment. May require 24-hour supervision.
0-10	Severe	Patient not likely to be testable.	Marked impairment. Likely to require 24-hour supervision and assistance with ADL.

Source:

- Folstein MF, Folstein SE, McHugh PR: "Mini-mental state: A practical method for grading the cognitive" state of patients for the clinician." *J Psychiatr Res* 1975;12:189-198.

VAMC

SLUMS ExaMination

Name _____ Age _____

Is the patient Alert? Level of education _____

1. What day of the week is it?
2. What is the year?
3. What state are we in?

4. Please remember these five objects; I will ask you what they are later.
Apple Pen Tie House Car

5. You have $100 and you go to the store and buy a dozen apples for $3 and a tricycle for $20.
How much did you spend?
How much do you have left?

6. Please name as many animals as you can in one minute.
0-4 animals 5-9 animals 10-14 animals 15+ animals

7. What were the five objects I asked you to remember? 1 point for each one correct.

8. I am going to give you a series of numbers and I would like you to give them to me backwards. For example, if I say 42, you would say 24.
37 548 2657

9. This is a clock face. Please put in the hour markers and the time at ten minutes to eleven o'clock.
Hour markers okay
Time correct

10. Please place an X in the triangle.

Which of the above figures is largest?

11. I am going to tell you a story. Please listen carefully because afterwards, I'm going to ask you some questions about it.

Jill was a very successful stockbroker. She made a lot of money on the stock market. She then met Jack, a devastatingly handsome man. She married him and had three children. They lived in Chicago. She then stopped work and stayed at home to bring up her children. When they were teenagers, she went back to work. She and Jack lived happily ever after.

What was the female's name?
When did she go back to work?
What work did she do?
What state did she live in?

TOTAL SCORE

SCORING

Raw Score Education	Adjust	Education Adjusted Score
27-30	+0	27-30
25-26	+1 if ≤ 12 years	26-27
1-24	+2 if ≤ 8 years	1-25

CLINICIAN'S SIGNATURE DATE TIME

MR Tariq S. Tumosa, JT Chibnall, RM Perry III, and JE Morley. The Saint Louis University Mental Status (SLUMS) Examination for detecting mild cognitive impairment and dementia is more sensitive than the Mini-Mental Status Examination (MMSE) - A pilot study. *Am J Geriatr Psych* 14:900-10, 2006.

Alabama Brief Cognitive screener (ABCs)		Instructions and scoring	Record specific answer (optional)	Scoring (1 if correct, 0 if incorrect)
e.g.	What is your full name?			
1	First and Last name	Score correct only when given name and surname are included and match the medical record. Examiner MAY prompt if only one name is provided initially.		
2	What year were you born?	Only correct year is needed		
3	Who is the current president of the United States?	Only surname is required		
	Repeat these words:			
4	Igor	Score only the number repeated on the 1st attempt. MAY give 2 attempts.		
5	Hope			
6	Bella			
	Draw the face of a clock, put the numbers on it, and show the hands as it was 11:10			
7	Circle	Examiner MAY clarify the time (Ten past eleven, ten after eleven) and MAY remind subject of the task they (e.g., now put the numbers on...)		
8	Numbers			
9	Hands			
	Tell me the three words I asked you to repeat a little while ago.			
10	Igor	NO hints or cues are permitted		
11	Hope			
12	Bella			
	Count backwards from 40 by 4's			
13	36	*Examiner MAY clarify instructions as needed for the subject to understand.		
14	32			
15	28	*Once subject has started, do NOT prompt or remind subject of intermediate subtractions.		
16	24			
17	20	*Score each subtraction independently, e.g., 36 32 28 24 21, would score 4 points.		
	Tell me:			
18	Today's date	Replies must be exactly correct		
19	The day of week			
20	The month	No NOT give credit for +/- 1		
21	The year			
22	What this building is called	Either "UAB" or the specific building name IS acceptable		
23	What city we are in			
24	What state we are in			

Patient name: Gen Practioner COG

Testing date: _____

STEP 1 – PATIENT EXAMINATION

Unless specified, each question should only be asked once.

Name and address for subsequent recall test

I am going to give you a name and address. After I have said it, I want you to repeat it. Remember this name and address because I am going to ask you to tell it to me again in a few minutes: John Brown, 42 West Street, Kensington. (Allow a maximum of 4 attempts.)

Time orientation	Correct	Incorrect
1. *What is the date?* (exact only)	☐	☐
Clock drawing (use blank page)		
2. *Please mark in all the numbers to indicate the hours of a clock.* (correct spacing required)	☐	☐
3. *Please mark in hands to show 10 minutes past eleven o'clock.* (11:10)	☐	☐
Information		
4. *Can you tell me something that happened in the news recently?* (Recently = in the last week. If a general answer is given, e.g. "war", "lot of rain", ask for details. Only specific answer scores.)	☐	☐
Recall		
5. *What was the name and address I asked you to remember?* John Brown 42 West (St) Kensington		☐ ☐ ☐ ☐ ☐

Add the number of items answered correctly: **Total score:** ☐ **out of 9**

9	**No significant cognitive impairment** Further testing is not necessary
5 – 8	**More information required** Proceed with informant interview in step 2 on next page
0 – 4	**Cognitive impairment is indicated** Conduct standard investigations

Patient name: _____

Testing date: _____

STEP 2: INFORMANT INTERVIEW

Informant name: _____

Relationship to patient, i.e. informant is the patient's: _____

Ask the informant:

Compared to 5–10 years ago,

	YES	NO	Don't know	N/A
1. *Does the patient have more trouble remembering things that have happened recently than s/he used to?*	☐	☐	☐	
2. *Does s/he have more trouble recalling conversations a few days later?*	☐	☐	☐	
3. *When speaking, does s/he have more difficulty in finding the right word or tend to use the wrong words more often?*	☐	☐	☐	
4. *Is s/he less able to manage money and financial affairs (e.g. paying bills and budgeting)?*	☐	☐	☐	☐
5. *Is s/he less able to manage his or her medication independently?*	☐	☐	☐	☐
6. *Does s/he need more assistance with transport (either private or public)? (If the patient has difficulties only due to physical problems, e.g. bad leg, tick 'no')*	☐	☐	☐	☐

Add the number of items answered with 'NO', 'Don't know' or 'N/A': **Total score:** ☐ **out of 6**

4 – 6 **No significant cognitive impairment**
Further testing is not necessary

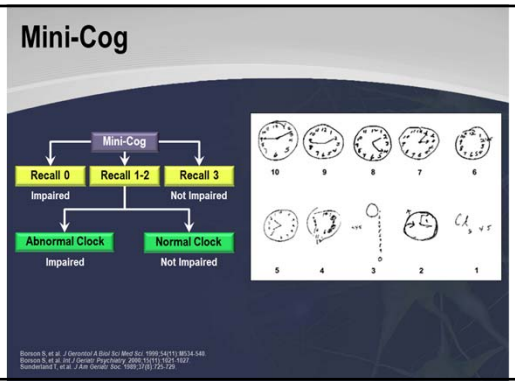
0 – 3 **Cognitive impairment is indicated**
Conduct standard investigations

When referring to a specialist, mention the individual scores for the two GPCOG test steps:

STEP 1 **Patient examination:** ___/ 9

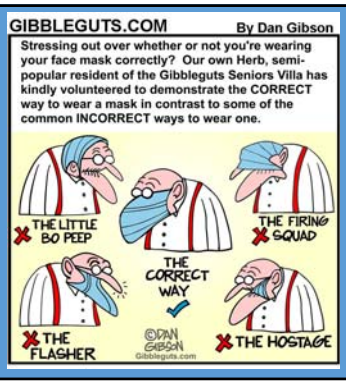
STEP 2 **Informant interview:** ___/ 6 or **N/A**

Mini-Cog



Borson S, et al. *J Gerontol A Biol Sci Med Sci.* 1999;54(11):M534-540.
Borson S, et al. *Int J Geriatr Psychiatry.* 2000;15(11):1021-1027.
Sunderland T, et al. *J Am Geriatr Soc.* 1989;37(8):725-729.

Prevalence of Neuropsychiatric Disturbances in Dementia



BPSD

- Behavioral and psychological symptoms of dementia (BPSD), also known as neuropsychiatric symptoms, represent a heterogeneous group of non-cognitive symptoms and behaviors occurring in subjects with dementia. BPSD constitute a major component of the dementia syndrome irrespective of its subtype. They are as clinically relevant as cognitive symptoms as they strongly correlate with the degree of functional and cognitive impairment. BPSD include agitation, aberrant motor behavior, anxiety, elation, irritability, depression, apathy, disinhibition, delusions, hallucinations, and sleep or appetite changes. It is estimated that BPSD affect up to 90% of all dementia subjects over the course of their illness, and is independently associated with poor outcomes, including distress among patients and caregivers, long-term hospitalization, misuse of medication, and increased health care costs. Although these symptoms can be present individually it is more common that various psychopathological features co-occur simultaneously in the same patient. Thus, categorization of BPSD in clusters taking into account their natural course, prognosis, and treatment response may be useful in the clinical practice.

What are "Behaviors?"

- Apathy, depression, anxiety and agitation were found to be the most frequent forms of BPSD.
- Delusions (distressing beliefs) Hallucination
- Agitation: – Easily upset – Repeating questions – Arguing/complaining- Pacing
- Hoarding
- Refusing care: -eating – bathing – meds- ADLs
- Inappropriate screaming, crying out, disruptive sounds
- Leaving home, attempting to leave/exit seeking
- Depression or dysphoria Anxiety: – Worrying – Shadowing (following care giver)
- Apathy or indifference Disinhibition: – Socially inappropriate behavior – Sexually inappropriate behavior
- Irritability or lability Motor disturbance (repetitive activities without purpose): – Wandering – Rummaging Night-time behaviors (waking and getting up at night)

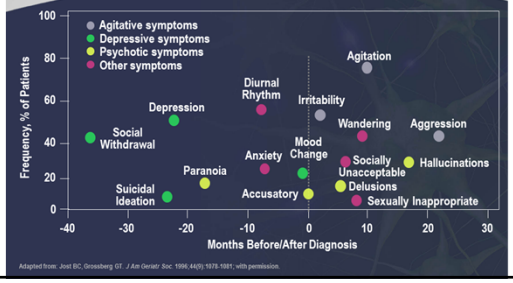
Neuropsychiatric Symptoms in Dementias

NPI Item	AD	PDD	DLB	VaD	FTD
Delusions	●	●	●●	●	—
Hallucinations	—	●●●	●●	●	—
Agitation	●●	●●	●●●	●●●	●●●
Depression	●●	●●●	●●●	●●	●●●
Anxiety	●●	●●●	●●●	●●	●
Apathy	●●●	●●●	●●●●	●●●	●●●●
Disinhibition	—	—	●	●	●●●●
Irritability	●●	●	●●●	●●	●●●
Sleep	●	●	●●●	●●	●●

— 0-14% ● 15-29% ●● 30-44% ●●● 45-59% ●●●● ≥60%

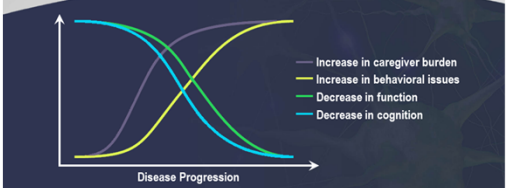
NPI=Neuropsychiatric Inventory. PDD=Parkinson's disease dementia. DLB=dementia with Lewy bodies. VaD=vascular dementia. FTD=frontotemporal dementia.
1. Ikenanarong V, et al. *Dement Geriatr Cogn Disord* 2004;17(1-2):14-20. 2. Aarsland D, et al. *J Neurol Neurosurg Psychiatry* 2007;78(1):36-42. 3. Tekin S, et al. *Ann Neurol* 2001;49(3):355-361. 4. Aarsland D, et al. *Int J Geriatr Psychiatry* 2001;16(2):184-191. 5. Kao AW, et al. *Alzheimer Dis Assoc Disord* 2009;23(4):360-370. 6. Craig D, et al. *Am J Geriatr Psychiatry* 2005;13(6):460-468. 7. Lyketsos CG, et al. *Am J Psychiatry* 2000;157(5):708-714. 8. Banks SJ, Weintraub S. *J Geriatr Psychiatry Neurol* 2008;21(2):133-141. 9. Caputo M, et al. *Acta Psychiatr Scand* 2008;117(6):455-464. 10. Aalten P, et al. *Dement Geriatr Cogn Disord* 2007;24(6):457-463. 11. Borroni B, et al. *Arch Gerontol Geriatr* 2008;46(1):101-106. 12. Fuh JL, et al. *J Neurol Neurosurg Psychiatry* 2005;76(10):1337-1341. 13. Sinkkanh S, et al. *J Neurol Sci* 2005;229(1-2):43-48. 14. Lyketsos CG, et al. *JAMA* 2002;288(12):1475-1483. 15. Liu W, et al. *Neurology* 2004;62(5):742-748.

Timeline and Epidemiology of Psychiatric Symptoms in AD



Adapted from: Jost BC, Grossberg GT. *J Am Geriatr Soc* 1996;44(9):1078-1081; with permission.

Dementia: Behavioral Symptoms Worsen as Cognition Declines[1]



Dementia patients who display marked behavioral disturbances in a given time frame are more likely to display them again in the future.[1]

1. Rabins PV, et al. *Am J Psychiatry* 2007;164(12 Suppl):5-56. 2. Holtzer R, et al. *J Am Geriatr Soc* 2003;51(7):953-960. 3. Aarsland D, et al. *Int J Geriatr Psychiatry* 2001;16(2):184-191. 4. Clarke DE, et al. *J Neuropsychiatry Clin Neurosci* 2008;20(3):337-347. 5. Dujardin K, et al. *Mov Disord* 2009;24(16):2391-2397. 6. Wilson RS, et al. *Am J Geriatr Psychiatry* 2005;13(11):984-990. 7. Scarmeas N, et al. *Arch Neurol* 2005;62(10):1601-1608.

Symptom Clusters

- Apathy, depression, anxiety and agitation were found to be the most frequent forms of BPSD.
- BPSD tends to cluster together, usually into four clusters – that is, the affective, psychotic, hyperactive and apathetic clusters.
- Pre-existing personality and psychiatric illnesses Clinical experience suggests that longstanding personality patterns and characteristics may affect the development of behavioral and psychological symptoms of dementia—the loss of inhibitory control may accentuate premorbid personality traits. Lifelong psychiatric disorders (such as major depression, anxiety, bipolar disorder, and schizophrenia) and their management (for example, treatment with antidepressants, anxiolytics, mood stabilizers, and antipsychotics) may also affect the development of these symptoms.

Pharmacological Management

(To give nonpharmacological treatment a better chance of success)

1) Cholinesterase inhibitors (donepezil, rivastigmine, and galantamine) are effective for cognition in mild to moderate Alzheimer's disease (A)
2) Memantine for moderate to severe Alzheimer's disease (A) and combination therapy (cholinesterase inhibitors and memantine) may be beneficial (B). Drugs should not be stopped just because dementia severity increases (A).
3) Neither cholinesterase inhibitors nor memantine are effective in those with mild cognitive impairment (A).
4) Cholinesterase inhibitors are not effective in frontotemporal dementia and may cause agitation (A), though selective serotonin reuptake inhibitors may help behavioral (but not cognitive) features (B)
5) Cholinesterase inhibitors should be used for the treatment of people with Lewy body dementias (both Parkinson's disease dementia and dementia with Lewy bodies), and memantine may be helpful (A).

6)No drugs are clearly effective in vascular dementia, though cholinesterase inhibitors are beneficial in mixed dementia (B)

7) Early evidence suggests multifactorial interventions may have potential to prevent or delay the onset of dementia (B).

8)Though the consensus statement focuses on medication, psychological interventions can be effective n addition to pharmacotherapy, both for cognitive and non-cognitive symptoms.

9)In MCI patients with a history of depression, long-term SSRI treatment (>4 years) was significantly associated with a delayed progression to Alzheimer's dementia by approximately 3 years, compared with short-term SSRI treatment, treatment with other antidepressants, or no treatment and compared with MCI patients without a history of depression.

Clinical practice with anti-dementia drugs; A revised (third) consensus statement from the British Association for Psychopharmacology John T O'Brien1, Clive Holmes2, Matthew Jones3,4,et al. Journal of Psychopharmacology, 2017.

Impact of SSRI Therapy on Risk of Conversion From Mild Cognitive Impairment to Alzheimer's Dementia in Individuals With Previous Depression. Claudia Bartels,PhD, Michael Wagner, PhD., et al. American Journal of Psychiatry, Nov 2017.

Pharmacotherapy for Behavioral Disturbances in Dementia: Overview

- There are no FDA-approved treatments for any behavioral disturbances associated with dementia
- Overall approach: "Start low and go slow" and periodic assessment[1]
  - Antidepressants
  - Antipsychotics*
  - Anticonvulsants
  - Anxiolytics
  - Hypnotics
- Overall, pharmacotherapy has only limited efficacy for neuropsychiatric disorders in dementia[1-3]
  - However, even a small improvement may be beneficial, for caregivers as well as patients
- Appearance of behavioral symptoms may require careful review of all medications, including those for dementia

*All antipsychotics carry black box warnings relating to elderly patients with dementia.[1,2]
1. Rayner AV, et al. *Am Fam Physician*. 2005;71(4):647-652. 2. Cummings JL, et al. *Am Fam Physician*. 2002;65(12):2525-2534. 3. Sink KM, et al. *JAMA*. 2005;293(5):596-608. 4. Schneider LS, et al. *N Engl J Med*. 2006;355(15):1525-1538. 5. Sultzer DL, et al. *Am J Psychiatry*. 2008;165(7):844-854.
This information includes a use that has not been approved by the US FDA.

Depression in Long-Term Care

JAMDA
Volume 9, Issue 2 , Pages 82-87, February 2008 Mugdha Thakur, MD
Affiliations
Mugdha Thakur, MD, Dan G. Blazer, MD, PhD

- Up to 35% of residents in long-term care facilities may experience either major depression or clinically significant depressive symptoms. These symptoms are often not recognized. Depression is frequently comorbid with other problems that are common in long-term care, such as cognitive impairment, medical illness, and functional impairment. Nevertheless, depression, once diagnosed, can be treated effectively in the nursing home setting. The foundation of treatment is pharmacotherapy, yet other therapeutic approaches, such as exercise and psychological therapies may be of value.

Depression and anxiety are among the most common BPSD and an effective antidepressive therapy in dementia can improve both cognition and affective symptoms as well as other forms of BPSD, such as agitation and aggressiveness.6,14,106 Tricyclic antidepressants are not recommended because of their anticholinergic adverse events. SSRIs have reasonable tolerability and favourable treatment response. In dementia, SSRIs (specifically citalopram) are as efficacious as atypical antipsychotics for treating agitation.107 SSRIs can be associated with severe adverse effects such as QT-prolongation and hyponatraemia.

From <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5518961/>

In MCI patients with a history of depression, long-term SSRI treatment (>4 years) was significantly associated with a delayed progression to Alzheimer's dementia by approximately 3 years, compared with short-term SSRI treatment, treatment with other antidepressants, or no treatment and compared with MCI patients without a history of depression. No differences in CSF biomarker levels were observed between treatment groups. Citalopram was used at 20-30mg/d.

Mirtazapine…Remeron
Sleep/appetite 15-30mg
Mood….30-60mg
Trazodone…
Sleep 25-200mg
Anxiety/depression
25-50mg, BID, TID, QID

Legal considerations
•Have you advised your patient and their caregiver(s) to seek legal advice with regard to planning for future incapacity?122
•Are you aware of the state requirements regarding medical fitness to drive for patients with AD?121
•Are you aware of your legal obligations/appropriate steps to take if you suspect abuse/neglect in the patient or caregiver?123
•Child Proof the house, guns, sharp utensils, etc over times and possibly get car keys

Inadequate Indications:

Antipsychotic medications in persons with dementia should not be used if the only indication is one or more of the following:

- *wandering*
- *poor self-care*
- *restlessness*
- *impaired memory*
- *mild anxiety*
- *insomnia*
- *inattention or indifference to surroundings*
- *sadness or crying alone that is not related to depression or other psychiatric disorders*
- *fidgeting*
- *nervousness*
- *uncooperativeness (e.g. refusal of or difficulty receiving care).*

First, it is important to state that antipsychotics have not been approved for clinical use in dementia, except for risperidone, at least in some countries.

From <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5518961/>

Indications to use antipsychotics for patients with dementia include:

•severe agitation and aggression associated with risk of harm

•delusions and hallucinations

•comorbid preexisting mental health conditions (eg, bipolar disorder, schizophrenia, treatment-resistant depression, etc.).

Symptoms that do not usually respond to an antipsychotic include wandering, social withdrawal, shouting, pacing, touching, cognitive defects, and incontinence.[12] These symptoms may respond to interventions such as changes to the environment.

Table 2

Psychopharmacologic treatments based on a psychobehavioral metaphor

Symptoms	Medication class
Depressed/anxious: agitated, socially withdrawn, dysphoric, irritable	Antidepressant
Manic: agitated, psychomotor activation, labile affect, rapid speech	Mood stabilizer
Psychotic: agitated, aggressive, delusional, hallucinating	Antipsychotic

Source: Reference 11

Black box warning

- **Increased Mortality in Elderly Patients with Dementia-Related Psychosis**
  Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of seventeen placebo controlled trials (modal duration of 10 weeks) in these patients revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times that seen in placebo-treated patients. Over the course of a typical 10 week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. RISPERDAL®. (risperidone) is not approved for the treatment of patients with Dementia-Related Psychosis.

"C'mon, c'mon — It's either one or the other."

Schizophrenia or Dementia?

- Dementia Praecox

The term "dementia praecox" was first used in 1891 by Arnold Pick (1851–1924), a professor of psychiatry at Charles University in Prague.

Dementia praecox (a "premature dementia" or "precocious madness") is a disused psychiatric diagnosis that originally designated a chronic, deteriorating psychotic disorder characterized by rapid cognitive disintegration, usually beginning in the late teens or early adulthood. Over the years, the term "dementia praecox" was gradually replaced by "schizophrenia", which remains in current diagnostic use.

If patient has primary schizophrenia, Bipolar DO, etc use standard medication protocols, adjusted for age.

While it's not part of the diagnostic criteria, they do consider someone's age. The typical age of schizophrenia diagnosis is between late adolescence and the mid-30s. This varies, though, with peak ages ranging from the early- to mid-20s for males and late-20s for females (Are Schizophrenia Symptoms in Males and Females Different?). Further, while it's rare, schizophrenia can be diagnosed as early as childhood and as late as the 40s.

If patient has primary schizophrenia, Bipolar DO, etc use standard medication protocols, adjusted for age.

Clarify Dx…
Misperceptions, confusion are not hallucinations!
"I have to go to work, pick up my children, fix my husband's dinner, etc."

No medications have an indication for use in this population. It is proposed that doses which have been used in completed randomized trials that reflect the best information available about the dose are likely to maximize benefit and minimize risk. On the basis of those trials, reasonable starting doses would be[15-22]:

- quetiapine 25 to 50 mg/d
- risperidone 0.5 to 1 mg/d
- aripiprazole 2 to 10 mg/d
- olanzapine 2.5 to 5 mg/d
- ziprasidone 20 mg/d

The highest doses tested for each of these compounds in randomized clinical trials for this population were: risperidone 2 mg/d, olanzapine 10 mg/d, and aripiprazole 15 mg/d. A wide variety of maximum doses of quetiapine were studied in clini- cal trials, with a top dose of 200 mg being most common. It is worth noting that doses higher than these have been used for other indications.[15-22]

Atypical antipsychotics such as risperidone and aripiprazole are among the most often (and probably too often) prescribed drugs in BPSD. They are effective in the treatment of psychotic symptoms, agitation and aggression.2,14,108,109

From <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5518961/

Most studies and reviews recommend Risperdal as 1st choice and either Seroquel or Abilify as a second choice.

Haloperidol may be considered in the treatment of delirium in dementia, but it is not recommended for a different use in dementia. And no longer recommended in Dementia either (twice the level of cardiac complications as Risperdal).

From <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5518961/

While the evidence on the efficacy of quetiapine for BPSD is mixed, it is widely used clinically.111 Due to its favourable side-effect profile, particularly regarding extrapyramidal signs, quetiapine may be of particular value for BPSD, especially in patients with Parkinsonian features, despite conflicting evidence.112

From <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5518961/>

Limit use, try 14-21d and try to re-evaluate

MOOD STABILIZERS

Although carbamazepine shows some benefit for agitation in dementia, mood stabilizers are often associated with severe side effects.2,14,113 Trileptal has similar action to CBZ with fewer side effects Valproic acid is not recommended..There is some clinical experience and limited evidence for gabapentine and lamotrigine in the treatment of BPSD.

From <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5518961/>

VPA has freq hepatoencephalopathy

ONE WAY TO FIND OUT IF YOU ARE OLD IS TO FALL DOWN IN FRONT OF A LOT OF PEOPLE. IF THEY LAUGH, YOU'RE STILL YOUNG. IF THEY PANIC AND START RUNNING TO YOU, YOU'RE OLD.

Benzodiazepines

Evidence for the efficacy of benzodiazepines in BPSD is lacking. Benzodiazepines are associated with sedation, dizziness, falls, worsening cognition, respiratory depression, dependency and paradoxical disinhibition in the elderly. They are thus only recommended for the management of an acute crisis,6,14 if other methods fail. Their use must be limited in time and they should not be prescribed as hypnotics. SNF prn Bz is 7-14d.

From <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5518961/>

Sedative/Hypnotics

Hypnotics such as zopiclone, zolpidem or zaleplone can have similar side-effects as benzodiazepines.[6] They are used for sleep disorders in dementia over a limited period of time and at small doses. Sedative antidepressants such as trazodone seem to improve sleep duration. Melatonin and melatonin receptor agonists can be effective in treating circadian sleep disorders.[34,35]

From <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5518961/>