

CCNA Webinar – September 8, 2021

The Impact of Lewy Body Dementia on Patients, Caregivers, and Society

Why We Should Care

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Disclosure of potential conflicts of interest



None to declare

Objectives

- 1 Describe the various clinical features of Lewy body dementia;
- 2 Understand the negative effects of Lewy body dementia on patients and caregivers;
- 3 Appreciate the socioeconomic consequences of Lewy body dementia;
- 4 Name resources available to mitigate the impact of Lewy body dementia on patients and caregivers.



Presentation Plan

1. Background

- Definitions;
- The history of LBD;
- Epidemiology;

3. The Impact of LBD

- On patients;
- On family and caregivers;
- On society.

2. Lewy Body Spectrum Disorders

- Clinical manifestations;
- Clinical diagnosis;
- Investigations;
- Clinical management.

4. Resources and Care

- Unmet needs;
- Resources;
- Key messages.



Background

Cognitive Neurology 101

- **Major neurocognitive disorder (*dementia*)**: significant cognitive deficits with functional impairment;
- **Minor neurocognitive disorder (*mild cognitive impairment*)**: significant cognitive deficits without functional impairment;
- **Alzheimer’s disease (AD)**: a specific neurodegenerative disease that causes dementia, secondary to amyloid beta;
- **Related dementias**: other neurodegenerative and non-neurodegenerative causes of dementia:
 - Behavioural variant – Frontotemporal Dementia (BvFTD);
 - Primary Progressive Aphasia (APP);
 - Corticobasal Syndrome (CBS);
 - Progressive Supranuclear Palsy (PSP);

secondary to frontotemporal lobar degeneration

 - Dementia with Lewy bodies (DLB);
 - Parkinson’s disease dementia (PDD);

secondary to alpha-synucleinopathy

 - Vascular dementia (VaD).

Lewy Body Spectrum Disorders

Parkinson's Disease (PD)

Mainly a movement disorder defined by the presence of parkinsonism: resting tremor, rigidity, bradykinesia, postural and gait changes

Parkinson's Disease Dementia (PDD)

When cognitive deficits emerge (late) during the course of Parkinson's disease and cause functional impairment

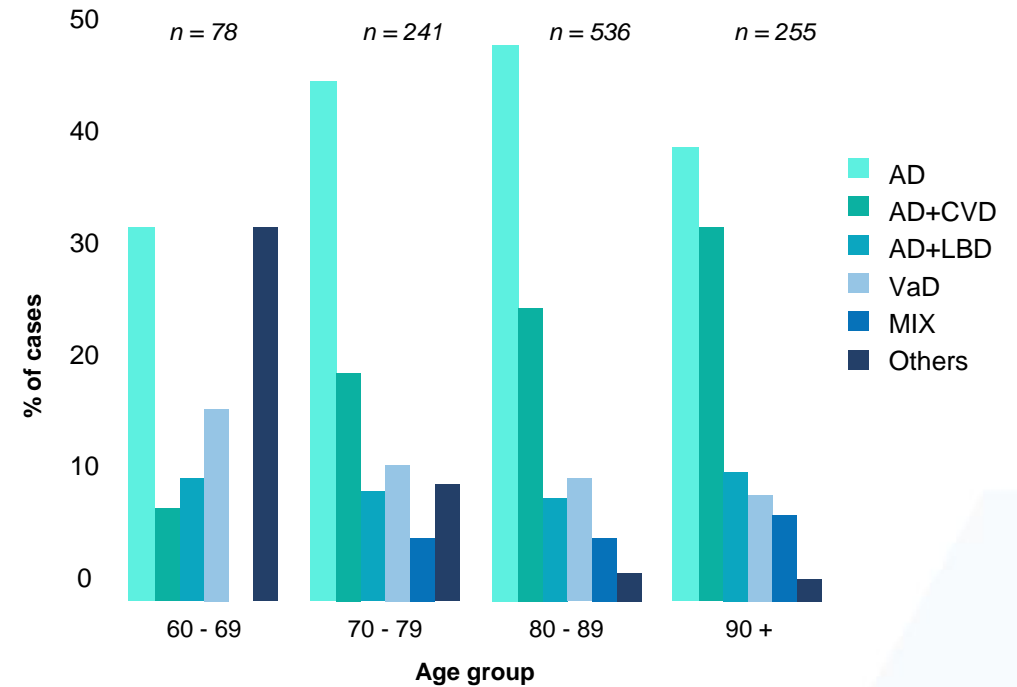
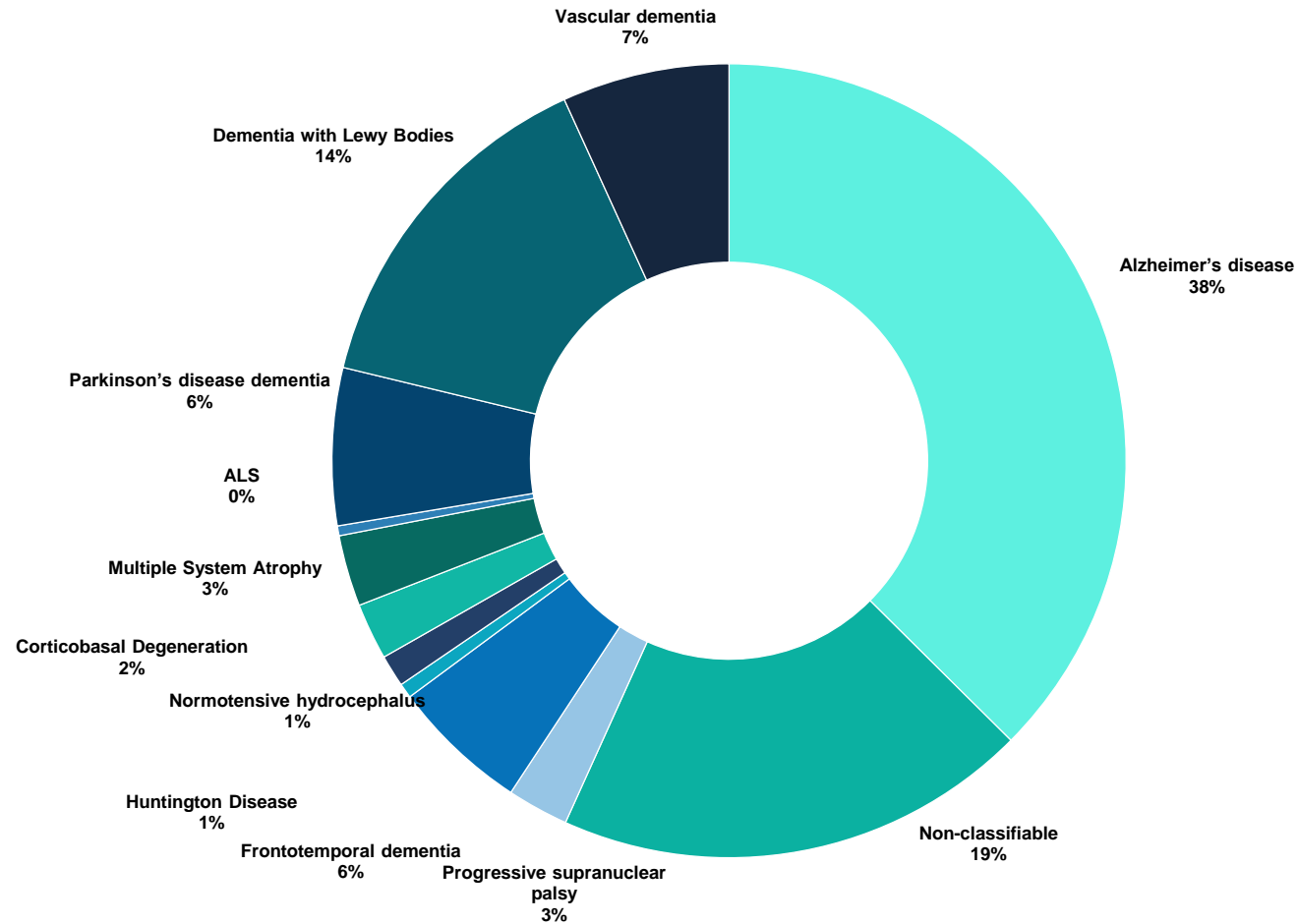
Dementia with Lewy bodies (DLB)

A disorder characterized by the presence of parkinsonism, cognitive changes (early), dysautonomic and neuropsychiatric manifestations

Lewy Body Dementia (LBD)

Umbrella term for both Dementia with Lewy bodies (DLB) and Parkinson's disease dementia (PDD)

Alzheimer's Disease and Related Disorders



Age-related frequency of neuropathologic types of dementing disorders

Adapted from Stoeck, Brain, 2012

P.Desmarais

Adapted from Jellinger, Acta Neuropathol, 2010

Lewy Pathology – A 100-Year-Old Pathology

James Parkinson



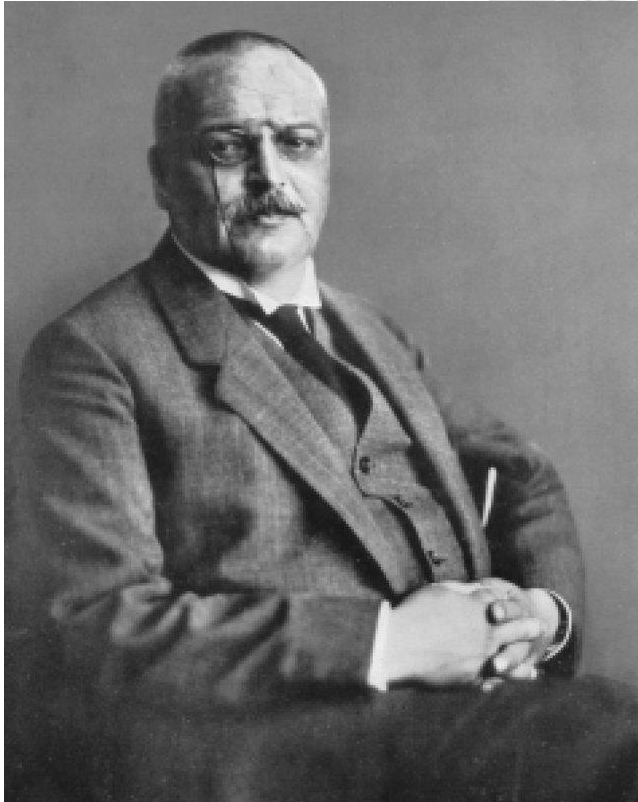
**Fritz Heinrich
Lewy**

**Lewy body within a
dopaminergic neuron**

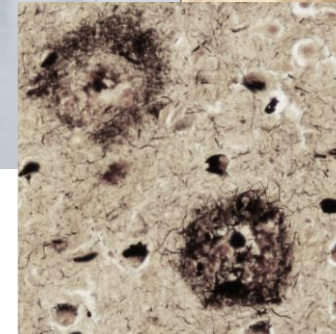
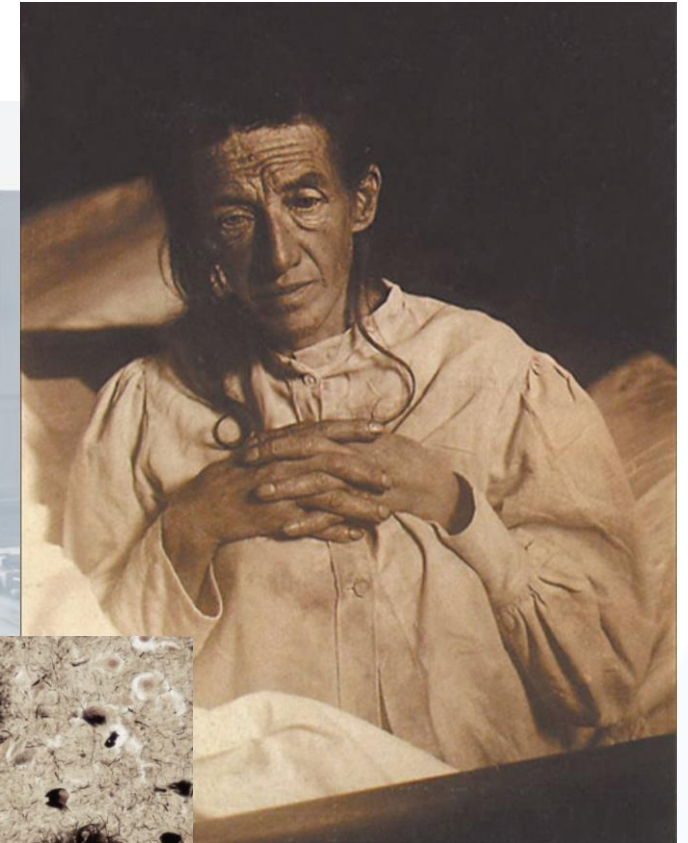


Alzheimer's Disease – Another 100-Year-Old Pathology

Dr Alois Alzheimer



Auguste Deter



Amyloid plaques

Epidemiology

- Parkinson's disease dementia (PDD)¹:
 - Incidence rate: 2.5 per 100 000 person-years.
- Dementia with Lewy bodies (DLB)¹:
 - Incidence rate: 3.5 per 100 000 person-years.
- Lewy Body Dementia (PDD + LBD)¹:
 - 50-59 yrs: 0.6 per 100 000 person-years;
 - 60-69 yrs: 13.7 per 100 000 person-years;
 - 70-79 yrs: 64.3 per 100 000 person-years;
 - 80-99 yrs: 77.2 per 100 000 person-years.
- Alzheimer's disease²:
 - 50-59 yrs: 18.9 per 100 000 person-years;
 - 60-69 yrs: 68.2 per 100 000 person-years;
 - 70-79 yrs: 619.1 per 100 000 person-years;
 - 80-99 yrs: 4835 per 100 000 person-years.

¹Savica et al., *JAMA Neurol.* 2013

²Jellinger et al., *Dement Geriatr Cogn Disord.* 2011

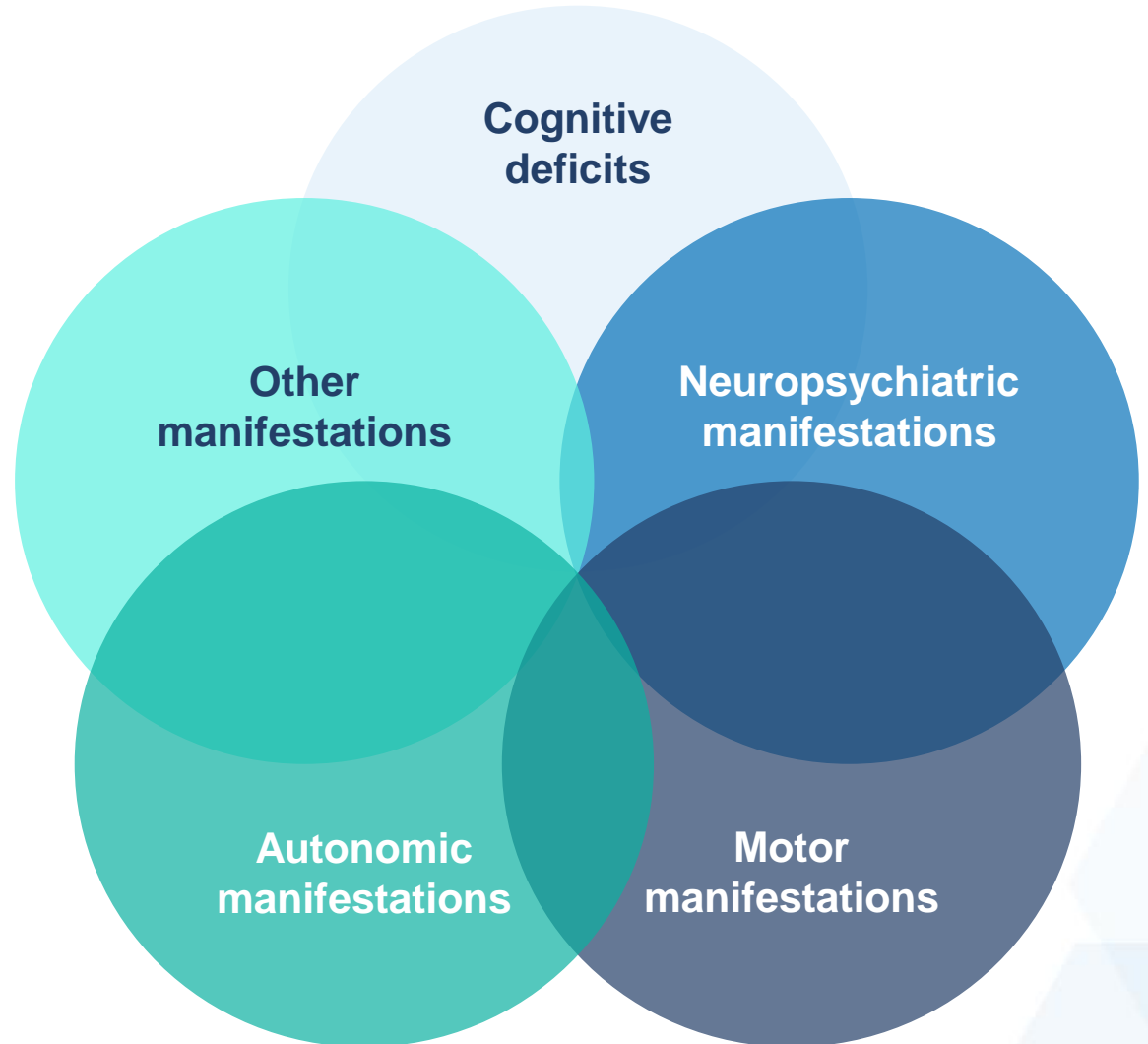


Lewy Body Spectrum Disorders



Clinical Manifestations

- 1 Cognitive deficits
- 2 Neuropsychiatric manifestations
- 3 Motor manifestations
- 4 Autonomic manifestations
- 5 Other manifestations

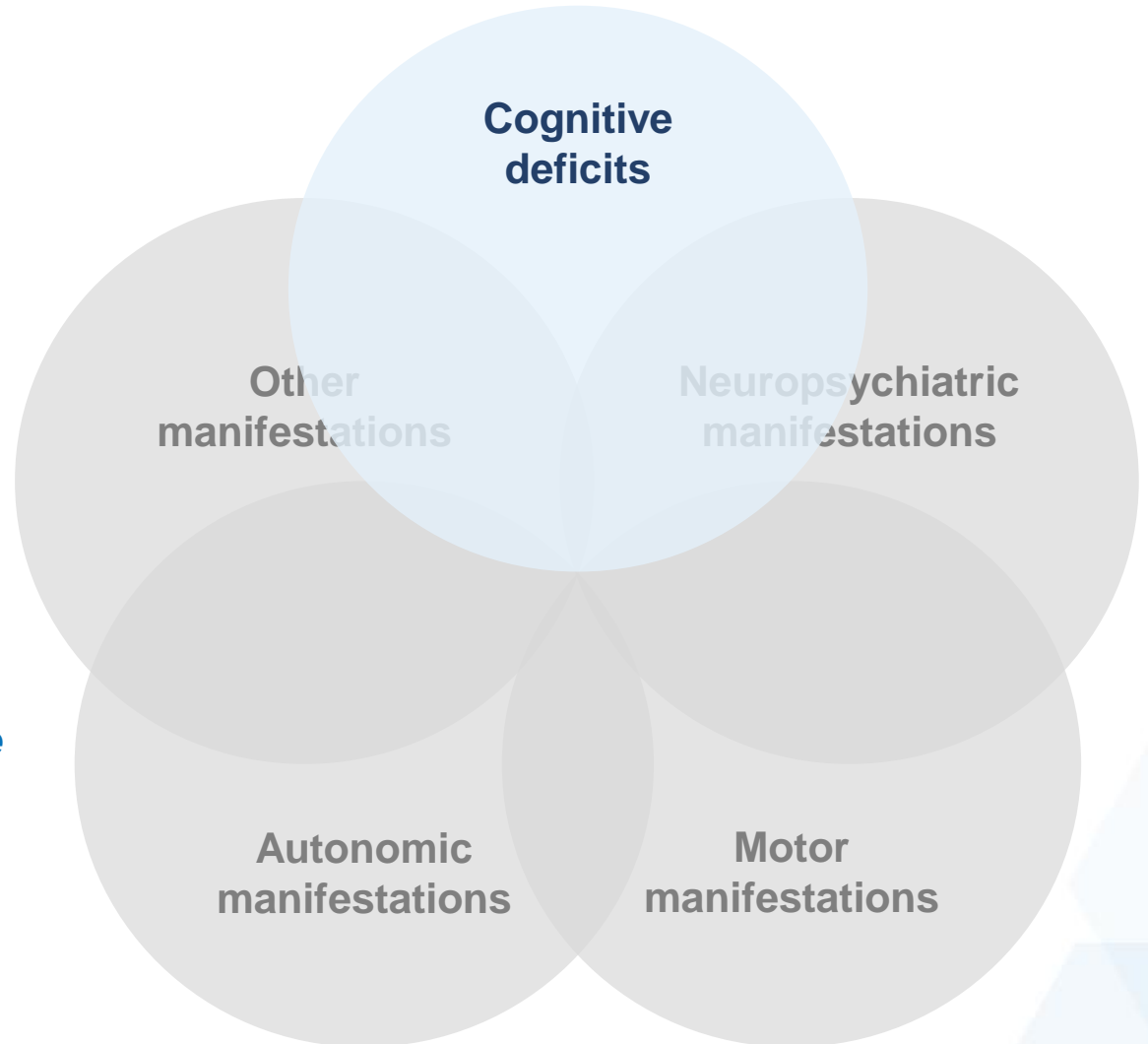


Cognitive Deficits

1 Cognitive domains impaired:

- Attention and alertness;
- Executive functions;
- Processing speed;
- Judgement;
- Visuoperceptual abilities;
- Episodic memory.

Cognitive difficulties tend to fluctuate over time

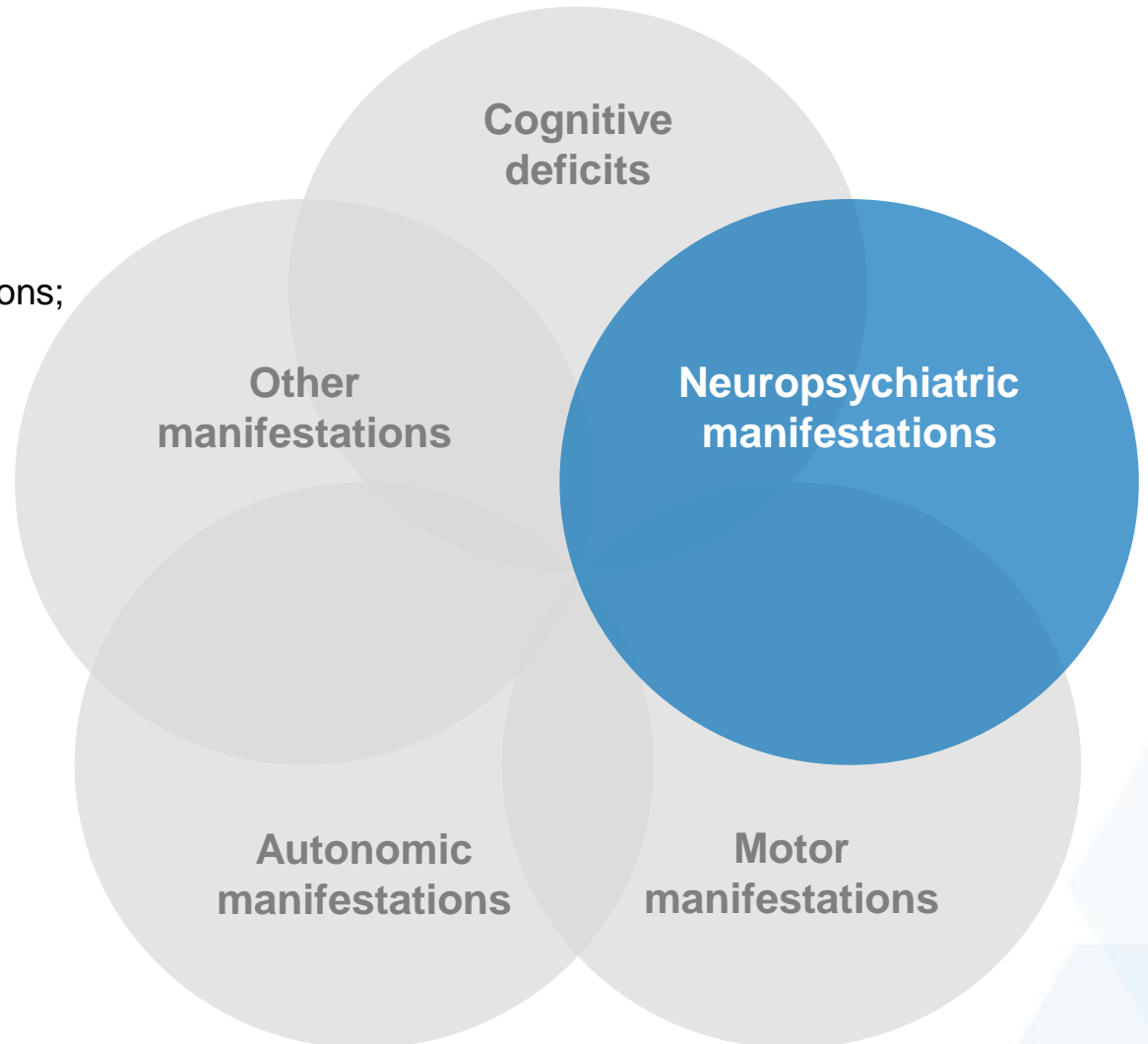


Neuropsychiatric Manifestations

2

Neuropsychiatric manifestations:

- Psychotic manifestations (57-76%):
 - Hallucinations, especially visual hallucinations;
 - Delusions.
- Mood:
 - Depressive symptoms (49%);
 - Anxiety and irritability (65%);
 - Apathy (57%).
- Sleep manifestations (80%):
 - REM sleep behaviour disorder;
 - Restless legs syndrome;
 - Hypersomnolence;
 - Insomnia;
 - Sleep fragmentation;
 - Wake-sleep cycle inversion.

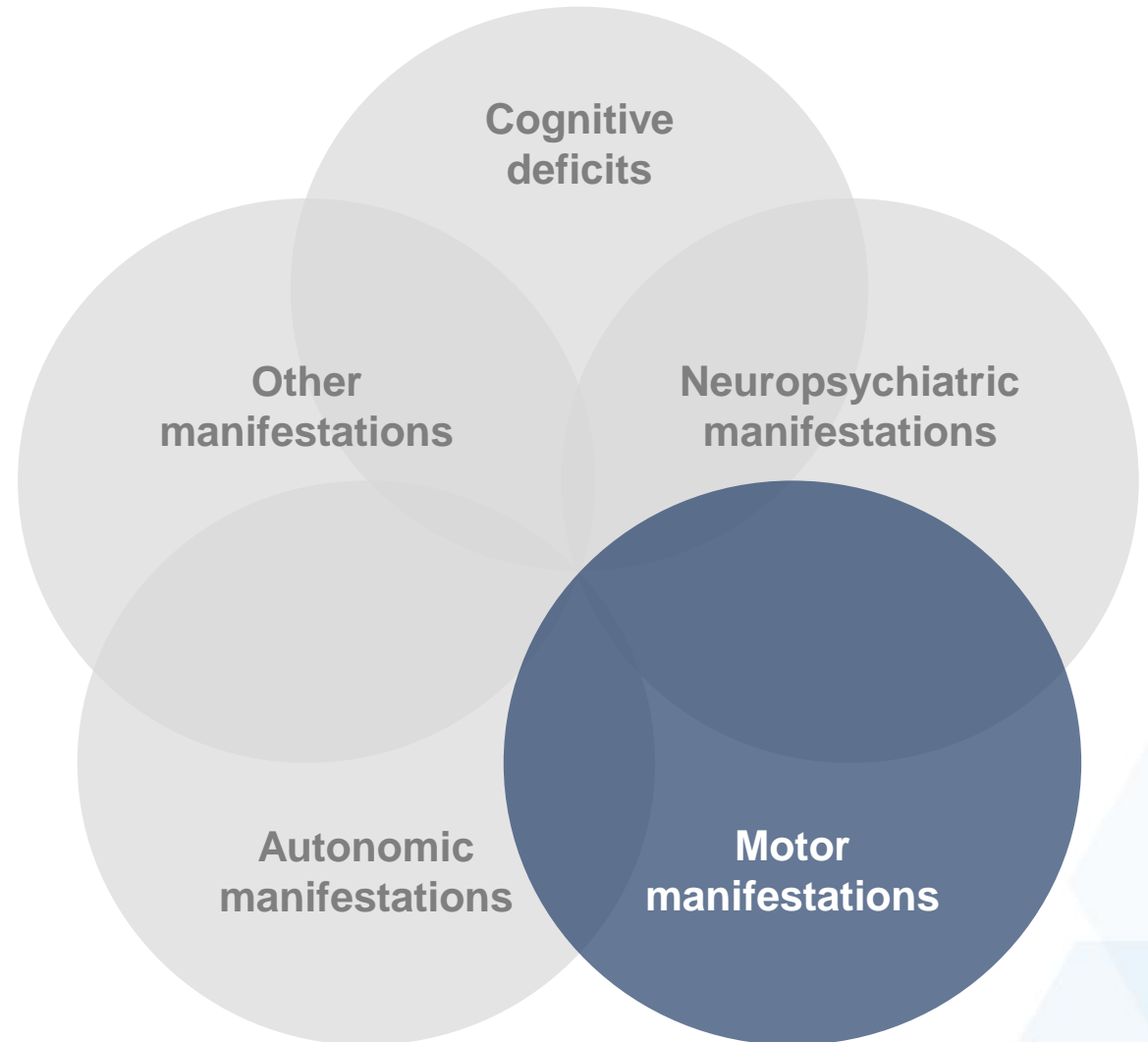


Motor Manifestations

3

Motor manifestations:

- Parkinsonism (85%):
 - Akinesia / bradykinesia;
 - Rigidity;
 - Gait issues;
 - Resting tremor;
- Falls;
- Immobility;
- Dysphagia;
- Dysphonia;
- Sialorhea.



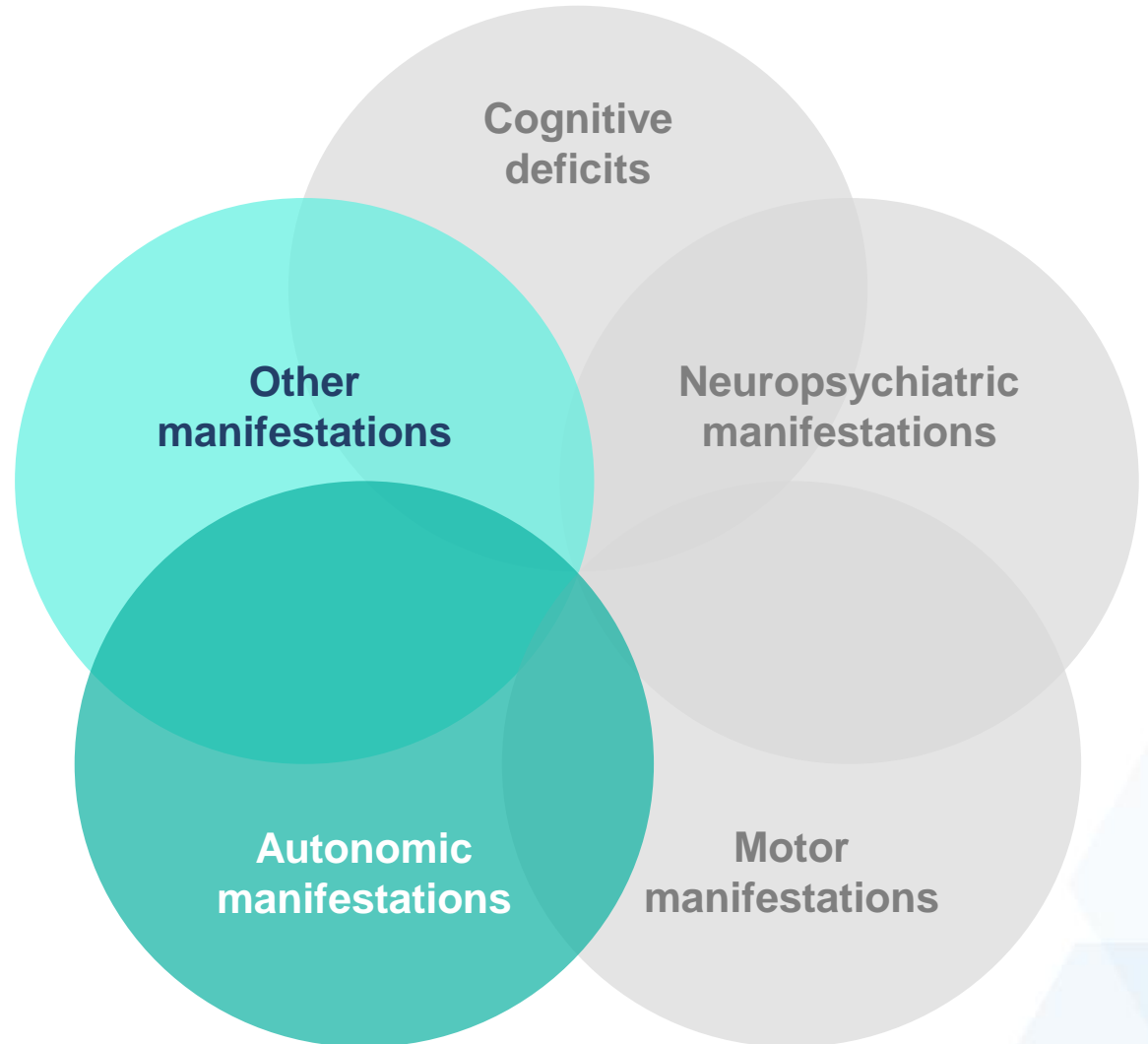
Dysautonomic and Other Manifestations

4 Dysautonomic manifestations (96%):

- Orthostatic hypotension (66%);
- Syncope (28%);
- Gastroparesia;
- Bladder dysfunction;
 - Urinary urgency / incontinence (97%);
 - Urinary retention (28%);
- Erectile dysfunction;
- Constipation (83%);
- Fecal incontinence;
- Sialorrhea/rhinorrhea;
- Hyperhidrosis.

5 Other manifestations

- Loss of smell;
- Seborrheic dermatitis.



Clinical Diagnosis

Revised criteria for the clinical diagnosis of probable and possible dementia with Lewy bodies

Essential

Dementia: a progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational functions, or with usual daily activities. Prominent or persistent memory impairment may not necessarily occur in the early stages but is usually evident with progression. Deficits on tests of attention, executive function, and visuo-perceptual abilities may be especially prominent and occur early.

Core clinical features

- Fluctuating cognition with pronounced variations in attention and alertness
- Recurrent visual hallucinations that are typically well formed and detailed
- REM sleep behavior disorder, which may precede cognitive decline
- Parkinsonism: bradykinesia, rest tremor, or rigidity.

Supportive clinical features

Severe sensitivity to antipsychotic agents; postural instability; repeated falls; syncope or other transient episodes of unresponsiveness; severe autonomic dysfunction (e.g., constipation, orthostatic hypotension, urinary incontinence); hypersomnia; hyposmia; hallucinations in other modalities; systematized delusions; apathy; anxiety and depression.

Indicative biomarkers

- Reduced dopamine transporter uptake in basal ganglia on SPECT or PET;
- Abnormal (low uptake) ¹²³Iodine-MIBG myocardial scintigraphy;
- Polysomnographic confirmation of REM sleep without atonia.

Supportive biomarkers

- Relative preservation of medial temporal lobe structures on CT/MRI scan;
- Generalized low uptake on SPECT/PET perfusion/metabolism scan with reduced occipital activity ± the cingulate island sign;
- Prominent posterior slow-wave activity on EEG with periodic fluctuations in the pre-alpha/theta range.

Probable DLB

- a. Two or more core clinical features of DLB are present, with or without the presence of indicative biomarkers, or;
- b. Only one core clinical feature is present, but with one or more indicative biomarkers.

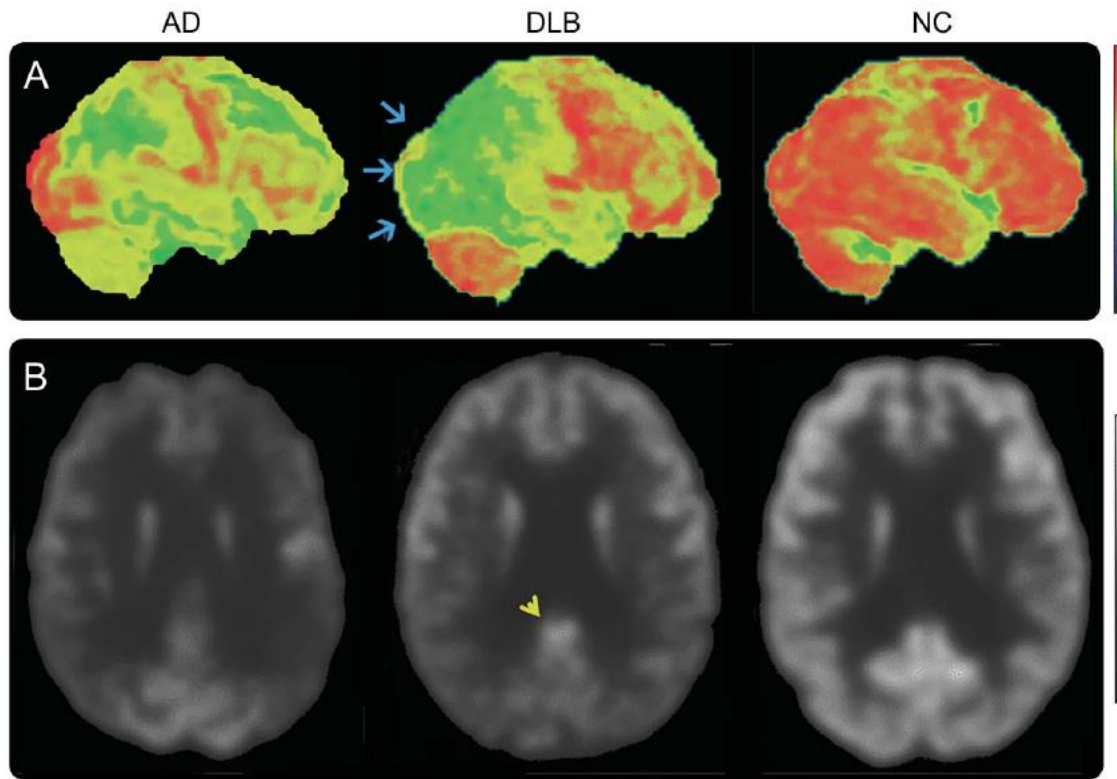
Possible DLB

- a. Only one core clinical feature of DLB is present, with no indicative biomarker evidence, or;
- b. One or more indicative biomarkers is present but there are no core clinical features.

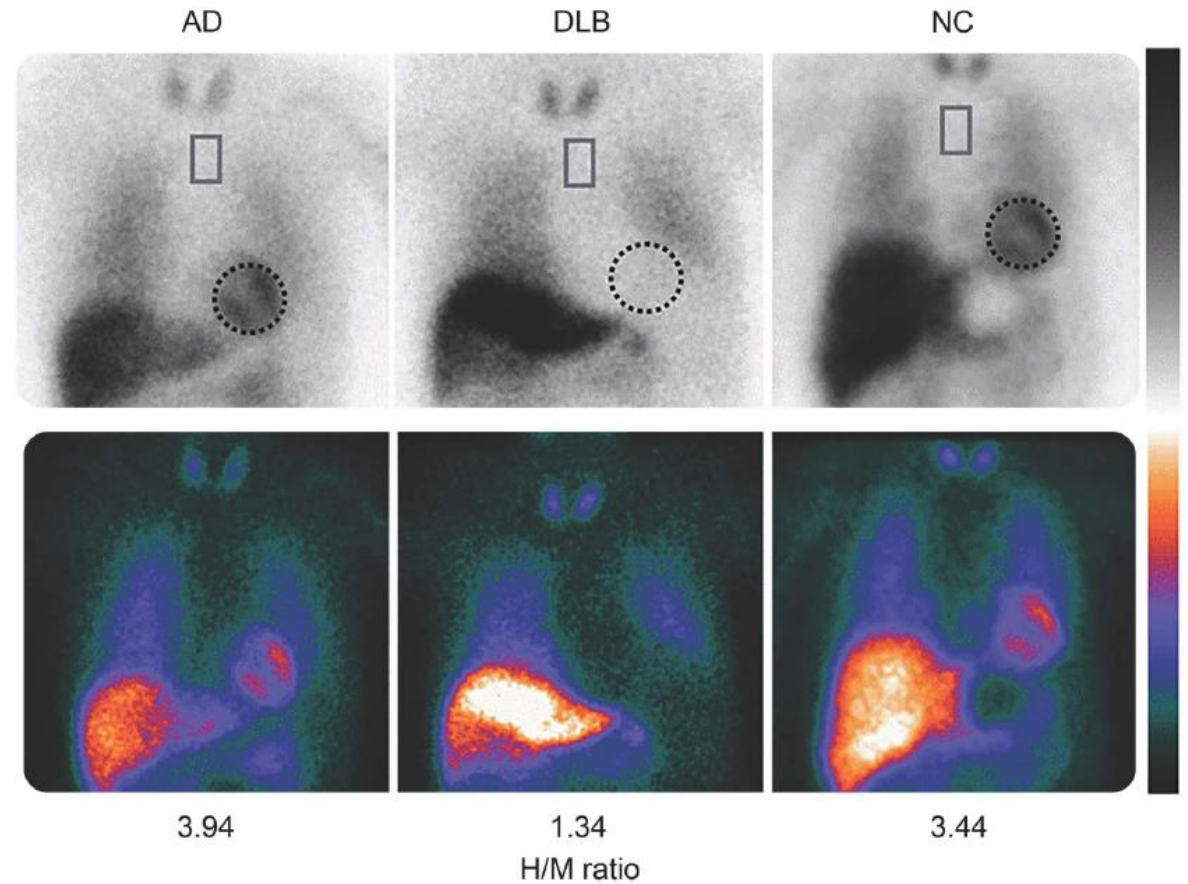
Adapted from McKeith et al. *Neurology*, 2017

Investigations

^{18}F -FDG-PET



^{123}I iodine-MIBG myocardial scintigraphy



Adapted from McKeith et al. *Neurology*, 2017

Clinical Management of Lewy Body Dementia

Clinical management has to be personalized to patients' manifestations, priorities, and objectives as well as their caregivers' priorities.

1. Cognitive impairment:

- Cholinesterase inhibitors:
 - Improve cognition;
 - Improve completion of activities of daily living;
 - Reduce global deterioration;
 - Reduce caregiver burden.

2. Neuropsychiatric manifestations:

- Cholinesterase inhibitors (*in general*):
 - May reduce delusions, hallucinations, apathy, cognitive fluctuations.
- Antipsychotics (*for psychosis*):
 - Efficacy is uncertain in LBD;
 - High-risk of severe sensitivity reactions (50%);
 - Enhanced mortality risk in the longer term.
- Antidepressants (*for depression and anxiety*):
 - Efficacy is uncertain but they can reduce depressive symptoms.
- Melatonin (*for sleep disorders*):
 - Improve sleep quality and is well tolerated;
 - Can reduce REM sleep behaviour disorder;

Clinical Management of Lewy Body Dementia

Clinical management has to be personalized to patients' manifestations, priorities, and objectives as well as their caregivers' priorities.

3. Motor manifestations:

- Levodopa therapy for parkinsonism:
 - May improve motor function in up to 50% of patients.

4. Autonomic dysfunction:

- Orthostatic hypotension:
 - Midodrine, fludrocortisone, and droxidopa can provide significant benefits.
- Constipation:
 - Polyethylene glycol and psyllium can provide significant benefits.



The Impact of Lewy Body Dementia

The Impact of Disease



The Impact on Patients



Quality of life (QOL) and well-being:

- ↓ in patients with LBD compared to patients with AD (patient-rated and caregiver-rated)^{1,2}:
 - Predictors of QOL in LBD:
 - Neuropsychiatric manifestations (especially depression, apathy, and psychosis);
 - Functional independence on activities of daily living and instrumental activities of daily living;
 - Autonomic dysfunction (orthostatic hypotension, syncope);
 - Living with caregiver and level caregiver's burden;
 - Mobility;
 - Constipation;
 - Use of antipsychotics.



Independence:

- ↓ in patients with LBD compared to patients with AD (at time of diagnosis):
 - Predictors of functional impairment:
 - Cognitive fluctuations;
 - Cognitive impairment;
 - Parkinsonism;
 - Apathy.

¹:van de Beek et al., *Journal of Alzheimer's Disease*. 2019

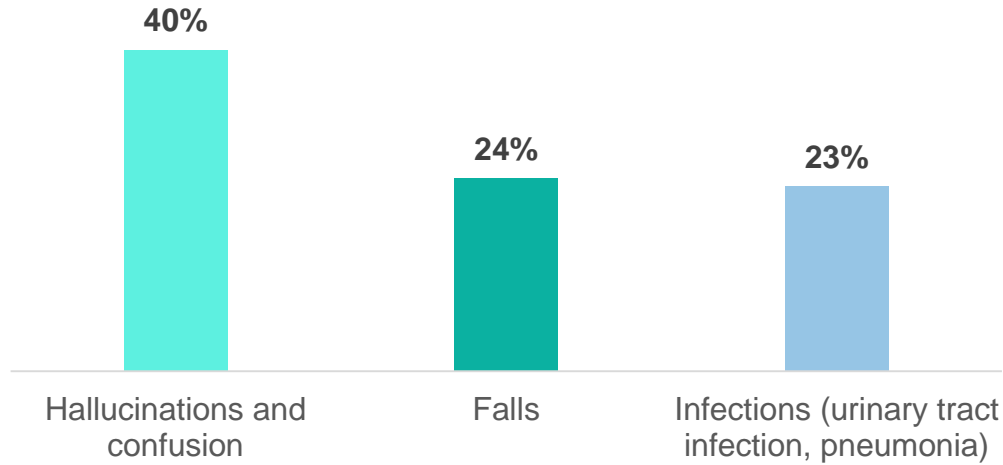
²: van de Beek et al., *Alzheimer's Research & Therapy*. 2021

The Impact on Patients

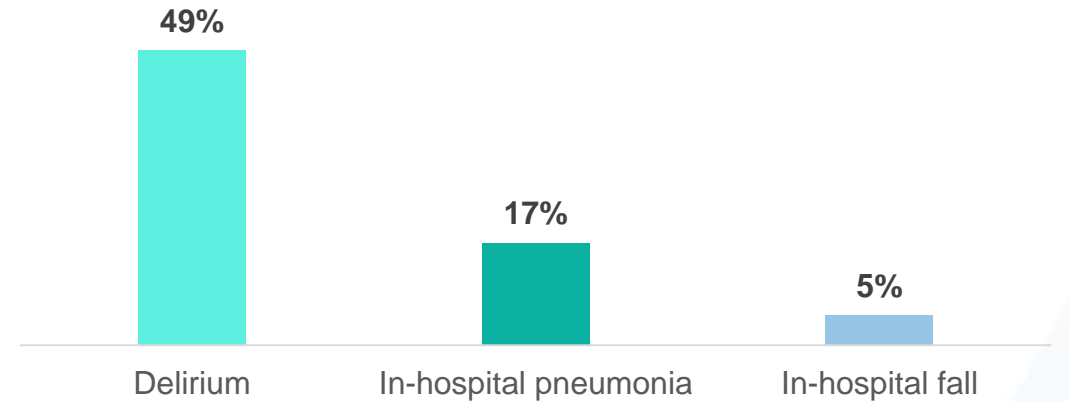


Hospitalisations

Causes of admission



High rate of in-hospital complications



38%

High exposure to antipsychotic medications

30%

High rate of transition to a higher level of care

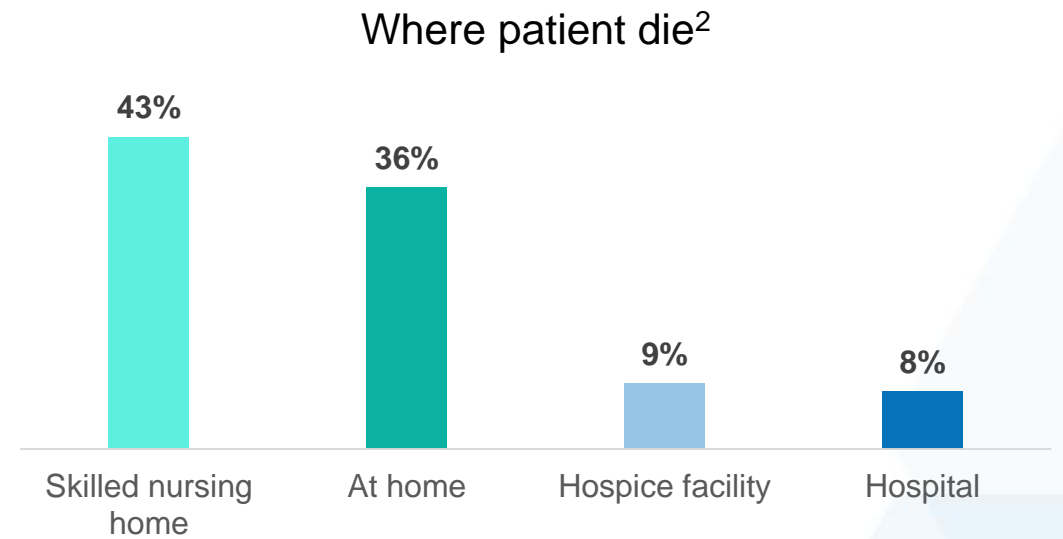
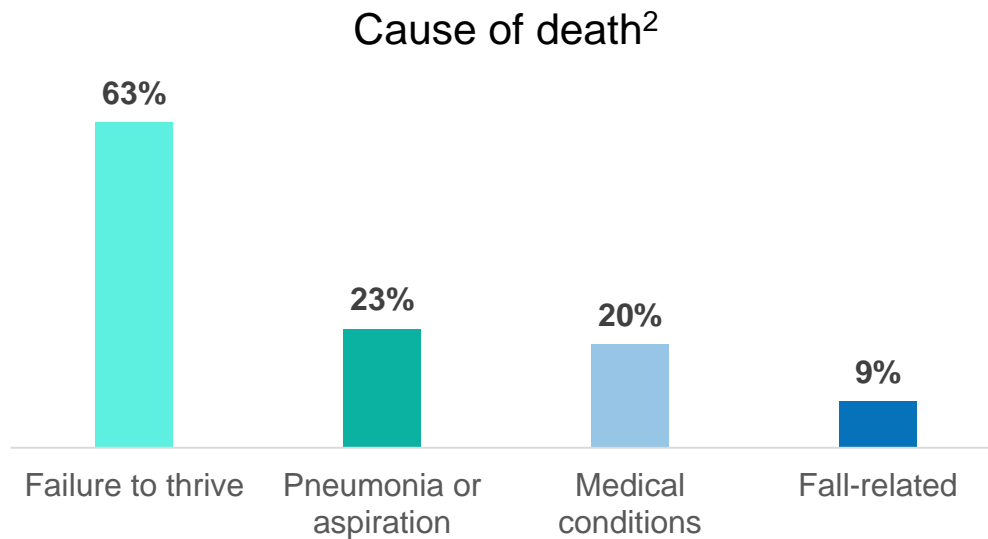
Adapted from Spears et al., *Parkinsonism and Related disorders*. 2019

The Impact on Patients



End of life:

- Survival is worse in LBD than in AD¹:
 - Survival estimate from diagnosis: 1.9 to 6.3 years;
 - Survival estimate from onset: 5.5 to 7.7 years.



¹Mueller et al., *Lancet Neurol.* 2017

²Adapted from Armstrong et al., *J Am Geriatr Soc.* 2019

The Impact on Patients



Obstacles in the patient's journey through the healthcare system:

- Delay in timely diagnosis:
 - Under-appreciation of the differences between age-associated slowing and dementia;
 - Under-appreciation of the importance of early diagnosis by some clinicians;
 - Long patient journey in the healthcare system, difficult access to specialized clinics, investigations, etc.
 - 68% of patients have consulted 3 different physicians before obtaining a diagnosis;
 - On average, patients obtained a diagnosis after 4 medical visits, 33% of patients obtained a diagnosis after 6 visits;
 - For 31% of patients, it took >2 years before obtained a diagnosis.
- Frequent alternative initial diagnosis (78%):
 - Parkinson's disease or PD with another condition (39%);
 - Alzheimer's disease (26%);
 - Frontotemporal dementia (4%);
 - Psychiatric diagnoses (24%): major depression, bipolar disorder, or schizophrenia.

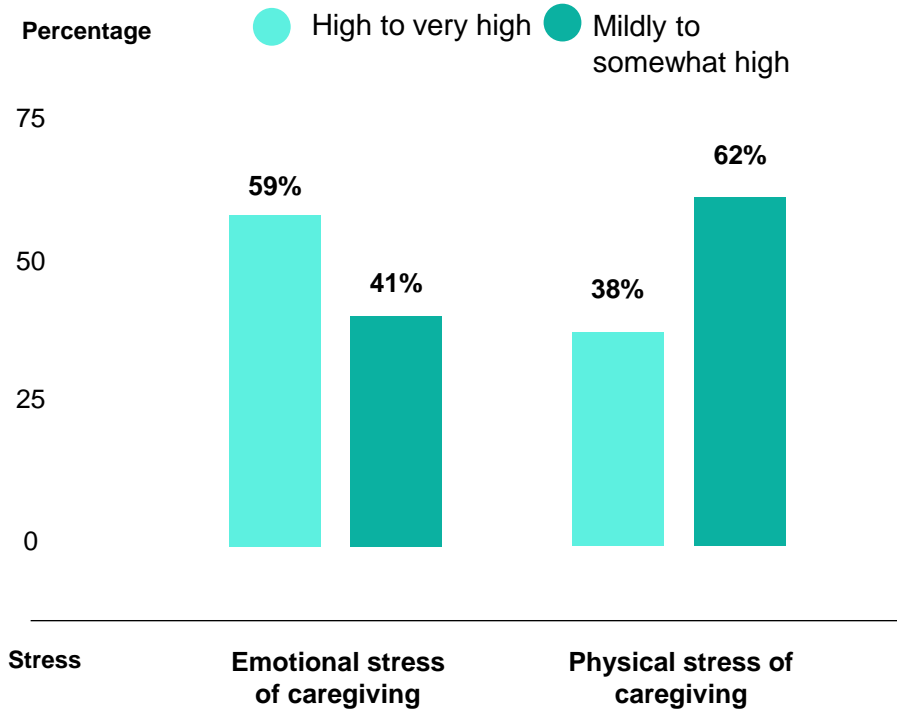
The Impact on Patients



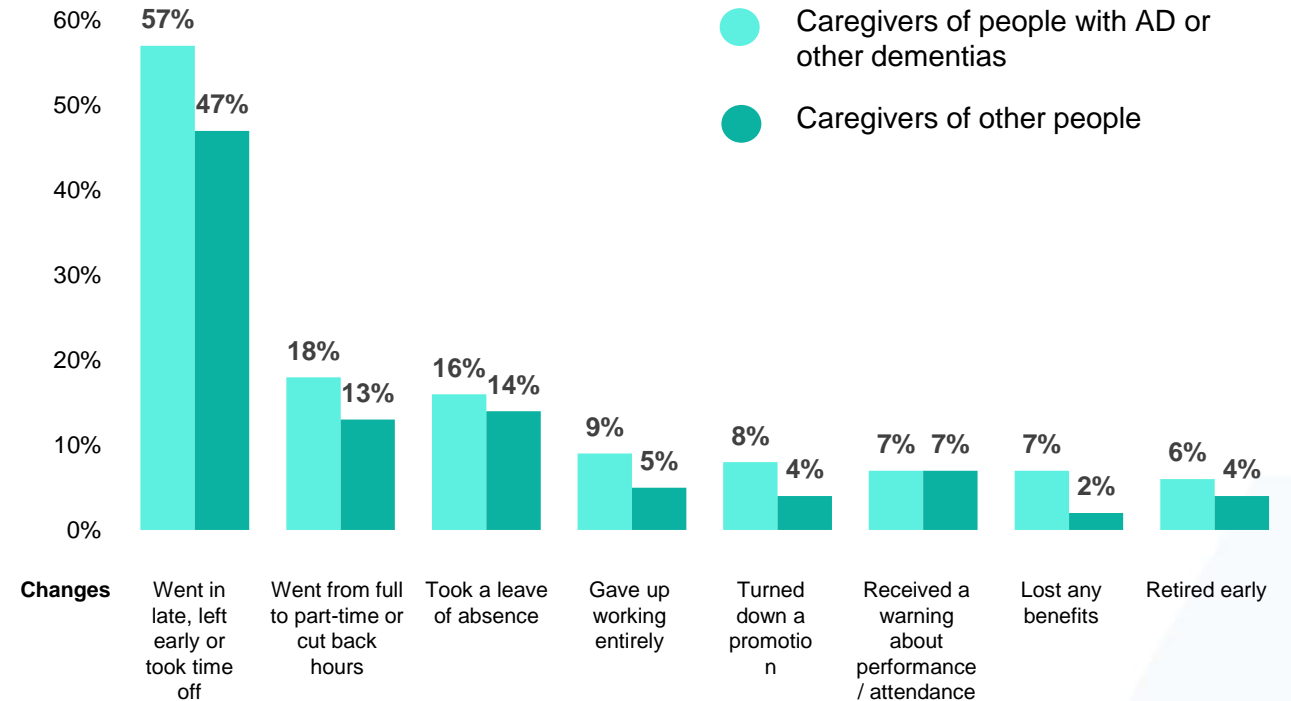
Obstacles in the patient's journey through the healthcare system:

- Exposure to medications and serious adverse events:
 - Exposure to antipsychotics for neuropsychiatric manifestations;
 - Neuroleptic malignant syndrome (NMS);
 - Neuroleptic sensitivity reactions:
 - Sedation;
 - Confusion;
 - Increased parkinsonism;
 - Immobility.
 - Exposure to anticholinergic medications for urinary incontinence, tremors, etc.:
 - Worsen cognition;
 - Exacerbate constipation
- Delay in receiving needed support services and longitudinal care:
 - 47% of patients are followed by the diagnosing physician;
 - 50% of patients are seeing 2 or more physicians for LBD-related problems.

The Impact on Caregivers and Family Members



Percentage of Caregivers Who Report High to Very High Stress Due Caregiving



Work-Related Changes Among Caregivers of People with Alzheimer's or Other Dementias Who Had Been Employed at Any Time Since They Began Caregiving

Adapted from Alzheimer's Disease Facts and Figures. *Alzheimers Dement.*, 2021

The Impact on Caregivers and Family Members



Caregivers of patients with LBD (*respondents in studies*):

- Female (>80%);
- Spouses (>40%).



Quality of life (QOL) and well-being:

- ↓ in caregivers of patients with LBD compared to caregivers of patients with AD:
 - Predictors of QOL:
 - Neuropsychiatric manifestations (notably psychosis, apathy, and night-time behaviours);
- Caregivers report medium to high levels of burden:
 - Fear of the future for their loved one;
 - Stress related to being a caregiver with other personal responsibilities;
 - Delay in receiving needed support services.

The Impact on Caregivers and Family Members



Obstacles in the caregiver's journey through the healthcare system:

- Misdiagnosis, underdiagnosis, delay in diagnosis, and conflicting diagnoses;
- Lack of knowledge regarding the diagnosis by healthcare providers;
 - 70% of caregivers report difficulties finding physicians who know the criteria for diagnosing LBD;
 - 77% of caregivers report difficulties finding physicians who know how to treat and care patients with LBD.
- Insufficient communication (*what's the diagnosis? what are the manifestations? what are the treatments?*);
- Poorly coordinated care across the healthcare system and cost;
- Access to facilities that can accept a person with DLB and behavioural manifestations;
- End-of-life care is particularly difficult:
 - Lack of recognition and knowledge about DLB by healthcare providers;
 - High use of antipsychotics to treat nausea, agitation, psychosis.

The Impact on Society



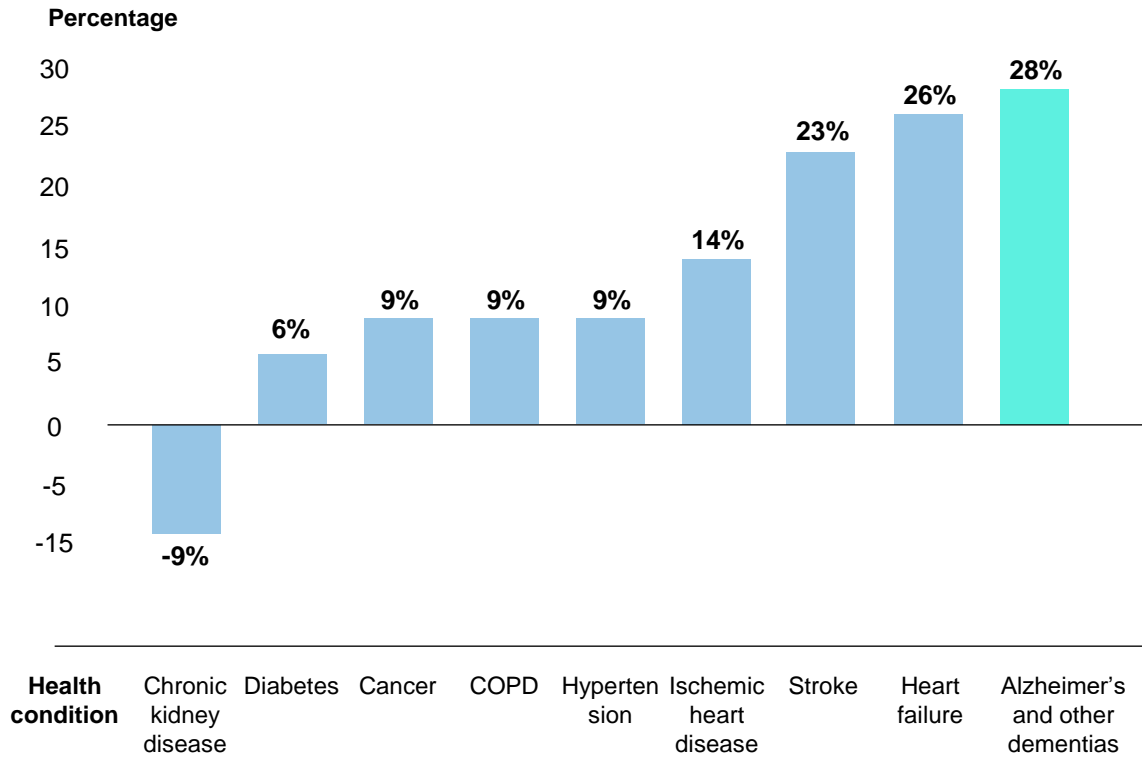
Total cost: \$355 Billion

- Medicare**
\$181B (51%)
- Medicaid**
\$59B (17%)
- Out of pocket**
\$76B (21%)
- Other**
\$39B (11%)

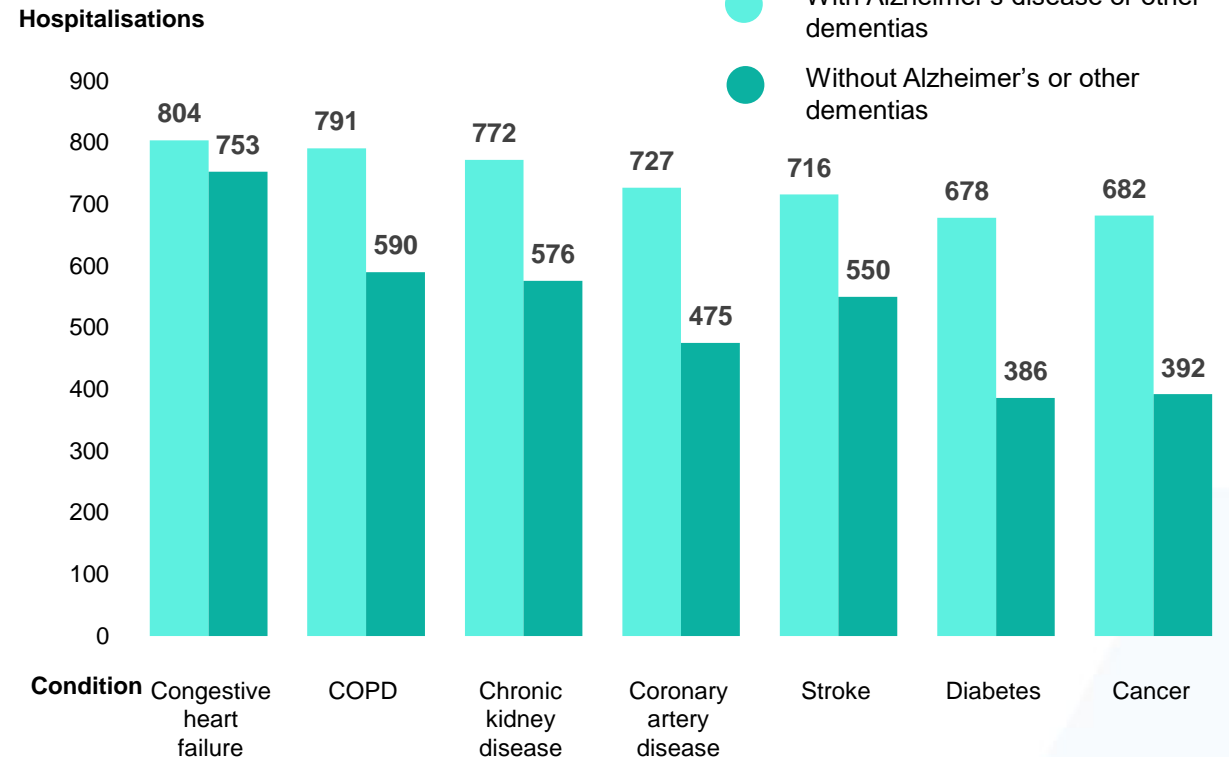
Distribution of Aggregate Costs of Care by Payment Source for Americans Age 65 and Older with Alzheimer's or Other Dementias, 2021

Adapted from Alzheimer's Disease Facts and Figures. Alzheimers Dement., 2021

The Impact on Society



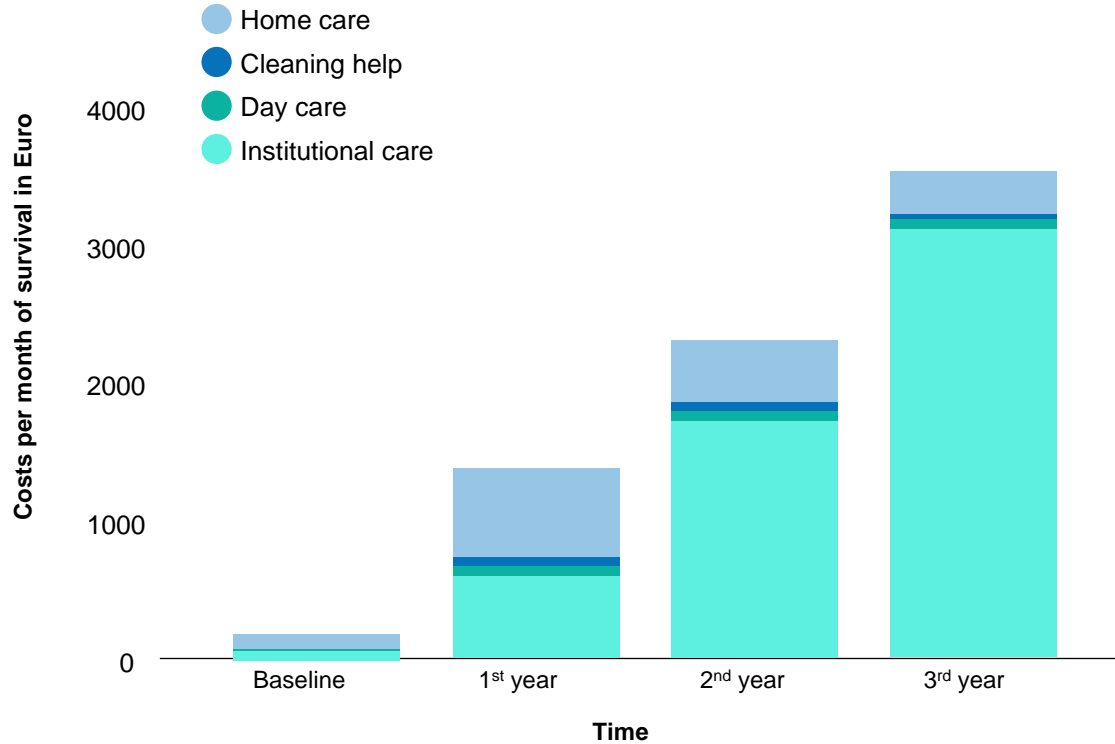
Percentage Changes in ED Visits per 1,000 Fee-for-Service Medicare Beneficiaries for Selected Health Conditions Between 2008 and 2018



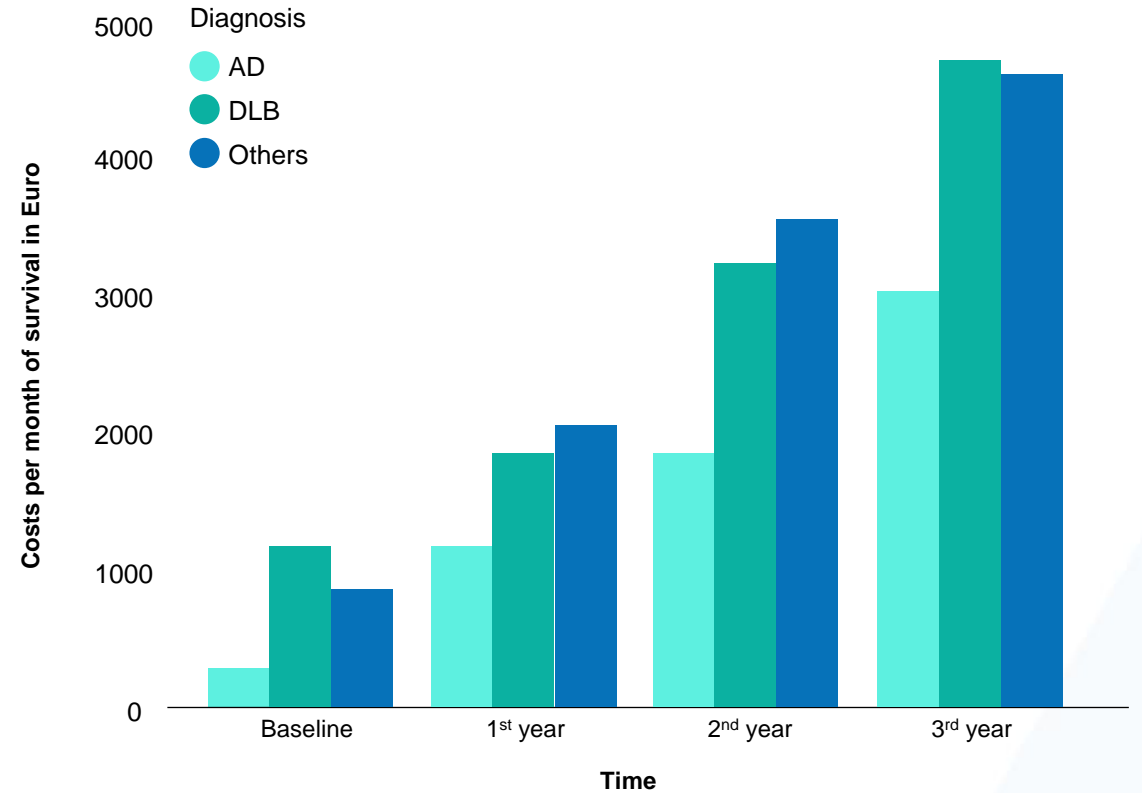
Hospital Stays Per 1,000 Medicare Beneficiaries age 65 and Older with Specified Coexisting Medical Conditions, with and without Alzheimer's or Other Dementias, 2014

Adapted from *Alzheimer's Disease Facts and Figures. Alzheimers Dement., 2021*

The Impact on Society



Mean costs per month of survival, specified by type of service.



Mean costs per months of survival, specified by diagnosis

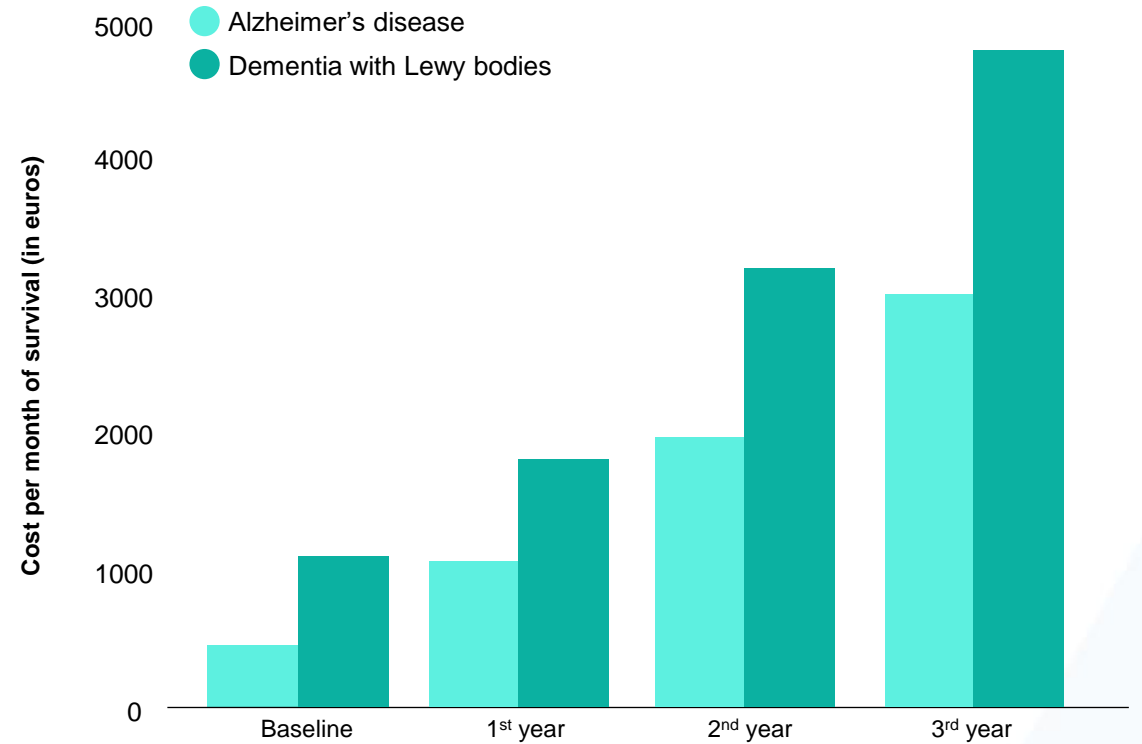
“others” = VaD, PDD, FTD, and alcoholic dementia
 Number of cases at baseline: AD = 73, DLB = 24, others = 12
 Number of cases at end of study: AD = 59, DLB = 18, others = 10

Adapted from Vossius et al, Am J Geriatr Psychiatry. 2014

The Impact on Society

- Progression to severe dementia and admission to nursing homes are costly;
- Predictors for increased cost:
 - Living alone;
 - Functional decline;
 - Comorbidity.
- Factors of increased cost in LBD compared to AD:
 - Hospital and nursing home admissions;
 - Pharmacotherapy;
 - Increased use of outpatient care;
 - Increased use of community services;
 - Increased of informal help.

Adapted from Mueller et al., *Lancet Neurol.* 2017



Mean costs of care per month of survival from dementia diagnosis for patients with Alzheimer's disease and dementia with Lewy bodies

The Impact on Society



A Commercial Database

DLB Feature	Total	Prescription	Outpatient	Inpatient	ER	Other
Autonomic	+\$21,076	+\$1,215	+\$886	+\$14,273	+\$788	+\$3,915
Delusions	+\$22,615	-\$1,303	-\$3,217	+\$17,882	+\$2,755	+\$6,498
Falls	+\$41,474	+\$1,201	+\$2,543	+\$28,575	+\$1,506	+\$7,650
Fluctuating cognition	+\$41,459	+\$1,484	+\$64	+\$29,012	+\$3,471	+\$7,428
Mood	+\$24,379	+\$3,231	+\$5,486	+\$10,852	+\$1,715	+\$3,095
Motor	+\$15,610	-\$223	-\$323	+\$12,440	+\$713	+\$3,002
RBD	-\$14,054	-\$1,606	-\$451	-\$6,690	-\$1,234	-\$4,074
Visual hallucinations	+\$24,173	-\$2,552	+\$1,765	+\$14,467	+\$1,280	+\$9,214

B Medicare Database

DLB Feature	Total	Prescription	Outpatient	Inpatient	ER	Other
Autonomic	+\$14,518	+\$182	+\$2,124	+\$7,189	+\$594	+\$4,430
Delusions	+\$522	-\$468	-\$547	+\$812	+\$342	+\$383
Falls	+\$12,323	-\$174	+\$450	+\$4,612	+\$1,119	+\$6,317
Fluctuating cognition	+\$22,924	-\$61	+\$1,864	+\$10,723	+\$1,393	+\$9,006
Mood	+\$12,284	+\$620	+\$908	+\$4,914	+\$842	+\$5,001
Motor	+\$10,078	+\$932	+\$1,189	+\$3,425	+\$450	+\$4,081
RBD	-\$8,640	-\$94	+\$1,332	-\$4,657	-\$535	-\$4,686
Visual hallucinations	-\$2,104	+\$74	+\$237	-\$878	+\$250	-\$1,786

Adapted from Espinosa et al., JAMDA. 2020



Resources and Care



Resources and Care

Patients and caregivers need:

Information

- About the disease (i.e., the precise name of the disease);
- About its nature (i.e., neurodegenerative, can fluctuate over time, but will progress inevitably);
- About its manifestations (i.e., not just cognition and movements, neuropsychiatric manifestations, dysautonomia, etc.);
- About its outcome (i.e., currently uncurable, but treatable).

Personalized, longitudinal, and holistic care

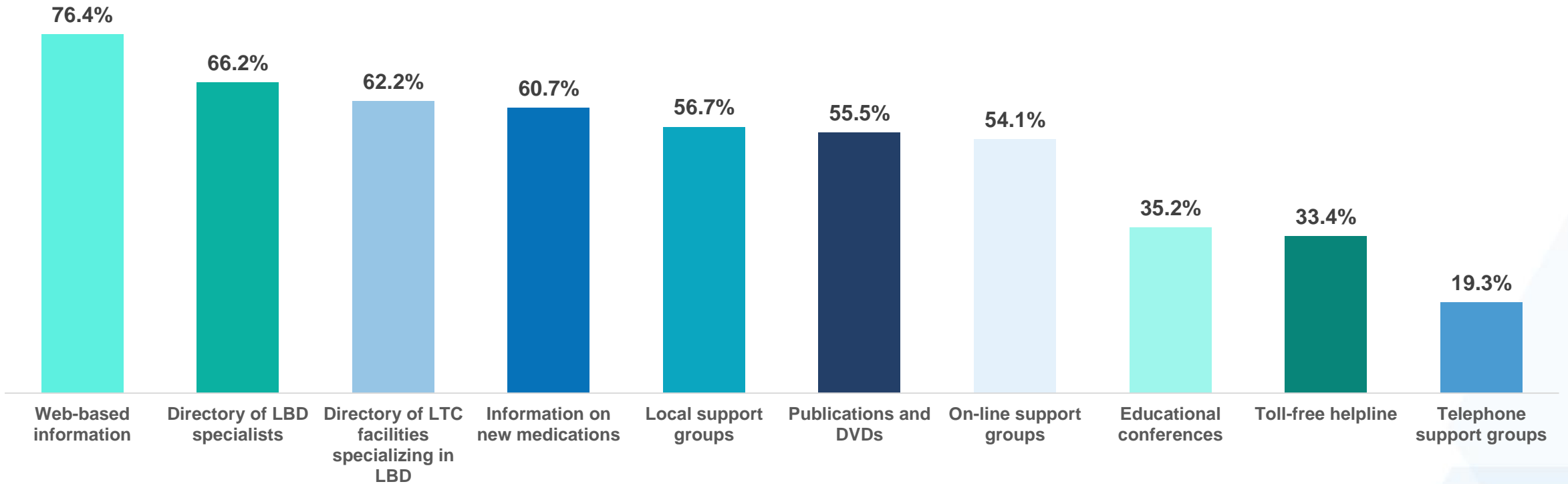
- Prioritization of the manifestations to address first;
- Simplification of medical care;
- Less fragmented care.

Preventive medicine and advance care planning

- Prevention of hospitalisations;
- Advance care planning and advanced directives;
- Enhanced end-of-life care.

Resources and Care

Most requested services by LBD caregivers:



Adapted from Galvin et al., Alzheimer Dis Assoc Disord. 2010



Resources and Care

- BrainXchange™ (www.brainxchange.ca)
- Alzheimer Society (www.alzheimer.ca)
- Lewy Body Dementia Association (www.lbda.org)
- Lewy Body Dementia Resource Center (www.lewybodyresourcecenter.org)
- Lewy Body Society (www.lewybody.org)
- National Institutes of Health (<https://order.nia.nih.gov>)



Conclusion



Key Messages

1

Lewy body dementia has several clinical manifestations, including cognitive, neuropsychiatric, motor, and autonomic manifestations, which all can affect negatively patients' quality of life.

2

Neuropsychiatric symptoms are the strongest predictors for poor QoL in patients and caregivers, as well as for hospital and LTC admissions, while cognitive deficits are the strongest predictors for functional decline.

3

Lack of awareness about the disease by patients, caregivers, and healthcare providers is frequently reported as an obstacle for quality of care and enhanced knowledge can mitigate the impact of the disease.

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Thank you!

Questions

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