

# Dementia with Lewy Bodies-Mild Cognitive Impairment: Beyond Medications

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# Disclosures

- PI for UF's Lewy Body Dementia Association Research Center of Excellence
- Member, Scientific Advisory Committee for Lewy Body Dementia Association
- Evidence-based medicine methodology consultant for the AAN
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- Royalties for publication of Parkinson's Disease: Improving Patient Care (Oxford University Press)

# Vocabulary

- **Lewy body dementia:** Umbrella term including clinically-diagnosed dementia with Lewy bodies and PD dementia
- **Dementia with Lewy bodies:** Dementia that occurs before or concurrently with parkinsonism or within 1 year of onset of motor symptoms
  - Parkinsonism not required for diagnosis
- **Parkinson's disease dementia:** Dementia starting  $\geq 1$  year after a diagnosis of Parkinson's disease
- **Lewy body disease:** Pathological diagnosis

**Table 1.** Clinical Features That Have Been Suggested as Indicative of Early LB Disease.

Early symptoms (typically 5-15 years pre-dementia)

- Decreased sense of smell
- REM sleep behavior disorder
  - Nightmares
  - Crying or shouting during sleep
  - Limb movements during sleep

- Constipation
- Dizziness on standing
- Urinary incontinence
- Increased saliva
- Increased sweating

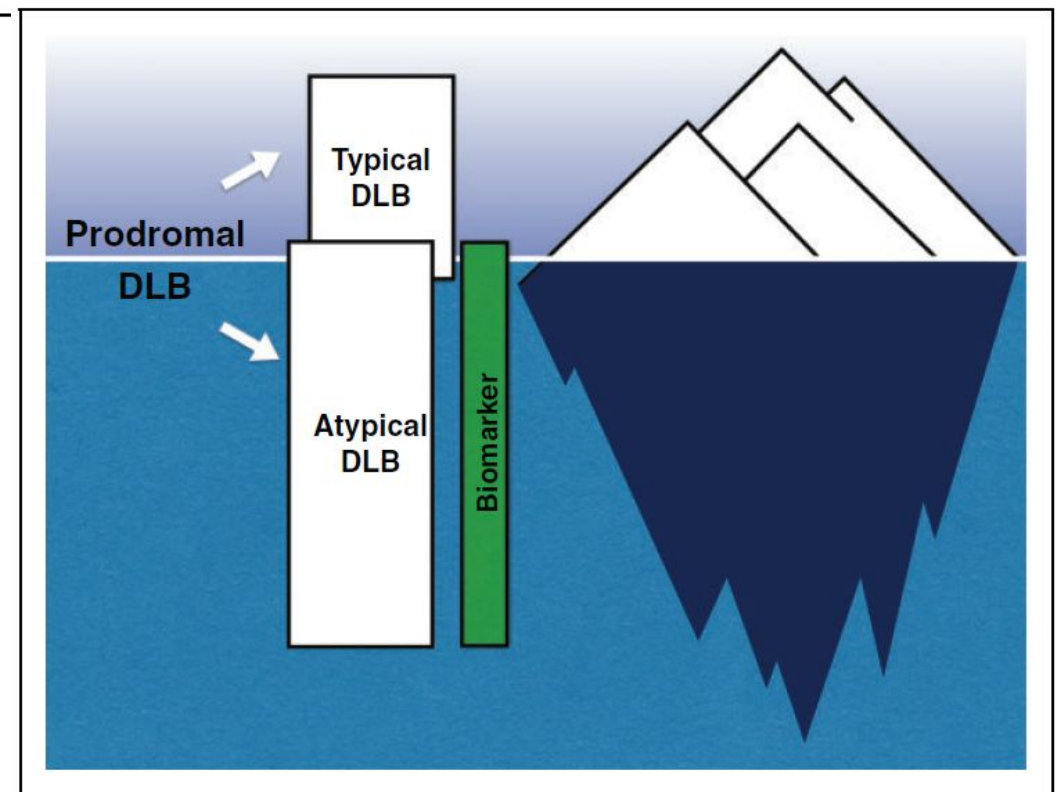
Intermediate symptoms

- Delirium: provoked or unexplained
- Late onset psychiatric disorder
  - Psychosis
  - Depression

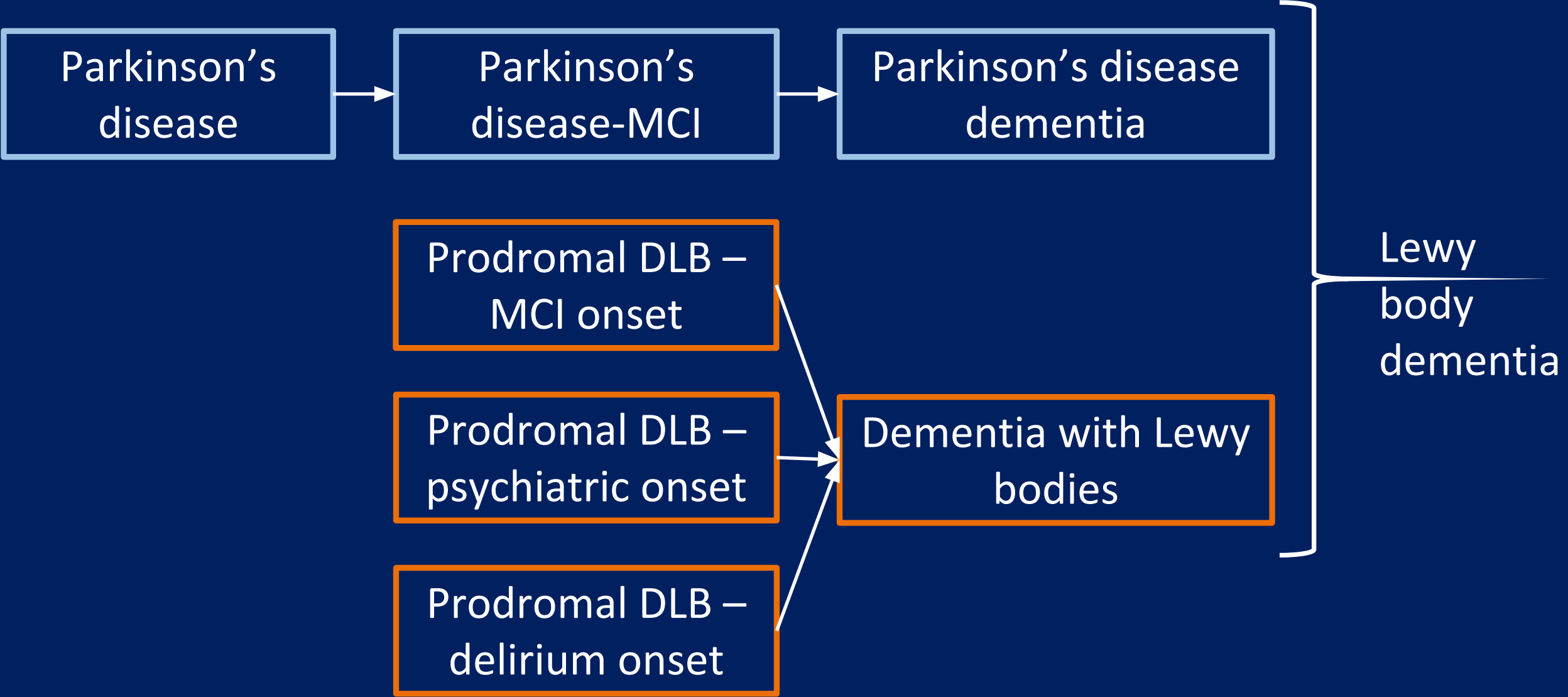
Later symptoms

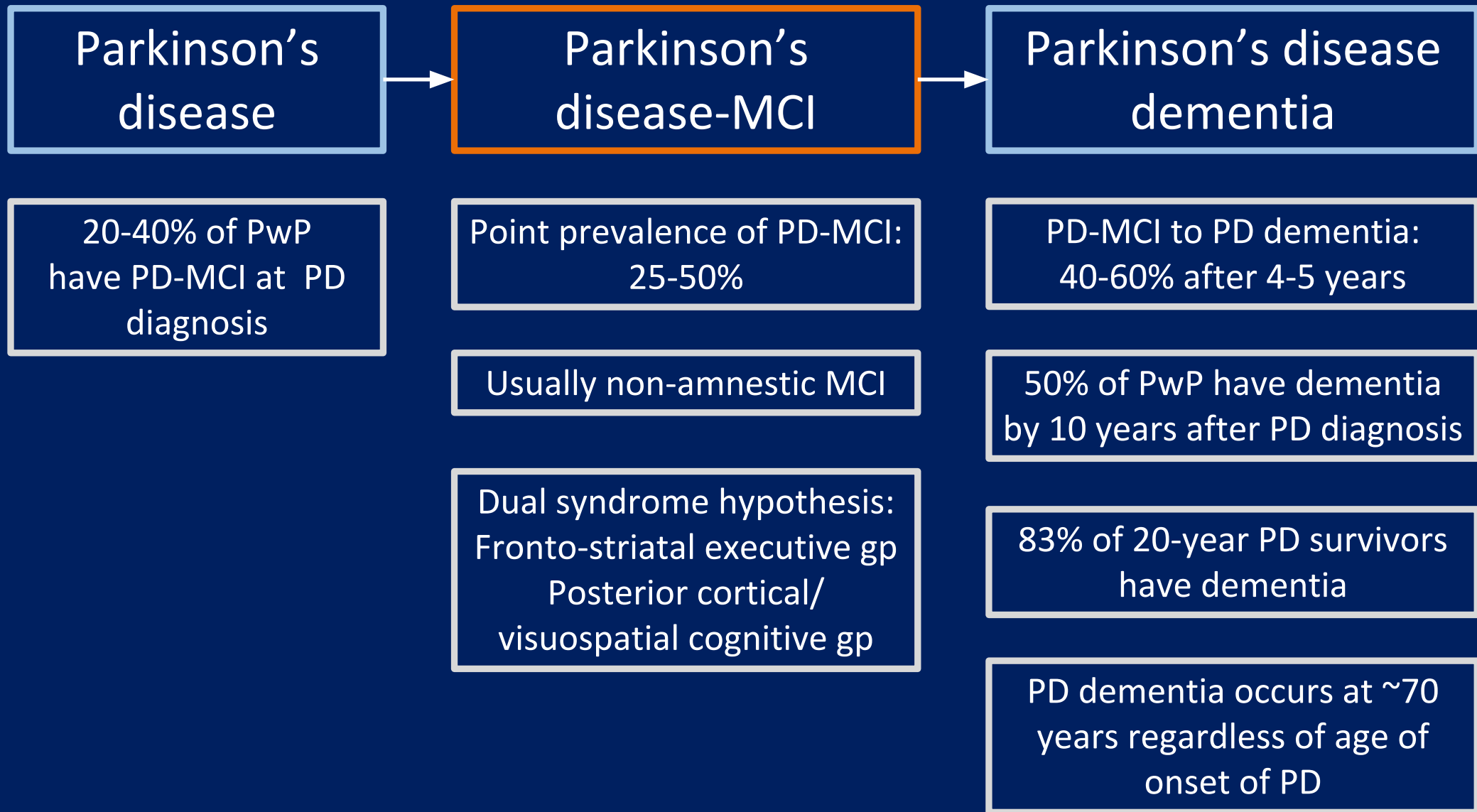
- Cognitive impairment (nonamnestic mild cognitive impairment)
- Visual hallucinations, illusions, and misconceptions
- Parkinsonism

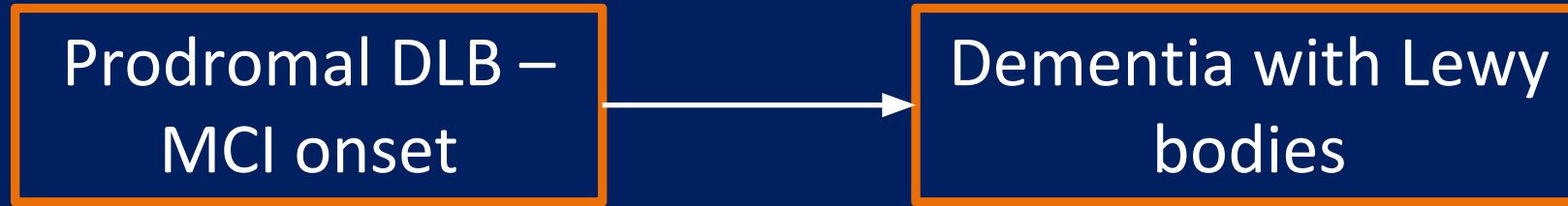
Abbreviations: LB, Lewy body; REM, rapid eye movement.



**Figure 1.** Schematic of the relationships between the prodromal and dementia stages of DLB.







- Non-amnestic MCI: 10x more likely to develop clinically probable DLB than clinically probable AD dementia
  - Non-amnestic MCI annual rate of transition to DLB: 20%
- MCI to probable DLB
  - Baseline attention and/or visuospatial deficits
  - REM sleep behavior disorder
  - Fluctuations
  - Subtle/mild parkinsonism

# DLB Diagnosis

- Likely underestimate: 1 in 3 DLB cases may be missed
- 68% saw more than 3 doctors before diagnosis (LBD)
  - 15% saw more than 5 different physicians
- Mean number of office visits to get diagnosis:  $3.7 \pm 1.9$ 
  - 33% required more than 6 office visits
  - 51% were diagnosed within the first year
  - >2 years from the start of symptoms for 31% to receive an LBD diagnosis



# Treating DLB-MCI Beyond Medications #1: Give the Diagnosis

Reasons to Give Dementia Diagnosis	Reasons to Give MCI Diagnosis
Understanding what is happening	Understanding what is happening
Validation that something is wrong	Validation that something is wrong
Establishing a treatment plan, connecting to resources	Establishing a treatment plan, connecting to resources
Improved decision-making, future planning	<b>Improved decision-making, future planning</b>
Right to know	Right to know
Improved family patients with person with dementia	

Giving the diagnosis is one of the 6 AAN quality improvement measures for MCI

van den Dungen P, et al. Preferences regarding disclosure of a diagnosis of dementia: a systematic review. *Int Psychogeriatr.* 2014;26:1603-1618.  
 Connell CM, et al. Attitudes toward the diagnosis and disclosure of dementia among family caregivers and primary care physicians. *Gerontologist.* 2004;44:500-507.  
 Karnieli-Miller O, et al. Expectations, experiences, and tensions in the memory clinic: the process of diagnosis disclosure of dementia within a triad. *Int Psychogeriatr.* 2012;24:1756-1770.  
 Riva M, et al. Diagnosis disclosure and advance care planning in Alzheimer disease: opinions of a sample of Italian citizens. *Aging Clin Exp Res.* 2014;26:427-434.  
 Petersen RC, et al. Practice guideline update: Mild cognitive impairment. *Neurology.* 2018;90:126-135.

# Treating DLB-MCI Beyond Medications #2: Tell Them What to Expect

- MCI progression
  - PD-MCI to PD dementia: 40-60% after 4-5 years
  - Non-amnestic MCI to DLB: 20% annually

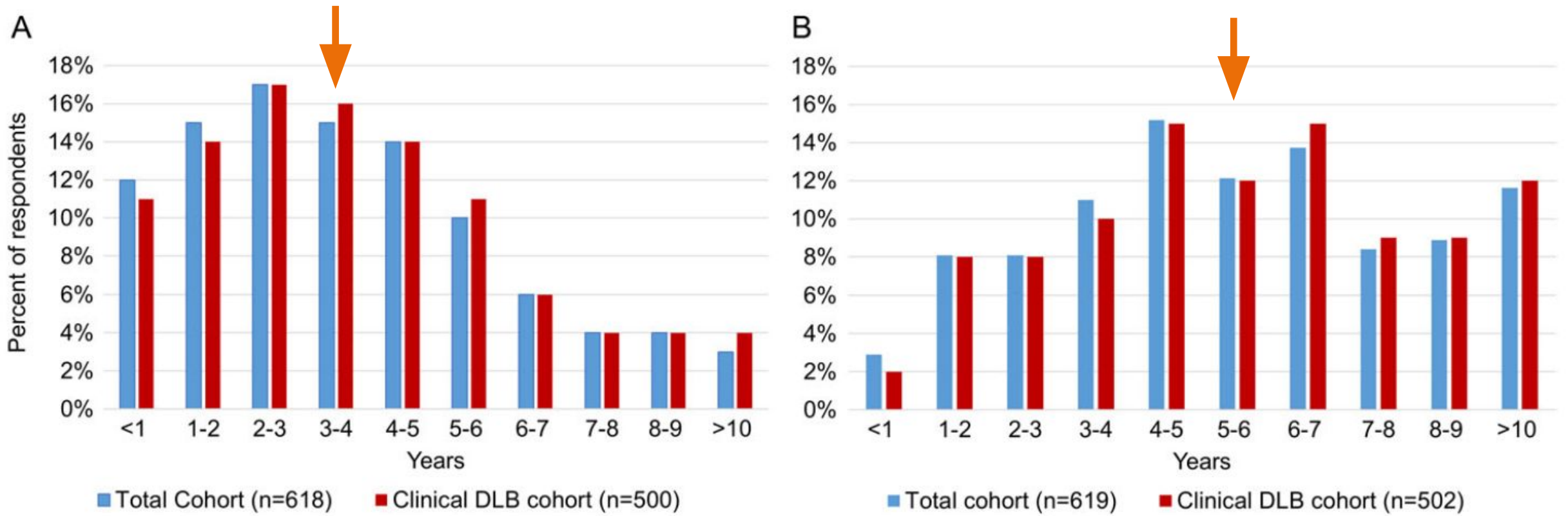


Figure 1. Respondent-reported time from (A) diagnosis to death and (B) symptom onset to death in individuals with dementia with Lewy bodies.

- Other clinical cohorts: 3.2-, 3.7-, 4.1- year disease durations
- Median 5.3-year duration between symptom onset and death

**Table 2. Reported Causes of Death in People with Dementia with Lewy Bodies (DLB)**

Cause of Death	Total Cohort, n = 646	Clinical DLB Cohort, n = 524
	n (%)	
DLB or failure to thrive	464 (72)	369 (70)
Failure to thrive (stopped eating, drinking)	421 (65)	334 (63)
DLB (no other cause listed) <sup>1</sup>	43 (7)	35 (7)
Pneumonia or aspiration	148 (23)	121 (23)
Pneumonia, complications from pneumonia	105 (16)	89 (17)
Aspiration or swallowing difficulties <sup>1</sup>	43 (7)	32 (6)
Medical condition <sup>1</sup>	125 (19)	103 (20)
Infection (not pneumonia)	51 (8)	40 (8)
Heart	25 (4)	22 (4)
Stroke	21 (3)	17 (3)
Lung	10 (2)	9 (2)
Cancer	10 (2)	8 (2)
Colon	6 (1)	6 (1)
Kidney	4 (0.6)	4 (0.8)
Cardiorespiratory	4 (0.6)	3 (0.6)
Neurological	3 (0.5)	3 (0.6)
Other	3 (0.5)	3 (0.6)
Fall, complications from a fall	65 (10)	49 (9)
Antipsychotic related <sup>1</sup>	8 (1)	7 (1)
Suicide <sup>1</sup>	5 (0.8)	4 (0.8)

<sup>1</sup>These include write-in responses under “other medical” and “other” fields rather than offered categories.

# Treating DLB-MCI Beyond Medications #3: Connect to Research

## Practice guideline update summary: Mild cognitive impairment

Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology

Ronald C. Petersen, MD, PhD, Oscar Lopez, MD, Melissa J. Armstrong, MD, MSc, Thomas S.D. Getchius, Mary Ganguli, MD, MPH, David Gloss, MD, MPH&TM, Gary S. Gronseth, MD, Daniel Marson, JD, PhD, Tamara Pringsheim, MD, Gregory S. Day, MD, MSc, Mark Sager, MD, James Stevens, MD, and Alexander Rae-Grant, MD

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### *Recommendation A7b*

For interested patients, clinicians may discuss the option of biomarker research or refer patients, or both, if feasible, to centers or organizations that can connect patients to this research (e.g., subspecialty centers, Trial Match, ClinicalTrials.gov) (Level C).

### *Recommendation*

For patients diagnosed with MCI who are interested in pharmacologic treatment, clinicians may inform these patients of centers or organizations that can connect patients to clinical trials (e.g., subspecialty centers, Trial Match, ClinicalTrials.gov) (Level C).

- DLB Consortium (U01, Leverenz)
- ADRCs
- Evaluate NYX-458 in Subjects With MCI-PD (NCT04148391)
  - Small module that modulates NMDA receptors
  - Phase 2
    - Primary outcome = safety
  - Posted 11/1/2019; not yet recruiting

# Treating DLB-MCI Beyond Medications #4: Therapy/Exercise

## REVIEW

### International Parkinson and Movement Disorder Society Evidence-Based Medicine Review: Update on Treatments for the Motor Symptoms of Parkinson's Disease

Interventions for general motor symptoms			
Cannabidiol		<i>Insufficient evidence</i>	<i>Investigational</i>
Bee venom		<i>Nonefficacious</i>	<i>Not useful</i>
Physiotherapy		<i>Likely efficacious</i>	<i>Clinically useful</i>
Movement strategy–exercise based		<i>Insufficient evidence</i>	<i>Possibly useful</i>
Movement strategy–technology based		<i>Insufficient evidence</i>	<i>Investigational</i>
Formalized patterned exercises		<i>Insufficient evidence</i>	<i>Possibly useful</i>
Speech therapy		Insufficient evidence for speech <i>Insufficient evidence for swallowing problems</i>	Possibly useful (overall)
Occupational therapy		<i>Insufficient evidence</i>	Possibly useful

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### Recommendation B5

#### Rationale

Although long-term studies are unavailable, 6-month studies suggest a possible benefit of twice-weekly exercise for cognition in MCI. Exercise also has general health benefits and generally limited risk.

#### Recommendation

For patients diagnosed with MCI, clinicians should recommend regular exercise (twice/week) as part of an overall approach to management (Level B).

Cochrane Database of Systematic Reviews

## Physiotherapy versus placebo or no intervention in Parkinson's disease

Cochrane Systematic Review - Intervention | Version published: 10 September 2011  
<https://doi.org/10.1002/14651858.CD002817.pub4>

## Long-term effects of exercise and physical therapy in people with Parkinson disease

Margaret K. Mak<sup>1</sup>, Irene S. Wong-Yu<sup>1</sup>, Xia Shen<sup>2</sup> and Chloe L. Chung<sup>1</sup>

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# Treating DLB Beyond Medications #5: Prepare Them for the Unexpected

- 64% caregivers reported crisis situation in prior year (survey n=962)
- Most frequent place to seek help for person with LBD:
  - Hospital emergency room (296 visits, 73%)
  - Emergency medical services or law enforcement
  - Fifty seven caregivers reported the need for inpatient psychiatric care

# Other Hospital Details

- Antipsychotic medications: 38% of hospitalizations
  - New or increased in 19%
  - Quetiapine most common, others also used
- Longer length of stay if:
  - Delirium present at admission (6 days vs 3 days,  $p=0.002$ )
  - In-hospital delirium (6 days vs 3 days,  $p<0.001$ ), pneumonia (6 days vs 4 days,  $p=0.007$ ), falls (8 days vs 4 days,  $p=0.011$ )
  - Antipsychotic administration other than quetiapine or clozapine (7.5 days vs 4 days,  $p=0.001$ )
- 1/3 hospitalizations resulted in a transition to a higher level of care
  - 15% (27/178): death or hospice
  - Inpatient antipsychotic use other than quetiapine or clozapine: increased odds of transition to higher level of care (OR 2.41; 95 CI 1.06, 5.47)



# Causes and outcomes of hospitalization in Lewy body dementia: A retrospective cohort study

C. Chauncey Spears<sup>a</sup>, Amir Besharat<sup>a</sup>, Erin Hastings Monari<sup>a</sup>, D Leonardo Almeida<sup>a</sup>, Melissa J. Armstrong<sup>a,\*</sup>

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- 117 patients with LBD admitted over 2-year period
  - 69%: 1 hospitalization
  - 20%: 2 hospitalizations
  - 11%: >2 hospitalizations

Reason	Frequency
Hallucinations or confusion	40%
Falls	24%
Infection	23%
<i>Urinary tract infection</i>	11%
<i>Pneumonia</i>	7%
<i>Sepsis</i>	6%
Gastrointestinal disease	7%
Cardiac disease	6%
Respiratory illness	5%
Failure to thrive/failure to cope	5%
Genitourinary disorder	3%
Elective surgery	3%

# #6: Make Decisions Together

## COMMENTARY

### Shared decision making in mild cognitive impairment

Andrea M. Mejia, MA, Glenn E. Smith, PhD, ABPP-cn, Meredith Wicklund, MD, and Melissa J. Armstrong, MD, MSc

Neurology: Clinical Practice April 2019 vol. 9 no. 2 160-164 doi:10.1212/CPJ.0000000000000576

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**Table 2** Strategies to improve SDM in MCI

Category	Facilitators of SDM for persons with MCI
<b>Overall approach</b>	Assess the presence of MCI vs dementia
	Clarify patient preferences regarding SDM, CP involvement
	Establish continuity of care
	Hold discussions in a quiet environment without distractions
	Allow adequate time
	Engage CPs with patient's permission
	Re-evaluate over time
<b>Value solicitation</b>	Identify short-term and long-term values and preferences
	Encourage patients to discuss values with identified healthcare surrogate decision makers/proxies
<b>Presentation of medical evidence, decision making</b>	Identify cognitive weaknesses and provide additional support
	Use print tools (e.g., guideline patient summaries, DAs)
	Employ teach-back methods
	Engage CPs with patient's permission

Abbreviations: CP = carepartner; DA = decision aid; MCI = mild cognitive impairment; SDM = shared decision making.

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- Mangurian Clinical-Research Headquarters for Lewy Body Dementia at the University of Florida
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- Lewy Body Dementia Association Research Center of Excellence
- Other funding:
  - AHRQ K08HS24159
  - 1Florida ADRC pilot grant (AG047266)
  - Michael J. Fox Foundation

# Summary

- MCI in Lewy body diseases: PD-MCI, DLB-MCI
- MCI progression
  - PD-MCI to PD dementia: 40-60% after 4-5 years
  - Non-amnestic MCI to DLB: 20% annually
- Treating PD/DLB MCI beyond medications
  - Give the diagnosis
  - Tell them what to expect
  - Connect them to research
  - Therapy/exercise
  - Prepare them for the ~~un~~expected
  - Make decisions together