



Duke Dementia Family Support Program

Caregiver Connections

An Educational Webinar Series with the Experts

The presentation will begin shortly.

dukefamilysupport.org

919-660-7510



Emerging Diagnostic Tools for Alzheimer's Disease & Dementia

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Outline

- Background & definitions
- The complexities of testing
- Currently-available tests
- Future directions



What do we mean by MCI and dementia?

Normal Aging

- You have occasional lapses in memory. You forget someone's name but remember it later.
- You takes more time to learn new information or a new skill but can still do it.
- You occasionally miss a payment or forget to take a medication.



Mild Cognitive Impairment (MCI)

- Significant change in memory and thinking that you and others notice.

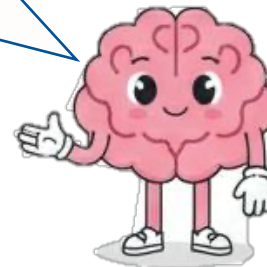
Is Alzheimer's the same as dementia?

psychiatric problem.



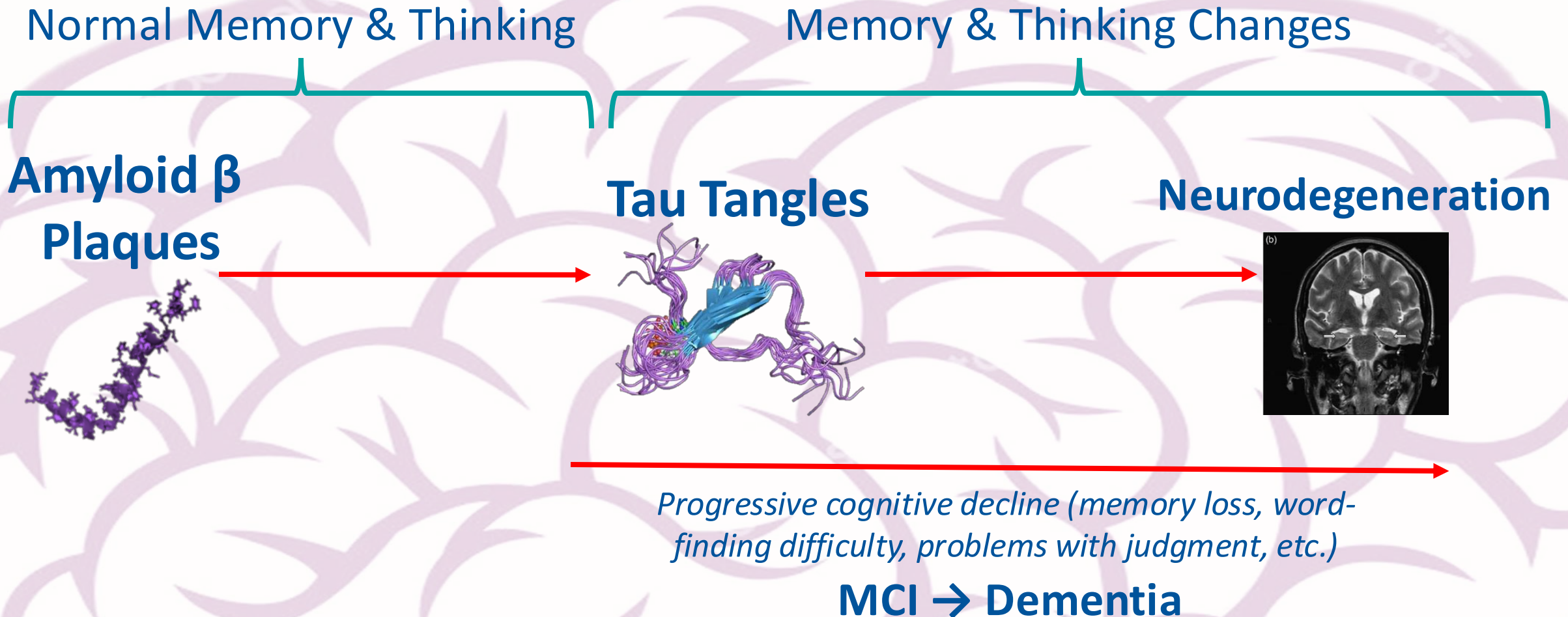
Dementia

- You have changes in memory and thinking that others notice.
- Changes make it so it's difficult for you to hold down a job and you need assistance to manage your finances and medications.
- Dementia Stages
 - Mild: Need help with finances
 - Moderate: Need help dressing/bathing
 - Severe: Not talking or moving around much



Alzheimer's Disease

The most common cause of dementia

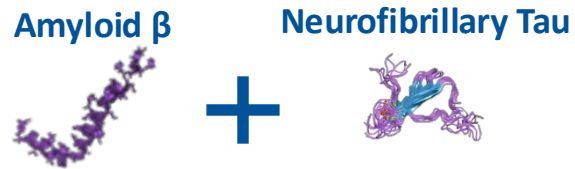




What diseases cause MCI/dementia?

Alzheimer's Disease

- Accounts for 60-80% of dementia
- Insidious and progressive short-term memory decline.
- Defined as the build up of two proteins:



Vascular Cognitive Impairment

- Often seen in combination with Alzheimer's.
- Dementia primarily caused by cerebrovascular disease or impaired brain blood flow.

Lewy Body Disease

- Accounts for 30% of dementia
- Progressive cognitive decline with cognitive fluctuations, visual hallucinations, REM sleep behavior disorder, and movement changes.



Many also have
Alzheimer's
Disease

Frontotemporal Disease

- Symptoms often develop at a younger age (50s). Accounts for ~10% of dementia in ≤ 65 years
- Can cause changes in behavior and problems with language.



And Others



Complexities of Testing

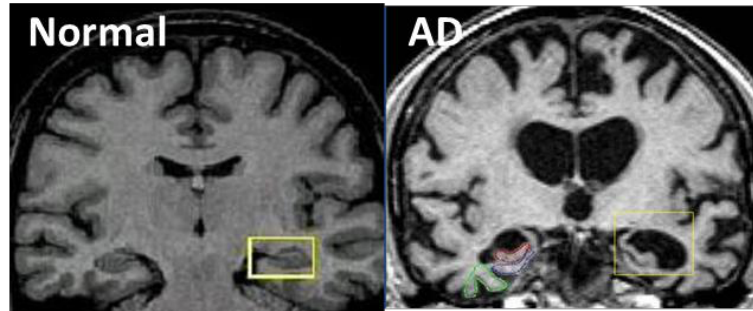
- No test is perfect. Testing should be used carefully in conjunction with information about symptoms, risk factors, and how common the disease is (prevalence).
- Tests answer different types of questions:
 - I don't have memory problems. Am I at risk of Alzheimer's disease? (*risk test*)
 - I have memory problems. Are they due to Alzheimer's disease? (*diagnostic test*)
 - I have Alzheimer's disease. How quickly will my symptoms progress? (*prognostic test*)
 - I have Alzheimer's disease. Will this new treatment help me? (*predictive test*)
- Some tests can answer more than one question, but separate studies are required to validate a test for each question.



Diagnosis of Alzheimer's Disease

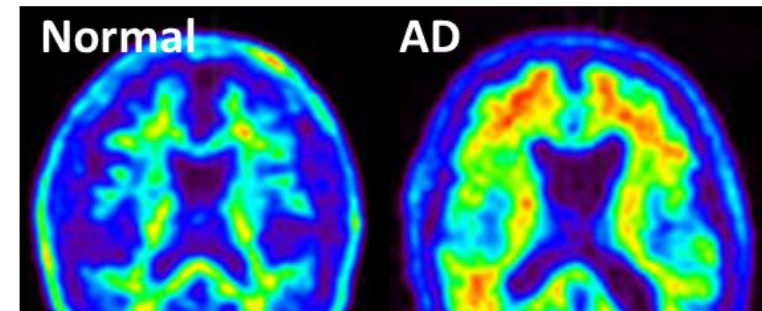
Imaging

MRI



Identifies neurodegenerative changes (damage to the brain) often seen with Alzheimer's disease.

Amyloid PET

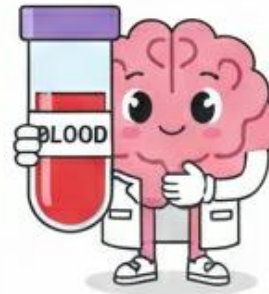


Tracer binds to the amyloid plaques and lights up, making the amyloid plaques visible.

Fluid

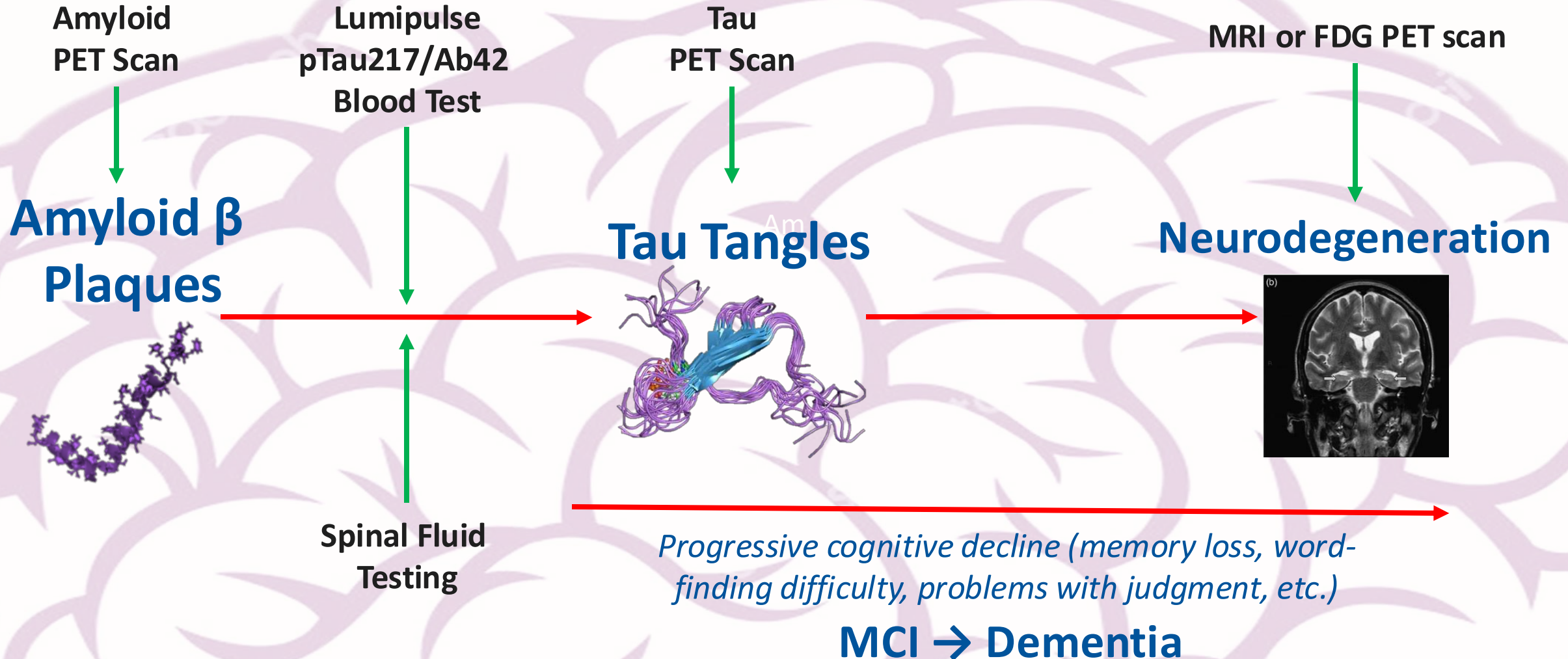


Measure Alzheimer's disease proteins in spinal fluid.



FDA approved the first blood test for Alzheimer's in May.

Alzheimer's Disease





Diagnosing other Causes of Dementia

Alzheimer's Disease

- Accounts for 60-80% of dementia
- Insidious and progressive short-term memory decline.
- Can be diagnosed in people with symptoms using imaging, spinal fluid, and now blood testing.

Vascular Cognitive Impairment

- Often seen in combination with Alzheimer's.
- Dementia primarily caused by cerebrovascular disease or impaired cerebral blood flow.
- Diagnosed based on imaging findings.

Lewy Body Disease

- Accounts for 30% of dementia
- Progressive cognitive decline with cognitive fluctuations, visual hallucinations, REM sleep behavior disorder, and movement changes.
- Diagnosed in people with symptoms using a skin biopsy, spinal fluid, or imaging testing.

Frontotemporal Disease

- Symptoms often develop at a younger age (50s). Accounts for ~10% of dementia in ≤ 65 years
- Can cause changes in behavior and problems with language.
- Diagnosed in people with symptoms using imaging and genetic testing.



Lumipulse pTau217/Ab42 Blood Test

- This test predicts whether a person over the age of 55 who has changes in memory and thinking concerning for Alzheimer's disease would have a positive amyloid PET scan.
- This test is not validated to predict whether someone without memory and thinking changes will develop Alzheimer's disease.
- This test will likely be covered by Medicare in early 2026.



Lumipulse pTau217/Ab42 Blood Test

- Measures two blood proteins linked to AD:
 - Ab42 is the sticky form of amyloid that clumps up in the brain in Alzheimer's disease. As Ab42 clumps up in the brain, levels go down in spinal fluid and blood.
 - pTau217 is a form of the tau protein that has been altered by increasing levels of amyloid plaques in the brain. pTau217 goes up in spinal fluid and blood in Alzheimer's disease.
 - We look at the ratio of the two proteins. A high ratio means that person would very likely have a positive amyloid PET scan.
- When used in the appropriate context:
 - A person with a positive result has a 92% chance of having a positive amyloid PET scan.
 - A person with a negative result has a 97% chance of having a negative amyloid PET scan.
 - 20% of people who get this test will have an intermediate result: not clearly positive or negative.



Lumipulse pTau217/Ab42 Blood Test

- This test determine whether there is Alzheimer's disease changes in the brain.
- A positive test result does not mean someone has dementia. Dementia is diagnosed when memory and thinking changes are present and interfere with day-to-day responsibilities.
- The test does not provide information about stage or the rate of progression.
- No test is perfect. A positive test result in someone without symptoms is likely a false positive.
- People who receive an intermediate test result will often need additional testing to confirm the diagnosis.



Test Report

pTau-217/Beta Amyloid 42 Ratio

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
pTau-217 ⁰¹	0.396 The reportable range of this assay is 0.041 to 10.000 pg/mL. The analytical measuring interval is 0.047 to 10.000 pg/mL.		pg/mL	Not Estab.
Beta-amyloid 42 ⁰¹	20.0 The reportable range of this assay is 0.2 to 500.0 pg/mL. The analytical measuring interval is 0.8 to 500.0 pg/mL.		pg/mL	Not Estab.
pTau-217/AB42 Ratio	0.01980	Negative <0.00371 Indeterminate 0.00371-0.00737 Positive >0.00737		
Interpretation ⁰¹	POSITIVE: A test result >0.00737 is a positive result which is consistent with patients who are likely to have amyloid pathology associated with Alzheimer's disease. This result does not establish a diagnosis of Alzheimer's disease or other cognitive disorders. The Lumipulse(R) G pTau-217/Beta-Amyloid 42 Ratio, plasma is indicated for adult patients, aged 50 years and older, presenting at a specialized care setting with signs and symptoms of cognitive decline. The ratio value reported is calculated in accordance with guidance documented in the FDA-approved instructions for use (IFU) for this assay. Please consult the official IFU for more information.			



Intermediate Results – 20% of Results

pTau-217/AB42 Ratio

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
pTau-217 ^{A, 01}	0.192 The quantitative range of this assay is 0.060 to 10.000 pg/mL.		pg/mL	Not Estab.
Beta-amyloid 42 ^{A, 01}	15.0 The quantitative range of this assay is 1.0 to 230.0 pg/mL.		pg/mL	Not Estab.
pTau-217/AB42 Ratio	0.0128			
		Low	<0.0086	
		Intermediate	0.0086 - 0.0152	
		High	>0.0152	
Interpretation ⁰¹	An intermediate pTau-217/Beta Amyloid 42 Ratio should be interpreted within the context of all clinical findings in symptomatic patients. Additional testing such as amyloid-positron emission tomography (PET) imaging or cerebrospinal fluid (CSF) biomarker assays is recommended to aid in the identification or exclusion of amyloid-related pathology, which is associated with Alzheimer's disease. Both pTau-217 and Beta Amyloid 42 are well documented indicators of pathological changes associated with Alzheimer's disease. Their ratio provides a higher level of sensitivity and specificity than their individual measurements alone. The performance of this test meets the criteria for a confirmatory test as defined by an international consortium of Alzheimer's experts (1). This test should not be used in asymptomatic individuals. (1) Schindler, Suzanne E., et al. "Acceptable performance of blood biomarker tests of amyloid pathology-recommendations from the Global CEO Initiative on Alzheimer's Disease." Nature Reviews Neurology 20.7 (2024): 426-439.			



Pitfalls of Diagnostic Testing

- **No test is perfect.** The performance of a test is described by its sensitivity and specificity.
- Sensitivity = “catch rate.” Among people who have the disease, how often is the test positive?
- Specificity = “false-alarm control.” Among people without the disease, how often is the test negative?

		Disease Status	
		Have the disease	Don't have disease
Test Result	+	True Positives	False Positives
	-	False Negatives	True Negatives

A good test generally has >90% sensitivity and specificity in the right context.



Pitfalls of Diagnostic Testing

- **No test is perfect.** Our test is 90% sensitive and 90% specific for Alzheimer's disease in people with memory problems.
- Around 15% of people age 60 to 69 will have Alzheimer's disease pathology.
- What happens when we test 10,000 randomly-selected people aged 60-69?

		Disease Status	
		Alzheimer's Disease	No Alzheimer's Disease
Test Result	+	1,350 (True Positive)	850 (False Positive)
	-	150 (False Negative)	7,650 (True Negative)

If the test is positive, it's truly positive 6 in 10 times. 4 in 10 positive results are false positives.



Summary

- We now have a variety of testing options to diagnose Alzheimer's disease and other causes of dementia.
- Tests should be used in people who have symptoms that are consistent with a particular disease (high pre-test probability).
- No test is perfect. People can have false positive test results and false negative test results. Using tests appropriately can reduce the chance that a positive test result is a false positive.
- The Lumipulse pTau217/Ab42 test is approved for ages 55 and up who have symptoms concerning for Alzheimer's disease.
- It does not predict the risk of developing Alzheimer's disease or provide information about stage or the rate of progression.



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Thank you for joining us today!

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