

The background of the slide is a soft, multi-colored watercolor wash in shades of pink, blue, and yellow, all contained within a thin red rectangular border. The text 'Lilly ConnectAD™' is centered horizontally and rendered in a vibrant red color. 'Lilly' is written in a classic cursive script, while 'ConnectAD™' is in a clean, bold, sans-serif font.

Lilly ConnectAD™

Diagnose

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Disclaimer

The content for this clinical case was developed in collaboration between a group of global clinicians who care for patients with Alzheimer's disease and Eli Lilly and Company.

A variety of cognitive and diagnostic tests can reasonably be used in the detection and diagnosis of Alzheimer's disease. Inclusion of specific cognitive and/or diagnostic tests in this case reflects some of the options available to clinicians, but the use of particular diagnostic tools does not imply endorsement or recommendation by Lilly.

Lilly ConnectAD™

Welcome to ConnectAD™, a clinical case series created by the Eli Lilly and Company Neuroscience medical education team. This series is intended to connect healthcare professionals to resources that help them understand biomarkers and biomarker testing for Alzheimer's disease.

Learning Objectives

By completing this course, you will have a deeper understanding of:

①

The clinical presentation of Alzheimer's disease

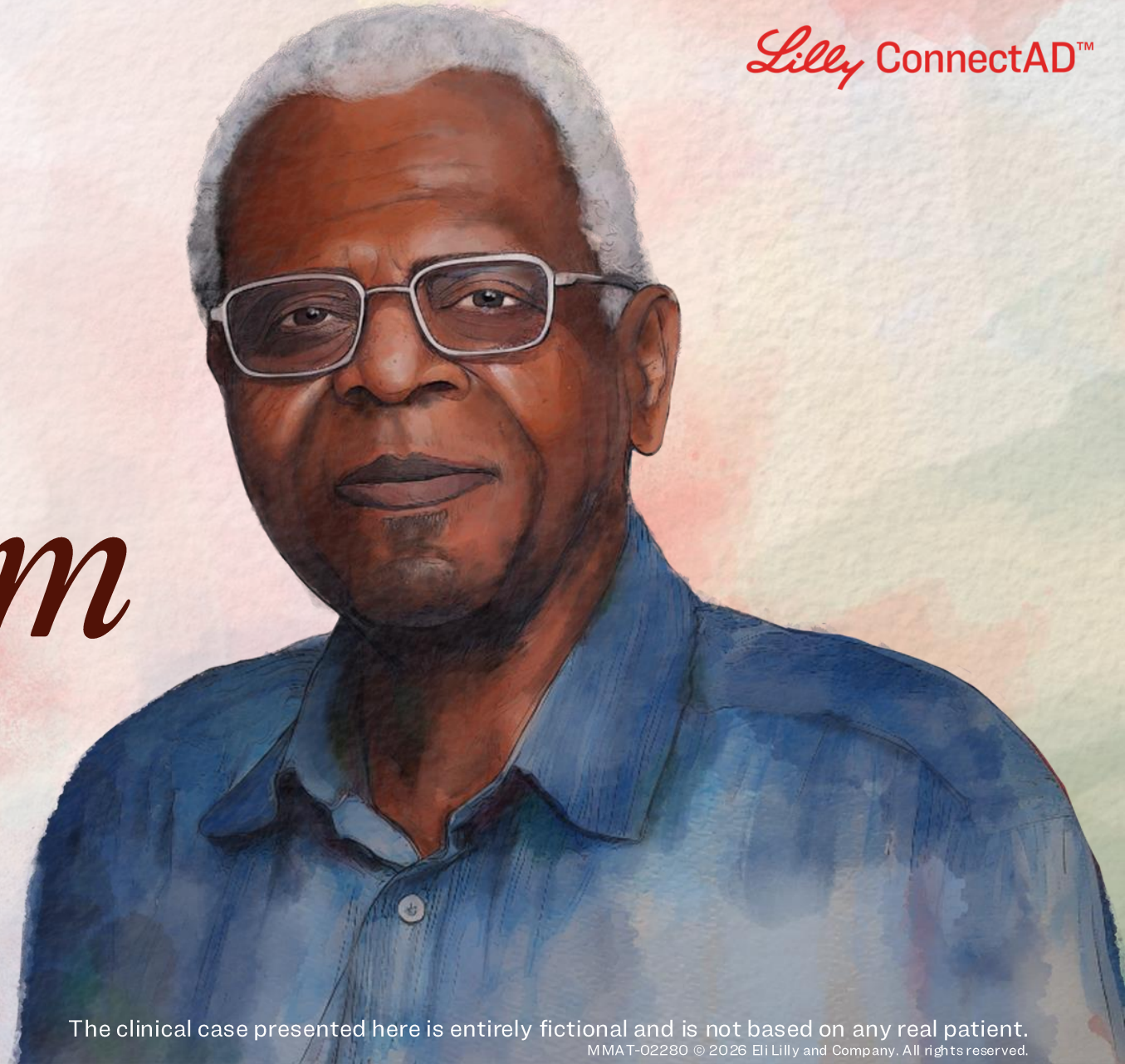
②

The role clinical and biomarker assessments can play in diagnosing early symptomatic Alzheimer's disease

Lilly ConnectAD™

Connect *with William*

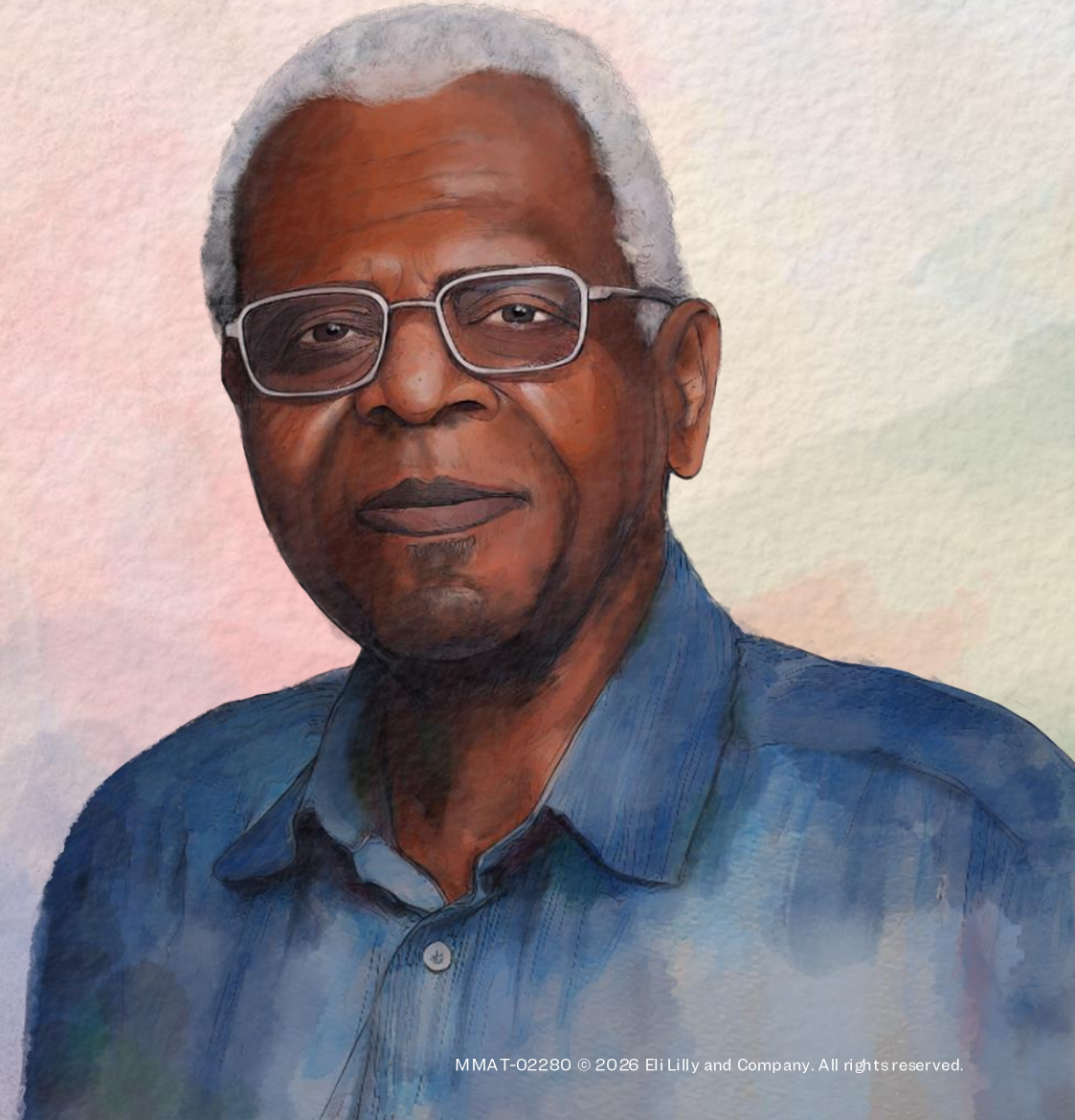
Diagnose



The clinical case presented here is entirely fictional and is not based on any real patient.
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Our Patient William

- 75 years old
- Male
- Black
- Married, lives with wife
- High school diploma
- Police officer (retired)
- Family history:
 - Prostate cancer
 - No family history of dementia



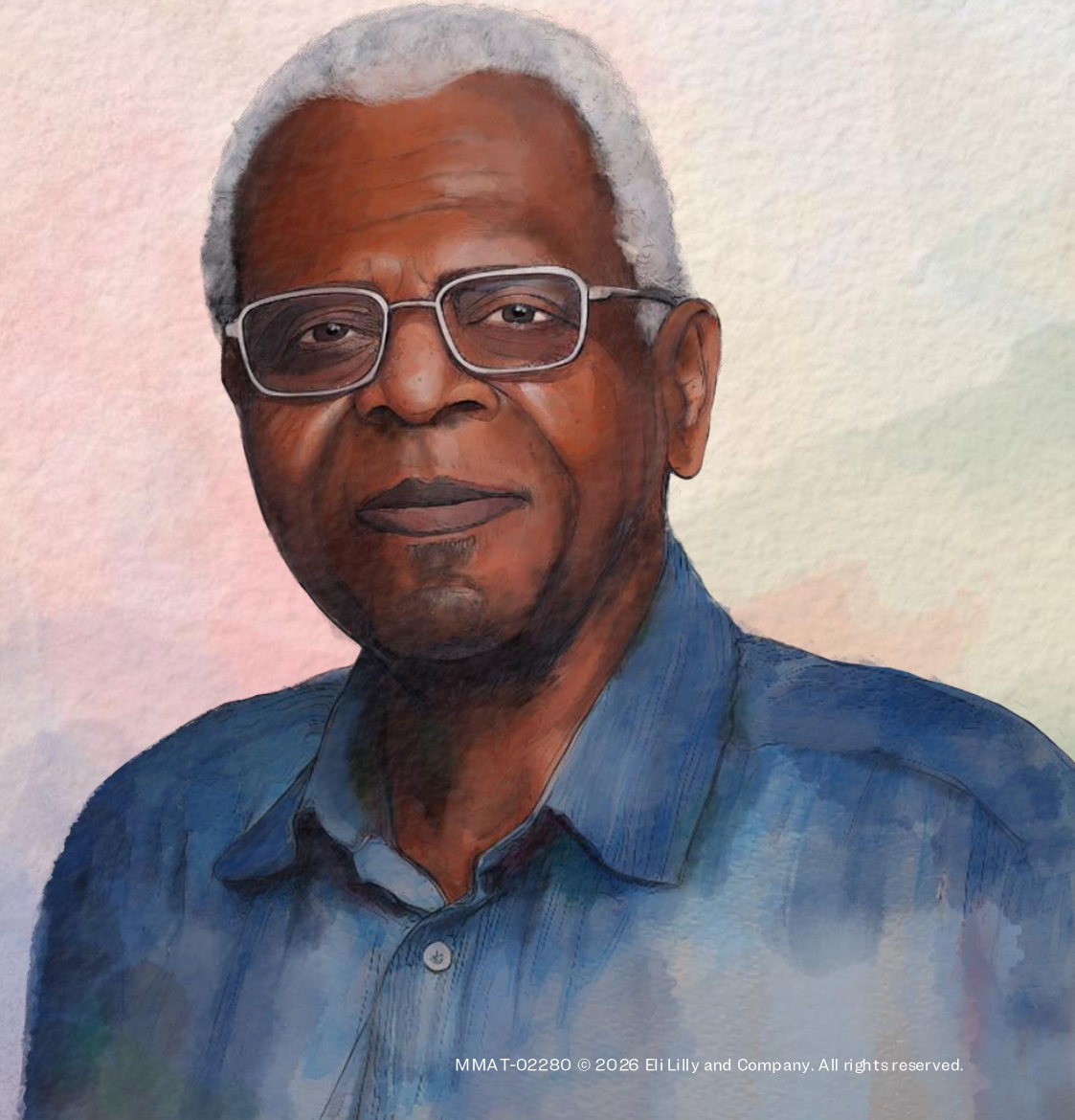
Clinical Information and History

William reports gradual worsening of cognitive symptoms and memory difficulties over the past 12 months.

He forgets details about recent activities, but he's able to remember devoting time and effort to the task.

His wife, concerned by these changes, encouraged him to seek medical attention.

He does not report changes in his personality, mood, or his ability to function.



Clinical Information and History

Clinical history

- Hypertension
- Type 2 diabetes

Current medication (class)

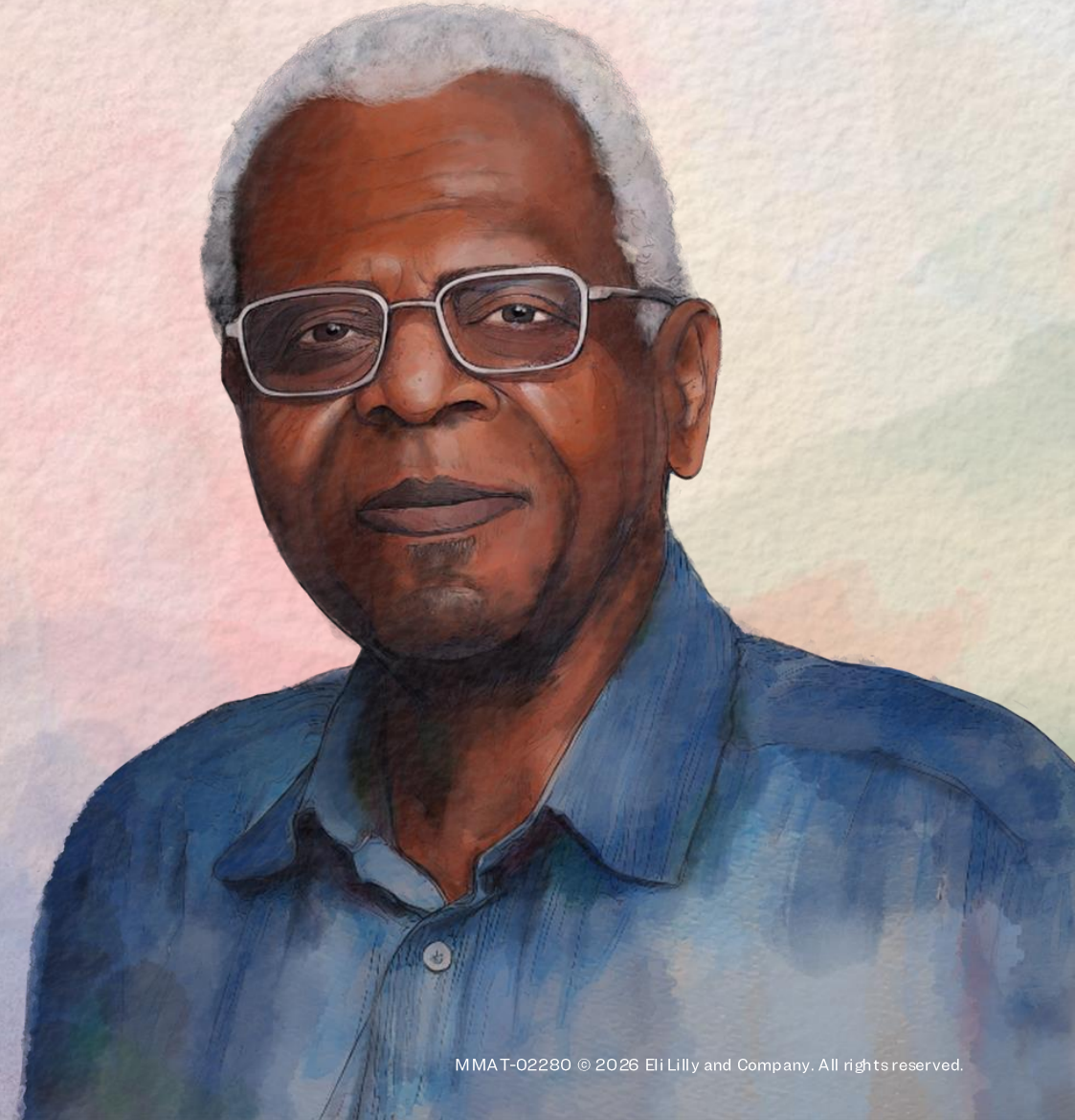
- Beta-blocker
- Biguanide

Vital signs

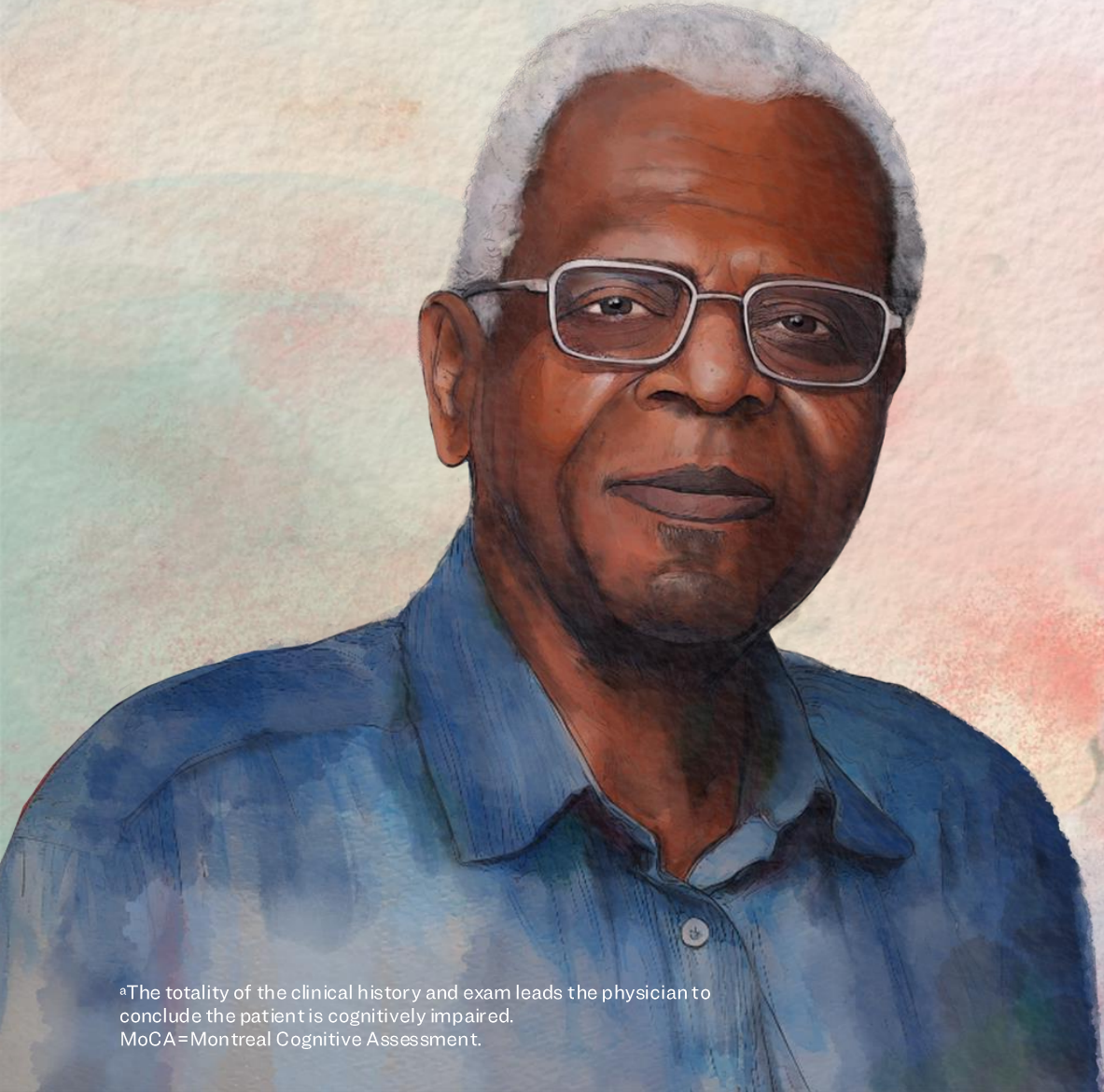
- Heart rate: 68 bpm
- Blood pressure: 130/80 mmHg

Physical exam

- Normal (no tremors or gait dysfunction)



Initial Clinical Assessment



General neurological exam

- Normal

Mental status

- Alert and responsive
- Oriented to person, time, and place
- Independent in all activities of daily living

Cognition

- MoCA: 26/30 (normal ≥ 26)^a

^aThe totality of the clinical history and exam leads the physician to conclude the patient is cognitively impaired.
MoCA=Montreal Cognitive Assessment.

Additional Findings: Routine Labs and Further Assessments

Blood work within normal limits, including:

- Complete blood count (CBC)
- Electrolytes
- Glucose
- Creatinine
- Thyroid stimulating hormone (TSH)
- Vitamin B12

Based on the differential diagnosis, the following were also ordered:

Brain MRI

- Bilateral lacunar infarcts
- Small vessel ischemic changes
- Age-appropriate atrophy

Blood biomarker assay

- P-tau217 test positive

Given the Patient Information Presented, What Are Possible Diagnoses the HCP Could Consider?

① Generalized anxiety

② MCI due to AD

③ Preclinical AD

④ Vascular cognitive impairment

⑤ Other



William

Given the Patient Information Presented, What Is the HCP's Diagnosis?

① Generalized anxiety

② MCI due to AD

③ Preclinical AD

④ Vascular cognitive impairment

⑤ Other



William

Why Is William Diagnosed with MCI Due to AD?

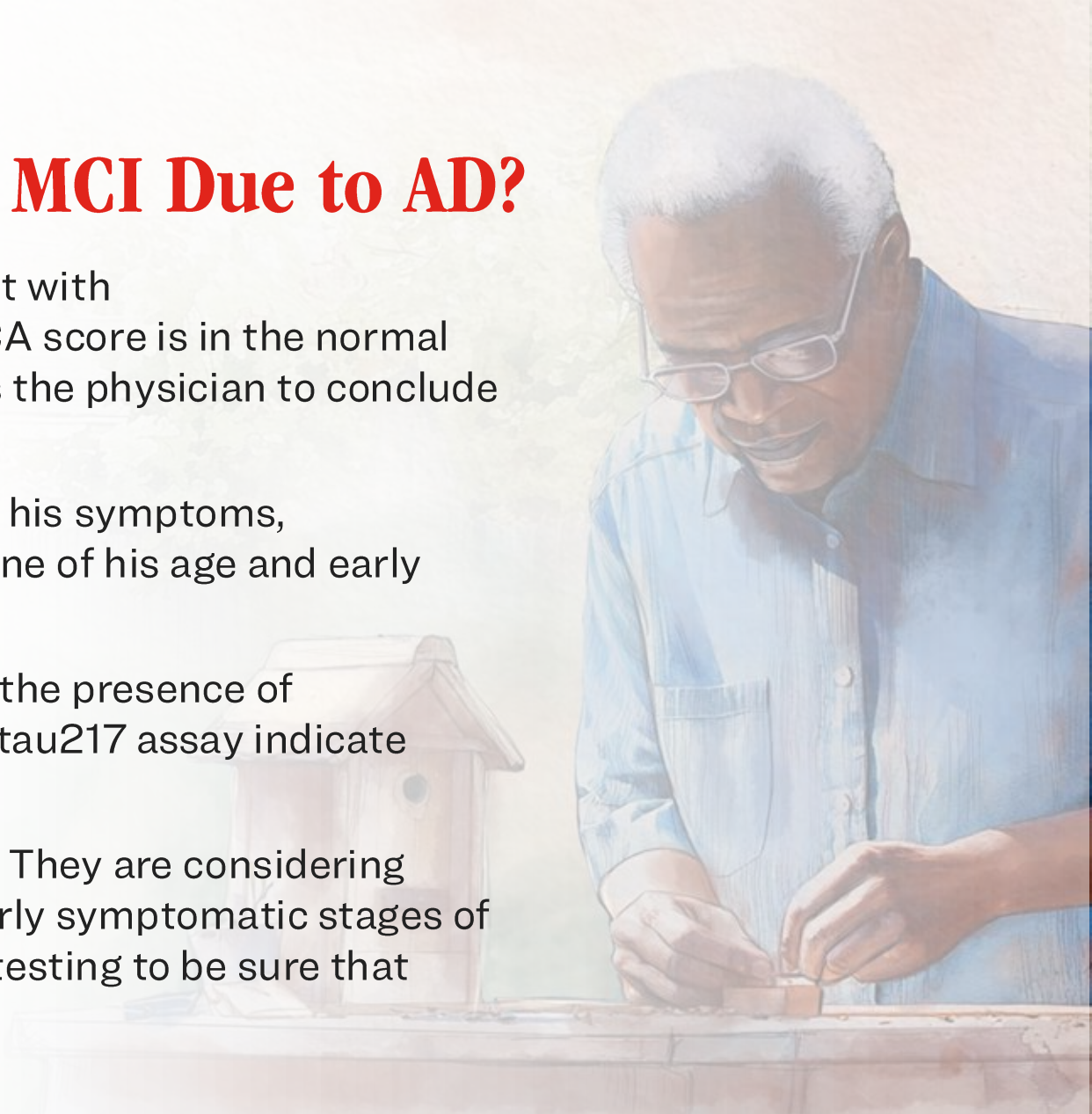
William is presenting with clinical symptoms consistent with the early symptomatic stages of AD. Although the MoCA score is in the normal range, the totality of the clinical history and exam leads the physician to conclude William is cognitively impaired.

His MRI results suggest a mild vascular contribution to his symptoms, but they are not definitive, which is common for someone of his age and early clinical presentation.

However, the results of his biomarker analysis confirm the presence of AD pathology. Specifically, the results of the plasma P-tau217 assay indicate amyloid pathology due to AD.^{1,2}

William's physician refers him to a dementia specialist. They are considering treatment with an amyloid-targeting therapy for the early symptomatic stages of AD. William's dementia specialist will order additional testing to be sure that William is an appropriate patient for the treatment.^a

^aFDA-approved amyloid-targeting therapies include donanemab and lecanemab.^{3,4}
AD=Alzheimer's Disease; FDA=Food and Drug Administration; MCI=Mild Cognitive Impairment; MoCA=Montreal Cognitive Assessment; MRI=Magnetic Resonance Imaging; P-tau217=Phosphorylated Tau at Position 217; PET=Positron Emission Tomography.
1. Hazan J, et al. *Alzheimers Dement*. 2025;21(3):e70113. 2. Hu S, et al. *Drug Discov Ther*. 2025;19(3):208-209.
3. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761248s0041bl.pdf (Accessed October 7, 2025).
4. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761269s0131bl.pdf (Accessed October 7, 2025).



Key Learnings in William's Case (1 of 3)

Positive P-tau217 means William is likely to have amyloid pathology.¹

The two hallmark pathological features of AD are²:

- Extracellular β -amyloid plaques
- Intracellular neurofibrillary tangles, which are composed of abnormally hyperphosphorylated tau protein, like P-tau217

Soluble $A\beta_{42}$ and P-tau217 appear at roughly the same time early in the disease process.³

- As AD progresses, $A\beta_{42}$ levels decline in CSF and blood (reflecting plaque formation), while P-tau markers rise in CSF and blood^{1,4-6}

$A\beta_{42}$ =42-Amino-Acid Version of Amyloid Beta; AD=Alzheimer's Disease; CSF=Cerebrospinal Fluid; P-tau=Phosphorylated Tau; P-tau217=Phosphorylated Tau at Position 217.

1. Teunissen CE, et al. *Alzheimers Dement.* 2025;21(1):e14397. 2. Palmqvist S, et al. *Alzheimers Dement.* 2025;21(7):e70535. 3. Arnsten AFT, et al. *Alzheimers Dement.* 2025;21(8):e70404. 4. Sunderland T, et al. *JAMA.* 2003;289(16):2094-2103. 5. Padala SP, Newhouse PA. *Metab Brain Dis.* 2023;38(1):185-193. 6. Graff-Radford NR, et al. *Arch Neurol.* 2007;64(3):354-362.

Key Learnings in William's Case (2 of 3)

A positive BBM test result provides evidence of amyloid pathology and is highly concordant with other amyloid biomarkers such as PET and CSF. ¹

BBM tests are anticipated to play two key roles: supporting triage decisions and confirming amyloid pathology¹

Triaging BBM tests

- A negative result suggests an individual is unlikely to have amyloid pathology and may benefit from evaluation for other causes of cognitive impairment¹
- A positive result indicates a higher likelihood of amyloid pathology, which should be confirmed with another method such as CSF biomarkers or amyloid PET imaging^{1,2}
- Performance threshold $\geq 90\%$ sensitivity with $\geq 85\%$ specificity in primary care and $\geq 75-85\%$ specificity in secondary care¹

Confirmatory BBM tests

- Positive result identifies the presence of amyloid pathology with strong concordance to amyloid PET¹
- Performance threshold $\geq 90\%$ sensitivity and $\geq 90\%$ specificity¹

Key Learnings in William's Case (3 of 3)

Comprehensive assessment involves: Medical evaluation, neurological exam, cognitive testing, laboratory assessment of potentially reversible etiologies of cognitive impairment, and structural neuroimaging.¹

- Cognitive symptoms often have multiple causes, and misdiagnosis may result in delayed care, inappropriate treatment, and inaccurate prognoses¹
- Many conditions other than AD can cause or exacerbate cognitive impairment; therefore, a comprehensive assessment should be used to identify the potential alternative etiologies¹

AD biomarker testing is not intended as a standalone diagnostic test for symptomatic AD; it should always be used in the context of a comprehensive assessment.¹

Thank you for
Connecting
with William



Diagnose