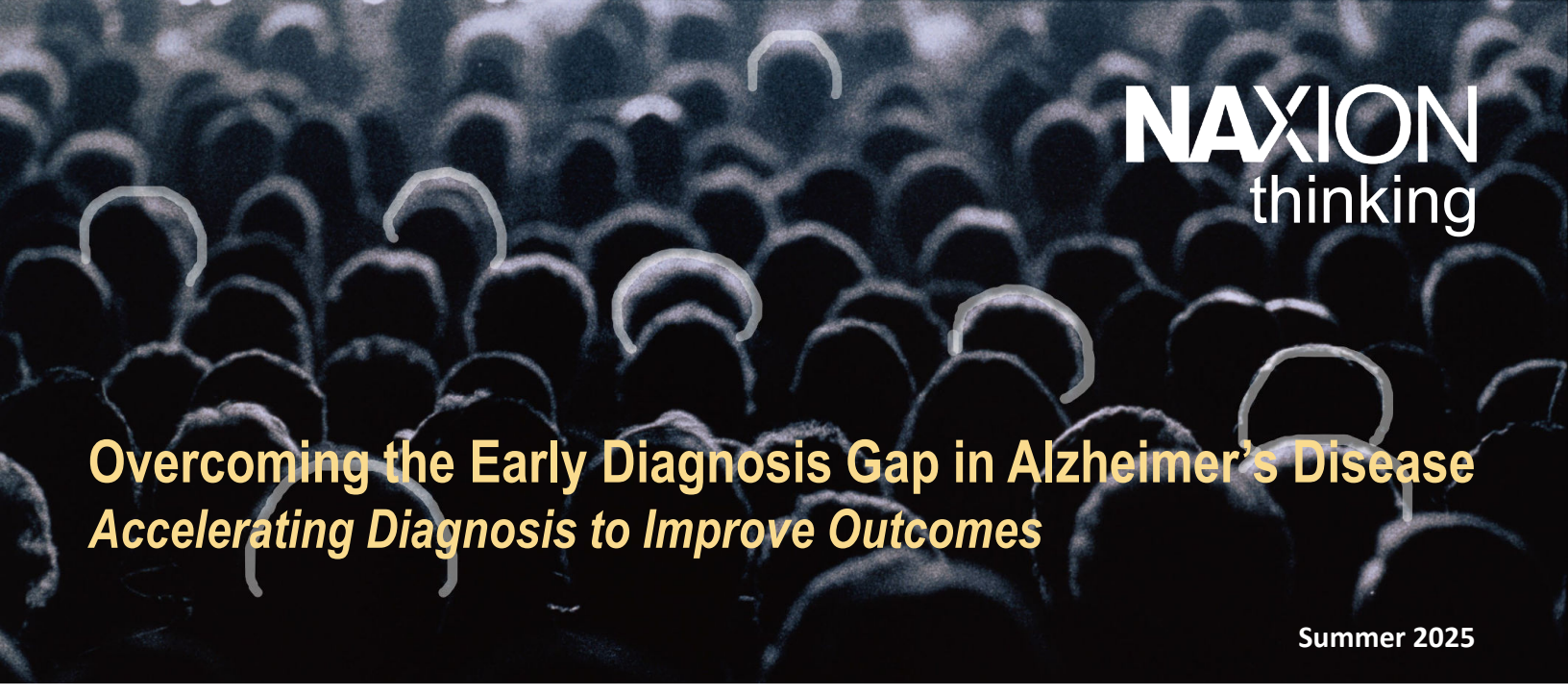

Overcoming the Early Diagnosis Gap in Alzheimer's Disease

Accelerating Diagnosis to Improve Outcomes

Summer 2025

Sometimes Hidden in Plain Sight

Alzheimer's Disease (AD) qualifies as a genuine medical crisis based on the burden it imposes and the growing population at high risk for developing it. But for all the attention it commands, it may well be one of the most underdiagnosed conditions in contemporary medicine. Long before the pharmaceutical industry trained its sights on AD, neuropsychologists already knew that individual differences in baseline cognition, combined with variability in normal aging, would make it difficult to diagnose people with a neurodegenerative condition based on cognitive changes alone.

Adding to the challenge of diagnosing AD early in the disease are the elaborate patterns of denial and compensatory behaviors used by patients and their families to camouflage the problem. For years, there was little incentive to uncover AD earlier than it could be "seen" because the interventions were largely unimpressive. But with higher aspirations for newer treatments, there is greater urgency to find relevant patients. Unfortunately, the pace of early diagnosis has yet to truly accelerate, making it difficult to recruit for clinical trials the very patients who are in the best position to benefit from treatment. Delayed diagnosis also makes it more challenging to demonstrate efficacy in the real world because many treated patients classified as "mild" are, in fact, moderately advanced in their disease trajectory by the time they begin therapy.

The Hunt for Preclinical Signals

The difficulty in diagnosing AD based on clinical presentation helps explain the excitement around a recently launched diagnostic blood test from Quest, AD-Detect, with roughly 90% sensitivity and 90% specificity. Still in its infancy, the test is marketed as a non-invasive screen for people already exhibiting symptoms. In that capacity, it will likely spur, but not dramatically accelerate, the speed of AD diagnosis. To have that effect, and potentially diagnose patients before cognitive decline is observed, it must become part of routine blood work as people age.

That prospect, along with the availability of new therapies that treat the underlying pathophysiology of the disease, has led the Alzheimer's Association Workgroup (AAW) to recommend defining AD based on biology rather than symptomatology. Notably, however, the AAW acknowledges that these criteria are not meant as guidelines for clinical practice because there is a shortage of facilities available to conduct the recommended diagnostic tests. Notably, in some communities, there is a backlog of patients waiting for even conventional neuropsych screening. Scaling up will take some time.

Serendipity to the Rescue

Meanwhile, as researchers try to validate other biomarkers or physiological changes that predict early AD (e.g., eye movements), a real-world experiment is taking place among patients with metabolic conditions (Type-2 diabetes and obesity) which may highlight the benefit of early diagnosis in dementia. Millions of diabetic and obese patients are now being treated with GLP-1 inhibitors, a relatively new class of medication that is also being trialed as a treatment for AD. Many of those patients are in their 50's and 60's, a period during which the preclinical brain changes that led the AAW to emphasize biology over symptoms may already be occurring. If patients who are taking GLP-1 inhibitors are diagnosed with AD less often (or later) than patients who receive other treatments for diabetes and obesity, it will represent proof-of-concept for an early treatment paradigm and provide an opportunity to wring extra value from a drug class whose safety and relative ease of use make early treatment practical.

The convergence of a diagnostic blood test, new AAW guidelines, and the potential for GLP-1 inhibitors to delay onset of clinical symptoms represent exciting changes to conceptualizations of the early stages of AD. Moving away from the clinical definition of AD to a biological definition is likely to broaden the treatment model to incorporate earlier intervention because early diagnosis and better treatments often chase one another.

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Michael is a neuropsychologist whose doctoral research addressed the effects of drugs on different types of memory tests in the broader context of organic amnesia. Prior to leaving academia, he also published on neuroanatomical correlates of various forms of memory loss, including prosopagnosia (face blindness). His 25-year career as an insights professional and marketing consultant has focused on the commercialization of new therapies for a wide variety of drugs, forecasting demand for novel products, and development of research methodologies to support regulatory policies concerning health and safety implications of new products. In his post-academic career, he continued to publish in peer-review journals on various topics including patient preferences for GLP-1 therapies and consumer recall of health and safety information. He has also written extensively on market research methodologies, including the role for neuroscience.

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