



Acurian on...

Alzheimer's: A Path Toward A Cure

Every major health epidemic has seemed daunting and insurmountable, until a single momentous discovery – or more often, a critical mass of accumulated knowledge – tips the balance toward a decisive treatment or cure.

Vaccines that took a hundred years to conceive are now viewed as a matter of routine care. Cancers that claimed every victim are now handily defeated with targeted drugs.

And so it will be one day with Alzheimer's disease, a looming epidemic that has thwarted every attempt to halt its progressive assault on the brain and its corresponding toll on families and society at large. Today, 46 million people around the world are afflicted with the disease. By 2050, that number is expected to reach 131 million.¹

Three momentous developments can rewrite this future:

- New biomarkers that serve as targets for early detection and early intervention
- Novel drugs that slow or prevent irreversible brain changes
- A massive effort to identify, screen and enroll healthy, at-risk adults in prevention trials before they become symptomatic.



Current and projected rates of Alzheimer's without new strategies and effective treatments

		Projected sufferers if Alzheimer's Disease is not stopped	
	2015	2030	2050
Americas	9.4m	15.8m	29.9m
Africa	4.0m	7.0m	15.8m
Europe	10.5m	13.4m	18.6m
Asia	22.9m	38.5m	67.2m
World	46.8m	74.7m	131.5m

<https://www.alz.co.uk/research/WorldAlzheimerReport2015.pdf>

99.6%
of investigational
Alzheimer's drugs have
yielded no benefit.²

¹ <https://www.alz.co.uk/research/statistics>

² <https://www.scientificamerican.com/article/why-alzheimer-s-drugs-keep-failing/>



Strength in Numbers

Scientists must attend to the first two tasks, elucidating the chemical culprits that trigger early Alzheimer's brain changes and accelerating the development of new compounds to block them.

Beyond the science, however, a logistical conundrum is unfolding. Tens of thousands of people – none of whom show symptoms – must agree to participate in prevention trials designed to monitor early disease progression and test new drugs that may slow or prevent disease onset.

The scale of these trials must exceed all previous Alzheimer's studies to ensure the data are sound and reproducible. The past 20 years have proven the futility of running studies that are short on time and people. Indeed, many an Alzheimer's drug candidate has shown promise in small groups of people, only to fail in larger studies or to pose unwanted side effects that were not initially evident.



To identify, screen and recruit large numbers of asymptomatic adults is a monumental undertaking that few organizations are equipped to handle. Acurian is uniquely positioned to meet this challenge, with an expansive reach into nearly one million homes with adults at risk for Alzheimer's as well as a robust technology built to pre-screen 10,000 people daily on a global scale.



The Prevention Paradigm

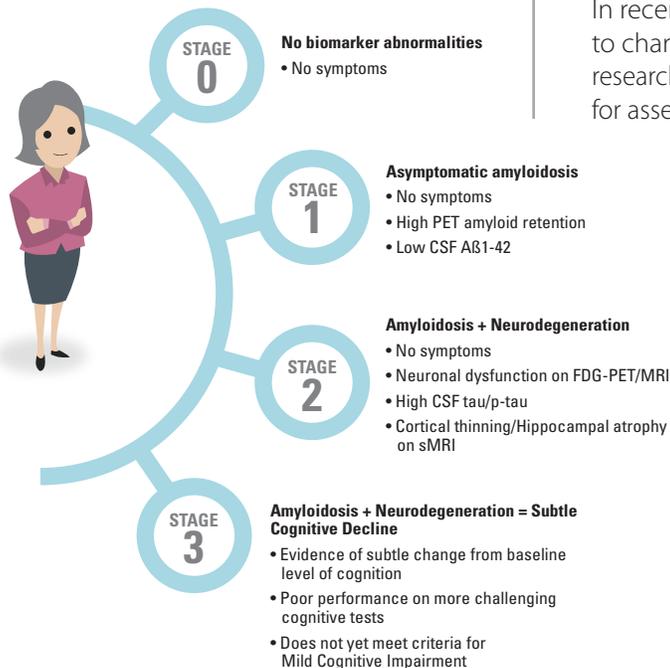
Much like dominoes falling in sequential order, the Alzheimer's brain predictably withers in size and function one structure at a time. Attempting to halt this process midstream – or restore lost neurons – has failed at every turn: 99.6 percent of investigational Alzheimer's drugs have yielded no benefit.²

Recognizing its flawed approach, the Alzheimer's community is now actively seeking to prevent the disease in its earliest stages, before the brain is irrevocably altered. This period is known as prodromal or preclinical Alzheimer's, a lengthy phase in which people are outwardly healthy but their brains are in slow pathological decline.

Evidence confirms these underlying brain changes begin 20 to 30 years before Alzheimer's symptoms are clinically detectable,³ providing ample windows of opportunity in which to test preventive therapies in large groups of at-risk individuals.

The key is to pinpoint, with as much precision as possible, the threshold at which these changes occur – a task that requires frequent screening with sensitive tools to detect slight changes in mood, memory or thinking.

In recent years, a whole new set of guidelines has emerged to characterize early disease progression as a means of aiding researchers and clinicians in establishing a common set of standards for assessing asymptomatic patients.



Acurian takes these guidelines to a higher level of analysis, applying its proprietary statistical modeling algorithm to identify the precise characteristics of an ideal randomized patient and matching these patients to prevention trials where they are most likely to randomize.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4285623/figure/F2/>

³ <http://jamanetwork.com/journals/jama/fullarticle/2293295>





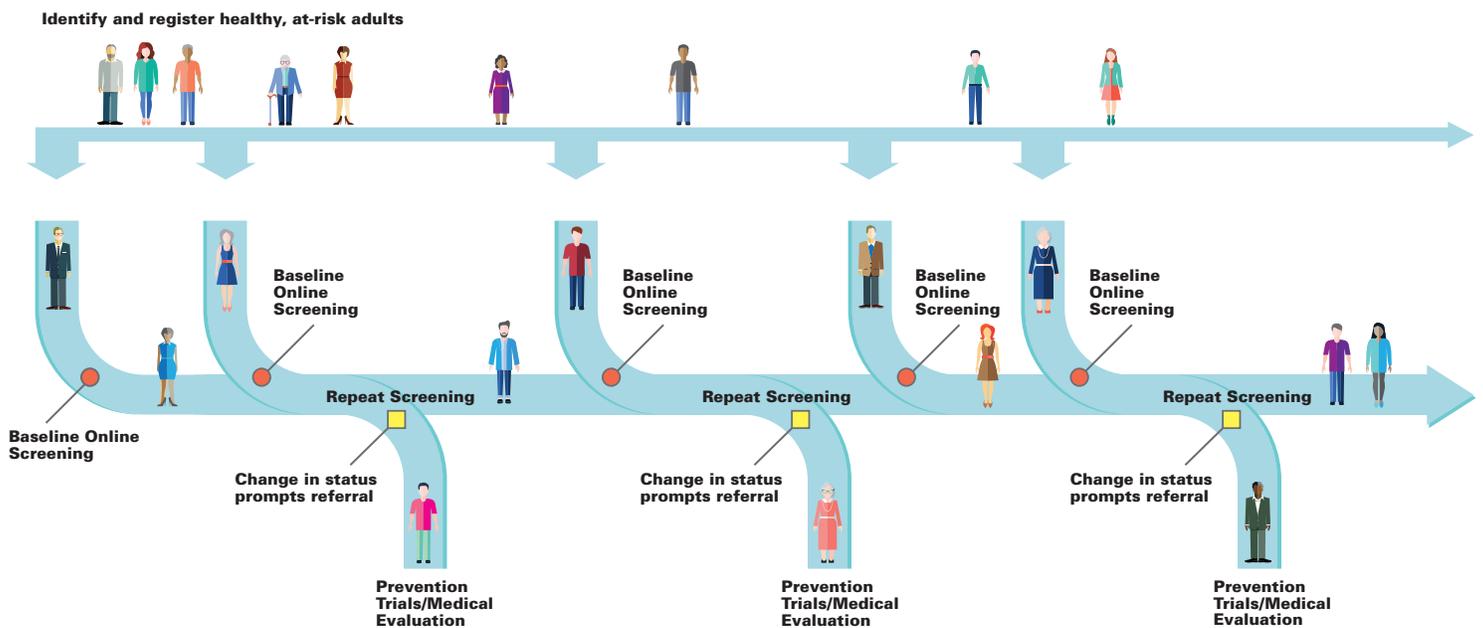
Longitudinal Screening

Alzheimer's prevention studies around the world are now tracking broad swathes of the population over years or decades to record incremental changes in memory, mood and function; assess the impact of genes and environment on brain health; and test the effects of new preventive agents long before individuals succumb to devastating brain changes.

Yet finding the estimated 70,000 people needed to fill global Alzheimer's prevention and treatment trials is a task of epic proportions, requiring **at least 700,000 people to be screened** – ten for each individual who ultimately meets study criteria.⁴

These expansive numbers call for aggressive measures to **identify and screen** sufficient numbers of people and combat the psychological barriers associated with a potential diagnosis of a fatal memory disorder.

Longitudinal Screening by Year



Acurian is capable of delivering huge numbers of qualified individuals through its global database of patients and caregivers as well as its predictive modeling algorithms that identify and target the right individuals for each respective trial.



Alzheimer's Registries

Engaging at-risk individuals early and often is essential to building and maintaining a ready-made source of clinical trial participants to tap into when new studies begin enrollment. In recent years, a multitude of Alzheimer's registries have arisen round the world to identify and pre-screen at-risk individuals long before they present with symptoms.

But names in a database do not translate into successful trial enrollment.

A successful registry must continually engage participants to maintain their interest and nurture their belief in the personal and societal benefits of advancing Alzheimer's clinical research.

Second, a registry must frequently assess an individual's cognitive status to pick up subtle shifts from baseline that might indicate readiness for a prevention trial. Most importantly, a registry must have a sophisticated system for matching participants with prevention trials that best fit their respective symptoms and geographical location.

Infrastructure challenges of an Alzheimer's registry



Acurian's 100-million-household database contains one million families who have indicated they are interested in, or affected by, Alzheimer's disease, providing a ready-made source of potential study participants. With an unmatched ability to reach interested participants through predictive modeling and the ability to deploy the optimal mix of outreach tactics, Acurian can recruit the right patients for the right study.



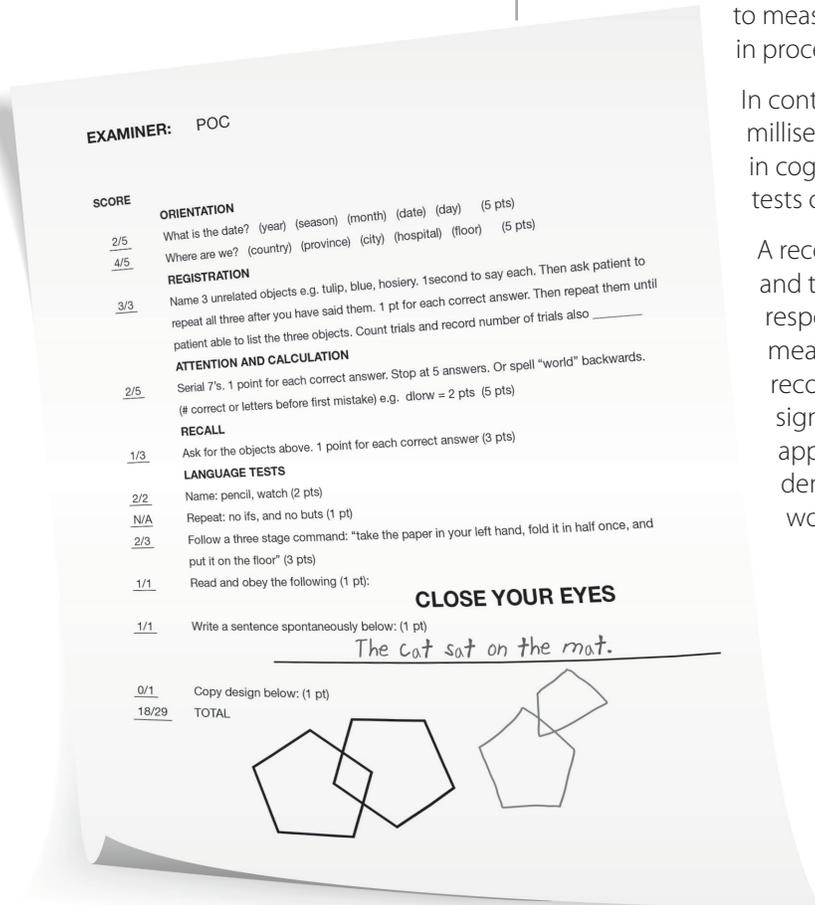
Assessing Cognitive Status

Screening millions of people for prodromal Alzheimer's necessitates a highly sensitive and cost-effective tool that can rapidly detect subtle shifts in status over short periods of time -- without the need for costly professional evaluation.

At present, no such tools exist. The most widely used tests in clinical practice must be administered and evaluated by a trained professional who uses pencil and paper to record responses, which could inadvertently introduce bias. Moreover, the tests were developed in the 1970s, '80s and '90s, long before prevention was a conceivable goal. As such, they lack the sensitivity required to measure minute cognitive changes and deficits in processing speed among prodromal individuals.

In contrast, newer online tests record answers with millisecond precision, easily detecting subtle delays in cognition and response time that pencil-and-paper tests cannot distinguish.⁵

A recent study found that both healthy people and those with mild cognitive impairment (MCI) responded with equal accuracy to questions measuring working memory and episodic recognition. However, response times were significantly slower in people with MCI, approaching the deficits seen in patients with dementia, a factor that pencil-and-paper tests would not have detected.⁶



The Mini Mental State Examination (MMSE)⁷



⁵ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4255527/>

⁶ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4255527/>

⁷ <https://www.mountsinai.on.ca/care/psych/on-call-resources/on-call-resources/mmse.pdf>



On a daily basis, Acurian makes contact with 10,000 people globally to gauge their interest and screen their eligibility to participate in clinical trials.

Similarly, the MMSE – a pencil-and-paper test widely used in clinical practice – has limited sensitivity in detecting mild cognitive impairment, as well as a “ceiling” effect that could overlook some people who have Alzheimer’s. As one researcher noted, “a highly educated individual could score well on the MMSE, but not be able to recognize their grandchildren.”⁸

Online screening is the most viable means for frequent, accessible, inexpensive and highly sensitive screening of people who are healthy and normal -- until the very moment when they are not. The medical community at large is now acknowledging this reality and has begun to validate the benefits of online screening over traditional pencil-and-paper testing for asymptomatic Alzheimer’s disease.

Acurian owns a custom-built software program that thoroughly prescreens individuals online when they respond to our marketing outreach tactics. The same platform could be used to screen Alzheimer’s registrants for their readiness to join prevention trials. Screener questions are carefully crafted and programmed by Acurian feasibility experts with advanced degrees who ensure that questions extract precision responses.

The infrastructure for launching this screening platform is already in place. On a daily basis, Acurian makes contact with 10,000 people globally to gauge their interest and screen their eligibility to participate in clinical trials.

The goal is to funnel a critical mass of vetted, screened participants with a high risk of developing Alzheimer’s into the appropriate prevention trials. Failure to enroll sufficient numbers of participants in a timely manner puts clinical development programs at risk for commercial failure⁹ -- a risk the Alzheimer’s community can no longer afford to take.

⁸ http://www.todaysgeriatricmedicine.com/news/ex_012511_01.shtml

⁹ <http://www.cambridgecognition.com/blog/entry/the-challenge-of-detecting-prodromal-alzheimers-disease-for-clinical-trials>



Taking Action

Global leaders have set a deadline of 2025 for finding an effective prevention or treatments. Without a change in strategy, the cost of caring for Alzheimer's patients is estimated to reach \$1 trillion by 2050.

The Alzheimer's mandate is clear. Without a change in strategy, the cost of caring for Alzheimer's patients is estimated to reach \$1 trillion by 2050.¹⁰ Global leaders have set a deadline of 2025 for finding an effective prevention or treatment¹¹ to stem the massive personal, healthcare and financial burden worldwide.

With this deadline looming, there is little time to waste on pursuing strategies that have failed to yield results. Novel drugs, new biomarkers, more sophisticated online screeners, and enhanced patient recruitment strategies must be immediately pursued if the goal is to be realized.

Irrefutable evidence highlights the importance of establishing and maintaining open channels of communication with potential trial participants. Frequent engagement is crucial to breaking down barriers created by the social stigma of Alzheimer's and mistrust of the medical research establishment. Clear and compelling information should awaken the public to the crucial roles of prevention, early detection and prompt intervention in lowering morbidity and mortality.

The significant reduction in heart disease deaths¹² and the exponential decline in U.S. tobacco use – down by nearly two-thirds since 1965¹³ – is testament to the power of knowledge and education to effect widespread change.

Proven methods to improve patient education and recruitment are widely available, but they require inordinate amounts of time, staffing and financial resources to implement.

It is time to reach outside the traditional framework and incorporate new partners in the recruitment of at-risk individuals for entire therapeutic areas – not just for individual trials – to more rapidly reduce the public burden of disease.

¹⁰ https://www.alz.org/documents_custom/trajectory.pdf

¹¹ <https://alzres.biomedcentral.com/articles/10.1186/s13195-016-0207-9>

¹² https://www.cdc.gov/pcd/issues/2016/16_0211.htm

¹³ https://www.cdc.gov/tobacco/data_statistics/fact_sheets/adult_data/cig_smoking/