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Health & Medicine

Would You Want to Know if Alzheimer's Were in Your Future?

New AI-based screening tools could help people who are falling through the cracks.

By
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One evening in the spring of 2021, Maryam Zolnoori, a data scientist and assistant professor of health-sciences research at the Columbia School of Nursing, settled into her office and pressed play on a series of quiet, intimate recordings of elderly New Yorkers speaking with the visiting nurses who cared for them. The audio had been gathered by the nonprofit nursing agency VNS Health, which had invited some of its nurses and home-care recipients to wear small microphones clipped to their clothing while they interacted. Zolnoori planned to transcribe the recordings and feed the resulting text into an artificial-intelligence program that she and her colleagues were developing to spot early signs of illness in older adults.

"Our models had previously identified people at risk of infections, adverse drug reactions, and other problems by analyzing medical records and clinical notes," says Zolnoori. "We thought that everyday conversations might teach us even more."

That evening, while listening back to the recordings, Zolnoori had a realization. "It dawned on me there might be valuable data not only in the words exchanged between caregivers and patients," she says, "but also in the sounds of their voices." The thought struck her while listening to the speech of some of the oldest study participants, which was marked by odd pauses, abrupt tonal shifts, and rough, garbled noises — like their mouths were struggling to form words. Curious, Zolnoori dove into the scientific literature. She discovered that such vocal distortions can

result from damage to the brain's motor-control systems, which are located next to its memory centers and are responsible for the complex muscular coordination required for fluent speech. Reading on, Zolnoori learned that Alzheimer's disease and other forms of dementia can ravage these networks in the earliest stages of decline, before memory problems became obvious.

"So that made me wonder: how early do these vocal changes begin?" she remembers. "Might we be able to detect them months, perhaps years, before dementia is diagnosed?"

To find out, Zolnoori soon undertook an ambitious study aimed at identifying people at risk of developing dementia. With $1.2 million in support from the National Institute on Aging, she set about building an AI model to analyze both the linguistic content and acoustic properties of a person's speech — looking not only for signs of forgetfulness and confusion but also for unusual sounds that indicated the brain was losing its grip on the diaphragm, larynx, mouth, and vocal cords. Her algorithm, trained on thousands of hours of publicly available recordings from cognitively healthy and impaired individuals, learned to detect the tiniest differences in their speech patterns. "Many of the differences the model picked up on are imperceptible to humans," says Zolnoori. "We're talking about rhythmic inconsistencies on the scale of milliseconds, involving the pacing of syllables within words or how long vowel sounds get drawn out." As the brain starts to lose control over motor functions, she explains, the cadence of speech becomes irregular in ways that the AI model can recognize — like a conductor noticing an orchestra falling out of sync.

Zolnoori's findings, published in a series of papers over the past two years, suggest that the model can predict whether people are at risk of developing dementia up to a decade in advance. In one experiment, the algorithm identified those with mild cognitive impairment — a precursor to Alzheimer's disease — with 90 percent accuracy. In another, it correctly flagged people with an even subtler form of memory loss that tends to emerge five to ten years before the onset of dementia. "It did so after listening to them speak for just thirty seconds," Zolnoori says. Neurologists, on the other hand, had to conduct lengthy examinations of the same people to detect their emerging cognitive issues.

Maryam Zolnoori (Len Small / Columbia Magazine)

The new Columbia technology, which Zolnoori and several colleagues are now fine-tuning to test in a clinical study, is part of a broader scientific push to revolutionize how and when Alzheimer's disease is diagnosed. Many scientists, armed with powerful new AI tools and a deeper understanding of the condition's wide-ranging neurological effects, have been racing to detect early warning signs of dementia by analyzing people's everyday activities. Sharon Di, a Columbia transportation engineer, has developed algorithms that assess driving behaviors recorded by in-vehicle sensors — like sudden braking or rapid acceleration — to spot emerging cognitive issues. Researchers at Ireland's Maynooth University and University College Dublin, meanwhile, have devised methods of tracking people's banking transactions for signs of cognitive decline, which they say can include missed payments and unusual spending patterns. Other scientists have explored monitoring people's sleep patterns, physical movements, and keyboard strikes for hints of trouble.

These techniques, which to date have been used only in research settings, aren't intended to replace traditional cognitive assessments. Rather, they're meant to

serve as preliminary screening tools, flagging people who might benefit from further testing. (A full workup for dementia typically starts with a memory test in a doctor's office and, if results warrant, is followed by a neurological exam including brain scans, blood analysis, and in some cases genetic tests.) Proponents say a key benefit of AI-based screening tools, which are designed to be used only with explicit consent, is their ability to detect neurological issues in people who haven't noticed any changes in themselves and therefore wouldn't think to seek a memory test. Widespread use of such tools, they argue, could help close a critical diagnostic gap in the US, where nearly half of people with Alzheimer's disease go undiagnosed, and most diagnoses come only in the disease's later stages.

"The reality is that most cognitive assessments don't happen unless a patient or family member raises concerns, and that often doesn't happen in the beginning," says James Noble '08PH, a Columbia neurologist and dementia expert who is helping Zolnoori prepare her technology for clinical study. He points out that memory tests take upwards of ten minutes to administer, which is a considerable amount of time in a primary-care visit, so they're not routinely done, even though Medicare reimburses physicians for conducting them annually for patients over 65. "If you could identify people who ought to be tested just by listening to them talk during a checkup, that would obviously make a big difference."

Driving the push for earlier detection of Alzheimer's risk is a growing awareness that the disease's underlying pathology begins long before symptoms are noticeable. A recent study by researchers at Columbia's Mailman School of Public Health adds weight to this idea, showing that people with well-known Alzheimer's risk factors —including poor cardiovascular health and chronic inflammation — exhibit slight declines in memory and cognition as early as their twenties and thirties. Notably, they also tend to have elevated levels of the brain proteins amyloid and tau, which have been implicated in neurodegeneration. The study, led by epidemiologist Allison Aiello '03PH, is the first large-scale US analysis ever to tie these biomarkers to cognitive performance so early in adulthood. "I was very surprised by our findings," says Aiello, who notes that she initially had trouble securing funding for the research because prevailing wisdom held that Alzheimer's pathology began in middle age. She says the discovery suggests that encouraging healthy habits in young people is crucial for preventing Alzheimer's disease. "To date, prevention efforts have focused on older adults — encouraging them to do crossword puzzles, stay socially connected, and exercise and eat well. But these conversations really need to start

much earlier.”

If we can spot the signs of Alzheimer’s earlier, do we have tools to help? There is growing optimism that we might. The FDA recently approved two drugs, lecanemab and donanemab, that are the first ever to alter the underlying disease process in Alzheimer’s, clearing away the sticky amyloid plaques that build up in the brain and damage neurons. The drugs are not curative, and they carry serious risks — including brain swelling and bleeding — but they appear to slow the disease’s progression by as much as 25 percent. That represents a major advance over traditional Alzheimer’s medications, which merely ease symptoms temporarily, often for just a few months. Clinical trials are now exploring whether the new anti-amyloid drugs might have an even greater impact if administered earlier, to people who have elevated levels of the protein and other biomarkers of the disease but no overt symptoms.

“There’s a lot of excitement in the field right now,” says Noble. “Many of us believe that even if these particular drugs don’t prove to be the answer, earlier diagnosis is still the way forward, and that eventually we’re going to find medications that can stop the disease before it takes hold.”

Yet the prospect of widely deploying risk-assessment tools like Zolnoori’s raises tricky ethical and logistical questions. Some experts fear that telling people they’re at risk of developing Alzheimer’s disease may simply provoke anxiety and feelings of helplessness. Others are concerned that that searching for cognitive issues too aggressively and too early will lead to excessive testing and flood neurologists’ offices with patients who may never develop dementia.

Meanwhile, public interest in early detection is soaring, driven in part by a recent boom in direct-to-consumer tests that claim to be able to assess Alzheimer’s risk. Noble says he’s seen a surge of patients worried about their memory. “Many arrive with test results from commercial labs in hand — blood panels, genetic readouts from companies like 23andMe,” he says. “We’re also seeing younger patients coming in now with milder symptoms.” While some of the commercial tests have scientific validity, Noble warns that their marketing materials often gloss over limitations. “The biggest issue is that no single test can tell you very much on its own.” He notes that even the gold-standard diagnostics for dementia, including spinal-fluid analyses and MRI scans, are imperfect and must be interpreted cautiously within the broader context of a neurological evaluation. “The thing to

remember is that everybody experiences a degree of age-related memory loss," says Noble, who is the author of *Navigating Life with Dementia*, a practical guidebook for patients and families. "It's when you see a sharp drop in your cognition, or when it impairs your ability to function in daily life, that it becomes a serious concern."

Even as millions of Americans are fretting over their potential risk, Noble says, many more remain unaware they're even vulnerable. "People who receive cognitive assessments and timely diagnoses of dementia tend to have more resources," he says. "They may have more education, time, money, access to health care, and family and friends who notice they're changing." An AI-enhanced system that passively monitors people's speech, he believes, could help secure care for people who might otherwise slip through the cracks.

Zolnoori, Noble, and several other colleagues are now preparing to put her technology to the test in the real world. With a new grant from the National Institute on Aging, the team is recruiting three hundred New Yorkers over the age of sixty who receive home care — none of whom have been diagnosed with dementia — along with their visiting nurses and primary-care physicians to participate in a study. "Our goal is to figure out exactly how the speech-analysis system can be integrated into the clinical workflow," Zolnoori says, noting that participants will agree to have their conversations with clinicians recorded in a variety of settings, including in their homes, in office visits, and on the phone. The Columbia researchers will then work with doctors to develop clear protocols for what to do when the software raises a red flag; this will mean teaching them how to interpret the risk scores and talk patients through the findings. Afterward, the researchers will interview patients about whether learning the results was helpful or distressing, and what, if anything, they decide to change in their lives as a result.

Zolnoori is confident that most people who learn they're at risk for dementia will use the information not only to consider medical options but to plan their care and future living arrangements, talk to their families, and put their affairs in order. "Even just having time to emotionally prepare can be huge," she says.

She has seen what happens when people don't have that opportunity. Back in Tehran, where she was born and raised, Zolnoori watched an aunt slip into dementia, oblivious to what was happening to her. "Over the course of several years, she became more confused and forgetful, which was terrifying to her and a

source of endless humiliations," she says. "By the time she was finally diagnosed, she was too far gone to understand."

For Zolnoori, that memory is never far from her work. "If people want to know if dementia may be in their future and prepare for it," she says, "they should have that choice."

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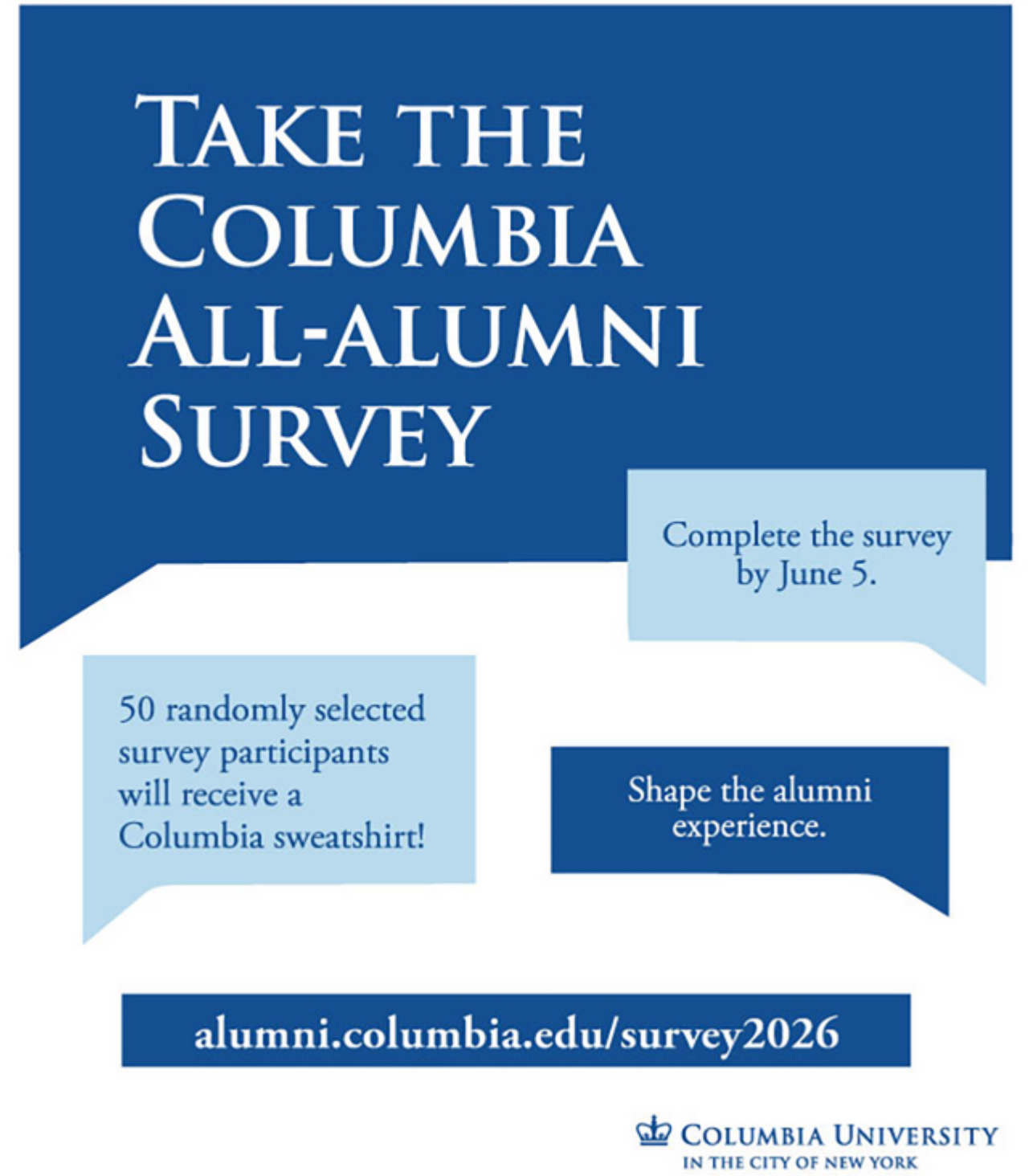

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