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Monitoring (on) Your Mind

Digital Biomarkers for Alzheimer's Disease

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I INTRODUCTION

What first comes to mind when you hear the words "Alzheimer's disease?"

For many, those words evoke images of an older adult who exhibits troubling changes in memory and thinking. Perhaps the older adult has gotten lost driving to church, although it's a familiar route. Perhaps they have bounced a check, which is out of character for them. Perhaps they have repeatedly left the stove on while cooking, worrying their spouse or adult children. Perhaps they have trouble finding words or are confused by devices like iPhones and, as a result, have lost touch with longtime friends.

Alzheimer's disease (AD) has traditionally been understood as a clinical diagnosis, requiring the presence of symptoms to be detected. The older adult we just envisioned might make an appointment with their physician. The physician would likely listen to the patient's medical history – noting the characteristic onset and pattern of impairments – and determine that the patient has *dementia*, a loss of cognitive and functional abilities severe enough to interfere with daily life. Dementia can have numerous causes, and so the physician would also conduct a comprehensive physical and cognitive examination, perhaps ordering lab tests or brain imaging scans, as well as neuropsychological testing. After excluding other causes, the clinician would diagnose the patient with "probable" AD, a diagnosis that can only be confirmed postmortem via autopsy. This approach to diagnosis interweaves the patient's experience of disabling cognitive and functional impairments (i.e., dementia) with the label of AD.[1]

Yet, our ability to measure the neuropathology of AD is rapidly evolving, as is our understanding of the preclinical and prodromal stages of disease. Thus, it is

[1] The utility of an AD diagnosis has been debated. Presently, there is no cure for dementia caused by AD; however, clinicians may prescribe a disease-modifying therapy or medications to temporarily improve or delay dementia symptoms or address other symptoms or conditions, such as depression or agitation. A diagnosis of AD can also be useful for informing lifestyle changes, providing clarity about what is happening, facilitating future planning, and accessing systems and support for the patient and caregiver.

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now possible to identify individuals who are *at risk* for developing dementia caused by AD years or even decades before the onset of cognitive decline through clinical but also digital monitoring. A key premise of this article is that, in the future, the identification of at-risk individuals will continue to occur in clinical settings using traditional biomarker testing; but, the identification of at-risk individuals will also increasingly occur closer to – or even in – one's home, potentially using digital biomarkers.

When you hear "Alzheimer's disease," in-home monitoring should come to mind.

Here, we argue that because AD affects the mind, the challenges associated with monitoring aimed at understanding the risk for disabling cognitive impairments are heightened as compared to the challenges of monitoring for physical ailments. In Section II, we discuss the biomarker transformation of AD, which is allowing us to see AD neuropathology in living persons and to identify individuals at increased risk for developing dementia caused by AD. In Section III, we outline empirical evidence regarding five different digital biomarkers; these digital biomarkers offer further insights into an individual's risk for cognitive impairment and could soon be used for in-home monitoring. Finally, in Section IV, we identify six challenges that are particularly pronounced when monitoring for AD.

II THE EVOLVING UNDERSTANDING OF AD

The field of AD research is rapidly moving from a syndromal definition of AD (see, e.g., the diagnostic process described in Section I) to a biological one. This shift reflects a growing understanding of the mechanisms underlying the clinical expression of AD.[2]

Biomarkers can now be used to identify AD neuropathology in vivo. A biomarker is a "defined characteristic that is measured as an indicator of normal biological processes, pathogenic processes or responses to an exposure or intervention."[3] Individuals are understood to have a biomarker profile, which (as we're using it here) describes the presence or absence in their brain of three AD biomarkers: Beta-amyloid, pathologic tau, or neurodegeneration. These biomarkers can be measured using various modalities, including positron emission tomography (PET), cerebrospinal fluid (CSF) sampling, or magnetic resonance imaging (MRI); moreover, that blood-based biomarker tests are now available.[4]

[2] Clifford R. Jack et al., A/T/N: An Unbiased Descriptive Classification Scheme for Alzheimer Disease Biomarkers, 87 Neurology 539 (2016); Clifford R. Jack et al., NIA-AA Research Framework: Toward a Biological Definition of Alzheimer's Disease, 14 Alzheimer's & Dementia: J. Alzheimer's Ass'n 535 (2018).

[3] FDA-NIH Biomarker Working Group, *BEST (Biomarkers, EndpointS, and other Tools) Resource* (2016).

[4] Suzanne E. Schindler & Randall J. Bateman, Combining Blood-based Biomarkers to Predict Risk for Alzheimer's Disease Dementia, 1 Nat. Aging 26 (2021).

In addition to the biomarker profile, a second, independent source of information is the individual's cognitive stage. An individual may be cognitively unimpaired – within the expected range of cognitive testing scores and functioning in daily life, have mild cognitive impairment (MCI) – a slight but noticeable decline in cognitive skills, or have dementia. The patient's biomarker profile can then be used in combination with the patient's cognitive stage to characterize the patient's place – and likely progression – along the Alzheimer's continuum. The continuum spans the preclinical (i.e., clinically asymptomatic with evidence of AD neuropathology) and clinical (i.e., symptomatic) phases of AD.[5]

Individuals in the preclinical stage have AD biomarkers but do not have clinically measurable cognitive impairment. They may be truly cognitively unimpaired, or they may have subjective cognitive decline – a self-experienced decline in cognitive capacity as compared to baseline.[6] Those with preclinical AD are understood to be at an increased risk of short-term cognitive decline.[7] An estimated 46.7 million Americans have preclinical AD (defined by amyloidosis, neurodegeneration, or both), though it's important to emphasize that not all of them will progress to a dementia-level of impairment.[8]

At present, preclinical AD remains a research construct. It is not yet diagnosed clinically. Researchers hope, however, that intervening earlier rather than later in the course of the disease will allow them to delay or prevent the onset of cognitive and functional impairment. Therefore, they are conducting secondary prevention trials, which recruit individuals who are asymptomatic but biomarker-positive for AD – that is, who have preclinical AD – to test new drugs or novel interventions. It is reasonable to assume that if the preclinical AD construct is validated and if a disease-modifying therapy for AD is found, preclinical AD will move from the research to the clinical context.

In the future, people who receive a preclinical AD diagnosis will have insight into their risk of developing MCI or dementia years or even decades before the onset of impairments.[9] Monitoring digital biomarkers in the home, the focus of Section III, will likely be complementary to clinical assessment. For instance, monitoring may be used to watch for incipient changes in cognition after a preclinical AD diagnosis. Or, conversely, data generated by in-home monitoring may suggest that it is time to see a clinician for an AD workup.

[5] Paul S. Aisen et al., On the Path to 2025: Understanding the Alzheimer's Disease Continuum, 9 Alzheimer's Rsch. & Therapy 60 (2017).

[6] Frank Jessen et al., The Characterisation of Subjective Cognitive Decline, 19 Lancet Neurol. 271 (2020).

[7] Jack et al., supra note 2.

[8] Ron Brookmeyer & Nada Abdalla, Estimation of Lifetime Risks of Alzheimer's Disease Dementia using Biomarkers for Preclinical Disease, 14 Alzheimer's & Dementia 981 (2018); Ron Brookmeyer et al., Forecasting the Prevalence of Preclinical and Clinical Alzheimer's Disease in the United States, 14 Alzheimer's & Dementia 121 (2018).

[9] Jack et al., supra note 2.

III DIGITAL BIOMARKERS OF AD

In parallel with our evolving understanding of beta-amyloid, pathologic tau, and neurodegeneration as "traditional" biomarkers of AD, there have been advances in our understanding of digital biomarkers for AD. Efforts to concretely and comprehensively define digital biomarkers are ongoing.[10] For the purposes of this chapter, we use the following definition: "Objective, quantifiable, physiological, and behavioral data that are collected and measured by means of digital devices, such as embedded environmental sensors, portables, wearables, implantables, or digestibles."[11]

Digital biomarkers have the potential to flag uncharacteristic behaviors or minor mistakes that offer insights into an older adult's risk of cognitive and functional decline or to indicate early cognitive decline. As noted above, the preclinical stage of AD is characterized by the presence of biomarkers in the absence of measurable cognitive impairment. Despite going undetected on standard cognitive tests, subtle cognitive changes may be present. There is, in fact, a growing body of evidence that subjective cognitive decline in individuals with an unimpaired performance on cognitive tests may represent the first symptomatic manifestation of AD.[12] These small changes from the individual's baseline may have downstream effects on complex cognitive and functional behaviors. Digital biomarkers offer a means of capturing these effects.

Here, we discuss five digital biomarkers for AD, highlighting both promising opportunities for monitoring the minds of older adults and limitations in our current knowledge and monitoring abilities. Crucially, these opportunities primarily reside outside of routine clinical settings. These examples are not meant to be exhaustive, but rather have been selected to highlight a range of monitoring modalities involving diverse actors. Moreover, they reveal a variety of potential challenges, which are the focus of Section IV.

A *Driving Patterns*

Due to the complex processes involved in spatial navigation and vehicle operation, an assessment of driving patterns offers an avenue for detecting changes in thinking and behavior. Indeed, prior studies demonstrate that those with symptomatic AD drive shorter distances and visit fewer unique destinations.[13] Research also

[10] Christian Montag, Jon D. Elhai & Paul Dagum, On Blurry Boundaries When Defining Digital Biomarkers: How Much Biology Needs to Be in a Digital Biomarker?, 12 Front. Psychiatry 740292 (2021).

[11] Antoine Piau et al., Current State of Digital Biomarker Technologies for Real-Life, Home-Based Monitoring of Cognitive Function for Mild Cognitive Impairment to Mild Alzheimer Disease and Implications for Clinical Care: Systematic Review, 21 J. Med. Internet Rsch. e12785 (2019).

[12] Frank Jessen et al., A Conceptual Framework for Research on Subjective Cognitive Decline in Preclinical Alzheimer's Disease, 10 Alzheimer's & Dementia 844 (2014).

[13] Lidia P. Kostyniuk & Lisa J. Molnar, Self-regulatory Driving Practices among Older Adults: Health, Age and Sex Effects, 40 Accid. Anal. Prev. 1576 (2008); Jennifer D. Davis et al., Road

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suggests that detectable spatial navigation deficits may precede AD symptom development in cognitively normal individuals with AD biomarkers.[14] A limitation of this work is that it was conducted using simulators, which only measure performance in very controlled settings and so are limited in their generalizability.[15] Studies have, therefore, shifted to a naturalistic approach to data collection to characterize daily driving patterns. Researchers can passively collect data using global positioning system (GPS) devices installed in participant vehicles. The resulting information includes average trip distance, number of unique destinations, number of trips with a speed of six miles per hour or more below the posted limit (i.e., underspeed), and a variety of other measures to quantify driving performance.[16] These studies have found differing behavior and driving patterns between cognitively unimpaired participants with and without AD biomarkers, including a greater decline in the number of days driving per month for those with AD biomarkers.[17]

These findings suggest that assessing driving patterns – as some insurers already do through standalone devices or apps[18] – may help identify individuals at risk for cognitive decline due to AD.

B *Banking and Finances*

Instrumental activities of daily living (IADLs) are complex activities necessary for individuals to live independently, such as managing one's finances. As AD progresses, IADLs become increasingly impaired. A 2021 study examined longitudinal credit report information for over 80,000 Medicare beneficiaries.[19] The researchers found that those with an AD or related dementia diagnosis were more likely to have missed bill payments over the six years prior to their dementia diagnosis. They also found that individuals with a dementia diagnosis developed subprime credit scores two-and-a-half years before their diagnosis. In a prospective study of cognitively

Test and Naturalistic Driving Performance in Healthy and Cognitively Impaired Older Adults: Does Environment Matter?, 60 J. Am. Geriatric Soc'y 2056 (2012).

[14] Samantha L. Allison et al., Spatial Navigation in Preclinical Alzheimer's Disease, 52 J. Alzheimers Dis. 77 (2016); Gillian Coughlan et al., Spatial navigation Deficits – Overlooked Cognitive Marker for Preclinical Alzheimer Disease?, 14 Nat'l Rev. Neurol. 496 (2018).

[15] Megan A. Hird et al., A Systematic Review and Meta-Analysis of On-Road Simulator and Cognitive Driving Assessment in Alzheimer's Disease and Mild Cognitive Impairment, 53 J. Alzheimers Dis. 713 (2016).

[16] Catherine M. Roe et al., A 2.5-Year Longitudinal Assessment of Naturalistic Driving in Preclinical Alzheimer's Disease, 68 J. Alzheimers Dis. 1625 (2019); Sayeh Bayat et al., GPS Driving: A Digital Biomarker for Preclinical Alzheimer Disease, 13 Alzheimer's Rsch. & Therapy 115 (2021).

[17] Roe et al., supra note 16; Bayat et al., supra note 16.

[18] Kristen Hall-Geisler & Jennifer Lobb, How Do Those Car Insurance Tracking Devices Work?, *US News & World Rep.* (March 9, 2022), www.usnews.com/insurance/auto/how-do-those-car-insurance-tracking-devices-work.

[19] Lauren Hersch Nicholas et al., Financial Presentation of Alzheimer Disease and Related Dementias, 181 JAMA Internal Med. 220 (2021).

unimpaired older adults, researchers found that a low awareness of financial and other types of scams was associated with an increased risk for MCI and dementia, though the measure was too weak for prediction at the individual level.[20]

More work is needed to characterize the timeframe of changes in financial management, but detecting changes such as missed payments, bounced checks, or altered purchasing behavior (e.g., repeated purchases) presents another opportunity to identify individuals with preclinical AD. Banking and financial institutions already use algorithms, behavioral analytics, and artificial intelligence (AI)-powered technology to identify unusual transactions or spending behaviors that may be suggestive of fraud.[21] Similar techniques could be adapted to monitor older adults and notify them of behaviors indicative of dementia risk.

C *Smart Appliances*

Sensors can be deployed in the home to detect cognitive changes in older adults.[22] In a task-based study, individuals with MCI have been shown to spend more time in the kitchen when performing a set of home-based activities.[23] While in the kitchen, participants with MCI open cabinets and drawers, as well as the refrigerator, more often than cognitively unimpaired participants.[24] Researchers are exploring whether it is possible to use similar techniques to differentiate between healthy controls and individuals with preclinical AD.[25] A challenge for such monitoring studies (and, by extension, for real-life uptake) is the need to deploy multiple sensors in the home. One study attempted to circumvent this issue by focusing on passive in-home power usage for large appliances; the team found, on average, lower daily and seasonal usage of appliances among people with cognitive impairment.[26]

Smart appliances, like refrigerators and ovens, connect to the internet and can sync with smartphones or other devices. They are already in many homes and are another alternative to sensor-based systems for detecting early cognitive changes. Smart refrigerators could track the frequency with which they are opened and for

[20] Patricia A. Boyle et al., Scam Awareness Related to Incident Alzheimer Dementia and Mild Cognitive Impairment: A Prospective Cohort Study, 170 Annals Internal Med. 702 (2019).

[21] Benjamin Pimentel, Banks Watch Your Every Move Online. Here's How It Prevents Fraud, *Protocol* (June 1, 2021), www.protocol.com/fintech/behavioral-analytics-bank-fraud-detection.

[22] Yuriko Nakaoku et al., AI-Assisted In-House Power Monitoring for the Detection of Cognitive Impairment in Older Adults, 21 Sensors (Basel) 6249 (2021).

[23] Piau et al., supra note 11; Nakaoku et al., supra note 22; Maxime Lussier et al., Smart Home Technology: A New Approach for Performance Measurements of Activities of Daily Living and Prediction of Mild Cognitive Impairment in Older Adults, 68 J. Alzheimers Dis. 85 (2019).

[24] Piau et al., supra note 11; Nakaoku et al., supra note 22; Lussier et al., supra note 23.

[25] The RADAR-AD Consortium et al., Remote Monitoring Technologies in Alzheimer's Disease: Design of the RADAR-AD Study, 13 Alzheimer's Rsch. & Therapy 89 (2021).

[26] Nakaoku et al., supra note 22.

how long. Similarly, smart ovens may track the time they are left on. Such usage information could then be shared with the consumer by the appliance itself, for example, via an app.

D *Speech*

Changes in speech have been used to characterize the progression of AD. Studies have often used active data collection in which individuals are recorded on a smartphone or similar device as they complete tasks associated with verbal fluency, picture description, and free speech. The voice recordings are then processed, sometimes using machine-learning techniques. Studies have found that short vocal tasks can be used to differentiate participants with MCI from those with dementia.[27] It remains an open question whether preclinical AD presents with detectable changes in speech. Yet, one study of speech changes found that cognitively unimpaired participants with AD biomarkers used fewer concrete nouns and content words during spontaneous speech.[28]

The interest in modalities for passive speech data collection – for example, conversations over the phone, communication with digital assistants, and texting related information – is mounting.[29] Improvements in machine-learning to reduce the burden of speech analysis, coupled with broad access to devices with microphones, are increasing the potential of passive speech data collection. Automatic speech recognition used for digital assistants like Amazon Alexa and Apple Siri has made strides in accuracy. As technological advancements further streamline transcription and analysis, speech data may be used to characterize changes related to preclinical AD. Simply put, Alexa may soon diagnose progression along the Alzheimer's continuum from preclinical AD to MCI to dementia.[30]

E *Device Use*

The ways people use their smartphones – including the amount of time spent on certain apps, login attempts, patterns of use, and disruptions in social interactions – may

[27] Alexandra König et al., Automatic Speech Analysis for the Assessment of Patients with Predementia and Alzheimer's Disease, 1 Alzheimer's & Dementia (Amst) 112 (2015); Alexandra Konig et al., Use of Speech Analyses within a Mobile Application for the Assessment of Cognitive Impairment in Elderly People, 15 Current Alzheimer Rsch. 120 (2018); Fredrik Öhman et al., Current Advances in Digital Cognitive Assessment for Preclinical Alzheimer's Disease, 13 Alzheimer's & Dementia (2021).

[28] Sander C.J. Verfaillie et al., High Amyloid Burden is Associated with Fewer Specific Words During Spontaneous Speech in Individuals with Subjective Cognitive Decline, 131 Neuropsychologia 184 (2019).

[29] Jessica Robin et al., Evaluation of Speech-Based Digital Biomarkers: Review and Recommendations, 4 Digit. Biomark 99 (2020); Lampros C. Kourtis et al., Digital Biomarkers for Alzheimer's Disease: The Mobile/Wearable Devices Opportunity, 2 npj Digit. Med. 9 (2019).

[30] David A. Simon et al., Should Alexa Diagnose Alzheimer's?: Legal and Ethical Issues with At-home Consumer Devices, Cell Reps. Med. 100692 (2022).

reveal signs of cognitive decline.[31] Studies examining patterns of smartphone use in older adults with and without cognitive impairment suggest that app usage is related to cognitive health.[32] There is much interest in leveraging device use as a potential marker of cognitive decline. The Intuition Study (NCT05058950), a collaboration between Biogen and Apple Inc., began in September 2021 with the aim of using multimodal passive sensor data from iPhone and Apple Watch usage to differentiate normal cognition from MCI; a secondary aim is to develop a function for predicting between individuals who will and will not develop MCI. With 23,000 participants, this observational longitudinal study will be the largest study to date collecting passive device use data.

Devices, like smartphones, could soon flag usage patterns that are suggestive of an increased risk of decline. Further, specific apps may be developed to detect concerning behavior changes by accessing meta-data from other apps and devices; this may streamline access to information and improve consumer friendliness.

IV CHALLENGES AHEAD

Here, we identify six ethical and legal challenges that will accompany the monitoring of digital biomarkers for AD. These are not exclusive, and many issues associated generally with measuring digital biomarkers will apply here as well. Moreover, the challenges outlined herein are not unique to digital biomarkers for AD. Rather, we would argue that they are heightened in this context because AD is a disease not just of the brain but the mind.

A *Consent to Collect and Consent to Disclose*

Although we hypothesize that preclinical AD will not be diagnosed clinically (i.e., using traditional biomarkers) until there is a disease-modifying therapy that renders the diagnosis medically actionable, in-home monitoring of digital biomarkers is not subject to this constraint. In fact, potential means of collecting and analyzing digital biomarkers for AD are already in our homes.

Yet, it is unlikely that individuals are aware that the GPS devices in their cars, the smart appliances in their kitchens, and the online banking apps on their phones can provide insights into their risk of cognitive and functional decline. Plugging in the GPS device, using the smart oven, or paying bills online, therefore, does not imply consent to having one's brain health measured. Nor can consent be presumed. Many individuals *do not* want to know about their risk of developing dementia

[31] Kourtis et al., supra note 29.

[32] Jonas Rauber, Emily B. Fox & Leon A. Gatys, Modeling Patterns of Smartphone Usage and Their Relationship to Cognitive Health (2019), https://arxiv.org/abs/1911.05683; Mitchell L. Gordon et al., App Usage Predicts Cognitive Ability in Older Adults, in *Proceedings of the 2019 CHI Conference on Human Factors in Computing Systems* 1 (2019), https://dl.acm.org/doi/10.1145/3290605.3300398.

caused by AD because there is little to be done about it.[33] Others eschew learning their dementia risk to avoid existential dread.[34] This all suggests that, if digital biomarkers for AD are to be collected, there must be explicit consent.

Even if individuals agree to having their digital biomarkers for AD monitored, they may ultimately choose against learning what is revealed therein. Some individuals who undergo testing to learn whether they are at risk for dementia caused by AD – whether due to genes or to biomarkers – subsequently decline to learn the results.[35]

This contrasts with – drawing an analogy to emergency medicine – our ability to presume consent for an Apple watch to monitor for and alert us to a possibly fatal arrythmia. But even there, where there is greater reason to presume consent, the evidence suggests we ought to eschew a "more is more" approach to disclosure. Apple watch monitoring for arrythmia can unduly worry people who receive a notification and subsequently follow-up with doctors, undergoing invasive and expensive tests only for the results to come back normal.[36] When the rate of false positives is unknown – or remains high – and when there are risks and burdens associated with disclosure, caution must accompany implementation.

B *Communicating Digital Biomarker Information*

To date, traditional AD biomarker information has been disclosed to cognitively unimpaired adults in highly controlled environments, mostly through research studies and with specialist clinical expertise.[37] Substantial work has gone into developing methods for disclosure, and the recommended steps include preparing people to learn about their biomarker information, maintaining sensitivity in returning the results, and following-up to ensure people feel supported after learning the results.[38] Digital biomarkers present an opportunity for individuals to learn that they are exhibiting subtle signs of cognitive decline or are at risk for dementia in the future from an app or from their banker or insurance agent – and without the option to speak directly and quickly about the results with a medical professional.

[33] Emily A. Largent et al., Disclosing Genetic Risk of Alzheimer's Disease to Cognitively Unimpaired Older Adults: Findings from the Study of Knowledge and Reactions to APOE Testing (SOKRATES II), 84 J. Alzheimer's Dis. 1015 (2021).

[34] Steven Pinker, My Genome, My Self, *The New York Times* (January 7, 2009), www.nytimes.com/2009/01/11/magazine/11Genome-t.html.

[35] Emily A Largent et al., "That Would be Dreadful": The Ethical, Legal, and Social Challenges of Sharing Your Alzheimer's Disease Biomarker and Genetic Testing Results with Others, J. Law & Biosciences lsab004 (2021).

[36] Larry Husten, Beware the Hype over the Apple Watch Heart App. The Device Could Do More Harm Than Good, *Stat* (March 15, 2019), www.statnews.com/2019/03/15/apple-watch-atrial-fibrillation/.

[37] Claire M. Erickson et al., Disclosure of Preclinical Alzheimer's Disease Biomarker Results in Research and Clinical Settings: Why, How, and What We Still Need to Know, 13 Alzheimer's; Dementia: Diagnosis, Assessment; Disease Monitoring (2021).

[38] Kristin Harkins et al., Development of a Process to Disclose Amyloid Imaging Results to Cognitively Normal Older Adult Research Participants, 7 Alzheimer's Rsch. & Therapy 26 (2015).

Although the disclosure of AD biomarkers has generally been found to be safe in pre-screened populations,[39] care should be taken when disclosing digital biomarker information more broadly. Here, the field may learn from discussions of direct-to-consumer genetic or biochemical testing.[40]

Another concern is that the monitoring of digital biomarker data could lead to the inadvertent disclosure of dementia risk. Imagine, for instance, that your changing device usage is flagged and then used to generate targeted advertisements for supplements to boost brain health or for memory games. You could learn you are at risk simply by scrolling through your social media feed. And, in that case, any pretense of thoughtful disclosure is dropped.

C *Conflicting Desires for Monitoring*

Studies suggest that some cognitively unimpaired older adults share their AD biomarker results with others because they would like to be monitored for – and alerted to – changes in cognition and function that might negatively affect their wellbeing.[41] Often, these individuals feel it is ethically important to share this information so as to prepare family members who might, in the future, need to provide dementia care or serve as a surrogate decision maker.[42] Other older adults, however, perceive monitoring as intrusive and unwelcomed.[43]

In an interview study of the family members of cognitively unimpaired older adults with AD biomarkers, some family members described watching the older adult more closely for symptoms of MCI or dementia after learning the biomarker results.[44] This may reflect family members' evolving understanding of themselves as pre-caregivers – individuals at increased risk for informal dementia caregiving.[45] Technology can allow family members to remotely monitor an older adult's location, movements, and activities, in order to detect functional decline and changes

[39] Erickson et al., supra note 37.

[40] Emily A. Largent, Anna Wexler & Jason Karlawish, The Future Is P-Tau – Anticipating Direct-to-Consumer Alzheimer Disease Blood Tests, 78 JAMA Neurol. 379 (2021).

[41] Sato Ashida et al., The Role of Disease Perceptions and Results Sharing in Psychological Adaptation after Genetic Susceptibility Testing: The REVEAL Study, 18 Eur. J. Hum. Genetics 1296 (2010); Largent et al., supra note 35.

[42] Largent et al., supra note 35.

[43] Clara Berridge & Terrie Fox Wetle, Why Older Adults and Their Children Disagree About In-Home Surveillance Technology, Sensors, and Tracking, *Gerontologist* (2020), https://academic.oup.com/gerontologist/advance-article/doi/10.1093/geront/gnz068/5491612; Marcello Ienca et al., Intelligent Assistive Technology for Alzheimer's Disease and Other Dementias: A Systematic Review, 56 J. Alzheimer's Disease 1301 (2017); Largent et al., supra note 35.

[44] Emily A Largent et al., Study Partner Perspectives on Disclosure of Amyloid PET Scan Results: Psychosocial Factors and Environmental Design/Living with Dementia and Quality of Life, 16 Alzheimer's & Dementia (2020).

[45] Emily A. Largent & Jason Karlawish, Preclinical Alzheimer Disease and the Dawn of the Pre-Caregiver, 76 JAMA Neurol. 631 (2019).

in cognition, as well as to intervene if needed. Despite these putative advantages, monitoring may be a source of friction if older adults and their families do not agree on its appropriateness or on who should have access to the resulting information.

V STIGMA AND DISCRIMINATION

Dementia caused by AD is highly stigmatized.[46] Research with cognitively unimpaired individuals who have the AD biomarker beta-amyloid suggests that many worry that this information would be stigmatizing if disclosed to others.[47] Unfortunately, this concern is likely justified; a survey experiment with a nationally representative sample of American adults found that, even in the absence of cognitive symptoms, a positive AD biomarker result evokes stronger stigmatizing reactions among members of the general public than a negative result.[48]

Discrimination occurs when stigmatization is enacted via concrete behaviors. Cognitively unimpaired individuals who have beta-amyloid anticipate discrimination across a variety of contexts – from everyday social interactions to employment, housing, and insurance.[49] It is not yet known whether – and if so to what extent – digital biomarkers will lead to stigma and discrimination. However, we must be aware of this possibility, as well as the scant legal protection against discrimination on the basis of biomarkers.[50]

VI INFORMATION PRIVACY

Digital biomarker information is health information. But it is health information in the hands of bankers and insurance agents or technology companies – individuals and entities that are not health care providers and are therefore not subject to the privacy laws that govern health care data. The Health Insurance Portability and Privacy Act (HIPAA) focuses on data from medical records; it does not, for instance, cover data generated by smartphone apps.[51] The need for privacy is intensified by the potential for stigma and discrimination, discussed above.

[46] Lynne Corner & John Bond, Being at Risk of Dementia: Fears and Anxieties of Older Adults, 18 J. of Aging Studs. 143 (2004); Perla Werner & Shmuel M. Giveon, Discriminatory Behavior of Family Physicians Toward a Person with Alzheimer's Disease, 20 Int. Psychogeriatr. 824 (2008); Alzheimer's Association, 2019 Alzheimer's Disease Facts and Figures, 15 Alzheimers Dementia 321 (2019).

[47] Largent et al., supra note 35.

[48] Shana D. Stites et al., The Relative Contributions of Biomarkers, Disease Modifying Treatment, and Dementia Severity to Alzheimer's Stigma: A Vignette-based Experiment, 292 Soc. Sci. & Med. 114620 (2022).

[49] Largent et al., supra note 35.

[50] Jalayne J. Arias et al., The Proactive Patient: Long-Term Care Insurance Discrimination Risks of Alzheimer's Disease Biomarkers, 46 J. Law. Med. Ethics 485 (2018).

[51] Nicole Martinez-Martin et al., Data Mining for Health: Staking Out the Ethical Territory of Digital Phenotyping, 1 npj Digit. Med. 68 (2018); Anna Wexler & Peter B. Reiner, Oversight of Direct-to-consumer Neurotechnologies, 363 Science 234 (2019).

Further, older adults with MCI and dementia are vulnerable – for example, to financial scammers. It is important to ensure that data generated by monitoring is not abused – by those who collect it or by those who subsequently access it – to identify potential targets for abuse and exploitation. Abuse and exploitation may occur at the hands of an unscrupulous app developer but also, or perhaps more likely, at the hands of an unscrupulous family member or friend.

VII DISPARITIES IN HEALTH AND TECHNOLOGY

The older population is becoming significantly more racially and ethnically diverse.[52] Black and Hispanic older adults are at higher risk than White older adults for developing AD, and they encounter disproportionate barriers to accessing health care generally, and dementia care specifically.[53] Health disparities are increasingly understood to reflect a broad, complex, and interrelated array of factors, including racism.[54] There are well-reported concerns about racism in AI.[55] Those are no less salient here and may be more salient, given disparities in care.

Further, monitoring may be cost prohibitive, impacted by the digital divide, or reliant on an individual's geographic location. For instance, older adults, especially adults from minoritized communities, may not have smart devices. According to a Pew report using data collected in 2021, only 61 percent of those aged 65 and older owned a smartphone and 44 percent owned a tablet.[56] As many of the digital biomarkers described in Section III require a smart device, uptake of monitoring methods may be unevenly distributed and exacerbate, rather than alleviate, disparities in AD care.

VIII CONCLUSION

The older adult we envisioned at the beginning of this chapter will not be the only face of AD much longer. We may soon come to think, too, of adults with preclinical AD. These individuals may learn about their heightened risk of cognitive and

[52] Sandra Colby & Jennifer Ortman, *Projections of the Size and Composition of the US Population: 2014 to 2060*, 13 (2015).

[53] María P. Aranda et al., Impact of Dementia: Health Disparities, Population Trends, Care Interventions, and Economic Costs, 69 J. Am. Geriatrics Soc'y 1774 (2021).

[54] Carl V. Hill et al., The National Institute on Aging Health Disparities Research Framework, 25 Ethn Dis 245 (2015); Camara P. Jones, Levels of Racism: A Theoretic Framework and a Gardener's tale, 90 Am. J. Pub. Health 1212 (2000).

[55] Effy Vayena, Alessandro Blasimme & I. Glenn Cohen, Machine Learning in Medicine: Addressing Ethical Challenges, 15 PLoS Med e1002689 (2018); Ravi B. Parikh, Stephanie Teeple & Amol S. Navathe, Addressing Bias in Artificial Intelligence in Health Care, 322 JAMA 2377 (2019).

[56] Michelle Faverio, Share of Those 65 and Older Who Are Tech Users Has Grown in the Past Decade, *Pew Rsch. Ctr.* (January 13, 2022), www.pewresearch.org/fact-tank/2022/01/13/share-of-those-65-and-older-who-are-tech-users-has-grown-in-the-past-decade/.

functional impairment from a clinician. Or they may learn about it because the GPS device plugged into their car has detected slight alterations in their driving patterns, because their smart refrigerator has alerted them to the fridge door staying open a bit longer, or because their phone has noted slight changes in speech.

AD is undergoing a biomarker transformation, of which digital biomarkers are a part. AD is a deeply feared condition, as it robs people of their ability to self-determine. Care must therefore be taken to address the multitude of challenges that arise when monitoring our minds.

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