



# Detecting Dementia

Emerging Innovations and Their Implications for  
American Adults and Their Health Care

**A NEHI Report**

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## Acknowledgments

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## About this report

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## About NEHI

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NEHI is a non-profit, unbiased organization with members, including providers, payers, hospitals and health systems, pharmaceutical and biotech companies, medical device, and technology providers, as well as associations and consultants. Through interdisciplinary collaboration and with our members' guidance, we research and examine tough and timely health care innovation issues from multiple, often divergent, perspectives. We then address policy and adoption challenges to promote the value of innovative products and processes.

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## Executive Summary

**Dementia is significantly under-detected and undiagnosed** among U.S. adults, with estimates indicating that up to 61% of dementia cases go undiagnosed.<sup>1</sup>

- Racial-ethnic disparities are also pronounced. Black and Latino Americans are 1.5 to two times as likely to develop Alzheimer's disease or other dementias compared to white peers, with a particularly underreported rate of missed diagnoses.<sup>2</sup>

**Under-detection and under-diagnosis of dementia results in a major gap in care for Medicare beneficiaries** and exacerbates the long-term burden of dementia, Alzheimer's disease, and related neurological disorders on patients, caregivers, and the Medicare program. The Alzheimer's Association has estimated that total annual costs per person for Medicare beneficiaries with dementia and related conditions is nearly triple the costs for beneficiaries with no dementia (\$43,644 vs. \$14,660, 2023 dollars).<sup>3</sup>

**Patients are missing opportunities for early intervention** to arrest or slow the progression of dementia, due to under-detection and under-diagnosis.

- Ongoing research indicates that as much as 40% of dementia cases can be attributed to modifiable risk factors such as exposure to pollutants, stress, and complications from chronic diseases.<sup>4</sup> Under-detection of dementia inhibits public health initiatives and preventive health measures that could address dementia.
- Multiple drug therapies for Alzheimer's disease are expected to emerge in the coming years. It is generally thought that drug therapy will be most effective when administered early in a patient's disease progression.

**Ongoing innovations create new capabilities to improve and scale-up dementia screening.** New tests, tools, and protocols for dementia screening are enabling capabilities to a) administer dementia screening more rapidly and more efficiently in primary health care settings, b) support testing and monitoring by patients and caregivers themselves, and c) support more comprehensive assessment by primary care teams, (i.e. capabilities for **"brain health assessment"**), and

d) reduce unnecessary or unproductive referrals to neurologists and specialty services by primary care teams.

Innovations for dementia screening and brain health assessment are driven by advances in biomarker development, testing technologies, data integration, and analytical methods, as seen in the launch of new digital tools and laboratory tests.

**Innovations are also accelerating the capability to detect risks or precursors of dementia among individuals who show no signs or symptoms (i.e. asymptomatic persons).**

Pre-symptomatic detection of dementia will create new opportunities for early intervention—but not all patients who test positive for early signs will develop full-blown dementia. Early detection presents important and unresolved issues of ethics and clinical utility.

**Substantial barriers to the uptake of innovative tools remain.** While innovations could improve the ability of primary care teams to assess brain health at scale, pressures on primary care, doubts about the clinical utility of dementia care, and limited incentives inhibit uptake.

### Recommendations

This report details the actions needed to realize the benefits of innovative dementia screening and brain health assessment. They include:

- Reevaluating the scope of Medicare benefits for cognitive impairment and dementia, Medicare quality and performance improvement incentives, and alternative payment models.
- Raising the priority of research on biomarker development and utilization of innovative tests, tools, and protocols among research grantmakers (federal agencies, private grantmakers), including research on safe and accurate use among historically marginalized and under-represented groups.
- Promoting open, transparent debate on the ethics and utility of pre-symptomatic detection of dementia.
- Identifying and filling gaps in procedural and billing codes that will support reimbursement for appropriate use of innovative dementia screening and brain health assessment.

<sup>1</sup> Lang L, Clifford A, Wei L, et al. Prevalence and determinants of undetected dementia in the community: a systematic literature review and a meta-analysis. *BMJ Open*. 2017;7(2):e011146. doi:10.1136/bmjopen-2016-011146

<sup>2</sup> Alzheimer's Association. 2019 Alzheimer's Disease Facts and Figures. 2019. Accessed August 10, 2024. <https://www.alz.org/media/Documents/alzheimers-facts-and-figures-2019-r.pdf>

<sup>3</sup> Pothen Skaria A. The Economic and Societal Burden of Alzheimer Disease: Managed Care Considerations. *AJMC*. Published online 2022. Accessed August 10, 2024. <https://www.ajmc.com/view/the-economic-and-societal-burden-of-alzheimer-disease-managed-care-considerations>

<sup>4</sup> Livingston G, Huntley J, Liu KY, Costafreda SG. Dementia prevention, intervention, and care: 2024 report of the Lancet standing Commission. *The Lancet*. Published online 2024. doi:[https://doi.org/10.1016/S0140-6736\(24\)01296-0](https://doi.org/10.1016/S0140-6736(24)01296-0)

# Dementia Screening and Detection Among U.S. Adults Today

**Clinical detection of dementia falls far short of its prevalence among U.S. adults.** Dementia is a condition that often begins with subtle changes in memory, cognition, mood, speech, and hearing. In many cases, a patient is only screened for dementia when the patient, a caregiver, or a clinician observes clear signs or symptoms of dementia or by a suspicion that the patient is already suffering from Alzheimer’s disease or another serious neurological condition. Recent estimates suggest that the true underlying prevalence of dementia and mild cognitive impairment (MCI) among U.S. adults ages 65 and older is as high as 10% and 22%, respectively,<sup>1</sup> but that the rate of undetected dementia may be as high as 61%.<sup>2</sup> It is estimated that the number of elder Americans with dementia—approximately 7 million in 2024—will grow to approximately 14 million by 2060.<sup>3</sup> (See **Appendix A** for greater detail.)

## **Significant racial-ethnic disparities exist in the prevalence of mild cognitive impairment or dementia.**

Multiple studies suggest that Black Americans are two times as likely to develop Alzheimer’s disease or other dementias compared to white peers, while Latino Americans are as much as 1.5 times as likely to develop these conditions.<sup>4</sup> Studies attribute these disparities largely to socioeconomic factors: low income, disparities in education level, exposure to environmental risk factors such as stress and pollution, and others.<sup>4</sup> A recent study of “traditional” (fee for service) Medicare beneficiaries found documented rates of dementia and Alzheimer’s disease of 12.2% among Hispanic individuals, 14% among Black Americans, and 10.3% among non-Hispanic white individuals.<sup>4,5</sup> Disparities among Medicare beneficiaries aged 85 or older are even wider, with an estimated 43% of Black beneficiaries and 40% of Hispanic beneficiaries suffering from dementia compared to 33% of non-Hispanic white beneficiaries.<sup>5</sup> A 2019 survey of Alzheimer’s research from the Alzheimer’s Association suggests that the rate of missed diagnoses of dementias among Black Americans is actually higher than generally reported rates.<sup>4</sup>

Individuals with Down syndrome are also significantly more likely to develop dementia and Alzheimer’s disease over their lifetime, with onset starting as early as the age of 35.<sup>6</sup> An estimated 60% of individuals with Down syndrome ages 65 and older have Alzheimer’s disease compared to 11% among

## **Detecting Brain Disorders: Clinical Practice Today vs. Clinical Practice of the Future**

### ***Screening and Diagnostic Practices Today***

There is great variability in patients’ experience with dementia screening, follow-up assessment, and diagnosis. Their experience often depends on whether a caregiver, clinician, or the patient themselves take the first step toward screening, and how far a patient’s dementia may have progressed.

Standard screening practices focus on detection of mild cognitive impairment (MCI). Patients often miss opportunities for early intervention to reverse, avert, or delay progression of MCI, dementia, or other dementia-related conditions such as Alzheimer’s disease. Diagnosis of specific types of dementia (differential diagnosis) is complex, and often involves referral to one or more clinical specialties.

### ***Screening and Diagnostic Practices in the Future***

Brain health is emerging as a new paradigm for public health and population health management as:

- The onset of dementia is associated with numerous modifiable risk factors.
- Preventive health measures could avert or delay dementia among many Americans if adopted at greater scale and maintained persistently.

Screening for MCI and dementia at greater scale will be necessary (as will follow-up through more holistic “brain health assessment”) for patients who could benefit from preventive health measures or, when necessary, active treatment for Alzheimer’s disease and other neurological disorders.

***See Appendix A for greater detail.***

adults without Down syndrome.<sup>6</sup> The high prevalence of Alzheimer’s disease in patients with Down syndrome is attributed to genetics, (the extra presence of chromosome 21), which has raised awareness in the Down syndrome community regarding the importance of adapting or developing innovative screening and diagnostic tests and tools that are configured around the unique genetic and health characteristics of individuals with Down syndrome.<sup>6</sup>

## Implications for Medicare

**Under-detection of dementia results in a major gap in care for Medicare beneficiaries.** The average total annual cost for Medicare beneficiaries 65 years and older with Alzheimer’s disease and other forms of dementia is estimated to be \$41,757 (2021 dollars), as compared to an annual cost of \$14,026 for those without dementia-related conditions.<sup>7</sup> Estimates of the financial burden of Alzheimer’s-related care alone (as distinct from care for other dementia-related conditions) surpassed \$500 billion per year in 2020, and is expected to rise to \$1.6 trillion per year by 2050.<sup>8</sup>

While Medicare covers cognitive assessment for adults over the age of 65, data suggests that routine uptake of cognitive assessment does not match the underlying prevalence of dementia among Medicare beneficiaries. Cognitive assessment is a required element of the Medicare Annual Wellness Visit (AWV), although it competes for clinicians’ attention with eight other required elements.<sup>9</sup> Approximately 50% of Medicare beneficiaries received an AWV according to a 2019 study, and only 20% of these visits included a cognitive assessment. Only 30% of Medicare beneficiaries received a cognitive assessment in any physician visit.<sup>10</sup> A dementia-specific benefit, the Medicare Cognitive Assessment and Care Plan Services benefit, covers a 60 minute visit designed both to conduct a patient cognitive assessment and design a care plan for the patient. A recent General Accountability Office (GAO) analysis suggests that uptake of the benefit remains low, with only 2.4% of beneficiaries with Alzheimer’s disease or a related disorder receiving the service.<sup>11</sup>

Despite (or perhaps, due to) the absence of health benefit coverage and provider incentives for cognitive assessment, U.S. professional societies have not ceased promoting stronger voluntary efforts to increase dementia screening and follow-up assessment among clinicians and caregivers. For example, the 5,500-member Gerontological Society of America promotes and routinely updates a compendium of best practices directed at primary care teams serving aging adults.<sup>12</sup>

## Targets for Innovation: Accurate, Efficient, and Rapid Dementia Screening and Follow-up Assessment

**Emerging innovations are now increasing the ability to screen and assess patients for dementia and related disorders and perform assessments in primary care and other non-specialty settings.** Emerging innovations include tests of both pathological (i.e. biological) markers and behavioral and neuropsychological markers of potential disease. Moreover, many are designed for administration in primary care or by caregivers and patients themselves in the home or other community-based settings. (See the “Innovations in Dementia Screening and Brain Health Assessment” text box for greater detail.)

**Successful innovations—those that improve patient care—will enable clinicians to overcome multiple challenges around initiating and monitoring dementia screening with patients and in follow-up assessment.** Despite the relatively high prevalence of MCI and dementia among older adults in the U.S., clinicians face numerous barriers to intensifying their efforts to screen and detect dementia. Innovative tests, tools, and protocols for dementia screening need to meet these challenges to prove their value. **Appendix B** outlines five trends in innovation for dementia screening and brain health assessment, including the new capabilities they present and the unmet needs they aim to address. Key attributes of the most promising innovations are:

1. Accurate detection of dementia based on an expanded set of detectable biomarkers—both pathological biomarkers and novel markers of patient behavior and neuropsychology.
2. Capability to administer testing rapidly so that screening and follow-up assessment are more easily integrated into patient visits with clinicians, thus enabling initiation of screening and follow-up assessment at greater scale compared to current rates of screening.
3. Tests, tools, and protocols designed for administration in non-specialty settings, including primary health care and among patients and caregivers whose reporting can complement or augment screenings and assessments conducted by clinicians.
4. Capability to assess the patient’s risk for dementia based on routinely collected data (e.g., electronic medical record [EMR] data, insurance claims data, etc.), potentially

supporting clinician counseling of patients and caregivers, and enabling prioritization of patients at elevated risks for screening and monitoring.

5. Delivery of results directly to primary care teams, enabling appropriate follow-up within primary care and ruling out low priority or unnecessary referrals to neurologists and other specialists—a critically needed capability given the limited number of neurologists in the U.S.—and uneven access to neurology services. (As of 2017, twenty U.S. states have been identified as “neurology deserts,” indicative of shortages in dementia specialists in over half of the U.S.)<sup>12-14</sup>

**Notably, emerging innovations may also enable early detection of dementia risks among asymptomatic patients.** The launch of blood-based biomarker tests for Alzheimer’s disease now enables the detection of Alzheimer’s pathologies in the brain, not only among persons suffering signs and symptoms of the disease, but also among persons with no signs or symptoms (i.e. asymptomatic persons). Early detection among asymptomatic individuals raises important but unresolved questions around medical ethics and clinical utility.<sup>15</sup> The current scientific consensus is that asymptomatic individuals found with early pathologies of Alzheimer’s disease will not necessarily progress into symptomatic disease. However, it is also generally believed that preventive health measures and treatment will be most effective in delaying or deterring dementia and related disorders when administered at the earliest possible point in the disease progression.<sup>16</sup>

## Innovations Will Create a New Capability for Brain Health Assessment in Primary Care

Innovations in screening and follow-up assessment could have a major impact on dementia care delivered by primary care teams. Whereas primary care teams today have limited capabilities and resources to conduct follow-up assessments when patients exhibit signs of dementia on standard assessments, new tools, tests, and protocols may enable primary care teams to conduct a more holistic assessment – a brain health assessment. Brain health assessment will be based on the capabilities to evaluate a patient’s neurological health based on the expanded set of markers (cognitive, functional, and pathological) that can be tested through new digital tools, laboratory tests, and analytical methods. This could have

### Innovations in Dementia Screening and Brain Health Assessment: What Are They? How Could They Change Health Care?

Two trends are driving innovations for dementia screening and brain health assessment: discovery and validation of biomarkers, and an expanding number of technologies for biomarker detection and analysis. Innovations are evident in several fields.

**Biomarkers.** New or emerging biomarkers include pathological biomarkers and behavioral/neuropsychological biomarkers.

**Genetic testing** for gene mutations or other genetic anomalies associated with the onset of Alzheimer’s disease or other neurological disorders.

**Neuropsychological testing** that utilizes digital devices that adapt standard tests for dementia (e.g., the Clock Drawing Test) with the capability to collect data on other markers of dementia, such as markers in speech patterns, patient movement, and hearing.

**Laboratory testing** for blood-based biomarkers of Alzheimer’s disease.

**Data integration.** Integration of data on multiple markers of dementia and related disorders is creating capabilities for more comprehensive assessment of patients.

**Predictive analytics.** Applications of artificial intelligence techniques to large datasets of patient health information are creating capabilities to identify patients at elevated risk for dementia before it is otherwise apparent or reported to clinicians.

*See Appendix B for greater detail.*

an important impact on improving dementia-related care provided by primary care teams and on prioritizing referrals to neurologists and other specialists by:

- “Ruling in” the need for further testing and assessment for patients at the highest risk for advanced dementia, Alzheimer’s disease, and other neurological conditions. This includes referral to more complex testing and specialist services, such as brain imaging or more advanced

laboratory testing that may be necessary to detect serious neurological conditions such as Alzheimer’s disease.

- “Ruling out” the need for further testing and assessment by specialists for patients not at high risk, thus enabling primary care teams to design appropriate care plans directly and promptly.
- Creating new capabilities for routine monitoring of patients for signs of dementia and the progression of dementia or more serious, dementia-related diseases such as Alzheimer’s disease.

## Nonetheless, Significant Scale-Up Barriers Remain

**Better tests, tools, and protocols for screening and brain health assessment will be integral to the scale-up of dementia prevention, care, and treatment. However, support for comprehensive dementia interventions is still necessary.** Substantial barriers to the scale-up of dementia care must be overcome:

- **Fear and stigma deter patients from seeking help.** Many patients hesitate to seek help for their cognitive concerns out of fear of dementia and its stigma, denial of signs of MCI and dementia symptoms, and a belief that little can be done to treat dementia or mitigate its progression meaningfully.<sup>17</sup>
- **Doubts over the clinical utility of screening and brain health assessment are still pervasive.** Doubts that dementia can be treated or managed effectively—or what clinicians describe as doubts over clinical utility—are still common in the medical community. Scientific evidence to support the clinical utility of screening continues to accumulate, including evidence that preventive measures (e.g., smoking cessation, improved nutrition, physical activity, and social engagement) can mitigate or delay the progression of dementia. New anti-amyloid treatments for Alzheimer’s disease are now an option for some patients and represent a new justification for the clinical utility of dementia screening and brain health assessment.

Nevertheless, widely accepted clinical practice guidelines supporting routine cognitive assessment among adults have yet to materialize, due to weak patient health outcomes identified in the overall body of peer-reviewed evidence. The nation’s leading neurology professional

society, the American Academy of Neurology, encourages physicians to routinely track and assess the cognitive health of U.S. adults ages 65 and older.<sup>18</sup> However, the nation’s leading societies of primary care physicians, the American Academy of Family Physicians and the American College of Physicians, follow the lead of the U.S. Preventive Services Task Force (USPSTF), which rates the evidence supporting routine assessment as inconclusive.<sup>19</sup>

### **Many primary care practices are not positioned to adopt innovative screening and brain health assessment.**

Many primary care teams in the U.S. are ill-equipped to take advantage of innovative tests, tools, and protocols for dementia screening and brain health assessment without greater support to offer testing to patients, process results, interpret them for patients, and make appropriate referrals to specialists when warranted. Key reasons include:

- **The overall crisis in primary health care.** Stress and burnout are widely reported among primary care teams and are ascribed to excessive burdens of services required by payers, low reimbursement rates, and diminished physician autonomy. The decrease in young physicians electing to practice in primary care has also diminished patient access to care and exacerbated longer waiting periods for routine visits.<sup>20</sup>
- **Limited incentives for the delivery of dementia-related care.** Performance metrics for dementia screening and cognitive assessment are not priorities or commonly selected as metrics qualifying clinicians for incentives under the value-based payment models implemented by most public and private sector health care payers. (One exception is the Healthcare Effectiveness Data and Information Set [HEDIS] measure of high-risk medications used among older patients, a measure designed to reduce risks often associated with medication use among older patients with dementia.) The Medicare program is taking a major step forward by launching a voluntary alternative payment model for dementia care, the GUIDE Model (Guiding an Improved Dementia Experience Model). Currently, the GUIDE Model will support care for patients previously identified with dementia, thus supporting the monitoring of dementia progression but not initial screening and assessment.<sup>21</sup>



## Improving Patient Care Through Innovative Dementia Screening and Brain Health Assessment: Next Steps

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Emerging innovations should enable more comprehensive, rapid, and scalable dementia screening and brain health assessment in the years ahead. Greater awareness of these capabilities among clinicians, caregivers, and patients could create stronger momentum for dementia screening and brain health assessment and overall improvements in primary health care. These innovations generate hard data on the prevalence of dementia among U.S. adults, including data on the early stages of dementia and risks for its progression. In the past, the launch of highly scalable screening and laboratory testing procedures has generated data on previously underestimated health risks and shifted clinical practice, public health guidelines, and payment policy. For example, the invention of highly scalable blood testing for lipid profiles in the 1980s led to new guidelines for cholesterol management and the widespread prescription of statin drugs to treat unhealthy cholesterol levels in patients.<sup>22</sup>

Nevertheless, widespread adoption of these innovations will likely depend on how readily they are integrated into primary care teams' routine workflows or how easily workflows can be adapted to accommodate new tests and tools. Integrating innovative dementia screening and brain health assessment into routine practice will be particularly challenging, especially at a time when U.S. primary care is under great stress and many patients have difficulty accessing care of any type.<sup>23</sup>

In our estimation, the ideal administration of innovations for dementia screening and brain health assessment would occur in three prototypical encounters among patients, caregivers, and clinicians:

1. **Routine screening:** Routine screening encompasses initial (first-ever) patient screening that establishes a baseline for a patient's cognition and function, subsequent, regularly occurring screenings, and for patients diagnosed with dementia, recurring screenings to monitor the progression of dementia or related conditions such as Alzheimer's disease. Routine screening today is most often conducted through standard tests such as the Montreal Cognitive Assessment (MoCA) and the Mini-Mental State Examination (MMSE).<sup>24</sup>

2. **Brain health assessment:** Ideally, new forms of patient appointments with primary care teams should accommodate brain health assessments that yield a more comprehensive assessment of a patient's susceptibility to (or progression of) dementia that is typically produced today in primary care. Brain health assessments will occur through innovative neuropsychological testing and laboratory tests commissioned before or during the primary care visit.
3. **Return of results from brain health assessment:** While emerging innovations for neuropsychological evaluation and pathological biomarker testing will enable additional testing during a primary care visit, the opportunity to analyze results may still occur outside the visit. For example, test data may be evaluated by third-party vendors and clinical laboratories or the testing device manufacturer. Once results are available to physicians, they may also require time with patients and caregivers to interpret results, offer counseling, devise care plans, or recommend referrals for further evaluation.

## Recommendations

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We foresee the need to reevaluate policy in three primary areas: Medicare, biomedical and health services research, and the reimbursement processes (including Medicare and all payers). Prioritizing these areas could promote the demonstration and validation of innovative dementia screening and brain health assessment tests, tools, and protocols, and support high-value utilization of these innovations.

### Medicare Benefits

Given the high rate of undetected dementia among Medicare beneficiaries, several Medicare benefits and Medicare payment and quality improvement programs should be reevaluated by the Medicare program and key stakeholders (i.e., patient advocates, providers, professional societies, and quality measure developers) for potential reforms. Reforms should aim to create payment mechanisms and quality improvement incentives that support the three key interventions identified above, including routine screening, brain health assessment, and timely return of results from brain health assessments to providers, patients, and caregivers.

**The Medicare Annual Wellness Visit should be reevaluated to determine the feasibility of promoting greater uptake of cognitive assessments.** Most health screenings, such as

cancer screenings for Medicare and non-Medicare patients, are often managed around annual physical examinations. Medicare's authorizing statute does not allow coverage of annual physical examinations (although some Medicare Advantage plans now offer physical examinations as a covered benefit). Beneficiaries of traditional, fee-for-service Medicare (now comprising slightly less than 50% of all beneficiaries) bear the cost of physical examinations. Medicare will cover patients for visits deemed "medically necessary," including visits patients and caregivers schedule themselves so that physicians can examine patients for signs of cognitive impairment.

Medicare's fragmented coverage of physical examinations deprives physicians of a regularly recurring opportunity to proactively spot and address MCI and apparent dementia in their patients.

As the name implies, Medicare's Annual Wellness Visit (AWV) benefit is a covered, annual benefit for all Medicare beneficiaries with no out-of-pocket cost. In theory, the AWV allows clinicians to proactively address signs of impairment in patients, provided that patients avail themselves of the benefit. Patient uptake of the AWV is low, as is the uptake of cognitive assessment within completed AWVs. Recent estimates suggest that fewer than half of eligible Medicare beneficiaries participate in an AWV and that cognitive assessments occur in less than half of AWVs completed.<sup>10</sup> As previously mentioned, cognitive assessment is one of nine processes required within a single AWV.

Typical AWV visits are estimated to run from 20 to 60 minutes. Some innovative dementia screening tools now entering the market can facilitate screening in less than 10 minutes, and some in as little as three minutes. However, given the relatively low utilization of AWVs and cognitive assessment within completed AWVs, the AWV could be reassessed to determine whether Medicare should offer greater incentives to physicians to promote AWVs with patients. The visit could also be reassessed to include thorough cognitive assessments, particularly for patients at increasing risk for dementia due to advancing age or other identifiable factors.

### **The Medicare Cognitive Assessment and Care Plan Services Benefit**

In 2017, Medicare initiated coverage of a new benefit for both comprehensive cognitive assessment by clinicians and the subsequent creation of dementia care plans for individual patients: the Cognitive Assessment and Care Plan Services (CACPS)

benefit. The CACPS is a benefit seemingly well-matched for comprehensive brain health assessments enabled by emerging innovations in neuropsychological and pathological biomarker laboratory testing. However, a recent evaluation by the GAO suggests that uptake of the CACPS benefit is limited, (less than 3% of eligible Medicare beneficiaries according to 2021 data).<sup>25</sup> Limited uptake of the benefit may be due to several factors that bear reevaluation, including:

- **Length of the assessment visit:** Provider reimbursement for the CACPS visit is based on a 60-minute visit; acknowledgment that typical 15- to 20-minute patient visits with primary care providers is not sufficient to conduct an adequate cognitive assessment and design an appropriate care plan. The GAO's 2023 review concluded that, at 60 minutes, the CACPS visit can be difficult for clinicians to schedule (given the volume of short visits they must schedule each day) but may still be too short to conduct a thorough assessment. The utilization of innovative neuropsychological tests (such as digitally enabled tests) promises to reduce the time necessary to conduct a full-scale CACPS assessment, but a thorough assessment may still require creating payment and performance incentives that facilitate scheduling adequate time.
- **Scope of the CACPS:** Innovative tests for dementia screening and brain health assessment may reduce the time needed to administer tests to patients when they visit primary care teams or are at a clinic. Data reported by patients and caregivers who test or monitor cognitive function in the home (again, via innovative digital tools) may also reduce the time clinicians need to administer tests. However, the use of innovative tests and tools may generate data that requires results to be evaluated after the patient visit. High-value use of innovative screening and brain health assessment tests and tools to create a rigorous CACPS care plan may require the benefit to cover appointments for test administration, results interpretation, and design of a patient-specific care plan.

## **Medicare Quality Improvement Programs**

Medicare's quality improvement programs and initiatives should be reevaluated for the feasibility of promoting uptake of dementia-related quality improvements on a scale that is more commensurate with the prevalence of MCI and dementia among Medicare beneficiaries. Providers serving patients in traditional (fee-for-service) Medicare are eligible to seek quality and performance incentives in either the Merit-based

Incentive Payment System (MIPS) or in alternative payment models (APMs). Private insurers offering Medicare Advantage plans are incentivized to promote quality and performance improvements among providers by competing for high ratings under the Medicare Star Ratings program.

### **The Merit-based Incentive Payment System**

Under the current MIPS programs health care providers are eligible for financial bonuses if they demonstrate high performance against a set of health care quality and performance measures of their choosing. Four dementia-related measures are included in Medicare's total roster of over 200 measures. Publicly available data suggests that the most frequently used MIPS measures are measures related to preventive health care (such as vaccinations and cancer screenings) and to chronic disease management (such as blood pressure and hemoglobin a1C control) – all measures that pertain to the health of Medicare beneficiaries of all ages and cognitive status.<sup>26</sup> Given the high underlying prevalence of dementia among Medicare patients and the long-term burden of dementia-related care, the MIPS program might be reevaluated usefully to ascertain how dementia screening, brain health assessment, and dementia care could be better incentivized, notwithstanding the continuing need to support preventive health care and chronic disease management. The four current dementia-related MIPS measures support a range of basic patient screening and assessment interventions, and caregiver education:

1. *Dementia: Cognitive Assessment.* Percentage of patients, regardless of age, with a diagnosis of dementia for whom an assessment of cognition is performed and the results reviewed at least once within a 12-month period.
2. *Dementia: Education and Support of Caregivers for Patients with Dementia.* Percentage of patients with dementia whose caregiver(s) were provided with education on dementia disease management and health behavior changes AND were referred to additional resources for support in the last 12 months.
3. *Dementia: Functional Status Assessment.* Percentage of patients with dementia for whom an assessment of functional status was performed at least once in the last 12 months.
4. *Dementia: Safety Concern Screening and Follow-Up for Patients with Dementia.* Percentage of patients with dementia or their caregiver(s) for whom there was a documented safety concerns screening in two domains of risk: 1) dangerousness to self or others, 2) environmental risks; and if safety concerns screening was positive in the last 12 months, there was documentation of mitigation

recommendations, including but not limited to referral to other resources.<sup>27</sup>

### **Medicare Advantage and Star Ratings**

Medicare Advantage is now the source of Medicare coverage for just over half of all Medicare beneficiaries and is expected to remain the source of coverage for a majority of beneficiaries. Research studies suggest that cognitive assessment uptake in AWWs is somewhat higher among Medicare Advantage beneficiaries than those covered under traditional Medicare.<sup>10</sup> While routine annual physical examinations are not covered under traditional, fee-for-service Medicare, some Medicare Advantage plans offer coverage. Annual physical examinations often serve as an opportunity for patients to update their health screenings and could provide opportunities for dementia screening.

Then again, the original rationale for the creation of Medicare Advantage as invoked by Congress was the capability of private insurers to manage patient care within overall, per-patient-per-month budgets while improving patient care quality measured against transparent benchmark measures, including Medicare's Star Ratings benchmarks. CMS might incentivize dementia screening and dementia care at a scale more commensurate with the burden of dementia-related illness by moving validated metrics of dementia screening, brain health assessment and dementia care into the yearly Star Ratings. This could include moving metrics of cognitive assessment and biomarker testing into the program's Staying Healthy measures, and measures of dementia care into the Chronic Conditions Management Star metrics.

### **Alternative Payment Models**

The Affordable Care Act authorized the creation of the CMS Innovation Center (CMMI) and granted CMMI broad authority to design and test alternative models of health care provider payment models (APMs) and health care delivery. Until recently, dementia screening, prevention, and care had not been specific, targeted priorities for CMMI programs. However, in 2024, CMMI launched an eight-year APM to demonstrate improvements in dementia care, including services that will lessen burdens on family members and other unpaid caregivers.<sup>21</sup> The GUIDE (Guiding an Improved Dementia Experience) Model will cover beneficiaries in traditional, fee-for-service Medicare and, by definition, service patients with existing dementia. Patients are eligible for services under GUIDE based on an attestation of dementia from their clinicians.

The GUIDE model could be a significant vehicle for demonstrating improvements in monitoring the progression of dementia and related disorders among patients who receive an attestation of dementia. Demand for attestations of dementia will also create an opportunity for use of innovative tests, tools, and protocols that support initial screening and assessment of patients.

CMS should evaluate and consider expansion of approved screening and brain health assessment tools to maximize the opportunity created by GUIDE and consider enhancement to its training program for GUIDE providers and caregivers that will spread greater understanding of emerging capabilities for timely and accurate screening, brain health assessment and diagnosis of dementia-related disorders. Results from the GUIDE model should also be evaluated to inform the health care quality and performance goals of CMMI's entire array of APMs that serve the chronic care needs of Medicare beneficiaries, including new consideration of coverage for preventive health interventions, dementia screening, brain health assessment, and dementia care planning.

## Biomedical and Health Services Research

Research grantmakers in the federal government (e.g., the National Institutes of Health [NIH], Agency for Healthcare Research and Quality [AHRQ], and the Patient-Centered Outcomes Research Institute [PCORI]) and the private sector have a key role in expediting the development and utilization of innovative tests, tools, and protocols for dementia screening and brain health assessment. Research support is needed for foundational biological research (e.g., research on biomarkers of dementia and related disorders), technology development (e.g., novel assays, laboratory testing, and digital tools), and health services research that will support appropriate adoption of innovative tests, tools, and protocols. We recommend research support priorities below.

**Expedite generation of evidence on cognitive assessment for review by the U.S. Preventive Services Task Force.** Recommendations made by the USPSTF are the most significant influences on preventive health service standards in the U.S. Health insurance plans regulated by the Affordable Care Act (ACA) are required to cover preventive health services receiving an A or B grade for effectiveness by the USPSTF. Medicare generally covers these services as well. Typically, preventive health services supported by the USPSTF become subject to

the development, validation, and adoption of widely used healthcare quality and performance metrics (e.g., HEDIS and Medicare Star ratings) used in provider payment models.

The USPSTF regularly reviews evidence on dementia screening (defined as cognitive assessment), most recently in 2019, when it reaffirmed its position that evidence on the effectiveness of cognitive assessment is inconclusive and merits a grade of "I" for "Incomplete." Numerous organizations in the U.S. Alzheimer's disease and neurology communities have pointed out that the USPSTF's 2019 evaluation cites a lack of evidence that cognitive assessment influences a reduction in "age-related dementia," yet scientific evidence on dementia also indicates that aging is only one of several risk factors for dementia and that the progression of dementia can be prevented or reduced by health promotion (sleep, nutrition, physical activity, social engagement, etc.).<sup>28</sup> (A recent systematic review by the Lancet Standing Commission on Dementia revised and expanded the number of modifiable risk factors implicated in the onset of dementia.<sup>29</sup>)

Critics also point out that data generated by screenings acts as an impetus for revising standards of care and improving care delivery. The introduction of innovative dementia screening and brain health assessment tools promises to deliver a greater wealth of data on the underlying prevalence and progression of dementia and related disorders and facilitate research on the impact of screening and brain health assessment on follow-up diagnoses and treatment of Alzheimer's disease and related disorders. Research priorities at funding organizations (e.g., the NIH, AHRQ, PCORI, and private grantmakers) could be usefully reassessed to reflect the potential impact of innovative diagnostics on dementia-related care and how greater support for outcome evaluation could expedite the review of new evidence by the USPSTF.

### Promote Further Research on Potential Uses of Predictive Analytics to Enable More Efficient Delivery of Dementia Screening.

Ongoing research is demonstrating capabilities to apply machine learning to large datasets of patient health information and create algorithms that identify patients who are reasonable candidates for dementia screening or more extensive brain health assessment.<sup>30,31</sup> This type of advanced risk identification could prove useful in signaling to clinicians which patients might be prioritized for dementia screening, given the limited time and resources available to many primary care teams. Ongoing research utilizing Artificial Intelligence (AI) techniques applied to multiple types of patient data (e.g.,

biomarker data, neuropsychological data, medical histories, etc.) is also creating capabilities to predict differential diagnosis; that is, differentiate one type of dementia from another, including Alzheimer's disease, Lewy Body dementia, vascular dementia, and so on.<sup>32</sup>

Eventually, with further development and validation of AI-based techniques, the identification of dementia risks among patients at a population level could facilitate population health management strategies for dementia management, akin to the population health management strategies now employed in APMs (such as Accountable Care Organization models) to treat major chronic conditions such as type 2 diabetes. Careful attention must be paid to designing risk identification and patient outreach strategies that are sensitive to the stigma, denial, and fear that patients often feel regarding the onset of dementia.

**Promote Further Research on the Adaptation and Use of Innovative Dementia Screening Tests and Tools Among Historically Marginalized and Under-served Patient Populations.** Ongoing research has substantiated racial-ethnic disparities in both the prevalence of dementia and related disorders and in its diagnosis. Black and Hispanic Americans experience a higher prevalence of dementia which may be linked to their comparatively higher level of exposure to risk factors for dementia.<sup>33</sup> Variations in the likelihood of dementia among different racial-ethnic groups can skew the accuracy of tests that are developed based on the characteristics of the majority white population. This kind of variation has already been noted as tests configured to the characteristics of patients without Down syndrome have been used with Down syndrome patients who have a unique genetic disposition towards Alzheimer's disease that is not present among non-Down syndrome individuals. Thus, continued research and development on innovative tests and tools for dementia screening and brain health assessment must be configured to unique risk factors faced by patient populations that suffer from a comparatively high prevalence of dementia.

Black and Latino Americans also suffer from a comparative lack of access to formal diagnosis of dementia; continued research on configuring dementia screening tools to the needs of these under-served populations, as well as research on best practices to administer them, should be a continuing priority.<sup>34</sup> Americans living in remote or under-served communities also suffer from lack of access to dementia screening and brain health assessment.<sup>35</sup> Remotely-delivered telehealth

services for dementia assessment and dementia care can provide a useful solution that bridges regional gaps in care. Telehealth services delivered to under-served communities should be a continuing research priority as well.

**Promote Open Debate on the Ethics and Clinical Utility of Early Detection of Dementia Pathology Among Asymptomatic Patients: The “Right to Know” vs. the “Right Not to Know.”** Continued advances in pathological biomarker testing are making it possible to identify biomarkers of Alzheimer's disease in patients who show no signs or symptoms of the disease. AI-enabled analysis of data integrated from biomarker data and neuropsychological testing may expand this capability even further. Findings from neurological research suggest that while some asymptomatic patients who test positive for Alzheimer's disease-related biomarkers will go on to develop the disease, others will not.

These new capabilities for early detection of dementia-related pathologies raise profound new issues for the prevention and treatment of dementia. Longstanding norms of clinical practice emphasize that the benefits of early screening and diagnosis of disease can be outweighed by the risks of exposing patients to unnecessary follow-up procedures when early detection proves false, or when there is little clinical utility in diagnosing disease in the first place. As noted earlier, patients, caregivers, and clinicians have often been reluctant to screen for dementia out of the sense that little can be done to help the patient.

This calculus may now be subject to change as dementia screening and brain health assessment capabilities improve and as the first in what will likely be a series of new pharmaceutical treatments for Alzheimer's disease reaches FDA approval (albeit subject to continuing debate among clinicians). Growing awareness of the ability to detect risk for dementia at early stages of onset could shift attitudes to favor screening asymptomatic patients (e.g., the usefulness of screening patients who may be asymptomatic but may be at an elevated level of risk as identified by advanced predictive analytics of patient data).

The debate over early detection is sometimes characterized as a debate over the patient's “right to know” versus the patient's “right *not* to know.”<sup>36</sup> In the future, patients who demand the right to know might also call for ongoing monitoring like the active surveillance (“watchful waiting”) offered to men at risk

for prostate cancer progression. Other patients may prefer not to know about early markers of dementia and avoid anxiety over the disease and the intrusion of active surveillance. The issues raised by early detection demand an open review of patient preferences regarding early detection and the ethics and practicality of its adoption.

## Reimbursement Processes (Medicare and Other Payers)

**Identify and Address Gaps in Procedural and Billing Codes.** Mismatches between the capabilities of new diagnostic products and diagnostic and billing codes necessary for payment are not uncommon, and often require a) a reassessment of existing codes and b) the need for new or more appropriate codes. Ongoing reassessment of codes by physician societies and Medicare may be necessary to enable easier adoption of new tests and tools for dementia screening and brain health assessment.

## Conclusion

To comprehensively enable earlier detection of dementia and related disorders, healthcare policies must focus on several critical areas. Reevaluating the scope of Medicare's Annual Wellness Visit (AWV) and Cognitive Assessment and Care Plan Services (CACPS) benefits, as well as creating greater incentives to report on dementia quality measures, could enhance cognitive assessment uptake and patient care plans. Monitoring progress on CMS's GUIDE Model will offer a promising avenue for comprehensive payments for dementia care and better care management. Expediting evidence generation for the U.S. Preventive Services Task Force could integrate regular cognitive screening and assessment within preventive care standards. Prioritizing additional research on the use of predictive analytics in dementia care will support the integration of innovative screening tools; research on innovative screening tools should be especially prioritized among populations at high risk for dementia and Alzheimer's disease. Considering the ethical implications of early dementia detection must balance patient autonomy with clinical utility. Furthermore, identifying and addressing gaps in diagnostic and billing codes is essential to facilitate the adoption of new diagnostic tools. Together, these steps can enable a collective advancement in quality and accessible dementia care and promote better outcomes for affected individuals.

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## Appendix A. Detecting Brain Disorders: Clinical Practice Today vs. Clinical Practice of the Future

### Screening and Diagnostic Practices Today

**There is great variability in patients' experience with dementia screening and assessment.** Patients at risk for dementia and related disorders such as Alzheimer's disease often start their personal "patient journeys" in very different places and points in time. Many factors influence when and how a patient may be screened for the first time.

The journey may begin when the patient is aware of a memory problem or problem related to the ability to think and decides to seek help from a clinician. In many cases, it is not the patient but a concerned family member or other caregiver who seeks help for the patient. In other cases, a primary care physician or other clinician may observe or suspect a problem and encourage the patient to undergo a formal screening or a more complex assessment.<sup>37</sup>

#### **Patients often miss opportunities for early intervention.**

An initial screening or cognitive assessment may occur when a patient's symptoms are mild or merely suspected, or it may only occur when signs and symptoms of a neurological problem are already obvious. If it is ultimately determined that the patient has a form of dementia, the severity or acuity of the dementia at the time the patient is assessed can be a critical factor in whether further dementia can be prevented or treated. It is generally thought that the earlier clinicians intervene with preventive or therapeutic health measures, the more likely it will be that a patient's dementia can be arrested or delayed.<sup>38</sup>

Whether an initial assessment takes place at all may depend on whether the patient has a trusted caregiver, a pre-existing relationship with a primary care physician or other qualified clinicians, or the clinicians' capabilities to conduct assessments under the patient's health insurance coverage.

#### **Screening practices focus on mild cognitive impairment.**

Medical best practice, defined by U.S. physician societies and their professional societies, recommends that aging patients

or patients with a known risk be screened for mild cognitive impairment (MCI).<sup>37</sup> MCI is defined as a decline in memory and thinking ability that exceeds expected, age-related cognitive declines, but does not impair a patient's ability to live independently or perform daily functions. MCI is typically differentiated from dementia, a condition in which patients experience limitations in the ability to perform daily activities of life due to declines in memory, thinking ability, movement, speech, and other behaviors.<sup>39</sup> Patients with MCI do not necessarily progress into dementia, although an estimated 10% to 15% of patients with MCI do develop dementia.<sup>40–42</sup> Dementia can be further differentiated as Alzheimer's disease (the most prevalent form of dementia) or other neurological disorders.<sup>39</sup>

Recommended screening practices focus primarily on the detection of MCI. For example, the U.S. Preventive Services Task Force (USPSTF) conducts recurring reviews of services (defined in USPSTF reviews as "cognitive assessments") that evaluate outcomes from the use of the most widely accepted instruments for detection of MCI, including the Mini-Mental State Examination (MMSE), the Mini-COG test, and the Montreal Cognitive Assessment (MoCA).<sup>43</sup>

#### **Diagnosis of specific types of dementia (differential diagnosis) is complex, often involving multiple clinical specialties.**

More extensive testing and assessment are necessary if MCI screening or observations from patients, caregivers, and clinicians suggest that a patient is experiencing a condition that is more serious than MCI. This process may include detailed and time-consuming reviews of the patient's physical condition, medical history, family medical histories, and medication reviews.<sup>44</sup> Many of these tasks can be performed by primary care teams. Many primary care teams, however, prefer to refer patients to experienced specialists (e.g., neurologists and geriatricians) or may be compelled to refer patients to specialists because of limitations in their capacity to rigorously evaluate patients.

### Screening and Diagnostic Practices in the Future

**Health care for the brain will be essential.** An accumulating body of scientific research indicates that the onset of dementia is associated with numerous modifiable risk factors, including risk factors that are also associated with the onset or progression of chronic diseases such as heart disease, stroke, and type 2 diabetes. This research has strengthened the proposition that preventive health measures could avert or delay dementia among many Americans if adopted at greater

scale and maintained persistently. These risk factors include hypertension, a history of smoking, poor nutrition and limited physical activity, exposure to air pollution, avoidable concussions, and traumatic brain injuries.<sup>29,45</sup> (While the precise relationship between COVID-19 and brain function is not yet clear, “Long COVID” may still emerge as a factor in the higher prevalence of brain disorders.) The advent of pharmacologic treatment for Alzheimer’s disease and other serious neurological disorders may strengthen the case for detecting brain disorders even further.<sup>46</sup>

As a result “brain health” has emerged as a new paradigm for public health and population health management. In a 2023 call to action the American Academy of Neurology (AAN) called brain health “an imperative for the 21st Century,” citing the estimated \$800 billion per year burden of the nine most common neurological disorders.<sup>47</sup> (At present, brain health disorders are seen as distinct from psychiatric and mental health disorders. The combined burden of neurological and psychiatric disorders in the U.S. has been estimated at upwards of \$1.5 trillion per year.<sup>48</sup>) Recommendations made by the AAN include validation and routine updating of public health practice and clinical practice guidelines for brain health preventive measures; adoption of routine brain health visits between clinicians and patients; and stronger public health campaigns to promote preventive measures that reduce or delay brain disorders and associated chronic diseases.

## Appendix B. Innovations in Dementia Screening and Brain Health Assessment: What Are They? How Could They Change Health Care?

Innovations in dementia screening and assessment are largely based on the convergence of two trends: discovery and validation of biomarkers, and an expanding number of technologies for biomarker detection.

### Biomarkers

The two most widely acknowledged markers of Alzheimer's disease pathology are abnormal concentrations in the brain of two proteins, amyloid-beta protein (including amyloid plaques) and tau protein (including tau tangles). Both are discoverable through advanced imaging techniques, such as positron emission tomography (PET), and cerebrospinal fluid analysis typically performed through a lumbar puncture (i.e., a spinal tap). Recent research has begun to establish the validity of other pathological disease biomarkers, such as brain inflammation markers.<sup>49</sup> Detection of these pathological biomarkers is generally performed by neurologists and in specialty care settings, however, biomarker development is also advancing in two directions that are creating capabilities to detect signs of Alzheimer's disease in non-specialty settings. Biomarker development is also identifying detectable markers of dementia, the precursor condition to Alzheimer's disease, and enabling its detection in primary care and other non-specialty settings. Leading examples include:

- **Pathological biomarkers:** Blood-borne markers of amyloid and tau proteins have been identified and are discoverable through analysis of blood samples drawn in standard phlebotomy laboratories.<sup>50</sup>
- **Behavioral and neuropsychological biomarkers:** Markers of dementia observed in gait (patterns of walking), eye movements, and speech patterns have been validated for accuracy in indicating the onset and progression of dementia.<sup>51</sup>

Consequently, a variety of innovative tests, tools, and protocols for dementia screening and brain health assessment are now emerging in the health care market or are in active development. Major innovations can be classified into several categories, although many tests and tools in development combine elements from several of these categories. In the

future, clinicians and health care delivery systems may deploy several types of innovative tests and tools to support a comprehensive approach to dementia risk evaluation, screening, brain health assessment, and disease diagnosis at scale.

### Genetic testing

Persons with Down syndrome are known to be at an extremely high, genetically-driven risk for the onset of Alzheimer's disease, with or without formal testing. Persons with a strong family history of Alzheimer's disease can also be at elevated risk for early onset Alzheimer's disease, a risk that research has tied to the presence of mutations in three single genes, (APP, PSEN1, PSEN2) which are now subject to genetic testing. The vast majority of Alzheimer's disease is classified as late-onset (65 years and older) disease. Genetic testing for late onset Alzheimer's disease has not been widely embraced, since the presence of genetic variants or mutations that predispose patients to the disease are not known to be strongly deterministic of disease. However, recent research suggests that as many as 15% of Alzheimer's disease cases can be linked to patients carrying two copies of the APOE4 gene, with most patients testing positive for abnormal concentrations of amyloid beta protein by the age of 65.<sup>52</sup>

### Neuropsychological testing

Widely accepted tests of Mild Cognitive Impairment (MCI) and dementia, such as the Clock Drawing Test, the Mini-Mental State Examination (MMSE), and the Montreal Cognitive Assessment (MoCA) are still often administered as paper-based tests, however, many have been adapted for administration on digital devices. Conversion to digital devices now offers opportunities to collect data on other markers of MCI and dementia that can be collected on smartphones, iPads, and other tablet devices, such as markers of speech (via device-based microphones), eye movements (via device-based cameras), and gait and body movement (via device-based motion sensors that also support fitness and exercise applications).

Enhancement of MCI and dementia screening through digital devices offers three potential improvements in patient care:

- **Rapid administration and rapid return of results.** Many of the newly emerging digital tools can be administered rapidly to patients (in some cases, less than 10 minutes). Results can be returned in real time or near real-time, since findings are generated by built-in algorithms. Lengthy tests are less likely to be adopted by clinicians and less likely to be integrated into the routine workflows of health care providers. Emerging tests are also designed

for self-administration by patients, or for administration guided by caregivers. This creates the potential for testing in advance of visits with clinicians, and testing that can be done repeatedly in the home or outside the clinic to monitor patient symptoms over time.

- **Holistic brain health assessment.** As noted, the built-in capabilities of digital devices (touch screens, microphones, accelerometers, etc.) not only allow for the collection of data on traditional core measures of MCI and dementia such as memory and cognition, but for the collection of data on new markers of MCI and dementia revealed in speech patterns, changes in gait and body movement, and eye movements. (Simultaneous collection of multiple dementia-related data points also enables analysis that integrates findings from these multiple data points; see “Data Integration,” below.)
- **Scalability.** Since many of the newly emerging neuropsychological tests are administered on now-common digital devices (e.g., smartphones and tablets), they create new potential for conducting MCI and dementia screening at greater scale than commonly seen today and screening that more closely matches the underlying prevalence of dementia among patients.

## Laboratory testing

**Blood and fluid-based laboratory testing for pathological biomarkers.** Advances in the identification of pathological biomarkers of Alzheimer’s disease and other neurological disorders are coinciding with the development of technologies that detect pathological biomarkers through specimens that can be collected from patients in routine physician visits. A first generation of laboratory tests for blood-based biomarkers of Alzheimer’s disease is now available and capable of detecting traces of amyloid beta and tau proteins associated with progression of the disease. Other fluid-based tests (e.g., saliva and urine) for biomarkers of disease are in development. Minimally intrusive tests capable of detecting other neurological conditions (conditions often co-occurring with dementias) are also now emerging: laboratory test on skin samples for detection of Parkinson’s disease, for example.

Definitive analysis of pathological biomarkers for Alzheimer’s disease is still reserved for more complex testing such as testing by positron emission tomography (PET) imaging or cerebrospinal fluid (CSF) analysis on samples collected by lumbar puncture. Nevertheless, the launch of novel laboratory tests now creates the capability to provide patients with minimally intrusive testing. (Ongoing advances in blood sample

collection, such as the introduction of microneedle devices, now promise to enable sample collection that may be even less intrusive than standard blood collection by phlebotomy.) Administration of minimally intrusive testing in primary care settings will enable greater capability for clinicians to rule out the need to refer patients for more complex (and often more expensive) testing such as PET imaging and CSF analysis that is typically administered by specialists.

### **Early detection: detection of pathological biomarkers of disease among asymptomatic patients.**

The advent of fluid biomarker testing also creates new capabilities to detect pathologies of Alzheimer’s disease among younger patients, and patients who otherwise exhibit no signs or symptoms of disease (i.e. asymptomatic patients). This capability is raising important and, as yet, unresolved issues for clinical practice.<sup>15</sup> For example, ongoing research indicates that some patients detected with early, asymptomatic accumulation of amyloid beta and tau proteins in the brain may not progress to full-blown Alzheimer’s disease. For these patients, positive findings from laboratory testing may create unnecessary anxiety or trigger further unnecessary testing. On the other hand, early detection of pathological biomarkers could motivate patients, caregivers, and clinicians to intensify preventive health measures (such as good control of blood pressure, type 2 diabetes, and other conditions associated with dementia), and trigger earlier use of drug therapies for patients who meet criteria for these drugs.

## Data integration

### **Comprehensive brain health assessment through integration of neuropsychological test results with laboratory test results.**

As noted above, smartphones, tablet computers (such as iPads), wearable sensors, and other devices have created capabilities to detect multiple markers of MCI and dementia simultaneously. Built-in microphones, motion sensors, cameras, and touch screens can record data that can be analyzed algorithmically for signs of dementia in speech patterns, gait, hand motions and tremors, eye movements, verbal recall, and other markers.

Simultaneous collection of these data points is creating capabilities to evaluate risks of dementia based on analysis that integrates data from these multiple markers and is further complemented with data from other sources, such as blood-based biomarker tests. Tests that are now actively marketed are promising a return of results in 10 minutes or less.<sup>53</sup>

## Predictive analytics

### **Risk identification through advanced analytical methods to personal health data and health insurance claims.**

Applications of machine learning and other artificial intelligence (AI) techniques to large datasets are creating capabilities to identify patients who are at elevated risk for the onset of dementia and potential progression of Alzheimer's disease prior to the onset of symptoms and before patients and caregivers may report signs or symptoms to clinicians.<sup>30,31</sup> Advance identification of patients at risk could enable clinicians to prioritize screenings for MCI and for more comprehensive brain health assessment. AI techniques are also showing promise in integrating data to create algorithms that are capable of generating probabilities of differential diagnoses of dementia (i.e., the probability that a patient's apparent dementia is due to a specific underlying condition such as Alzheimer's disease, vascular dementia, Lewy Body dementia, or the interaction of co-morbid conditions).<sup>32</sup>