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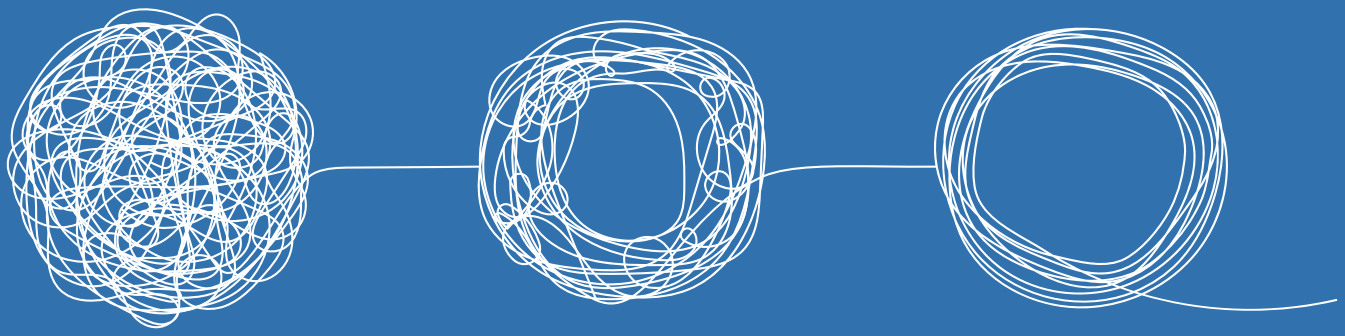


Alzheimer's Roundtable discussion brief

Identifying the scope for a potential Alzheimer's NEWDIGS Case Study

Patients, caretakers, providers, payers, and drug research organizations are eager for advances in pre-symptomatic and early symptomatic Alzheimer's identification, diagnosis, treatment, and care. Health care costs due to Alzheimer's disease in the U.S. are currently estimated at more than $300 billion a year, with costs expected to triple by 2050 as the population continues to age[1]. Medical interventions that slow patients' progression to moderate Alzheimer's by 3 years could reduce those costs by an estimated $212 billion to $1,274 billion over a decade if 50% of mild AD patients can be treated and have been granted traditional approvals[2]. To date, the FDA has approved three medications, two of which currently remain on the market[3]; Leqembi (July 2023) and Kisunla (July 2024), that are meant to slow or delay symptoms of Alzheimer's disease in the early and mild cognitive impairment stage of the disease[4]. Moreover, screening and diagnostic testing options are also gaining ground, underscoring the importance of early testing. With over 150 PhII and PhIII clinical trials continuing across the globe[5], it is incumbent upon Alzheimer's healthcare stakeholders to test the healthcare systems' readiness to bring these advancements to the right patients in the right timeframe.

Providing equitable and appropriate access in a financially and clinically feasible manner will require downstream system innovation to match the upstream scientific innovation leading to these diagnostics and therapies. In preparation for the November Alzheimer's Roundtable, this Brief outlines challenges to patient care that will require multi-stakeholder engagement if we are to equip current healthcare systems to fully utilize these innovations for Alzheimer's patients.

The Roundtable is expected to spark a collaborative process that will lead to concrete, cross-organization actions to mitigate the existing challenges and to enhance the overall utility of Alzheimer's patient care. As medical science progresses, patient access to the new care environment can be destabilized if the overall system is not prepared to uniformly incorporate care solutions in a timely manner. The incorporation of new care solutions is not a given but requires a systematic assessment to understand the current hurdles to embracing the new interventions. Systemically, patient access can also be hindered by policy barriers and by provider constraints. These interdependent themes influence aspects of the patient journey, the practicalities of coverage policies, payment models, and delivery structures that must be developed to foster appropriate Alzheimer's care.

If we assume that advanced diagnostics and treatments will be available, how might stakeholders adjust the distribution of action, burden, benefits, and costs across the system, and what new structures for care could be required? Changes may affect most healthcare elements, from new coverage policies and benefit designs to sites of care, provider roles, behavioral health, and ancillary services, as well as the funding and payment models for them all. Issues of patient access, equity, value tracking, and privacy need addressing. Each of these elements (listed below) could benefit from a coordinated change process that can build solutions that are sustainable for all stakeholders:

- The patient odyssey: Screening, diagnostics, and treatment
- Value distribution: A patient perspective
  - Stigma & privacy
- Provider capacity and capability
- Value: A payer perspective
  - Coverage policies
  - Patient churn and delayed benefits
  - Reimbursement mechanics and motivation
- Outcomes tracking infrastructure

The patient odyssey

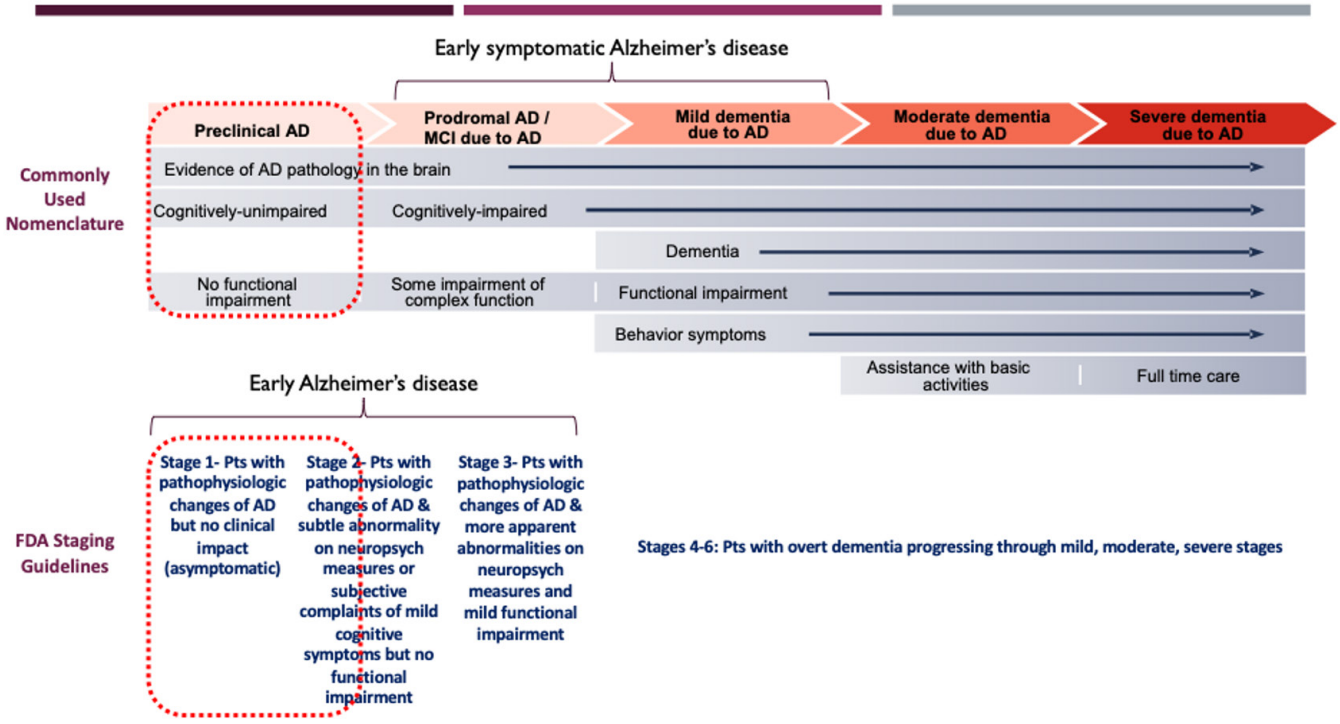
Scientists have long known that decades before Alzheimer's symptoms present, amyloid protein plaque builds in the brain, yet progression to severe dementia takes time. Now, leading patient groups and government agencies have begun to map this journey into stages, beginning with a pre-symptomatic phase often called "preclinical" and progressing to ever greater cognitive and functional decline.

Alzheimer's patients follow varying journeys for risk identification/screening, diagnosis, and treatment. To complicate things further, the disease can be caused by a combination of genetics, lifestyle, and environmental factors and the vast majority of patients will present, long after symptoms begin, with a mix of dementias (e.g., Alzheimer's disease and vascular dementia), requiring treatment of the full burden of cognitive impairment. Currently, standard screening practices look to detect mild cognitive impairment (MCI), but the application and coverage of these diagnostic practices vary[6]. Current diagnostic practices use qualitative physician assessments in tandem with spinal taps and/or PET scans to measure sentinel proteins that indicate Alzheimer's disease. Blood tests are also being developed as a more accessible diagnostic for the presence of beta-amyloid or tau proteins. MRI scans can also be useful to identify any shrinkage of the brain over time, also a sign of cognitive decline caused by Alzheimer's disease.

With two new therapies approved by the FDA, treatment of Alzheimer's Disease has entered a new era, shifting from treating symptoms to where medical professionals can change disease progression[7]. The treatment process requires regular doctor visits for an infusion (1x/month for Kisunla, or bi-weekly for Leqembi). As effective, disease modifying therapies continue gaining approval, what coordinated actions are needed to:

- Encourage patients to seek out screening, diagnosis and treatment?
- Create ubiquitous, efficient screening and diagnosis programs that incorporate new diagnostic tools as available and provide adequate reimbursement?
- Develop improved tools, risk projections, and testing strategies?
- Ensure equitable and secure access?

Figure 1. FDA staging guidelines for Alzheimer's Disease



Further research and development, FDA-approval, at-scale deployment, and reimbursement of diagnostic tools to support time-sensitive Alzheimer's detection will require policy makers, regulators, developers, payers, healthcare providers, and patients to create effective collaboration structures.

Value: A patient perspective

Ultimately, the value to patients, their families, and caregivers of these diagnostic and treatment innovations can be significant, but realizing the value for all eligible patients will not happen without systemic changes. The health system must normalize screening and diagnosis of Alzheimer's at a population health level, including more nuanced cognitive screening tests, healthcare practitioners trained in dementia diagnosis and care, and patients who can access appropriate experts when needed (e.g., across geographies, with sufficient populations of experts).

Stigma & privacy

At a population health level, the innovations in Alzheimer's screening, diagnosis and treatment could dramatically improve the lives of patients, their families and caregivers[8]. However, patients today are reluctant to seek diagnosis, as it could lead to stigma and negative consequences from friends, family members and work colleagues. Stigma concerns may contribute to the average 15-month delay from patient/caretaker observed symptom onset and an initial physician discussion[9]. From a privacy level, patients may not seek early diagnosis, worried that once diagnosed, it could have a negative impact on their employment, property insurance, credit, or other potentially unprotected uses of their health information. As early diagnosis can improve a patient's treatment outcomes, it is imperative that stigma and privacy challenges be addressed more directly.

Provider capacity and capability

Currently, patients with Alzheimer's disease require healthcare providers to manage the appropriate use of available treatment options. A patient's caregivers also require healthcare support to understand the disease and the growing needs of the patient over time. In future, providers may face a very different patient population (i.e., pre-symptomatic or mildly symptomatic that may not be immediately noticed) that will require broader outreach for diagnosis and longer preventive treatment follow-up.

The primary care physician's office (PCP) is likely the best point of contact for early screening and diagnosis of Alzheimer's disease. Yet, if treatments remain complicated, for example requiring regular infusions and monthly assessments, the PCP's office may not be equipped to manage the scope of care required for medicine administration and the ancillary services often needed by Alzheimer's patients. Simpler modes of administration in the future may alleviate some of the medication burden on the PCP, but not the ancillary care coordination burden.

Significant training and personnel increases will likely be required to provide the emerging higher standard of care. Growing the care provider system capacity through technology and new organizational structures in addition to expanding existing PCP, neurologist and memory care professional staffing may be needed[10].

Additional questions may also need addressing such as:

- How will patient adherence be tracked and what infrastructure will be required for long-term treatment maintenance?
- How will medical management be compensated (under current and future needs)?
- Will there be enough care providers trained to support the Alzheimer's patient population? Can medical schools and schools of nursing, pharmacy, and allied health professionals tailor training to current needs?
- How could digital/telehealth expand and extend provider capacity?
- How will PCPs have the time to coordinate this care?

Providers will have to adapt to the changing condition of diagnosis and care of Alzheimer's patients but will require support for the systemic changes they will have to make.

Value distribution: A payer perspective

Emerging diagnostics and therapeutics in the hands of skilled providers are creating value for those impacted by Alzheimer's disease. While the pricing of new medications is out of scope for this work, it will be important to have a model that can estimate financial challenges and benefits for all stakeholders as Alzheimer's treatment evolves over the near- and mid-term. For example:

- How will provider capacity impact annual spending and equity in patient care?
- Will coverage policies delay patient access?
- With patients transitioning between private insurance groups or from private insurance to Medicare in signif-

icant numbers, should the later payers benefiting from delay or milder patients contribute to the costs incurred by earlier payers?
- How might the benefits of reduced assisted living/memory unit utilization and caregiver burden be recognized?

A multi-stakeholder collaboration could improve our knowledge of what budget impact challenges might exist and how those challenges might impact patient access.

Payer value: Coverage policies

Coverage policies and quality ratings for new diagnostic and treatment innovations are crucial aspects of care in our multi-payer healthcare systems. Physician associations, working with regulatory agencies, payers and patient groups will require updated coverage policies in public and private insurance programs for patient pathways that include, for example, preventive care designations (as new treatments evolve) and coverage for early and regular screening for the disease. Timely USPSTF recommendations regarding cognitive health screening will be needed that balance evidence maturity with the opportunity costs of untreated MCI. Coverage policies work best for patients when the appropriate quality coding and rating systems are in place to measure the successful application of new coverage policies. Updating the infrastructure to care provision requires input from across the healthcare system.

Payer value: Patient churn and delayed benefits

As of June 2023, Medicare covers medications to treat Alzheimer's disease for patients enrolled in a Coverage with Evidence Development (CED) registry[11]. This coverage is an important factor to ensure equitable access to treatment for all patients eligible for Medicare. This coverage also highlights the challenges faced by private payers, who are likely to support patients prior to Medicare eligibility, thus covering early screening, diagnostic tests and early treatment costs for Alzheimer's patients. While encouraged to detect this progressive disease early, it will unfortunately land as a significant cost to private health insurance to establish early treatment programs, after which patients will likely switch to Medicare for what could be only short-term Alzheimer's care[12]. The patient turnover, or churn, for private payers is a significant challenge to health systems' viability over the long-term.

Payer value: Reimbursement mechanics and motivation

In support of patients, provider and payers, the mechanics of how reimbursement for Alzheimer's care develops will be crucial to the effective and efficient utilization of diagnostic and treatment innovations. As the medical science of both diagnostics and treatment is still developing for this complicated and progressive disease, the patient pathways still require further investigation. Ongoing research is needed; payers will need more evidence to understand what treatment pathways work best for each subpopulation (e.g., dementia patients with more than one form of cognitive disability). They will need to better understand when to start treatments and what a successful outcome looks like, the ideal length of treatment for various subpopulations, etc. Payers will also need to understand if they can secure adequate numbers of trained care providers to satisfy their patient populations. Reimbursement policies, and potentially the creation of new payment models, will be needed for financially sustainable access to both Alzheimer's diagnostics and drug therapy.

Outcomes tracking infrastructure

As is true with all diagnostic and treatment innovations, there will be evidence gaps to be identified and managed. Ongoing data generation and analysis will be necessary for the continued improvement of Alzheimer's care[13]. The infrastructure to monitor and improve patient care such as described in the CMS Innovation Center GUIDE model[10], will need further development, but such improvements could also aid patients and their providers. How this new infrastructure will be sustained and paid for demands further dialogue.

As new treatments evolve, and patient pathways become consistent, real-world data generation could be an important opportunity to further investigate new treatments' value to patients. Innovative contracts that include data generation would benefit from improved tracking and reporting capabilities. Such contracts with evidence generation might be sponsored by the Alzheimer's Network (ALZ-NET), or in value-based contracts agreed upon between manufacturers and payer organizations. In addition, the CMS CED clinical studies could be built upon to analyze the Medicare-insured population[14]. How will this data be utilized and how broadly will it be disseminated? Early models of health outcomes tracking can set standards, establishing points in the patient journey to measure and reward.

Conclusion

Alzheimer's is an age-related disease that will impact a larger number of people because of increasing life expec-

tancy. As diagnostic and treatment advances continue to provide us with stronger tools to combat this disease, our current healthcare systems must be improved in ways that will accommodate these new opportunities efficiently and effectively for the most patients possible. Beyond individual organization's action, cross-stakeholder groups collaborative design and preparation may be needed for the US healthcare system to succeed on a population health level to optimally and equitably utilize these innovations.

NEWDIGS at Tufts Medical Center is dedicated to improving health out-comes by accelerating appropriate and timely access for patients to biomedical products, in ways that work for all stakeholders. NEWDIGS designs, evaluates, and catalyzes the real-world implementation of system innovations that are too complex and cross-cutting to be addressed by a single organization or market sector. Its members include global leaders from patient advocacy, payer organizations, biopharmaceutical companies, regulatory agencies, clinical care, academic research, and investment firms. https://newdigs.tuftmedicalcenter.org.

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10. On July 1, 2024, CMS launched the GUIDE Model. With 390 organizations participating, "The Guiding an Improved Dementia Experience" (GUIDE) model will run for 8 years, testing care scenarios with the aim to support people with dementia and their unpaid caregivers. See: https://www.cms.gov/priorities/innovation/innovation-models/guide. Accessed 10/16/2024.
11. CMS Consumer Fact Sheet: Medicare Coverage for Alzheimer's Drugs: Things to know for people with Medicare. See https://www.cms.gov/files/document/fact-sheet-june-2023.pdf
12. Note that early clinical trial results show data where patients can stop treatment after 12- or 18- months. See USA Today, *FDA approves a new Alzheimer's drug. What to know about Eli Lilly's Kisunla* by Ken Alltucker, July 2, 2024. https://www.usatoday.com/story/news/health/2024/07/02/alzhiemers-drug-kisunla-donanem-ab-fda-approval-eli-lilly/74282636007/
13. Note that both Kisunla and Leqembi gained FDA approval via the Accelerated Approval Pathways process, where developers are required to continue with a clinical development plan to be met post-launch. See NEWDIGS work on Accelerated Approval Pathways.
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