

Alzheimer's disease (AD) is a global healthcare challenge characterized by progressive cognitive decline, memory loss, and behavioral change that increases in prevalence with age. As put by Phyllis Barkman-Ferrell, Eli Lilly's global head of external engagement for Alzheimer's disease, there are "10,000 Baby Boomers turning 65 every day" in the United States, and the burden of AD will grow significantly, making it a priority in healthcare innovation. In 2023, more than 6 million Americans are living with Alzheimer's disease and this number is projected to rise to 13 million by 2050. Alzheimer's disease and other dementias represent a projected financial burden of \$345 billion in 2023 in the United States alone, and as the prevalence is skyrocketing, the cost for disease management should reach close to \$1 trillion by 2050.



Beyond numbers, AD is wreaking havoc among families, posing a huge socioemotional toll on patients, their caregivers, and their relatives. As adequate medical and medically related resources are scarce, the challenges of dealing with AD and adapting resources will become more difficult. The Alzheimer's Association publication shows that "the largest segment of the workforce that supports people living with dementia is the direct care workforce." Finally, the field of Alzheimer's disease is filled with drug development failures, with an attrition rate of 99.6% over the 2002-2012 decade<sup>1</sup>.

Despite these gloomy perspectives, recent progress in drug development gives hope to provide patients with candidates that can slow down disease progression at the early stage of development. While they will not cure Alzheimer's disease, they induce a paradigm shift: we may have soon a therapeutic arsenal and options that physicians can prescribe to this neglected patient population. In this new paradigm, health technology will play a role in supporting patient identification, early diagnosis, monitoring disease progression and supporting patients and their caregivers daily.

In this paper, we will frame the challenges and pain points posed by Alzheimer's disease for all populations involved. We will then showcase digital interventions that can alleviate these challenges. Finally, we will discuss the expected value of digital health solutions in the field of Alzheimer's disease and how Aptar Digital Health intends to contribute to improve the lives of people with Alzheimer's disease.

1 Cummings, J.L., Morstorf, T. & Zhong, K. Alzheimer's diseasedrug-development pipeline: few candidates, frequent failures. Alz Res Therapy 6, 37 (2014). https://doi.org/10.1186/alzrt269

### Underlying Challenges in Alzheimer's Disease Management

Alzheimer's disease impacts multiple stakeholders beyond patients themselves and better understanding the challenges for each population is paramount to imagine the best possible strategies to manage the disease as it will expand in the coming decades.

Initially, patients are faced with challenges very early in their journey. It starts before diagnosis since many individuals with AD face delayed diagnosis due to the stigma of having dementia and the insidious onset of symptoms. This can lead to missed opportunities for early intervention. As for many other diseases, the interviews we conducted with Alzheimer's disease patients show that an early diagnosis would help them and their relatives prepare for the challenges ahead.

> "If I knew this [AD] was going to happen, I would have prepared or started long-term care much sooner"

After diagnosis comes treatment: currently there is no cure for Alzheimer's disease, available treatments provide only symptomatic relief, and it is difficult for patients to know if the medications they are taking improve their wellbeing. Remembering to take medications requires layers of reminders. As the disease progresses, the ability for patients to selfmanage diminishes. This decline has a deep negative psychosocial impact on patients and caregivers as they depend more and more on others to provide physical, emotional, and logistical support.

- Subsequently, caregivers are particularly impacted by Alzheimer's disease. The condition their loved ones is living with is emotionally stressful and physically exhausting. They can also experience a lack of support and trustworthy sources for recommendations on how to cope with the disease on a daily basis. Taking care of their relatives also means they are less able to manage their own activities, potentially leading to caregiver burnout and physical decline. Finally, the financial toll of Alzheimer's disease often comes back to them, putting additional stress on the situation. It's also worth noting that in the US, about 30% of caregivers are 65+ years old and have their own set of clinical, and physical challenges to face.
- In addition, Alzheimer's Disease is also complex to handle for providers. This starts early in the process as Alzheimer's disease symptoms are often dismissed as signs of normal aging, sometimes by patients who want to hide or avoid discussing Mild Cognitive Impairment (MCI) symptoms, sometimes by providers who are ill equipped to identify the signs. A survey from the Alzheimer's Association showed that 39% of PCPs are uncomfortable making an Alzheimer's disease diagnosis, 55%

are concerned that there are not enough specialists to meet demand today and 22% had no dementia training during their residency. Finally, most recent AD drugs that hit the market are expensive and the assessment of their impact in real-world setting is just starting. Providers can feel conflicted when they have no therapeutic options that would be affordable and clinically proven to provide to patients. Providers also struggle with providing affordable memory care facilities to patients and families.

• Finally, the pharmaceutical industry also faces a range of challenges in this disease state. Alzheimer's disease landscape is characterized by a notorious difficulty to develop diseasemodifying treatments. According to a recent review, there are currently 187 trials assessing 141 drugs for the treatment of Alzheimer's disease<sup>2</sup>. Several drugs such as Aduhelm (2021), Legembi (2022) and donanemab (decision for approval expected by end of 2023), followed this complex path and provide a new set of options in the fight against Alzheimer disease. Beyond these, the current therapeutic environment must lead pharma to consider additional services and offerings to support patients, caregivers and providers in navigating their own challenges. As a recent press article stated, the emergence of new treatments for dementia raises hope but brings additional concerns such as affordability, patient eligibility, management of side-effects and increasing complexity to an already complex patient journey (punctuated with cognitive tests, MRI scans, infusions, genetic tests, spinal taps, PET scans...).



2 Cummings, J, Zhou, Y, Lee, G, Zhong, K, Fonseca, J, Cheng, F. Alzheimer's disease drug development pipeline: 2023. Alzheimer's Dement. 2023; 9:e12385. https://doi.org/10.1002/trc2.12385

We are entering a new age for Alzheimer's disease as new standards for diagnosis and management are emerging. In this new framework, digital health has a role to play, and we will focus now on how it can be an effective contributor to improve the overall care experience for all parties involved.

### The value of Digital Health in Alzheimer's Disease and Other Dementia

#### Early Detection and Diagnosis

A recent report published by the American Academy of Neurology<sup>3</sup> shortage of neurologists in the US (ang globally) is seen as a "grave threat" to public health. While digital health is not a "silver bullet" and people with Alzheimer's need to pursue education, training, care planning, there is a call for leveraging technologies to screen for disease sooner. As mentioned before, the combination of a globally population with ageing emerging treatments and new diagnostics tools will increase the demand and cause a major supply issue. An example of a digital solution is Cognigram<sup>™</sup>, a simple and validated computerized tests system to aid healthcare professionals with rapid assessment of cognition in individuals. The tool is developed by Cogstate and has been cleared by the U.S Food and Drug Administration (FDA) as a Class II Medical device. Beyond real-world medicine, digital screening for dementia can also be of help for Decentralized Clinical Trials (DCTs) as slow recruitment and missing data are quoted as regular pain points in dementia clinical research<sup>4</sup>.

#### Patient and caregiver support

Once a diagnosis of dementia has been established, technology can be used to help with different aspects of daily life. Such digital solutions go far beyond traditional care delivery and can be of assistance for other applications (for instance, sensors that can detect floods, shut off the waters and raise the alarm).

"I use Alexa to set alarms for everything and to remind me to take laundry out of the washer or the dryer, or if I'm supposed to call my sister back, I try and tell Alexa"

Beyond domotics and smart homes, a 2023 review published by Zhai et al<sup>5</sup>. showed that across chronic diseases, including Alzheimer's disease, digitally-enhanced interventions provide *"high-quality* assistance and support to caregivers by improving their health, self-efficacy, caregiving skills, quality of life, social support and problem-coping abilities".

There are multiple ways a digital solution can help caregivers including:

- Increase disease awareness and education,
- Facilitate real-time communication with the care team,

<sup>3</sup> A Shortage of Neurologists – We Must Act Now – A Report From the AAN 2019 Transforming Leaders Program; Jennifer J. Majersik, Aiesha Ahmed, I-Hweii A. Chen, Holly Shill, Gregory P. Hanes, Victoria S. Pelak, Jennifer L. Hopp, Antonio Omuro, Benzi Kluger, Thabele Leslie-Mazwi; Neurology Jun 2021, 96 (24) 1122-1134; DOI: 10.1212/WNL.000000000012111

<sup>4</sup> Leroy, V., Gana, W., Aïdoud, A. et al. Digital health technologies and Alzheimer's disease clinical trials: might decentralized clinical trials increase participation by people with cognitive impairment?. Alz Res Therapy 15, 87 (2023). https://doi.org/10.1186/s13195-023-01227-4

<sup>5</sup> Zhai S, Chu F, Tan M, Chi NC, Ward T, Yuwen W. Digital health interventions to support family caregivers: An updated systematic review. Digit Health. 2023 May 19;9:20552076231171967. doi: 10.1177/20552076231171967. PMID: 37223775; PMCID: PMC10201006.

- Give access to coaches or other type of coordinator,
- Support data collection and monitoring,
- Provide psychotherapy services,
- Build a caregivers' community to find support and relief.

#### Disease management

Digital solutions can also be of help when focused on the disease itself. On one hand, solutions like companion apps can act as daily support for patients and their caregivers. These apps, packaged into a disease management platform, can benefit patients on multiple fronts:

- Maintain patients active and engaged with their condition and therapy,
- Facilitate the bilateral communication with the care team, providing important real-world insights on patients status,
- Support elderly patients (as it is often the case in dementia) in dealing with comorbidities and multiple medications,
- Remind patients to take their dose at the right time through audible or visual cues,
- Report any specific event in a journal to facilitate consultations.

Some of these features can be embedded into wearable devices to monitor specific par ameters like sleep quality, physical activity or heart rate, all of which are important factors in an Alzheimer's disease patient quality of life<sup>6</sup>.

These benefits also impact caregivers who can rely on a 24/7 solution that will reduce the psychosocial burden and the anxiety of monitoring these parameters themselves. Our interviews with people with AD showed that they are keen on to use devices to make their lives easier, relying for instance on Alexa to set reminders, or on an Apple Watch to alert care teams in case of emergency.

On the other hand, there is growing interest among the scientific and entrepreneurs' communities for new, tech-enabled methods to create new treatments in the digital therapeutics space. Brain+ for instance develops a Cognitive Stimulation Therapy (CST) to treat dementia. It uses psychosocial interaction to stimulate cognition and provide a structured way for patients to interact with their caregivers. Another example is the neuromodulation platform currently developed by Cognito Therapeutics, where a headset (which obtained FDA Breakthrough Device Designation) can help modulate neuronal network activity and regulate gamma wave patterns.

#### Research and Drug Development

Digital biomarkers for clinical trial optimization are a major area for digital health to benefit research on new treatments for Alzheimer's disease. For instance, pharmaceutical companies such as Biogen, Eisai, Eli Lilly and Merck joined forces with the non-profit Digital Medicine Society (DiME), American universities (Boston University and Oregon Health & Science University) and the Alzheimer's drug discovery Foundation.

The goal of the group is to identify and develop the most effective techenabled biomarkers helping to find out which prospective treatments are slowing cognitive decline associated with

<sup>6</sup> Salehi W, Gupta G, Bhatia S, Koundal D, Mashat A, Belay A. IoT-Based Wearable Devices for Patients Suffering from Alzheimer Disease. Contrast Media Mol Imaging. 2022 Apr 22;2022:3224939. doi: 10.1155/2022/3224939. PMID: 35542758; PMCID: PMC9054450.

neurodegenerative conditions. This is of importance when we consider that there are more than 300 digital endpoints in the open-source library curated by DiME. Integrating more diversified measures may open new windows of understanding about disease progression. Such efforts help designing more accurate trials but beyond that, it guides us toward a more personalized approach to Alzheimer's disease and other dementia management. Alzheimer's disease comes to us with multiple types of needs across a variety of stakeholders. While the era of "point solutions" in digital health should be over, this is even truer in this area. If we want to significantly tackle AD challenges, we must build digital health solutions that are broad and holistic enough to include expectations beyond patients, and beyond the clinical setting.

# Towards an Alzheimer's Disease management platform

At <u>Aptar Digital Health</u>, we qualify this integrative, holistic approach as "disease management platforms" and define them as comprehensive drug-agnostic solution elevating standards of care for chronic conditions. In the context of Alzheimer's disease, a successful disease management platform must be built according to two guiding principles:

- Beyond patients: the digital ecosystem must consider and provide value to other stakeholders who gravitate around patients and are significantly impacted by AD burden today.
- Beyond clinical: a large part of needs from platform end-users are not clinical but relate to the ability of patients and caregivers to live every day with the disease and maintain life as normal as possible with the right level of support.



With these two principles in mind, Aptar Digital Health's vision of a platform for AD needs to be broad, flexible and configurable, which means:

- Broad: must include a large set of features such as medication management, alerts, ePROs, symptom management functions and digital diagnostic capabilities to monitor disease evolution.
- Flexible: we can anticipate that some functions and algorithms would be considered as medical devices and some would not, hence the need for a platform that can seamlessly cope with both options. The solution also needs to be geographically flexible, meaning compliant with national/international regulations.
- Configurable: specific features can be activated or deactivated at user or user category levels, keeping in mind that as each type of user will have their own expectations, different portals and interfaces are needed to access services of interest.

To be successful, a disease management platform in Alzheimer's disease needs to meet the needs and expectations from the four populations we described above: patients, caregivers, providers, and pharma. On top of these considerations, it must respect foundational characteristics related to:

- **Trustability**: robustness of shared information and ethical aspects related to data processing and automation
- Security: compliance with national and international guidance on data safety, privacy and cybersecurity requirement.
- Interoperability: ability to interface seamlessly from one software environment to another, for example from hospital-care to primary-care, from providers' to patients' ecosystems...



#### ALZHEIMER'S DISEASE MANAGEMENT PLATFORM CONCEPT

Such platform should aim to deliver value at 3 levels:

- Better outcomes: focused on collecting data about the impact of AD on certain behaviors (symptom management, adherence...) and organizational aspects (optimization of resources use, total costs...).
- Improved Quality of Life: relates to the non-medication side of the platform and aims to demonstrate that patients and their relatives are coping better with their daily challenges (for instance, stress and anxiety management, overall mental well-being, ...).
- Real-World Evidence impact: relates to data that can help payers and regulators assess the best ways to financially manage the implementation of health technology, and potentially lead to reimbursement.

The development of a disease management platform as described above is of value for all stakeholders including life sciences and pharmaceutical companies. Pharma for instance can use Real-World Evidence for R&D - refine clinical development strategies - and commercialization - and launch value-based care contracts with payers. Datapoints generated through the platform can also shed light on good use (or not) of innovative medications that hit the market. Furthermore, being an active contributor to the development and rollout of a disease management platform is a strong differentiating asset, giving access to a diverse population of end-users that may not otherwise have access and would benefit from additional services.

#### Conclusion

Alzheimer's disease wreaks havoc globally and has a huge social, economic, and clinical impact. However, its management is under a paradigm shift: new therapies are emerging, and hold promises for the entire community of stakeholders. We can expect digital health solutions to become an important contributor to the development of new frameworks to diagnose patients earlier, better manage the disease and help patients, providers, and caregivers to cope with the massive organizational burden of Alzheimer's disease and other related dementias. A successful digital health approach in Alzheimer's disease needs to be "beyond patients" and "beyond clinical challenges". We consider that the way forward is a flexible disease management platform that can deliver value and better outcomes for all involved stakeholders if we hope to make a tangible positive impact on the huge set of challenges that this disease presents.



# **About Aptar Digital Health**

Aptar Digital Health creates end-to-end solutions to enhance patient experiences every day, leveraging a holistic ecosystem of digital interventions. Amplified by an industry-leading portfolio of products and solutions, Aptar Digital Health's offerings combine mobile and web apps, connected drug delivery systems, onboarding, training and advanced data analytics services to actively empower patients and create a positive treatment journey.

<u>Aptar Pharma</u>'s Digital Health division is part of AptarGroup, Inc., a global leader in drug and consumer product dosing, dispensing and protection technologies.

Ready to take the next step? Contact us for a detailed discussion on how we can collaborate to enhance Alzheimer's care through digital health.

## **Contact Us!**

