**Title:** How Registries Can Facilitate Holistic Value Assessments of New Therapies in Alzheimer’s Disease

**Authors:**

Samantha Benham-Hermetz – Alzheimer’s Research UK

Anders Gustavsson – Quantify Research

Alessandro Padovani – University of Brescia

Paola Barbarino – Alzheimer’s Disease International

Lydia Lanman – F. Hoffmann-La Roche Ltd, Basel, Switzerland

Antonella S. Chadha – Biogen, Inc.

**Abstract**

As Alzheimer’s research accelerates, holistic value assessments for new disease modifying therapies are urgently needed. Alzheimer’s registries collect crucial data that can be used to assess the clinical efficacy of therapies and quantify their social and economic benefits. However, optimizing the use of registries remains an urgent next step for European stakeholders to enable the assessment of the clinical and economic value of new Alzheimer’s disease therapies. To better-facilitate holistic value assessments, registries must incorporate more biomarker and digital phenotyping data, be flexible, and reflect multiple disease hypotheses. Registries should also serve to foster greater public trust in and engagement with registries by incorporating robust legal frameworks that protect data privacy.

**Introduction**

As Europe’s populations age and life expectancies rise, the prevalence of Alzheimer’s disease is rapidly increasing. Current projections show a staggering 18.8 million Europeans will be living with Alzheimer’s disease by 2050.[[1]](#endnote-1) As researchers identify and develop new treatment breakthroughs, policymakers and healthcare providers must collaborate to collect, store, share, and standardize the data needed to guide treatment decisions and assessments of the value of new therapies. As of 2021, 28 Alzheimer’s therapies were undergoing phase III trials, and 61% of these were disease-modifying treatments (DMTs) designed to slow the progression of Alzheimer’s by altering its underlying pathophysiology.[[2]](#endnote-2) The United States Food and Drug Administration (FDA) recently approved aducanumab, making it the first DMT approved.[[3]](#endnote-3)

DMTs present unique challenges to drug value assessments. Drug assessment models that rely primarily on clinical trial data often cannot accurately quantify the full range of health and cost-saving benefits of DMTs. This is because the efficacy of DMTs extend beyond the clinical symptoms of Alzheimer’s disease. The scientific community is aligning on the fact that DMTs must be used earlier in the disease course, to realise the benefits of delayed disease progression. To better assess these the full value of these benefits, real-world data following patients over the entirety of the disease course is needed to ensure proper patient selection, identify appropriate therapeutic timing and duration, and reduce societal and health system costs.

Alzheimer’s disease registries have already collected much of the data needed to better assess the health, social, and cost-saving value of these emerging Alzheimer’s therapies and treatments. Registries can track large cohorts of patients and caregivers across a broad range of metrics over long periods of time. When aggregated and analysed, this data can help health systems and payers to assess the clinical efficacy of different therapies and quantify their broader socioeconomic benefits.

**Methods**

To examine unmet needs, the potential benefits of registry data, and recommendations for leverage registries, we conducted desk research. We also drew on professional expertise and experiences in diverse segments of the Alzheimer’s space, including research, advocacy, and industry.

We structured our research and analysis around the following questions:

* How can registry data be used to create drug value assessments that discern the full benefits of emerging therapies?
* How can this registry data be leveraged to secure payer support and patient access?
* What are the current barriers to using Alzheimer’s disease registry data, including any “data gaps,” in the creation of new drug value assessments?
* Can registries help bridge between clinical trial data and insights to real world evidence needs?
* How can digital biomarkers be used in registries? How do these technologies potentially change the landscape in the future?

**Results**

Optimizing the use of Alzheimer’s disease registries remains an urgent next step for European stakeholders seeking to advance new therapies and the funding models that support them. To make the most of the opportunities offered by registries, we must:

1. Increase biomarker and digital phenotyping data in the registries.

2. Ensure registries are flexible and not built around a single disease hypothesis.

3. Foster public trust and engagement by establishing robust legal structures that protect data privacy.

By taking these steps, we can elevate the potential of Alzheimer’s registries operating today, inform how to construct these tools in the future, deepen our understanding of the disease, and catalyze innovation and access in Alzheimer’s treatment.

**Discussion**

Because Alzheimer’s is marked by gradual progression over the course of many years, long-term data on large populations is essential. By adopting a broad scope and collecting patient data from pre-clinical Alzheimer’s to its terminal stages, registries can facilitate and add to the extrapolation of randomized clinical trial data for better understanding. Three steps are essential for maximizing the potential of registries:

1. Increase biomarker and digital phenotyping data in the registries.

Ideally, the most effective DMTs would be administered early in the disease course. Advanced biomarker and digital phenotyping data can facilitate early treatment by helping pinpoint who will benefit the most from new Alzheimer’s therapies. If registries can collect biomarker and phenotyping data from large, diverse populations, health systems can use the data to determine which patients will benefit most from DMTs.

Registry data can also be used to build and validate modelsusing real-world data. These biomarker and digital phenotyping-informed models can offer a wealth of information on long-term time horizons (10-20 years), broader settings (e.g. markets not included in clinical trials, subgroups that require specific assumptions) and outcomes that cannot be adequately assessed in clinical trials.

1. Ensure registries are flexible and not built around one disease hypothesis.

Many biomarkers—representing diverse disease hypotheses—are currently being researched and developed, and registries need to support the full scope of these scientific efforts. For example, we need to expand the use of diagnostics that measure the APOE-4 gene, which is linked to a greater risk of Alzheimer’s; beta-amyloid, a protein that disrupts brain cell function; cerebrospinal fluid biomarkers such as the protein tau -- which is abnormally shaped in the brains of Alzheimer’s patients; and passive digital data on cognitive function, which can be measured by mobile phone apps or wearables.

Digital tools are especially helpful, as they allow the collection of a wide range of data—leading to new or unexpected discoveries. By passively collecting vast amounts of data, digital technologies can pick up on trends outside the bounds of what researchers are looking for, leading to discoveries that otherwise would not have been made., This can help investigators assess the appropriateness of a given approach in the context of full data.

1. Foster public trust and engagement by establishing robust legal structures that protect data privacy.

Because registry data offers real-world information about patients, structures for gaining consent and using data are critical—to meet legal obligations, ensure ethical operations, and foster public trust and engagement. Citizens are protective of their health data, and we need to show them that registries are reliable custodians of data. If we fail to do this, the public will be unwilling to share health information with registries, limiting the effectiveness of registry informing scientific and policy decisions.

Information should be collected under a framework that protects data and incorporates important considerations that define when and how consent is gathered. These factors include frequency of informed consent gathering, the purpose of informed consent collection, and the specificity of informed consent. Frameworks should also ensure data safety and integrity (through technical fire walls, encryption, data access controls etc.) where necessary—and open access of anonymized health data whenever possible.

Despite the progress being made in the development of Alzheimer’s registries, costs of data collection remain a barrier, often meaning long-term data goes uncollected. Clinical trials are historically too short to demonstrate the value of new drugs over an extended timespan. Drug funds are one measure that could be used to overcome these challenges. By absorbing the costs of DMTs over an extended period, drug funds can support pharmacovigilance and identifying adverse events, patient follow-up, informing treatment duration, and the assessment of potentially useful surrogate endpoints.

**Key Points**

* Optimizing the use of Alzheimer’s disease registries remains an urgent next step for European stakeholders seeking to advance new therapies and the funding models that support them. To make the most of the opportunities offered by registries, we must:
	+ Increase biomarker and digital phenotyping data in the registries.
	+ Ensure registries are flexible and not built around one disease hypothesis.
	+ Foster public trust and engagement by establishing robust legal structures that protect data privacy.
1. Data Sharing in Dementia Research - The EU Landscape [Internet]. CORDIS. 2021 [cited 2021 Jun 8]. Available from: https://cordis.europa.eu/article/id/429232-alzheimer-europe-sets-out-recommendations-to-improve-data-sharing-in-dementia-research/it [↑](#endnote-ref-1)
2. Cummings J, Lee G, Zhong K, et al. Alzheimer's disease drug development pipeline: 2021. Alzheimer’s Dement (NY). 2021 May 25;7(1):e12179. doi: 10.1002/trc2.12179. [↑](#endnote-ref-2)
3. BBC News. US approves first new Alzheimer’s drug in 20 years. BBC [Internet]. 2021 Jun 7 [cited 2021 Jun 9]; Available from: https://www.bbc.com/news/health-57383763 [↑](#endnote-ref-3)