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New Anti-Amyloid Therapies - Where we are Wrong and about What do we have to Take Care of

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ABSTRACT

The numbers affected by Alzheimer's and other dementias has accelerated pace of increasing and still has no tendency to decrease. Effects of the current therapies are quite modest. These effects contribute to negative attitude toward anti dementia drugs, delaying in establishing a diagnosis, postponing of beginning of pharmacological therapy or refusal of using therapy and disbelief in success of other measures like: life style changing, adoption to a new life habit or using non pharmacological therapies. The outcome of these attitudes is significantly faster cognitive decline which is reflected in changes in behavior with more severe episodes of maladaptive behavior that require additional use of medications such as: antipsychotics, hypnotics, benzodiazepines, anti-depressants and anxiolytics.

Unfortunately, although non-pharmacological therapies have a real effect in improving the condition of people with dementia, they are not talked about enough. Professional health meetings do not include non-health professionals who do the hard work of improving a patient's condition every day. Also, health professionals do not refer patients to non-pharmacological therapy although there are science researches which prove efficiency. We want to believe that this is because there are few professional institutions that deal with non-pharmacological interventions, but also experts who have the knowledge, skills and tools for that job. National health and social care systems that either do not recognize these services as useful therapies or offer these services under limited conditions certainly contribute to this serious deficiency. This issue also shows the non-harmonious functioning of the health and social sectors, although non-pharmacological interventions has potential to decline fees these systems.

A new generation of AD therapies are passive anti-amyloid immunotherapies that modify the course of the disease. It is expected that only 13% of people with MCI and 17% with mild dementia are eligible for therapy. The task of these products is cleansing the brain from Beta amyloid (Aß) deposits during 18 months. According to the words of producers, therapy allows slowing the decline of executive functions, maintaining social cognition and preserving short-term and working memory. Therapy has side effects which can worse patient health condition.

Here we ask: "Where we go wrong and why proper communication with stakeholders regarding anti-amyloid therapies is important? What after anti-amyloid therapy?"

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Introduction

The numbers affected by Alzheimer's and other dementias has accelerated pace of increasing and still has no tendency to decrease. Lately regarding prevention, we speak about 10 or 12, or more, risk factors of developing dementia but that is story about 40% possible causes which could contribute in development of dementia.

With what are faced those are coming in touch with dementia? Those that are faced with dementia we can divide into two groups: those who provide and those who receive therapy. Those who are providing therapy are health workers - for medical care and non-health workers - for non-medical care. The common barriers for all (both groups) are prejudice and stigma.

What are resources for health workers? Current therapies in use are: Donepezil, Rivastigmine, Galantamine and Memantine. The youngest therapy in use for Alzheimer's disease (AD) is more than 20 years old, and it is memantine, while Donepezil is a therapy that has been used for almost 30 years. The effects of these therapies are quite modest, and slightly better effects are recorded, especially in the treatment of behavioral deterioration, with a combination of therapies, e.g. donepezil and memantine.

What are options for non-health workers if their patients have no cure for disease they suffer and they are loaded with prejudice and stigma? That is: providing of non-pharmacological therapies, advising and raising awareness at patients and their family members.

People with dementia and their families? The key for therapy success lay on three legs: - accepting of the disease and her requires bring with herself; - understanding of course of disease which brings cognitive decline and changing in behavior; - wish for living.

Timely diagnosis, life style changing, making and adoption to a new life habits and full access to non-pharmacological therapies are resources for people with dementia and their families. Stated belongs to non-medical care.

Today's Challenges on the Dementia Field

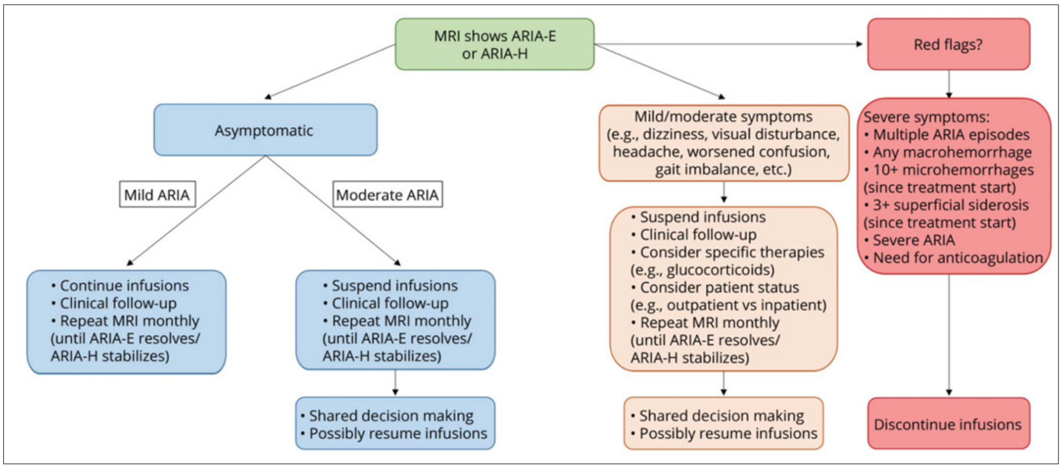
What is consequence of the modest therapeutic effect of today's therapies in conjunction with prejudices and stigma? The consequence is creating of a negative attitude toward anti-dementives which results in delaying in establishing a diagnosis, postponing of beginning of pharmacological therapy or refusal of using therapy and disbelief in success of other measures like: life style changing, adoption to a new life habit or using non pharmacological therapies. What does it lead to? It leads to: significantly faster cognitive decline which is reflected in changes in behavior with more severe episodes of maladaptive behavior that require additional use of medications such as: antipsychotics, hypnotics, benzodiazepines, anti-depressants and anxiolytics. Very often, as a result of sudden cognitive declines, there is also a worsening of the somatic condition, and the involvement of health workers is necessary.

All of the above drastically increases the costs of the health system because requires complex therapeutic care provided by good trained professionals in special equipped spaces. Also, it increases the costs of social expenditures, but also worsen quality of life of people with dementia but and their families and drastically reduces the life expectancy of a person with dementia. This process which take place in front of eyes of family, environment and health care workers encourage prejudice with reflection on strengthening stigma Because of that grow distrust that has reflection in modest success in raise awareness campaigns.

Anti-Amyloid Therapies for AD - New Challenge

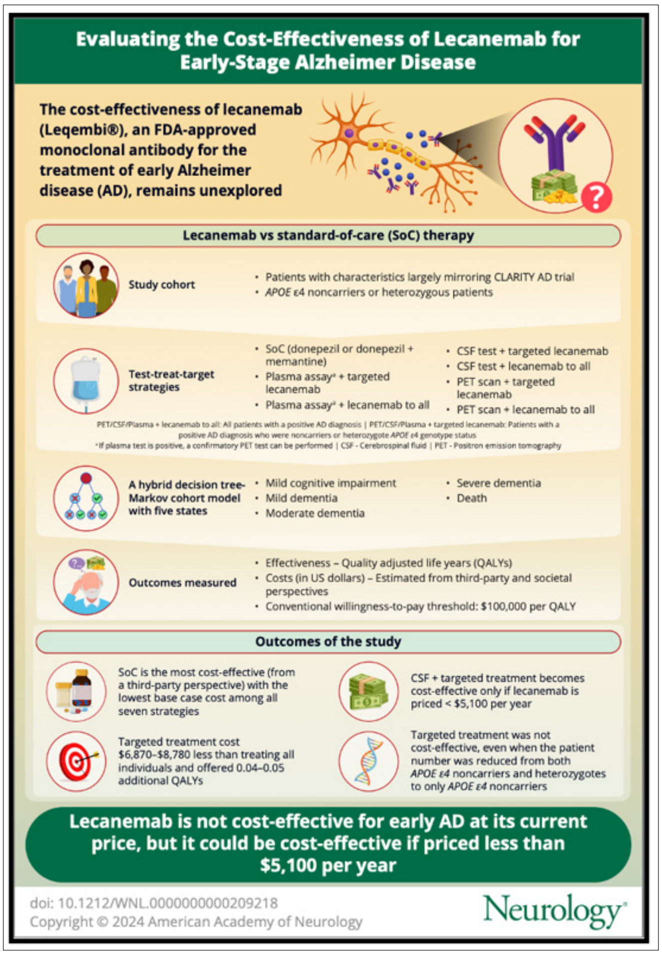
A new generation of AD therapies are passive anti-amyloid immunotherapies that modify the course of the disease. It is expected that only 13% of people with MCI and 17% with mild dementia are eligible for therapy. The task of these products is cleansing the brain from Beta amyloid (Aß) deposits during 18 months. According to the words of producers, therapy allows slowing the decline of executive functions, maintaining social cognition and preserving short-term and working memory.

Withal, therapies can have a serious side effect, which is why it is necessary monitoring the patient's health condition. Because of these facts, manufacturers have set up research protocols that select candidates for anti-amyloid therapy. At the same time, manufacturers set strict requirements regarding patient monitoring before and after therapy. In this way, manufacturers direct the patient to the provider from the research that establishes the diagnosis to the very end of treatment, which increases the cost of anti-amyloid therapy. This limitation will especially affect patients who do not live near the location of the anti-amyloid therapy provider. This is an additional and certainly a big discouraging factor of the number of people who will access to therapy.



Source: Neurology 2023; 101:842-852. doi: 10.1212/WNL.0000000000207757.

When we speak about anti -amyloid therapies then we have to mention price. The annual price of Lecanemab therapy is $26,500, while the price of Donanemab is slightly higher at $32,000. It means that the full therapy with Lecanemab is almost 40.000$ or 48.000$ with Donanemab. This price doesn't include other costs like: transport, accommodation, findings before and after therapy and non-pharmacological therapy as well.



Evaluating the Cost-Effectiveness of Lecanemab for Early-Stage Alzheimer Disease

The cost-effectiveness of lecanemab (Leqembi®), an FDA-approved monoclonal antibody for the treatment of early Alzheimer disease (AD), remains unexplored

Lecanemab vs standard-of-care (SoC) therapy

Study cohort
- Patients with characteristics largely mirroring CLARITY AD trial
- *APOE* ε4 noncarriers or heterozygous patients

Test-treat-target strategies
- SoC (donepezil or donepezil + memantine)
- Plasma assay[a] + targeted lecanemab
- Plasma assay[a] + lecanemab to all
- CSF test + targeted lecanemab
- CSF test + lecanemab to all
- PET scan + targeted lecanemab
- PET scan + lecanemab to all

PET/CSF/Plasma + lecanemab to all: All patients with a positive AD diagnosis | PET/CSF/Plasma + targeted lecanemab: Patients with a positive AD diagnosis who were noncarriers or heterozygote *APOE* ε4 genotype status

[a] If plasma test is positive, a confirmatory PET test can be performed | CSF - Cerebrospinal fluid | PET - Positron emission tomography

A hybrid decision tree-Markov cohort model with five states
- Mild cognitive impairment
- Mild dementia
- Moderate dementia
- Severe dementia
- Death

Outcomes measured
- Effectiveness – Quality adjusted life years (QALYs)
- Costs (in US dollars) – Estimated from third-party and societal perspectives
- Conventional willingness-to-pay threshold: $100,000 per QALY

Outcomes of the study

SoC is the most cost-effective (from a third-party perspective) with the lowest base case cost among all seven strategies

CSF + targeted treatment becomes cost-effective only if lecanemab is priced < $5,100 per year

Targeted treatment cost $6,870–$8,780 less than treating all individuals and offered 0.04–0.05 additional QALYs

Targeted treatment was not cost-effective, even when the patient number was reduced from both *APOE ε4* noncarriers and heterozygotes to only *APOE ε4* noncarriers

Lecanemab is not cost-effective for early AD at its current price, but it could be cost-effective if priced less than $5,100 per year

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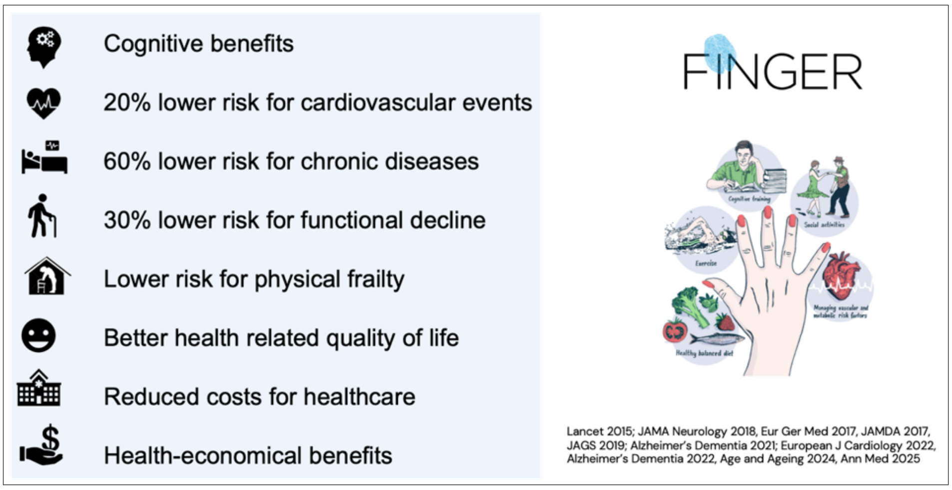
Justification of Non-Medical Interventions

The very important information is that therapy does not prevent the progression of the disease and the transition of the affected person to the next phase of the disease!

As with current therapies there is no mention of the accompanying and parallel activities that we mentioned above implemented by non-healthcare workers as non-medical care. One gets the impression that other activities are unimportant and that the success of anti-amyloid therapy does not directly depend on other measures but rather enables them through its effects on the brain. The manufacturer’s recommendations and reports include medical protocols but nowhere is there any mention non-medical care.

Below we will describe Two Studies:

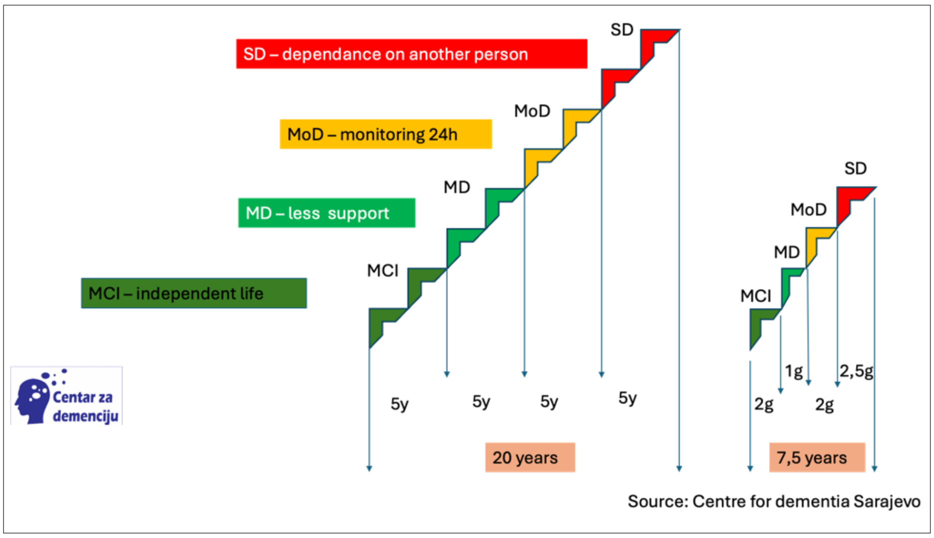
- Therefore, we will look at the outcomes of the FINGER study that present a post-diagnostic non-pharmacological individualized approach to a person with dementia supported by pharmacological therapy of AD (donepezil, memantine, rivastigmine and galantamine). The FINGER study proves that adjusting the lifestyle can influence the improvement of a person's overall condition and the prevention of cognitive decline. These are interventions in 5 components: nutrition, exercise, cognitive training, social activities and monitoring of vascular risk factors. Interventions respect health advice. The subjects were studied for 5, 7 and 11 years. Improvements in the condition of the monitored individuals were recorded in the following segments:
- overall cognition by 25%,
- information processing speed by 150%,
- memory improvements by 40% and
- executive function improvements by 83% [1]
- a better response to the interventions was seen in APOE ε4 carriers as well as in men [2].


Cognitive benefits
20% lower risk for cardiovascular events
60% lower risk for chronic diseases
30% lower risk for functional decline
Lower risk for physical frailty
Better health related quality of life
Reduced costs for healthcare
Health-economical benefits

Lancet 2015; JAMA Neurology 2018, Eur Ger Med 2017, JAMDA 2017, JAGS 2019; Alzheimer's Dementia 2021; European J Cardiology 2022, Alzheimer's Dementia 2022, Age and Ageing 2024, Ann Med 2025

- Research conducted by the Center for Dementia; Sarajevo; Bosnia and Herzegovina in the period 2013-2022. in Bosnia and Herzegovina, how long do people with dementia live from the onset of dementia symptoms up to death. Sample was on 4.000 cases. It should be noted that the respondents were not provided with any significant post-diagnostic non-pharmacological intervention nor are adopted life style. According to the statements of the families, they relied exclusively on pharmacological therapy. The collected data from research showed that in Bosnia and Herzegovina people with dementia live an average of 7.5 years from the onset of symptoms and that they spend the longest time in advanced dementia (4.5 years vs. 3 years).

We think that the conclusion is self-imposed and that is: relying exclusively on pharmacological therapy does not give the expected result. Dementia therapy is much more than just taking pharmacological therapy. At the same time, I want to believe that anti-amyloid therapies of the new generation are much more effective from current.



Source: Centre for dementia Sarajevo

Preparedness of the System for Dementia Care

Very interesting research was conducted under the name of PANEUCARE (Multidirectional Knowledge Transfer of Dementia Research and Care between European and International Regions) with funding from the EU Joint Programme on Neurodegenerative Disease Research (JPND) which has finalized in summer 2025. but not yet published. The project brought together researchers, practitioners, policymakers, caregivers, and people living with dementia from 17 European countries, particularly emphasizing the inclusion of Southern and Eastern European countries. Through collaborative workshops and focus groups, PANEUCARE identified shared challenges, good practices, and strategic priorities for strengthening dementia care across diverse European contexts. In the top 10 challenges in these 17 societies are: increasing prevalence of dementia and demographic challenges, access to specialized care, lack of manpower, delay or absence of diagnosis, caregiver burnout and system support, lack of trained professionals, quality of care provided, friendly communities, poorly organized home care in urban areas and lack of services in rural areas, financial challenges. In the 13th place out of thirty-one places is the fragmentation of health and social care.

It is very clear from this research that national systems are completely unprepared to implement the necessary care for people with dementia [3-24].

Conclusion

From above stated challenges it is very clear that a lack of educated and trained staff causes insufficient or lower quality services and that ill-adapted health and social care systems create a gap between needs and supply, this is not the root of the problem. The root of the problem is fragmented systems, the social system from the health system, which is not holistic but curative. These two systems does not allow, even they are payed from one budget, for joint actions, determined with a single goal, which in the case of dementia should be the completely, somatic and cognitive, improvement of the patient's condition as a result of coordinated and centrally managed activities that have equal importance. This root of the problem arises in the educational system that builds illusions on a one-sided approach to the problem of each profession individually. Such educational systems have built completely separate systems and services that are not parallel but follow each other without mutual connection and communication. Although there is more and more talk about multi-disciplinary and inter-professional, the substrate (educational systems) is completely wrong and it is quite normal that it is very difficult to reorganize the system and make it harmonized without first changing of these substrates, which takes time.

From the FINGER study we saw that it is possible to achieve favorable care outcomes if there is cooperation between all stakeholders with designed, managed and coordinated parallel activities. At the same time, from the research of the Center for Dementia Sarajevo we see the disaster for the patient, family, community and system that a one-sided approach based on pharmacological therapy brings.

Therefore, the question arises, what if in real circumstances a person is accepted as a potential patient for anti-amyloid therapy, secures the necessary funds and receives all 18 therapies without at the same time carrying out the parallel activities non-medical care (adopting new life habits, changing life style, using non-pharmacological therapies etc) and at the end of the cycle is disappointed with final outcome. Also, what if the patient starts receiving therapy and after a couple of therapies the process has to be interrupted due to side effects. Is it okay to just say we're sorry? Nevertheless, this is a person who, with good care, could live quite well 10 or 15 years. What is her/his future after the complications caused by the therapy or how will she/he find the strength to fight on?
How will such reports affects the future of public raise awareness campaigns and fight against prejudice and stigma as well as improving trust in non-pharmacological therapies that the patient should continue with for the rest of his or her life?

The answers are before us. Since anti-amyloid therapies do not stop the progression of the disease, those who successfully received the therapy or the therapy was interrupted for some reason have the only way out to return with non-pharmacological therapies that are not carried out by health professionals. Therefore, isn't it logical to open the process from the very beginning and make it multi-professional and parallel, which continues after pharmacological therapy.

We are aware that anti-amyloid therapy is on the beginning. Closed pharmacological approach can be wrong strategy which in connection with miscommunication that could turn hope into disappointment with perhaps more serious consequences than we can imagine. Miscommunication can:

- discourage policy makers, medical and other professionals, and
- discourage the general public,
- warn scientist in medical agencies to be more careful in communication because they can make it difficult for all those involved in raising awareness about dementia, who are crucial to the mission of improving the state of dementia, recruiting and encouraging sufferers to access the process of diagnosis and use of therapy.

Persons with dementia and their families had high expectations from existing pharmacological therapies that these therapies cannot meet. Therefore, it is not surprising that people have high expectations from anti-amyloid therapies that are coming into use. With this paper we do not want to criticize but to draw attention to the following:

- anti-amyloid therapy protocols must also include other content related to non-medical measures as parallel activities
- when it is about therapy and not medicine communication with all stakeholders should be open and carefully designed with special sense
- the nervousness of investors and their demand for return of investment in the research or positioning of their therapy before outbreak of a new therapy doesn't instill confidence.

We have witness that the interest in new anti-amyloid therapies is not great or expected in countries where the application is approved and supported by the health system, which should be carefully analyzed.

Therefore, we should look for solutions that provide the best outcomes in a situation where there is no cure but life goes on!

References

1. Tiia Ngandu, Jenni Lehtisalo, Alina Solomon, Esko Levälahti, Satu Ahtiluoto, et al. (2015) A 2year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial, The LancetVol 385: 2255-2263.
2. Kučuk Osman, Jochen Rene Thyrian, Nenad Bogdanović, Boris Rogelj, Emanuele Buratti (2025) iCoDem/25 Conclusions, Research Gate.
3. Gustavsson A, Norton N, Fast T, Frölich L, Georges J et al. (2022) Global estimates on the number of persons across the Alzheimer's disease continuum. Alzheimer's & Dementia 19: 658-670.
4. Anna Rosenberg, Ulf Öhlund-Wistbacka, Anette Hall, Alexandre Bonnard, Göran Hagman, et al. (2022) β-Amyloid, Tau, Neurodegeneration Classification and Eligibility for Anti-amyloid Treatment in a Memory Clinic Population. Neurology 99: 2102-2113.
5. Vijay K Ramanan, Melissa J Armstrong, Parichita Choudhury, Katherine A Coerver, Roy H Hamilton, et al. (2023) Antiamyloid Monoclonal Antibody Therapy for Alzheimer Disease. Neurology 101: 842-852.
6. Hai V Nguyen, Shweta Mital, David S Knopman, G Caleb Alexander (2024) Cost-Effectiveness of Lecanemab for Individuals With Early-Stage Alzheimer Disease. Neurology 102: e209218.
7. Whittington MD, Campbell JD, Rind D, Fluetsch N, Lin GA, et al. (2022) Cost-effectiveness and value-based pricing of aducanumab for patients with early Alzheimer disease. Neurology 98: 968-977.
8. Sinha P, Barocas JA (2022) Cost-effectiveness of aducanumab to prevent Alzheimer's disease progression at current list price. Alzheimers Dement (NY) 8: 12256.
9. Ross EL, Weinberg MS, Arnold SE (2022) Cost-effectiveness of aducanumab and donanemab for early Alzheimer disease in the US. JAMA Neurol 79: 478-487.
10. KFF (2023) New Alzheimer's Drugs Spark Hope for Patients and Cost Concerns for Medicare. kff.org/policy-watch/new-alzheimers-drugs-spark-hope-for-patients-and-cost-concerns-for-medicare/.
11. Eisai Co (2023) Ltd. EISAI's Approach to U.S. Pricing for

Leqembi™ (Lecanemab), a Treatment for Early Alzheimer's Disease, Sets Forth Our Concept of "Societal Value of Medicine" in Relation to "Price of Medicine" https://media-us.eisai.com/2023-01-06-EISAIS-APPROACH-TO-U-S-PRICING-FOR-LEQEMBI-TM-LECANEMAB-,-A-TREATMENT-FOR-EARLY-ALZHEIMERS-DISEASE,-SETS-FORTH-OUR-CONCEPT-OF-SOCIETAL-VALUE-OF-MEDICINE-IN-RELATION-TO-PRICE-OF-MEDICINE.

12. Institute for Clinical and Economic Review (2023) Alzheimer's Disease: An Assessment of Lecanemab. ICER. 2022. https://icer.org/wp-content/uploads/2023/04/ICER_Alzheimers-Disease_Final-Report_For-Publication_04172023.pdf.
13. Sanders GD, Neumann PJ, Basu A (2016) Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses: second panel on cost-effectiveness in health and medicine. JAMA 316: 1093-1103.
14. Landeiro F, Mughal S, Walsh K (2020) Health-related quality of life in people with pre-dementia Alzheimer's disease, mild cognitive impairment or dementia measured with preference-based instruments: a systematic literature review. Alzheimers Res Ther 12: 154.
15. Alzheimer's Association (2023) Lecanemab Approved for Treatment of Early Alzheimer's Disease. Alzheimer's Disease and Dementia. 2023. alz.org/alzheimers-dementia/treatments/lecanemab-leqembi.
16. The Alzheimer's Organization. ApoE4 Genetic Test (2023) alzheimersorganization.org/alzheimers-test.
17. Andersen K, Lolk A, Martinussen T, Kragh-Sørensen P (2010) Very mild to severe dementia and mortality: a 14-year follow-up–the Odense study. Dementia Geriatric Cognitive Disorders 29: 61-67.
18. Yunusa I, Alsahali S, Rane A, Eguale T (2021) Comparative value of cholinesterase inhibitors and memantine in persons with moderate-to-severe Alzheimer's disease in the United States: a cost-effectiveness analysis. J Alzheimers Dis Rep 5: 705-713.
19. Yan Li, Suzanne E Schindler, James G Bollinger, Vitaliy Ovod, Kwasi G Mawuenyega, et al. (2022) Validation of plasma amyloid-β 42/40 for detecting Alzheimer disease amyloid plaques. Neurology 98: 688-699.
20. Herring WL, Gould IG, Fillit H, Peter Lindgren, Fiona Forrestal, et al. (2021) Predicted lifetime health outcomes for aducanumab in patients with early Alzheimer's disease. Neurology 10: 919-940.
21. Neumann PJ, Hermann RC, Kuntz KM, Araki SS, Duff SB, et al. (1999) Cost-effectiveness of donepezil in the treatment of mild or moderate Alzheimer's disease. Neurology 52: 1138-1145.
22. Monfared AAT, Tafazzoli A, Chavan A, Ye W, Zhang Q (2022) The potential economic value of lecanemab in patients with early Alzheimer's disease using simulation modeling. Neurol Ther 11: 1285-1307.
23. van Dyck CH, Swanson CJ, Aisen P, Randall J Bateman, Christopher Chen, et al. (2023) Lecanemab in early Alzheimer's disease. N England J Med 388: 9-21.
24. United States Joint Economic Committee (2022) The Economic Costs of Alzheimer's Disease. 2022 jec.senate.gov/public/index.cfm/democrats/issue-briefs?id=02F4CADC-954F-4E3B-8409-A4213E3C0759.