



When precision innovation meets health system realities:

The case of amyloid-targeting treatments for Alzheimer's disease

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Precision Medicine in Neuroscience

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Disclosures



Soeren Mattke serves on the board of directors of Senscio Systems, Inc., and scientific advisory boards of Alzpath, BMS and Boston Millennia Partners. He has received consulting fees from Biogen, C2N, Eisai, Eli Lilly, Novartis, Novo Nordisk and Roche/Genentech. Outside of this work, USC has research contracts on which Dr. Mattke is PI with Biogen, C2N, Eisai, Eli Lilly and Roche/Genentech.

The case of aducanumab



Major breakthrough for precision treatment of Alzheimer's disease

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The antibody aducanumab reduces A β plaques in Alzheimer's disease

- First drug to remove beta-amyloid plaques from the brain and reduce progression of cognitive decline

Sevigny, J., Chiao, P., Bussière, T. *et al.* The antibody aducanumab reduces A β plaques in Alzheimer's disease. *Nature* **537**, 50–56 (2016). <https://doi.org/10.1038/nature19323>

Lack of health systems preparedness to identify patients and deliver drug

The Edinburgh Consensus: preparing for the advent of disease-modifying therapies for Alzheimer's disease



Craig W. Ritchie^{1,2†}, Tom C. Russ^{1,2,3,4†}, Sube Banerjee⁵, Bob Barber⁶, Andrew Boaden⁷, Nick C. Fox⁸, Clive Holmes⁹, Jeremy D. Isaacs¹⁰, Ira Leroi¹¹, Simon Lovestone¹², Matt Norton¹³, John O'Brien¹⁴, Jim Pearson¹⁵, Richard Perry¹⁶, James Pickett⁷, Adam D. Waldman¹⁸, Wai Lup Wong¹⁷, Martin N. Rossor^{8†} and Alistair Burns^{11†}



Assessing the Preparedness of the U.S. Health Care System Infrastructure for an Alzheimer's Treatment

Jodi L. Liu, Jakub P. Hlavka, Richard Hillestad, Soeren Mattke

Ritchie, C., et al. (2017). The Edinburgh Consensus: Preparing for the advent of disease-modifying therapies for Alzheimer's disease. *Alzheimer's research & therapy*. <https://doi.org/10.1186/s13195-017-0312-4>

Liu, Jodi L., Jakub P. Hlavka, Richard Hillestad, and Soeren Mattke, Assessing the Preparedness of the U.S. Health Care System Infrastructure for an Alzheimer's Treatment. Santa Monica, CA: RAND Corporation, 2017. https://www.rand.org/pubs/research_reports/RR2272.html.

Why were we so concerned about health systems preparedness?



Today's paradigm for memory care



Required future state



What happened in the early roll-out years?



- Aducanumab received accelerated approval in 2021 and two similar drugs, lecanemab and donanemab, were FDA approved in 2022 and 2023, respectively
- Aducanumab was discontinued in 2022 for lack of commercial viability
- By the end of 2023, 924 patients had been started on treatment by 410 prescribers in the full Medicare fee-for-service population
- Detection rates of mild cognitive impairment, the state at which the drugs would ideally be started, hover around 8-10%

Mattke, S., et al. (2025). "Demographic and clinical characteristics of initial patients receiving amyloid-targeting treatments in the United States after regulatory approval." *Alzheimers Dement* **21(3)**: e70054.

Mattke, S., et al. (2023). "Expected and diagnosed rates of mild cognitive impairment and dementia in the U.S. Medicare population: observational analysis." *Alzheimer's Research & Therapy* 15(1).

Which factors contributed to the limited uptake?



- Skepticism, even among specialists, about clinical benefit of treatment
 - Concerns about adverse events
- Lack of capacity given limited prescriber base
- Uncertainty about coverage of diagnostic tests and treatment itself
- Reluctance of health systems to invest in needed infrastructure
- Lack of engagement of PCPs to detect and refer patients with early-stage cognitive impairment
 - Aggravated by lack of confidence and knowledge

What are the implications for precision neuroscience?



- We are witnessing unprecedented progress in our understanding of, particularly, neurodegenerative disorders
 - Basis for biologic disease definitions and subsequent development of biomarkers and targeted treatments
- Several of those diseases are too common to remain in the hands of specialists, let alone sub-specialists, alone as neurology/neuropsychiatry is not a large specialty
 - Also, treatment-oriented neurologists have historically gravitated towards MS and stroke
- Urgent need to grow specialist capacity and develop care models to leverage scarce specialists better

Contact information



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