

Alzheimer's Disease and Related Dementia (ADRD) Risk-Reducing Benefits Offered by HMG-CoA Reductase Inhibitors, or Statins

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Presented 11/13/2023 at ISPOR Europe

Disclosures

- Mohin Chanpura, the presenting author, is presently employed by Magnit (formerly PRO Unlimited) as contractor for Novartis Pharmaceuticals Corp., was previously employed by Deallus Consulting as a consultant to AbbVie Inc., Bristol Myers Squibb, Daiichi Sankyo, Inc., and Sage Therapeutics whilst researching this topic as a master's student at Rutgers University, and presently owns stock in Marinus Pharmaceuticals, Inc.
- All views expressed by the presenting author are the presenting author's own and do not represent those of any past or present employers, nor any other companies done business with.
- No research funding was associated with this study.

Recent Headlines Featuring Novel Alzheimer's Txs

The hard math on the new \$56,000 Alzheimer's drug



Analysis by Zachary B. Wolf, CNN

🕒 6 minute read · Updated 8:11 PM EDT, Tue July 20, 2021

FDA's Approval of Biogen's New Alzheimer's Drug Has Huge Cost Implications for Medicare and Beneficiaries

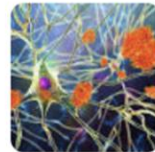
Juliette Cubanski and Tricia Neuman



New Alzheimer's drug Aduhelm flops with doctors and patients : Shots - Health News

The new Alzheimer's drug Aduhelm isn't reaching many patients. And doctors say reasons include its high cost, insurers' reluctance to cover...

Nov 8, 2021



House investigation says FDA approval process of Alzheimer's drug was 'rife with irregularities'



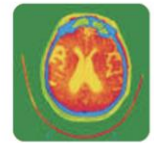
By Jen Christensen, CNN

🕒 5 minute read · Updated 4:53 PM EST, Thu December 29, 2022



A new Alzheimer's drug will cost \$26,500 a year. Who will be able to get it?

A newly approved drug intended to slow the progression of Alzheimer's disease offers patients hope, but it will come with a steep price tag:...



News > Medscape Medical News

Annual Costs of Lecanemab Estimated to Be Upwards of \$2 Billion

Megan Brooks

May 12, 2023



Donanemab Alzheimer Drug Fast Approval Shutdown by FDA

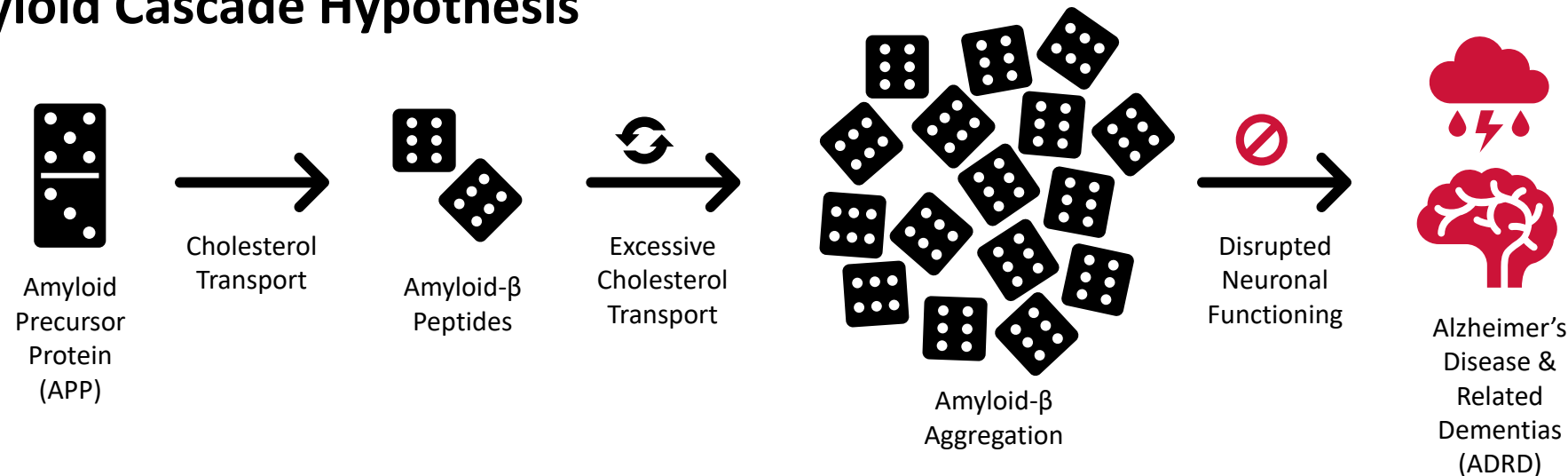
Eli Lilly's bid for an accelerated approval of Alzheimer's disease drug donanemab has been shut down by the FDA.

Jan 19, 2023



ADRD Prevention: Learnings from UK's Whitehall II

Amyloid Cascade Hypothesis



Singh-Manoux et al. (2008)

- Low HDL-C levels (<40 mg/dL) show significant association with **declining short-term memory** in Whitehall II Study participants ages 55-61

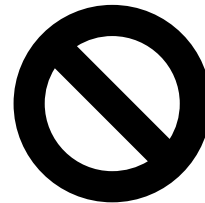
Statins as ADRD Prophylaxis?

HMG-CoA Reductase Inhibitors (Statins)

- Block cholesterol synthesis through inhibition of HMG-CoA reductase enzyme
- Have been used to treat dyslipidemia since 1987 (United States)
- Taken by more than 200 million patients worldwide today
- Loss of patent exclusivity as of 2017 has dropped annual wholesale acquisition costs (WACs) to <\$40/patient in US



Safe.



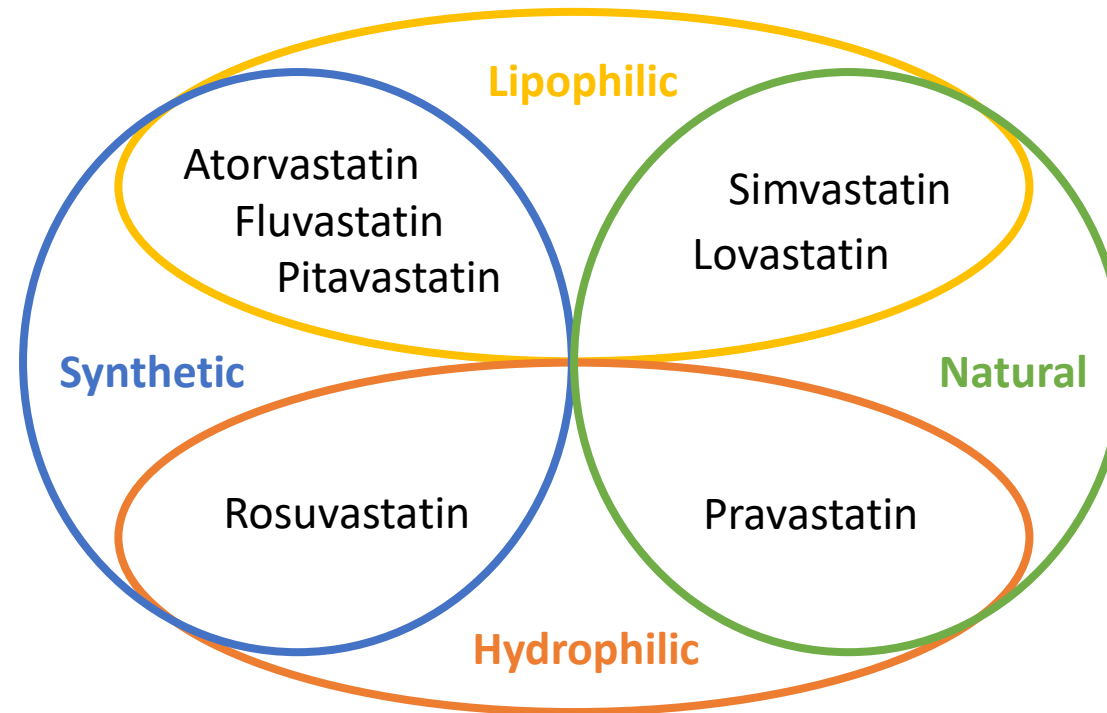
Effective.



Affordable.

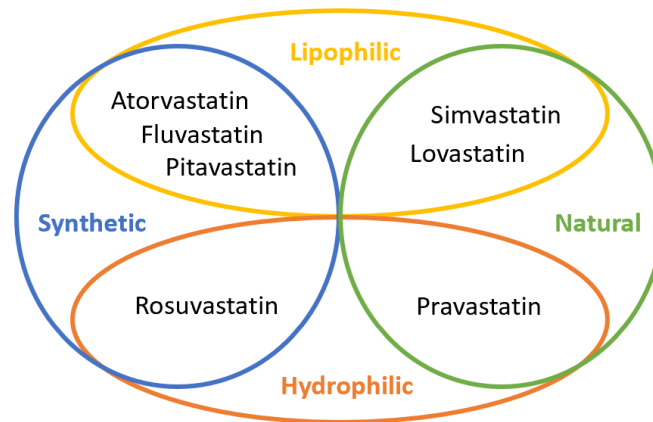
Statins as ADRD Prophylaxis?

Not all statins are created equal!



Objectives

1. To determine whether statins as an overall drug class significantly decrease ADRD risk in older adults (ages 45+)
2. To compare the degrees by which different statin drugs reduce ADRD risk



Data Source: Medicare Current Beneficiary Survey

What is MCBS?

- Longitudinal, multipurpose panel survey studying HCRU among Medicare beneficiaries
- Conducted annually by US Centers for Medicare & Medicaid Services since 1991
- Surveys nationally representative cohorts of ~15,000 beneficiaries each year
- Complete annual data sets (excluding PHI) publicly available to researchers



Study Design

A retrospective, matched case-control analysis of 2019 and 2020 MCBS data

- Cases defined as respondents ages 45+ with self/proxy reported diagnoses of either Alzheimer's disease OR other dementias

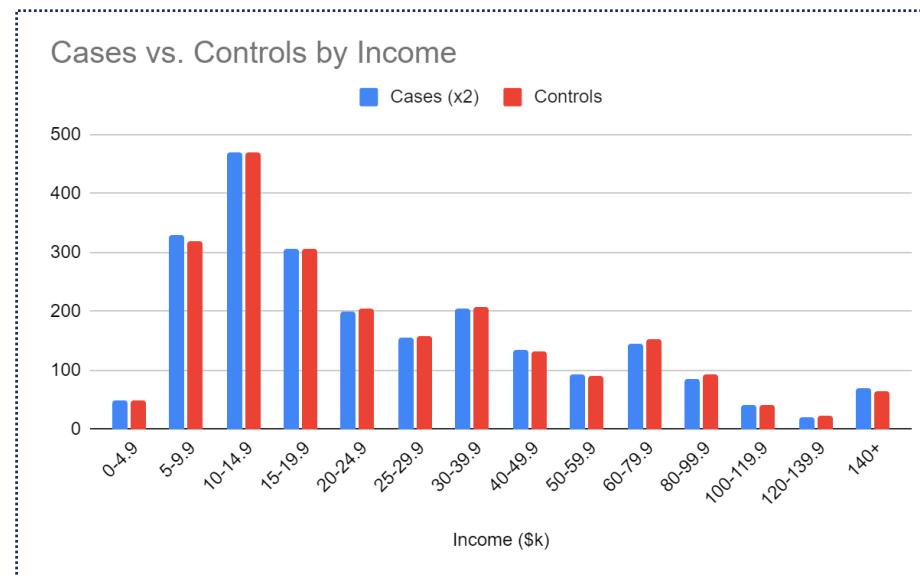
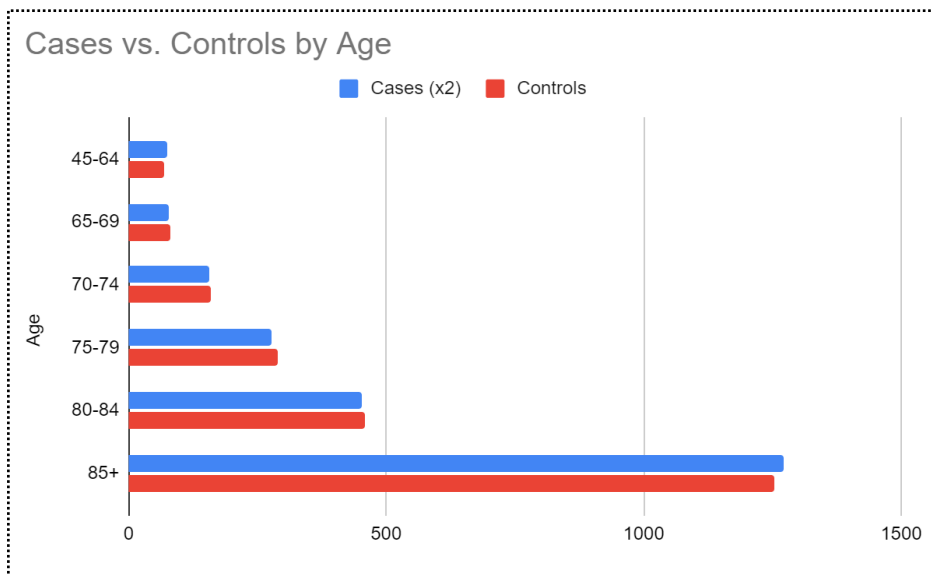
Cases and controls matched at 1:2 ratio based on:

- Sex
- Race (and ethnicity if available)
- Age stratum
- Income level

Results: Study Sample

3,468 respondents included (n=1,156 cases; n=2,132 controls)

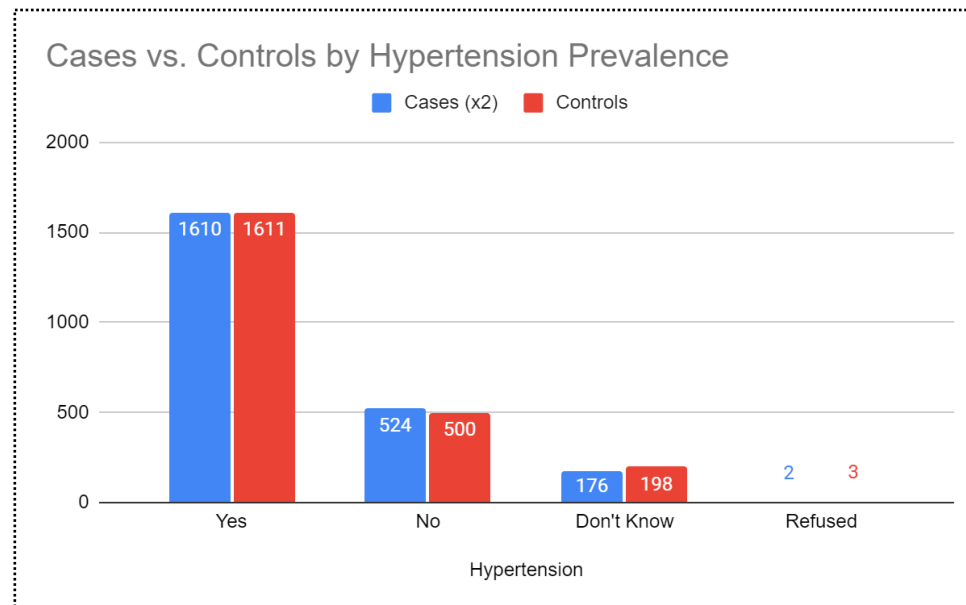
- Matched perfectly by **sex** (65.3% female) & **race** (75.2% white, 12.0% Hispanic, 9.7% black)
- Matched closely by **age** ($\chi^2 = 1.621$; $p=0.8987$), **income** ($\chi^2 = 2.002$; $p=0.9998$), and **ethnicity** ($\chi^2 = 4.176$; $p=0.9645$)



Results: Prevalence of Hypertension in Sample

Hypertension is known to be associated with cognitive impairment and dementia

- Chi-square testing showed **no significant difference** in hypertension prevalence among cases and controls ($\chi^2 = 4.350$; $p=0.2261$)



Results: Statin Utilization Among Selected Sample

1,898 statin users (55% of sample) reported taking one or more of the following:

- n=945 (50% of users) taking atorvastatin (including amlodipine/atorvastatin)
- n=432 (23% of users) taking simvastatin (including ezetimibe/simvastatin)
- n=220 (11% of users) taking pravastatin
- n=204 (11% of users) taking rosuvastatin
- n=97 (5% of users) taking other statins (lovastatin, fluvastatin, or pitavastatin) or taking multiple statins equally

1,570 selected respondents (45% of sample) reported not using statins

ADRD Diagnosis Less Likely Among Statin Users

Table 3: Diagnosis of ADRD (Alzheimer's + Other Dementia) among all statin users versus nonusers.

	Diagnosed ADRD	No Diagnosis	Total
Statin User	558 (29.4%)	1340 (70.6%)	1898
Statin Nonuser	598 (38.1%)	972 (61.9%)	1570
Total	1156	2312	3468

OR: 0.6769 (0.5873, 0.7800); $p < 0.0001$

Regardless of Diagnosis Type (Alzheimer's or Other)

Table 4: Diagnosis of Alzheimer's disease among all statin users versus nonusers.

	Diag. Alzheimer's	No Diagnosis	Total
Statin User	209 (13.5%)	1340 (86.5%)	1549
Statin Nonuser	239 (19.7%)	972 (80.3%)	1211
Total	448	2312	2760

OR: 0.6343 (0.5177, 0.7772); $p < 0.0001$

Table 5: Diagnosis of Other Dementias among all statin users versus nonusers.

	Diag. Dementia	No Diagnosis	Total
Statin User	349 (20.7%)	1340 (79.3%)	1689
Statin Nonuser	359 (27.0%)	972 (73.0%)	1331
Total	708	2312	3020

OR: 0.7052 (0.5956, 0.8349); $p < 0.0001$

All Statins Significantly Reduced ADRD Risk

Table 6: Diagnosis of ADRD among atorvastatin users versus all statin nonusers.

	Diagnosed ADRD	No Diagnosis	Total
Atorvastatin User	306 (32.4%)	639 (67.6%)	945
Statin Nonuser	598 (38.1%)	972 (61.9%)	1570
Total	904	1611	2515

OR: 0.7784 (0.6566, 0.9927); $p=0.0040$

Table 7: Diagnosis of ADRD among simvastatin users versus all statin nonusers.

	Diagnosed ADRD	No Diagnosis	Total
Simvastatin User	120 (27.7%)	312 (72.3%)	432
Statin Nonuser	598 (38.1%)	972 (61.9%)	1570
Total	718	1284	2002

OR: 0.6252 (0.4989, 0.7899); $p<0.0001$

Table 8: Diagnosis of ADRD among pravastatin users versus all statin nonusers.

	Diagnosed ADRD	No Diagnosis	Total
Pravastatin User	58 (26.4%)	162 (73.6%)	220
Statin Nonuser	598 (38.1%)	972 (61.9%)	1570
Total	656	1134	1790

OR: 0.5819 (0.4240, 0.7988); $p=0.0007$

Table 9: Diagnosis of ADRD among rosuvastatin users versus all statin nonusers.

	Diagnosed ADRD	No Diagnosis	Total
Rosuvastatin User	49 (24.0%)	155 (76.0%)	204
Statin Nonuser	598 (38.1%)	972 (61.9%)	1570
Total	647	1127	1774

OR: 0.5138 (0.3668, 0.7197); $p<0.0001$

Rosuvastatin Deemed Best at Reducing ADRD Risk

Table 10: Treatment effect comparison matrix - odds of ADRD diagnosis among users of treatment versus control statin.

Control	Treatment		
	Simvastatin	Pravastatin	Rosuvastatin
Atorvastatin	0.8032 (p=0.0901)	0.7476 (p=0.0900)	0.6602 (p=0.0193)
Simvastatin		0.9309 (p=0.7804)	0.8219 (p=0.3373)
Pravastatin			0.8830 (p=0.6546)

Hydrophilicity Significantly Reduced ADRD Risk

Table 11: Diagnosis of ADRD among users of hydrophilic statins versus users of lipophilic statins.

	Diagnosed ADRD	No Diagnosis	Total
Hydrophilic Statin (Pravastatin, Rosuvastatin)	107 (25.2%)	317 (74.8%)	424
Lipophilic Statin (Atorvastatin, Simvastatin, Fluvastatin, Lovastatin, Pitavastatin)	448 (30.5%)	1021 (69.5%)	1469
Total	555	1338	1893

OR: 0.7693 (0.6017, 0.9835); p=0.0394

Conclusions

1. **Statin use significantly decreased ADRD risk** compared to non-use, suggesting viable use as a preventative therapy
2. **Rosuvastatin significantly reduced ADRD risk** relative to atorvastatin, the most prescribed statin in the United States
3. **Hydrophilic statins significantly reduced ADRD risk** relative to lipophilic statins

Limitations

Cross-sectional nature of MCBS data

- Rutgers' availability of data from only 2015 onward made it impossible to establish temporality, and therefore causation
- All findings from this analysis were simply associations, nothing more
- Future retrospective research still necessary to determine how long patients need to be on statin therapy before realizing ADRD risk reduction

Thank You!

For additional information please reach out at

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Backup

Algorithm for Case-Control Matching

Steps

1. Look for exact matches
2. Look for matches to the nearest income level
3. Look for matches of a different ethnicity within the same race (if applicable), repeating steps 1 and 2
4. Look for matches of the same income level from the closest age stratum
5. Look for matches to the nearest income level from the closest age stratum

