NEW & NOTABLE IN CARING FOR OLDER ADULTS

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Primary Care Review | February 2026

Objectives

- Appraise a selection of recently published studies on caring for older adults
- Consider new and updated information for its ability to affirm or change current practice

Updated Beers List

Pruritus	First-generation antihistamines *Recommendation: Avoid*	Generalized pruritus is generally not responsive to antihistamines unless specifically due to a histamine-mediated etiology like urticaria. Tailor treatment of generalized pruritus to the etiology, typically either dry skin, medications (opioids, CNS medications, diuretics, many others), or underlying medical conditions. For dry skin, consider: – Hydrating emollient twice daily – Short showers (< 3 min) in lukewarm water – Humidifiers – For other causes of generalized pruritus, address underlying conditions For localized pruritus, consider topical agents such as: – Topical anesthetics (e.g., lidocaine, pramoxine) – Cooling agents (e.g., menthol) – Topical steroids (e.g., hydrocortisone, triamcinolone) – Topical antihistamines (e.g., topical doxepin) – Capsaicin If using an oral antihistamine, prefer 2nd or 3rd generation agents, e.g., loratadine, cetirizine, levocetirizine, fexofenadine.[a,b]	**For patients and caregivers:** Information on causes of itching (AAFP) https://www.aafp.org/pubs/afp/issues/2022/0100/p55-s1.html Information on causes of itching and self-care (MedlinePlus) https://medlineplus.gov/itching.html **For clinicians:** Chronic pruritus review (JAMA 2024) https://jamanetwork.com/journals/jama/fullarticle/2819296

AGS Beers' Criteria Alternatives Panel. Alternative treatments to selected medications in the 2023 AGS Beers Criteria. J Am Geriatr Soc. 2025; https://doi.org/10.1111/jgs.19500

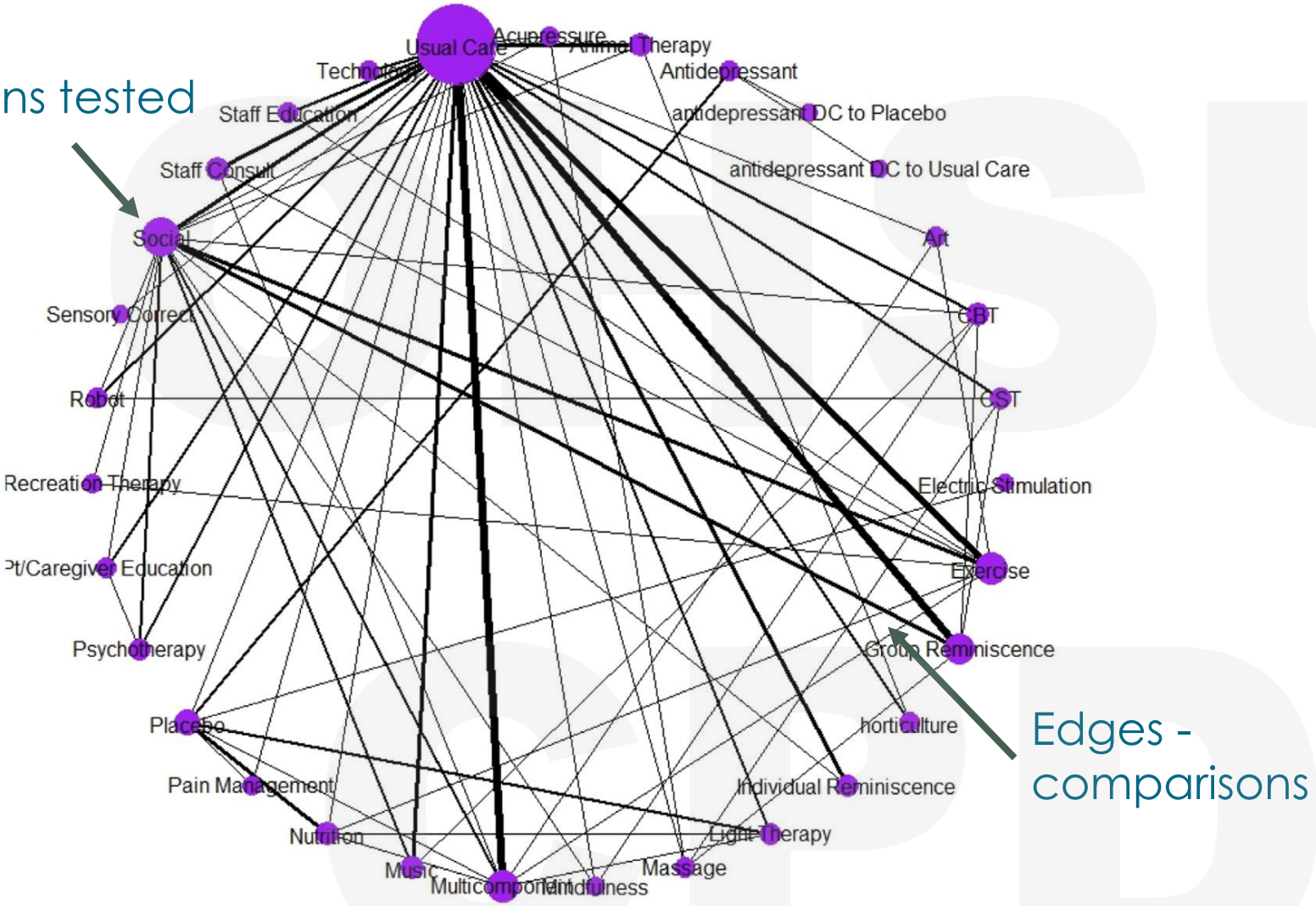
Depression in Long Term Care

Depression Treatments in LTC

- Network meta-analysis of 31 medication & non-pharmacologic treatments across 147 RCTs

OHSU CPD

Nodes – interventions tested



Edges - comparisons

Fig. 3. Network diagram of 31 treatment conditions from studies evaluating depression symptom reduction in residents of LTC. Antidepressant DC to Placebo, antidepressant discontinuation to placebo; Antidepressant DC to Usual Care, antidepressant discontinuation to usual care; CBT, cognitive behavioral therapy; CST, cognitive stimulation therapy; Multicomponent, multicomponent nonpharmacologic intervention; Pt/Caregiver Education, patient and/or caregiver education; Robot, robotic toy/therapy doll; Sensory Correct, sensory correction; Social, socialization interventions; Staff Consult, staff consultation team.

Atchison K, Hoang PM, Merrikh D, et al. Treatments for depression for older adults living in long term care: A systematic review and network meta analysis. J Am Med Dir Assoc. 2025;26:105435

What is a Network Meta Analysis

Statistical technique to simultaneously compare multiple interventions via both direct and indirect evidence

Node size & edge thickness = number of comparisons

Depression Treatments in LTC

- Network meta-analysis of 31 medication & non-pharmacologic treatments across 147 RCTs from 28 countries
  - All LTC residents aged 70-89, baseline MMSE scores 6-27
  - Included residents with MDD, non-specific depressive symptoms or neither
  - Most common outcome measures → GDS, Cornell Depression Scale (CSDD), Beck Depression Inventory (BDI)

Pharmacologic	Non-pharmacologic
Antidepressants, analgesics, nutrient augmentation	Multicomponent, exercise, group reminiscence, art, social groups, horticulture, CBT, massage, light, robotic pet / doll, and more!

Atchison K, Hoang PM, Merrikh D, et al. Treatments for depression for older adults living in long term care: A systematic review and network meta analysis. J Am Med Dir Assoc. 2025;26:105435

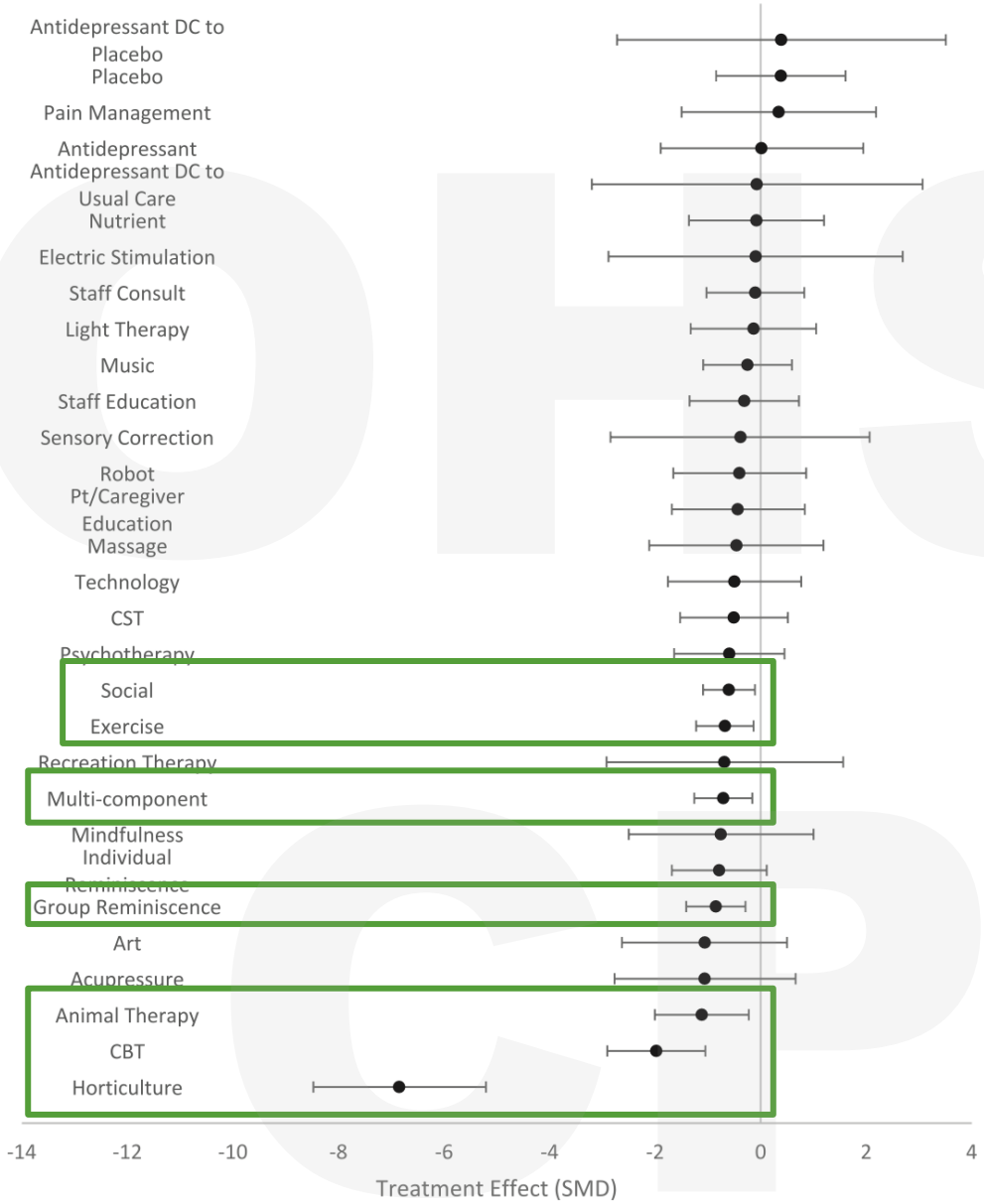


Fig. 4. Forest plot of relative treatment effect vs usual care SMD median value. Negative values indicate improved outcomes relative to usual care. Error bars represent 95% CrI. Antidepressant DC to Placebo, antidepressant discontinuation to placebo; Antidepressant DC to Usual Care, antidepressant discontinuation to usual care; CBT, cognitive behavioral therapy; CST, cognitive stimulation therapy; Multicomponent, multicomponent nonpharmacologic intervention; Pt/Caregiver Education, patient and/or caregiver education; Robot, robotic toy/doll therapy doll; Sensory Correct, sensory correction; Social, socialization interventions; Staff Consult, staff consultation team.

Results

Regular planting & gardening had 99% odds of imparting the most impact to residents

Atchison K, Hoang PM, Merrikh D, et al. Treatments for depression for older adults living in long term care: A systematic review and network meta analysis. J Am Med Dir Assoc. 2025;26:105435

2022 Flashback

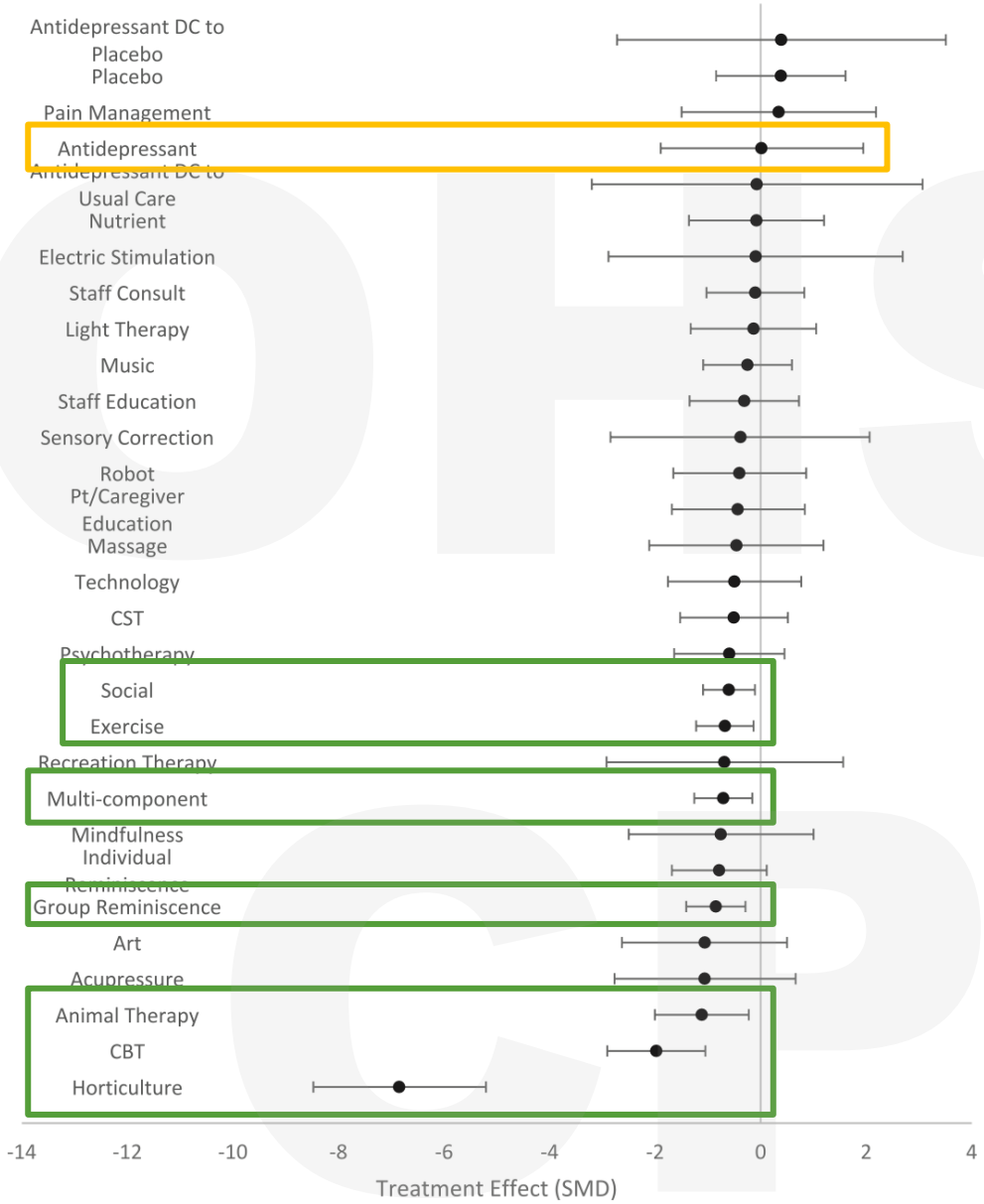
NMA of drug and non-drug interventions for depressive symptoms in dementia

Table 2 | Efficacy of interventions for reducing symptoms of depression in people with dementia without a diagnosis of major depressive disorder

		Network meta-analysis			Meta-analysis†		
Intervention v usual care	Studies in pairwise treatment comparison (participant*)	SMD (95% CrI)	SMD re-expressed as MD on CSDD (95% CrI)	Probability of MD >0.4 SDs‡ (%)	SMD (95% CrI)	SMD re-expressed as MD on CSDD (95% CrI)	Probability of MD >0.4 SDs‡ (%)
Animal therapy[44]	1 (23)	−0.45 (−1.24 to 0.39)	−2.30 (−6.34 to 1.97)	55.6	−0.94 (−1.76 to −0.16)	−4.82 (−8.97 to −0.8)	90.9
Cognitive stimulation[34 45-56]	13 (805)	−0.57 (−0.85 to −0.30)	−2.93 (−4.35 to −1.52)	90.4	−0.67 (−1.02 to −0.33)	−3.42 (−5.19 to −1.69)	94.1
Cognitive stimulation+cholinesterase inhibitor	-	−2.23 (−3.60 to −0.77)	−11.39 (−18.38 to −3.93)	99.3	-	-	-
Exercise[57-62]	6 (581)	−0.27 (−0.58 to 0.03)	−1.39 (−2.94 to 0.14)	21.9	−0.47 (−0.89 to −0.07)	−2.42 (−4.55 to −0.34)	63.9
Exercise+social interaction+cognitive stimulation[63]	1 (14)	−2.43 (−3.73 to −1.05)	−12.37 (−19.01 to −5.36)	99.8	−2.40 (−3.41 to −1.43)	−12.28 (−17.41 to −7.30)	100
Massage and touch therapy[64-66]	3 (219)	−1.77 (−2.41 to −1.15)	−9.03 (−12.28 to −5.88)	100	−1.77 (−2.42 to −1.12)	−9.05 (−12.35 to −5.70)	100
Multidisciplinary care[67-73]	7 (838)	−0.39 (−0.74 to −0.03)	−1.98 (−3.80 to −0.16)	49.1	−0.48 (−0.90 to −0.05)	−2.44 (−4.62 to −0.23)	63.9
Occupational therapy[74-78]	5 (497)	−0.51 (−0.92 to −0.08)	−2.59 (−4.70 to −0.40)	69.0	−0.5 (−1.02 to 0.02)	−2.56 (−5.20 to 0.12)	64.8
Psychotherapy+reminiscence therapy+environmental modification[79]	1 (51)	−1.00 (−2.05 to 0.08)	−5.12 (−10.46 to 0.40)	87.2	−0.99 (−1.53 to −0.45)	−5.06 (−7.82 to −2.28)	98.4
Reminiscence therapy[14 22 80-91]	14 (1163)	−0.45 (−0.72 to −0.18)	−2.30 (−3.68 to −0.93)	65.8	−0.50 (−0.81 to −0.21)	−2.57 (−4.12 to −1.06)	75.1

CSDD=Cornell scale for depression in dementia; MA=pairwise meta-analysis; MD=mean difference; CrI=credible interval; SMD=standardised mean difference.
*Sample sizes adjusted for clustering effect, when appropriate.
†Pairwise meta-analysis.
‡Minimum clinically important difference estimated to be 2.0 at 0.4 standard deviations (SDs) and 2.5 at 0.5 SDs.

Watt JA, Goodarzi Z, Veroniki AA, et al. Comparative efficacy of interventions for reducing symptoms of depression in people with dementia: systematic review and network meta-analysis. BMJ. 2021;372:n532



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Results

No significant effect of medications, including individual control studies where meds are swapped to placebo

Atchison K, Hoang PM, Merrikh D, et al. Treatments for depression for older adults living in long term care: A systematic review and network meta analysis. J Am Med Dir Assoc. 2025;26:105435

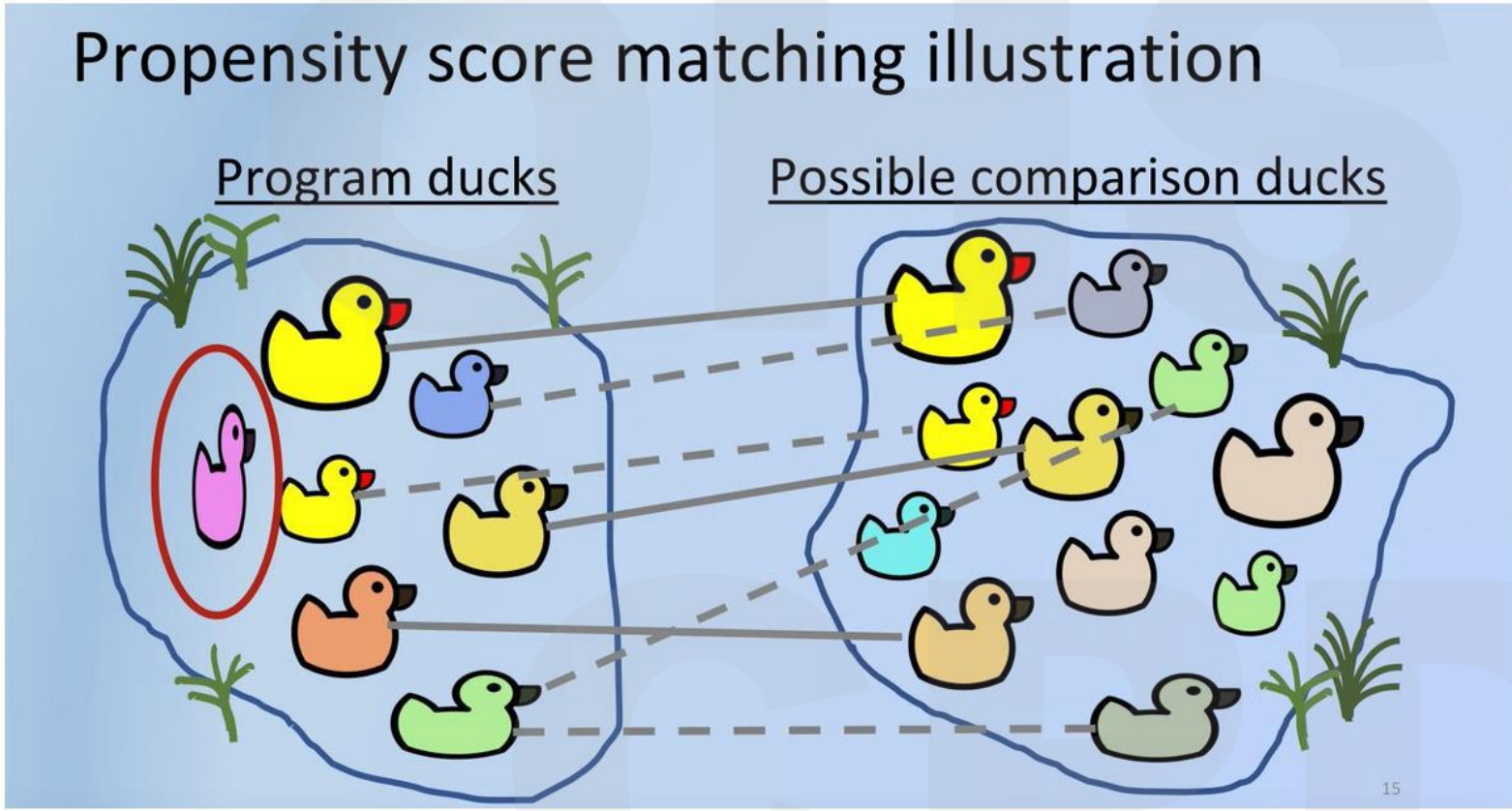
Anti-Depressant Pitfalls

- Australian retrospective cohort study of 5409 LTC residents newly starting mirtazapine vs sertraline within 60 days of LTC entry
  - Registry data from ROSA (Registry of Senior Australians) from 2015-2019, median age 84

Exposure	Outcomes
LTC residents newly prescribed mirtazapine or sertraline within 60 days of moving to LTC	All cause mortality, falls & fractures, CV events, dementia & delirium related hospitalizations while treated with the agent of interest

- Enrollees censored at med discontinuation (avg ~150-160 days), exit from LTC or death
- Adjusted for individual, pharmaceutical, system / facility covariates and propensity risk score matched

Hughes GA, Inacio MC, Rowett D, et al. Risk of adverse outcomes associated with mirtazapine compared to sertraline use among older people living in long term care facilities. Age Ageing. 2025;54:afaf074



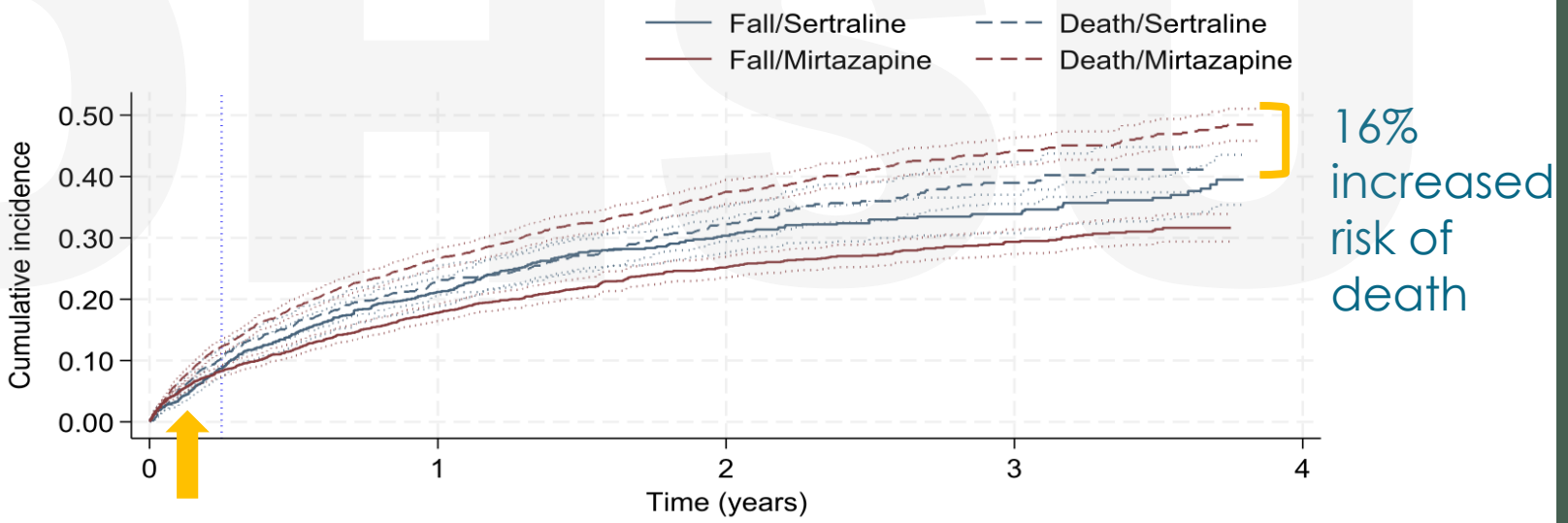
What is Propensity Score Matching?

Aka. IPTW

Statistical method for identifying the closest "pair" and minimizing more bias than regular adjustment

Often a sign of a well done observational study

All Cause Mortality, Falls & Fractures



16% increased risk of death

1st 90 days – sertraline safer than mirtazapine
After 90 days – mirtazapine safer than sertraline

Number at risk:					
Overall	5228	1831	796	300	90
Sertraline	1517	535	238	91	24
Mirtazapine	3711	1296	557	209	66

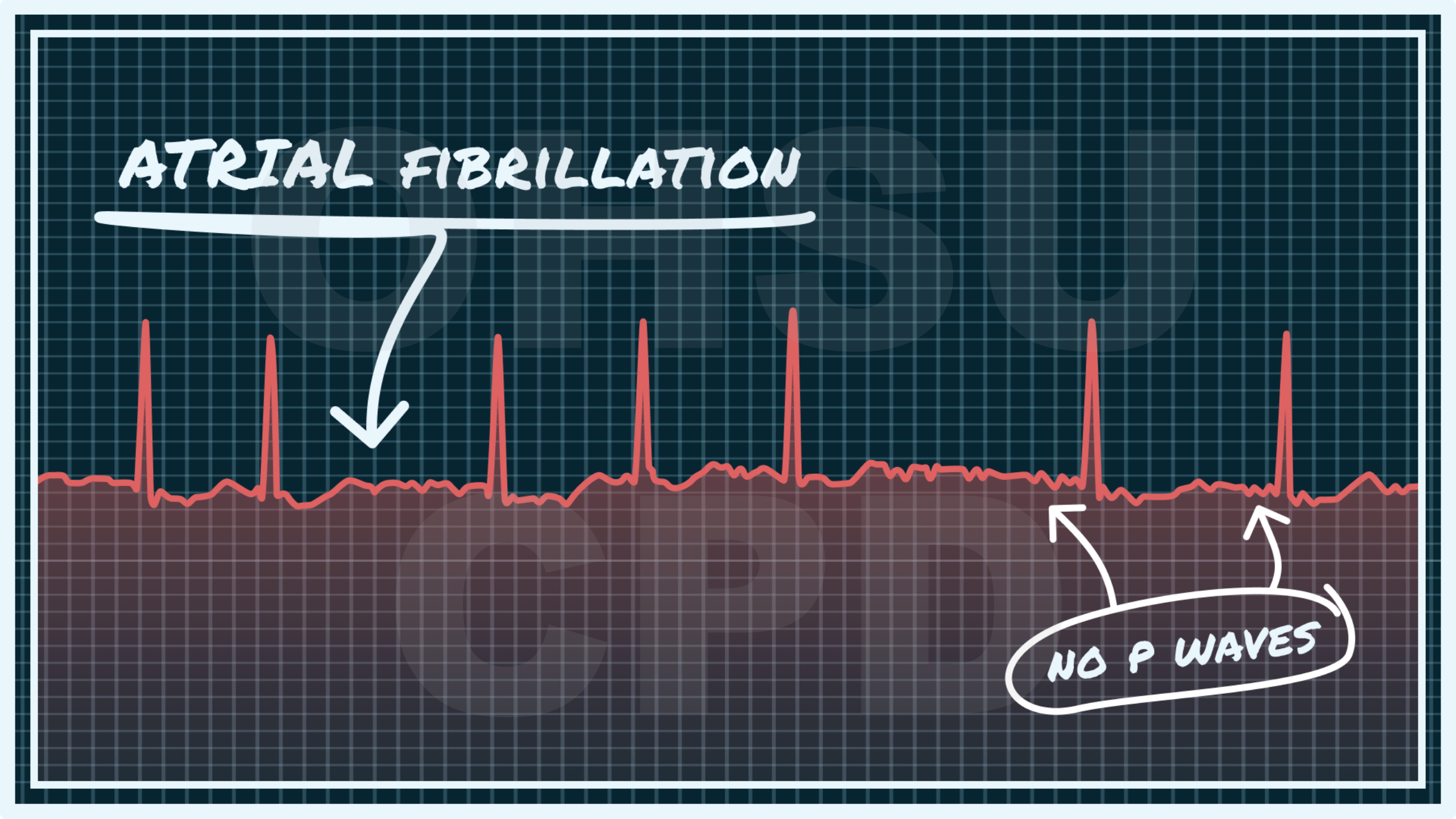
Figure 2. Cumulative incidence of falls and competing risk of death among the weighted cohorts, by antidepressant type. Cumulative incidence of falls, and death as the competing event, is plotted. Dotted vertical line at 90 days for time-varying effects. Plot truncated to 4 years due to low numbers at risk thereafter. Numbers at risk of the IPTW cohort are listed by exposure group at bottom of plot.

Hughes GA, Inacio MC, Rowett D, et al. Risk of adverse outcomes associated with mirtazapine compared to sertraline use among older people living in long term care facilities. Age Ageing. 2025;54:afaf074

Takeaways

- Gardening for everyone!
  - There are multiple non-medication interventions with more efficacy than antidepressants
  - Combining interventions is also more effective than many on their own
- LTC residents with and without dementia benefit from various non-pharmacologic interventions for depression and depressive symptoms

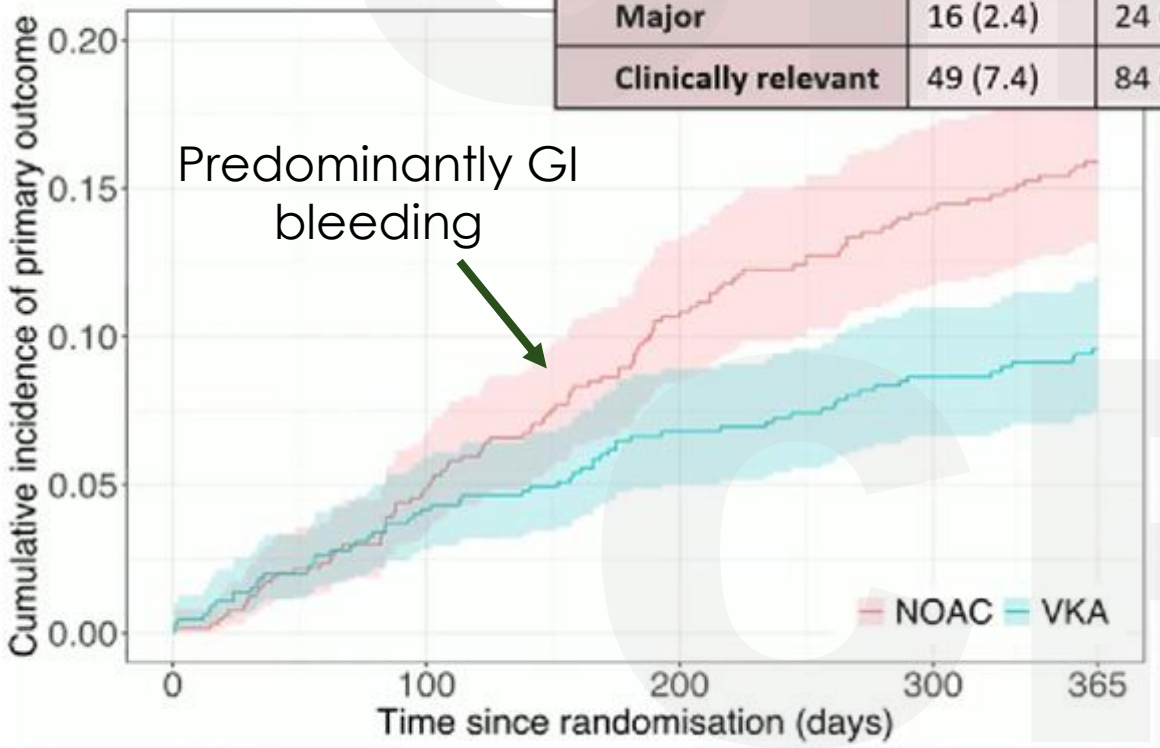
- Mirtazapine increases risk of death throughout course of treatment but sertraline carries a higher risk of falls & fractures after 3 months of use
  - Another reminder to de-prescribe, even in LTC


ATRIAL FIBRILLATION
NO P WAVES

A Bit of Flashback …

Primary outcome

	VKA-arm no. (%)	NOAC-arm no. (%)	Hazard ratio (95% CI)	P-value
Bleeding	62 (9.4)	101 (15.3)	**1.69 (1.23-2.32)**	**0.00112**
Major	16 (2.4)	24 (3.6)	1.52 (0.81-2.87)	
Clinically relevant	49 (7.4)	84 (12.7)	1.77 (1.24-2.52)	



54% of DOAC arm switched to rivaroxaban

ESC Congress 2023
Amsterdam & Online

FRAIL-AF RCT

2023 RCT from Netherlands

75+ with frailty randomized to continue warfarin or switch to DOAC

Warfarin or DOAC?

- Patient level meta-analysis of 5,913 frail enrollees in the original DOAC vs warfarin RCTs (COMBINE-AF database)
  - 3 inclusion criteria: age 75+, frail (as defined by Frailty Index), warfarin "experienced"
  - Secondary analysis including younger, non-frail, warfarin naïve patients from those same RCTs
  - Duration – 26.7 months

Efficacy Outcomes	Safety Outcomes
Stroke, systemic embolic events composite outcome All cause mortality, CV events, hemorrhagic stroke, ischemic stroke, embolic events	Major bleeding Fatal bleeding, any bleeding, ICH, GI bleeding

- Net clinical outcomes – composites of stroke/SEE/major bleed/death

Nicolau AM, Giugliano RP, Zimmerman A, et al. Outcomes in older patients after switching to a newer anticoagulant or remaining on warfarin. JACC. 2025;86(6):426-439

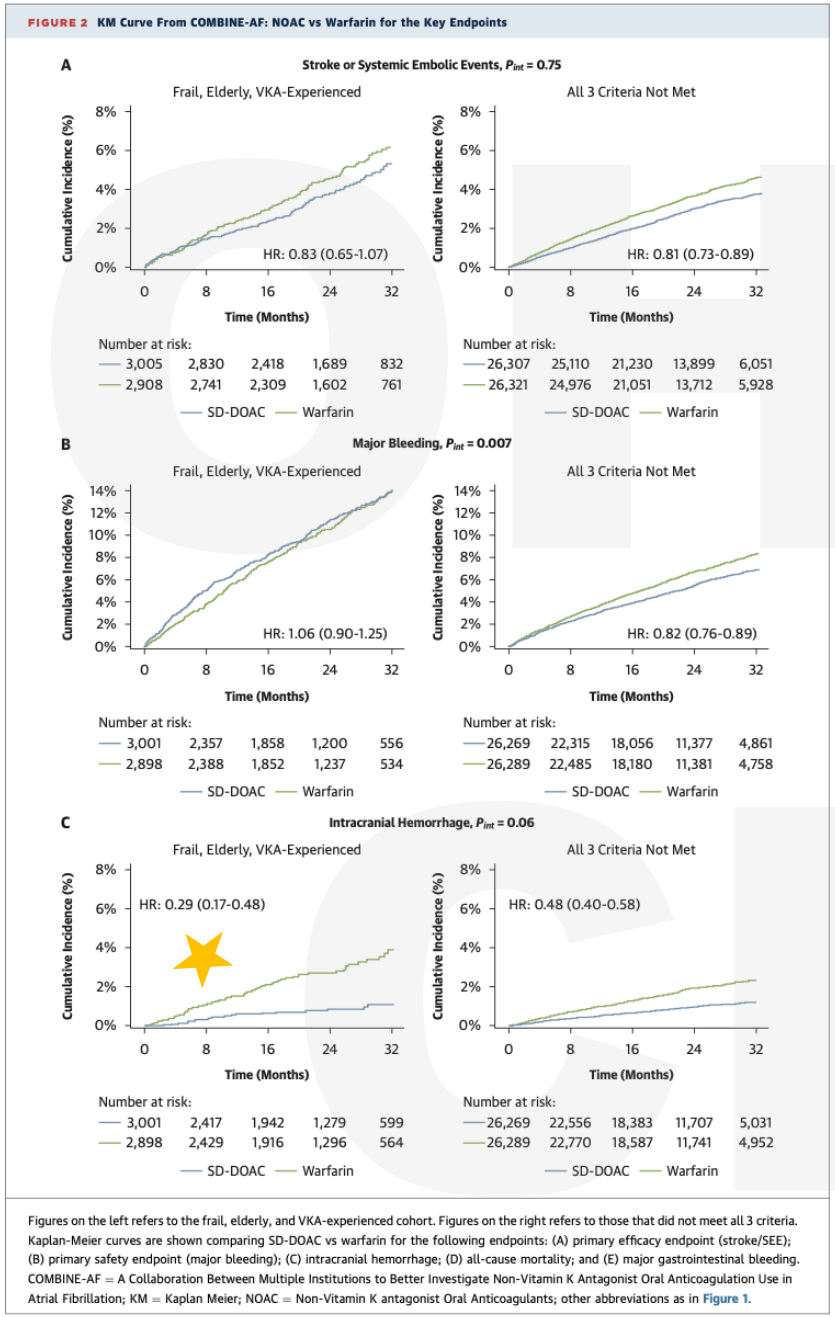
TABLE 1 Baseline Characteristics of the COMBINE-AF in Patients Who Were Frail, Elderly, and VKA-Experienced vs Those Who Were Not

	Frail, Elderly, and VKA-Experienced (N = 5,913)		All 3 Criteria Not Met (N = 52,721)	
	SD-DOAC (n = 3,005)	Warfarin (n = 2,908)	SD-DOAC (n = 26,357)	Warfarin (n = 26,364)
Age, y	79.8 ± 3.7	79.7 ± 3.7	69.4 ± 9.3	69.4 ± 9.2
Female	1,239 (41.2)	1,211 (41.6)	9,730 (36.9)	9,655 (36.6)
Paroxysmal AF	469 (15.6)	467 (16.1)	5,881 (22.3)	6,028 (22.9)
CCI score	2 (0-2)	2 (0-2)	1 (0-2)	1 (0-2)
Frailty index 18	7 (6-8)	7 (6-8)	5 (4-6)	5 (4-6)
Number of comedications	4 (3-5)	4 (3-5)	3 (2-4)	3 (2-4)
CHA_2DS_2-VASc score	5 (4-6)	5 (4-6)	4 (3-5)	4 (3-5)
Heart failure	1,563 (52)	1,462 (50.3)	12,170 (46.2)	12,165 (46.1)
Coronary artery disease	1,495 (49.8)	1,444 (49.7)	7,225 (27.4)	7,267 (27.6)
Hypertension	2,778 (92.4)	2,716 (93.4)	23,006 (87.3)	23,050 (87.4)
Diabetes	1,111 (37)	1,099 (37.8)	8,012 (30.4)	7,912 (30)
History GI bleeding	179 (7.5)	177 (7.5)	697 (3.3)	734 (3.5)
History non-GI bleeding	349 (14.5)	333 (14.1)	1,412 (6.8)	1,372 (6.6)
Prior stroke or TIA	950 (31.6)	958 (32.9)	7,519 (28.5)	7,519 (28.5)
Body mass index, kg/m^2	28.8 ± 5.3	28.8 ± 5.4	29.2 ± 5.9	29.2 ± 6
Creatinine clearance, mL/min	56.9 ± 18.8	56.8 ± 18.5	77.8 ± 31.2	77.7 ± 36.7
Concurrent platelet inhibitor use	775 (25.8)	761 (26.2)	9,101 (34.5)	9,137 (34.7)
TTR (% for each patient)	Not applicable	68.6 (56.6-78.4)	Not applicable	64.7 (50.5-75.8)
Direct acting oral anticoagulant		Not applicable		Not applicable
Rivaroxaban	554 (18.4)		6,577 (25)	
Apixaban	849 (28.3)		8,271 (31.4)	
Edoxaban	997 (33.2)		6,038 (22.9)	
Dabigatran	605 (20.1)		5,471 (20.8)	

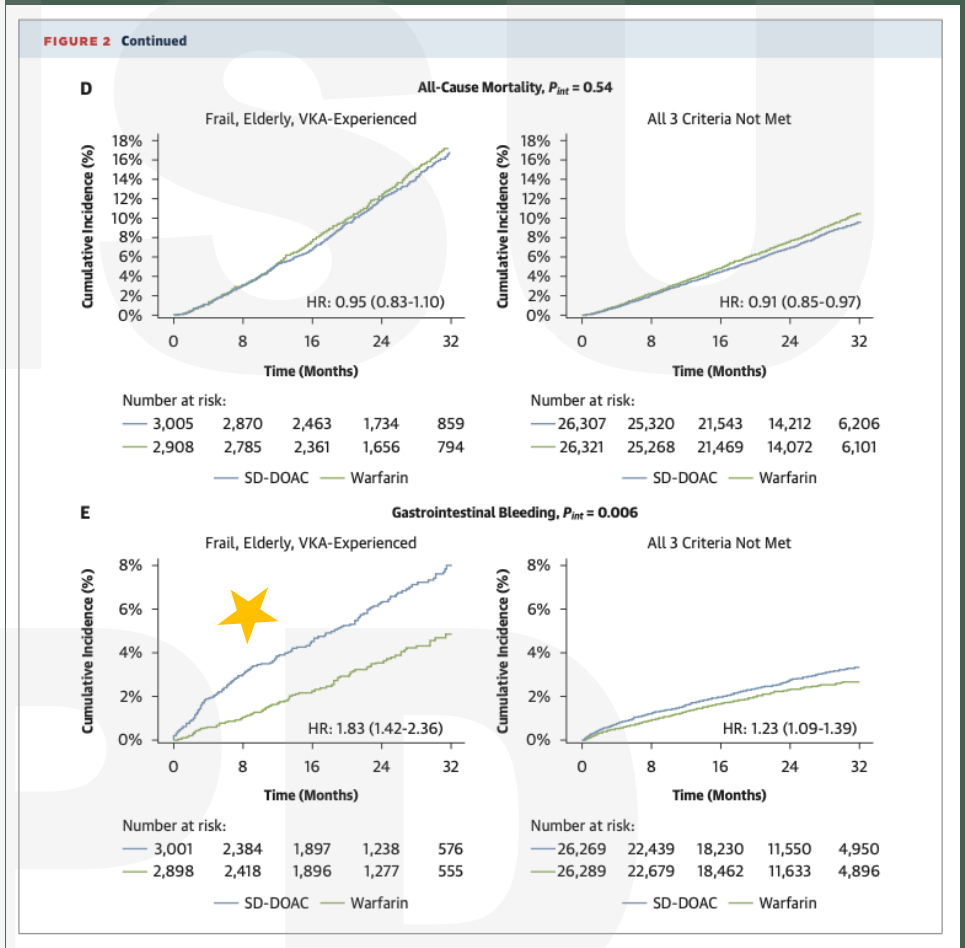
Values are mean ± SD, n (%), or median (Q1-Q3). Frail considered frailty index (FI)-18 ≥6 or FI >0.33 (see Methods section for details). Elderly considered age ≥75 years. All *P* values comparing baselines characteristics with standard-dose direct oral anticoagulant (SD-DOAC) vs warfarin within the same group were nonsignificant ($P > 0.05$). Creatinine clearance calculated with Cockcroft Gault formula in mL/min. All baseline characteristics differed significantly ($P < 0.05$) between those who were frail, elderly, and vitamin K antagonist (VKA)-experienced vs those who were not.

AF = atrial fibrillation; CCI = Charlson Comorbidity Index; GI = gastrointestinal; TIA = transient ischemic attack; TTR = time in therapeutic range.

Demographics



Figures on the left refers to the frail, elderly, and VKA-experienced cohort. Figures on the right refers to those that did not meet all 3 criteria. Kaplan-Meier curves are shown comparing SD-DOAC vs warfarin for the following endpoints: (A) primary efficacy endpoint (stroke/SEE); (B) primary safety endpoint (major bleeding); (C) intracranial hemorrhage; (D) all-cause mortality; and (E) major gastrointestinal bleeding. COMBINE-AF = A Collaboration Between Multiple Institutions to Better Investigate Non-Vitamin K Antagonist Oral Anticoagulation Use in Atrial Fibrillation; KM = Kaplan Meier; NOAC = Non-Vitamin K antagonist Oral Anticoagulants; other abbreviations as in Figure 1.



NCOs – no difference between DOAC & warfarin

Sensitivity Analyses

TABLE 4 Comparison of Outcomes in the FRAIL-AF Trial With the Frail, Elderly, VKA-Experienced Population in COMBINE-AF

	FRAIL-AF (n = 1,330)	COMBINE-AF: All SD-DOAC (n = 5,913)[a]	COMBINE-AF: Same DOAC Mix as FRAIL-AF (n = 2,046)	COMBINE-AF: Apixaban and Edoxaban Only (n = 3,637)	COMBINE-AF: Age ≥80 y (n = 2,755)	COMBINE-AF: Age ≥85 y (n = 760)
Stroke/SEE[b]	1.26 (0.60-2.61)	0.83 (0.65-1.07)	0.92 (0.71-1.18)	0.92 (0.67-1.27)	0.96 (0.68-1.35)	0.90 (0.49-1.67)
All stroke	1.30 (0.59-2.87)	0.84 (0.65-1.08)	0.91 (0.69-1.17)	0.95 (0.68-1.32)	0.89 (0.62-1.28)	0.85 (0.44-1.64)
Ischemic stroke	NA	1.04 (0.78-1.40)	1.17 (0.85-1.56)	1.14 (0.78-1.66)	1.14 (0.75-1.73)	1.24 (0.56-2.73)
Hemorrhagic stroke	NA	0.37 (0.19-0.70)	0.35 (0.15-0.64)	0.48 (0.22-1.07)	0.35 (0.15-0.83)	0.38 (0.07-1.99)
Major bleeding	1.52 (0.81-2.87)	1.06 (0.90-1.25)	1.21 (1.00-1.44)	0.83 (0.67-1.04)	0.99 (0.78-1.26)	0.96 (0.61-1.49)
ICH	NA	0.29 (0.17-0.48)	0.48 (0.32-0.73)	0.16 (0.07-0.36)	0.37 (0.20-0.71)	0.48 (0.15-1.57)
GI bleeding	NA	1.83 (1.42-2.36)	2.16 (1.68-2.72)	1.36 (0.97-1.91)	1.72 (1.19-2.47)	1.99 (1.02-3.91)
Major or CRNM	1.69 (1.23-2.32)	1.00 (0.90-1.12)	1.15 (1.04-1.26)	0.84 (0.74-0.97)	0.99 (0.85-1.16)	1.03 (0.77-1.39)
CRNM	1.77 (1.24-2.52)	0.97 (0.85-1.11)	1.13 (1.02-1.25)	0.85 (0.72-1.00)	0.97 (0.80-1.18)	1.02 (0.70-1.49)
Mortality	0.96 (0.64-1.45)	0.95 (0.83-1.10)	0.88 (0.75-1.01)	0.94 (0.78-1.13)	0.98 (0.81-1.19)	0.87 (0.63-1.21)
Primary NCO	NA	1.01 (0.91-1.13)	1.03 (0.92-1.16)	0.94 (0.82-1.08)	1.02 (0.88-1.18)	0.91 (0.69-1.18)
Secondary NCO	NA	0.91 (0.80-1.03)	0.90 (0.79-1.03)	0.88 (0.75-1.04)	0.97 (0.81-1.15)	0.90 (0.66-1.22)

Values are HR (95% CI). [a]n for COMBINE-AF: same DOAC mix as FRAIL-AF based on 1,000 samples with same mix of DOACs. [b]Stroke/SEE for FRAIL-AF trial was a composite of ischemic stroke, transient ischemic attack, and peripheral arterial thromboembolism. Primary NCO: stroke/SEE, major bleeding, or death; secondary net clinical outcome: stroke/SEE, intracranial hemorrhage (ICH), or death.

NA = not available; other abbreviations as in Tables 1 and 2.

Takeaways

- Rotating from warfarin to a DOAC is safer and just as effective
  - May start to show up in guidelines soon
- More support for preferential use of apixaban, edoxaban

"There's a blood bank, not a brain bank"
Dr Tom DeLoughery


Hearing loss, communication ability and social isolation

Hearing Aids & Communication

- Secondary analysis of ACHIEVE RCT
  - 2023 RCT of 977 community dwelling older adults (ages 70-84) with intact cognition and untreated hearing loss randomized to hearing aid intervention or health education control

Control	Intervention
Chronic disease, disability prevention counseling & education (10 Keys to Healthy Aging Program) every 6 months with an individual health educator	Audiology assessment, provision of hearing aids + adaptive devices like connections for TVs & smartphones with counseling on use and troubleshooting every 6 months

- Outcomes → HHIE (Hearing Handicap Inventory for the Elderly) score

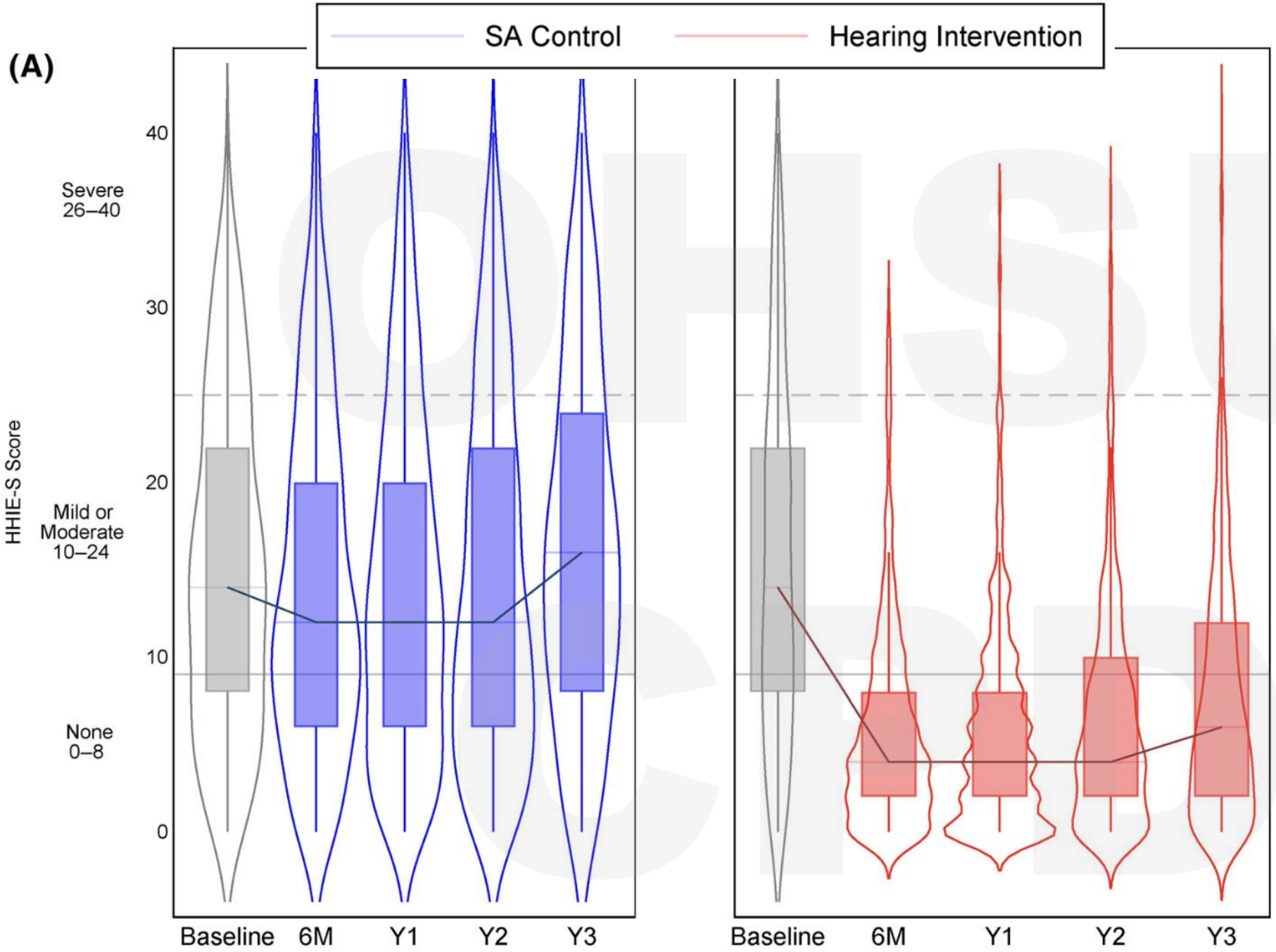
Sanchez VA, Arnold ML, Garcia Morales EE, et al. Effect of hearing intervention on communicative function: A secondary analysis of the ACHIEVE RCT. J Am Geriatr Soc. 2024;72:3784-3799

	Item	Yes (4 pts)	Sometimes (2 pts)	No (0 pts)
E	Does a hearing problem cause you to feel embarrassed when meeting new people?	_____	_____	_____
E	Does a hearing problem cause you to feel frustrated when talking to members of your family?	_____	_____	_____
S	Do you have difficulty hearing when someone speaks in a whisper?	_____	_____	_____
E	Do you feel handicapped by a hearing problem?	_____	_____	_____
S	Does a hearing problem cause you difficulty when visiting friends, relatives, or neighbors?	_____	_____	_____
S	Does a hearing problem cause you to attend religious services less often than you would like?	_____	_____	_____
E	Does a hearing problem cause you to have arguments with family members?	_____	_____	_____
S	Does a hearing problem cause you difficulty when listening to TV or radio?	_____	_____	_____
E	Do you feel that any difficulty with your hearing limits or hampers your personal or social life?	_____	_____	_____
S	Does a hearing problem cause you difficulty when in a restaurant with relatives or friends?	_____	_____	_____
	TOTAL SCORE = _____ (sum of the points assigned to each of the items)			

HHIE

Functional hearing inventory focused on actual communication ability, social consequences

Higher score = greater impairment

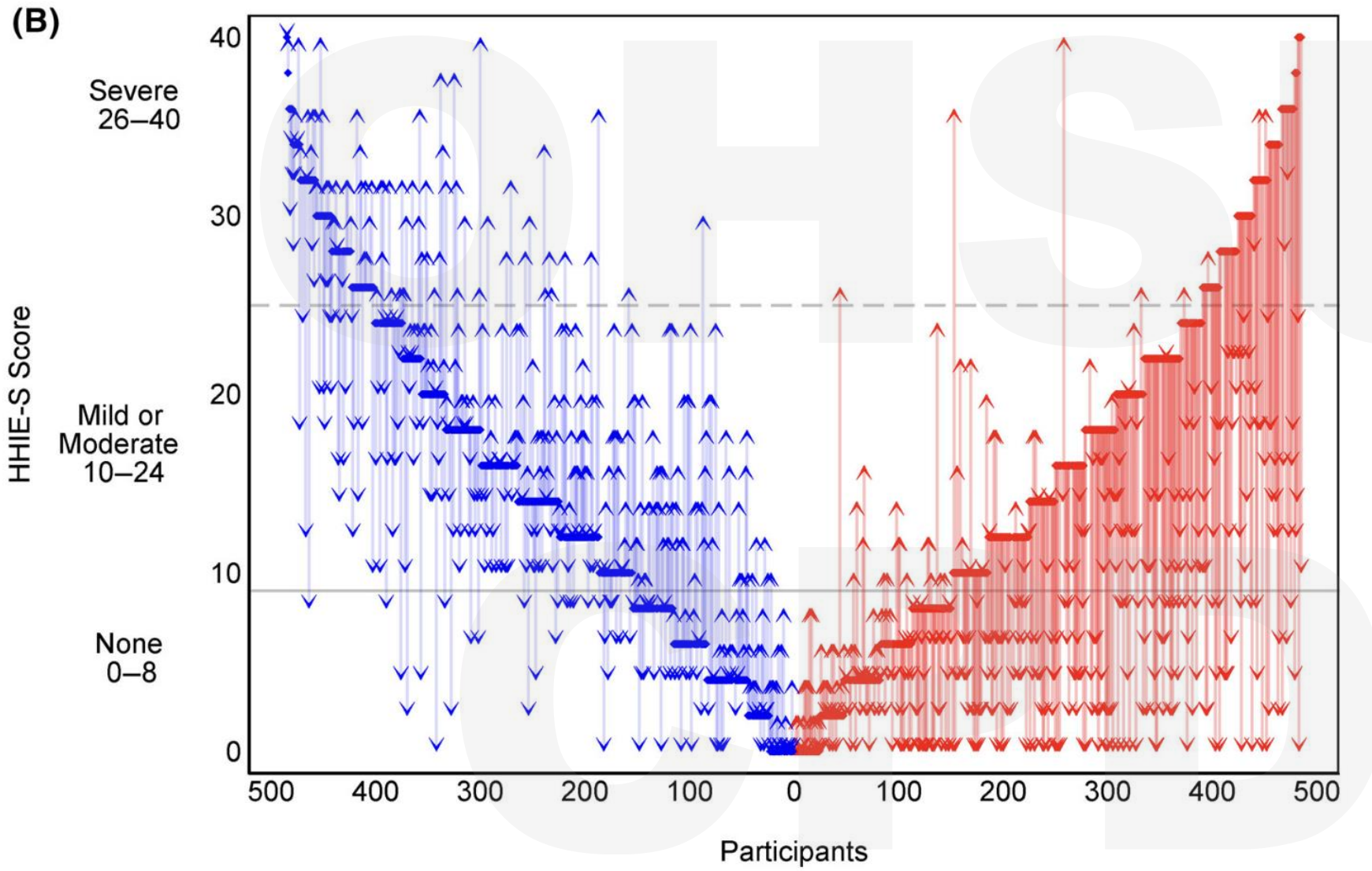


Results

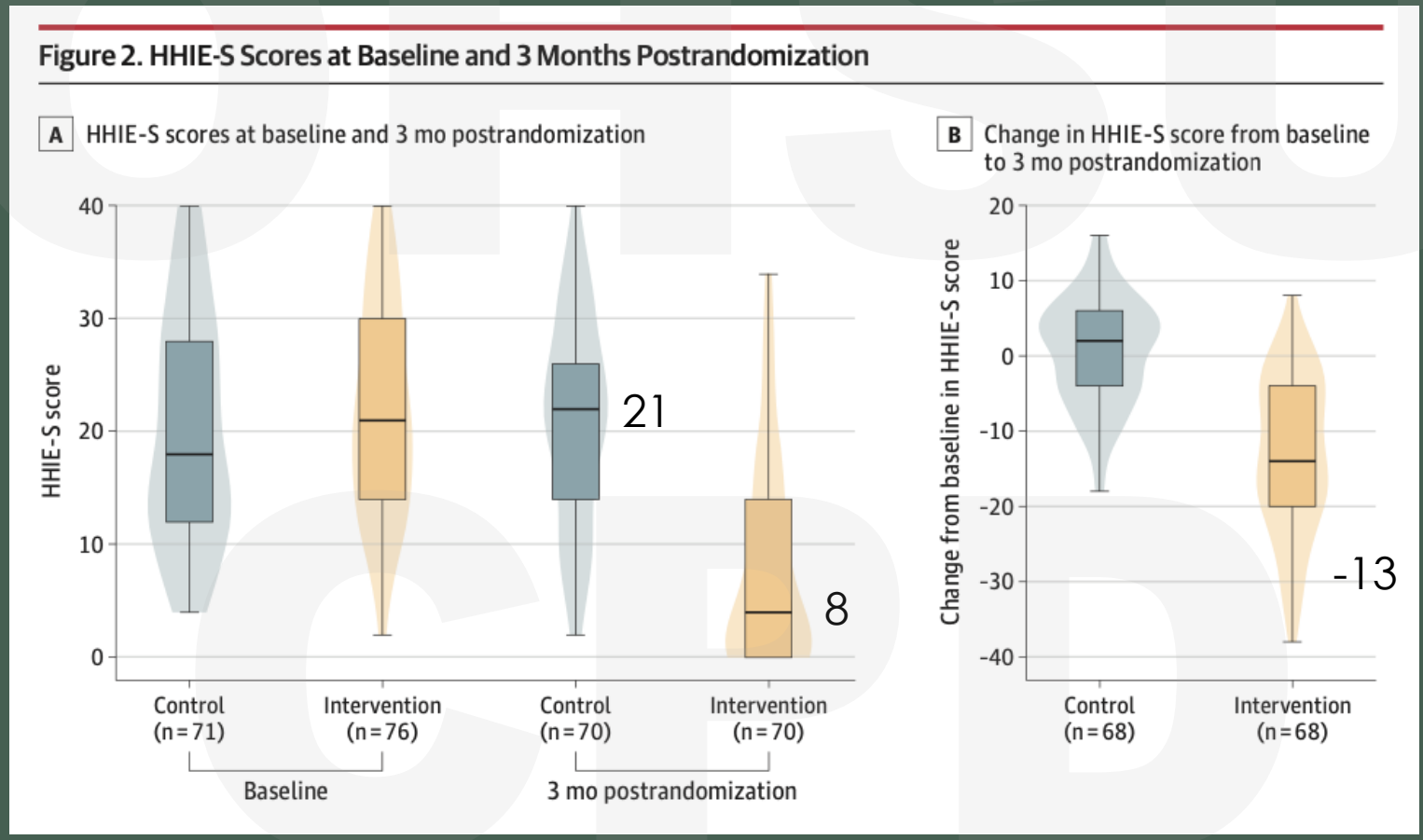
Most of the bell curve improved to "no impairment" range

Improvements sustained for the 3 year follow up with minimal "booster" supports

Individual HHIE Score Changes



I've seen these before …



Nieman CL, Betz J, Garcia Morales EE, et al. Effect of a community health worker-delivered personal sound amplification device on self-perceived communication function in older adults with hearing loss. JAMA 2022;328(23):2324-2333

Hearing Aids, Social Contacts & Loneliness

- Another secondary analysis of ACHIEVE RCT focused on social function and loneliness

- Outcomes → Size, diversity & embeddedness of social network (Cohen Social Network Index), loneliness (UCLA Loneliness Scale)

OHSU CPD

6. How many close friends do you have? (meaning people that you feel at ease with, can talk to about private matters, and can call on for help)

____0 ____1 ____2 ____3 ____4 ____5 ____6 ____7 or more

6a. How many of these friends do you see or talk to at least once every 2 weeks?

____0 ____1 ____2 ____3 ____4 ____5 ____6 ____7 or more

7. Do you belong to a church, temple, or other religious group? (If not, check 'no' and skip to question 8.)

_____ no _____ yes

7a. How many members of your church or religious group do you talk to at least once every 2 weeks? (This includes at group meetings and services.)

____0 ____1 ____2 ____3 ____4 ____5 ____6 ____7 or more

8. Do you attend any classes (school, university, technical training, or adult education) on a regular basis? (If not, check 'no' and skip to question 9.)

_____ no _____ yes

8a. How many fellow students or teachers do you talk to at least once every 2 weeks? (This includes at class meetings.)

____0 ____1 ____2 ____3 ____4 ____5 ____6 ____7 or more

9. Are you currently employed either full or part-time? (If not, check 'no' and skip to question 10.)

____ (0) no _____ (1) yes, self-employed _____ (2) yes, employed by others

9a. How many people do you supervise?

____0 ____1 ____2 ____3 ____4 ____5 ____6 ____7 or more

9b. How many people at work (other than those you supervise) do you talk to at least once every 2 weeks?

____0 ____1 ____2 ____3 ____4 ____5 ____6 ____7 or more

Cohen Social Network Index

12 question inventory

Use combination of Q&As to determine:

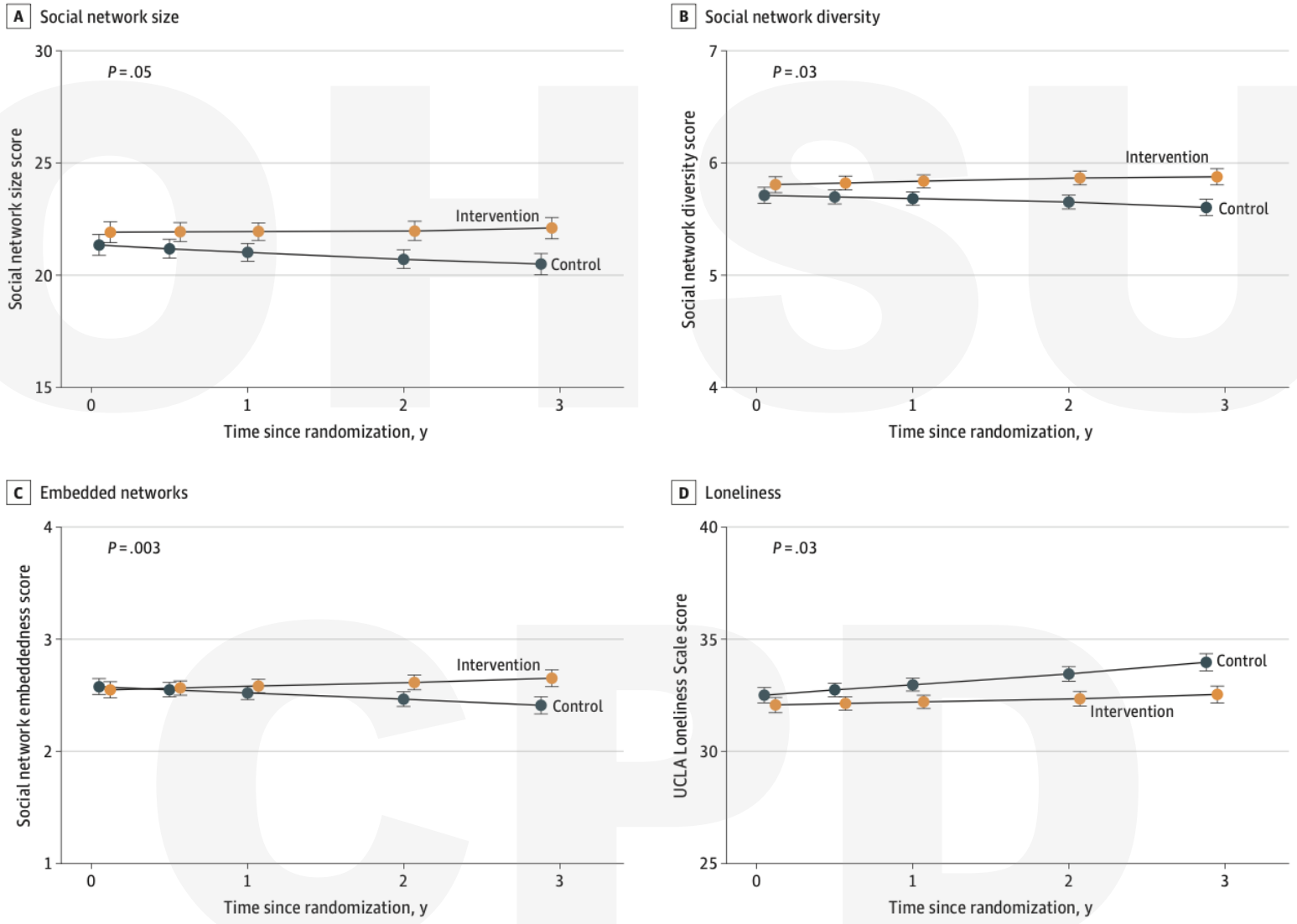
- # of high contact roles (0-12)
- # of people in social network (0-84)
- # of embedded networks (0-8)

Wait … what about the COVID years?

Specific adjustment called Time Varying Covariates

Predictor adjustment to account for Within-Individual changes that can influence the outcome

Figure 2. Trajectories and Pointwise Estimates of Social Network Characteristics and Loneliness by Randomly Assigned Treatment Among the Total Cohort of 977 Participants



Y-axis values are social network characteristics and loneliness scores that were developed using the linear mixed-effect model. Parameter estimates and 95% CIs (indicated by whiskers) were calculated from a linear mixed-effects model that adjusted for baseline age, sex, education, field site, better-ear pure-tone average, speech-in-noise understanding, hearing handicap inventory for the elderly score, marital status, living alone, global cognition, Center for Epidemiologic Studies depression scale, antidepressant use, and whether the participant was part of a recruited spousal pair. Multiple imputation by chained equations was used to impute missing covariates.

Takeaways

- Hearing aids for patients with hearing loss, with basic Audiologic support, improves ability to communicate with others, maintain social connectedness and slow the development of loneliness

- Consider the potential return on investment related to hearing loss, loneliness and dementia …

OHSU CPD

Alzheimer's, anxiety and amyloid antibodies

Anxiety: A Risk for Dementia?

- 15 year Prospective cohort study of 2132 cognitively healthy, community dwelling adults ages 55-85 in Australia
- Study participants assessed at enrollment and every 5 years for total of 3 assessments
  - Kessler Psychological Distress Scale (K10) – assessment for anxiety & depression

Exposure		
Chronic Anxiety	Resolved Anxiety	New Anxiety during Follow Up
(+) K10 at assessments 1 and 2	(+) K10 only at assessment 1	(+) K10 only at assessment 2
Outcome		
All cause dementia diagnosis as determined by ICD-10 F00-F03, G30 Stratified by age of exposure to anxiety		

Khaing K, Dolja-Gore X, Nair BR, et al. The effect of anxiety on all cause dementia: A longitudinal analysis from the Hunter Community Study. J Am Geriatr Soc. 2024;72:3327-3334

TABLE 2 Association between anxiety groups and incidence all-cause dementia.

	Model 1			Model 2			Model 3		
	HR	95% CI	*p*-value	HR	95% CI	p-value	HR	95% CI	*p*-value
No anxiety ($N = 1418$)	1			1			1		
Chronic anxiety ($N = 202$)	2.57	1.27–5.20	0.01	2.80	1.35–5.72	0.01	2.94	1.42–6.11	0.004
Resolved anxiety ($N = 247$)	1.02	0.41–2.55	0.96	1.06	0.40–2.81	0.90	1.10	0.41–2.92	0.85
New anxiety at follow-up ($N = 85$)	3.20	1.37–7.43	0.01	3.20	1.40–7.45	0.01	2.80	1.16–6.78	0.02

Note: Model 1—adjusted age, gender. Model 2—adjusted Model 1+ depression. Model 3—excluded participant developed dementia within 5 years from baseline, adjusted Model 2 variables.

TABLE 3 Association between anxiety groups of different age groups and incidence all-cause dementia.

	Model 2 Chronic anxiety			Model 2 Resolved anxiety			Model 2 New anxiety		
Within group comparison	HR	95% CI	*p*-value	HR	95% CI	*p*-value	HR	95% CI	*p*-value
Age 60–70 years $N = 925$	4.58	1.12–18.81	0.03	0.92	0.11–7.67	0.94	7.21	1.86–28.02	0.004
Age 71–80 years $N = 447$	2.42	0.90–7.25	0.08	1.03	0.22–4.88	0.97	0.98	0.13–7.16	1.0
Age 80+ $N = 91$	0.84	0.24–2.94	0.80	0.56	0.10–5.24	0.61	2.52	0.52–12.32	0.25

Note: Model 1—adjusted age, gender. Model 2—adjusted Model 1+ depression.

Mean time to diagnosis = 10 years

"Perhaps the biggest question is: What does anxiety in the years before the diagnosis of all cause dementia represent? Is it a prodrome of the neurodegenerative disease … or is it a true risk factor that is mechanistically linked with the development or hastening of neurodegeneration or cognitive or behavioral changes? A cohort study such as this can establish an association but cannot disambiguate prodrome from risk factor."

- Dr Jordan Karp and Dr Eric Lenze

Karp JF and Lenze EJ. Anxiety and aging: A marker of brain changes and potential treatment target to promote brain health. J Am Geriatr Soc. 2024;72:3294-3295

Amyloid Antibodies

- Meta analysis of 18,826 patients from 16 Phase 3 placebo controlled RCTs of 6 different amyloid antibodies
  - All included studies had arms with 200+ participants
  - Average follow up: 76-80 weeks
  - Mix of subjects with early AD and mild-moderate AD

- Primary outcomes → CDR-SB (Clinical Dementia Rating – Sum of Boxes), ADAS-cog
- Safety outcomes → rates of ARIA-E, ARIA-H, cerebral macro-hemorrhages, persistent headache

Tonegawa-Kuji R, Hou Y, Hu B, et al. Efficacy and safety of passive immunotherapies targeting amyloid beta in Alzheimer's disease: a systematic review and meta analysis. PLoS Med. 2025;22(3):e1004568

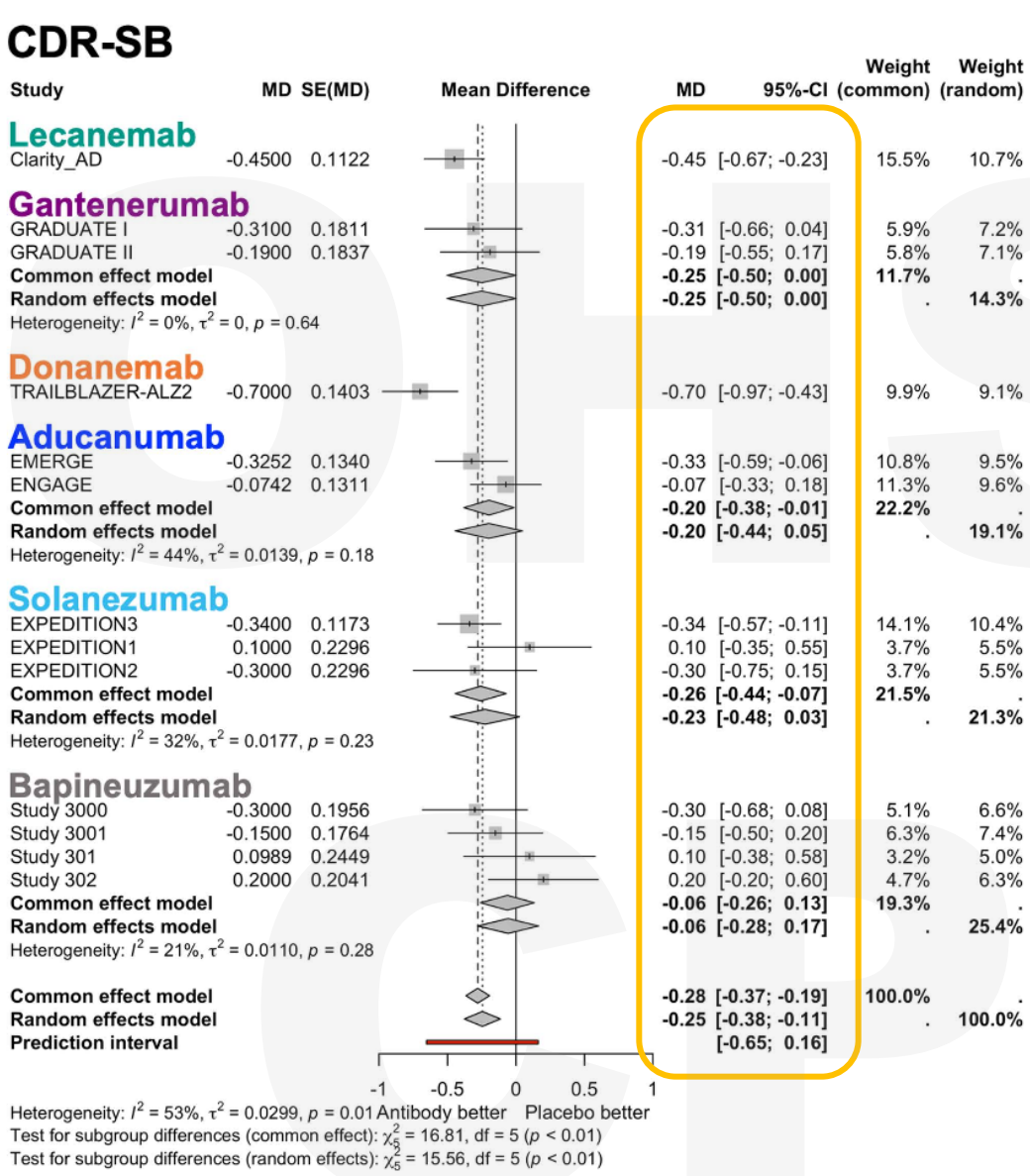


Fig 2. Forest plots for change in Clinical Dementia Rating-Sum of Boxes (CDR-SB). The summary measure of CDR-SB was expressed as Mean difference (MD), and the standard errors (SE) and 95% confidence interval (CI) are presented. The overall results are shown for both the random effects Model and the common effect model, along with the results of the subgroup analysis by antibody. Forest plots show the effect size and its 95% CI, with the size of the gray squares representing the weight of each study. I^2 value, τ^2 value calculated using the Mandel–Paule algorithm, and the P-value from Cochran's Q test for heterogeneity are provided. The χ^2 value, degrees of freedom (df), and P-values from the test for subgroup differences are also reported.

NNT = 8

Results

MCID for CDR-SB = 0.5 pts

None reach this effect size individually or in the pooled result

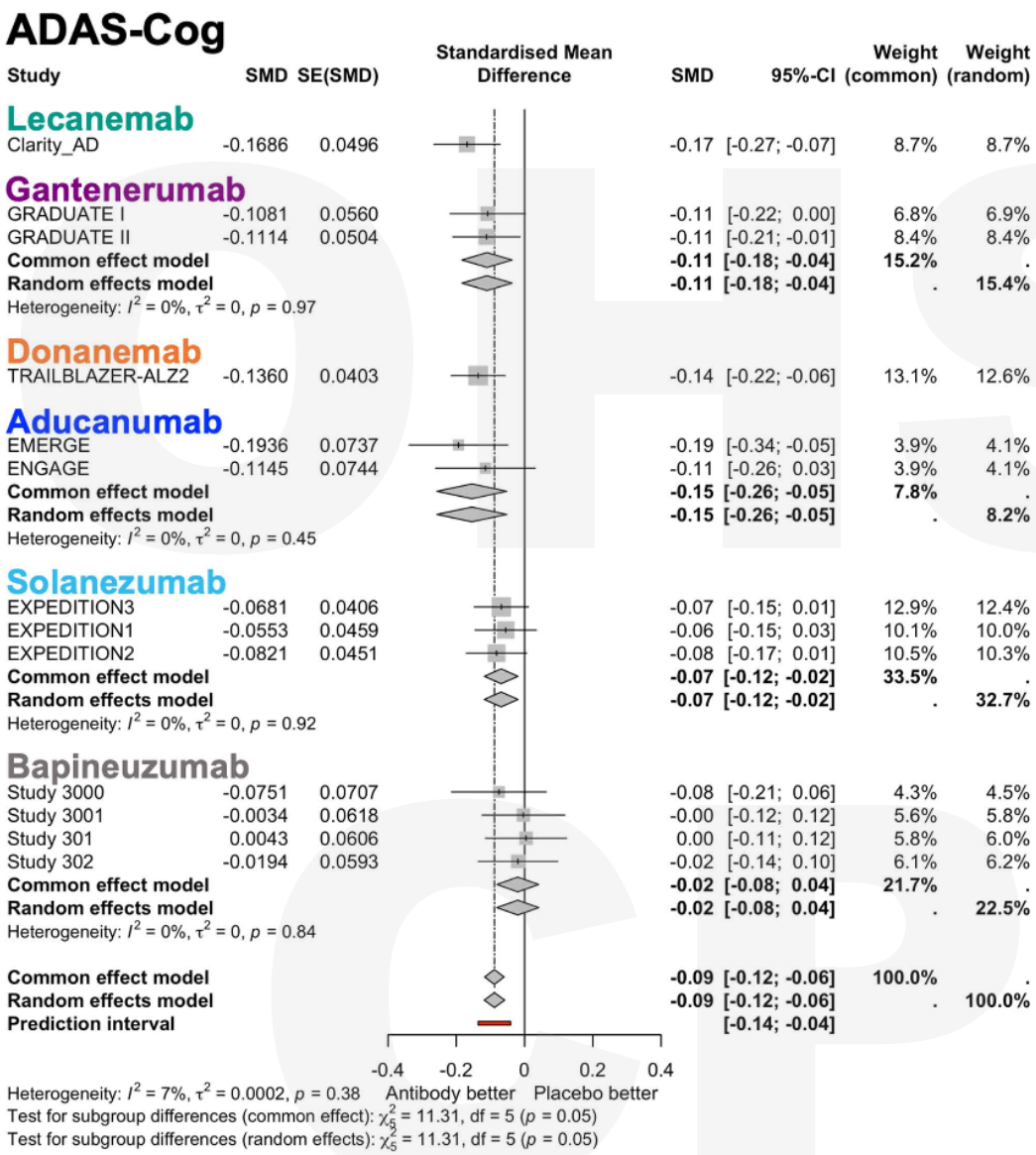


Fig 3. Forest plots for change in Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog). The summary measure of ADAS-Cog was expressed as standardized mean difference (SMD), with the standard errors (SE) and 95% confidence interval (CI) presented for each study. The overall results are shown for both the random effects model and the common effect model, along with the results of the subgroup analysis by antibody. Forest plots show the effect size and its 95% CI, with the size of the gray squares representing the weight of each study. I^2 value, τ^2 value calculated using the Mandel–paule algorithm, and the P value from Cochran's Q test for heterogeneity are provided. The χ^2 value, degrees of freedom (df), and P-values from the test for subgroup differences are also reported.

NNT = 4

Results

MCID for ADAS-cog = 2-3 pts

None reach this effect size individually or the pooled result

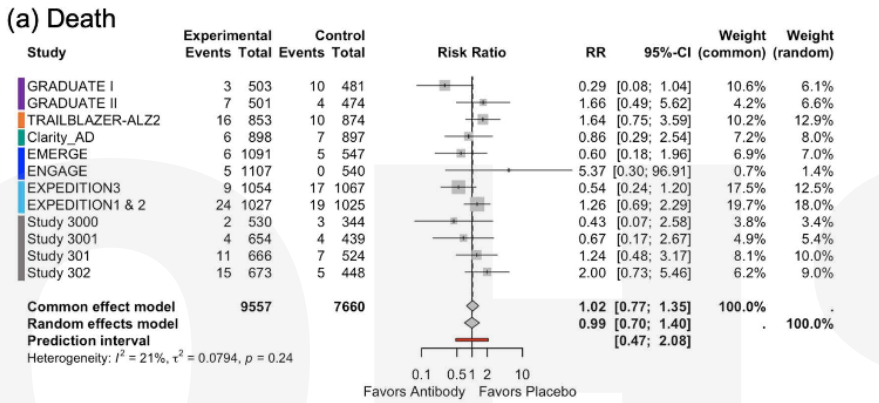


Fig 4. Forest plots for safety outcomes. (**a**) Death, (**b**)ARIA-E, and (**c**) ARIA-H. A number of events in experimental and control groups, risk ratio (RR), and its 95% confidence interval (CI), and weights are shown. The overall results are shown for both the random effects model and the common effect model. Forest plots show the effect size and its 95% CI, with the size of the gray squares representing the weight of each study. I^2 value, τ^2 value calculated using the Mandel–Paule

NNH = 7

NNH = 10

Safety Outcomes

No difference in cerebral macro-hemorrhages

1.2x increased risk of headaches

- More common in those with mild-mod AD

What's Coming …

JAMA | Original Investigation

Blood Biomarkers to Detect Alzheimer Disease in Primary Care and Secondary Care

Operating characteristics of blood tau and amyloid levels in primary care and specialty memory care practices in Sweden

Palmqvist S, Tideman P, Mattsson-Calgren N, et al. JAMA. 2024;332(15):1245-1257

Takeaways

- There is a relationship between persistent anxiety (especially in mid-life) or new anxiety in later life and development of dementia
  - Prodrome or risk factor clarification needs more study
  - Akin to the relationship between depression and dementia

- Minimal to no clinical improvement from mAbs is counter-balanced by significant risks of CNS side effects, even in a large pooled meta-analysis


ODDS &
ENDS

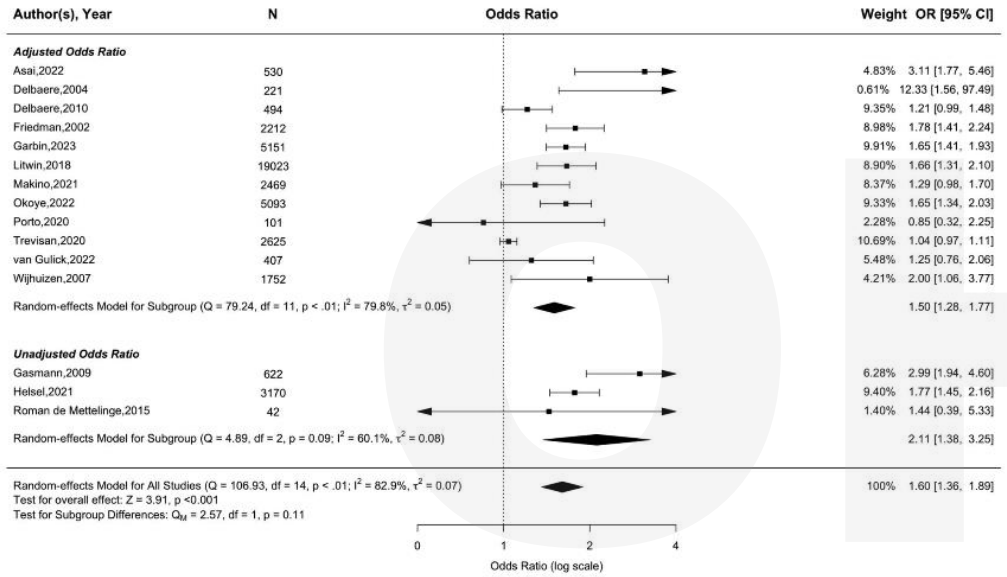


Figure 4. Forest plot of the association between single-item measures of concerns about falling and future any-type falls.

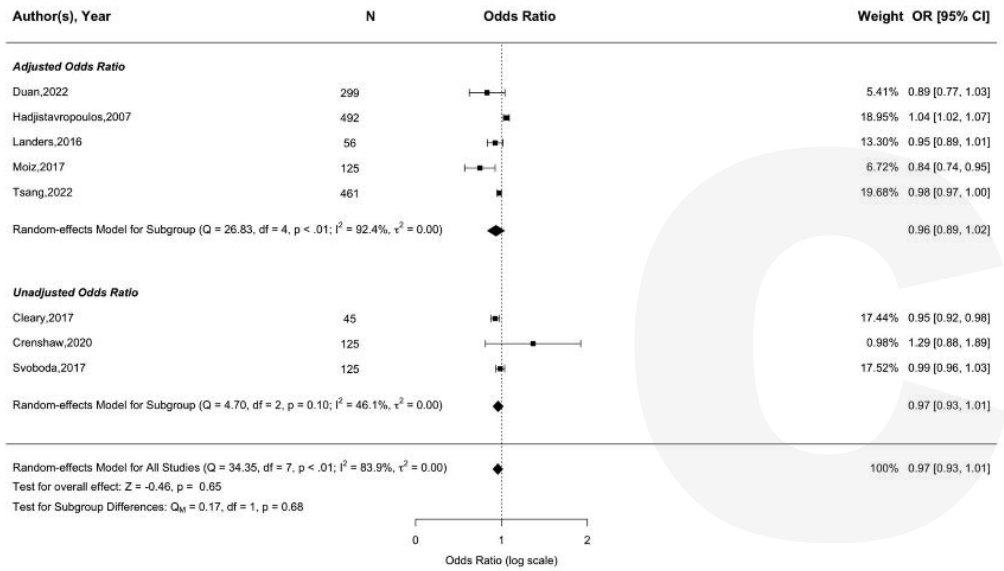
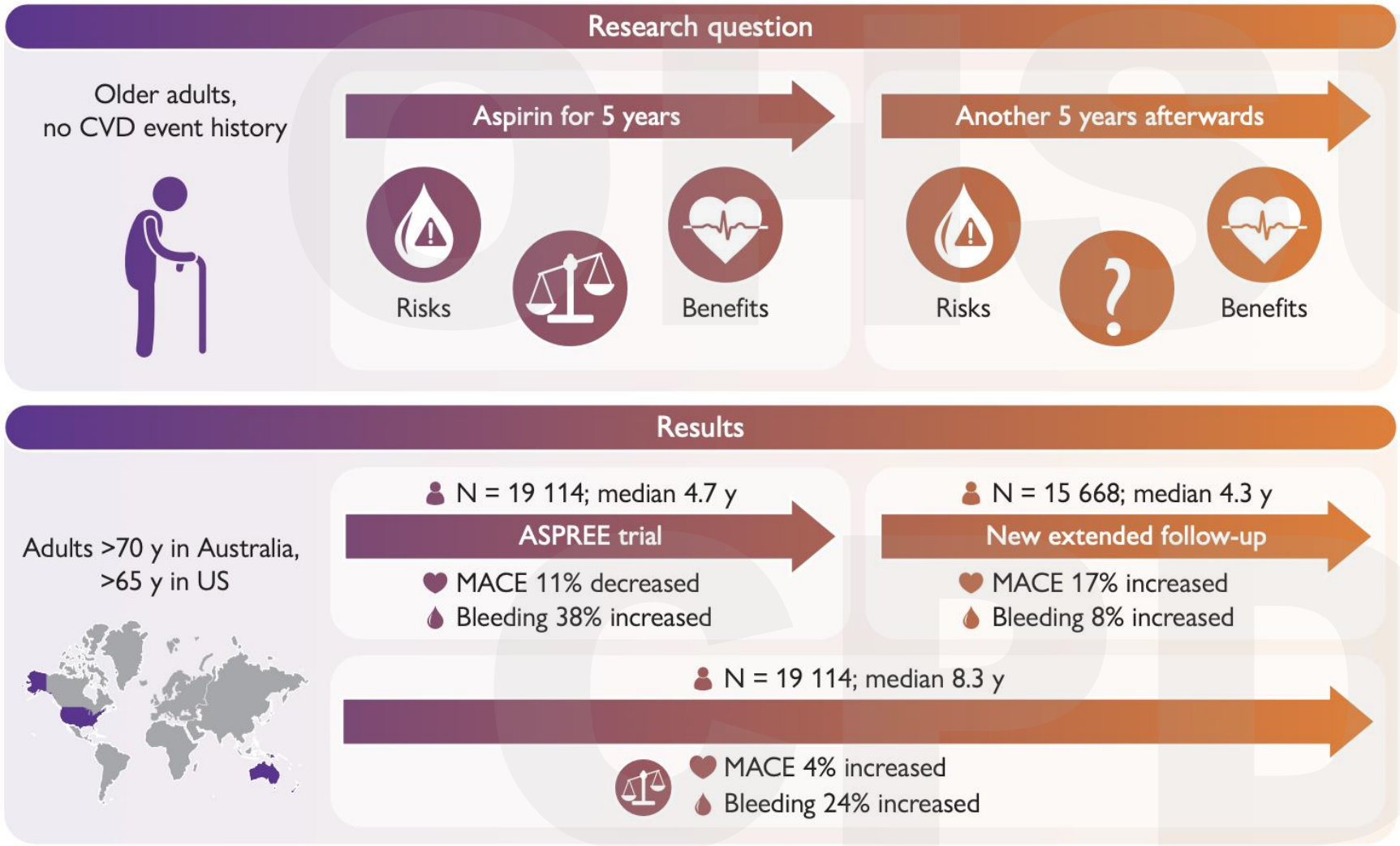


Figure 5. Forest plot of the association between balance confidence (Activities-Specific Balance Confidence Scale [ABC]) and future any-type falls.

Fear of falling but NOT balance confidence is associated with increased risk of falling

Ellmers TJ, Ventre JP, Freiberger E, et al. Does concern about falling predict future falls in older adults?: A systematic review and meta analysis. Age Ageing. 2025;54:afaf089



ASPREE Follow Up

Persistent increased risk of bleeding and increased risk of MACE in 4 years post-trial follow up

- ITT analytic approach

Wolfe R, Broder JC, Zhou Z, et al. Aspirin, cardiovascular events, and major bleeding in older adults: Extended follow up of the ASPREE trial. Eur Heart J. 2025; https://doi.org/10.1093/eurheartj/ehaf514

Table. Strategies to Prevent Recurrent Urinary Tract Infection in Women Older Than 65 Years in Outpatient Settings

Agent	Common formulations/regimens	Special considerations for older women
Antibiotic strategies		
Nitrofurantoin	Daily oral dose of 50-100 mg at bedtime or 100 mg as a single dose within 2 h of sexual intercourse[a]	Risk of pulmonary toxic effects, hepatic toxic effects, and peripheral neuropathy if CrCl is <30 mL/min; conversely, lower rates of drug-drug interactions and antimicrobial resistance[b]
Trimethoprim-sulfamethoxazole	Daily or 3 times weekly oral dose of 40 mg or 200 mg (half a single-strength tablet), respectively[a]	Greater risk of kidney failure or hyperkalemia if CrCl is <30 mL/min or with concomitant angiotensin-converting enzyme inhibitor or receptor antagonist therapy; multiple potential other drug-drug interactions[b]
Trimethoprim	Daily dose of oral 100 mg[a]	50% Dose decrease indicated if CrCl is 15-30 mL/min; multiple potential drug-drug interactions[b]
Fosfomycin	Oral dose of 3 g every 7-10 d (or every 3 d to maintain higher blood levels)[a]	Dose adjustment indicated if CrCl is <50 mL/min; lower rates of drug-drug interactions than some alternatives[b]
Cephalexin	Daily oral dose of 125-250 mg or 250 mg as a single dose just before or after sexual intercourse[a]	Potential for increased kidney toxic effects with concomitant loop diuretic therapy; drug-drug interactions with metformin and warfarin[b]
Antibiotic-sparing strategies		
Vaginal estrogen	No evidence to compare formulations; past trials with estradiol cream (0.5 mg nightly for 2 weeks then twice weekly) or estradiol ring (2 mg, every 3 mo)[a]	In contrast to vaginal estrogen, no evidence of reduced UTI risk with oral estrogen, which has other long-term health risks in older women
Methenamine	Oral methenamine hippurate, 1 g, tablet twice daily[a]	Evidence of noninferiority based on trials in women of all ages (only 0.49 more episodes per year with methenamine vs nitrofurantoin),[8] but no age-specific data
Cranberry supplements	No single definitive regimen—past trials reporting benefit with juice, tablets, or powder[a]	Relative risk of 0.74 in a meta-analysis of trials of women of all ages,[9] but unclear benefit in the subgroup of older adults in long-term care
Hydration	A trial reporting benefit with 1.5 L water over daily intake, but other solutions possible	Hydration with water preferable to electrolyte beverages in older women with conditions worsened by salt load; diuretics may be held in acute UTI

Abbreviations: CrCl, creatinine clearance; UTI, urinary tract infection.

[a] Past trials limited to 6 to 12 months for antibiotic prophylaxis, 8 to 9 months for vaginal estrogen, 12 months for methenamine, and 12 months for cranberry products.

[b] Consider evaluation of antimicrobial sensitivities through urine culture before initiating antibiotics in clinically stable older patients.

Huang AJ, Grady D and Mody L. Recurrent urinary tract infection in older outpatient women. JAMA IM. 2024;184(8):971-972

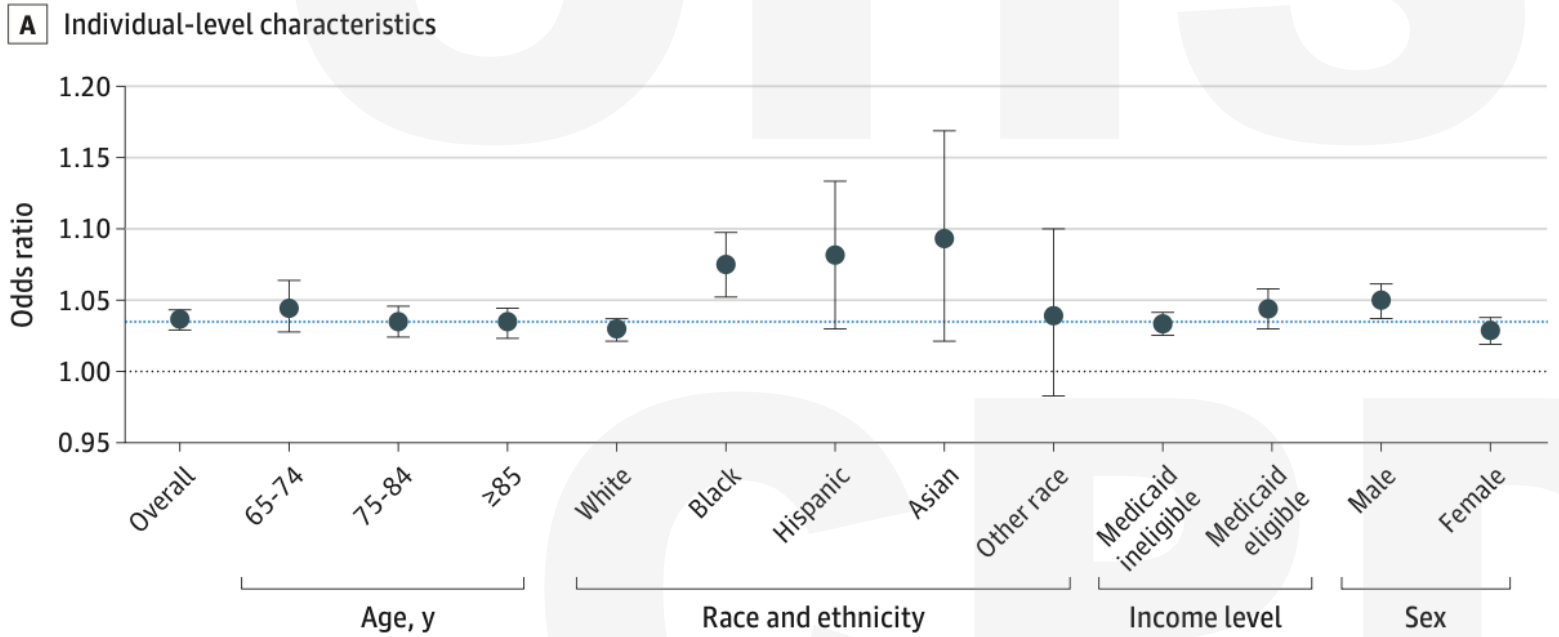
Table 2. Cumulative Odds Ratios of Hospitalization With Alzheimer Disease and Related Dementias After 1 to 4 Days of Sustained Exposure to Extreme Heat, 2000 to 2018[a]

Days of sustained exposure[b]	Percentiles of the Climate-Specific Heat Index distribution[c]		
	90th vs 50th	95th vs 50th	99th vs 50th
Nationwide (all climates combined)			
1	1.014 (1.010-1.018)[c]	1.015 (1.010-1.021)[c]	1.017 (1.011-1.023)[c]
2	1.022 (1.017-1.026)[c]	1.025 (1.020-1.030)[c]	1.027 (1.021-1.034)[c]
3	1.025 (1.020-1.030)[c]	1.030 (1.024-1.035)[c]	1.033 (1.027-1.040)[c]
4	1.026 (1.021-1.031)[c]	1.031 (1.025-1.037)[c]	1.036 (1.029-1.043)[c]
Temperate climates PNW			
1	1.016 (1.011-1.020)[c]	1.018 (1.012-1.024)[c]	1.020 (1.013-1.027)[c]
2	1.024 (1.017-1.030)[c]	1.028 (1.020-1.036)[c]	1.031 (1.022-1.040)[c]
3	1.026 (1.020-1.033)[c]	1.031 (1.023-1.040)[c]	1.035 (1.026-1.045)[c]
4	1.026 (1.019-1.034)[c]	1.032 (1.023-1.040)[c]	1.036 (1.026-1.046)[c]

Dose-response relationship between consecutive days of heat exposure and hospitalization risk for those with ADRD

Delaney SW, Stegmuller A, Mork D, et al. Extreme heat and hospitalization among older persons with Alzheimer's disease and related dementias. JAMA IM. 2025;185(4):412-421

Figure 3. Odds Ratios (ORs) of Hospitalization With Alzheimer Disease and Related Dementias (ADRD) After Sustained Exposure to 4 Days of Extreme Heat, by Population Subgroup



ADRD patients of color may be at even greater risk of heat related hospitalization

Delaney SW, Stegmuller A, Mork D, et al. Extreme heat and hospitalization among older persons with Alzheimer's disease and related dementias. JAMA IM. 2025;185(4):412-421