

# Top 10 Geriatric Medicine Papers 2022

University of British Columbia, McGill, University of Toronto  
Canadian Geriatrics Society ASM  
Saturday, April 15<sup>th</sup>, 2023

**Geriatric Medicine**



Medicine  
UNIVERSITY OF TORONTO

# Speakers

## Dr. Carolyn Pavoni

- MDCM, FRCPC
- PGY – 4, Geriatric Medicine, McGill University



## Dr. Natanya Russek

- MD
- PGY-3 IM, UBC
- Incoming PGY -4 GM, UBC



# Speakers

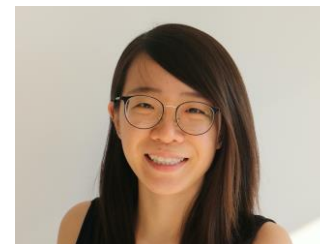
## Dr. Natasha Lane

- MD, PhD, MSc
- PGY – 3 IM, UBC
- Incoming PGY – 4 GM, U of T



## Dr. Carolyn Tan

- MD, MSc (QIPS), FRCPC
- PGY – 5, Geriatric Medicine, U of T
- Incoming Clinical Pharmacology and Toxicology Resident, U of T



# Speakers

## Dr. Dov Gandell

- Staff physician, Sunnybrook Hospital
- Assistant Professor, University of Toronto
- Program Director, Geriatric Medicine, University of Toronto



# Disclosures

- No conflicts of interest from any speaker to declare



# Article Selection

- CGS survey to members
- Drs. Gary Naglie, Sharon Marr, Arielle Berger, Janice Lee
- University of Toronto Geriatric Medicine Journal Club
- EvidenceAlerts
- Hand search major journals



ORIGINAL ARTICLE

# Lecanemab in Early Alzheimer's Disease

C.H. van Dyck, C.J. Swanson, P. Aisen, R.J. Bateman, C. Chen, M. Gee, M. Kanekiyo,  
D. Li, L. Reyderman, S. Cohen, L. Froelich, S. Katayama, M. Sabbagh, B. Vellas,  
D. Watson, S. Dhadda, M. Irizarry, L.D. Kramer, and T. Iwatsubo

N Engl J Med 2023; 388:9-21



# Background

- Amyloid  $\beta$  is implicated in the pathophysiology of Alzheimer's Disease (AD) and clearance of amyloid  $\beta$  is theorized to be disease modifying
- Lecanemab is a monoclonal antibody targeting soluble amyloid  $\beta$  protofibrils





# Objective

- Does Lecanemab 10mg/kg IV Q 2 weeks x 18 months reveal clinical benefit in mild cognitive impairment or mild dementia due to AD?

N Engl J Med 2023; 388:9-21



# Methods

CDR Sum of Boxes Range	Staging Category
0	Normal
0.5–4.0	Questionable cognitive impairment
0.5–2.5	Questionable impairment
3.0–4.0	Very mild dementia
4.5–9.0	Mild dementia
9.5–15.5	Moderate dementia
16.0–18.0	Severe dementia

N Engl J Med 2023; 388:9-21



# Methods

- **Secondary End Points**

- ADAS-cog14 (cognition)
- ADCOMS (behaviour)
- ADCS-MCI-ADL (function)

- **Biomarker sub-studies**

- PET Amyloid burden
- PET Tau burden
- CSF
- Plasma



# Results

- N = 1795
- 235 sites in North America, Europe, and Asia
- **Average participant**
  - 71, female 52%
  - White 77%
  - Mild cognitive impairment 60%
  - MMSE score 25.5
  - CDR-SB score 3.2
  - ApoE  $\epsilon$ 4 carriers 70%

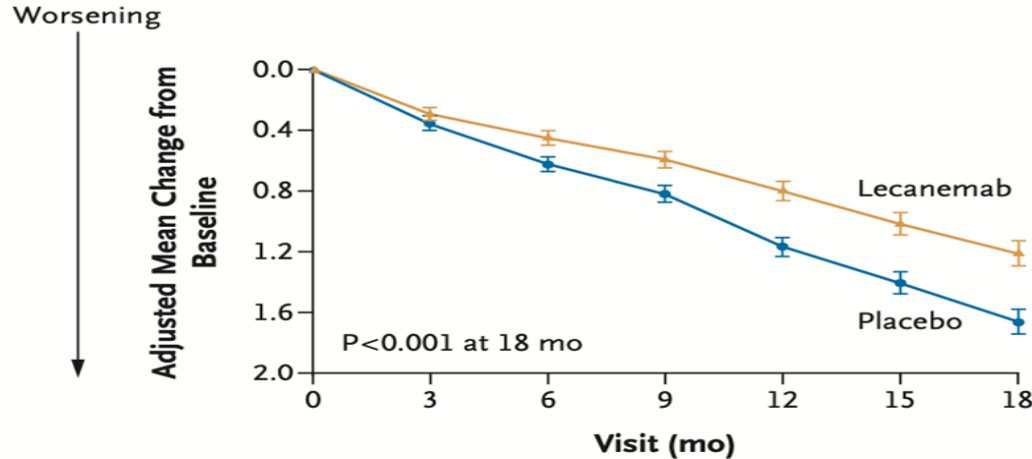
N Engl J Med 2023; 388:9-21



# Results

- CDR-SB Score

- Adjusted mean difference vs placebo **-0.45** (-0.67 to -0.23),  $p < 0.001$



### No. of Participants

Lecanemab	859	824	798	779	765	738	714
Placebo	875	849	828	813	779	767	757

N Engl J Med 2023; 388:9-21



# Results

- **Secondary End Points**

- Small improvements favouring Lecanemab

ADAS-cog14 (cognition):	<b>-1.44</b>	(-2.27 to -0.61), p<0.001
ADCOMS (behavior):	<b>-0.05</b>	(-0.07 to -0.03), p<0.001
ADCS-MCI-ADL (function):	<b>2.00</b>	(1.20 to 2.80), p<0.001

- Biomarkers favored Lecanemab

- PET amyloid/tau

- CSF

- Plasma



# Results

- **Safety**

- Adverse events (%)

	<b>Lecanemab</b>	<b>Placebo</b>
<b>Total</b>	44.7	22.0
<b>Trial discontinuation</b>	6.9	2.9
<b>Infusion-related reaction</b>	26.4	7.4
<b>ARIA-hemorrhage</b>	17.3	9.0
<b>ARIA-edema</b>	12.6	1.7

- ARIA – **A**myloid **R**elated **I**maging **A**bnormalities

N Engl J Med 2023; 388:9-21



# Cautions

- VERY modest difference in CDR-SB (0.45)
  - Minimal clinically important difference in CDR-SB
    - **0.98** for MCI
    - **1.63** for mild dementia
- Real life adverse effect rates unknown
- Lack of diversity
  - ? generalizable

Alzheimer's & Dementia: Translational Research and Clinical Interventions 2019; 5:354-363  
N Engl J Med 2023; 388:9-21





# Bottom Line

Would you support Lecanemab approval by Health Canada?





ORIGINAL ARTICLE

# Variation in bone mineral density and fractures over 20 years among Canadians: a comparison of the Canadian Multicenter Osteoporosis Study and the Canadian Longitudinal Study on Aging

Nazila Hassanabadi<sup>1,2</sup> · Claudie Berger<sup>2</sup> · Alexandra Papaioannou<sup>3</sup> · Angela M. Cheung<sup>4</sup> · Elham Rahme<sup>1,2</sup> · William D. Leslie<sup>5</sup> · David Goltzman<sup>1,2</sup> · Suzanne N. Morin<sup>1,2</sup> 



# Background

- Osteoporosis (OP) is a disease of aging.
  - 2.3 million Canadians affected and counting
- Temporal trends in other countries have revealed improved bone mineral density (BMD) and reduced incidence of fragility fractures over time



# Objective

- Over 20 years, compare two population-based cohorts:
  - Bone Mineral Density (BMD)
  - FRAX score
  - Major osteoporotic fractures (MOF)
  - Vitamin D supplementation
  - Calcium supplementation
  - Osteoporosis medication



# Methods

- **Canadian Multicenter OP Study (CaMos)**
  - 1995 - 1997
  - Focus
    - Osteoporosis and fracture risk
  
- **Canadian Longitudinal Study on Aging (CLSA)**
  - 2012 – 2015
  - Focus
    - Determinants of healthy aging



# Results

- **N = 26 013**

- CaMos 6 479 (25%)
- CLSA 19 534 (75%)

- **Baseline characteristics**

- 64 years old
- White
  - > 92% in both cohorts
- Women
  - 55%



# Results: Women

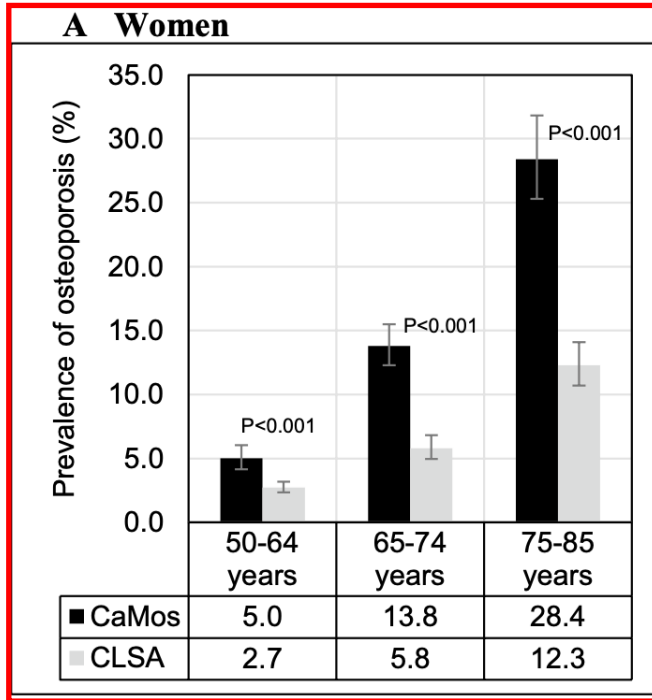
Women	CaMos	CLSA
Weight	69.0kg	72.5kg
BMI	27.1	27.8
Smokers	13.5%	7%
Post-secondary degree	44%	77%
Alcohol	0.9%	3.2%

Osteoporos Int 2023; 34:357–367





# Results: Women - Osteoporosis



**Femoral neck BMD (adjusted)**

CaMos < CLSA

**-0.017 g/cm<sup>2</sup>** [95% CI -0.021;-0.014], p<0.05



# Results

- **Higher risk major osteoporotic fracture, adjusted, CaMos**

- Women **OR 1.99** [95% CI 1.71, 2.30],  $p < 0.05$

- Men **OR 2.33** [95% CI 1.82, 3.00],  $p < 0.05$



# Results: Supplement/medication

Women, FRAX > 20%	Calcium & Vitamin D (%)	Bisphosphonate (%)
CaMos (1995-1997)	30.5	7.2
CLSA (2012-2015)	52.8	20.6

Osteoporos Int 2023; 34:357–367



# Strengths

- Canadian data over 20 years
  - Results consistent with expectations over time
- Multiple adjustments for covariates



# Cautions

- Despite adjustments, were groups similar enough for comparison to draw conclusions?
  - Selection bias
- Improvement in risk factors over time for BMD and MOF do not fully account for results
  - Secular trends
- Lack of diversity in both samples



# Bottom Line

Canadian bones appear to be more dense and less fragile over time. It is more certain that the more our population changes, the more the osteoporosis care gap persists.



# *The* NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

JULY 28, 2022

VOL. 387 NO. 4

## Supplemental Vitamin D and Incident Fractures in Midlife and Older Adults

Meryl S. LeBoff, M.D., Sharon H. Chou, M.D., Kristin A. Ratliff, B.A., Nancy R. Cook, Sc.D., Bharti Khurana, M.D.,  
Eunjung Kim, M.S., Peggy M. Cawthon, Ph.D., M.P.H., Douglas C. Bauer, M.D., Dennis Black, Ph.D.,  
J. Chris Gallagher, M.D., I-Min Lee, M.B., B.S., Sc.D., Julie E. Buring, Sc.D., and JoAnn E. Manson, M.D., Dr.P.H.

**Geriatric Medicine**



Medicine  
UNIVERSITY OF TORONTO

# Background

- Osteoporosis Canada recommends vitamin D supplementation at 400–1000 IU daily
- Meta-analyses of small RCTs have been inconsistent regarding the potential fracture-lowering benefit of supplemental vitamin D

Best Pract Res Clin Endocrinol Metab 2011;25: 585-91.  
CMAJ. 2010;182(17):1864-1873  
Endocr Rev 2019;40: 1109-51





# Objective

- Does supplementation with oral vitamin D decrease rate of fracture among older adults?



# Methods

- Double-blind, placebo-controlled, randomized trial
  - **Vitamin D3**, cholecalciferol, **2000 IU per day**
  - 6 years follow-up
- **Primary Outcomes**
  - First incident fractures
    - Total
    - Non-vertebral
    - Hip

N Engl J Med. 2022; 387(4):299-309

Contemp Clin Trials 2015;41:259-68



# Results

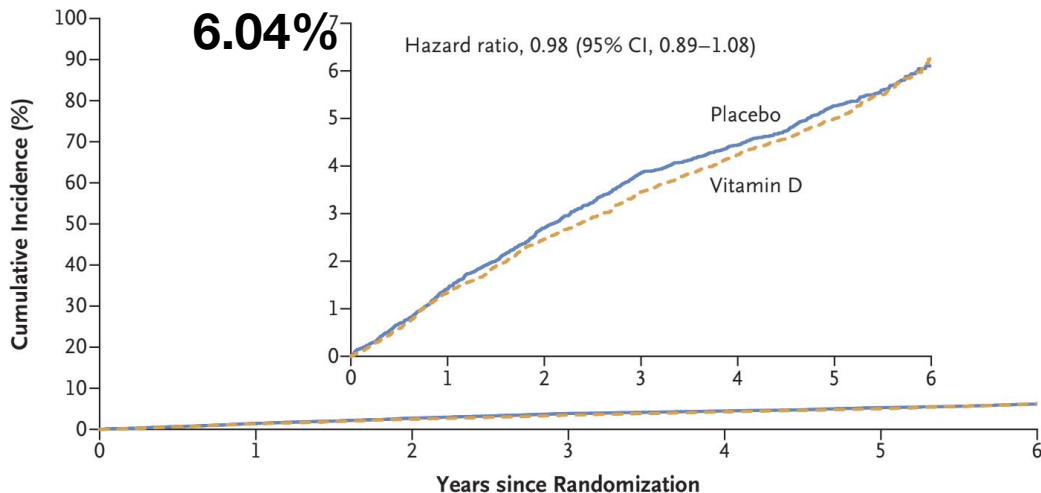
- N = 25 871 across the USA
- **Average participant**
  - 67 years
  - 50.6% female
  - 70% white, 20% black, 1.5% Asian
  - BMI 28
  - 5% taking osteoporosis medications at baseline
  - 10% had history of fragility fracture prior to enrollment
  - FRAX risk 8% in females and 5% in males
  - Baseline vitamin D level 75 nmol/L

N Engl J Med. 2022; 387(4):299-309  
Statistics Canada; Canada at a Glance, 2022



# Results

- Total confirmed incident fractures
  - **Vitamin D 5.93% vs Placebo 6.04%**



- No difference between subgroups
  - Age
  - Sex
  - Baseline vitamin D level

- Vitamin D  $\leq 60$  nmol/L
  - N = 4270
  - HR 1.04 (0.80 – 1.36)



# Discussion

- Strengths
  - Sample size and multi-centre
  - Fractures were adjudicated by blinded chart review
- Cautions
  - Amount of weight-bearing physical activity
  - Falls
  - Few had very low vitamin D levels

N Engl J Med. 2022; 387(4):299-309, Statistics Canada; Canadian Health Measures Survey, 2012 to 2013  
Zeitschrift für Gerontologie und Geriatrie 2013; 46: 403–409, BMC Geriatr. 2017;17(1):229.



# Bottom Line

Vitamin D supplementation is not protective against fractures in patients at a low risk of fracture.



# **Over-the-counter hearing aids: What will it mean for older Americans? Canadians?**

**Jan Blustein MD, PhD<sup>1,2</sup> | Barbara E. Weinstein PhD<sup>3,4</sup> |  
Joshua Chodosh MD, MSHS<sup>2,3,5</sup>**

<sup>1</sup>Robert F Wagner Graduate School, New York University, New York, New York, USA

<sup>2</sup>Department of Population Health, NYU Grossman School of Medicine, New York University, New York, New York, USA

<sup>3</sup>Division of Geriatric Medicine and Palliative Care, Department of Medicine, NYU Grossman School of Medicine, New York University, New York, New York, USA

<sup>4</sup>Doctor of Audiology Program, CUNY Graduate Center, The City University of New York, New York, New York, USA

<sup>5</sup>VA New York Harbor Health Care System, New York, New York, USA



# Background

- Hearing loss impacts 94% aged 70 to 79
- Hearing loss is
  - A risk factor for dementia
  - Associated with social isolation and depression
  - Often perceived as cognitive impairment

J Am Geriatr Soc. 2022 Jul;70(7):2115-2120

Statistics Canada, Hearing health of Canadian adults; Canadian Health Measures Survey 2012-2013 and 2013-2014

Government of British Columbia; Medical Equipment - Hearing Instruments

Lancet; 2020;396(10248):413-446





# Hearing Aids

## Access

- Audiology assessment
  - Prescription only
- Education on use

## Barriers

- Cost
  - Minimum \$2000 CAN / pair
  - Are not less costly with time
  - Funding varies by province
- Health care system navigation

# Over-the-Counter (OTC) Hearing Aids

- FDA authorized OTC hearing aids for mild to moderate hearing loss
- Significant cost savings
  - \$200 - \$1000 USD per pair
- Self-fit without health professional
  - Most devices require linkage with smartphone



# How will US OTC hearing aids impact Canadians?

- Pressure on Health Canada to follow
  - Medical Device License for specific products
  - Provinces to lift requirement for prescription
- Patients travel or order cross border devices to overcome barriers in Canada



# How will US OTC hearing aids impact Canadians?

- Ease of use
  - Need for smartphone app registration/programming
  - Ear molds not custom
- Severity of hearing loss
- Still other options
  - Personal amplifiers
  - Air Pods Pro



# Bottom Line

OTC hearing aids are removing barriers to access in the US and likely in Canada too – a major health equity improvement.



## ORIGINAL RESEARCH

# “I Hope That the People Caring for Me Know About Me”: Exploring Person-Centred Care and the Quality of Dementia Care



Bryan B Franco, MD<sup>1</sup>, Veronique M. Boscart, RN, MSCN, MED, PhD<sup>2</sup>, Jacobi Elliott, PhD<sup>3</sup>, Sherry Dupuis, PhD<sup>4</sup>, Lisa Loiselle, MA<sup>5</sup>, Linda Lee, MD, CCFP(COE), FCFP, MCISC(FM)<sup>6,7</sup>, George A. Heckman, MD, FRCP(C)<sup>3,8</sup>

Can Geriatr J. 2022; 25(4): 336-346.



# Background

- Patient-centered care is highly valued in Geriatric Medicine.
- Persons with dementia are rarely included in qualitative studies on quality of care in Geriatrics.

J Alzheimer's Disease 2021; 80(1):103-111.

Can Geriatr J. 2022; 25(4): 336-346.



# Objective

- To explore the perspectives of people living with dementia and their caregivers on the intersection of patient-centredness and high-quality care.

Can Geriatr J. 2022; 25(4): 336-346.





# Methods

- **Semi-structured interviews**
  - 9 persons living with dementia and 8 care partners.
  - Interviews conducted by a medical student using semi-structured interview guide
- **Content analysis**
  - Thematic coding, two interviews coded by researcher dyads to confirm consistency in coding.

Can Geriatr J. 2022; 25(4): 336-346.



# Results: participants

- Mean age 75
- 4 ♀ 5 ♂
- 8 had post-secondary education
- 8 needed help with ADLs
- Care partners (n=8)
  - 5 spouses, 1 without a care partner



# Results

- Person-centered care is “seeing me as a person”
- “I hope that people looking after me know about me.”
- “The specialist people do special things. So when they’re talking to the normal people. They don’t realize that we don’t understand the words that they’re saying.”
- Quality indicators are “not all of it.”

Can Geriatr J. 2022; 25(4): 336-346.



# Results

- “He isn’t the disease; he’s still the person he was before.”
- Value “someone [that] that has time to just be with them – not fixing them or changing them.”
- “I like to understand [what’s happening] as we go down the road.”
- “NPs seem to have a mandate to take time with their patients. I don’t know why the doctor doesn’t have that same mandate.”
- “They strive for 10 minutes. Write a prescription, take the pill, good bye.”

Can Geriatr J. 2022; 25(4): 336-346.



# Discussion

- Strengths
  - Interviewed individuals living with dementia and their care partners
- Cautions
  - Select population of highly-educated English-speaking persons

JAMA. 2001; 286(2):180-187.

Can Geriatr J. 2022; 25(4): 336-346.



# Bottom Line

*“The whole system needs a quantum shift.”*

Everyone caring for older adults with dementia should consider aspects of person-centred care identified in this article that they can improve on.



JAMA Internal Medicine | [Original Investigation](#)

# Development and External Validation of a Mortality Prediction Model for Community-Dwelling Older Adults With Dementia

W. James Deardorff, MD; Deborah E. Barnes, PhD, MPH; Sun Y. Jeon, PhD; W. John Boscardin, PhD;  
Kenneth M. Langa, MD, PhD; Kenneth E. Covinsky, MD, MPH; Susan L. Mitchell, MD, MPH;  
Elizabeth L. Whitlock, MD, MS; Alexander K. Smith, MD, MS, MPH; Sei J. Lee, MD, MAS

JAMA IM. 2022; 182(11): 1161-1170.



# Background

- Prognosticating survival in people with dementia is important and challenging
- A well-validated and easy to apply prognostic model for mortality in community-dwelling older adults with dementia did not exist prior to this study<sup>1</sup>

1. J Alzheimer's Disease 2021; 80(1):103-111.

JAMA IM. 2022; 182(11): 1161-1170.





# Objective

- To develop and externally validate a mortality prediction model in nationally representative cohorts of community-dwelling older adults with dementia in the US

JAMA IM. 2022; 182(11): 1161-1170.



# Methods

- **Cohorts**

- Community-dwelling, > 65, probable dementia
- Derivation cohort (n = 4267)
  - Health and Retirement Study (HRS)
- Validation cohort (n = 2404)
  - National health and Aging Trends Study (NHATS)

- **Primary Outcome**

- All-cause mortality

- **Methods**

- Cox proportional hazards model

JAMA IM. 2022; 182(11): 1161-1170.



# Results

- Mean age 82
- 1/4 to 1/3 live alone
- 1/3 with  $\geq 1$  ADL dependence
  
- Comparable burden chronic disease to Ontario cohort persons with dementia<sup>1</sup>

1. PLOS Med 2017; 7;14(3):e1002249.

JAMA IM. 2022; 182(11): 1161-1170.



# Results

- Variables included in final model
  - Age, sex
  - BMI
  - smoking status
  - ADL/IADL dependence count
  - Difficulty walking several blocks
  - Regular vigorous physical activity
  - Diabetes
  - heart/lung disease
  - non-skin cancer

JAMA IM. 2022; 182(11): 1161-1170. PLOS Med 2017; 7;14(3):e1002249.



# Results

- Discrimination, Area Under Curve (AUC)
  - 0.76 at 1 year
  - 0.84 at 10 years
- Accuracy
  - Integrated Brier score 0.1
- Calibration between predicted and expected outcomes good

JAMA IM. 2022; 182(11): 1161-1170.



# Discussion

- Strengths
  - Based on variables most of us would have in our consults
    - does not require cognitive testing
  - Discrimination, accuracy, calibration on par with other heavily used predictive scores
- Cautions
  - Dementia etiology not included
  - Tailor prognostication information to patient and their family

JAMA IM. 2022; 182(11): 1161-1170.

JAMA. 2001; 286(2):180-187.



# Bottom Line

The mortality prediction tool for persons with dementia is as accurate a prediction score as others we routinely use in clinical practice – practice changing - start using this today at [eprognosis.com](http://eprognosis.com)



ORIGINAL ARTICLE

# Haloperidol for the Treatment of Delirium in ICU Patients

N.C. Andersen-Ranberg, L.M. Poulsen, A. Perner, J. Wetterslev, S. Estrup, J. Hästbacka, M. Morgan, G. Citerio, J. Caballero, T. Lange, M.-B.N. Kjær, B.H. Ebdrup, J. Engstrøm, M.H. Olsen, M. Oxenbøll Collet, C.B. Mortensen, S.-O. Weber, A.S. Andreasen, M.H. Bestle, B. Uslu, H. Scharling Pedersen, L. Gramstrup Nielsen, H.C. Toft Boesen, J.V. Jensen, L. Nebrich, K. La Cour, J. Laigaard, C. Haurum, M.W. Olesen, C. Overgaard-Steensen, B. Westergaard, B. Brand, G. Kingo Vesterlund, P. Thornberg Kyhnauv, V.S. Mikkelsen, S. Hyttel-Sørensen, I. de Haas, S.R. Aagaard, L.O. Nielsen, A.S. Eriksen, B.S. Rasmussen, H. Brix, T. Hildebrandt, M. Schønemann-Lund, H. Fjeldsøe-Nielsen, A.-M. Kuivalainen, and O. Mathiesen, for the AID-ICU Trial Group\*

DECEMBER 29, 2022





# Background

- Delirium affects about 70% of older adults in the ICU
- Associated with increased mortality, LOS, functional decline, long-term cognitive impairment, and institutionalization
- Haloperidol is not supported by clinical practice guidelines due to lack of evidence

J Am Geriatr Soc 2003; 51(5):591-8  
Arch Intern Med 2007; 167(15):1629  
Acta Anaesthesiol Scand 2019;64(2):254-66  
Semin Respir Crit Care Med 2001;22(02):115-26



# Methods

- **Design:** multicenter, double-blind, randomized, placebo-controlled
- **Population:** adults with delirium (CAM-ICU or ICDSC) in the ICU
- **Intervention:** haloperidol 2.5mg IV TID and PRN (daily max 20mg) vs. placebo



# Methods

- **Primary outcome**
  - Number of days alive and out of hospital at 90 days after randomization
  
- **Secondary outcomes**
  - Serious adverse reactions
  - Use of rescue medications
  - # of days without delirium or coma
  - # of days without mechanical ventilation
  
- **Analysis:** intention-to-treat



# Results

- 1000 adults aged 18+ with delirium in the ICU
- 16 centers in Europe
- **Average participant**
  - Age 70, male
  - 66% medical admission
  - 55% hypoactive delirium
  - 63% on mechanical ventilation
  - 52% on vasopressors or inotropes
  - < 1% with neurodegenerative disease



# Results

Outcome	Haloperidol	Placebo	Adjusted Absolute Difference (95% or 99% CI)†	Adjusted Relative Risk (95% or 99% CI)†	P Value
<b>Primary outcome</b>					
Days alive and out of hospital at 90 days — raw mean no. (95% CI)‡	35.8 (32.9 to 38.6)	32.9 (29.9 to 35.8)	2.9 (-1.2 to 7.0)§	NC	0.22¶
Death — no./total no. (%)	182/501 (36.3)	210/485 (43.3)	-6.9 (-13.0 to -0.6)**	0.84 (0.72 to 0.98)	
Length of hospital stay — raw mean no. of days (95% CI)††	28.8 (26.7 to 30.8)	26.4 (24.4 to 28.5)	2.3 (-0.6 to 5.1)§	NC	



# Results

- No heterogeneity by:
  - Type of delirium
  - Age (< 69, ≥ 69)
  - Sex
  - Admission type
  - Delirium risk factors
  - Predicted 90-day mortality
  
- Secondary outcomes were similar in both groups



# Discussion

- Large, well-conducted RCT that addressed an area of great clinical need
- Haloperidol was given standing for both hypoactive and hyperactive delirium
- Very low rates of underlying neurodegenerative disease
- Haloperidol dose differs from our typical practice



# Bottom Line

Use of haloperidol for patients with delirium in the ICU should continue to be an individualized decision





Received: 1 November 2021

Revised: 8 March 2022

Accepted: 12 March 2022

DOI: 10.1111/jgs.17788

Journal of the  
American Geriatrics Society

# Patient outcomes related to receiving care on a dedicated Acute Care for Elders (ACE) unit versus with an ACE order set

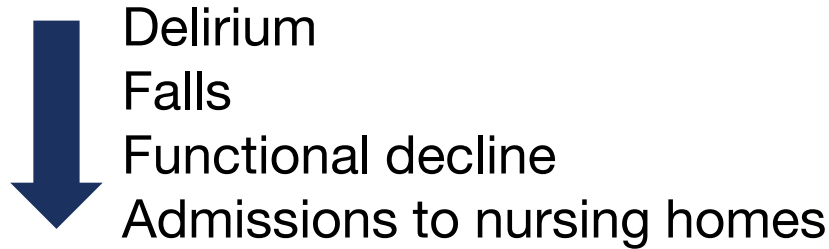
Richard E. Norman MD, MASC, MSc<sup>1,2</sup>  | Samir K. Sinha MD, DPhil<sup>1,2</sup>



J Am Geriatr Soc. 2022; 70:2101-06

# Background

- Older adults are at increased risk of adverse outcomes during hospitalization which contribute to further loss of independence



- # of patients who could benefit often exceeds ACE unit capacity

# Objective

- Protocolized order sets have been developed to provide patients bed-spaced on non-ACE units with several aspects of the ACE model of care
- Is the ACE model equally effective when applied this way?



# Methods

- **Design:** retrospective cohort of ACE-eligible patients aged 65+
- **Location:** Mount Sinai Hospital, Toronto
- **Intervention:** admission to 28-bed ACE unit vs. bed-spaced with protocolized ACE order set



# Methods

- **Primary outcomes**
  - Discharge disposition (home or other location)
  - In-hospital mortality
  
- **Data collection:** over 5 years, ending in 2018



# Methods

Intervention	ACE Unit	ACE Order Set (Bed-Spaced)
Dedicated daily interdisciplinary rounds on geriatric-specific issues	Yes	No
<b>Physical Environment</b>		
Prominent clocks and calendars in every room	Yes	No
High contrast environment, enhanced lighting	Yes	No
<b>Patient Care</b>		
Supervision by geriatric nursing practitioner	Yes	No
Specialized geriatric nursing training	Yes	No
Specialized nursing training in prevention and management of delirium	Yes	No
Specialized continence training	Yes	No



# Results

Characteristic	ACE Unit (n = 1499)	Bed-Spaced (n = 1547)
<b>Age in years (mean)</b>	<b>83.5</b>	<b>82.6</b>
Sex, No. (%)		
Male	589 (39.3)	608 (39.3)
Female	910 (60.7)	939 (60.7)
Resource use as defined by RIW		
Median	1.06	0.97
Mean	1.48	1.35
Length of stay, days		
Median	5.9	4.8
Mean	8.4	7.3
Discharge diagnosis, No. (%)		
Functional decline	116 (7.7)	105 (6.8)
Pneumonia	92 (6.1)	103 (6.7)
Congestive heart failure	86 (5.7)	85 (5.5)



# Results

Characteristic	ACE Unit (n = 1499)	Bed-Spaced (n = 1547)
<b>Age in years (mean)</b>	<b>83.5</b>	<b>82.6</b>
Sex, No. (%)		
Male	589 (39.3)	608 (39.3)
Female	910 (60.7)	939 (60.7)
Resource use as defined by RIW		
Median	1.06	0.97
Mean	1.48	1.35
Length of stay, days		
Median	5.9	4.8
Mean	8.4	7.3
Discharge diagnosis, No. (%)		
Functional decline	116 (7.7)	105 (6.8)
Pneumonia	92 (6.1)	103 (6.7)
Congestive heart failure	86 (5.7)	85 (5.5)





# Results

- Patients on the ACE unit were more likely to be discharged home
  - **OR 1.31**, 95% CI 1.12-1.54,  $p = 0.001$
- And less likely to die in hospital
  - **OR 0.70**, 95% CI 0.51-0.95,  $p = 0.02$



# Results

- Post-hoc analysis adjusted for potential case mix differences
- Patients on the ACE unit still more likely to be discharged home
  - **OR 1.23**, 95% CI 1.02-1.50,  $p = 0.033$
- Mortality benefit no longer present
  - **OR 0.89**, 95% CI 0.60-1.33,  $p = 0.63$



# Cautions

- Single institution
- Non-randomized study
- Fidelity to ACE interventions was not tracked



# Cautions

- Impact of bed-spacing to different floors and surgical units
- No comparison to usual care
- Readmission and cost data would be helpful



# Bottom Line

ACE units reflect a synergy of staff expertise, resources, and a culture that values caring for older adults

The whole is likely greater than the sum of its parts



# *The* NEW ENGLAND JOURNAL *of* MEDICINE

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## Polypill Strategy in Secondary Cardiovascular Prevention

J.M. Castellano, S.J. Pocock, D.L. Bhatt, A.J. Quesada, R. Owen, A. Fernandez-Ortiz, P.L. Sanchez, F. Marin Ortuño, J.M. Vazquez Rodriguez, A. Domingo-Fernández, I. Lozano, M.C. Roncaglioni, M. Baviera, A. Foresta, L. Ojeda-Fernandez, F. Colivicchi, S.A. Di Fusco, W. Doehner, A. Meyer, F. Schiele, F. Ecartot, A. Linhart, J.-C. Lubanda, G. Barczi, B. Merkely, P. Ponikowski, M. Kasprzak, J.M. Fernandez Alvira, V. Andres, H. Bueno, T. Collier, F. Van de Werf, P. Perel, M. Rodriguez-Manero, A. Alonso Garcia, M. Proietti, M.M. Schoos, T. Simon, J. Fernandez Ferro, N. Lopez, E. Beghi, Y. Bejot, D. Vivas, A. Cordero, B. Ibañez, and V. Fuster, for the SECURE Investigators\*

N Engl J Med. 2022;387:967-977



# Background

- Adherence, secondary prevention
  - Estimated at 50%
    - associated with worse outcomes
- Pill burden, regimen
- Fixed dose combination, polypill strategy
  - Increased adherence via simplification
  - Infectious disease



# Methods

- Multicenter, randomized, non-inferiority
  - 113 European centers, 36 months
- **Intervention**
  - **Polypill (AAR 40, AAR 20)**
    - ASA 100mg
    - Atorvastatin 20mg, 40mg
    - Ramipril 2.5mg, 5mg, 10mg
  - **Usual care**
    - European Society of Cardiology guidelines

N Engl J Med. 2022;387:967-977





# Methods

- **Primary Outcome, composite**
  - Cardiovascular death
  - Non-fatal myocardial infarct
  - Non-fatal stroke
  - Urgent coronary revascularization
  
- **Secondary Outcomes**
  - Treatment adherence
  - Risk factor control
  - Treatment satisfaction

N Engl J Med. 2022;387:967-977



# Methods

- **Inclusion**

- Myocardial infarction within previous 6 months AND
- Age > 75 OR
- Age > 65 and at least 1 of
  - Diabetes mellitus
  - Kidney dysfunction (creat clearance 30 to 60ml/min)
  - Prior coronary revascularization
  - Prior stroke



# Results

N = 2499

## Average participant

- 76
- 69% male
- 78% HTN, systolic mean 129mmHg
- LDL 2.3mmol/L
- 57% diabetes
- 51% history of tobacco use



# Results

- **Primary outcome**

- **9.5%** polypill vs **12.7%** usual care
  - **HR 0.76** (95 CI 0.60 – 0.96,  $p < 0.001$ )
  - **NNT 31**



# Results

- **Secondary outcomes**

- Death from any cause
  - HR 0.97 (95 CI 0.75 – 1.25)
- Adherence
  - 24 months 74.1% vs 63.2%
- Biomarkers did not differ
  - Blood pressure
  - Cholesterol
- Treatment satisfaction did not differ

- **Adverse events**

- 32.7% polypill vs 31.6% usual care



# Discussion

- Higher adherence, no change biomarkers?
  - Greater ASA use
  - Pleiotropic effects statins
  - High intensity statins 90% vs 50%
- Not blinded
  - Greater healthy lifestyle behaviors
- Satisfied test for superiority



# Bottom Line

A patient-centered view would call this a two-for-one bottom line, a superior outcome and reduced pill burden.

Industry's view may struggle to find the bottom line at all



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Antidepressant Augmentation versus Switch  
in Treatment-Resistant Geriatric Depression

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N Engl J Med 2023;388:1067-1079





# Background

- Depression treatment failure is common and associated with
  - Decreased psychological well-being
  - Disability
  - Cognitive decline
- Augmenting with aripiprazole effective vs placebo
  - Canadian Coalition For Senior's Mental Health 2021

Lancet 2015;386:2404-2412

CCSMH 2021 Canadian Guidelines on Prevention, Assessment and Treatment of Depression Among Older Adults

N Engl J Med 2023;388:1067-1079



# Methods

- Pragmatic, open label trial
- Treatment resistant depression
  - 2 trials, adequate dose and duration
- Dementia excluded
- Randomized 1:1:1 ratio
  - Augmentation to aripiprazole
  - Augmentation to bupropion
  - Switch to burpropion

N Engl J Med 2023;388:1067-1079



# Methods

- **Primary Outcome**

- Psychological well-being
  - National Institutes of Health Toolbox
    - Positive Affect & General Life Satisfaction subscales
  - Population mean score 50
    - Higher score, greater well-being

- **Secondary Outcomes**

- Montgomery-Asberg Depression Rating Scale (MADRS)
  - Lower scores greater well-being, 60 points
  - Remission of depression (< 10)



# Results

- N = 611
  - $\approx$  200 per treatment arm

## Average participant

- 69 years old, White, Female
- 14 years education
- MADRS 23
- 2.3 # of medication trials prior to enrolment
- 8.7 Cumulative Illness Severity Score – Geriatric
  - 0 – 56, higher score = greater impairment
- 40%  $\geq$  1 fall in last 6 months



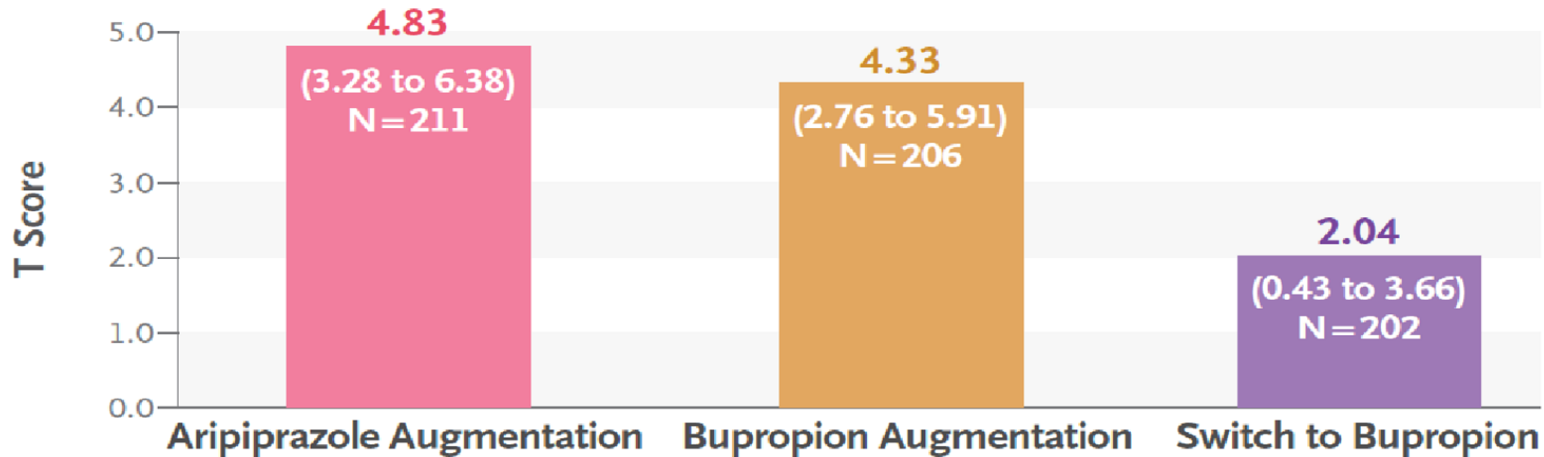
N Engl J Med 2023;388:1067-1079



# Results

## Step 1

### Change in Psychological Well-Being (95% CI)



**Aripiprazole augmentation vs. switch to bupropion** 2.79 points (0.56 to 5.02); P=0.014

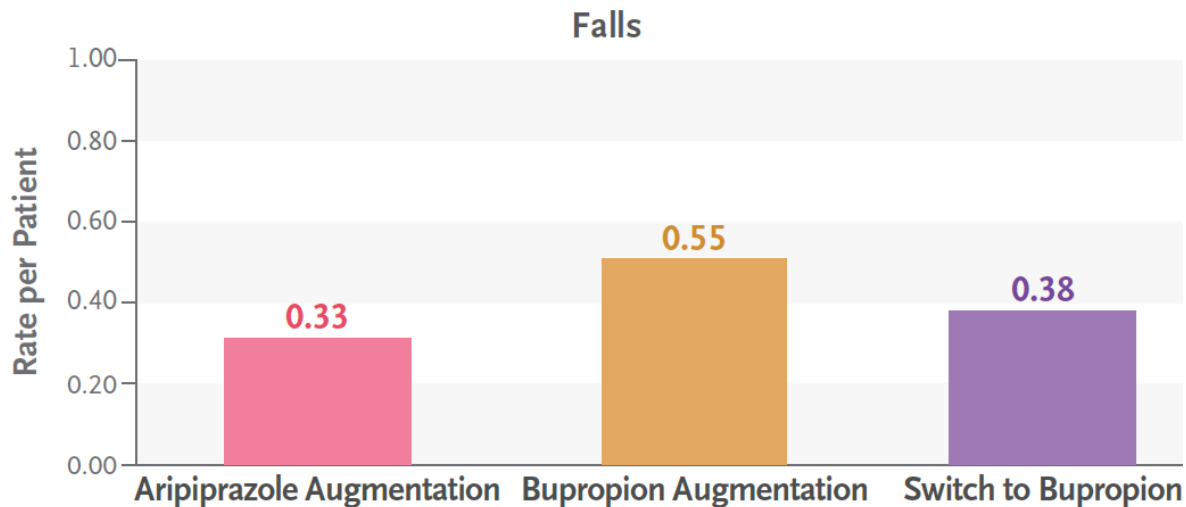
**Aripiprazole augmentation vs. bupropion augmentation** 0.50 points (-1.69 to 2.69)

# Results

	Step 1		
	Aripiprazole- Augmentation Group (N= 211)	Bupropion- Augmentation Group (N= 206)	Switch-to- Bupropion Group (N= 202)
Remission¶			
No. (%)	61 (28.9)	58 (28.2)	39 (19.3)
Risk ratio vs. switch group (95% CI)	1.50 (1.06 to 2.13)	1.49 (1.04 to 2.12)	1.00 (reference)



# Results



**Aripiprazole augmentation vs. bupropion augmentation** 0.59 (0.38 to 0.92); P=0.02

# Discussion

- Consistent with prior RCT data on augmentation
- Remission rates only 30%
- Short duration likely underestimates adverse effects
- Younger older adults





# Bottom Line

Augmentation should also augment management to include a referral for balance training and prevention

N Engl J Med 2023;388:1067-1079



# More great papers, 2022

- The High Price of Aduhelm's Approval: An investigation into FDA's Atypical Review Process and Biogen's Aggressive Launch Plans. Staffs of the Committee on Oversight and Reform and Committee on Energy and Commerce. **US House of Representatives. December 2022**
- Geriatric Surgical service interventions in older emergency general surgery patients: Preliminary results. **J Am Geriatr Soc. 2022;70:2404-2414**
- Impact of Geriatric Assessment and Management on Quality of Life, Unplanned Hospitalizations, Toxicity, and Survival for Older Adults With Cancer: The Randomized 5C Trial. **Journal of Clinical Oncology 2023;41:847-858**



# More great papers, 2022

- Trial of Cinpanemab in Early Parkinson's Disease. *N Engl J Med* 2022;387:408-420
- Trial of Prasinezumab in Early-Stage Parkinson's Disease. *N Engl J Med* 2022;387:421-432
- Six-Year Cognitive Trajectory in Older Adults Following Major Surgery and Delirium. *JAMA Intern Online* 2023.doi:10.1001/jamainternalmed.2023.0144



# More great papers, 2022

- Experiences of Everyday Ageism and the Health of Older US Adults. *JAMA Network Open*. 2022;5(6):e2217240. doi:10.1001/jamanetworkopen.2022.17240
- The Intersections of Structural Racism and Ageism in the Time of COVID-19. *Research in Gerontological Nursing* 2022;15:6-13
- The Safety of Inpatient Health Care. *N Engl J Med* 2023;388:142-153



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