

# Literature Update 2019

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UNIVERSITY OF  
**TORONTO**



**Sunnybrook**  
HEALTH SCIENCES CENTRE



# Conflicts of Interest

- None



# Methods: article selection

- Canvassed Geriatricians from across the province
- Scanned table of contents and read major journals/reviews
- Reviewed articles presented at the Geriatric Medicine Journal Club



# Interactive

- Question to consider
- Poll the audience for the answer
- Review the evidence
- Moment of reflection



# Dementia





# What is new regarding dementia in 2019?

- A) A new dementia syndrome and pathophysiological process has been described
- B) Canada's National Dementia Strategy resulted in a commitment of 1% of dementia care costs to researching dementia
- C) A systolic blood pressure target of 120mmHg reduces incident MCI and subsequently dementia
- D) Models of care for dementia that rely on telephone support failed to demonstrate benefit



**REVIEW****Limbic-predominant age-related TDP-43 encephalopathy (LATE): consensus working group report**

Peter T. Nelson,<sup>1</sup>  Dennis W. Dickson,<sup>2</sup> John Q. Trojanowski,<sup>3</sup> Clifford R. Jack Jr.,<sup>4</sup> Patricia A. Boyle,<sup>5</sup> Konstantinos Arfanakis,<sup>5,6</sup> Rosa Rademakers,<sup>2</sup> Irina Alafuzoff,<sup>7</sup> Johannes Attems,<sup>8</sup> Carol Brayne,<sup>9</sup> Ian T.S. Coyle-Gilchrist,<sup>9</sup> Helena C. Chui,<sup>10</sup> David W. Fardo,<sup>1</sup> Margaret E. Flanagan,<sup>11</sup> Glenda Halliday,<sup>12</sup> Suvi R.K. Hokkanen,<sup>9</sup> Sally Hunter,<sup>9</sup> Gregory A. Jicha,<sup>1</sup> Yuriko Katsumata,<sup>1</sup> Claudia H. Kawas,<sup>13</sup> C. Dirk Keene,<sup>14</sup> Gabor G. Kovacs,<sup>15</sup> Walter A. Kukull,<sup>14</sup> Allan I. Levey,<sup>16</sup> Nazanin Makkinejad,<sup>6</sup> Thomas J. Montine,<sup>17</sup> Shigeo Murayama,<sup>18</sup> Melissa E. Murray,<sup>2</sup> Sukriti Nag,<sup>5</sup> Robert A. Rissman,<sup>19</sup>  William W. Seeley,<sup>20</sup> Reisa A. Sperling,<sup>21</sup> Charles L. White III,<sup>22</sup> Lei Yu<sup>5</sup> and Julie A. Schneider<sup>5</sup>

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# Two cases

- 72 female
- No CVD, mental health
- 2-3 years gradual short-term
- **Amyloid – Alzheimer's Disease**
- Lack of insight, head turn sign
- Stopped driving and banking
- MMSE 22/30

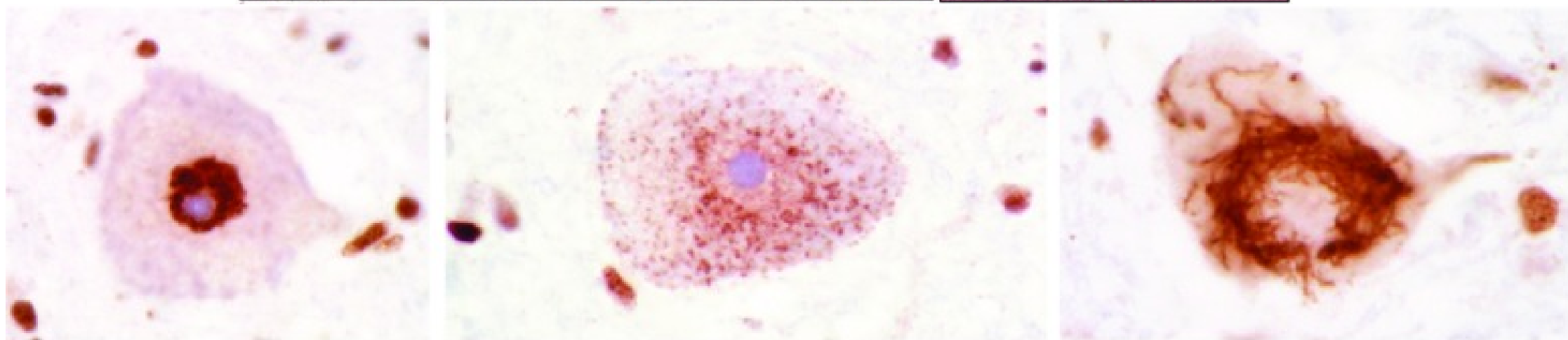
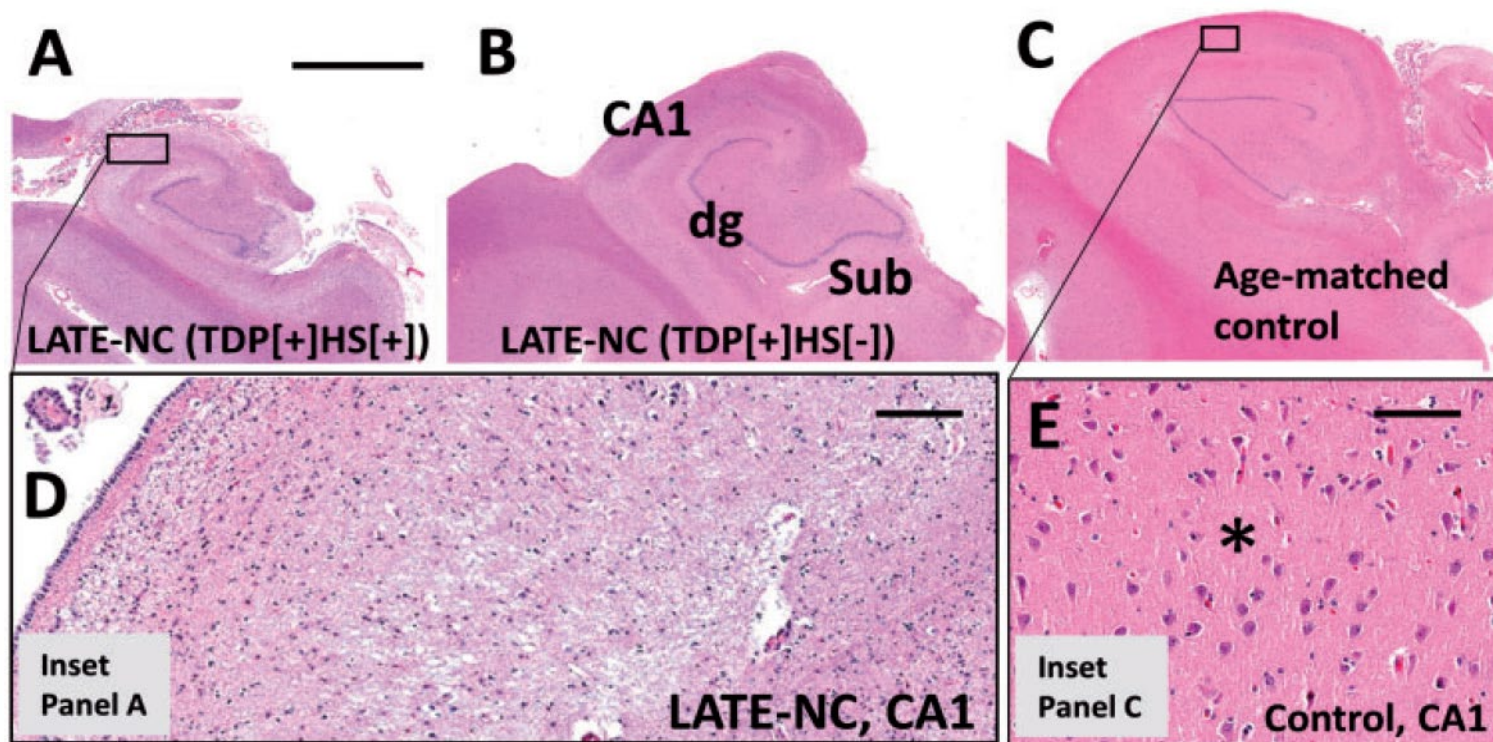
- 93 female

- ?
- **TDP – 43 – Limbic predominant age related TDP 43 encephalopathy**
- MMSE 22/30



- **Transactive response DNA binding protein of 43 kilodaltons TDP 43**
  - Protein that binds RNA, DNA
  - Multiple functions in gene expression, transcription and translation
  - Normal state non-phosphorylated, within nuclei
  - Disease state phosphorylated, translocated and deposited in cytoplasm
  - 2006 – Amyotrophic Lateral Sclerosis/Fronto-Temporal Lobar Degeneration
- **LATE**
  - **L**imbic-predominant **A**ge-related **T**DP – 43 **E**ncephalopathy
  - TDP 43 localized to limbic brain structures in subjects past 80 years of age





Nucleus



Cytoplasm



- **LATE neuropathological change**
  - 20% to 50% of individuals > 80 years
  - Increases with advanced age
  - 100-fold more prevalent than FTD syndromes
  - No gender differences or ethno-cultural predilection

Neuropathological indices	Fraction attributable % (95% CI) <sup>a</sup>
Alzheimer's disease (ADNC)	39.4 (31.5–47.4)
Vascular disease pathology <sup>b</sup>	24.8 (17.3–32.1)
<b>LATE-NC</b>	<b>17.3 (13.1–22.0)</b>
$\alpha$ -Synucleinopathy/Lewy body pathology	11.9 (8.4–15.6)



- **Clinical**

- Bottom Line

- Practice changing with regard to diagnosis
    - No data on prognosis, no change to management
    - Hope for a biomarker soon...





# A **Dementia** STRATEGY FOR CANADA

*Together We Aspire*





- **History**

- **June 22, 2017**

- **Bill C233 – A National Strategy for Alzheimer’s Disease and Other Dementias Act**

- **May 14 – 15, 2018**

- **National Dementia Conference**

- **June 17, 2019**

- **National Strategy**
    - **\$50 million over 5 years**
    - **Ministerial Advisory Board**



- **Vision**

- A Canada in which all people living with dementia and caregivers are valued and supported, quality of life is optimized, and dementia is prevented, well understood, and effectively treated

- **5 Principles**

- Quality of life, diversity, human rights, evidence-informed, results-focused

- **Main objectives**

- Prevent Dementia
  - Advance therapies and find a cure
  - Improve the quality of life of people living with dementia and caregivers



- **Achievements**
  - **Emphasis on prevention**
  - **Focus**
    - **Women**

CURRENT STATUS	ASPIRATION
Widespread stigma within communities and a lack of understanding of dementia.	All people living in Canada understand dementia and stigma no longer exists in Canada.

- **Eliminating stigma**
  - **Dementia**
  - **Ageism**



- Bottom Line
- Great document and first step
- Muted reaction if improvement on the front lines desired in the near term



JAMA | Original Investigation

# Effect of Intensive vs Standard Blood Pressure Control on Probable Dementia

## A Randomized Clinical Trial

The SPRINT MIND Investigators for the SPRINT Research Group



- **Double-blind, randomized, placebo-controlled trial**
- **N = 9361, 3.3 years**
- **Intervention**
  - **Systolic blood pressure goal of < 120mmHg versus < 140mmHg**
- **Primary outcome**
  - **Probable dementia**
    - **3 part process (screen, functional assessment, neuropsychological battery)**
  - **Mild cognitive impairment**
    - **2 or more consecutive adjudicated conclusions of MCI**
  - **Mild cognitive impairment and dementia**



- **Inclusion**

- **Clinical or subclinical cardiovascular disease**
- **Chronic kidney disease**
- **Framingham risk score greater than 15%**
- **Age >75**

- **Exclusion**

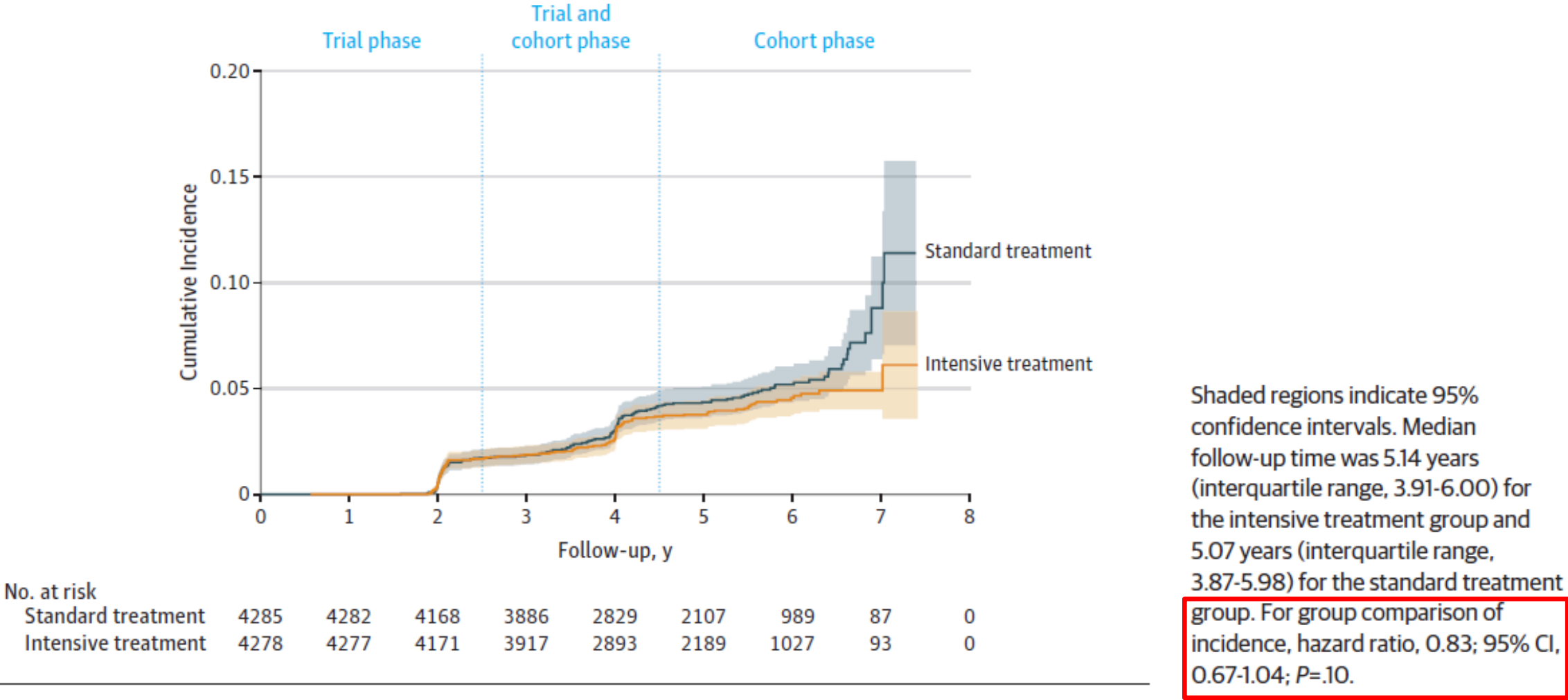
- **Diabetes**
- **Stroke**
- **LTC residents**
- **Prevalent dementia or on dementia pharmacotherapy**



- **Average participant**
  - **68 years old**
  - **64% male**
  - **30% black**
  - **33% SBP > 145**
  - **MoCA score 23/30**



Figure 2. Probable Dementia by Treatment Group





- **Results**

- **Probable dementia**

**7.2 vs 8.6 / 1000 pyrs**

HR 0.83 CI (0.67-1.04), p = 0.10

- **Mild Cog Impairment**

**14.6 vs 18.3 / 1000 pyrs**

HR 0.81 CI (0.69-0.95), p = 0.007

- **MCI or Prob Dementia**

**20.2 vs 24.1 / 1000pyrs**

HR 0.85 CI (0.74-0.97), p = 0.01

- **All subgroups**

**NS**




- **Discussion**

- Trial terminated early due to cardiovascular benefit

- Bottom Line

- Wind out of my sails
    - SPRINT MIND 2.0 to the rescue?





Research

JAMA | **Original Investigation**

# Association of Intensive vs Standard Blood Pressure Control With Cerebral White Matter Lesions

The SPRINT MIND Investigators for the SPRINT Research Group



- **Double-blind, randomized, placebo-controlled trial**
- **N = 449**
- **4 years**
- **Intervention**
  - **Systolic blood pressure goal of < 120mmHg versus < 140mmHg**
- **Primary outcome**
  - **MRI change in total white matter lesion volume**
  - **MRI change in total brain volume**



- **Inclusion**

- **Clinical or subclinical cardiovascular disease**
- **Chronic kidney disease**
- **Framingham risk score greater than 15%**
- **Age >75**

- **Exclusion**

- **Diabetes**
- **Stroke**
- **LTC residents**
- **Prevalent dementia or on dementia pharmacotherapy**



- **Average participant**
  - **67 years old**
  - **60% men**
  - **30% black**
  - **BP 138/78**
  - **MoCA 24**
  - **White matter lesion (WML) volume 3 cm<sup>3</sup>**
  - **Total brain volume (TBL) 1150 cm<sup>3</sup>**



## • Results

• WML change 0.23cm<sup>3</sup> /yr intensive versus 0.37cm<sup>3</sup> /yr standard, p<0.001

• TBV change -3.7cm<sup>3</sup> /4yrs more loss intensive versus standard, p=0.006

Table 2. Estimated Changes in Structural Magnetic Resonance Imaging Outcomes by Treatment Group<sup>a</sup>

	Volume (95% CI), cm <sup>3</sup>							
	Intensive Treatment			Standard Treatment			Estimated Difference in Change	P Value
Outcome	Baseline	Follow-up	Change	Baseline	Follow-up	Change		
WML volume, asinh	1.99 (1.86 to 2.13)	2.14 (2.01 to 2.28)	0.15 (0.11 to 0.19)	1.96 (1.82 to 2.10)	2.25 (2.10 to 2.39)	0.28 (0.24 to 0.33)	-0.13 (-0.19 to -0.07)	<.001
WML volume	4.57 (4.00 to 5.14)	5.49 (4.91 to 6.07)	0.92 (0.69 to 1.14)	4.40 (3.80 to 5.00)	5.85 (5.23 to 6.47)	1.45 (1.21 to 1.70)	-0.54 (-0.87 to -0.20)	
Annualized change			0.23 (0.17 to 0.29)			0.37 (0.30 to 0.43)		
Total brain volume	1134.5 (1125.1 to 1144.0)	1104.0 (1094.5 to 1113.4)	-30.6 (-32.3 to -28.8)	1134.0 (1124.4 to 1143.6)	1107.1 (1097.4 to 1116.8)	-26.9 (-28.8 to -24.9)	-3.7 (-6.3 to -1.1)	.006
Annualized change			-7.7 (-8.1 to -7.3)			-6.8 (-7.3 to -6.3)		



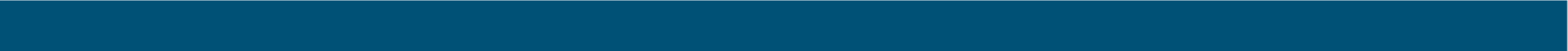
- Discussion

- ~~WML can be closed by intensive systolic blood pressure target~~

- Bottom Line

- Results do not justify intensive targets
- Still haven't found what I am looking for





Research

JAMA Internal Medicine | [Original Investigation](#) | HEALTH CARE REFORM

# Effect of Collaborative Dementia Care via Telephone and Internet on Quality of Life, Caregiver Well-being, and Health Care Use

## The Care Ecosystem Randomized Clinical Trial

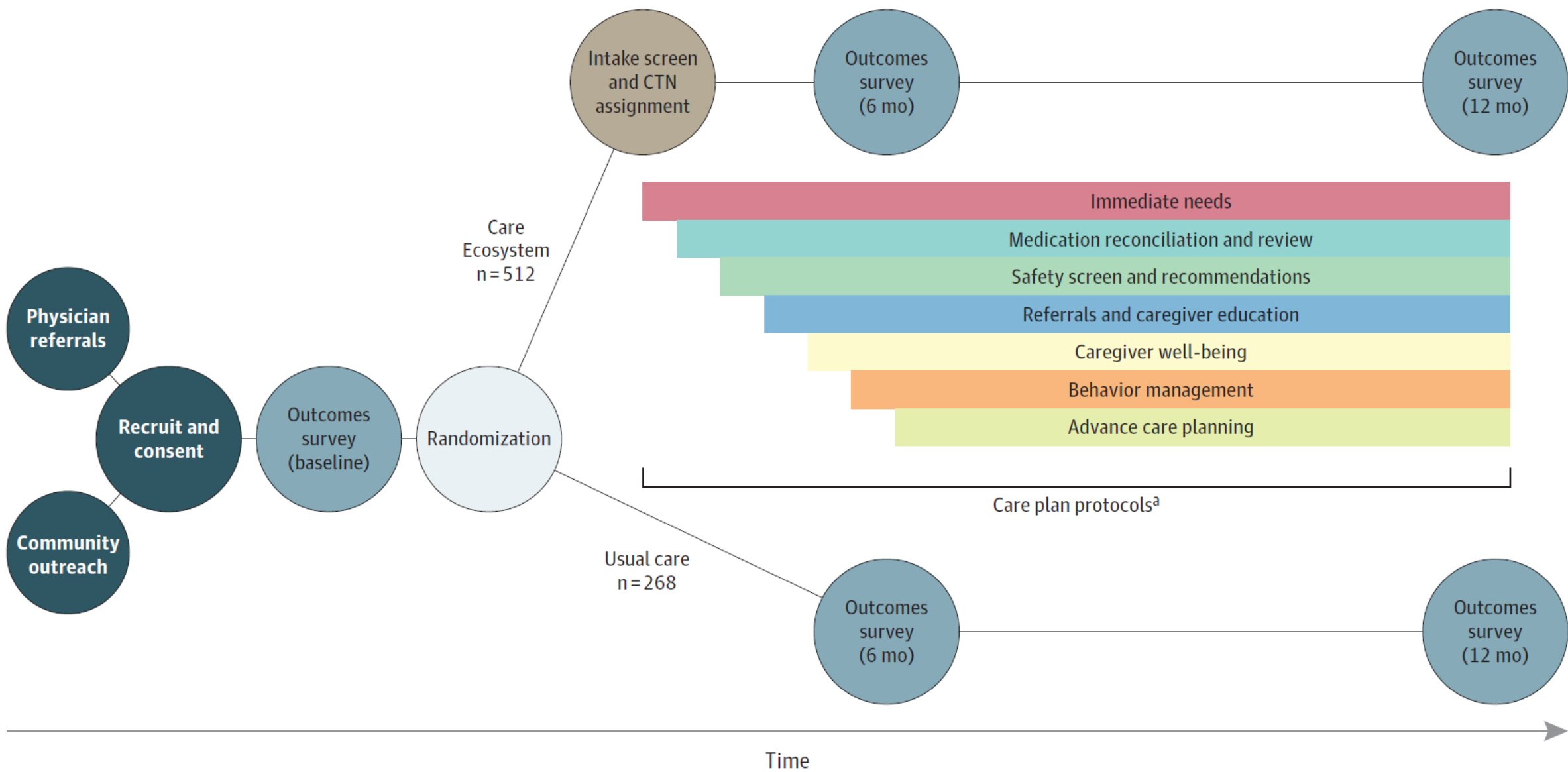
Katherine L. Possin, PhD; Jennifer J. Merrilees, RN, PhD; Sarah Dulaney, RN, MS, CNS; Stephen J. Bonasera, MD; Winston Chiong, MD, PhD; Kirby Lee, PharmD; Sarah M. Hooper, JD; Isabel Elaine Allen, PhD; Tamara Braley, MSN, APRN; Alissa Bernstein, PhD, MPH; Talita D. Rosa, MS, MD; Krista Harrison, PhD; Hailey Begert-Hellings, BA; John Kornak, PhD; James G. Kahn, MD, PhD; Georges Naasan, MD; Sergio Lanata, MD, MS; Amy M. Clark, PhD, MSW; Anna Chodos, MD; Rosalie Gearhart, RN, MS, CNS; Christine Ritchie, MD, MSPH; Bruce L. Miller, MD



- **Pragmatic, single-blind, randomized controlled trial**
- **N = 780, 12 months**
- **Intervention**
  - **Care Team Navigator (CTN) telephone based collaborative dementia care**
    - **Weekly case reviews with advance practice nurse or social worker**
    - **Pharmacist review all meds on entry and based on need or changes**
  - **Control**
- **Primary outcome**
  - **Quality of Life in Alzheimer's Disease (QoL AD)**
    - **13 aspects of person with dementia (PWD) life**
    - **4-point scale (13 to 52), higher better QoL**



Figure 2. The Care Ecosystem Trial Design





- **Inclusion**
  - **Dementia with caregiver who agreed to co-enroll**
  - **Age  $\geq$  45**
  - **Enrollment or eligible for Medicare or Medicaid**
  - **Resident of California, Nebraska, Iowa**
  - **Nursing home excluded**
- **Average participant**
  - **78 years old**
  - **55% female**
  - **80% white, 92% English**
  - **70% < \$50 000 yearly income**
  - **50% mild**



## • Results

- Mean number of phone calls per dyad 15.3 (SD 11.9)
- CTN case load (maximum 90)
  - UCSF 35
  - UNMC 49
- Quality of Life AD
  - B, 0.53; 95 CI 1.30 – 0.25,  $p = 0.04$
- Rate of ED use
  - B, -0.14, 95 CI (-0.29 - -0.01),  $p = 0.04$       NNT 5
  - 16 ambulance events, 13 hospitalizations prevented
- Caregivers
  - Depression and burden both improved



- **Discussion**

- Bottom Line

- Fundamentally believe in more care
    - Scalable



# What is new regarding dementia in 2019?

- A) A new dementia syndrome and pathophysiological process has been described – LATE
- B) Canada's National Dementia Strategy resulted in a commitment of 1% of dementia care costs to researching dementia
- C) A systolic blood pressure target of 120mmHg reduces incident MCI and subsequently dementia
- D) Models of care for dementia that rely on telephone support failed to demonstrate benefit



## **Please identify the correct statement?**

- A) Informal caregiver is an acceptable term to describe a family member providing care to an older adult in need
- B) Formal caregiver is an acceptable term to describe a health care worker providing care to an older adult in need
- C) Biomarkers of subclinical cardiovascular disease are associated with falls
- D) Biomarkers of subclinical cardiovascular disease are not associated with falls



# Caregivers



# Words Matter: The Language of Family Caregiving

Increased attention has been paid recently to the central role of language in shaping the culture of aging.<sup>1</sup> This includes the notable adoption of the modified American Medical Association style by the *Journal of the American Geriatrics Society*, recognizing that word choices can frame important aging issues in judgmental and counterproductive ways.<sup>2,3</sup> For example, using catastrophic metaphors like “silver tsunami” and “tidal wave” to frame demographic changes may garner

common perception that caregiving is limited to basic personal care and household chores.<sup>11</sup> *Home Alone* highlighted how the caregiving role had become increasingly complex, demanding, and stressful. With little to no training or support, caregivers are tasked with providing medical and nursing care in the home, navigating health and long-term care systems, and serving as substitute decision makers.<sup>6,7,11-13</sup> AARP recently released its 2019 follow-up study, *Home*



- **Editorial**
- **Importance of language**
  - **Journal of the American Geriatrics Society**
  - **Alzheimer's Society of Canada**
- **Language of Caregivers**
  - **No consensus language for family or paid caregivers**
  - **Informal caregiver**
  - **Care partner**
  - **Carer**



Caregiving role	Terms to be avoided	Less optimal terms	Preferred terms
Provide care primarily because of a <i>personal</i> relationship. They are usually next of kin (spouses, children, or other relatives) but may sometimes be friends or neighbors.	<i>"Informal caregiver"</i> Family caregivers may find this term insulting and invalidating, and it is an inaccurate description of the complex tasks performed by today's caregivers.	<i>"Care partner" or "Carer"</i> In North America, these terms do not clearly distinguish family caregivers from paid care providers.	<i>'Family caregiver'</i> <i>"Family/Friend caregiver"</i> <i>"Unpaid caregiver"</i>



- Bottom Line

- Increases your sensitivity which translates to effectiveness
- Suggest adherence to better language
- [https://alzheimer.ca/sites/default/files/2017-11/Person\\_Centred\\_Language\\_Guidelines-e.pdf](https://alzheimer.ca/sites/default/files/2017-11/Person_Centred_Language_Guidelines-e.pdf)





Falls



## CLINICAL INVESTIGATIONS

# Subclinical Cardiovascular Disease and Fall Risk in Older Adults: Results From the Atherosclerosis Risk in Communities Study

*Stephen P. Juraschek, MD, PhD,\*  Natalie Daya, MHS,<sup>†</sup> Lawrence J. Appel, MD, MPH,<sup>†</sup> Edgar R. Miller III MD, PhD,<sup>†</sup> Kunihiro Matsushita, MD, PhD,<sup>†</sup> Erin D. Michos, MD, MHS,<sup>†</sup>  B. Gwen Windham, MD, MHS,<sup>‡</sup> Christie M. Ballantyne, MD,<sup>§</sup> and Elizabeth Selvin, PhD, MPH\**

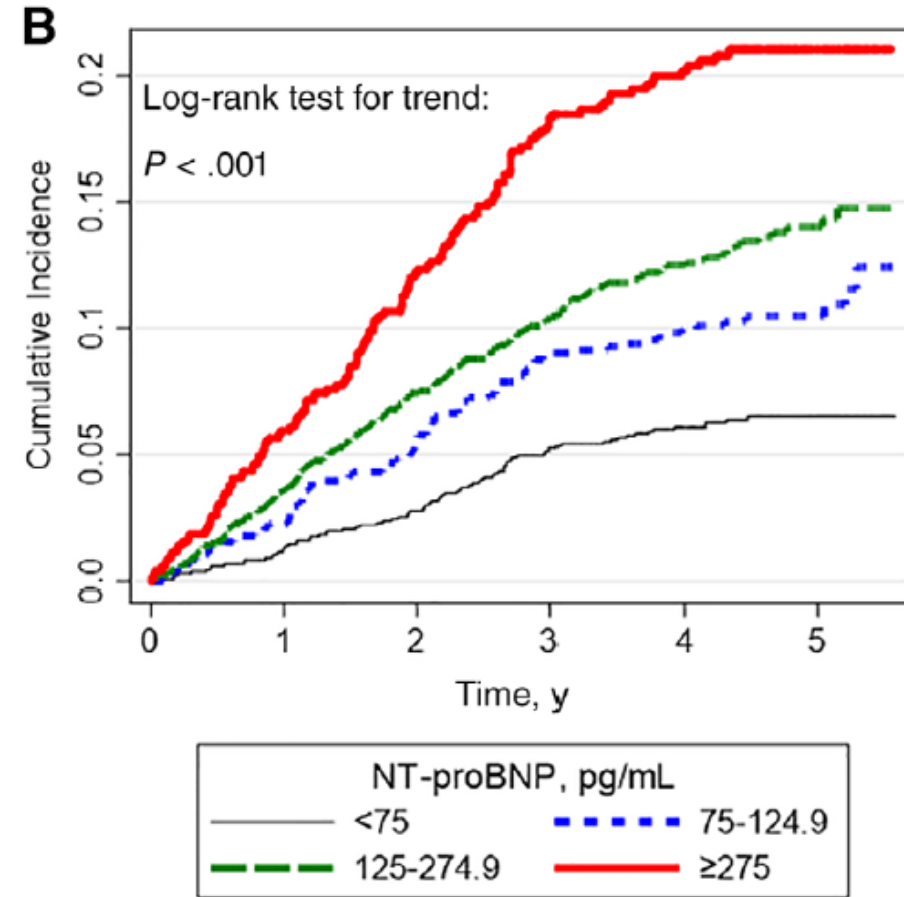
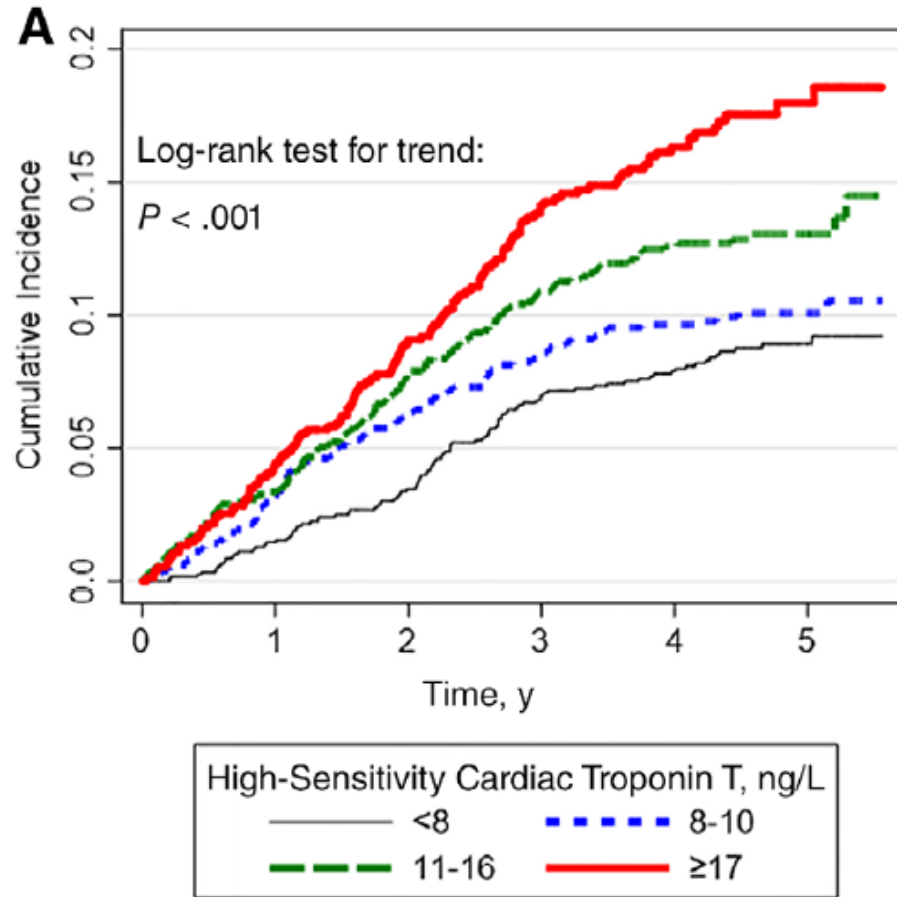


- **Prospective cohort study**
  - **Atherosclerosis Risk In Communities Study (ARIC)**
- **N = 3973**
- **4.5 years**
- **Intervention**
  - **To determine if levels of high-sensitivity cardiac troponin T (hs-cTnT) and N terminal pro-B-type natriuretic peptide (NT-proBNP) in subjects without cardiovascular disease is associated with risk of falls**
- **Primary outcome**
  - **Falls requiring medical attention**
    - **Diagnostic codes for inpatient or outpatient services after baseline visit**



- **Inclusion**
  - **Participants in ARIC cohort without cardiovascular disease**
    - myocardial infarct
    - heart failure
    - stroke
- **Average participant**
  - Age 76
  - 62% female
  - 22% black
  - BMI 29
  - 70% HTN
  - 50% alcohol use
  - 30% DM
  - 10% depressed







- **Results**

- Association remained consistent after adjusting for

- Bottom Line

- Hypothesis generating, do not suggest to measure Tn or BNP for this purpose
      - Unclear if interventions to lower Tn/BNP subsequently reduce falls



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Thank you!