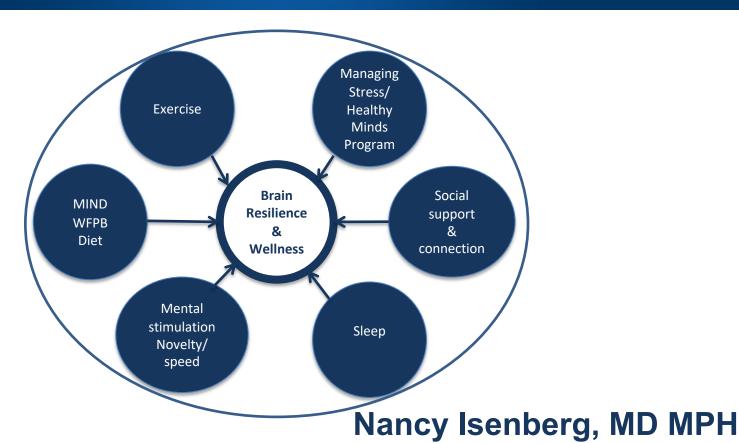
Vascular Cognitive Impairment



Center for Healthy Aging
Swedish Neuroscience Institute
Clinical Associate Professor, Department of Neurology
Project ECHO Dementia 6/26/20

Overview

Learning Objectives

- Define & Identify different types of Vascular Cognitive Impairment (VCI)
- –Understand relationship between VCI and LOAD
- Implement Prevention and RiskReduction strategies

Why is VCI important?

VD is 2nd most common cause of Dementia

May be the most preventable and treatable cause of dementia.

120/80, lipids at goal (LDL-C < 70 post stroke), A1c 5.4,

asp. If TIA/stroke







Amarenco P, Kim JS, Labreuche J, et al., on behalf of the Treat Stroke to Target (TST) Committees and Investigator Centers. Benefit of Targeting a LDL (Low-Density Lipoprotein) Cholesterol <70 mg/dL During 5 Years After Ischemic Stroke. *Stroke* 2020;Feb 20:[Epub ahead of print].

Amarenco P, Kim JS, Labreuche J, et al., on behalf of the Treat Stroke to Target Investigators. A Comparison of Two LDL Cholesterol Targets After Ischemic Stroke. *N Engl J Med* 2020;382:9-19.

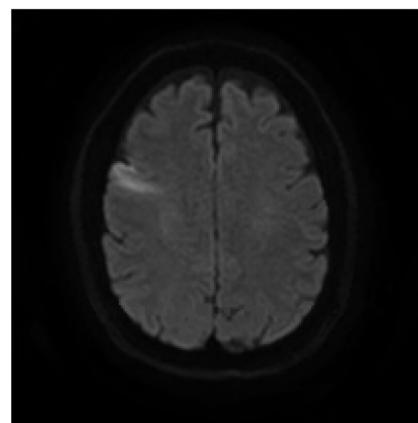
VCI CASE seen this week

47 yo man/weightlifter on testosterone, CAD s/p stenting seen for persistent memory and attentional issues following stroke in 2019

Stoke Risk Factors include: CAD, HLD, PFO s/p repair, anabolic steroids, chewing tobacco, sleep apnea using CPAP, animal protein Mild retrieval inefficiency, disorganized, less efficient.

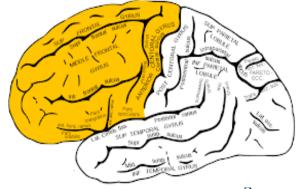
Anxious, irritable

,



Assessing Cognition

- Executive function and speed processing are frequently affected in patients with VCI
 - Why these areas of cognition?
 - Frontal lobe difficulty, reduced phonemic fluency on testing, difficulty organizing and planning a trip, or learning a hand sequence.
 - May test well in structured setting, with significant challenges in real world
 - Often with Neuropsychiatric sx/PBA/Gait dysfunction/LBP
 - Many patients are Mixed LOAD/VD
- Consider Neuropsychological testing



Vascular Cognitive Impairment (VCI)

- Some degree of cognitive impairment + evidence cerebral vascular disease (CVD)
- VCI encompasses a spectrum of severity

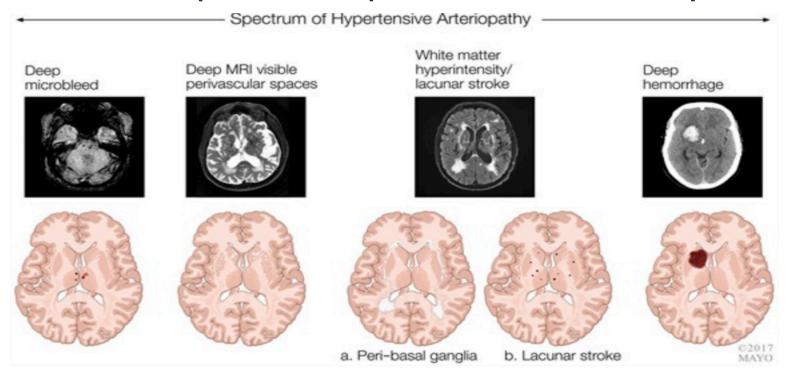
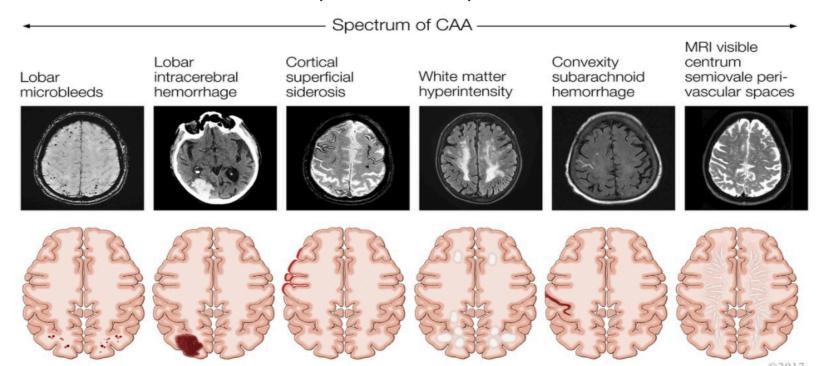


FIGURE 7-1. Spectrum of imaging changes with hypertensive arteriopathy. MRI = magnetic resonance imaging.

CAA spectrum (rare familial assc w/ mutations in APP, ITM2B and CST3 genes)

- Lobar microbleeds
- Lobar ICH
- Cortical superficial siderosis
- WMH
- Convexity subarchnoid hemorrhage
- MRI visible centrum semiovale perivascular spaces

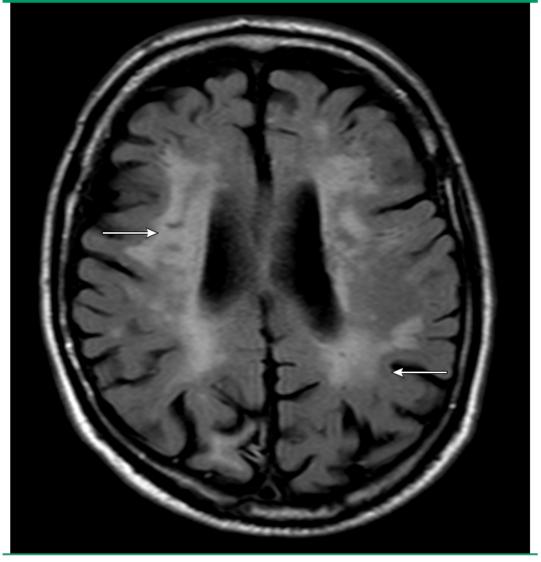


Stroke Statistics by Race and Ethnicity

- Stroke is the fifth leading cause of death for Americans, but the risk of having a stroke varies with race and ethnicity.
- Risk of having a first stroke is nearly twice as high for blacks as for whites, and blacks have the highest rate of death due to stroke. Hispanics have seen an increase in death rates since 2013
- Stroke risk increases with age
- In 2009, 34% of people hospitalized for stroke were less than 65 years old.

CDC.gov

White matter hyperintensities of presumed vascular origin

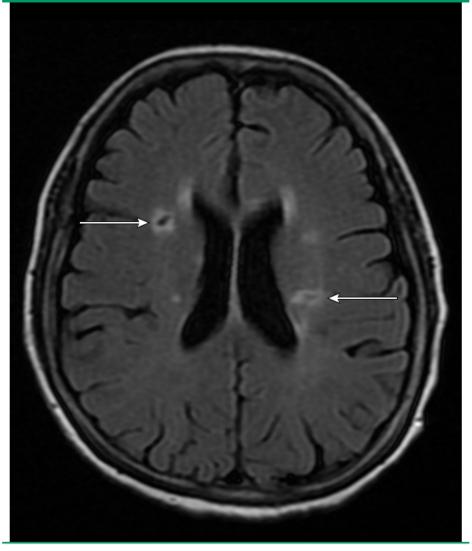


Axial FLAIR magnetic resonance imaging demonstrating white matter hyperintensities of presumed vascular origin (arrows).

 ${\it FLAIR: fluid-attenuated inversion \, recovery.}$

UpToDate[®]

Lacunar brain infarcts



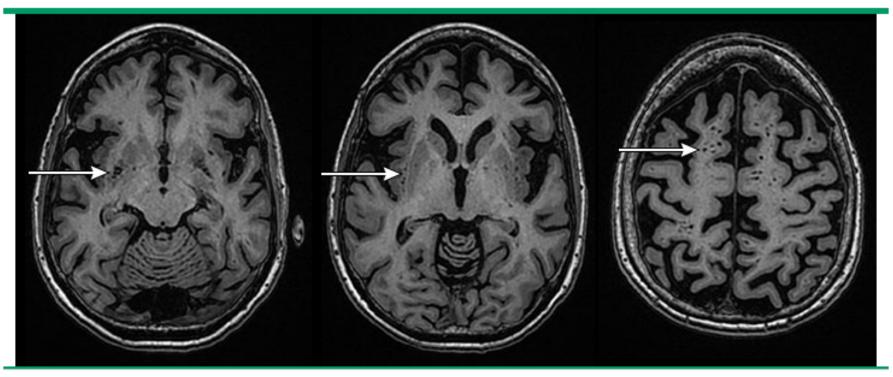
Axial FLAIR magnetic resonance imaging demonstrating lacunar infarcts (arrows). Lacunes are defined radiologically as round or ovoid, subcortical, fluid-filled cavities (signal similar to cerebrospinal fluid) of between 3 and approximately 15 mm in diameter.

FLAIR: fluid-attenuated inversion recovery.

Courtesy of Eric Smith, MD.

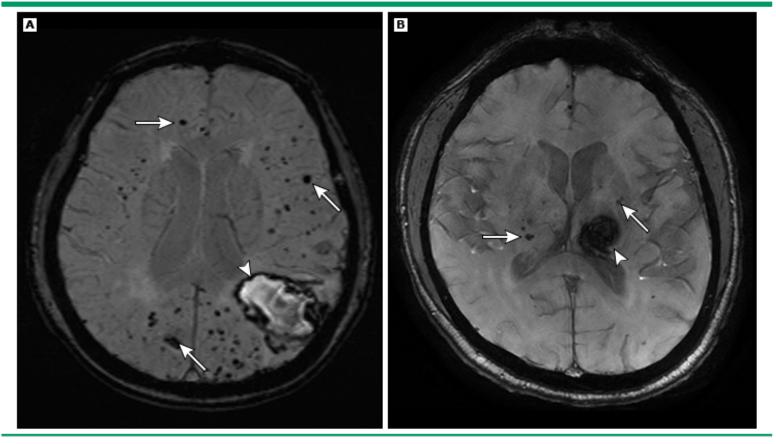
UpToDate°

Prominent perivascular spaces



Axial T1-weighted magnetic resonance images demonstrating prominent perivascular spaces (arrows)pToDate°

Lobar versus nonlobar hemorrhage and microbleeds

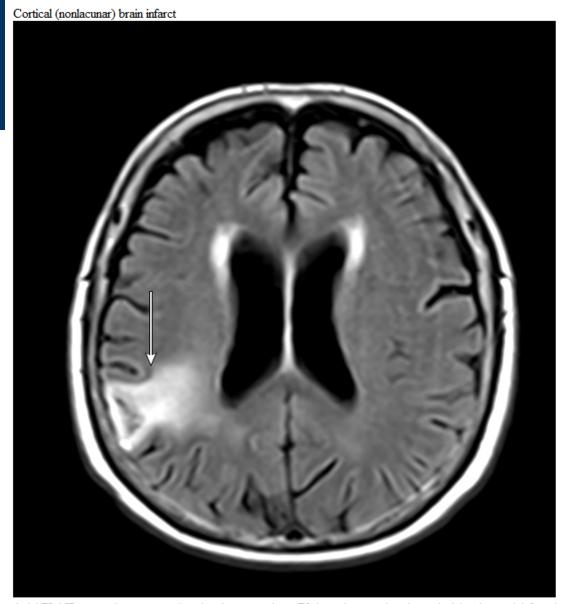


Axial SWI magnetic resonance imaging from two different patients. In panel A, there are multiple lobar hemorrhages including a left parietal lobar hematoma (arrowhead) and many lobar microbleeds (arrows), without microbleeds in the basal ganglia or brainstem (not shown), meeting criteria for probable cerebral amyloid angiopathy. In panel B, there is a left thalamic hematoma (arrowhead) with microbleeds in the basal ganglia (arrows). This pattern of nonlobar hemorrhages is not consistent with cerebral amyloid angiopathy, and instead is probably caused by hypertension.

SWI: susceptibility-weighted imaging.

Courtesy of Eric Smith, MD.





Axial FLAIR magnetic resonance imaging demonstrating a T2-hyperintense chronic cortical (nonlacunar) infarct in the right parietal lobe (arrow).

FLAIR: fluid-attenuated inversion recovery.

Courtesy of Eric Smith, MD.

O'Donnell MJ, Chin SL, Rangarajan S, et al.

Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE):

a case-control study

The Lancet. Published online July 15 2016

9 in 10 strokes are preventable

The 10 main risk factors for stroke are:

HTN~60% risk

Smoking. Nurses Health study RR 2.58 v never smokers

Heavy alcohol

Diabetes RR 2

Poor diet veg diet assc. With 28 % lower incidence CVD

Lack of exercise

HLD

Heart disease (Afib/CAD/CHF)

Obesity

Stress

Other factors sleep apnea, carotid dx, metabolic syndrome, hypercoagulability, inf. (COVID-19), radiotherapy

©2750000 people

Pathologic basis of vascular cognitive impairment

Parenchymal lesions of vascular etiology*

- 1. Large vessel or atherothromboembolic disease
 - a. Multiple infarcts
 - b. Single strategically placed infarct
- 2. Small vessel disease
 - a. Multiple lacunar infarcts in white matter and deep gray matter nuclei
 - b. Ischemic white matter change
 - c. Dilatation of perivascular spaces
 - d. Cortical microinfarcts and microhemorrhages
- 3. Hemorrhage
 - a. Intracerebral hemorrhage
 - b. Multiple cortical and subcortical microbleeds
 - c. Subarachnoid hemorrhage
- 4. Hypoperfusion
 - a. Hippocampal sclerosis
 - b. Laminar cortical sclerosis

Types of vascular lesions

- 1. Atherosclerosis
- 2. Cardiac, atherosclerotic, and systemic emboli
- Arteriolosclerosis
- 4. Lipohyalinosis
- 5. Amyloid angiopathy
- 6. Vasculitis infectious and noninfectious
- 7. Venous collagenosis
- 8. Arteriovenous fistulae dural or parenchymal
- 9. Hereditary angiopathies CADASIL, CARASIL, etc.
- 10. Giant cell arteritis
- 11. Berry aneurysms
- 12. Miscellaneous vasculopathies fibromuscular dysplasia, Moya-Moya
- 13. Systemic microangiopathies without vascular inflammatory cell infiltrates
- 14. Cerebral venous thrombosis

CADASIL: cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy; CARASIL: cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy.

* Microinfarcts may be localized in cortical and subcortical structures because of different etiologies.

From: Sachdev P, Kalaria R, O'Brien J, et al. Diagnostic criteria for vascular cognitive disorders: a VASCOG statement. Alzheimer Dis Assoc Disord 2014; 28:206. DOI:

10.1097/WAD.0000000000000034. Copyright © 2014. Reproduced with permission from Wolters Kluwer Health. Unauthorized reproduction of this material is prohibited.

Cognitive and physical activity and dementia

A 44-year longitudinal population study of women

Jenna Najar, Svante Östling, Pia Gudmundsson, Valter Sundh, Lena Johansson, Silke Kern, Xinxin Guo, Tore Hällström, Ingmar Skoog First published February 20, 2019, DOI: https://doi.org/10.1212/WNL.00000000000007021

- A population-based sample of 800 women aged 38–54 years (mean age 47 years) was followed from 1968 to 2012
- Cognitive activities conferred protection for AD
- Physical activities were protective for mixed dementias and VCI
- Dementia behaves like cardiovascular disease
- Heart health is Brain health
- We need population approach to foster a culture of BRAIN HEALTH



@ Relation of cerebral vessel disease to Alzheimer's disease dementia and cognitive function in elderly people: a cross-sectional study

Zoe Arvanitakis, Ana W Capuano, Sue E Leurgans, David A Bennett, Julie A Schneider

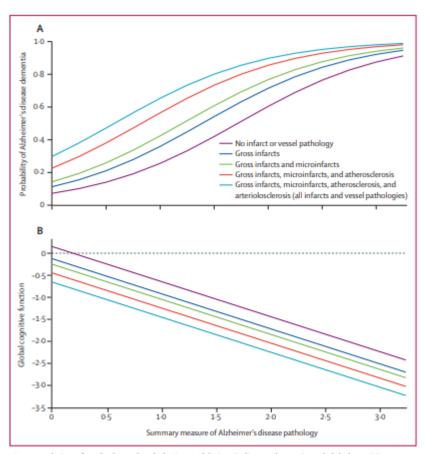


Figure 2: Relation of cerebral vessel pathologies to Alzheimer's disease dementia and global cognitive function

(A) The probability of Alzheimer's disease dementia by Alzheimer's disease pathology, showing separate effects of infarcts and cerebral vessel pathologies. (B) The relation of Alzheimer's disease pathology to global cognitive function, showing separate effects of infarcts and cerebral vessel pathologies.

Review

> Ageing Res Rev. 2020 Mar;58:101002. doi: 10.1016/j.arr.2019.101002.

Epub 2019 Dec 30.

A Third of Community-Dwelling Elderly With Intermediate and High Level of Alzheimer's Neuropathologic Changes Are Not Demented: A Meta-Analysis

Mahmoud Reza Azarpazhooh ¹, Abolfazl Avan ², Lauren E Cipriano ³, David G Munoz ⁴, Mahdiyeh Erfanian ⁵, Amin Amiri ⁶, Saverio Stranges ⁷, Vladimir Hachinski ⁸

Viewpoint

ONLINE FIRST

April 27, 2020

White Matter Degeneration—A Treatable Target?

Austyn Roseborough, MSc¹; Vladimir Hachinski, MD, DSc²; Shawn Whitehead, PhD¹

Author Affiliations | Article Information

JAMA Neurol. Published online April 27, 2020. doi:10.1001/jamaneurol.2020.0814

Healthy lifestyle and the risk of Alzheimer dementia

Findings from 2 longitudinal studies

Klodian Dhana, MD, PhD, Denis A. Evans, MD, Kumar B. Rajan, PhD, David A. Bennett, MD, and Martha C. Morris, ScD

Neurology® 2020;95:1-10. doi:10.1212/WNL.00000000009816

Correspondence

Dr. Dhana klodian_dhana@rush.edu

Figure HRs of AD according to the combination of healthy lifestyle factors in the prospective cohort studies

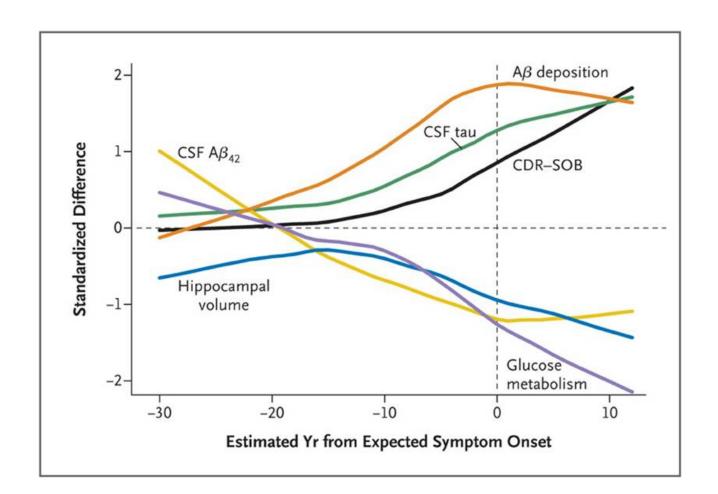
Number of healthy	N	% of AD		Unroud votic (OFN/ CI)
lifestyle factors	IN	% OF AD		Hazard ratio (95% CI)
0–1 healthy factor				
CHAP 0-1	322	24.4		1.00 (1.00, 1.00)
MAP 0-1	123	31.7		1.00 (1.00, 1.00)
2–3 healthy factors				
CHAP 2-3	1,073	15.4	⊢	0.58 (0.37, 0.93)
MAP 2-3	507	26.4	⊢	0.66 (0.46, 0.94)
Combined (p for heterogeneity = 0.7)	ĺ			0.63 (0.47, 0.84)
4–5 healthy factors				
CHAP 4-5	450	8.1	·	0.33 (0.18, 0.61)
MAP 4-5	290	19.3	⊢	0.43 (0.28, 0.66)
Combined (p for heterogeneity = 0.5)				0.40 (0.28, 0.56)
			 	\neg
		0.10	0.25 0.50 1.00	2.00
			Hazard ratio	

Model adjusted for age, sex, race, education, $APOE \ \epsilon A$, and prevalence of cardiovascular disease (including heart disease or stroke). A random-effects metaanalysis was used to combine cohort-specific results. AD = Alzheimer dementia; CHAP = Chicago Health and Aging Project; CI = confidence interval; HR = hazard ratio; MAP = Rush Memory and Aging Project; N = number of participants in each group. "Should we begin to think of lifelong control of Aβ metabolism in the same way that we now think of lifelong control of cholesterol metabolism? The lesson of the DIAN study and of the study on the protective APP mutation is that reduction of the risk of late-life dementia requires a long-term and possibly lifelong effort."

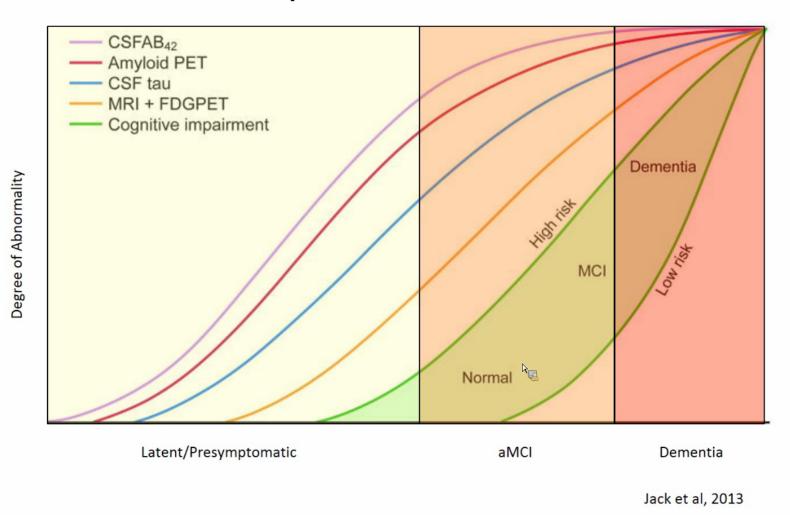
S. Gandy MD

N. Front Limed 2012, Nature 2012

Early Detection and Intervention

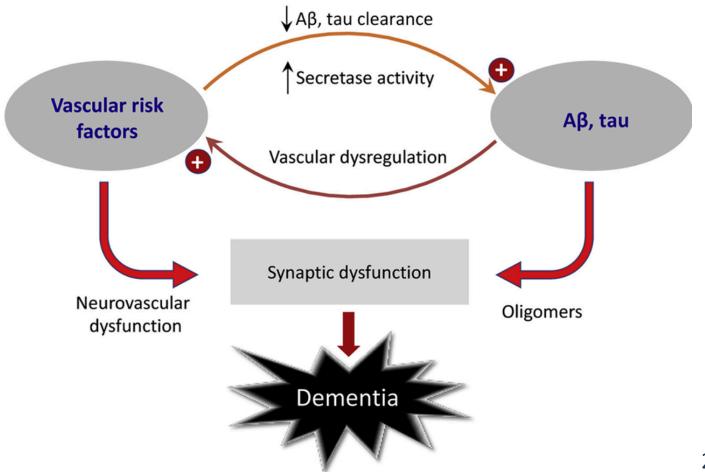


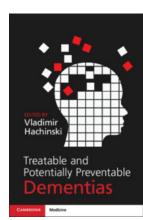
Canonical Sequence of AD Biomarkers



Preventing Dementia by Preventing Stroke: The Berlin Manifesto

Vladimir Hachinski ¹, Karl Einhäupl ², Detlev Ganten ³, Suvarna Alladi ⁴, Carol Brayne ⁵, Blossom C M Stephan ⁶, Melanie D Sweeney ⁷, Berislav Zlokovic ⁷, Yasser Iturria-Medina ⁸, Costantino ladecola ⁹, Nozomi Nishimura ¹⁰, Chris B Schaffer ¹⁰, Shawn N Whitehead ¹¹, Sandra E Black ¹², Leif Østergaard ¹³, Joanna Wardlaw ¹⁴, Steven Greenberg ¹⁵, Leif Friberg ¹⁶, Bo Norrving ¹⁷, Brian Rowe ¹⁸, Yves Joanette ¹⁹, Werner Hacke ²⁰, Lewis Kuller ²¹, Martin Dichgans ²², Matthias Endres ²³, Zaven S Khachaturian ²⁴





WORLD STROKE ORGANIZATION DECLARATION



Emphasis on population-wide strategies (reduction of exposure to risk factors among the whole population and motivational population-wide prevention strategy with the control of risk factors in all people with increased stroke risk regardless of the level of risk)



Abandoning categorisation of people into low, moderate, and high risk; advocating an holistic prevention approach



Ideally combining community interventions (eg, health workers in low-income and middle-income countries, nurse educators in high-income countries), pharmacological (eg, polypill), and non-pharmacological (eg, lifestyle modification via the Stroke Riskometer app) interventions for people at risk of stroke

Figure: Key principles of the WSO Declaration on the primary prevention of stroke and dementia globally

Lancet Neurology June 2020 50% reduction stroke incidence, 30% reduction dementia incidence globally

> Public Health Rep. 2020 Jan;135(1):132-140. doi: 10.1177/0033354919893030.

Cognitive Impairment and Cardiovascular Disease: A Comparison of Risk Factors, Disability, Quality of Life, and Access to Health Care

Mary L Adams ¹, Joseph Grandpre ², David L Katz ³, Douglas Shenson ⁴ ⁵

DM

Ever smoked

HTN

HLD

Poor veg /fruit intake

Obesity

Sedentary

Behavioral risk factor surveillance system (BRFSS)

Ageing without Dementia

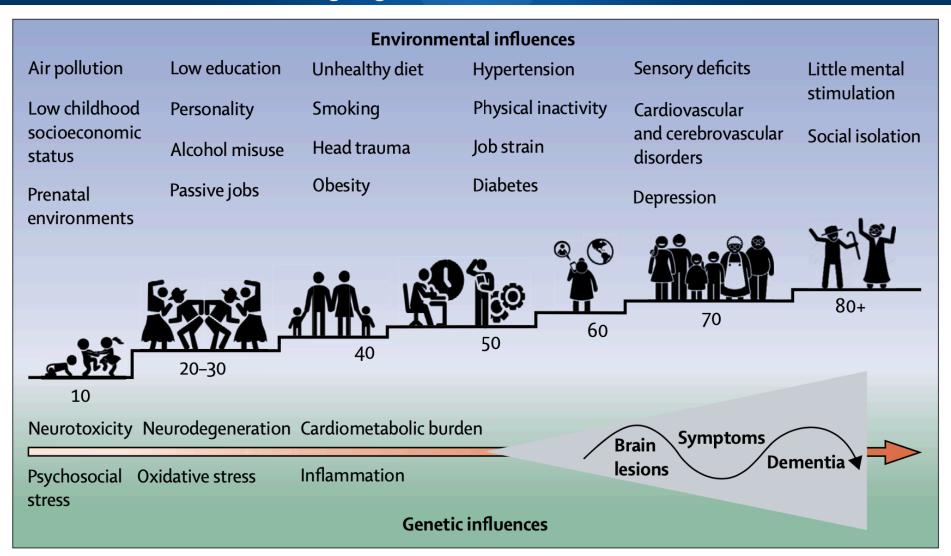


Figure 1: A life course model of dementia development

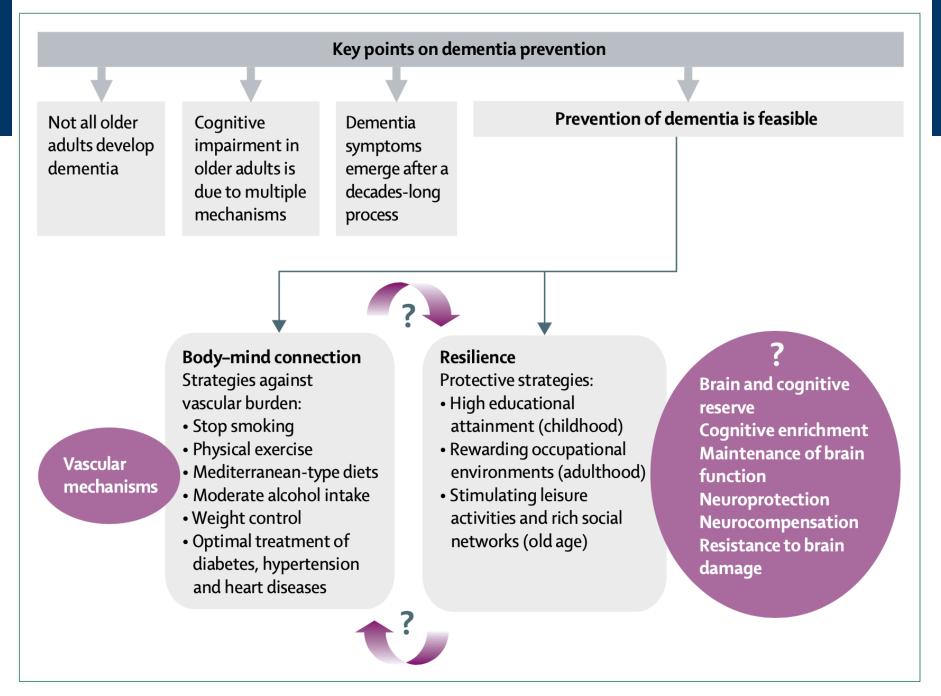


Figure 2: Preventive strategies in dementia

Teaching Resources

- -https://www.aarp.org/health/brain-health/global-council-on-brain-health/heart-health/
- -www.stroke.org health tools
- -https://www.alz.org/alzheimersdementia/what-is-dementia/types-ofdementia/vascular-dementia
- -https://tryhealthyminds.org

Brain Health & Wellness

Conditions • Brain Games • Global Council on Brain Health • Staying Sharp



To Protect Your Brain, Take Care of Your Heart



Report finds evidence cardio health is directly linked to cognition













Evidence to support harm

Sugar-sweetened beverages increase risk of type 2 diabetes and obesity

Red and processed meats increase CVD and cancer risk

Coconut oil, butter, margarine and other oils that congeal at room temperature increase CVD risk

Excess alcohol intake increases CVD and cancer risk

CAUTION!

Weak/insufficient evidence to support benefit

Juicing fruits and vegetables concentrates calones and reduces fiber content

Moderate alcohol consumption may have a positive CVD benefit but increases risk of cancer^a

Low carbohydrate
high fat diets may
promote weight-loss,
although long-term
effects on CVD outcomes
are unclear



Strong evidence to support benefit

Leafy green vegetable consumption improves CVD risk

Legume consumption offers a sustainable source of protein and promotes weight loss

Moderate coffee consumption has been shown to have a CVD protective effect

Low sodium intake lowers blood pressure and risk of hypertension

Mediterranean diet, DASH diet, and plantbased diet are recommended by multiple societies for their CVD benefit

Contact Information

Center for Healthy Aging



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