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# Lifestyle Medicine and Dementia

- Beth Frates, MD FACLM DipABLM
- Harvard Medical School
- Assistant Clinical Professor
- Department of PM&R
- President of American College of Lifestyle Medicine (ACLM)

# Disclosures

- Scientific Advisory Board of Jenny Craig
- Medical Advisory Board of obVus Solutions
- Private Practice-lifestyle medicine consulting-Wellness Synergy

# Goals

- Define Lifestyle Medicine
- Review 6 Pillars
- Examine each pillar in relation to dementia
- Tips and strategies for patients with dementia
- Consider the care-givers



# How is Lifestyle Medicine Defined?

- Lifestyle medicine is a medical specialty that uses therapeutic lifestyle interventions as a primary modality to treat chronic conditions including, but not limited to, cardiovascular diseases, type 2 diabetes, and obesity. Lifestyle medicine certified clinicians are trained to apply evidence-based, whole-person, prescriptive lifestyle change to treat and, when used intensively, often reverse such conditions. Applying the six pillars of lifestyle medicine—a whole-food, plant-predominant eating pattern, physical activity, restorative sleep, stress management, avoidance of risky substances and positive social connections—also provides effective prevention for these conditions.
- -ACLM website

# The 6 Pillars of Lifestyle Medicine



# Preventing Dementia

- Don't smoke.
- Stay at a healthy weight.
- Get plenty of exercise.
- Eat healthy food.
- Manage health problems including diabetes, high blood pressure, and high cholesterol.
- Stay mentally alert by learning new hobbies, reading, or solving crossword puzzles.
- Stay involved socially. Attend community activities, church, or support groups.
- If your doctor recommends it, take aspirin.

- <https://stanfordhealthcare.org/medical-conditions/brain-and-nerves/dementia/prevention.html>

# Risk Factors for Dementia-NHS in UK

- age: the older you are, the more likely you are to develop dementia. However, dementia is not a natural part of ageing
- genes: in general, genes alone are not thought to cause dementia. However, certain genetic factors are involved with some of the less common types. Dementia usually develops because of a combination of genetic and "environmental" factors, such as smoking and a lack of regular exercise
- lower levels of education
- <https://www.nhs.uk/conditions/dementia/dementia-prevention/>

# Risk Factors for Dementia

- [hearing loss](#)
- untreated [depression](#)
- [loneliness](#) or social isolation
- sitting for most of the day
- <https://www.nhs.uk/conditions/dementia/dementia-prevention/>



# Nutrition

- **The risk:** a diet that's high in saturated fat, salt and sugar, and low in fibre, can increase your risk of [high blood pressure](#), [high cholesterol](#), becoming overweight or obese, and type 2 diabetes.
- <https://www.nhs.uk/conditions/dementia/dementia-prevention/>

# Recommendations:

- eating a healthy, balanced diet
- maintaining a healthy weight
- exercising regularly
- keeping alcohol within recommended limits
- stopping smoking
- keeping your [blood pressure](#) at a healthy level
- <https://www.nhs.uk/conditions/dementia/dementia-prevention/>

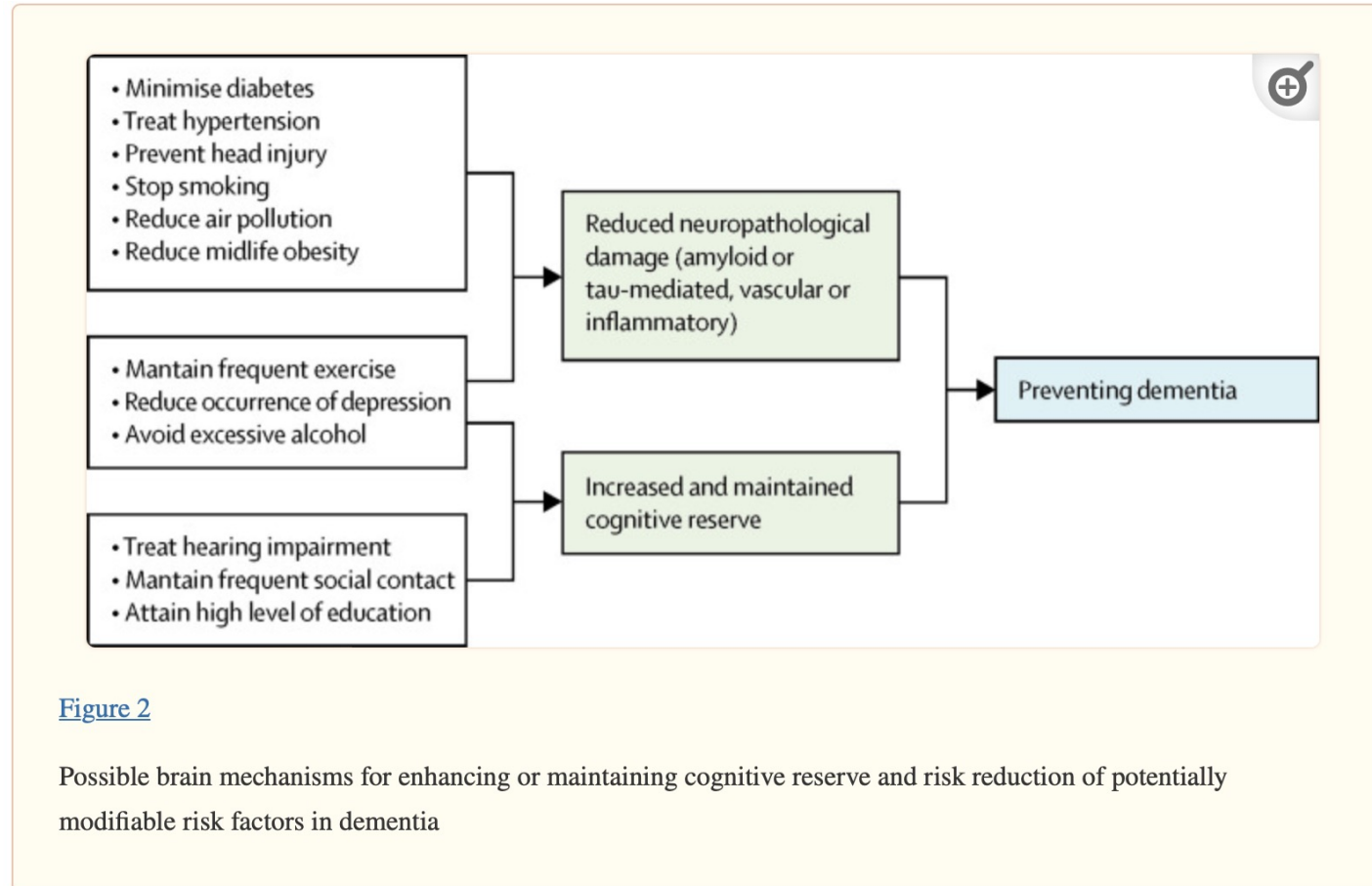
# Taking into account different populations

- Research shows that African Americans, American Indians, and Alaska Natives have the highest rates of dementia.
- <https://www.alzheimers.gov/life-with-dementia/can-i-prevent-dementia>

# Lancet 2020 Dementia Prevention

- Livingston G, Huntley J, Sommerlad A, Ames D, Ballard C, Banerjee S, Brayne C, Burns A, Cohen-Mansfield J, Cooper C, Costafreda SG, Dias A, Fox N, Gitlin LN, Howard R, Kales HC, Kivimäki M, Larson EB, Ogunniyi A, Orgeta V, Ritchie K, Rockwood K, Sampson EL, Samus Q, Schneider LS, Selbæk G, Teri L, Mukadam N. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission.
- Lancet. 2020 Aug 8;396(10248):413-446.

# Figure 2



# Three new modifiable risk factors for dementia

- New evidence supports adding three modifiable risk factors
- **AVOID: excessive alcohol consumption, head injury, and air pollution—**
- 2017 *Lancet* Commission on dementia prevention, intervention, and care life-course model of nine factors (avoid-- less education, hypertension, hearing impairment, smoking, obesity, depression, physical inactivity, diabetes, and infrequent social contact).
- 12 FACTORS

- *Lancet*. 2020 Aug 8;396(10248):413-446

Prevent or delay up to  
40% of dementia cases

- Modifying 12 risk factors might prevent or delay up to 40% of dementias.

- Lancet. 2020 Aug 8;396(10248):413-446

# Be ambitious about prevention

- Prevention is about policy and individuals.
- Contributions to the risk and mitigation of dementia begin early and continue throughout life, so it is never too early or too late.
- These actions require both public health programs and individually tailored interventions.
- In addition to population strategies, policy should address high-risk groups to increase social, cognitive, and physical activity; and vascular health.

- Lancet. 2020 Aug 8;396(10248):413-446



## Specific Recommendations:

- Aim to maintain systolic BP of 130 mm Hg or less in midlife from around age 40 years.
- Encourage use of hearing aids for hearing loss and reduce hearing loss by protection of ears from excessive noise exposure
- Reduce exposure to air pollution and second-hand tobacco smoke.
- Prevent head injury.

- Lancet. 2020 Aug 8;396(10248):413-446

# Leading Causes of Traumatic Brain Injury in the United States (2013)



# Substance Use

- Limit alcohol use, as alcohol misuse and drinking more than 21 units weekly increase the risk of dementia.
  - Avoid smoking uptake and support smoking cessation to stop smoking, as this reduces the risk of dementia even in later life.
- Lancet. 2020 Aug 8;396(10248):413-446

## Recommendations Continued

- Provide all children with primary and secondary education.
- Reduce obesity and the linked condition of diabetes. Sustain midlife, and possibly later life physical activity.
- Addressing other putative risk factors for dementia, like sleep, through lifestyle interventions, will improve general health.

• Lancet. 2020 Aug  
8;396(10248):413-446

# Tackle inequality and protect people with dementia

- Many risk factors cluster around inequalities, which occur particularly in Black, Asian, and minority ethnic groups and in vulnerable populations.
- Tackling these factors will involve not only health promotion but also societal action to improve the circumstances in which people live their lives.
- Examples include creating environments that have physical activity as a norm, reducing the population profile of blood pressure rising with age through better patterns of nutrition, and reducing potential excessive noise exposure.

- Lancet. 2020 Aug 8;396(10248):413-446

# Addressing dementia in other countries

- Dementia is rising more in low-income and middle-income countries (LMIC) than in high-income countries, because of population aging and higher frequency of potentially modifiable risk factors.
- Preventative interventions might yield the largest dementia reductions in LMIC.

• Lancet. 2020 Aug 8;396(10248):413-446

# Pillar 1: Increase Physical Activity

- Six minutes of high-intensity cycling intervals increased every metric of circulating BDNF by 4 to 5 times more than prolonged low-intensity cycling.
  - Six 40-s intervals at 100% of  $\dot{V}O_{2\text{peak}}$  increased plasma and serum BDNF
  - Working with a dozen men and women
  - BDNF increased four to five times more compared to fasting, which showed no BDNF change, or prolonged activity, which showed a slight increase in BDNF.
- Gibbons TD, Cotter JD, Ainslie PN, Abraham WC, Mockett BG, Campbell HA, Jones EMW, Jenkins EJ, Thomas KN.
  - Fasting for 20 h does not affect exercise-induced increases in circulating BDNF in humans. *J Physiol.* 2023 Jan 11



# Physical Activity

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9484730/>

Zhu J, Ge F, Zeng Y, Qu Y, Chen W, Yang H, Yang L, Fang F, Song H. Physical and Mental Activity, Disease Susceptibility, and Risk of Dementia: A Prospective Cohort Study Based on UK Biobank. *Neurology*. 2022 Aug 23;99(8):e799-e813.

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# Results

- The mean age at recruitment was 56.53, and 45.60% of the participants were male.
- UK Biobank, 501,376 dementia-free participants were recruited
- Follow up of 10.66 years—prospective study
- 5,185 dementia cases were identified
- When analyzed separately, multiple studied items related to physical and mental activity showed significant associations with the risk of dementia.
- The pattern analyses revealed that a higher level of adherence to activity patterns related to
  - frequent vigorous and other exercises (hazard ratio 0.65, 95% CI 0.59–0.71),
  - housework-related activity (0.79, 0.72–0.85), and
  - friend/family visit (0.85, 0.75–0.96)
- was associated with a lower risk of dementia.

# Strength Training

- Broadhouse, K. M., Singh, M. F., Suo, C., Gates, N., Wen, W., Brodaty, H., Jain, N., Wilson, G. C., Meiklejohn, J., Singh, N., Baune, B. T., Baker, M., Foroughi, N., Wang, Y., Kochan, N., Ashton, K., Brown, M., Li, Z., Mavros, Y., ... Valenzuela, M. J. (2020).
- Hippocampal plasticity underpins long-term cognitive gains from resistance exercise in MCI.
- NeuroImage: Clinical, 25, 102182.

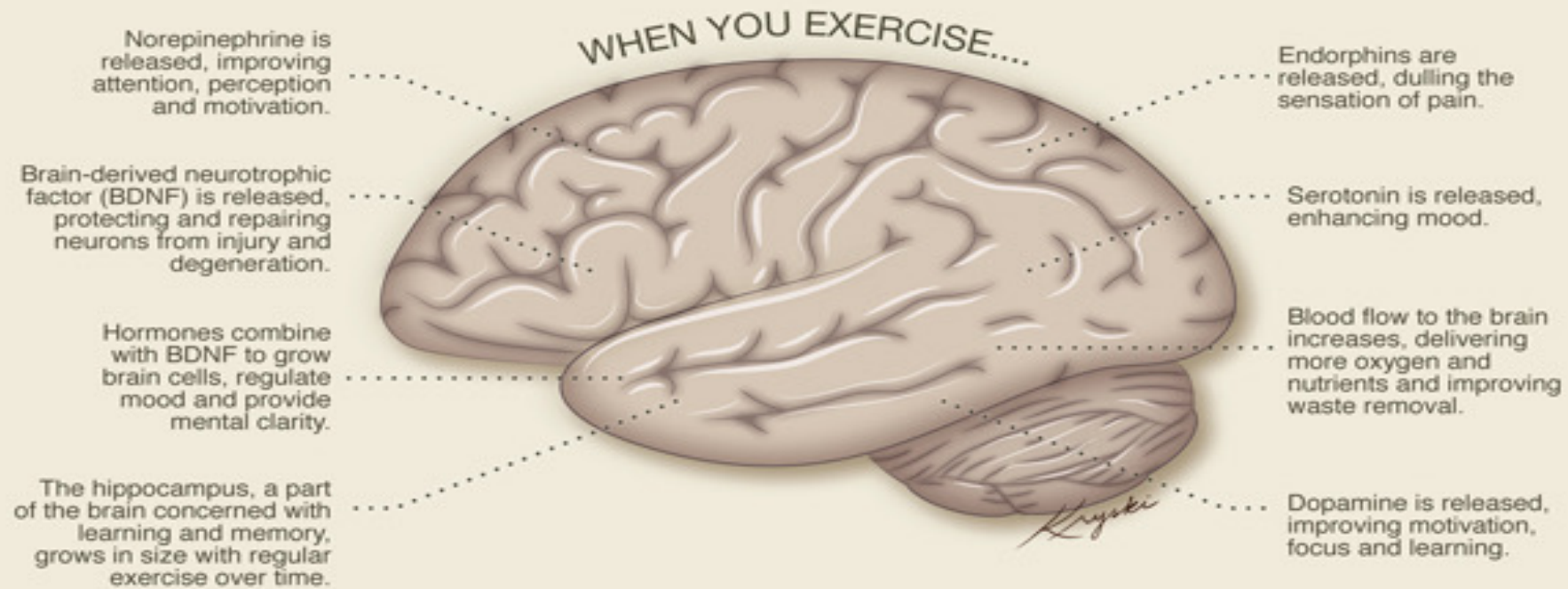
# Study

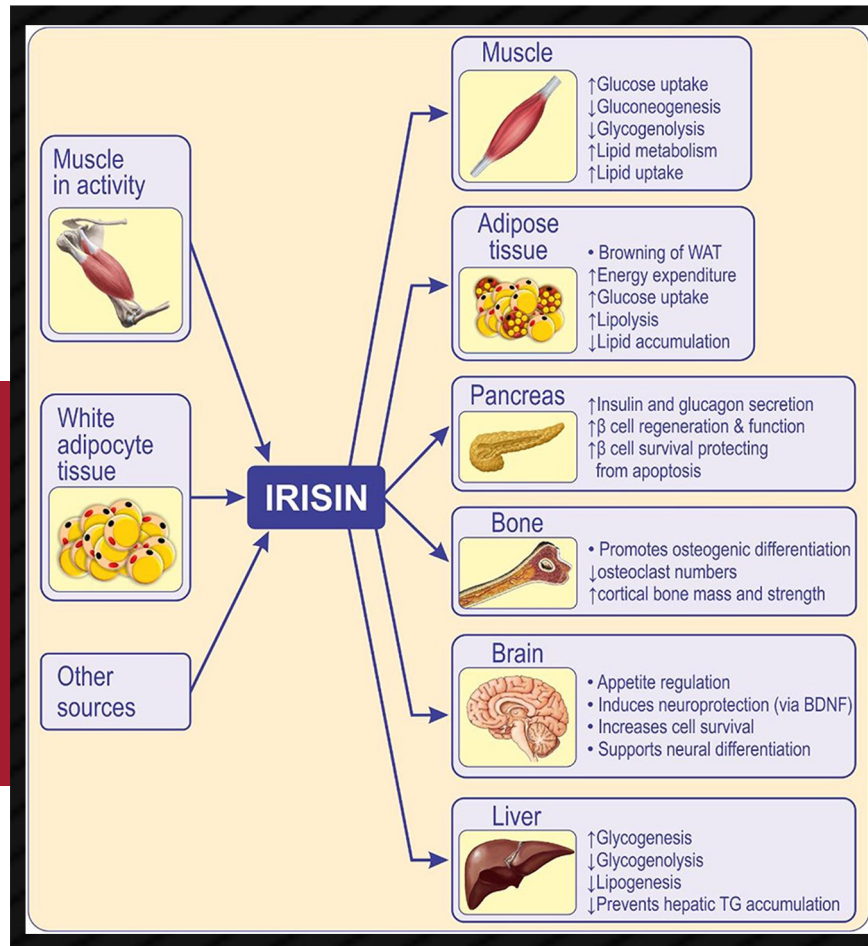
- One hundred MCI participants
- Participants in this study did supervised strength training for just 90 minutes in total each week, over two or three weekly sessions for 6 months
- The hippocampus subregions targeted by the strength training were those especially vulnerable to Alzheimer's disease. In the control condition, where no strength training was undertaken hippocampal subregions shrunk by 3-4 percent over the 18-months, whilst those undergoing strength training saw only 1-2 percent reductions, and in some areas, none at all.

# Why exercise?

Table 1. B
Variable
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Myocardia
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High dens
Triglycerid
Body weig
Insulin res
<b>Physical f</b>
Fitness/st
Exercise c
Performanc
Return to v
<b>Psycholog</b>
Depressio
Anxiety
Quality of

## YOUR BRAIN LOVES THE GYM (OR SIDEWALK, BIKE TRAIL, POOL,...)





Arhire, Lidia I., Laura Mihalache, and Mihai Covasa. "Irisin: a hope in understanding and managing obesity and metabolic syndrome." *Frontiers in endocrinology* 10 (2019): 524.

# Lac Phe

nature

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Article | [Published: 15 June 2022](#)

## An exercise-inducible metabolite that suppresses feeding and obesity

[Veronica L. Li](#), [Yang He](#), [Kévin Contrepois](#), [Hailan Liu](#), [Joon T. Kim](#), [Amanda L. Wiggenhorn](#), [Julia T. Tanzo](#), [Alan Sheng-Hwa Tung](#), [Xuchao Lyu](#), [Peter-James H. Zushin](#), [Robert S. Jansen](#), [Basil Michael](#), [Kang Yong Loh](#), [Andrew C. Yang](#), [Christian S. Carl](#), [Christian T. Voldstedlund](#), [Wei Wei](#), [Stephanie M. Terrell](#), [Benjamin C. Moeller](#), [Rick M. Arthur](#), [Gareth A. Wallis](#), [Koen van de Wetering](#), [Andreas Stahl](#), [Bente Kiens](#), ... [Jonathan Z. Long](#)  [+ Show authors](#)

[Nature](#) **606**, 785–790 (2022) | [Cite this article](#)

**51k** Accesses | **7** Citations | **1940** Altmetric | [Metrics](#)

### Abstract

Exercise confers protection against obesity, type 2 diabetes and other cardiometabolic diseases<sup>1,2,3,4,5</sup>. However, the molecular and cellular mechanisms that mediate the metabolic benefits of physical activity remain unclear<sup>6</sup>. Here we show that exercise stimulates the production of *N*-lactoyl-phenylalanine (Lac-Phe), a blood-borne signalling metabolite that suppresses feeding and obesity. The biosynthesis of Lac-Phe

• “metabolite as a molecular effector associated with physical activity across multiple activity modalities and mammalian species.”

# Pillar 2- Nutrition

- It has been proven that dietary habits, which lead to the development of cardiovascular and metabolic diseases, significantly increase the risk of dementia.
- On the other hand, a Mediterranean diet rich in antioxidants, fiber and omega-3 polyunsaturated fatty acids may have a protective effect on the neurodegenerative process.
- The beneficial effect of many nutrients on the course of AD has been demonstrated. These include: glutathione, polyphenols, curcumin, coenzyme Q10, vitamins B6, B12, folic acid, unsaturated fatty acids, and caffeine.
- A diet rich in saturated fatty acids promotes the progression of dementia.
- Dietary intervention should be introduced as early as possible to minimize the risk of developing dementia.
- The Mediterranean and DASH diets have been documented to protect against AD.
- However, the MIND diet is reported to be much more effective in preventing cognitive decline/dementia than either the Mediterranean or DASH diets alone.

Co Enzyme Q10 soybeans, nuts, seeds

- Śliwińska S, Jeziorek M. The role of nutrition in Alzheimer's disease. Rocz Panstw Zakl Hig. 2021;72(1):29-39.

Glutathione-Sulfur containing vegetables:

cruciferous vegetables like broccoli, Brussels sprouts, cauliflower, kale, watercress and mustard greens.

Allium vegetables, including garlic, shallots and onions, also boost glutathione levels — likely due to their sulfur-containing compounds

# Nutrition Continued

- A combination of the Mediterranean and DASH diets is called the MIND diet (MIND stands for Mediterranean-DASH Intervention for Neurodegenerative Delay).
- This diet is designed to improve cognitive performance and lower the risk of developing neurodegenerative diseases such as AD.
- In addition to DASH and Mediterranean diets, MIND diet emphasizes the consumption of food products that have a positive effect on brain function such as green leafy vegetables (spinach, kale, lettuce) and berries (strawberries, blueberries, blueberries and raspberries).
- These products should be eaten 6 times a week.
- Other food products recommended on the MIND diet include **vegetables, nuts, pulses, whole grains, fish, poultry, olive oil, and red wine.**
- On the other hand, the MIND diet encourages limiting the consumption of **red meat, butter, margarine, cheese, sweets and fried foods.**



# Nutrition Information Specifics

The diet of patients with AD should be balanced and provide the right amount of energy.

The clinical value of antioxidants for the prevention of AD is ambiguous.

Vitamins C and A do not inhibit the progression of cognitive disorders.

Research on the protective effect of vitamin E is contradictory.

Research has revealed that curcumin not only prevents aggregation of new amyloid- $\beta$  deposits, but also reduces the size of remaining ones.

Vitamins B6, B12 and folic acid maintain a healthy nervous system and may be helpful in the treatment of AD.

Excessive intake of saturated fatty acids can aggravate cognitive disorders.

Consuming unsaturated fatty acids prevents cognitive decline.

Caffeine may protect against cognitive disorders and dementia due to its neuroprotective and neuromodulatory properties.

The Mediterranean diet not only reduces inflammation and oxidative stress, but is also associated with reduced loss of brain volume and slower AD progression.

DASH diet has positive results if followed for a longer period of time, even before the first symptoms of dementia begin to appear, and therefore it can only be used as the prevention of cognitive decline.

The MIND diet turned out to be much more effective in preventing dementia than the Mediterranean and DASH diets alone.



# Data Vegetables and Fruits

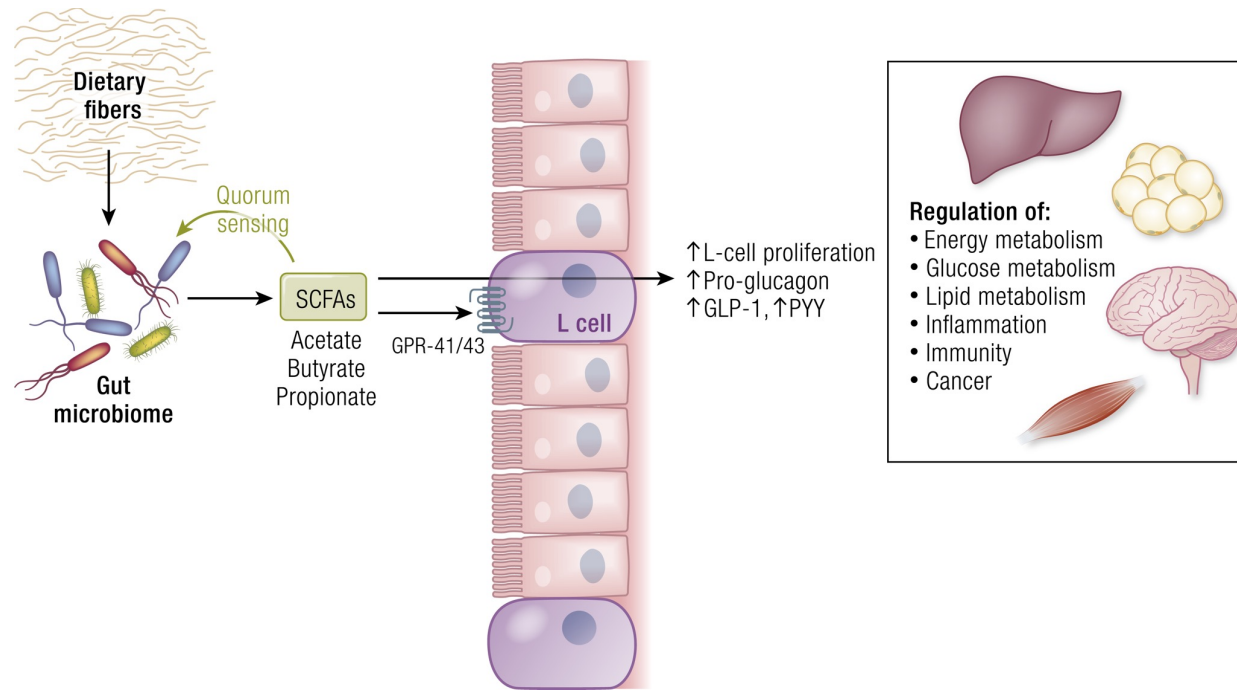
- A meta-analysis of cohort studies following 469,551 participants found that a higher intake of fruits and vegetables is associated with a reduced risk of death from CVD
  - an average reduction in risk of 4% for each additional serving per day of fruit and vegetables.
    - [BMJ](#). 2014 Jul 29;349:g4490
- Nurses Study-Compared with those in the lowest category of fruit and vegetable intake (less than 1.5 servings a day), those who averaged 8 or more servings a day were 30% less likely to have had a heart attack or stroke.
  - [Journal of the National Cancer Institute](#). 2004 Nov 3;96(21):1577-84.
- Individuals who ate more than 5 servings of fruits and vegetables per day had roughly a 20% lower risk of coronary heart disease and stroke, compared with individuals who ate less than 3 servings per day.
  - [Journal of human hypertension](#). 2007 Sep;21(9):717.
  - [The Lancet](#). 2006 Jan 28;367(9507):320-6.

# Fiber helps increase number and diversity of friendly bacteria in the microbiome



- WHO recommends 25 and 29 gms of fiber each day
- Lower incidence of [type 2 diabetes](#), [heart disease](#), [stroke](#), and [colon cancer](#).
- Eat fiber and then friendly bacteria ferment it.
- SCFAs--acetate, propionate, and butyrate.
- SCFAs play key roles in regulating host metabolism, immune system, and cell proliferation.

**Figure 2.** Microbiota-derived SCFAs influence host endocrine functions. Dietary fibers are substrates of the microbial ...



# Pillar 3: Sleep

- People who slept six hours or less per night in their 50s and 60s were more likely to develop dementia later in life.



[Association of sleep duration in middle and old age with incidence of dementia.](#)

Sabia S, Fayosse A, Dumurgier J, van Hees VT, Paquet C, Sommerlad A, Kivimäki M, Dugravot A, Singh-Manoux A. *Nat Commun*. 2021 Apr 20;12(1):2289.

doi: 10.1038/s41467-021-22354-2. PMID: 33879784.

# Sleep

- In a small study, losing just one night of sleep led to an increase in beta-amyloid, a protein in the brain associated with impaired brain function and Alzheimer's disease.



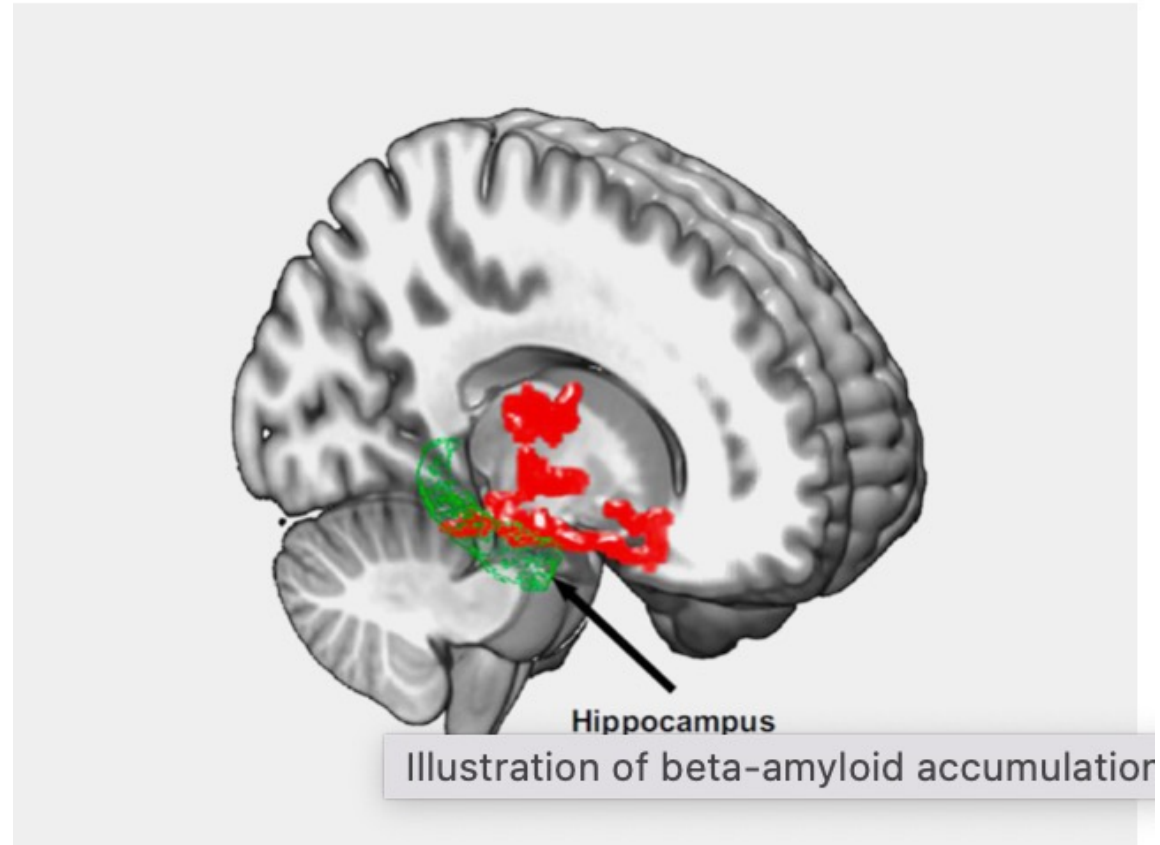
## [β-Amyloid accumulation in the human brain after one night of sleep deprivation.](#)

Shokri-Kojori E, Wang GJ, Wiers CE, Demiral SB, Guo M, Kim SW, Lindgren E, Ramirez V,

Zehra A, Freeman C, Miller G, Manza P, Srivastava T, De Santi S, Tomasi D, Benveniste H, Volkow ND.

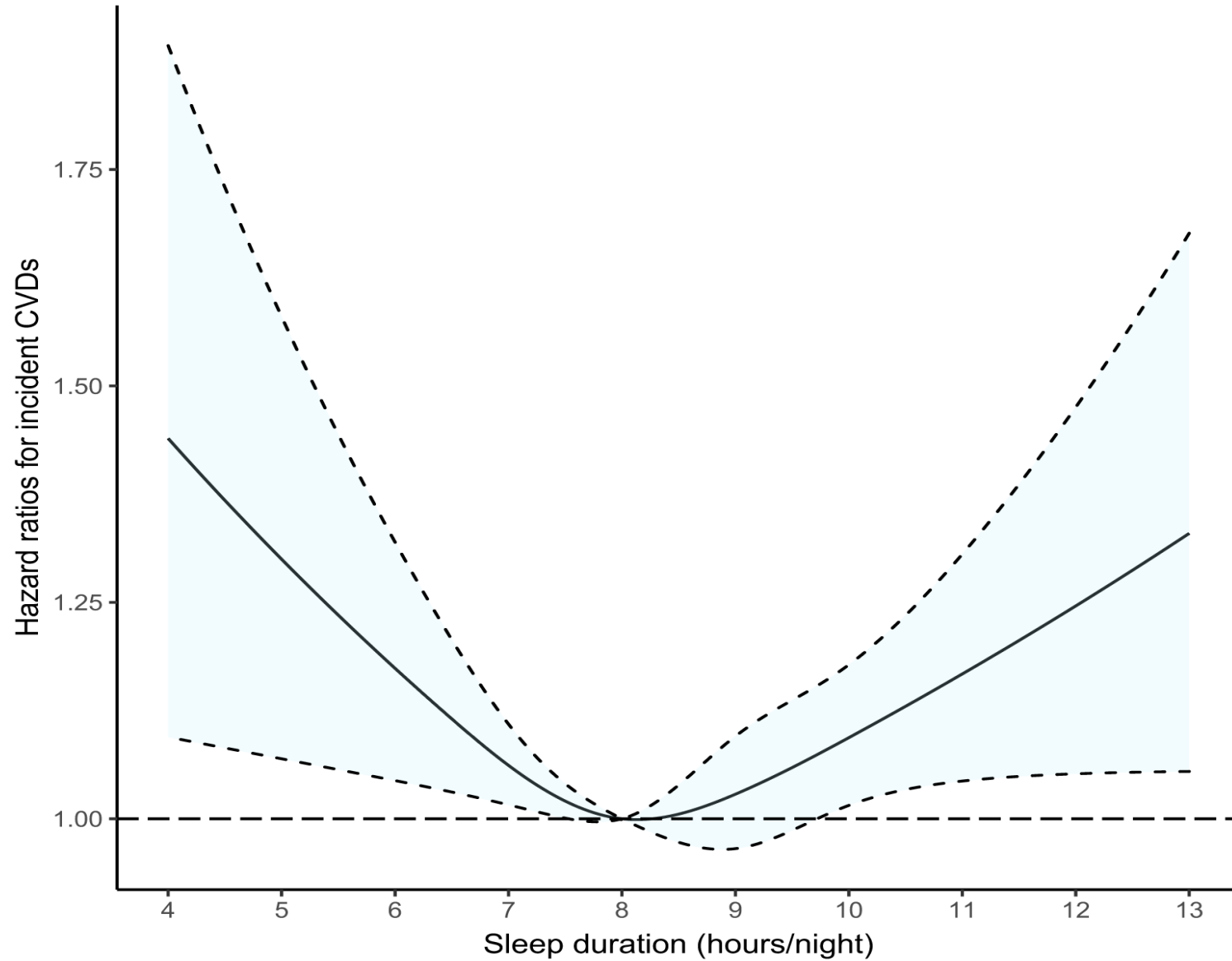
*Proc Natl Acad Sci USA*. 2018 Apr 9. pii: 201721694. doi: 10.1073/pnas.1721694115. [Epub ahead of print]

PMID: 29632177.



Brain imaging after one night of sleep deprivation revealed beta-amyloid accumulation (red) in the hippocampus and nearby regions. *Proceedings of the National Academy of Sciences*

# Cardiovascular diseases



Zhiyu Wang. Journal of the American Heart Association. Association of Sleep Duration, Napping, and Sleep Patterns With Risk of Cardiovascular Diseases: A Nationwide Twin Study, Volume: 11, Issue: 15, DOI: (10.1161/JAHA.122.025969)

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# Pillar 4: Stress



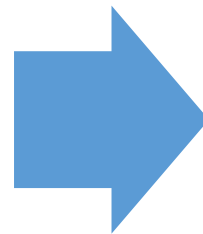
Günak MM, Billings J, Carratu E, Marchant NL, Favarato G, Orgeta V. Post-traumatic stress disorder as a risk factor for dementia: systematic review and meta-analysis. Br J Psychiatry. 2020 Nov;217(5):600-608.

This is the first meta-analysis quantifying the association of PTSD and risk of dementia showing that PTSD is a strong and potentially modifiable risk factor for all-cause dementia.

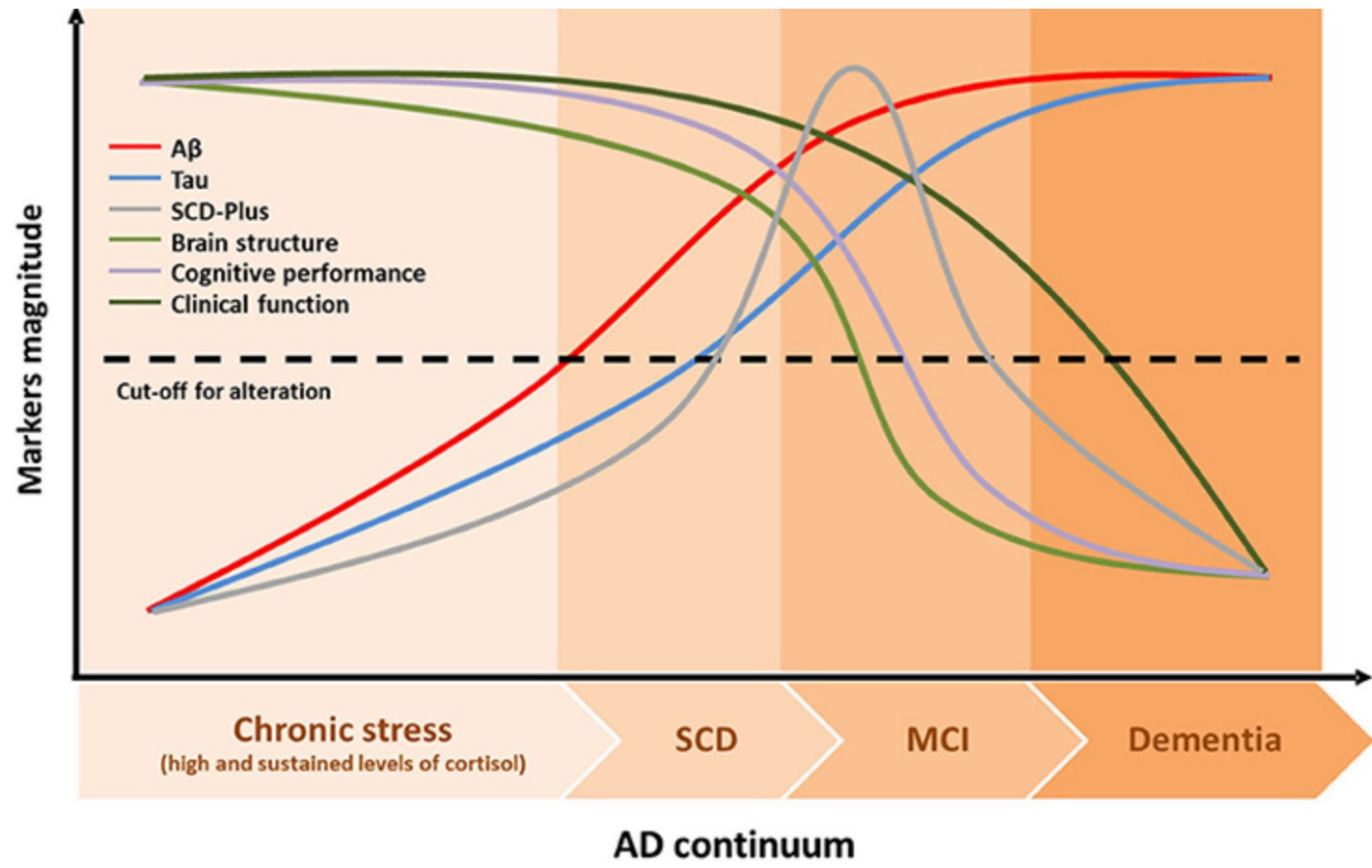
# Stress and multiple mechanisms



Venero C, Ávila J, Fernández-Blázquez MA. The Role of Chronic Stress as a Trigger for the Alzheimer Disease Continuum. *Front Aging Neurosci.* 2020 Oct 22;12:561504.

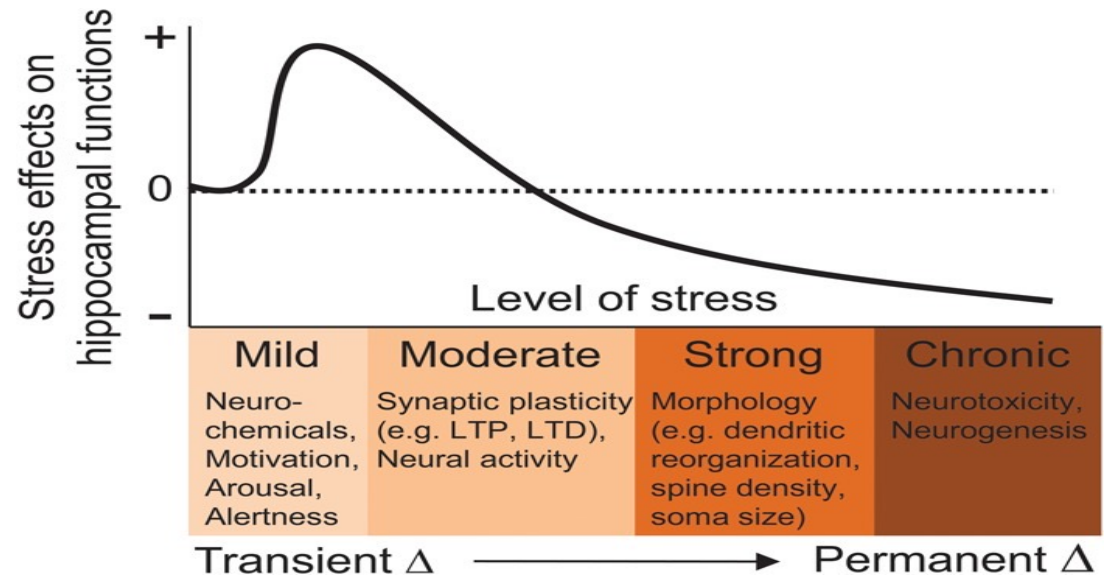


It is likely that the excess of corticosteroids is not the only mechanism by which stress exacerbates AD neuropathology, since manipulations of the neuropeptide released by stress Corticotropin Releasing Factor can also alter beta-amyloid release and tau aggregation



# Stress Levels and Hippocampus

- Some stress is good.
- Excessive stress or strain may cause damage.



Learn Mem. 2015 Sep; 22(9): 411–416.

# STRESS RESPONSE

(Involuntary/reflexive)

# RELAXATION RESPONSE

(Requires conscious elicitation and repeated practice)

Pro-Inflammatory Cytokines  
IL1 + TNF alpha

↑ sympathetic nervous system activity

Adrenocorticotrophic hormone

sympathetic nerve terminals (various organs)

Rippe Lifestyle Medicine Textbook: Page 282

↑ Cort

↑ Ne

↑ Epi

↓ NO

Epi ↓

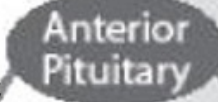
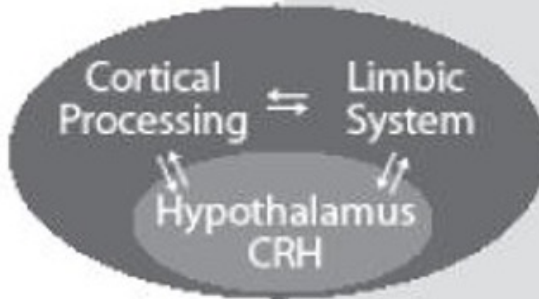
Ne ↓

Cort ↓

NO ↑

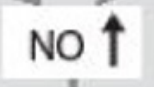
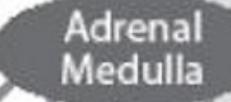
↓ sympathetic nervous system activity

sympathetic nerve terminals (various organs)



↑ ACTH

ACTH ↓



# Pillar 5: Social Connection

Of 5022 older adults, 1172 (23.3%) were socially isolated, and 3850 (76.7%) were not socially isolated.

Adjusting for demographic and health factors, being socially isolated (vs. not socially isolated) was associated with a 1.28 (95% CI: 1.10–1.49) higher hazard of incident dementia over 9 years.

There was no statistically significant difference by race and ethnicity.

# Pillar 6: Substance Use

Limit alcohol use, as alcohol misuse and drinking more than 21 units weekly increase the risk of dementia.

AHA –0-1 drinks for a woman and 0-2 drinks for a man per day

If you don't drink, don't start

Avoid smoking uptake and support smoking cessation to stop smoking, as this reduces the risk of dementia even in later life.



# Stress and the Caregivers

- The Health of the Caregivers for people with dementia needs to be addressed and prioritized as well.
- Agitation, aggression, disinhibition, delusions and mood disturbance. There can be psychosis and insensitivity.
- Disruptive behaviors
  - Cheng ST. Dementia Caregiver Burden: a Research Update and Critical Analysis. *Curr Psychiatry Rep.* 2017 Aug 10;19(9):64.
- “Behavioural problems or psychological symptoms were the primary factor of the person with dementia that is associated with caregiver burden.”
  - Chiao CY, Wu HS, Hsiao CY. Caregiver burden for informal caregivers of patients with dementia: A systematic review. *Int Nurs Rev.* 2015 Sep;62(3):340-50.
- “Caregivers with higher levels of self-compassion report lower levels of burden and this is at least partly due to the use of less dysfunctional coping strategies.”
  - Lloyd J, Muers J, Patterson TG, Marczak M. Self-Compassion, Coping Strategies, and Caregiver Burden in Caregivers of People with Dementia. *Clin Gerontol.* 2019 Jan-Feb;42(1):47-59.



# Guidelines with all 6 Pillars will help

1

Evidence for prevention of dementia is strongest.

2

Focus on 6 pillars through the lifespan is key.

3

Follow the literature for specifics.