

**NAPA Council Meeting  
July 28, 2017**

# **Interventions to Prevent or Slow Cognitive Decline, MCI and Dementia in Individuals without Dementia**

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## **Disclosures**

- **No conflicts of interest to disclose**
- **None of the interventions are FDA approved to prevent or slow cognitive decline in patients without dementia**

## Objective

- Review evidence on efficacy & harms of interventions to prevent or delay cog decline, MCI & dementia in individuals without dementia

## Nonpharmacological Treatments Evaluated

### Any Low/Mod RoB Studies

- Cognitive Training
- Physical Activity
- Diet
- Multimodal
- Nutraceuticals
- Vitamins

### No or only High RoB Studies

- Social Engagement
- Sleep Disorder
- Music-based
- Transcranial random noise stimulation
- Depression Treatment
- Smoking Cessation
- Community-level

# Pharmacological Treatments Evaluated

## Any Low/Mod RoB Studies

- Dementia meds\*
- Anti-hypertensives
- Diabetes meds
- Lipid lowering meds
- NSAIDs / ASA
- Hormones

## No or only High RoB Studies

- Antidepressants
- Smoking cessation meds
- Sleep disorder meds

\*FDA approved for treatment of diagnosed dementia

# Cognitive Training

- **Individuals with MCI:**
  - Insufficient evidence about incident dementia, patient-reported memory
- **Individuals with normal cognition:**
  - Cognitive performance **improved** in trained domain (mod SoE at 2 yr, low SoE at 5-10 yr)
  - Processing speed training may be associated with less IADL decline over 2-5 yr
  - No evidence about commercial “brain training” programs

# Physical Activity

- **Individuals with MCI:**
  - No or insufficient evidence for cog tests, dementia
- **Individuals with normal cognition**
  - Pattern of results across variety of physical activity provides indication of effectiveness for cognitive performance (Resistance training, aerobic training)

# Multimodal

- **Individuals with MCI:**
  - No evidence
- **Individuals with normal cognition:**
  - One lifestyle-based behavioral intervention **improved** cog test performance (low SoE) (FINGER)
  - One lifestyle advice plus drug management **no diff** (low SoE) (PreDIVA)
  - Remaining studies were insufficient evidence



# Diet

- **Individuals w MCI:**
  - No evidence
- **Individuals with normal cognition:**
  - **No diff** vs. control for risk of MCI, dementia, or cog tests (insuff SoE)

# Nutraceuticals

- **Individuals with MCI:**
  - Insufficient evidence for Omega-3, ginkgo biloba
- **Individuals with normal cognition:**
  - Omega-3, ginkgo biloba **no diff** vs. placebo for dementia risk, cog tests (low SoE)
  - Insufficient evidence for resveratrol, plant sterol/stanol esters, multicomponent supplement

# Vitamins

- **Individuals with MCI:**
  - Vit E **no better** than placebo on risk of dementia (low SoE), insufficient for cog tests
- **Individuals with normal cognition:**
  - B12 + folic acid > placebo for memory, not other cog tests in individuals w low B12 levels (low SoE)
  - MVI, vit D + calcium **no diff** vs. placebo on risk of MCI, dementia, or cog tests (low SoE)
  - Omega-3+B, vit C, beta carotene, vit E **no diff** vs. placebo for cog tests in women (mostly low SoE)

# Dementia Medications

- **Individuals with MCI:**
  - AChEI **do not** reduce risk of dementia or improve cog tests vs. placebo (low SoE)
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- **Individuals with normal cognition:**
  - No evidence

# Anti-hypertensive Medications

- **Individuals with MCI:**
  - Insufficient evidence for anti-HTN
- **Individuals with normal cognition:**
  - Anti-HTN **reduced risk** of dementia vs. placebo in 1 of 4 RCTs (low SoE)
  - **No diff** cog tests or incident cognitive impairment for anti-HTN vs. placebo or between intensive vs. standard anti-HTN rx (low-mod SoE)

# Diabetes Medications

- **Individuals with MCI:**
  - Insufficient evidence for DM medication treatment
- **Individuals with normal cognition:**
  - Intensive & standard glucose control **no diff** for incident cog impairment or cog tests (low SoE)

# Lipid Lowering Medications

- **Individuals with MCI**
  - No evidence
- **Individuals with normal cognition:**
  - Statins **no diff** than placebo for cog tests (low SoE); insufficient evidence for risk of dementia

# NSAIDs / ASA

- **Individuals with MCI:**
  - No evidence
- **Individuals with normal cognition:**
  - NSAIDs **no diff** vs. placebo risk of dementia (low SoE)
  - ASA & NSAIDs **no diff** vs. placebo any cog tests (low SoE)



# Hormones

- **Individuals with MCI:**
  - Insufficient evidence for treatment effect on cog tests
- **Individuals with normal cognition:**
  - E & E+P **increase risk** of dementia/MCI (low SoE)
  - High (not low) dose raloxifene **reduce risk** of MCI but not of dementia (low SoE)
  - No hormone treatments improve cog tests
  - Important harms noted for all hormone treatments

# Summary

- Cognitive training improves cog tests in domain trained
- Aerobic & resistance exercise w mixed benefits/no diff across multiple cog domains
- Mixed benefits/no diff for multimodal interventions vs. control on cog tests
- Other nonpharm treatments evaluated have little to no benefit for preventing or delaying cog decline, MCI or dementia (low-insuff SoE)
  - **Diet**
  - **Nutraceuticals**
  - **Vitamins**

## Summary

- Estrogen +/-progestin increases risk of dementia/MCI
- Other pharm treatments evaluated have little to no benefit for preventing or delaying cog decline, MCI, or dementia in individuals without dementia (low-insuff SoE)
  - Dementia medications
  - Anti-hypertensives
  - Diabetes medications
  - Lipid lowering medications
  - NSAIDs/ASA

## Limitations

- Many trials not designed to assess cog outcomes
  - Possible reporting bias since these are minority of trials of these interventions
- Trials too short to show meaningful cog change in cognitively normal participants
- High attrition

## **Limitations**

- **Cog outcomes heterogeneous between trials**
- **Incident MCI & dementia not often reported**
- **Little subgroup data reported**
- **Adverse events poorly reported**

## July 28, 2017 -- Advisory Council Meeting #25

The meeting was held on Friday, July 28, 2017, in Washington, DC. The Advisory Council spent the morning discussing information gaps across the three areas of research, clinical care, and long-term services and supports. There was also a presentation on the recently released National Academy of Sciences, Engineering, and Medicine (NASEM) report on preventing cognitive decline. Additional presentations included a presentation on planning and progress towards the October Care and Services Summit and federal workgroup updates. Material available from this meeting is listed below and is also available at <https://aspe.hhs.gov/advisory-council-alzheimers-research-care-and-services-meetings#Jul2017>.

Comments and questions, or alerts to broken links, should be sent to [napa@hhs.gov](mailto:napa@hhs.gov).

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### General Information

<b>Agenda</b>	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
<b>Meeting Announcement</b>	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
<b>Meeting Summary</b>	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
<b>Public Comments</b>	<a href="#">[HTML Version]</a>

### Presentation Slides

2017 National Plan Update and Non-Federal Recommendations	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
Clinical Services Subcommittee Federal Update	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
CommunityRx for Community-Residing People with Dementia and Their Caregivers	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
Dementia Caregiving in the U.S.	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
Development of the FY 19 NIH Bypass Budget for Alzheimer's Disease and Related Dementias	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
Implications of a Biologically Based Definition of Alzheimer's Disease	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
Increasing Opportunities for Choice and Control for Persons with Dementia	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
Interventions to Prevent or Slow Cognitive Decline, MCI and Dementia in Individuals without Dementia	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
Living Alone With Dementia	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>



Long-Term Services and Supports Committee Update	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
Managing Chronic Conditions in People Living with Dementia	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
Preventing Cognitive Decline and Dementia	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
Research Summit on Dementia Care	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
The Many Challenges of Alzheimer's Disease	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>

## **Videos**

Welcome thru Clinical Care	<a href="#">[Video]</a>
LTSS Research	<a href="#">[Video]</a>
Public Comments thru Federal Workgroup Updates	<a href="#">[Video]</a>
Recommendations thru Adjourn	<a href="#">[Video]</a>

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