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

Mary Butler & Howard Fink
Minnesota Evidence-Based Practice Center
Minneapolis VA Health Care System

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 cognitive decline, MCI & dementia in individuals without dementia

Nonpharmacological Treatments Evaluated

<table>
<thead>
<tr>
<th>Any Low/Mod RoB Studies</th>
<th>No or only High RoB Studies</th>
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<td>• Cognitive Training</td>
<td>• Social Engagement</td>
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<td>• Physical Activity</td>
<td>• Sleep Disorder</td>
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<td>• Diet</td>
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<td>• Multimodal</td>
<td>• Transcranial random noise stimulation</td>
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<td>• Nutraceuticals</td>
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<td>• Vitamins</td>
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<td>• Community-level</td>
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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, gingko 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)

- 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](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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