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Committee on Preventing Dementia and Cognitive Impairment

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The Task

Examine the evidence on interventions for delaying or slowing ARCD and preventing, delaying, or slowing MCI and CATD, and recommend:

- Interventions supported by sufficient evidence to be incorporated into public health strategies and messages
- Areas for future research

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A Novel Study Model

Phase I: NASEM committee informs the design of an AHRQ systematic review

- Committee met with EPC December 2015
- AHRQ draft review released in September 2016 (final review, January 2017)

Phase II: NASEM Committee draws from the AHRQ systematic review and other evidence sources

- Testimony at Oct 2016 public workshop,
- Observational studies

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Why Supplemental Sources?

- AHRQ review focused only on RCT data
- RCTs challenging (e.g., long follow up requirement, comorbid conditions, secular dementia trends) and, in some cases, unethical
- Supplemental sources of evidence
  - Testimony from public workshop
  - Prospective cohort studies (intervention and risk factor studies)
  - Neurobiological studies (mechanistic and brain imaging biomarker studies)
  - Knowledge of benefits, harms, and costs

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Strength of the Evidence for Interventions

- Insufficient evidence to justify a public health information campaign to encourage adoption of specific interventions
- Three interventions supported by encouraging, but inconclusive evidence
  - Cognitive training
  - Blood pressure management for people with hypertension
  - Increased physical activity
- All have minimal risk of harm, and two known to be beneficial for other conditions

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Cognitive Training – Supplemental Evidence

- No observational studies identified for cognitive training
- Observational studies have suggested participating in cognitively stimulating activities (reading, games, learning a new language) may lower risk of cognitive impairment
- Low educational attainment known modifiable risk factor for dementia

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Cognitive Training – Conclusions

- Despite limitations of ACTIVE trial, moderate strength RCT evidence suggests cognitive training can delay or slow ARCD
- No evidence that such beneficial long-term cognitive effects obtained with commercial, computer-based "brain training" applications
- No evidence that cognitive training prevents, delays, or slows MCI and CATD

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Blood Pressure Management – Supplemental Evidence

- Cerebrovascular disease linked to dementia, vascular component of mixed dementia increasingly recognized
- Antihypertensives known to reduce stroke risk and subclinical cerebrovascular disease
- Prospective cohort studies have more consistently found associations between BP lowering and improved cognitive outcomes (dementia and cognitive performance)

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Blood Pressure Management – Conclusions

- RCT data do not offer strong support for BP management in patients with hypertension for delaying or slowing ARCD or preventing, delaying, or slowing MCI and CATD, although Syst-Eur trial provides some evidence of impact on risk of CATD
- Add-on trials with cardiovascular primary endpoints may not have been optimally designed to detect impact on cognitive outcomes
- Using Hill criteria, data from non-RCT studies suggest effects of BP management on incident CATD in hypertensives are consistent with a causal relationship

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Recommendation 1
Communicating with the Public

NIH, CDC and other organizations should make clear that positive effects of the following interventions are supported by encouraging although inconclusive evidence:

- *cognitive training* to delay or slow ARCD;
- *blood pressure management for people with hypertension* to prevent, delay, or slow CATD; and
- *increased physical activity* to delay or slow ARCD.

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Common Methodological Limitations

- Initiation of interventions at later life stages that may be outside optimal window for prevention
- Inadequate follow up to assess effects of interventions on long-term clinical outcomes
- Use of heterogeneous outcome measures and assessment tools precluded pooling results across studies
- Failure to collect baseline data on cognition
- Small sample sizes, underpowered studies, attrition
- Homogeneous study populations
- Suboptimal control groups

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Recommendation 2
Methodological Improvements

NIH and other interested organizations should support studies that:

- identify individuals at higher risk of cognitive decline and dementia and tailor interventions accordingly
- increase participation of underrepresented populations to study intervention effectiveness in these populations
- begin more interventions earlier with longer follow-up
- use consistent cognitive outcome measures to enable pooling
- integrate robust cognitive outcome measures into trials with other primary purposes
- include biomarkers as intermediate outcomes
- conduct large trials in broad, routine clinical practices

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Recommendation 3
Highest Priorities for Future Research

NIH and other interested organizations should support further research to strengthen the evidence base on the following categories of interventions supported by encouraging but inconclusive evidence:

- *cognitive training* – e.g., components of ACTIVE trial responsible for benefits of intervention
- *blood pressure management* – e.g., optimal targets and timing
- *increased physical activity* – e.g., comparative effectiveness of different regimens

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Recommendation 4
Additional Priorities for Future Research

NIH and other interested organizations should support further research to strengthen the evidence base on:

- new antidementia treatments
- diabetes treatment
- depression treatment
- dietary interventions
- lipid-lowering treatment/statins
- sleep quality interventions
- social engagement interventions
- vitamin B_{12} plus folic acid supplementation

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Other Cross-Cutting Considerations for Research

- Multimodal approaches – can combining interventions improve outcomes beyond those achieved by single interventions?
- Optimizing dose, timing, delivery schedule, and duration to maximize cognitive outcomes.
- How can adherence to an intervention best be promoted and measured?
- Making use of new adaptive designs for clinical trials and statistical methodologies

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Final Thoughts

- This report represents a snapshot of the state of the science in 2017 but new data constantly emerging and recommendations will need to be reassessed
- NIA and others need to consider criteria used for public health messaging as RCTs may not always be possible or able to yield needed evidence
- RCTs and other studies have yielded encouraging data for some interventions and public should have access to this information to inform choices
- Committee is optimistic much more will be known on preventing ARCD and dementia in the near future

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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.

General Information

Agenda	[HTML Version] [PDF Version]
Meeting Announcement	[HTML Version] [PDF Version]
Meeting Summary	[HTML Version] [PDF Version]
Public Comments	[HTML Version]

Presentation Slides

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

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

Videos

Welcome thru Clinical Care	[Video]
LTSS Research	[Video]
Public Comments thru Federal Workgroup Updates	[Video]
Recommendations thru Adjourn	[Video]

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