Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Practice guideline update summary: mild cognitive impairment: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology.

Bibliographic Source(s)

Petersen RC, Lopez O, Armstrong MJ, Getchius TSD, Ganguli M, Gloss D, Gronseth GS, Marson D, Pringsheim T, Day GS, Sager M, Stevens J, Rae-Grant A. Practice guideline update summary: mild cognitive impairment: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2018 Jan 16;90(3):126-35. [90 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Petersen RC, Stevens JC, Ganguli M, Tangalos EG, Cummings JL, DeKosky ST. Practice parameter: Early detection of dementia: Mild cognitive impairment (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2001 May 8;56(9):1133-42. [47 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

NEATS Assessment

National Guideline Clearinghouse (NGC) has assessed this guideline's adherence to standards of trustworthiness, derived from the Institute of Medicine's report Clinical Practice Guidelines We Can Trust.

= Poor = Fair = Good = Very Good = Excellent

Assessment	Standard of Trustworthiness
YES	Disclosure of Guideline Funding Source
	Disclosure and Management of Financial Conflict of Interests

	Guideline Development Group Composition
YES	Multidisciplinary Group
YES	Methodologist Involvement
▮▮▯▯▯	Patient and Public Perspectives
	Use of a Systematic Review of Evidence
▮▮▮▮▮	Search Strategy
▮▮▮▮▮	Study Selection
▮▮▮▮▮	Synthesis of Evidence
	Evidence Foundations for and Rating Strength of Recommendations
▮▮▮▮▯	Grading the Quality or Strength of Evidence
▮▮▮▮▯	Benefits and Harms of Recommendations
▮▮▮▮▮	Evidence Summary Supporting Recommendations
▮▮▮▮▮	Rating the Strength of Recommendations
▮▮▮▮▮	**Specific and Unambiguous Articulation of Recommendations**
▮▮▮▮▯	**External Review**
▮▮▮▮▮	**Updating**

Recommendations

Major Recommendations

Definitions of the levels of the recommendations (A, B, C, U) and classification of the evidence (Class I-IV) are provided at the end of the "Major Recommendations" field.

Note from the National Guideline Clearinghouse (NGC) and the American Academy of Neurology (AAN):

In addition to evidence, AAN guidelines incorporate several consensus-based factors into constructing practice recommendations. The following four premise types are part of that process:

- Evidence from the systematic review
- Strong evidence from related conditions
- Axiomatic principles of care
- Inferences made from one or more statements in the rationale

The above-listed premise types are presented as rationales before each recommendation statement. The premises contribute to the strength of those recommendation statements.

See the full-length guideline (see the "Availability of Companion Documents" field) for a fuller

understanding of the recommendation statements.

Recommendations for Assessing for Mild Cognitive Impairment (MCI)

Recommendation A1

For patients for whom the patient or a close contact voices concern about memory or impaired cognition, clinicians should assess for MCI and not assume the concerns are related to normal aging (Level B).

Recommendation A2

When performing a Medicare Annual Wellness Visit, clinicians should not rely on historical report of subjective memory concerns alone when assessing for cognitive impairment (Level B).

Recommendation A3

For patients for whom screening or assessing for MCI is appropriate, clinicians should use validated assessment tools to assess for cognitive impairment (Level B). For patients who test positive for MCI, clinicians should perform a more formal clinical assessment for diagnosis of MCI (Level B).

Recommendation A4

For patients with MCI, clinicians should assess for the presence of functional impairment related to cognition before giving a diagnosis of dementia (Level B).

Recommendation A5

For patients suspected to have MCI, clinicians who lack the necessary experience should refer these patients to a specialist with experience in cognition (Level B).

Recommendation A6

For patients diagnosed with MCI, clinicians should perform a medical evaluation for MCI risk factors that are potentially modifiable (Level B).

Recommendation A7a

For patients and families asking about biomarkers in MCI, clinicians should counsel that there are no accepted biomarkers available at this time (Level B).

Recommendation A7b

For interested patients, clinicians may discuss the option of biomarker research or refer patients, or both, if feasible, to centers or organizations that can connect patients to this research (e.g., subspecialty centers, Trial Match, ClinicalTrials.gov) (Level C).

Recommendation A8

For patients diagnosed with MCI, clinicians should perform serial assessments over time to monitor for changes in cognitive status (Level B).

Recommendations for Management of MCI

Recommendation B1

For patients diagnosed with MCI, clinicians should wean patients from medications that can contribute to cognitive impairment (where feasible and medically appropriate) and treat modifiable risk factors that may be contributing (Level B).

Recommendation B2

For patients diagnosed with MCI, clinicians should counsel the patients and families that there are no pharmacologic or dietary agents currently shown to have symptomatic cognitive benefit in MCI and that

no medications are U.S. Food and Drug Administration (FDA)-approved for this purpose (Level B).

Recommendation B3a

For patients diagnosed with MCI, clinicians may choose not to offer cholinesterase inhibitors (Level B).

Recommendation B3b

If clinicians choose to offer cholinesterase inhibitors, they must first discuss with patients the fact that this is an off-label prescription not currently backed by empirical evidence (Level A).

Recommendation B4

For patients diagnosed with MCI who are interested in pharmacologic treatment, clinicians may inform these patients of centers or organizations that can connect patients to clinical trials (e.g., subspecialty centers, Trial Match, ClinicalTrials.gov) (Level C).

Recommendation B5

For patients diagnosed with MCI, clinicians should recommend regular exercise (twice/week) as part of an overall approach to management (Level B).

Recommendation B6

For patients diagnosed with MCI, clinicians should discuss diagnosis and uncertainties regarding prognosis. Clinicians should counsel patients and families to discuss long-term planning topics such as advance directives, driving safety, finances, and estate planning (Level B).

Recommendation B7

Clinicians should assess for behavioral and neuropsychiatric symptoms in MCI and treat with both pharmacologic and nonpharmacologic approaches when indicated (Level B).

Recommendation B8

In patients with MCI, clinicians may recommend cognitive interventions (Level C).

Definitions

American Academy of Neurology Rules for Classification of Evidence for Risk of Bias

Screening Scheme

Class I

A statistical, population-based sample of patients studied at a uniform point in time (usually early) during the course of the condition. All patients undergo the intervention of interest. The outcome, if not objective, is determined in an evaluation that is masked to the patients' clinical presentations.

Class II

A statistical, non-referral-clinic-based sample of patients studied at a uniform point in time (usually early) during the course of the condition. Most patients undergo the intervention of interest. The outcome, if not objective, is determined in an evaluation that is masked to the patients' clinical presentations.

Class III

A sample of patients studied during the course of the condition. Some patients undergo the intervention of interest. The outcome, if not objective, is determined in an evaluation by someone other than the treating physician.

Class IV

Studies not meeting Class I, II, or III criteria, including consensus, expert opinion, or a case report.

Prognostic Accuracy Scheme

Class I

A cohort study of a broad spectrum of persons at risk for developing the outcome (e.g., target disease, work status). The outcome is defined by an acceptable reference standard for case definition. The outcome is objective or measured by an observer who is masked to the presence of the risk factor. Study results allow calculation of measures of prognostic accuracy.

Class II

A case-control study of a broad spectrum of persons with the condition compared with a broad spectrum of controls, or a cohort study of a broad spectrum of persons at risk for the outcome (e.g., target disease, work status) where the data were collected retrospectively. The outcome is defined by an acceptable reference standard for case definition. The outcome is objective or measured by an observer who is masked to the presence of the risk factor. Study results allow calculation of measures of prognostic accuracy.

Class III

A case-control study or a cohort study where either the persons with the condition or the controls are of a narrow spectrum where the data were collected retrospectively. The outcome is defined by an acceptable reference standard for case definition. The outcome is objective or measured by an observer who did not determine the presence of the risk factor. Study results allow calculation of measures of a prognostic accuracy.

Class IV

Studies not meeting Class I, II, or III criteria, including consensus, expert opinion, or a case report.

Therapeutic Scheme

Class I

A randomized, controlled clinical trial of the intervention of interest with masked or objective outcome assessment, in a representative population. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

The following are also required:

- Concealed allocation
- No more than 2 primary outcomes specified
- Exclusion/inclusion criteria clearly defined
- Adequate accounting for dropouts (with at least 80% of enrolled subjects completing the study) and crossovers with numbers sufficiently low to have minimal potential for bias
- For noninferiority or equivalence trials claiming to prove efficacy for one or both drugs, the following are also required*:
  - The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or noninferiority
  - The standard treatment used in the study is substantially similar to that used in previous studies establishing efficacy of the standard treatment (e.g., for a drug, the mode of administration, dose, and dosage adjustments are similar to those previously shown to be effective)
  - The inclusion and exclusion criteria for patient selection and the outcomes of patients on the standard treatment are comparable to those of previous studies establishing efficacy of the standard treatment

The interpretation of the study results is based on a per-protocol analysis that accounts for dropouts or crossovers

For crossover trials, both period and carryover effects examined and statistical adjustments performed, if appropriate

Class II

A randomized controlled trial (RCT) of the intervention of interest in a representative population with masked or objective outcome assessment that lacks one criteria a–e above (see Class I) or a prospective matched cohort study with masked or objective outcome assessment in a representative population that meets b–e above (see Class I). (Alternatively, a randomized crossover trial missing 1 of the following 2 characteristics: period and carryover effects described or baseline characteristics of treatment order groups presented.) All relevant baseline characteristics are presented and substantially equivalent among treatment groups, or there is appropriate statistical adjustment for differences.

Class III

All other controlled trials (including studies with external controls such as well-defined natural history controls). (Alternatively, a crossover trial missing both of the following 2 criteria: period and carryover effects described or baseline characteristics of treatment order groups presented.) A description of major confounding differences between treatment groups that could affect outcome.** Outcome assessment is masked, objective, or performed by someone who is not a member of the treatment team.

Class IV

Studies that (1) did not include patients with the disease, (2) did not include patients receiving different interventions, (3) had undefined or unaccepted interventions or outcomes measures, or (4) had no measures of effectiveness or statistical precision presented or calculable.

*Note that numbers 1–3 in Class Ie are required for Class II in equivalence trials. If any one of the three is missing, the class is automatically downgraded to Class III.

**Objective outcome measurement: an outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data).

Assigning a Level of Strength to the Recommendation

When there is sufficient evidence to support an inference for the use of an intervention (i.e., the balance of benefits and harms favors the intervention), the author panel assigns one of three recommendation designations: A, B, or C. Each designation corresponds to a helping verb that denotes the level of strength of the recommendation. Level A is the strongest recommendation level and is denoted by the use of the helping verb *must*. *Must* recommendations are rare, as they are based on high confidence in the evidence and require both a high magnitude of benefit and low risk. Level B corresponds to the helping verb should. Should recommendations tend to be more common, as the requirements are less stringent but still based on the evidence and benefit–risk profile. Finally, Level C corresponds to the helping verb may or might. *May* and *might* recommendations represent the lowest allowable recommendation level the American Academy of Neurology (AAN) considers useful within the scope of clinical practice and can accommodate the highest degree of practice variation.

Level A denotes a practice recommendation that "must" be done. In almost all circumstances, adherence to the recommendation will improve health-related outcomes. A Level B indicates a recommendation that "should" be done. In most circumstances, adherence to the recommendation will likely improve health-related outcomes. A Level C represents a recommendation that "might" be done. In some circumstances, adherence to the recommendation might improve health-related outcomes.

When there is insufficient evidence to support an inference for the use of an intervention (i.e., the balance of benefits and harms is unknown) a Level U or Level R designation is appropriate.

A Level U indicates that the available evidence is insufficient to support or refute the efficacy of an intervention. A Level R is assigned when the balance of benefits and harms is unknown and the

intervention is known to be expensive or have important risks. A Level R designates that the intervention should not be used outside of a research setting. Non-evidence-based factors that need to be transparently and systematically considered when formulating recommendations include the following:

- The relative value of the benefit as compared with the risk; this is derived from consideration of:
  - The importance to patients of the health related-outcomes (both benefits and harms)
  - The size of the intervention's effect
  - The risk of harm of the intervention (i.e., tolerability and safety)
- The feasibility of complying with the intervention (e.g., the intervention's availability)
- The cost of the intervention
- The expected variation in patient preferences relative to the risks, burdens, and benefits of the intervention

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Idiopathic or neurodegenerative mild cognitive impairment (MCI)—particularly relating to Alzheimer disease (AD)

Note: Mild cognitive changes relating to potentially reversible causes (e.g., metabolic, vascular, systemic, or psychiatric disorders) or Parkinson disease–MCI or vascular cognitive impairment are not within the scope of this guideline.

Guideline Category

Diagnosis

Management

Risk Assessment

Screening

Treatment

Clinical Specialty

Family Practice

Geriatrics

Internal Medicine

Neurology

Psychiatry

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Nurses

Psychologists/Non-physician Behavioral Health Clinicians

Social Workers

Guideline Objective(s)

- To update the 2001 American Academy of Neurology (AAN) practice parameter with recommendations concerning the diagnosis and treatment of mild cognitive impairment (MCI)
- To address the following 4 questions:
  1. What is the prevalence of MCI in the general population?
  2. What is the prognosis for patients diagnosed with MCI for progression to a diagnosis of dementia, and how does this compare with an age-matched general population?
  3. What pharmacologic treatments are effective for patients diagnosed with MCI?
  4. What nonpharmacologic treatments are effective for patients diagnosed with MCI?

Note: This guideline does not review the rapidly evolving field of biomarker research in MCI; the guideline panel determined that this should be the subject of a future guideline or systematic review. In addition, the potential psychological distress of a diagnosis of MCI (which has been discussed in the literature) was not one of the questions reviewed by the expert panel for this guideline.

Target Population

Persons with mild cognitive impairment (MCI)

Interventions and Practices Considered

Assessment

Assessment for mild cognitive impairment (MCI)
Use of validated assessment tools
Formal clinical assessment for diagnosis of MCI
Assessment for functional impairment related to cognition
Referral of patients with suspected MCI to specialist
Medical evaluation for potentially modifiable risk factors
Counseling on biomarkers
Referral to biomarker research
Serial assessments

Management/Treatment

Weaning from medications that can contribute to cognitive impairment
Treatment of modifiable risk factors
Counseling patients and families on pharmacologic or dietary agents
Cholinesterase inhibitors
Informing patients of centers/organizations that can connect them to clinical trials
Regular exercise
Counseling of patients and families on long-term planning topics (e.g., advance directives, living will)
Assessment for behavioral and neuropsychiatric symptoms in MCI
Pharmacologic treatment, when indicated
Nonpharmacologic treatment, when indicated
Cognitive interventions

Major Outcomes Considered

- Progression of disease
- Cognitive function
- Effectiveness of pharmacologic treatments
- Effectiveness of nonpharmacologic treatments
- Quality of life

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The guideline panel included articles in humans related to mild cognitive impairment (MCI) and cognitively impaired no dementia (CIND) under the headings of prevalence, prognosis, treatment (both pharmacologic and nonpharmacologic). The panel excluded pharmacologic treatment trials with fewer than 50 participants. The complete search strategy is presented in appendix e-3 in the full guideline (see the "Availability of Companion Documents" field). The panel engaged a medical librarian to search the MEDLINE, CINAHL, EMBASE, and PsycINFO databases from January 2000 to December 2008. An updated literature search was completed from January 2008 to April 2014. An additional updated search was performed in December 2015 to include prevalence, prognosis, and cognitive therapy articles. Two panel members working independently of each other reviewed each of the 11,530 abstracts retrieved for basic inclusion criteria: (1) article was relevant to at least one of the clinical questions; (2) article described MCI, cognition disorders, or memory disorders, unrelated to dementia; (3) study population was greater than or equal to 50 to reduce the likelihood of spurious results due to small samples; (4) article was not a single-patient case report, review, or editorial. Of the 11,530 abstracts reviewed, the panelists identified 315 as pertinent, for which they obtained and reviewed the full-text articles.

For the prevalence and prognosis questions, the guideline panel excluded from analysis articles that reanalyzed cohorts (substudies) or assessed secondary outcomes of a parent treatment study. For the treatment question, the guideline authors excluded articles that assessed mixed populations (e.g., persons with MCI or dementia). Also excluded were pharmacologic treatment studies totaling fewer than 50 participants and cognitive intervention studies lacking control groups and totaling fewer than 50 participants. Class III studies are discussed in the guideline text only when no Class I or Class II studies were identified. Class IV studies were excluded from consideration because of their high risk of bias.

Number of Source Documents

Of the 315 reviewed articles, 68 met inclusion criteria and were reviewed and classified.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

American Academy of Neurology Rules for Classification of Evidence for Risk of Bias

Screening Scheme

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Class IV

Studies not meeting Class I, II, or III criteria, including consensus, expert opinion, or a case report.

Prognostic Accuracy Scheme

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A case-control study of a broad spectrum of persons with the condition compared with a broad spectrum of controls, or a cohort study of a broad spectrum of persons at risk for the outcome (e.g., target disease, work status) where the data were collected retrospectively. The outcome is defined by an acceptable reference standard for case definition. The outcome is objective or measured by an observer who is masked to the presence of the risk factor. Study results allow calculation of measures of prognostic accuracy.

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A case-control study or a cohort study where either the persons with the condition or the controls are of a narrow spectrum where the data were collected retrospectively. The outcome is defined by an acceptable reference standard for case definition. The outcome is objective or measured by an observer who did not determine the presence of the risk factor. Study results allow calculation of measures of a prognostic accuracy.

Class IV

Studies not meeting Class I, II, or III criteria, including consensus, expert opinion, or a case report.

Therapeutic Scheme

Class I

A randomized, controlled clinical trial of the intervention of interest with masked or objective outcome assessment, in a representative population. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for

differences.

The following are also required:

- Concealed allocation
- No more than 2 primary outcomes specified
- Exclusion/inclusion criteria clearly defined
- Adequate accounting for dropouts (with at least 80% of enrolled subjects completing the study) and crossovers with numbers sufficiently low to have minimal potential for bias
- For noninferiority or equivalence trials claiming to prove efficacy for one or both drugs, the following are also required*:
  - The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or noninferiority
  - The standard treatment used in the study is substantially similar to that used in previous studies establishing efficacy of the standard treatment (e.g., for a drug, the mode of administration, dose, and dosage adjustments are similar to those previously shown to be effective)
  - The inclusion and exclusion criteria for patient selection and the outcomes of patients on the standard treatment are comparable to those of previous studies establishing efficacy of the standard treatment
  - The interpretation of the study results is based on a per-protocol analysis that accounts for dropouts or crossovers
- For crossover trials, both period and carryover effects examined and statistical adjustments performed, if appropriate

Class II

A randomized controlled trial (RCT) of the intervention of interest in a representative population with masked or objective outcome assessment that lacks one criteria a–e above (see Class I) or a prospective matched cohort study with masked or objective outcome assessment in a representative population that meets b–e above (see Class I). (Alternatively, a randomized crossover trial missing 1 of the following 2 characteristics: period and carryover effects described or baseline characteristics of treatment order groups presented.) All relevant baseline characteristics are presented and substantially equivalent among treatment groups, or there is appropriate statistical adjustment for differences.

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All other controlled trials (including studies with external controls such as well-defined natural history controls). (Alternatively, a crossover trial missing both of the following 2 criteria: period and carryover effects described or baseline characteristics of treatment order groups presented.) A description of major confounding differences between treatment groups that could affect outcome.** Outcome assessment is masked, objective, or performed by someone who is not a member of the treatment team.

Class IV

Studies that (1) did not include patients with the disease, (2) did not include patients receiving different interventions, (3) had undefined or unaccepted interventions or outcomes measures, or (4) had no measures of effectiveness or statistical precision presented or calculable.

*Note that numbers 1–3 in Class Ie are required for Class II in equivalence trials. If any one of the three is missing, the class is automatically downgraded to Class III.

**Objective outcome measurement: an outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data).

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Of the 315 reviewed articles, 68 met inclusion criteria and were reviewed and classified by 2 panel members, working independently of each other, for quality of evidence on the basis of the American Academy of Neurology (AAN) screening (frequency), prognostic, and therapeutic classification schemes rating risk of bias pertaining to study characteristics (see the "Rating Scheme for the Strength of the Evidence" field). Discrepancies were reconciled between the 2 reviewers or by a third reviewer. Appendix e-5 in the full guideline (see the "Availability of Companion Documents" field) presents the rules for determining confidence in the evidence.

The panelists noted that various definitions of mild cognitive impairment (MCI), and of related terms, such as cognitively impaired no dementia (CIND), were used in the reviewed literature. Variation was based on different ascertainment methods, different neuropsychological (NP) measures, different measure thresholds, and requirements for different cognitive deficits. There also was variation in the use of aMCI and nonamnestic MCI in these studies. To address these discrepancies, the panelists reflected the specific definition used for a study where feasible in the evidence table and guideline text, and provided specific comments on the potential effect of differing definitions.

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

In 2008, after reviewing potential members' conflict of interest statements and curriculum vitae, the American Academy of Neurology (AAN) Guideline Development, Dissemination, and Implementation Subcommittee convened a multidisciplinary panel of experts in mild cognitive impairment (MCI) to develop this guideline. The original panel consisted of 6 neurologists, 1 geriatric psychiatrist, 1 neuropsychologist, 1 geriatrician, and 1 AAN staff member. Additional assistance was later provided by 2 guideline methodology specialists and another guideline subcommittee member. The panel determined at project initiation that the literature on "biomarkers" to predict progression to Alzheimer disease (AD) is changing rapidly and should be the subject of a future guideline or systematic review. This view was reaffirmed in 2016. The panel developed research questions in PICO format: patient, intervention, comparison, outcome.

The guideline panel used a modified form of the Grading of Recommendations Assessment, Development and Evaluation process to develop conclusions (see appendix e-6 in the full guideline for evidence synthesis tables) and a modified Delphi process to achieve consensus regarding recommendations. In accordance with the 2011 guideline manual, recommendations were based not only on the evidence in the systematic review, but also on strong related evidence, established principles of care, and inferences. The level of obligation for each recommendation was based on the strength of these premises and the risk–benefit ratio of following the recommendation, with adjustments based on importance of outcomes, variation in patient preferences, feasibility/availability, and patient costs. Consensus was determined by a modified Delphi voting process in accordance with prespecified rules. Appendix e-7 in the full guideline delineates the steps and rules for formulating recommendations, and appendix e-8 in the full guideline presents the rationale of factors considered during recommendation development.

Rating Scheme for the Strength of the Recommendations

Assigning a Level of Strength to the Recommendation

When there is sufficient evidence to support an inference for the use of an intervention (i.e., the balance of benefits and harms favors the intervention), the author panel assigns one of three recommendation designations: A, B, or C. Each designation corresponds to a helping verb that denotes the level of strength of the recommendation. Level A is the strongest recommendation level and is denoted by the use of the helping verb *must*. *Must* recommendations are rare, as they are based on high confidence in the evidence and require both a high magnitude of benefit and low risk. Level B corresponds to the helping verb should. Should recommendations tend to be more common, as the requirements are less stringent but still based on the evidence and benefit–risk profile. Finally, Level C corresponds to the helping verb may or might. *May* and *might* recommendations represent the lowest allowable recommendation level the American Academy of Neurology (AAN) considers useful within the scope of clinical practice and can accommodate the highest degree of practice variation.

Level A denotes a practice recommendation that "must" be done. In almost all circumstances, adherence to the recommendation will improve health-related outcomes. A Level B indicates a recommendation that "should" be done. In most circumstances, adherence to the recommendation will likely improve health-related outcomes. A Level C represents a recommendation that "might" be done. In some circumstances, adherence to the recommendation might improve health-related outcomes.

When there is insufficient evidence to support an inference for the use of an intervention (i.e., the balance of benefits and harms is unknown) a Level U or Level R designation is appropriate.

A Level U indicates that the available evidence is insufficient to support or refute the efficacy of an intervention. A Level R is assigned when the balance of benefits and harms is unknown and the intervention is known to be expensive or have important risks. A Level R designates that the intervention should not be used outside of a research setting. Non-evidence-based factors that need to be transparently and systematically considered when formulating recommendations include the following:

- The relative value of the benefit as compared with the risk; this is derived from consideration of:
  - The importance to patients of the health related-outcomes (both benefits and harms)
  - The size of the intervention's effect
  - The risk of harm of the intervention (i.e., tolerability and safety)
- The feasibility of complying with the intervention (e.g., the intervention's availability)
- The cost of the intervention
- The expected variation in patient preferences relative to the risks, burdens, and benefits of the intervention

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Drafts of the guideline have been reviewed by at least 3 American Academy of Neurology (AAN) committees, a network of neurologists, *Neurology* peer reviewers, and representatives from related fields.

This guideline was approved by the Guideline Development, Dissemination, and Implementation Subcommittee on July 16, 2016; by the Practice Committee on August 22, 2016; and by the AAN Institute Board of Directors on October 5, 2017.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Although long-term studies are unavailable, 6-month studies suggest a possible benefit of twice-weekly exercise for cognition in mild cognitive impairment (MCI). Exercise also has general health benefits and generally limited risk.
- In patients with MCI, cognitive interventions may be beneficial in improving measures of cognitive function.

Potential Harms

- Appropriate diagnosis of mild cognitive impairment (MCI) is important in order to assess for reversible causes of cognitive impairment, to help patients and families understand the cause of their cognitive concerns, and to discuss the prognostic possibilities with the provider so they can plan accordingly, although sharing the diagnosis must be balanced with the potential harm of anxieties from diagnosing a patient with a condition that may not progress.
- In addition to lacking efficacy, side effects of cholinesterase inhibitors are common, including gastrointestinal symptoms and cardiac concerns.

Qualifying Statements

Qualifying Statements

Disclaimer

Clinical practice guidelines, practice advisories, systematic reviews, and other guidance published by the American Academy of Neurology (AAN) and its affiliates are assessments of current scientific and clinical information provided as an educational service. The information (1) should not be considered inclusive of all proper treatments, methods of care, or as a statement of the standard of care; (2) is not continually updated and may not reflect the most recent evidence (new evidence may emerge between the time information is developed and when it is published or read); (3) addresses only the question(s) specifically identified; (4) does not mandate any particular course of medical care; and (5) is not intended to substitute for the independent professional judgment of the treating provider, as the information does not account for individual variation among patients. In all cases, the selected course of action should be considered by the treating provider in the context of treating the individual patient. Use of the information is voluntary. The AAN provides this information on an "as is" basis and makes no warranty, expressed or implied, regarding the information. The AAN specifically disclaims any warranties of merchantability or fitness for a particular use or purpose. The AAN assumes no responsibility for any injury or damage to persons or property arising out of or related to any use of this information or for any errors or omissions.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Patient Resources

Quick Reference Guides/Physician Guides

Resources

Slide Presentation

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Petersen RC, Lopez O, Armstrong MJ, Getchius TSD, Ganguli M, Gloss D, Gronseth GS, Marson D, Pringsheim T, Day GS, Sager M, Stevens J, Rae-Grant A. Practice guideline update summary: mild cognitive impairment: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2018 Jan 16;90(3):126-35. [90 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2018 Jan 16

Guideline Developer(s)

American Academy of Neurology - Medical Specialty Society

Source(s) of Funding

This practice guideline was developed with financial support from the American Academy of Neurology.

Guideline Committee

Guideline Development, Dissemination, and Implementation Subcommittee

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Financial Disclosures/Conflicts of Interest

Conflict of interest

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Disclosure

R. Petersen has served as a consultant for Roche Inc., Merck Inc., Genentech Inc., and Biogen Inc.; receives publishing royalties from Oxford University Press; performs clinical procedures relating to mild cognitive impairment in his clinical neurology practice; and receives research support from the National Institute on Aging of the NIH. O. Lopez has been a consultant for Grifols Inc., Lundbeck, and Raman Technologies and has received grant support from the NIH. M. Armstrong serves on the Level of Evidence editorial board for *Neurology*® (but is not compensated financially) and serves as an evidence-based medicine methodologist for the American Academy of Neurology (AAN). T. Getchius was an employee of

the AAN and has nothing to disclose. M. Ganguli has served on the data safety and monitoring board for Indiana University and on the advisory committee for Biogen Inc. and has received research support from the National Institute on Aging of the NIH. D. Gloss serves as an evidence-based medicine methodologist for the AAN. G. Gronseth serves as associate editor for *Neurology*, serves on the editorial advisory board for *Neurology Now*, and is compensated by the AAN for methodologic activities. D. Marson serves as a consultant for and received royalties from Janssen Pharmaceuticals and receives research support from the National Institute on Aging for the NIH. T. Pringsheim has received financial reimbursement for travel to attend the Movement Disorder Society Meeting from Allergan Canada and Teva Canada Innovation and has received research support from Shire Canada Inc. and the Canadian Institutes of Health Research. G. Day received honoraria for serving as faculty at the 2016 AAN Annual Meeting and holds stock (>$10,000) in ANI Pharmaceuticals (generic manufacturer). M. Sager, J. Stevens, and A. Rae-Grant report no disclosures relevant to the manuscript. Go to Neurology.org for full disclosures.

Guideline Endorser(s)

Alzheimer's Association - Disease Specific Society

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Petersen RC, Stevens JC, Ganguli M, Tangalos EG, Cummings JL, DeKosky ST. Practice parameter: Early detection of dementia: Mild cognitive impairment (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2001 May 8;56(9):1133-42. [47 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

A list of American Academy of Neurology (AAN) guidelines, along with a link to this guideline, is available from the AAN Web site.

Availability of Companion Documents

The following are available:

- Practice guideline update: mild cognitive impairment: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Full guideline. Minneapolis (MN): American Academy of Neurology; 2018 Jan. 110 p. Available from the Neurology Journal Web site.
- Practice guideline update summary: mild cognitive impairment: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Summary of full guideline. Minneapolis (MN): American Academy of Neurology; 2018 Jan. 10 p. Available from the Neurology Journal Web site.
- Practice guideline update summary: mild cognitive impairment: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Clinician summary. Minneapolis (MN): American Academy of Neurology; 2018 Jan. 4 p. Available from the American Academy of Neurology (AAN) Web site.
- Practice guideline update summary: mild cognitive impairment: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Slide presentation. Minneapolis (MN): American Academy of Neurology; 2018 Jan. 46 p. Available from the AAN Web site.

Practice guideline update summary: mild cognitive impairment: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Podcast. Minneapolis (MN): American Academy of Neurology; 2018 Jan. Available from the AAN Web site .

American Academy of Neurology (AAN). Clinical practice guideline process manual, 2004 Ed. St. Paul (MN): American Academy of Neurology. 2004. 57 p. Available from the AAN Web site .

American Academy of Neurology (AAN). Clinical practice guideline process manual, 2011 Ed. St. Paul (MN): American Academy of Neurology. Available from the AAN Web site .

Patient Resources

The following is available:

Mild cognitive impairment. AAN summary of practice guideline for patients and their families. Minneapolis (MN): American Academy of Neurology; 2018 Jan. 2 p. Available from the American Academy of Neurology (AAN) Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

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