

# Amendments to the 2011 American Academy of Neurology Clinical Practice Guideline Process Manual

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# Amendments to the 2011 American Academy of Neurology Guideline Development Process Manual

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The following amendments apply to the indicated processes which are outlined in the 2011 process manual<sup>1</sup>

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# Amendment I: Addition of Level R Recommendation Level

**The AAN added recommendation level R to its scheme for rating guideline recommendations. Level R recommendations are those that the guideline authors assert should be applied only in research settings.**

**The text shown below replaces the applicable text that appears on page 20 of the AAN's *Clinical Practice Guideline Process Manual*, 2011 edition,<sup>1</sup> as per the AAN Institute Board of Directors' approval on June 3, 2012.**

## Assigning a Level of Strength to the Recommendation:

### Recommendation Development Process Step 4

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 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

# Amendment II: Updated Scheme for Classification of Evidence — Therapeutic Studies

**The classification schemes used to rate articles for systematic reviews are periodically revised when clarifications or changes are needed. This amendment reflects updates to the scheme for classification of therapeutic studies. The changes to the criteria decrease the ambiguity in the assessment of the presence of a primary outcome and provide additional criteria for rating randomized, crossover studies.**

**The text shown below reflects the altered or added criteria for rating randomized, crossover studies and is a change to the processes outlined on page 10 of the AAN's *Clinical Practice Guideline Process Manual*, 2011 edition.<sup>1</sup> These changed criteria were approved by the AAN Institute Board of Directors on June 21, 2014.**

## Primary Outcome

When designing a study, investigators are expected to designate a primary outcome. Often they do not. In addition, sometimes authors will designate multiple outcomes as “primary,” thereby defeating the purpose of designating a single primary outcome. Moreover, there are times when it may be impossible to determine whether study authors have reported all the outcomes they have measured.

To be rated Class I, a study must have no more than two prespecified primary outcomes. If there are three or more prespecified primary outcomes, the highest rating the study is eligible for is Class II. This rating affects all outcomes, whether primary or secondary.

Another requirement for a Class I rating is that the outcome pertinent to the guideline (regardless of whether it is a primary or secondary outcome in the original study) must have been specified a priori in the original study. This applies as well to subgroup analyses. If the article does not explicitly state that the outcome pertinent to the guideline was prespecified, then the class of evidence for the outcome is to be downgraded by one level.

## Secondary Outcomes

When several tests are performed on the same data set, there is a chance that false-positive results (type I errors) can occur. For example, if there are five hypotheses tested, there is a 23-percent chance one of them will be significant, even if all the tests are actually not significant. For  $n$  tests, the chance of a type I

error is  $1-(1-\alpha)^n$ . Ideally, the study authors would have adjusted for their secondary outcomes, and in this case, the guideline authors should use the study authors' reported values.

If the study authors did not adjust for multiple secondary outcomes, guideline authors may perform a correction. The simplest and most conservative correction is the Bonferroni correction. One way to perform a Bonferroni correction is to multiply the observed  $p$ -values by the number of comparisons measured. For articles that report five or fewer secondary outcomes, guideline authors should perform the Bonferroni correction.

A uniformly more powerful method to correct for multiple outcomes is the Holm-Bonferroni method.<sup>2</sup> This is the preferred method in cases where there are more than five secondary outcomes.

As an option, instead of making these corrections, the guideline panel may correct confidence intervals. In this case, the confidence intervals would be adjusted on the basis of the corrected alpha of the  $p$ -value, and then the corrected alpha would be reverse-imputed.

2 Kung J, Chiappelli F, Cajulis OO, et al. From systematic reviews to clinical recommendations for evidence-based health care: Validation of Revised Assessment of Multiple Systematic Reviews (R-AMSTAR) for grading of clinical relevance. *Open Dent J* 2010;4:84–91.

## Crossover Trials

A crossover trial is a type of clinical study in which the study participants are randomly assigned to receive each treatment in a

different order. For example, some patients receive placebo for several weeks followed by an active drug for several weeks, whereas others receive that active drug for several weeks followed by placebo for several weeks. Often, between treatments (placebo vs. active) there is a period of no treatment called a “washout” period. With this type of study, every patient serves as his or her own control. Crossover studies are often used to increase the statistical precision of a study.

In the setting of a crossover trial, confusion can arise because the patients are serving as their own controls and so, by definition, are substantially equivalent on baseline characteristics. However, in crossover trials there can be an effect related to treatment order. Hence, it is important to ensure that the patients randomized to different treatment orders (e.g., active followed by placebo vs. placebo followed by active) are substantially equivalent on baseline characteristics.

For a crossover trial to be rated Class I, the following criteria must be met:

1. There must be a comparison of baseline characteristics demonstrating substantial equivalence, or with adjustments for differences (if present).
2. Statistics must describe period and carryover effects, with adjustments if significant effects are present.

If the trial meets only one of these two criteria, it can be rated no higher than Class II.

If it meets neither criterion, it can be rated no higher than Class III.

# Appendix 3

Appendix 3 shown below comes from pages 35 and 36 of the AAN's *Clinical Practice Guideline Process Manual, 2011 edition*,<sup>1</sup> and reflects changes to the processes outlined as per the AAN Institute Board of Directors' approval on June 21, 2014. Text shown in strikethrough font with accompanying boldface font indicates that the former text has been replaced by the latter text. Text shown in boldface font without accompanying text in strikethrough font indicates the former is in addition to existing text.

## Appendix 3: Classification of Evidence Matrices

Classification of Evidence Matrix for Therapeutic, Causation, and Prognostic Questions			
Clinical Question Type			
Class	Therapeutic	Causation	Prognostic
I	<ul style="list-style-type: none"> <li>▪ Randomized, controlled clinical trial (RCT) in a representative population</li> <li>▪ Masked or objective outcome assessment</li> <li>▪ Relevant baseline characteristics are presented and substantially equivalent between treatment groups, or there is appropriate statistical adjustment for differences</li> <li>▪ Also required:               <ol style="list-style-type: none"> <li>a. Concealed allocation</li> <li>b. <del>Primary outcome(s) clearly defined.</del> <b>No more than two primary outcomes specified</b></li> <li>c. Exclusion/inclusion criteria clearly defined</li> <li>d. Adequate accounting for dropouts (with at least 80 percent of enrolled subjects completing the study) and crossovers with numbers sufficiently low to have minimal potential for bias</li> <li>e. For noninferiority or equivalence trials claiming to prove efficacy for one or both drugs, the following are also required*:                   <ol style="list-style-type: none"> <li>1. The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or noninferiority</li> <li>2. 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)</li> <li>3. 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</li> <li>4. The interpretation of the study results is based on a per-protocol analysis that accounts for dropouts or crossovers</li> </ol> </li> <li>f. <b>For crossover trials, both period and carryover effects examined and statistical adjustments performed, if appropriate</b></li> </ol> </li> </ul>	<ul style="list-style-type: none"> <li>▪ Cohort survey with prospective data collection</li> <li>▪ All relevant confounding characteristics are presented and substantially equivalent between comparison groups or there is appropriate statistical adjustment for differences</li> <li>▪ Outcome measurement is objective or determined without knowledge of risk factor status</li> <li>▪ Also required:               <ol style="list-style-type: none"> <li>a. Primary outcome(s) defined</li> <li>b. Exclusion/inclusion criteria defined</li> <li>c. Accounting of dropouts (with at least 80 percent of enrolled subjects completing the study)</li> </ol> </li> </ul>	<ul style="list-style-type: none"> <li>▪ Cohort survey with prospective data collection</li> <li>▪ Includes a broad spectrum of persons at risk for developing the outcome</li> <li>▪ Outcome measurement is objective or determined without knowledge of risk factor status</li> <li>▪ Also required:               <ol style="list-style-type: none"> <li>a. Inclusion criteria defined</li> <li>b. At least 80 percent of enrolled subjects have both the risk factor and outcome measured</li> </ol> </li> </ul>

## Appendix 3 (Continued)

Classification of Evidence Matrix for Therapeutic, Causation, and Prognostic Questions			
Clinical Question Type			
Class	Therapeutic	Causation	Prognostic
II	<ul style="list-style-type: none"> <li>Cohort study meeting criteria a–e (see Class I) or an RCT that lacks one or two criteria b–e (see Class I)</li> <li><b>An RCT that lacks one or two criteria a–e (see Class I) or a cohort study meeting criteria b–e (see Class I)</b></li> <li><b>Randomized, crossover trial missing one of the following two criteria:</b> <ol style="list-style-type: none"> <li><b>Period and carryover effects described</b></li> <li><b>Baseline characteristics of treatment order groups presented</b></li> </ol> </li> <li>All relevant baseline characteristics are presented and substantially equivalent among treatment groups, or there is appropriate statistical adjustment for differences</li> <li>Masked or objective outcome assessment</li> </ul>	<ul style="list-style-type: none"> <li>Cohort study with retrospective data collection or case-control study. Study meets criteria a–c (see Class I)</li> <li>All relevant confounding characteristics are presented and substantially equivalent among comparison groups or there is appropriate statistical adjustment for differences</li> <li>Masked or objective outcome assessment</li> </ul>	<ul style="list-style-type: none"> <li>Cohort study with retrospective data collection or case-control study. Study meets criteria a and b (see Class I)</li> <li>Includes a broad spectrum of persons with and without the risk factor and the outcome</li> <li>The presence of the risk factor and outcome are determined objectively or without knowledge of one another</li> </ul>
III	<ul style="list-style-type: none"> <li>Controlled studies (including studies with external controls such as well-defined natural history controls)</li> <li><b>Crossover trial missing both of the following two criteria:</b> <ol style="list-style-type: none"> <li><b>Period and carryover effects</b></li> <li><b>Baseline characteristics presented</b></li> </ol> </li> <li>A description of major confounding differences between treatment groups that could affect outcome**</li> <li>Outcome assessment masked, objective, or performed by someone who is not a member of the treatment team</li> </ul>	<ul style="list-style-type: none"> <li>Cohort or case-control study designs</li> <li>A description of major confounding differences between risk groups that could affect outcome**</li> <li>Outcome assessment masked, objective or performed by someone other than the investigator that measured the risk factor</li> </ul>	<ul style="list-style-type: none"> <li>Cohort or case control study</li> <li>Narrow spectrum of persons with or without the disease</li> <li>The presence of the risk factor and outcome are determined objectively, without knowledge of the other or by different investigators</li> </ul>
IV	<ul style="list-style-type: none"> <li>Did not include patients with the disease</li> <li>Did not include patients receiving different interventions</li> <li>Undefined or unaccepted interventions or outcome measures</li> <li>No measures of effectiveness or statistical precision presented or calculable</li> </ul>	<ul style="list-style-type: none"> <li>Did not include persons at risk for the disease</li> <li>Did not include patients with and without the risk factor</li> <li>Undefined or unaccepted measure of risk factor or outcomes</li> <li>No measures of association or statistical precision presented or calculable</li> </ul>	<ul style="list-style-type: none"> <li>Did not include persons at risk for the outcome</li> <li>Did not include patients with and without the risk factor</li> <li>Undefined or unaccepted measures of risk factor or outcomes</li> <li>No measures of association or statistical precision presented or calculable</li> </ul>

\* 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)

# Appendix 4

Appendix 4 shown below comes from page 38 of the AAN's *Clinical Practice Guideline Process Manual*, 2011 edition,<sup>1</sup> and reflects changes to the processes outlined as per the AAN Institute Board of Directors' approval on June 21, 2014. Text shown in strikethrough font with accompanying boldface font indicates that the former text has been replaced by the latter text. Text shown in boldface font without accompanying text in strikethrough font indicates the former is in addition to existing text.

## Appendix 4: Narrative Classification of Evidence Schemes

### Therapeutic

#### Class I

- Randomized, controlled clinical trial (RCT) in a representative population
- Masked or objective outcome assessment
- Relevant baseline characteristics are presented and substantially equivalent between treatment groups, or there is appropriate statistical adjustment for differences
- Also required:
  - a. Concealed allocation
  - b. Primary outcome(s) clearly defined  
**No more than two primary outcomes specified**
  - c. Exclusion/inclusion criteria clearly defined
  - d. Adequate accounting for dropouts (with at least 80 percent of enrolled subjects completing the study) and crossovers with numbers sufficiently low to have minimal potential for bias
  - e. For noninferiority or equivalence trials claiming to prove efficacy for one or both drugs, the following are also required\*:
    1. The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or noninferiority
    2. 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)

3. 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
4. The interpretation of the study results is based on a per-protocol analysis that accounts for dropouts or crossovers

#### **f. For crossover trials, both period and carryover effects examined and statistical adjustments performed, if appropriate**

#### Class II

- Cohort study meeting criteria a–e (see Class I) or an RCT that lacks one or two criteria b–e (see Class I) **An RCT that lacks one or two criteria a–e (see Class I) or a cohort study meeting criteria b–e (see Class I)**
- **Randomized, crossover trial missing one of the following two criteria:**
  - a. **Period and carryover effects described**
  - b. **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
- Masked or objective outcome assessment

#### Class III

- Controlled studies (including studies with external controls such as well-defined natural history controls)
- **Crossover trial missing both of the following two criteria:**
  - a. **Period and carryover effects**
  - b. **Baseline characteristics presented**
- A description of major confounding differences between treatment groups that could affect outcome\*\*
- Outcome assessment masked, objective, or performed by someone who is not a member of the treatment team

#### Class IV

- Did not include patients with the disease
- Did not include patients receiving different interventions
- Undefined or unaccepted interventions or outcome measures
- No measures of effectiveness or statistical precision presented or calculable

\* 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)



## Amendment III: Guideline Topic Nomination Process

**Until June 2014, the AAN maintained a list of topic nominations that the Guideline Development, Dissemination, and Implementation Subcommittee (GDDI) had accepted and reviewed quarterly but did not formally prioritize. For many topics, the AAN did not have the resources available in order to initiate development. In June 2014, the AAN initiated use of a Guideline Nomination Priority Score (GNPS) 1) to ensure that the most impactful topics for the AAN membership are undertaken in a timely manner, and 2) to increase the transparency of GDDI processes.**

**The text shown below replaces the applicable text that appears on pages 22 and 23 of the AAN's *Clinical Practice Guideline Process Manual*, 2011 edition,<sup>1</sup> as per the AAN Institute Board of Directors' approval on June 21, 2014.**

### Nominating the Topic

Any AAN member, Committee, or Section, or an outside organization (e.g., an organization responsible for generating health policy), may suggest a guideline topic using the Guideline Topic Nomination Form available at [AAN.com/guidelines/home/development](http://AAN.com/guidelines/home/development).

The GDDI evaluates nominated topics quarterly using a ranking tool known as the Guideline Nomination Priority Score (GNPS). The GDDI Chair designates one GDDI member with content expertise in the area of the nominated topic, and who does not have any relevant conflicts of interest, to rank the proposed topic (or the Chair may select a topic expert with no relevant conflicts from outside GDDI if necessary). To do so, the GDDI member or designated expert uses the GNPS tool to rank the position of the topic in the development priority hierarchy (i.e., the degree of impact the topic has for the AAN membership). The following criteria are taken into account:

- Relevance to neurologists
- Disease prevalence
- Degree of practice variation or controversy
- Project feasibility (amount of evidence, whether collaboration with one or more external societies is required)
- Impact on patient care and outcomes

Not all topics are accepted for development. In addition, the GDDI limits the existing topic list to 25 topics awaiting development at any one time.

The GNPS tool is presented on the next page.

# Amendment III: Guideline Topic Nomination Process

## American Academy of Neurology Guideline Nomination Priority Score Instructions

The Guideline Nomination Priority Score (GNPS) should be completed by an AAN GDDI member, or designated expert, with content expertise in the area of the nominated topic who does not have any relevant conflicts of interest. The individual nominating the topic will remain anonymous.

The GDDI member, or designated expert, assigned to complete the GNPS should review the information submitted in the Guideline Topic Nomination Form. The member may supplement this with his or her own literature search if needed. After reviewing the relevant information, the member will grade each question below on a scale of 1 to 5 according to the provided instructions.

1. Title/topic: \_\_\_\_\_
2. How relevant to neurologists is the proposed guideline question?  
(1 = minimally relevant, 5 = extremely relevant)  
 1    2    3    4    5
3. What is the prevalence of this disease?  
(1 = extremely rare, 5 = extremely common)  
 1    2    3    4    5
4. What is the amount of practice variation or controversy? When answering this, please consider both scientific issues and cost. Are nearly all neurologists handling this issue the same way, or are many neurologists handling it differently? What is the cost of the screening test or therapy (or other relevant intervention for the proposed question)? What are the cost implications of the guideline? Are there articles on the cost-effectiveness of the proposed guideline?  
(1 = minimal practice variation or controversy, minimal cost implications; 5 = significant practice variation or controversy, significant cost implications)  
 1    2    3    4    5
5. How feasible is the proposed project? Please consider the amount of evidence and published data to answer the proposed question, whether a preexisting systematic review might be able to inform the guideline, the number of questions proposed, and whether the AAN could collaborate with an associated society to complete the guideline.  
(1 = not feasible, 5 = easy to complete in a timely manner)  
 1    2    3    4    5
6. How might this guideline improve patient care and outcomes? When weighing this, please consider whether this guideline might inform the creation of a related AAN quality measure or whether it lends itself to use of certain dissemination and implementation tools.  
(1= small impact, 5 = large impact)  
 1    2    3    4    5
7. Please provide any additional comments regarding your prioritization of this guideline. The total score will be calculated in the spreadsheet fed by the Google Docs. The lowest possible score is 5, and the highest possible score is 25.

## Amendment III: Guideline Topic Nomination Process (Continued)

### American Academy of Neurology Evidence-based Guideline Topic Nomination Form

Please complete each of the required fields. The information you provide will be used to grade and prioritize the topic's importance. Please include specific references where requested.

1. Title/topic:
2. Clinical question(s) – Please provide in PICO format. For assistance, please see page 3 in AAN's *Clinical Practice Guidelines Process Manual* ([AAN.com/Guidelines/Home/Development](http://AAN.com/Guidelines/Home/Development))
3. Background on the topic and disease:
  - a. Why is this topic important and relevant?
  - b. What is the prevalence of this disease?
  - c. Describe the amount of practice variation or controversy.
  - d. Provide cost information relevant to the proposed guideline: What is the cost of the screening test or therapy (or other relevant intervention for the proposed question)? What are the cost implications of the guideline? Are there papers regarding the cost-effectiveness of the proposed guideline? Please provide references regarding cost.
4. How much evidence and published data are there to answer the proposed question? Please provide references to key systematic reviews or seminal high-quality research papers. Please comment on whether there are existing guidelines on this topic.
5. How might this guideline improve patient care and outcomes?
6. What implementation and development tools might be relevant to the proposed guideline (e.g., clinician summary, patient summary, algorithm, app, etc.)? Could this guideline be used to develop an AAN quality measure? Please describe.
7. Please suggest proposed authors for this guideline.

# Amendment IV: Focused Systematic Reviews and Practice Advisories

**Focused systematic reviews (focused SRs) and practice advisories are evidence-based documents the AAN develops in addition to SRs and evidence-based guidelines. Focused SRs and practice advisories have these features:**

- Both document types are briefer and more narrowly focused than full-length SRs and evidence-based guidelines.
- Both document types seek to answer two or fewer clinical questions.
- As with full-length SRs, focused SRs do not make recommendations.
- As with evidence-based guidelines, practice advisories make recommendations.

**The AAN is committed to producing SRs and evidence-based guidelines that are compliant with the 2011 Institute of Medicine (IOM) “Finding What Works in Health Care: Standards for Systematic Reviews” and “Clinical Practice Guidelines We Can Trust” (IOM standards).<sup>2,3</sup> However, SRs and evidence-based guidelines produced in full compliance with IOM standards take considerable resources and time to develop. Recognizing there may be clinical questions that warrant timely evidence-based review and guidance, the AAN approved development of focused SRs and practice advisories that are partially compliant with the IOM standards.**

**The text shown below updates the applicable text that appears on page 22 of the AAN’s *Clinical Practice Guideline Process Manual*, 2011 edition,<sup>1</sup> as per the AAN Institute Board of Directors’ approval on June 21, 2014.**

## Identifying the Five Document Types

### Systematic Reviews (Evidence Reports)

Systematic reviews (SRs) are documents developed using the AAN’s EBM approach to guideline development. These documents do not include practice recommendations. However, the SRs provide neurologists with information about the state of the evidence and often serve as an impetus for researchers to design studies to address the current knowledge gaps. SRs are developed in full compliance with the 2011 IOM standards.

### Focused Systematic Reviews

The AAN develops focused systematic reviews (focused SRs) in circumstances where only one or two clinical questions are posited. In contrast, comprehensive SRs address three or more clinical questions. Focused SRs do not

include practice recommendations. Focused SRs are developed in partial compliance with the IOM standards.

### Evidence-based Guidelines

These document types make actionable practice recommendations based on SRs developed with a methodologic rigor equivalent to or greater than the AAN’s. As with SRs, guidelines are documents that assess the safety, utility, and effectiveness of new, emerging, or established therapies and technologies in the field of neurology. Contrary to SRs, evidence-based guidelines also address strategies for patient management that assist physicians and patients in clinical decision making, focusing on a series of specific, evidence-based practice recommendations that answer one or more important clinical questions. Evidence-based guidelines are developed in full compliance with the IOM standards.

### Practice Advisories

Based on focused SRs, practice advisories also make recommendations. The AAN develops these documents in order to provide guidance in less time than is involved with the full development process. These documents are narrowly focused, typically limited to one or two clinical questions. Practice advisories are developed in partial compliance with the IOM standards.

### Case Definitions

Case definitions are documents developed for conditions for which there is no validated reference standard. In these circumstances, evidence cannot adequately define the condition; therefore these documents are developed using a formal, validated expert consensus approach (e.g., modified Delphi).

## Amendment IV: Focused Systematic Reviews and Practice Advisories (Continued)

**The text below updates the applicable text that appears on page 24 of the AAN's *Clinical Practice Guideline Process Manual*, 2011 edition,<sup>1</sup> as per the AAN Institute Board of Directors' approval on June 21, 2014.**

### Completing the Project Protocol

The following information is included in the draft protocol:

- Author panel, degrees, affiliations, and disclosures
- Justification for development
- Analytic frame used to help frame the questions
- Clinical questions (use the PICO format described in section 2 of this manual)
- Terms and databases to be used in the literature search
- Inclusion and exclusion criteria for article selection
- Proposed project timeline

The AAN is committed to producing SRs and evidence-based guidelines that are compliant with the 2011 IOM standards. However, SRs and evidence-based guidelines produced in full compliance with IOM standards take considerable resources and time to develop. Recognizing there may be clinical questions that warrant timely evidence-based review and guidance, the AAN approved development of focused SRs and practice advisories that are partially compliant with the IOM standards. The authors, in consultation with the GDDI and methodologists, may recommend opting out of any or all of the milestones outlined below. Any decision made to opt out of these milestones will require a justification to be included in the final manuscript for publication.

- Provide a public comment period for the protocol and refine each question based on feedback.
- Engage a librarian/information specialist to perform the literature search.
- Assign an independent librarian or other information specialist to review the search results.
- Conduct a "hand search" of the selected journal and conference abstracts.
- Conduct a web search.
- Search for studies in languages other than English.
- Search the "grey" literature databases, clinical trial registries, and other sources of unpublished information about studies.
- Invite study researchers and sponsors to clarify information in their studies and to provide unpublished data.
- Train screeners with written documentation and test and retest screeners to improve accuracy and consistency.
- Provide a public comment period for the report and publicly report on the disposition of comments.

## Amendment IV: Focused Systematic Reviews and Practice Advisories (Continued)

The table below shows the elements involved in development of the AAN's evidence-based documents, as per the AAN Institute Board of Directors' approval on June 21, 2014.

### Elements of AAN Evidence-based Documents

	Case Definition	Systematic Review		Guideline	
		Focused Systematic Review	Comprehensive Systematic Review	Practice Advisory	Evidence-based Guideline
Number of Clinical Questions Typically Addressed		≤ 2	≥ 2	≤ 2	≥ 2
Number of Databases Searched	Minimum of 1	Minimum of 1	At least 2 required	Minimum of 1	At least 2 required
Search of Grey Literature	Optional	Optional	Yes	Optional	Yes
Practice Recommendations Included	No	No	No	Yes	Yes
Public Comment Period Included	Optional	Optional	Yes	Optional	Yes
Patient/Patient Advocate on Panel Included	Optional	Optional	Yes	Optional	Yes

# Amendment V: Change in Steps for External Review Process and Option of Publication of Areas of Controversy

**In 2013, the AAN President convened the Guideline Publications Task Force to review and suggest improvements to the intersection of the AAN guideline development process and the *Neurology*<sup>®</sup> journal review process. As a result, the AAN Institute Board of Directors established the following process changes:**

1. The order of steps for SR and guideline external review now positions *Neurology* journal peer review to take place after the public comment period and before AAN internal committee final approval for an SR or guideline.
  - a. The authors review the comments from journal peer review and determine which changes to make.
  - b. After the authors have incorporated their changes, AAN staff present the revised documents to the GDDI for final review and approval.
  - c. After the GDDI approves the document changes, AAN staff presents the documents to the AAN Practice Committee for review and approval.
  - d. After the Practice Committee approves the documents, AAN staff submits the documents to the journal for re-review.

Note:

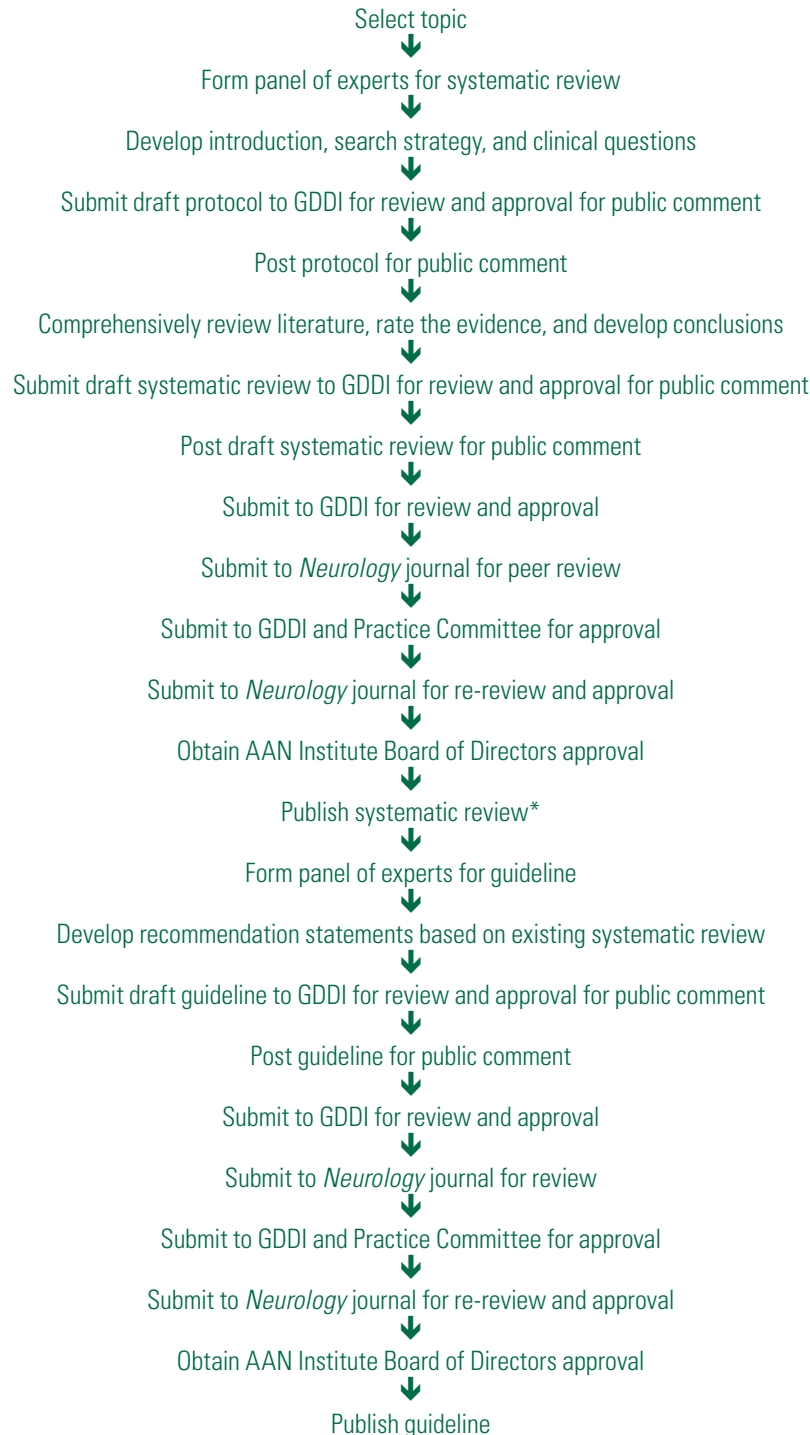
- Many SR/guideline projects were initiated before the AAN instituted the IOM standards-based methodology in 2011. The AAN has a “grandfather” allowance that permits these projects to follow the AAN methodology established in 2004. These projects are exempt from the process described in this amendment because these documents are not distributed for public comment.
2. The option is available to publish a report on areas of controversy in an instance in which the *Neurology* journal peer review process conflicts with the SR or guideline development process. In this situation, the *Neurology* journal and GDDI leadership determine the extent to which the generation of such a report would occur. The options include, but are not limited to, the following:

- An update of the text of the SR or guideline to identify areas of controversy
- Publication of a separate editorial or companion article to the SR or guideline

# Amendment V: Change in Steps for External Review Process and Option of Publication of Areas of Controversy (Continued)

The figure shown below replaces figure 7 as it appears on page 22 of the AAN's *Clinical Practice Guideline Process Manual*, 2011 edition,<sup>1</sup> as per the AAN Institute Board of Directors' approval on June 21, 2014.

**Figure 7. Steps in AAN Systematic Review and Guideline Development**



\* Not all SRs will serve as the basis for guidelines. In some cases, author panels or content reviewers will recommend against the development of guideline recommendations from a particular SR. In such cases, the AAN will publish the SR in final form as a standalone document.



# Amendment V: Change in Steps for External Review Process and Option of Publication of Areas of Controversy (Continued)

The text shown below replaces the applicable text that appears on page 30 of the AAN's *Clinical Practice Guideline Process Manual*, 2011 edition.<sup>1</sup>

## Reviewing and Approving SRs and Guidelines

### Stages of Review

AAN staff and the GDDI will review the SR and CPG at several stages during the development process. These stages are outlined below:

Stage	Reviewer
General topic	GDDI
Author panel* composition	GDDI leadership and AAN staff
Protocol	GDDI, AAN staff, public
Evidence tables	GDDI, AAN staff
SR/CPG draft	GDDI, AAN staff, AAN peer review network, public
SR/CPG draft post-public comment	GDDI, AAN staff, <i>Neurology</i> peer reviewers
GDDI-approved systematic review or CPG	AAN staff, Practice Committee, <i>Neurology</i> peer reviewers, AAN Institute Board of Directors

\*The author panel includes members of the facilitation team.

The following text replaces the applicable text that appears on page 31 of the AAN's *Clinical Practice Guideline Process Manual*, 2011 edition,<sup>1</sup> as per the AAN Institute Board of Directors' approval on June 21, 2014.

### GDDI Re-review (Post-public Comment)

AAN staff sends the GDDI the revised documents and revision table (reflecting input from public comment, as applicable) for review and a vote at the next GDDI meeting. GDDI approval may be contingent on additional requested revisions.

### Journal Review

The *Neurology* journal solicits reviewers from its network to review and comment on the manuscript. Comments are sent directly to the lead author and AAN staff. The lead author drafts a revision letter presenting all comments from *Neurology* peer reviewers. Authors are encouraged to consider all revisions suggested by the journal peer reviewers. Authors are to contact the facilitator if the reviewers' requested changes conflict with AAN requirements for SRs or CPGs, particularly if reviewers request substantial revisions to the wording of conclusions or recommendations. The lead author then submits the revised draft to AAN staff (not directly to the journal) with the completed revision letter denoting the panel's responses to all of the journal reviewers' comments. The revised draft must show all changes made to the manuscript, using an

electronic editing tool (e.g., Track Changes, strikethrough font, or highlighted font). AAN staff then submits the manuscript to GDDI.

### GDDI Re-review and Approval

AAN staff sends the revised documents, the revision table (reflecting input from public comment), and the *Neurology* peer review comments for a review and an official vote at the next GDDI meeting.

### Practice Committee Review and Approval

When the GDDI gives final approval of the manuscript, AAN staff submits the manuscript to the Practice Committee for approval. The Practice Committee may have additional revision requests, and if these revisions are substantial, the changes are reviewed by the GDDI Chair. Substantial revisions—particularly those that change the conclusions and recommendations—may require GDDI reapproval.

In some instances, the guideline authors, GDDI Subcommittee members, and Practice Committee members may disagree substantially with requested changes received from *Neurology* peer review that cannot be resolved with manuscript revisions. In cases of disagreement, the AAN EBM Methodologist,

GDDI Chair, and *Neurology* Editor-in-Chief convene a meeting to discuss whether the disagreement warrants publication of a report on the pertinent area(s) of controversy. If the AAN EBM Methodologist, GDDI Chair, and *Neurology* Editor-in-Chief determine such a report is needed, the author panel generates a discussion section for inclusion in the final publication to highlight the point of disagreement. The *Neurology* journal may choose to write a separate editorial or companion document for simultaneous publication that articulates how the areas of controversy related to the SR or guideline affect the field.

### Journal Re-review

At the time of revision submission, authors are required to provide AAN staff with updates to disclosures they have deemed to be relevant to the project. Later, at the point of journal provisional acceptance, authors must complete comprehensive disclosures on the journal's Authorship Agreement, Disclosure Agreement, and Publication Agreement Forms through their online *Neurology* author accounts.

The journal may request additional rounds of reviews prior to accepting the manuscript for publication.

# References

1. American Academy of Neurology. 2011. *Clinical Practice Guideline Process Manual*, 2011 ed. St. Paul, MN: The American Academy of Neurology.
2. Institute of Medicine of the National Academies. Finding What Works in Health Care: Standards for Systematic Reviews. <http://www.iom.edu/Reports/2011/Finding-What-Works-in-Health-Care-Standards-for-Systematic-Reviews.aspx>. Released March 23, 2011. Accessed January 11, 2013.
3. Institute of Medicine of the National Academies. Clinical Practice Guidelines We Can Trust: Standards for Developing Trustworthy Clinical Practice Guidelines (CPGs). <http://www.iom.edu/Reports/2011/Clinical-Practice-Guidelines-We-Can-Trust.aspx>. Released March 23, 2011. Accessed January 11, 2013.