Stroke Council Guideline Development Manual

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Section I: Overview of Methodology and Purpose of the Manual

Importance of AHA Stroke Council Guidelines
The creation development of stroke clinical practice guidelines has been a major activity of the American Heart Association/Stroke Association Stroke Council since the 1980s. The guidelines advance the mission of the Stroke Council by providing clinical recommendations to health care providers for the purpose of improving cerebrovascular health. The Institute of Medicine defines practice guidelines as, "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances." (1990) Well developed guidelines have the potential to enhance the appropriateness of clinical practice, improve the quality of care, lead to better patient outcomes, improve cost-effectiveness, and identify areas of further research needs.

Purpose and Scope of the Manual
To continue as a leader in the field of clinical practice guidelines, the Stroke Council Scientific Statements Oversight Committee has overseen the creation of this manual to assist guideline writing committees in navigating guideline creation. The purpose is to support the integrity of the Guideline process by using transparent, uniform procedures and to ensure that Stroke Council statements adhere to the highest standards of guideline development to increase their impact and adoption by other organizations involved in the care of stroke patients. The bulk of this manual consists of tools to assist guideline writers in interpreting and applying standardized methodology. A flowchart highlighting the key steps in the development of evidence-based guidelines (Figure 1) serves as the basis for organizing the manual. Foundational elements for the writing of this manual include AHA Policies on Conflicts of Interest, the AHA-ACC Manual on Guideline Development, and the Stroke Council Scientific Statement Oversight Committee Standing Manuscript Writing Committee Policy.

The Stroke Council Scientific Statements Oversight Committee (SOC) understands the challenges in applying a uniform methodology to guidelines that represent diverse diseases, conditions, diagnostics, and interventions. In all cases, writing group members should familiarize themselves thoroughly with the manual, as these policies and standards provide the framework for guideline creation. Under unusual circumstances, SOC may allow exceptions to these written policies.

Staff Support
AHA/ASA provides scientific and administrative staff to support the creation of evidence-based guidelines. A Scientific Liaison and an Administrative Assistant Manager are assigned to each guideline to assist writers with the methodology and process of guideline development.

Figure 1. Steps in the Development of Evidence-Based Guidelines
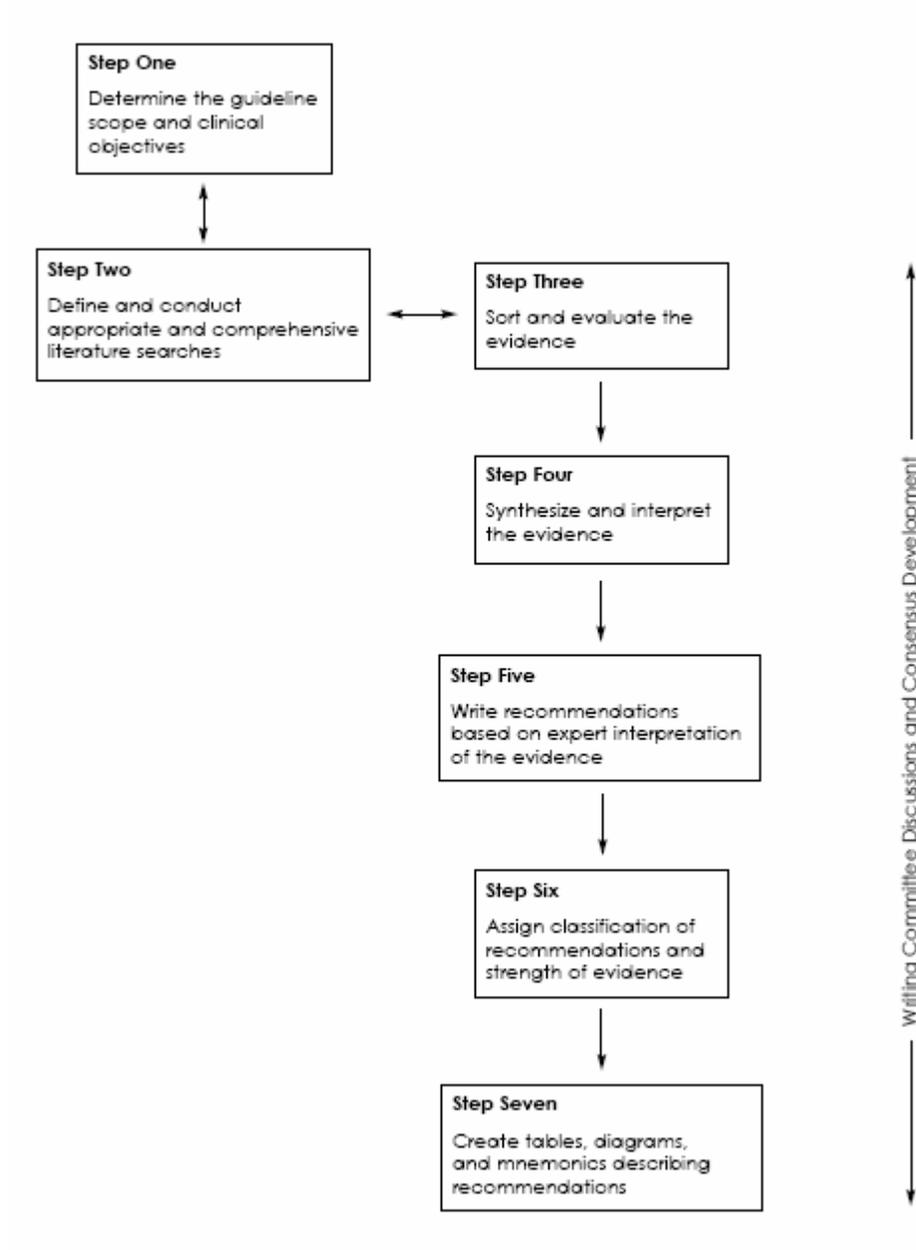
Section II: Tools and Methods for Creating Guidelines

Step One: Determine the Guideline Scope and Clinical Objectives

Topic Selection
AHA Stroke Council clinical practice guidelines are written on three topic areas: diagnosis of conditions, treatment of conditions, and performance of procedures. The Stroke Council Scientific Statements Oversight Committee determines the topics for guidelines and selects the writing committee members, while the writing committee is responsible for developing the guideline's content.

Determining the Guideline's Scope
Before and during the first meeting, the writing committee primarily focuses on coming to consensus about the guideline's scope (see **Checklist 1**). AHA Stroke Council guidelines are usually intended to provide recommendations applicable in the United States, with conclusions and recommendations based on expert judgment applied to clinical evidence. Although some guidelines also address issues of cost-effectiveness and related economic analyses, ACC/AHA guidelines are generally intended to provide clinically relevant information outside of the context of costs and reimbursement. If cost issues must be included, guideline writers should limit the scope to previously published analyses and not attempt to develop any new economic analysis within the document.

Checklist 1. Determining the Guideline Scope and Clinical Objectives

Questions related to the guideline overall

- o What is the guideline's targeted health condition, procedure, or diagnostic?
- o What is the purpose of the guideline?
- o What is within the scope of the guideline?
- o What is outside the scope of the guideline?
- o Who are the guideline's intended users?
- o What is the epidemiology of the topic?
- o What is the target patient population to be addressed in the guideline?
- o How does the guideline relate to other existing ASA and AHA guidelines?
- o Can a few flow diagrams summarize the guideline, or at least key sub-sections?

Questions related to the guideline's clinical objectives

- o What are the important clinical objectives related to the guideline

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topic?
- o What sub-topics and related topics must be included in the guideline?
- o Are flow diagrams appropriate to these sub-topics and related topics?
- o What are the potential benefits and risks for individual patients associated with an intervention or procedure?
- o What amount of clinical flexibility is appropriate for the topic area?
- o What clinical options are available?
- o What topics have already been covered in existing ASA and AHA guidelines?

Guideline Updates and Revisions

In order to ensure up-to-date guideline content, AHA Stroke Council has established Standing Manuscript Writing Committees to issue regularly updated guidelines addressing key domains of stroke care. Each Standing Manuscript Writing Committee will produce a fully updated comprehensive manuscript not less than once every 3 years. These comprehensive Guidelines will ordinarily be published in full in the journal <u>Stroke</u> and, if appropriate, in additional AHA journals. The Standing Manuscript Writing Committee may produce a fully updated comprehensive Guideline at a more frequent interval if the Standing Manuscript Writing Committee feels that research and clinical advances warrant accelerated publication of an updated comprehensive Guideline Statement. At the 3 year interval, the Standing Manuscript Writing Committee may determine that no changes or no substantial changes are warranted in a previous comprehensive Guideline. In this event, the previous comprehensive Guideline will be republished as reviewed and revalidated at the later date. This will be done to ensure that no comprehensive Manuscript is ever more than 3 years old.

Each Standing Manuscript Writing Committee will continuously monitor advances in the field for new findings that are of sufficient clinical and/or scientific significance to warrant a revision of a portion of the existing Guidelines at an interim timepoint in the usual 3 year cycle. If such major interval advances occur, the Standing Manuscript Writing Committee may choose to, or be tasked by the Stroke Council Leadership Committee, to produce a focused interim update of the comprehensive Guidelines. These interim updates will ordinarily be published on the website of the American Stroke Association. If appropriate, because of their clinical and/or scientific significance, they may also be published in the journal <u>Stroke</u> and additional AHA journals.

In addition to the Standing Manuscript Writing Committees, the Stroke Council Leadership Committee occasionally initiates other, one-time Manuscript Writing Committees addressing additional topics in stroke care. The Stroke Scientific Statement Oversight Committee will review all one-time Writing Committee Guidelines every 2 years following publication and determine if the guideline is a) still current, b) requires an update, or c) should be retired.

Guideline Structure

Guideline writers are encouraged to define as precisely as possible the overall guideline structure at the early stages of guideline creation. The standard guideline outlines in Table 1 are recommended. These outlines improve consistency across guidelines and facilitate the effectiveness of on-line searching of guidelines. They provide a common structure while allowing for flexibility as the topic demands. Guideline writers should determine at the outsets which "standard concepts" apply to their guideline, then proceed with creating detailed clinical objectives under each concept. The standard outlines are not prescriptive, nor are they meant to encourage the creation of textbook-style guidelines.

Table 1. Standard Guideline Outlines

Disease or Condition Guidelines

Standard Concepts	Possible Content
Abstract	Structured format
Introduction	Purpose of the guideline
	Scope
Methods	Intended audience and topic
	Literature search strategy and dates
	Levels of evidence / planned update
Definition of the Disease/Condition	Overview
	Epidemiology
	Classifications
	Characterizations
Clinical Evaluation	Recognition
	Methods for Risk Stratification
	Other issues related to clinical assessment
Diagnosis and Testing	Non-invasive testing
	Invasive testing
	Laboratory testing
	Risk assessment
Treatment	Principles of management
	Therapy
	Medication
	Procedures
	Interventions
	Alternative/complementary medicine
	Monitoring
Special Populations	Concomitant disorders
	Patient groups
Follow-up	Discharge
	Long-term management
Summary of Recommendations	Recommendation list
COI//Funding Source	Conflict of interest statements
	Description of funding source

Intervention Guidelines

Standard Concepts	Related Content
Abstract	Structured format
Introduction	Purpose of the guideline
	Scope

Methods	Intended audience and topic
	Literature search strategy and dates
	Levels of evidence / planned update
Definition of Intervention/Procedure	General considerations
	Background
Indications	Clinical uses
Management Strategies	Procedure-specific considerations
	Associated medical therapies
	Procedural complications
	Reducing risk
Outcomes	Definitions of success
	Short-term and long-term outcomes
	Comparisons with other interventions
Institutional/Operator issues	Quality assurance/improvement
	Volume considerations
Special Populations	Patient groups
Summary of Recommendations	Recommendation list
COI//Funding Source	Conflict of interest statements
	Description of funding source

Diagnostic Guidelines

Standard Concepts	Related Content
Introduction	Purpose
	Scope
Abstract	Structured format
Methods	Intended audience and topic
	Literature search strategy and dates
	Levels of Evidence/Planned update
Description of the Diagnostic Tool	Specific procedures
	Equipment
	Sensitivity/specificity
	General considerations
	Comparison with other diagnostic tools
Specific Conditions	Clinical uses (note: diagnostic guideline usually subdivided by the disease/conditions that they can diagnose. These discussions included diagnosis, assessment, prognosis, risk stratification, screening, etc.)
Special populations	Patient groups
Summary of Recommendations	Recommendation list
COI//Funding Source	Conflict of interest statements
	Description of funding source

Identifying the Clinical Objectives

The main goal a guideline is to develop recommendations that allow the public and healthcare providers to understand the evidence related to the topic and apply it in clinical practice. As such, guideline writers should progress with specific clinical objectives in mind. It may be very helpful

at the outset to consider what kind of guidance the readers will expect in the completed document, such as:

- The role of carotid imaging in asymptomatic patients
- The use of warfarin in patients with atrial fibrillation
- Managing cerebral vasospasm medically versus procedurally

A comprehensive collection of clinical objectives should be created within each main concept addressed by the guideline outline. These clinical objectives serve as the basis for literature searching and sorting, and later for the compilation of guideline recommendations.

Step Two: Define and Conduct Appropriate and Comprehensive Literature Searches

Finding and Managing the Evidence
Once the scope of the guideline has been determined, the next step is to conduct a comprehensive search of the published literature. A key component of guideline generation is the creation of recommendations based on the entirety of the evidence currently available. The Institute of Medicine describes literature searching as the key step in developing valid guidelines.

Recommended databases to include in a Stroke Council guideline development search are MEDLINE, EMBASE, the Cochrane Library, and Best Evidence. A Research Librarian and a Copy Editor can assist the Writing Committee in conducting searches and will forward relevant citations to the writers.

Literature Search Methodology
Figure 2 outlines the ASA process for conducting comprehensive literature searches for the guidelines. Initial literature searching focuses on published meta-analyses and systematic reviews. If high-quality, relevant, and up-to-date meta-analyses or systematic reviews are found, these articles allow writers to focus on critiquing and updating an existing review as opposed to creating one. For the majority of topics, literature searching also includes randomized clinical trials, and is expanded to non-randomized studies, case studies, and opinion documents until the evidence-base is sufficient for each clinical question identified in Step One. Each article should be critically evaluated as to quality and clinical limitations, as discussed in Step Three.

Figure 2. Process for Conducting Comprehensive Literature Searches for Guidelines
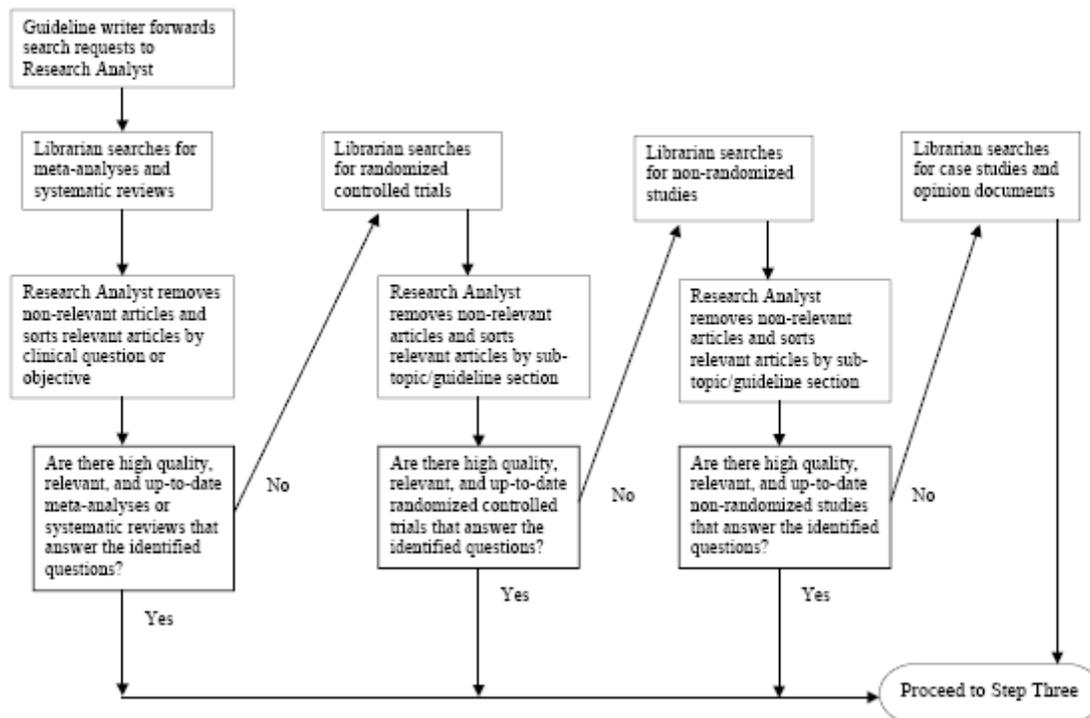
Documentation of Searching
All literature must be documented by the searcher and stored at the ASA offices. This allows the chair and Copy Editor to construct the text of the guideline describing the literature search criteria, thereby allowing guideline users to assess the comprehensiveness of the search strategy and allowing it to be updated for future guidelines.

In addition to searches conducted by staff, writing committee members are welcome to conduct their own literature searches, including search criteria beyond what the AHA/ASA resources are able to provide. The documentation for all literature searches must be forwarded to the Chair and Copy Editor using the **Template: Literature Searches for AHA Stroke Council Guidelines** (Appendix A).

Standard Search Criteria for AHA Stroke Council Guidelines

- Literature searching includes the following on-line databases:
    - MEDLINE/PubMed
    - EMBASE
    - Cochrane Library
    - Best Evidence
- Searches are limited to English language. (Searches will be expanded to languages other than English on a case-by-case, as requested basis.)
- Searches are limited to human subjects.
- In the case of a guideline update, searches are limited to the time period following the publication of the last version of the guideline.
- In the case of a new guideline or new guideline section, no time limits on searches are imposed, unless the writing committee determines that a different time frame is appropriate (for example, a guideline on a diagnostic that did not exist before a certain date).
- Gender and age are not limited, except when a specific clinical objective applies only to a particular sex or age group.
- Publication type is initially limited to randcomized clinical trials, meta-analyses and systematic reviews. Publication type is then expanded on an as-needed basis to include non-randomized studies, case studies, and opinion documents.
- If an acceptable systematic review or meta-analysis is identified, searches to update it are typically limited to the time period following the search cut-off date reported in the review.

Supplementing Retrieved Articles with Additional Articles Known to Committee Members
As content experts, Committee Members may be aware of published articles relevant to a guideline topic that do not appear among the article list yielded by the formal literature search. Committee Members should add these articles to the article database and include these articles in subsequent article filtering process.

Step Three: Sort and Evaluate the Evidence

Stages of Sorting Evidence
After the literature search results have been imported into the computerized database managed at the ASA, the Copy Editor and/or Requestor reviews the abstracts and removes non-relevant citations. At this step, only the article's title and abstract are assessed, so any article likely to be relevant to the guideline is maintained. Additionally, the Copy Editor and/or Requestor sorts the abstracts to correspond with the specific clinical objectives identified in Step One. This initial sort creates a comprehensive set of potentially relevant studies.

Although the Copy Editor and/or Requestor do a preliminary level of sorting, the clinical expertise of writing committee members is necessary to make the final decision as to whether the article is relevant and should be included in the formulation of a recommendation. This often requires review of the article's full text and critique of the research methodology employed. As necessary, guideline writer(s) should review the full text of all peer-reviewed, published:

- Randomized controlled trials
- Meta-analysis
- Systematic reviews of evidence
- Diagnostic studies using comparison with a gold standard

Along with each full text article, the writer will receive the Article Evaluation Checklist (Appendix B), which asks the writer to make the final determination of the article's role within the guideline. Documentation of completed checklists will be maintained by the ASA in the methodology files for the guideline.

Unpublished Data
Guideline writers are frequently familiar with data from abstracts and late-breaking trials that may be relevant to the guideline's content. The results from unpublished data should not be included. Inclusion of unpublished, non-peer reviewed, unfinalized analyses could introduce several biases. If new data that would change a guideline recommendation or lead to a new recommendation that would change practice is published as a peer-reviewed report subsequent to Guideline publication, the Standing Guideline Writing Group or the Stroke Scientific Statement Oversight Committee can initiate a Practice Advisory that would appear promptly as an amendment to issued Guideline.

Balancing Scientific Rigor with Feasibility
The Cochrane Collaboration publishes perhaps the most rigorous and comprehensive guide to conducting systematic reviews of evidence, and their methodology has provided the basis for much of this manual. However, due to time and economic constraints, some components of their methodology (such as creating and validating criteria for which articles to include, and removing the journal and author names from articles being reviewed) are beyond the resources of AHA Stroke Council.

A less resource-intensive, more feasible approach is to establish a few basic criteria (such as randomized controlled trials only or studies with at least six month follow-up) and be as

inclusive and unbiased as possible. The Stroke Council Scientific Statements Oversight Committee recommends rigorous review of the articles used in evidence tables and meta-analyses—those articles that are fundamental to the guideline recommendations. Documentation of why individual studies are included and excluded from consideration will provide additional scientific rigor to the document. If this documentation is performed, it can be published on the ASA web site as a component of the guideline methodology or included as an Appendix to the Guideline..

Checklist 2. Determining the Evidence Basis for Guideline Recommendations*

Guideline writers are asked to consider the merits, quality, and generalizability of each article relevant to the clinical objective. This checklist should be completed only for articles from the peer-reviewed, published literature that are:

- o   randomized controlled trials,
- o   meta-analysis/systematic reviews, or
- o   diagnostic studies using comparison with a gold standard.

Article/Author and Year:
Please indicate one of the following conclusions about the article:

_____ **Yes**, this is a relatively high quality study that provides credible results and should be included in the evidence table and references that support the recommendation(s) for this clinical objective.

_____ **No**, this study is not of sufficient quality to be included in the evidence table, but Yes, this study contains some useful information about the clinical objective and should be maintained as a reference for the text accompanying the recommendation.

_____ **No**, this is a relatively poor study that should not be used in the evidence table or in the references for this clinical objective.

_____ **No**, this study is not directly relevant to the clinical objective

Comments:

Step Four: Synthesize and Interpret the Evidence

Guideline Authoring Template
To improve the consistency of guideline content, both within and between guidelines, the Scientific Statement Oversight Commitee has created a guideline authoring template. Guideline writers will receive one template for each clinical objective they are responsible for writing. The following is a brief introduction to using the template:

- The fields for **guideline**, **author**, **section name**, and **clinical objective** will be completed by staff.
- The **evidence base** field will consist of the articles gathered through the literature search and sorting (**Steps Two** and **Three**). Writers whose clinical objectives have a large evidence base may also receive full text articles or an evidence table along with the template.
- There are four fields for **recommendation**, including a checklist for classification and level of evidence for each recommendation (more than four recommendations can be written). After reviewing the evidence base, the writer should create recommendations that answer the clinical objective. See **Steps Five** and **Six** for details on writing recommendations.
- The **text** field is used for placing recommendations in context (see "Narrative synthesis of evidence" below).
- The **additional references** field can be completed by a writer who references other sources than those provided in the evidence base field.
- If the clinical objective has a **diagram**, **table**, or **graphic** associated with it, it can be added or referenced in this field (see **Step Seven**).

Synthesizing the Evidence: Techniques

Narrative Synthesis of Evidence
Summaries of evidence should generally be in tabular form, and not in the text of the guideline. Text should be reserved for qualifying or clarifying interpretation of the evidence tables and for stating and clarifying guideline recommendations. When multiple trials have yielded similar, non-controversial results, a single sentence with appropriate references may suffice. Long, descriptive paragraphs of the methodology and findings of individual trials are discouraged.

Visual Synthesis of Evidence
Preparing an evidence table involves identifying and extracting the key data from the relevant studies. The Cochrane Collaboration recommends beginning by deciding what comparisons need to be made, then identifying the data elements necessary to make those comparisons. Salient data elements may include, but are not limited to, number of patients, morbidity, mortality, dose-response, sensitivity, specificity, p-values, confidence intervals, positive predictive value, negative predictive value, and relative risk.

The next step is to prepare visual summaries of the results of the studies included in each comparison. The data are often usefully displayed in a table that allows the studies' designs and results to be easily compared. However, sometimes the data are better summarized in a bar chart,

Forrest plot, or other graphic summary. Information presented graphically can replace the need for "text-heavy" sections of the guideline. Examples of visual synthesis of evidence from published ACC/AHA guidelines are shown in Appendix C.

Analytical Synthesis of Evidence
Sometimes recommendations can confidently be written based on the organization of evidence in tables or graphs. Other times, a further step is necessary; analyzing the data statistically to obtain an estimate of the heterogeneity of the individual effect sizes, an estimate of the summary effect size, and a measure of its variance. Guideline writers generally rely upon meta-analytic methods to conduct such analyses.

A detailed guide to the methods of meta-analysis is beyond the scope of this manual. The manual and software (RevMan) employed by the Cochrane Collaboration are useful resources. RevMan allows for entry of the characteristics of studies and their findings, and the creation of comparison tables. It can perform meta-analysis of the data entered, and present the results graphically. A comprehensive handbook for conducting systematic reviews can be printed from the same web site accompanies the software.

Use of Other Guidelines/Authorities
Guideline text, recommendations, and evidence tables may be replicated from previous ASA guidelines and statements, other AHA guidelines and statements, and guidelines from external guidelines and statements formally endorsed by ASA/AHA. Consensus statements or guidelines developed by others and not endorsed by the ASA/AHA should generally not be cited or referenced, as this implies AHA/ASA endorsement of their content.

Discussing Pharmacotherapy in Guidelines
SOC has provided in Checklist 3 a detailed list of policies on discussing pharmacotherapy in guidelines. In addition, a pharmacologist may be assigned to a guideline writing committee or used in a consulting role to review the guideline's pharmacotherapy discussions before publication.

Investigational treatments or drugs that are not available for general use may be mentioned, but should be clearly described as such and not given Class I, IIa, or IIb recommendations. The writing committee should decide whether to list them as Class III, or not to list them at all. The presence or absence of FDA or CMS approval of a drug or device for a specific purpose should generally not be mentioned. The criteria used by regulatory authorities are frequently different, and the ASA process should be independent of these regulatory issues.

> **Checklist 3. Discussing Pharmacotherapy in Guidelines**
>
> o Use generic or chemical name not trade name
>   - e.g., simvastatin, not Zocor
> o Use broadest and most generic name of class appropriate
>   - e.g., thiazide diuretic, not "hydrochlorthiazide"
> o Discuss evidence for or against "class effect"

- o If there is no evidence for differential application/effectiveness/side effects of subclasses of drug or individual drugs within classes, either list all drugs alphabetically or list none
- o If there is evidence for differential application/effectiveness/side effects of subclasses of drug or individual drugs within classes, discuss only according to evidence-based rationale, stating clearly the rationale.
  - e.g., first-line, second-line or side effects or cost-effectiveness
  - If no evidence-based rationale, list alphabetically
- o When so-called "alternative medicines" are known to be widely used, discuss the evidence about them and the issues raised by their use.
  - e.g., possible interactions
- o Avoid the use of symbols and abbreviations when discussing drug dosing and timing.
  - e.g., use "micrograms" or "mcg" instead of "µg"
  - The Institute for Safe Medication Practices has issued a drug error alert regarding some commonly used abbreviations.
- o Whenever a guideline includes specific drug information, such sections of the guideline should be reviewed by a pharmacologist during peer review.

Step Five: Formulate Recommendations

Recommendations: The Essence of Guidelines
Guideline development goes beyond the compilation and analysis of data to include formulation of recommendations to guide clinical practice. Guideline writers are challenged with considering a vast array of evidence and creating clinically applicable and clear recommendations.

As the evidence is considered, conclusions and recommendations naturally evolve. The recommendations are the core guideline content, while the text enhances the recommendations by providing further descriptive information, such as exceptions to the recommendations and clinical options.

If **Step One** determined that flow diagrams were appropriate, recommendations should be incorporated into the flow diagrams where appropriate (see **Step Seven**).

Because guidelines are increasingly serving as the basis for other ASA/AHA activities (such as pocket guides, performance measures, data standards, and Get With the Guidelines Projects), recommendations should be stand alone text that is written in complete sentences with as much detail as possible. Guidelines are intended to be applied by health care providers in real world settings, so the recommendations should be practical, feasible, and flexible, thus facilitating the translation and implementation of recommendations.

The wording of the complete sentences stating recommendations should closely reflect the formal Evidence Level and Class of Recommendation assigned to the recommendation. The following phrases should be employed:
Class I: "should," "is recommended," "is indicated," "is useful/effective/beneficial"
Class IIa: "is reasonable," "can be useful/effective/ beneficial," "is probably recommended or indicated"
Class IIb: "may/might be considered," "may/might be reasonable," "usefulness/effectiveness is unknown /unclear/uncertain or not well established"
Class III: "is not recommended," "is not indicated," "should not," "is not useful/effective/beneficial", "may be harmful"

Expert Interpretation of the Evidence
Despite all the evidence that may be available for writing the guideline, expert interpretation will always be necessary. Expert interpretation serves as a funnel through which evidence on multiple questions and clinical situations is combined, condensed, and formulated into recommendations.
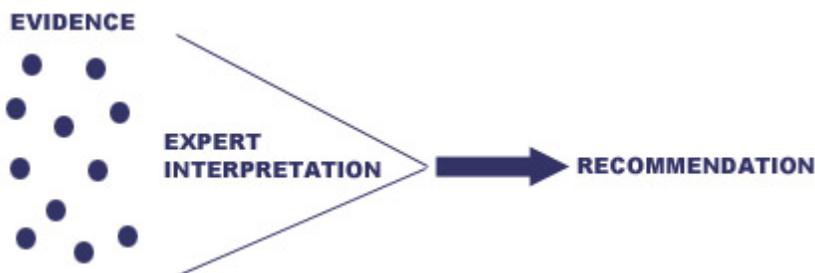
Sometimes there is an abundance of evidence available that leads directly to an indisputable recommendation. Other times the evidence may be less clear-cut. The evidence from different trials may lead to divergent conclusions, the evidence may only apply to specific sub-populations, the evidence may be from methodologically weak studies, or the evidence may simply be insufficient to support a recommendation.

Checklist 4 contains suggested approaches to recommendation formulation and writing.

Checklist 4. Writing Guideline Recommendations

- Write all recommendations in complete sentences.
- Write separate recommendations that apply to specific clinical objectives.
- Write recommendations that are practical in the real world setting.
- Describe the patients to whom the recommendation applies.
- Use unambiguous language and clearly defined terms when writing recommendations, including the AHA/ASA preferred phrases calibrated to Recommendation Grade.
- Write recommendations in terms of active/positive actions rather than passive/negative actions.
- When there are areas of uncertainty or controversy include this information in the recommendation.
- Quantify as much as possible benefits, harms, and timeframes.
- Write recommendations that incorporate data on patient preferences, when applicable.
- Specify sub-population variability and exceptions in the recommendations. List the exceptions whenever possible.
- Include flexibility in applying the recommendations, where applicable.
- Recommendations must be consistent with previous ASA/AHA guidelines, unless there is new evidence to justify a change. Both the new evidence and the change must be described in detail.

Step Six: Assign Classification of Recommendations and Level of Evidence

A formal Classification of Recommendation and Level of Evidence grade must be assigned to each recommendation. A following standard AHA algorithm for determining Classification of Recommendations and Level of Evidence has been established by a Task Force of the AHA-ACC[1]:

Classification of Recommendations

Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective.

Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.
                 IIa. Weight of evidence/opinion is in favor of usefulness/efficacy
                 IIb. Usefulness/efficacy is less well established by evidence/opinion.

Class III: Conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful/effective, and in some cases may be harmful.

Level of Evidence

Level of Evidence A   Data derived from multiple randomized clinical trials
Level of Evidence B   Data derived from a single randomized trial, or non-randomized studies
Level of Evidence C   Consensus opinion of experts

Applying the Classifications and Levels
The Classification of Recommendations and Level of Evidence are considered by many to be the core of the guidelines. As such, they are among the most debated aspects of the guideline within the writing group. See **Step Eight** for guidance on coming to group consensus on recommendations.

Any combination of Classification of Recommendation and Level of Evidence is possible. For example, a recommendation can have a Class I, even if it is based entirely on expert opinion and no research studies have ever been conducted on the recommendation (Level C). Similarly, a Class IIa or IIb can be assigned a Level A if there are multiple randomized controlled trials coming to divergent conclusions.

Assigning a Level of Evidence B or C should not be construed as implying that the recommendation is weak. Many important clinical questions addressed in the guidelines either do not lend themselves to experimentation or have not yet been addressed by high quality investigations. Even though randomized controlled trials may not be available, the clinical question may be so relevant that it would be delinquent to not include it in the guideline.

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[1] The Stroke Statements Oversight Committee is pursuing modification of this algorithm for Stroke Council Statements. Until modification is approved, the standard algorithm should be employed by Stroke Council writing committees.

Table 2 provides detailed descriptive and quantitative criteria for the standard AHA algorithm for assigning the classification and evidence ratings. Additionally, it displays the intersections between each rating.

Table 2. Applying Classification of Recommendations and Level of Evidence

<div align="center">"SIZE of TREATMENT EFFECT"</div>

"Estimate of Certainty (Precision) of Treatment Effect"	Class I *Benefit >>> Risk* Procedure/Treatment SHOULD be performed/administered	Class IIa *Benefit >> Risk* *Additional studies with focused objectives needed* IT IS REASONABLE to perform procedure/administer treatment	Class IIb *Benefit ≥ Risk* *Additional studies with broad objectives needed; Additional registry data would be helpful* Procedure/Treatment MAY BE CONSIDERED	Class III *Risk ≥ Benefit* *No additional studies needed* Procedure/Treatment should NOT be performed/administered SINCE IT IS NOT HELPFUL AND MAY BE HARMFUL
Level A *Multiple (3-5) population risk strata evaluated** *General consistency of direction and magnitude of effect*	· Recommendation that procedure or treatment is useful/effective · Sufficient evidence from multiple randomized trials or meta-analyses	· Recommendation in favor of treatment or procedure being useful/effective · Some conflicting evidence from multiple randomized trials or meta-analyses	· Recommendation's usefulness/efficacy less well established · Greater conflicting evidence from multiple randomized trials or meta-analyses	· Recommendation that procedure or treatment not useful/effective and may be harmful · Sufficient evidence from multiple randomized trials or meta-analyses
Level B *Limited (2-3) population risk strata evaluated**	· Recommendation that procedure or treatment is useful/effective · Limited evidence from single randomized trial or non-randomized studies	· Recommendation in favor of treatment or procedure being useful/ effective · Some conflicting evidence from single randomized trial or non-randomized studies	· Recommendation's usefulness/efficacy less well established · Greater conflicting evidence from single randomized trial or non-randomized studies	· Recommendation that procedure or treatment not useful/effective and may be harmful · Limited evidence from single randomized trial or non-randomized studies
Level C *Very limited (1-2) population risk strata evaluated**	· Recommendation that procedure or treatment is useful/effective · Only expert opinion, case studies, or standard-of-care	· Recommendation in favor of treatment or procedure being useful/ effective · Only diverging expert opinion, case studies, or standard-of-care	· Recommendation's usefulness/efficacy less well established · Only diverging expert opinion, case studies, or standard-of-care	· Recommendation that procedure or treatment not useful/effective and may be harmful · Only expert opinion, case studies, or standard-of-care
Suggested phrases for writing recommendations †	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/ beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown /unclear/uncertain or not well established	is not recommended is not indicated should not is not useful/effective/beneficial may be harmful

* Data available from clinical trials or registries about the usefulness/efficacy in different sub-populations, such as gender, age, history of diabetes, history of prior MI, history of heart failure, and prior aspirin use.

† The ACC/AHA Task Force on Practice Guidelines recently provided a list of suggested phrases to use when writing recommendations. All recommendations in the guideline have been written in full sentences that express a complete thought, such that a recommendation, even if separated and presented apart from the rest of the document (including headings above sets of recommendations), would still convey the full intent of the recommendation. It is hoped that this will increase readers' comprehension of the guidelines and will allow queries at the individual recommendation level.

Supplemental Stroke Council Classification of Recommendations and Level of Evidence Algorithms

The standard AHA (ACC/AHA) algorithm for classifying recommendations and levels of evidence focuses on therapeutic questions and, consequently, emphasizes evidence from randomized clinical trials. Clinical practice guidelines sometimes address other aspects of care, including diagnostic tests or prognostic algorithms. For these, SOC has developed supplemental algorithms, modified from the Guideline manual of the American Academy of Neurology.

Classifying Evidence for Diagnostic or Prognostic Accuracy Questions

Comparison (Control) Group
To be useful, a study of prognostic or diagnostic accuracy should include patients with and without the disease or outcome of interest. Quantitative measures of accuracy cannot be calculated from studies without a comparison group. These studies are judged to have a high risk of bias and are graded Level B.

Study Design
A Level A study of diagnostic or prognostic accuracy would be a prospective cohort survey. Investigators would start with a group of patients suspected of having a disease (the cohort). The diagnostic test would be performed on this cohort. Some patients would have a positive test, others a negative test. The cohort would then have the actual presence or absence of the disease determined by an independent reference standard (the gold standard). Quantitative measures of the diagnostic accuracy of the test (or predictor) such as the sensitivity or specificity could then be calculated. Studies of diagnostic accuracy are often done backwards. Rather than starting with a group of patients suspected of having the disease, investigators often start by selecting a group of patients who clearly have the disease (cases) and a group of patients who clearly do not have the disease (control). The test is then performed on both cases and controls and measures of diagnostic accuracy are calculated. Although this case-control study is easier to execute, its retrospective design introduces several potential biases. Thus, at best, such studies can only be graded Level B.

Patient Spectrum
One of the dangers of the case-control design is that sometimes only patients who clearly have the disease or clearly do not have the disease might be included. Including such unambiguous cases can exaggerate the diagnostic accuracy of the test. To avoid this, it is important for a study employing a case-control design to include a wide spectrum of patients. A wide spectrum would include patients with mild forms of the disease and patients with clinical conditions that could be easily confused with the disease. Studies employing a case-control design with a wide spectrum of patients should be given greater weight than those employing a narrow spectrum, although both are graded Level B.

Reference Standard
It is essential for any study of diagnostic or prognostic accuracy that a valid reference standard be used to confirm or refute the true presence of the disease or outcome. This reference standard should be independent of the diagnostic test or prognostic predictor in question. The reference standard could consist of pathological, laboratory, or radiological confirmation of the presence or absence of the disease. At times, the reference standard might even consist of a consensus-based case definition. Panel members should grade studies without a valid reference standard as Level C.

Completeness
Ideally, all patients enrolled into the cohort should have the diagnostic test result (presence of the prognostic variable) and the true presence or absence of the disease (outcome) measured. A

study should be downgraded to Level B if less than 80% of subjects have these variables measured.

Masking

For a study to be graded Level A, an investigator who is unaware of the results of the diagnostic test (presence or absence of the prognostic predictor) should apply the reference standard to determine the true presence of the disease (outcome). In the circumstance of the case-control design (Level B), greater weight should be given to studies in which an investigator who is unaware of the presence or absence of the disease (outcome) performs the diagnostic test (measure the prognostic predictor) of interest, intermediate weight to studies in which the investigators performing the diagnostic test (or measuring the prognostic predictor) are different than the investigator who determines the true presence or absence of disease (or the outcome), and least weight to studies in which the same investigator performed the diagnostic test (or measured the prognostic predictor) and determined the true presence or absence of disease (or the outcome). The requirement for masked or independent assessment to achieve Level A rating can be waived if the reference standard for determining the presence of the disease (outcome) and the diagnostic test (prognostic predictor) of interest are objective. An objective measure is one that is unlikely to be affected by expectation bias.

Classifying Evidence for Screening Questions

Data Collection

Retrospective collection of data, such as chart reviews, commonly introduces errors related to sub-optimal, incomplete measurement. Thus, data collection should be prospective to classify a study Level A.

Setting

Population-based studies tend to be the most representative and can be graded Level A. Studies of patients recruited from hospitals and/or outpatient clinics are Level B. Among Level B studies, greater weight should be given to studies in which patients were recruited from non-referral clinics (as they are more representative) and less weight to studies in which patients were recruited from referral centers. Occasionally, the screening question's population of interest is primarily patients referred to specialty centers. For example, some rare or difficult-to-treat conditions may only be managed at referral centers. Under these circumstances, such studies should be considered high weight Level B.

Sampling

The ideal methods of selecting patients for a study designed to answer a screening question are to 1) take all patients or 2) take a statistical sample of patients. This ensures that the patients are representative. Thus, a consecutive sample, a random sample, or a systematic sample of patients (e.g., every other patient) warrants a Level A grade. Because patients referred for a test may potentially be non-representative, a study using only such patients should be considered a lesser weight Level B study.

Completeness

For reasons similar to that discussed under sampling, it is important that all patients included in the cohort undergo the test of interest. If less than 80% of subjects receive the intervention of interest, the study can be graded no better than Level B.

Masking
To be graded Level A for a screening question, the interpretation of the intervention of interest (usually a diagnostic test) should be done without knowledge of the patient's clinical presentation. Among level B studies, greater weight should be given to studies in which someone other than the treating physician performed the interpretation of the diagnostic test. The requirement for independent or masked assessment can be waived if the interpretation of the diagnostic test is unlikely to be changed by expectation bias (i.e., is objective).

Classifying Evidence for Agreement Studies

Study Design
Agreement studies evaluate the degree to which two (or more) different tests or test operators agree when applied to the same diagnostic system. Agreement studies apply the different testing systems to the same population (i.e., subjects). One of the testing methods is often the more commonly applied or accepted method ("the status quo") and functions as the reference standard. In contrast to many diagnostic accuracy studies which have a group of patients with "disease" and a group of patients "without disease", agreement studies have one group of subjects and the type of subject population may vary depending on the study objectives. For Agreement Studies where a highly reliable, objective and reproducible reference standard exists, then likelihood ratios, sensitivity, specificity, ROC or other appropriate statistical comparisons should be used; when the reference standard lacks these qualities, levels of agreement between the test method and reference standard should be analyzed using Kappa scores or other appropriate statistical comparisons.

Level A Agreement Studies should be designed as a prospective study where the data collection efforts were planned before the test method and reference standard were applied. In addition, there should be an adequate description of the inclusion and exclusion criteria, setting and location as well as where data were collected. The study population should be from a consecutive series of patients defined by the inclusion and exclusion criteria. Level B Agreement studies use a retrospective design where the data collection efforts were planned after the test method and reference standard where applied. In addition, Level B studies occur where there is an inadequate description of the inclusion and exclusion criteria, setting or location.

Subject Spectrum
For level A studies, the subjects (patients or healthy individuals depending on the objectives of the study), should include the broad spectrum of characteristics that would be reflective of clinical practice. Level B studies, the spectrum of characteristics omit several important variables that may be found in routine clinical practice.

Test Method - Reference Standard
For Level A studies, the rationale for the test method and reference standard should be described in sufficient detail; this should include the technical specifications for applying the test method and reference standard, and the training and expertise of those performing or reading the test method and reference standard. Level B studies are those that provide some description of the test method and reference standard but lack sufficient detail for replication. Level C studies are

those that lack adequate descriptions to understand or replicate either the test method or the reference standard.

Masking
Masking of test/reference standard data: Level A studies are those where the persons executing or reading the test are unaware of the results of the reference standard and those executing or performing the reference standard are unaware of results of the test method. Level B studies occur when there is lack of complete masking.
Masking of subject characteristics: Level A studies are those where the persons executing or reading the test or the reference standard are unaware of detailed population or clinical characteristics of subjects that would effectively unmask the results of either the test method or reference standard. Level B studies occur when there is lack of masking.

Completeness
Level A studies should have sufficiently complete comparisons to be able to determine the relative strengths or weaknesses of the diagnostic methods for the particular clinical application. If this is not sufficient, the study should be graded as level B.

Statistical Methods and Results
Level A studies should describe methods for calculating measures of agreement including methods used to quantify uncertainty. In addition, the report should adequately describe the subject population, setting, and any adverse events from performing the test method and reference standard. Finally, it should discuss the clinical applicability of the findings. Level B studies do not adequately present the data to allow the reader to fully understand the clinical applicability of the finding.

Classifying Evidence for Agreement Studies

Level A:	Prospective Masked Broad/representative subject spectrum Complete Assessment Adequate description of test method/reference standard Adequate description of test results/study finding
Level B:	One or more of the following: Retrospective Unmasked Narrow spectrum Incomplete Assessment Inadequate description of test method/reference standard Inadequate description of test results/study finding

Level C:	Two or more of the following: Retrospective Unmasked Narrow spectrum Incomplete Assessment Inadequate description of test method/reference standard Inadequate description of test results/study finding

Writing Committee Discussions and Consensus Development

As shown in **Figure 1**, writing committee discussions and forging of consensus are ongoing at all stages of guideline development. Since ASA/AHA guidelines are team-written documents, coming to agreement on the scope, clinical objectives, evidence tables, text, recommendations, and visual summaries occurs throughout the document development process. Subsection writers often come to consensus through phone calls or e-mail exchanges of information, while the entire writing committee comes to consensus during the face-to-face meetings.

In evidence-based documents such as clinical practice guidelines, consensus development is often most important around topics that have a sparse literature base. Writing groups are faced with the challenge of addressing an important clinical question despite a lack of data. The ASA/AHA guideline development process allows for the incorporation of minority opinions within the document if consensus cannot be reached.

Step Seven: Create Tables, Diagrams, and Mnemonics Describing Recommendations

Once the evidence tables and recommendations have been created, guideline writers should look for ways to visually summarize the key points in tables, diagrams, and mnemonics. The flow diagrams identified in **Step One** should be considered again in light of the evidence collected and recommendations written. Frequently, the text and/or recommendations can be condensed into a clinical pathway, algorithm, or decision-tool. These visual summaries assist physicians in understanding and applying the best care for individual patients. Visual presentations should be:

- Written in clear and unambiguous language.
- Logically organized.
- Easy to follow.
- Specific about relevant populations and clinical circumstances.
- Specific about which elements of care are appropriate, inappropriate, and equivocal.

Guideline readers will examine the evidence presented to assess the quality of the recommendations. However, *in clinical circumstances, the key points of how the evidence applies to patients are the take-home messages that must be clearly presented and easily accessible in the guideline*.

Examples of good tables, diagrams, and mnemonics are shown in Appendix D.

Preparing the Summary of Recommendations
A bulleted list should be accompany the document, restating in one place all the recommendations scattered throughout the guideline. Optimally,, the Summary of Recommendations will be between 250-750 words in length. The Summary will provide readers of the Guidelines with a handy, quick view section for use in varied clinical settings. The Summary will also facilitate adaptation of the guideline into a format (e.g., pocket guide, web, PDA) that will facilitate implementation at the point of care.

Step Eight: Abstract, Methods, Conflict of Interest and Other Guideline Sections

The quality of a guideline is determined by the transparency and rigor of its methodology. Consequently, in addition to the core recommendations, the framework in which they are reported is vitally important. The Conference on Guideline Statements (COGS) and other organizations have issued widely accepted statements regarding desirable component elements in clinical practice guidelines.

Structured Abstract

A structured abstract is generally recognized as an element of best practices in Guideline development. The abstract should specifically state the guideline's status (original, revised, updated); the methods used to gather, select, and synthesize evidence and the date of the most recent evidence obtained; if space permits, a brief and specific list of key recommendations. It is required that each Stroke Council Guideline Statement have a structured abstract. Example abstracts are provided in Appendix F.

Methods Paragraph

The methods paragraph should concisely summarize the methodology used in Guideline development in a manner that assures readers that high quality processes were employed.(ref) The following general format for the Methods paragraph is recommended, adapted to the specifics of each Committee's workflow. Each sentence in the below paragraph satisfies a quality criterion of the Conference on Guidelines Statements (COGS) recommendations for Guideline elements.

> "This guideline is intended for use by physicians and allied health personnel caring for patients with <<insert condition here>>. A formal literature search was performed of the following databases: <<insert database 1>>, <<insert database 2>>, <<insert database 3>>, etc, employing the search strategy <<search term 1>> or <<search term 2>>, and or <<search term 3>>, covering the dates <<insert start date>> to <<insert end date>>. <<Insert person or persons here>> filtered the retrieved articles employing the following criteria: <<criterion 1>>, <<criterion 2>>, etc. Data was synthesized employing <<insert all that apply: evidence tables, meta-analyses, pooled analysis, and decision analysis>>. The AHA-ACC Levels of Evidence grading algorithm was employed to grade each recommendation. Prerelease review of the draft guideline was performed by x expert peer reviewers and by the members of the Stroke Council Leadership Committee. It is intended that this Guideline be fully updated in 3 years time.

Conflict of Interest

ASA Guidelines are intended to promote the best care of patients. Guideline authors are obligated to consider only the best interest of patients in formulating guideline recommendations, and not any personal interest or personal gain, and to disclose all relevant facts in any situation where a potential conflict of interest may arise (or be perceived). Members of the guideline writing committee will declare all potential conflicts of interest (COIs) in accordance with AHA COI Policy. A table or paragraph showing all declared COIs will be included in the print and electronic published versions of the Guideline Statement.

Funding Source
Statement of the funding sources supporting development is a best practice, as it allows guideline readers to assess potential competing interests affecting guideline generation. It is Stroke Council SOC policy that funding support for guideline development come from for-profit entities. A statement identifying funding sources for the guideline should appear in the acknowledgements or COI paragraph section of the guideline.

Step Nine: Finalizing the Document

At the final stages of guideline development, writers should re-examine the original goals regarding the scope of the guideline. Any identified gaps should be filled or explained before the document is sent to peer review. The writing group will be asked to give formal approval of the document both before peer review and after peer review edits have been incorporated. **Checklist 5** is provided as a tool to conduct an internal review of the guideline recommendations at both of these junctures.

<div style="background-color:#FAFABE; padding:1em;">

Checklist 5. Reviewing Guideline Recommendations

- o Are the recommendations within the stated purpose and scope of the guideline?
- o Are all recommendations assigned a Classification of Recommendation and a Level of Evidence?
- o Are clinically important and feasible recommendations made?
- o Are areas of uncertainty and exceptions to the rule clearly identified?
- o Are evidence tables and appropriate text provided to support recommendations, where applicable?
- o Are recommendations and key clinical points displayed visually, when possible?
- o Are the recommendations consistent with other ASA/AHA guidelines and other ASA/AHA documents on the same or related topics?

</div>

Appendix A

Literature Search Request Form for AHA Stroke Council Guidelines

The AHA Stroke Council methodology for guideline development requires the documentation of all literature searches performed for the creation of guidelines. Please complete this form for each literature search requested or conducted and return it to your AHA Stroke Council guideline committee Chair and Copy Editor.
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TO BE COMPLETED BY THE REQUESTOR

Name of Guideline: _____

Name of Requestor: _____ **DATE:** _____

Years Requested: _____ – _____

Publication Types:

    Meta-analyses & systematic reviews   Randomized controlled trials
    Non-randomized studies   Case studies
    Opinion documents/letters

Describe Keywords/Search Strategy:

Exclusions:

TO BE COMPLETED BY THE SEARCHER

Database(s) Searched: **DATE:** _____

    MEDLINE/PubMed   EMBASE
    Best Evidence   Cochrane Library
    Other, specify _____

Number of References Retrieved: _____

Notes/Comments:

Appendix B

Article Evaluation Checklist

Guideline writers are asked to consider the merits, quality, and generalizability of each article relevant to the clinical objective. This checklist should be completed only for articles from the peer-reviewed, published literature that are:

- o randomized controlled trials,
- o meta-analysis/systematic reviews, or
- o diagnostic studies using comparison with a gold standard.

Article/Author:
Please indicate one of the following conclusions about the article:

_____ **Yes**, this is a relatively high quality study that provides credible results and should be included in the evidence table and references that support the recommendation(s) for this clinical objective.

_____ **No**, this study is not of sufficient quality to be included in the evidence table, but Yes, this study contains some useful information about the clinical objective and should be maintained as a reference for the text accompanying the recommendation.

_____ **No**, this is a relatively poor study that should not be used in the evidence table or in the references for this clinical objective.

_____ **No**, this study is not directly relevant to the clinical objective

Comments:

Appendix C

Examples of Visual Synthesis of Evidence from Published ACC/AHA Guidelines

1) Forrest Plots

Acute Myocardial Infarction **Guideline**, Figure 7

Examples of visual synthesis of evidence from published ACC/AHA guidelines

Presentation features	Percent of patients dead		Stratified statistics		Odds ratio & CIs		Chi-square test of odds ratios in different patient categories:	
	Fibrinolytic	Control	O-E	Variance	Fibrinolytic better	Control better	Heterogeneity	Trend
ECG								
BBB	18.7%	23.6%	-24.5	83.3				
ST elev, anterior	13.2%	16.9%	-122.0	420.6				
ST elev, inferior	7.5%	8.4%	-27.1	237.4			21.28 on 6 df	
ST elev, other	10.6%	13.4%	-42.1	159.6			(P<.01)	
ST depression	15.2%	13.8%	12.9	108.7				
Other abnormality	5.2%	5.8%	-9.6	103.2				
Normal	3.0%	2.3%	3.4	12.9				
Hours from onset								
0-1	9.5%	13.0%	-29.3	83.3				
2-3	8.2%	10.7%	-100.2	354.8			9.69 on 4 df	9.55 on 1 df
4-6	9.7%	11.5%	-78.5	387.6			(P<.05)	(2P=0.002)
7-12	11.1%	12.7%	-51.5	336.7				
13-24	10.0%	10.5%	-11.1	212.6				
Age (years)								
<55	3.4%	4.6%	-45.9	155.6				
55-64	7.2%	8.9%	-86.3	360.0			8.27 on 3 df	6.58 on 1 df
65-74	13.5%	16.1%	-113.7	533.0			(P<.05)	(2P=0.01)
75+	24.3%	25.3%	-12.6	266.6				
Gender								
Male	8.2%	10.1%	-208.1	928.0			1.99 on 1 df	
Female	14.1%	16.0%	-62.2	436.8			(NS)	
Systolic BP (mm Hg)								
<100	28.9%	35.1%	-38.7	132.2				
100-149	9.6%	11.5%	-168.9	850.0			1.31 on 3 df	0.68 on 1 df
150-174	7.2%	8.7%	-59.2	290.0			(NS)	(NS)
175+	7.2%	8.2%	-10.8	74.1				
Heart rate								
<80	7.2%	8.5%	-83.2	464.9				
80-99	9.2%	11.3%	-65.8	287.2			0.51 on 2 df	0.31 on 1 df
100+	17.4%	20.7%	-51.7	238.6			(NS)	(NS)
Prior MI								
Yes	12.5%	14.1%	-43.7	322.4			2.09 on 1 df	
No	8.9%	10.9%	-228.5	1001.9			(NS)	
Diabetes								
Yes	13.6%	17.3%	-41.4	145.7			1.57 on 1 df	
No	8.7%	10.2%	-142.6	830.4			(NS)	
■ ALL PATIENTS	2820/29315 9.6%	3357/29285 11.5%	-269.5	1377.4	18% SD 2 odds reduction 2P<0.00001			

0.5   1.0   1.5

Adjusted-Dose Warfarin Compared with Placebo

2) Table

Chronic Stable Angina Guideline, Table 21

Table 21. Prognostic Value of Stress Myocardial Imaging in Definite or Suspected Chronic Stable Angina

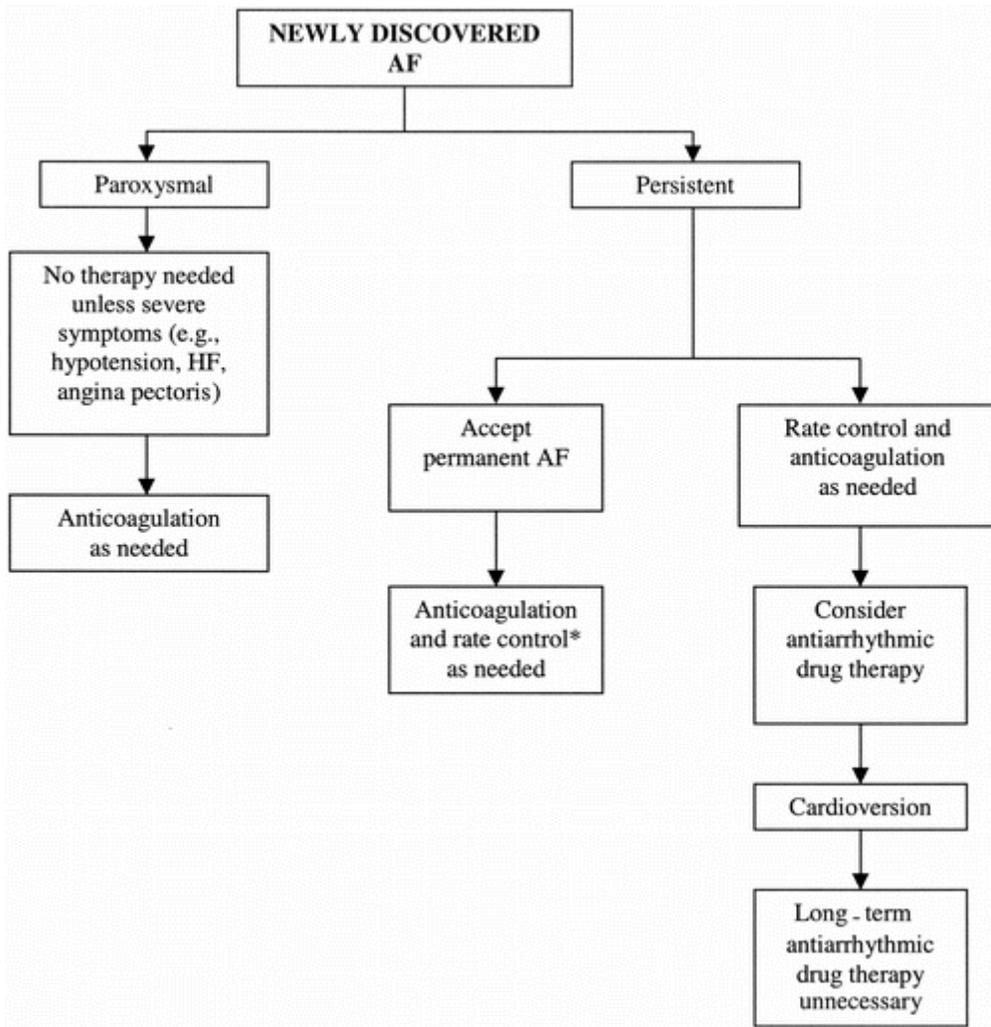| Author	Test	No.	Patient Population	Avg f/u (mo.)	% Abn Test	Event %	Pos. Pred. Value %	Neg. Pred. Value %	Relative Risk	Events
Ladenheim 1986 (441)	Tl-201 (planar) ETT	1689	CAD symptoms	12	50	4.4	7.5	98.7	10.6	Death, MI, CABG
Pollock 1992 (454)	Tl-201 (planar) ETT	501	Suspected CAD	52.8	N/A	18.5	N/A	N/A	2.2	Death or MI
Machecourt 1994 (455)	Tl-201 (SPECT) ETT or Dyp.	1929	Angina, prior MI, CABG, PTCA	33	63	5.2	3.8	99.4	9.1	Death or MI
Marie 1995 (456)	Tl-201 (SPECT) ETT	217	Suspected CAD	70	N/A	13.47	N/A	N/A	1.04	Death or MI
Kaul 1988 (444)	Tl-201 (planar) ETT	299	Suspected CAD	55.2	50	30	41.0	81.22	2.20	Death, MI or CABG
Hachamovitch 1998 (431)	Tl-201 + (SPECT) sestamibi, ETT, or adenosine	5183	Suspected CAD	21.4	43	5.3	5.3 (per yr)	99.2 (per yr)	6.5	Death or MI
Geleijnse 1996 (457)	Sestamibi (SPECT) dobutamine	392	CAD, Suspected CAD	22	67	11	16	98.5	14.5	Death or MI
Kamal 1994 (458)	Tl-201 (SPECT) adenosine	177	CAD	22	83	8	9.5	100	∞	Death or MI
Stratmann 1994 (459)	Sestamibi (SPECT) dipyrida-mole	534	Suspected CAD	13	66.5	11	15.4	98.3	8.4	Death or MI
Stratmann 1994 (460)	Sestamibi (SPECT) exercise	521	Stable angina	13	60.5	4.6	7.3	99.5	13.8	Death or MI
Iskandrian 1988 (443)	Tl-201 (planar) exercise	404	Suspected CAD, age >60	25	54.7	4	7.7	99.5	14.1	Death or MI
Iskandrian 1985 (461)	Tl-201 (planar) exercise	743	Suspected CAD	13	46	2.7	4.4	98.8	3.5	Death or MI

CAD indicates coronary artery disease; MI = myocardial infarction; ETT = exercise treadmill test; CABG = coronary artery bypass graft surgery; SPECT = single photon emission commuted tomography; Dyp = dipyridamole; PTCA = percutaneous transluminal coronary angioplasty.

Appendix D

Example Formats for Tables, Diagrams, and Mnemonics to Describe Recommendations

1) Simple Flow Diagram

- Atrial Fibrillation Guideline, Figure 9

```
                        NEWLY DISCOVERED
                              AF
                               |
            ┌──────────────────┴──────────────────┐
            ▼                                      ▼
       Paroxysmal                             Persistent
            │                                      │
            ▼                          ┌───────────┴───────────┐
    No therapy needed                  ▼                       ▼
    unless severe                   Accept              Rate control and
    symptoms (e.g.,              permanent AF           anticoagulation
    hypotension, HF,                  │                   as needed
    angina pectoris)                  │                       │
            │                         ▼                       ▼
            ▼                   Anticoagulation            Consider
      Anticoagulation         and rate control*         antiarrhythmic
      as needed                  as needed              drug therapy
                                                            │
                                                            ▼
                                                       Cardioversion
                                                            │
                                                            ▼
                                                      Long - term
                                                      antiarrhythmic
                                                      drug therapy
                                                      unnecessary
```

2) Mnemonic

- [Chronic Stable Angina Guideline, Figure 5](#)

ACC/AHA/ACP-ASIM
Guidelines for Management of Stable Angina

Aspirin and anti-anginals

Beta blocker and blood pressure

Cholesterol and cigarettes
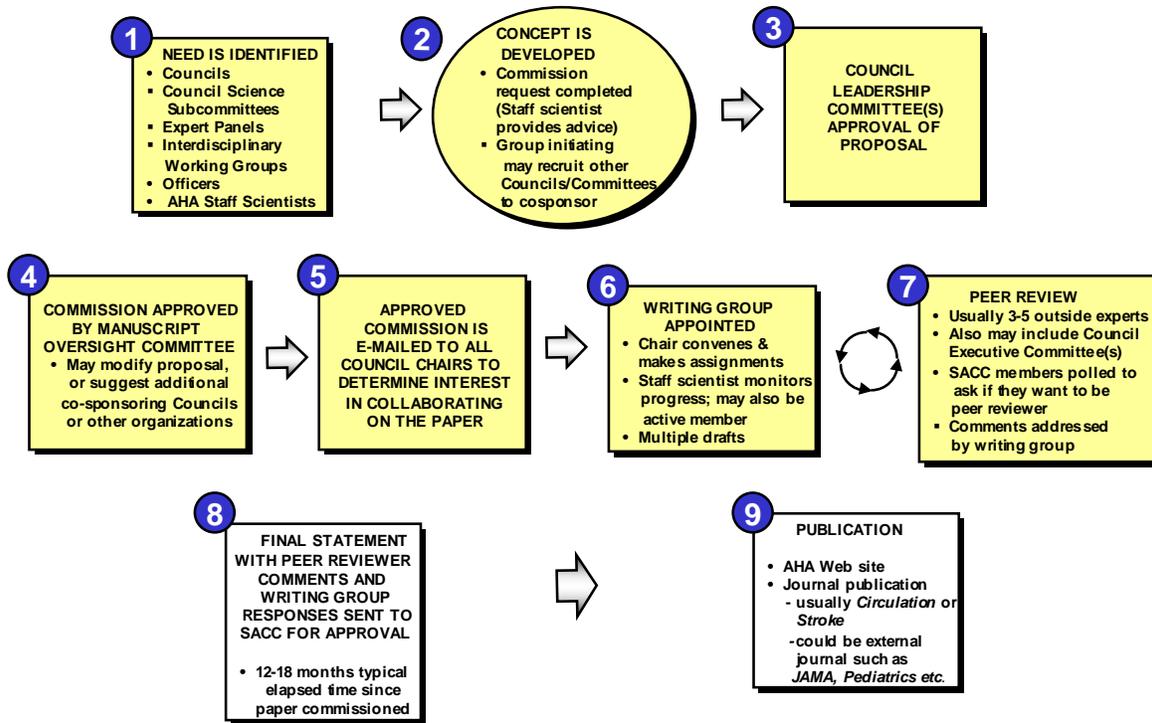
Diet and diabetes

Education and exercise
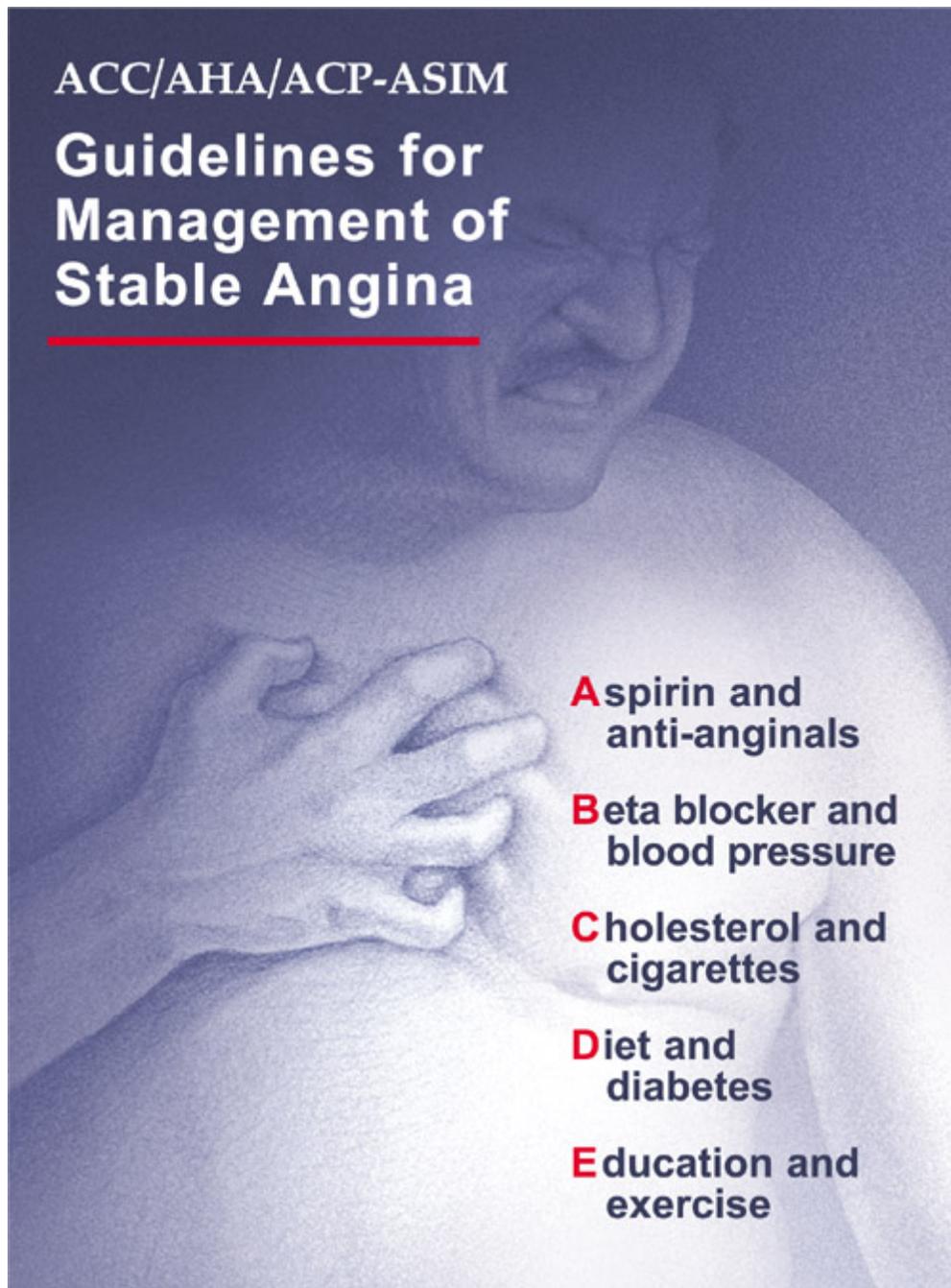
Appendix E

Background: Steps in the Production of an AHA Paper
(Guidelines, Scientific Statements, and Advisories)

(Guidelines are statements that require a certain "high" level of evidence. Papers that contain the following words in their titles: "Recommendations, Standards, procedures...etc" would be classified as Scientific Statements or Advisories. Advisories are usually short and straight to the point about one basic point to be conveyed. Scientific Statements are more far-ranging.)

1. A Council reaches the decision to initiate a paper (For the Stroke Council, this decision is made by the Stroke Scientific Statements Oversight Committee, based on suggestions/input from Stroke Council members).
2. The Council frames the topic of the paper and selects a Chair and Vice-Chair. In concert with the Chair, the Council selects additional members of the writing committee, chosen for multidisciplinary expertise in the subject area.
3. The Chair of the writing group, assisted by the SOC Chair and the Scientific Officer, completes the AHA Manuscript Commissioning Form.
4. The Commissioning Form is submitted to the AHA Manuscript Oversight Committee (MOC).
5. Before review by AHA's Manuscript Oversight Committee, the Commissioning Form proposal is circulated to the leadership of the other Councils and the Interdisciplinary Working Groups of the AHA. Any Council may choose to become a Co-Sponsor of the paper and place one of its Council members on the writing committee.
6. The proposal is reviewed by the Manuscript Oversight Committee, which meets monthly by teleconference.
7. The MOC needs to approve the proposal - with or without comments for change and/or suggestions for modification of the names of the members of the writing group and their specialties.
8. If approved, the writing group proceeds with developing and writing the manuscript, assisted by ASA/AHA staff.
9. When the manuscript is completed, it is sent to external peer reviewers. If the paper is a clinical practice guideline, it is also sent, at the same time, to members of the Stroke Leadership Committee.
10. Comments from the peer reviewers (and, for guidelines, Stroke Leadership Committee members) are relayed to the writing group (through the Chair). The manuscript is revised and submitted for a second round of peer review.
11. Once the revised manuscript passes peer review, it is forwarded to the AHA Science Advisory Cooperation Committee (SACC) for final review and approval.
12. SACC may approve the paper as is or request further modifications prior to approval. (Rarely SACC may reject the paper.)
13. Upon approval, the manuscript is sent for publication in the journal Stroke and on the ASA web site.
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DEVELOPING AHA SCIENTIFIC STATEMENTS/ADVISORIES

1 **NEED IS IDENTIFIED**
- Councils
- Council Science Subcommittees
- Expert Panels
- Interdisciplinary Working Groups
- Officers
- AHA Staff Scientists

2 **CONCEPT IS DEVELOPED**
- Commission request completed (Staff scientist provides advice)
- Group initiating may recruit other Councils/Committees to cosponsor

3 **COUNCIL LEADERSHIP COMMITTEE(S) APPROVAL OF PROPOSAL**

4 **COMMISSION APPROVED BY MANUSCRIPT OVERSIGHT COMMITTEE**
- May modify proposal, or suggest additional co-sponsoring Councils or other organizations

5 **APPROVED COMMISSION IS E-MAILED TO ALL COUNCIL CHAIRS TO DETERMINE INTEREST IN COLLABORATING ON THE PAPER**

6 **WRITING GROUP APPOINTED**
- Chair convenes & makes assignments
- Staff scientist monitors progress; may also be active member
- Multiple drafts

7 **PEER REVIEW**
- Usually 3-5 outside experts
- Also may include Council Executive Committee(s)
- SACC members polled to ask if they want to be peer reviewer
- Comments addressed by writing group

8 **FINAL STATEMENT WITH PEER REVIEWER COMMENTS AND WRITING GROUP RESPONSES SENT TO SACC FOR APPROVAL**
- 12-18 months typical elapsed time since paper commissioned

9 **PUBLICATION**
- AHA Web site
- Journal publication
  - usually *Circulation* or *Stroke*
  - could be external journal such as *JAMA, Pediatrics etc.*

Appendix F

Example Abstracts

Abstract for the 2005 AHA Scientific Statement on Infective Endocarditis
Circulation. 2005;111:e394-e434.)

Background— Despite advances in medical, surgical, and critical care interventions, infective endocarditis remains a disease that is associated with considerable morbidity and mortality. The continuing evolution of antimicrobial resistance among common pathogens that cause infective endocarditis creates additional therapeutic issues for physicians to manage in this potentially life-threatening illness.
Methods and Results— This work represents the third iteration of an infective endocarditis "treatment" document developed by the American Heart Association under the auspices of the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease of the Young. It updates recommendations for diagnosis, treatment, and management of complications of infective endocarditis. A multidisciplinary committee of experts drafted this document to assist physicians in the evolving care of patients with infective endocarditis in the new millennium. This extensive document is accompanied by an executive summary that covers the key points of the diagnosis, antimicrobial therapy, and management of infective endocarditis. For the first time, an evidence-based scoring system that is used by the American College of Cardiology and the American Heart Association was applied to treatment recommendations. Tables also have been included that provide input on the use of echocardiography during diagnosis and treatment of infective endocarditis, evaluation and treatment of culture-negative endocarditis, and short-term and long-term management of patients during and after completion of antimicrobial treatment. To assist physicians who care for children, pediatric dosing was added to each treatment regimen.
Conclusions— The recommendations outlined in this update should assist physicians in all aspects of patient care in the diagnosis, medical and surgical treatment, and follow-up of infective endocarditis, as well as management of associated complications. Clinical variability and complexity in infective endocarditis, however, dictate that these guidelines be used to support and not supplant physician-directed decisions in individual patient management.

Abstract for the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7), JAMA 2003;89: 2560-2572

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure" provides a new guideline for hypertension prevention and management. The following are the key messages (1) In persons older than 50 years, systolic blood pressure (BP) of more than 140 mm Hg is a much more important cardiovascular disease (CVD) risk factor than diastolic BP; (2) The risk of CVD, beginning at 115/75 mm Hg, doubles with each increment of 20/10 mm Hg; individuals who are normotensive at 55 years of age have a 90% lifetime risk for developing hypertension; (3) Individuals with a systolic BP of 120 to 139 mm Hg or a diastolic BP of 80 to 89 mm Hg should be considered as prehypertensive and require health-promoting lifestyle modifications to prevent CVD; (4) Thiazide-type diuretics should be used in drug treatment for most patients with uncomplicated hypertension, either alone or combined with drugs from other classes. Certain high-risk conditions are compelling indications for the initial use of other antihypertensive drug classes (angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, beta-blockers, calcium channel blockers); (5) Most patients with hypertension will require 2 or more antihypertensive medications to achieve goal BP (<140/90 mm Hg, or <130/80 mm Hg for patients with diabetes or chronic kidney disease); (6) If BP is more than 20/10 mm Hg above goal BP, consideration should be given to initiating therapy with 2 agents, 1 of which usually should be a thiazide-type diuretic; and (7) The most effective therapy prescribed by the most careful clinician will control hypertension only if patients are motivated. Motivation improves when patients have positive experiences with and trust in the clinician. Empathy builds trust and is a potent motivator. Finally, in presenting these guidelines, the committee recognizes that the responsible physician's judgment remains paramount.

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