NSGC Evidence-Based Clinical Practice Guideline Development Manual

(A Living Document)

Authors: Practice Guidelines Committee (2014-present)
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The NSGC Practice Guidelines Committee ratified this revised policy on August 10, 2015 and the NSGC Board of Directors approved these revisions on September 16, 2015.

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SECTION 1. Rationale for Revised Policy

The National Society of Genetic Counselors’ (NSGC’s) Practice Guidelines Committee (PGC) was established as a Full Committee in 2012 (see Appendix A for list of committee members). Prior to that, it was a subcommittee of the Access and Service Delivery Committee. As of December 2014, 14 publications with “Practice Guidelines” or “Recommendations” in the title have been published by NSGC or jointly with other professional organizations (http://nsgc.org/p/cm/ld/fid=70) through the efforts of the PGC or its predecessor. Per one of NSGC’s goals, the majority of these publications have been posted on the National Guideline Clearinghouse (NGC: www.guideline.gov), facilitating broad dissemination of these NSGC documents. Beginning June 1, 2014 the NGC required practice guidelines to adhere to new criteria in order to be eligible for posting on their website (see Appendix B). These criteria are meant to minimize bias, enhance the evidence base, and increase the trustworthiness of guideline recommendations. The PGC has been operating under a practice guideline development policy that was approved by the NSGC Board of Directors on February 18, 2012. However, the new NGC criteria are not addressed or met by that policy.

This manual revises and replaces the 2012 NSGC Practice Guidelines policy. The purpose of the revision is to describe a process for producing evidence-based NSGC practice guidelines that conform to the new NGC criteria. The revisions are informed by the Institute of Medicine’s standards for developing trustworthy clinical practice guidelines (Figure 1), the new NGC criteria effective June 2014, PGC member discussions and experiences with current policy, review of guideline policies used by other professional organizations, and the 2014 New York Academy TEACH conference. Major revisions were made to how guideline topics are generated and prioritized, how author groups are formed and their roles, the process for external review of guidelines, and to the guideline renewal process. Major additions to the guideline development process include incorporating the new NGC criteria, the GRADE system for evaluating the quality of evidence and the strength of recommendations, a systematic approach for developing recommendations using expert opinion only when necessary, and mechanisms for assessing the quality of practice guidelines. Another major change was implementing a process of endorsing practice guidelines from external organizations was also researched and delineated. Minor revisions were made to the Conflict of Interest (COI) policy for authors. See Appendix E for a list of retired PGC documents.

To help distinguish NSGC practice guidelines approved following this revised policy (after January 1, 2015), those approved NSGC Practice Guidelines will include “Evidence-Based Practice Guidelines” in the title. The NSGC Practice Guidelines Committee will oversee the process for developing Evidence-Based Practice Guidelines. The PGC will also be involved in endorsement requests for external practice guidelines. The NSGC Board reviews/approves all Evidence-Based Practice Guidelines before publication. NSGC Evidence-Based Practice Guidelines will typically be published in Journal of Genetic Counseling. Completely referenced statements, or their summaries, will be available on the NSGC website and may be submitted to other media sources at the discretion of the NSGC Executive Office. The NSGC Executive Office will submit NSGC Evidence-Based Practice Guidelines to the National Guideline Clearinghouse for posting.
Figure 1. AT-A-GLANCE: Standards for Developing Trustworthy Clinical Practice Guidelines (CPGs)

Standard 1: Establishing transparency
Standard 2: Management of COI
Standard 3: CPG development group composition

Standard 4: CPG-Systematic review intersection
Standard 5: Establishing evidence foundations for/rating strength of recommendations
Standard 6: Articulation of recommendations

Standard 7: External review of CPG
Standard 8: Updating the CPG

From “Clinical Practice Guidelines We Can Trust,” Institute of Medicine, March 2011
SECTION 2. What is a Genetic Counseling Clinical Practice Guideline?

“Clinical practice guidelines are statements that include recommendations intended to optimize patient care. They are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options.”

Clinical Practice Guidelines We Can Trust, Institute of Medicine, March 23, 2011

As noted previously in Section 1, in 2011, at the request of the United States Congress, the Institute of Medicine (IOM) published 8 standards for the development of rigorous, trustworthy Clinical Practice Guidelines. The IOM standards have quickly become a benchmark by which all guidelines are evaluated, and many professional societies are now developing their guidelines accordingly. Importantly, in 2013, the National Guideline Clearinghouse (NGC) revised their inclusion criteria to be in alignment with the IOM standards, and the NGC began to implement this change in 2014.

A critical aspect of the practice guideline development process is an understanding of the differences between rigorous, evidence-based Clinical Practice Guidelines that conform to IOM standards and other forms of clinical guidance that are less rigorous (yet still essential for clinical care). With this in mind, the NSGC PGC has defined two types of clinical guidance documents that affect the practice of genetic counseling:

1. **Clinical Practice Guidelines**, which offer evidence-based recommendations and supporting documentation that attempt to conform to IOM standards.
2. **Practice Resources**, which includes a broad category of less rigorous documents relating to information-sharing, and genetic counseling best practices that do not require evidence-based recommendations.

It should be noted that Clinical Practice Guidelines are the gold standard document and the PGC prioritizes overseeing their development and publication. However, Practice Resources may be considered if an appropriate Clinical Practice Guideline cannot be written; a PGC member can help authors facilitate their development. The aims of both documents are similar: to assist genetic counselors and other healthcare professionals with clinical decision-making and to promote consistent, high-quality care. The primary difference between the two documents lies in the rigor of their development, with Clinical Practice Guidelines being the more rigorous and evidence-based of the two. Additional details regarding the level of rigor, focus, and distribution of these two documents are provided in **Table 1**.

Genetic Counseling Clinical Practice Guidelines and Practice Resources are extensions of the NSGC’s efforts to demonstrate that genetic counseling is an integral part of healthcare delivery and quality care. NSGC Clinical Practice Guidelines, Practice Resources, and joint guidelines developed with other organizations should be consistent with NSGC’s mission, vision, scope of practice, code of ethics, and
strategic priorities. Clinical Practice Guidelines and Practice Resources can address the recommended use of certain genetic information in healthcare, which include, but are not limited to, referral practices, disease screening, predictive testing, disease diagnosis or treatment. They may also address access to, assessment of, or delivery of, genetic counseling services.

Of note, this manual does not pertain to documents handled by other NSGC Committees/SIGs/groups (like Position Statements, handled by the Public Policy Committee). Those processes will remain the same.

**Table 1. NSGC Clinical Guidance Documents: Clinical Practice Guidelines and Practice Resources**

<table>
<thead>
<tr>
<th>Level of Rigor</th>
<th>Clinical Practice Guideline (CPG)</th>
<th>Practice Resource*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Very rigorous</td>
<td>• Variable rigor</td>
</tr>
<tr>
<td></td>
<td>• Evidence-based</td>
<td>• Evidence-informed</td>
</tr>
<tr>
<td></td>
<td>• Aims to conform to IOM standards</td>
<td>• Does not require a systematic review</td>
</tr>
<tr>
<td></td>
<td>• Requires an explicit and transparent process of development (e.g. GRADE)</td>
<td>• Does not require a formal assessment of the quality of evidence</td>
</tr>
<tr>
<td></td>
<td>• Requires a systematic review of evidence</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Requires an assessment of the relative benefits and harms of the recommended interventions/test/practices</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Focus of Content</th>
<th>Clinical Practice Guideline (CPG)</th>
<th>Practice Resource*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Focuses on genetic counseling best practices that are enhanced by evidence-based recommendations</td>
<td>• Focuses on information-sharing and genetic counseling best practices that do not require evidence-based recommendations</td>
</tr>
<tr>
<td></td>
<td>• Typically focused on a narrow patient population with a specific phenotype or genetic diagnosis</td>
<td>• May be focused on a narrow patient population with a specific phenotype or genetic diagnosis or more “universal” practices that apply to broad categories of patients</td>
</tr>
<tr>
<td></td>
<td>• Examples include indications for referral to genetic counseling, indications for genetic testing, treatment of genetic conditions, and other management options</td>
<td>• Examples include an overview of the natural history of a condition, issues surrounding informed consent, and proper elicitation and documentation of family history</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Posting of Content, Distribution</th>
<th>Clinical Practice Guideline (CPG)</th>
<th>Practice Resource*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Published in <em>Journal of Genetic Counseling</em></td>
<td>• Likely published in <em>Journal of Genetic Counseling</em></td>
</tr>
<tr>
<td></td>
<td>• Posted on NSGC web site</td>
<td>• Likely posted on NSGC web site</td>
</tr>
<tr>
<td></td>
<td>• Submitted for inclusion in the National Guideline Clearinghouse (NGC)</td>
<td></td>
</tr>
</tbody>
</table>
**Stakeholders in Approval Process**

- Clinical Practice Guideline authors
- PGC members
- NSGC membership
- NSGC Ethics Advisory Board
- NSGC Legal
- NSGC Board of Directors
- Co-endorsing organization (if applicable)
- Relevant members of joint/partnering organization (if applicable)

- Practice Resource authors
- PGC members
- NSGC membership
- NSGC Ethics Advisory Board
- NSGC Legal
- NSGC Board of Directors
- Co-endorsing organization (if applicable)
- Relevant members of joint/partnering organization (if applicable)

GRADE, Grading of Recommendations Assessment, Development, and Evaluation; IOM, Institute of Medicine; NSGC, National Society of Genetic Counselors; PGC, Practice Guidelines Committee

*Although these documents are commonly referred to as “guidelines” (with a small “g”) because they provide practice guidance to clinicians, they do not meet the rigorous standards and definitions that are used for Guidelines (with a capital “g”) as established by the IOM.*
SECTION 3. Life of an NSGC Evidence-Based Practice Guideline – from Conception to Delivery

Figure 2. The 12-Step Process to an Evidence-Based Clinical Practice Guideline

The 12 Steps Explained:

1. PGC or external groups initiate this. A broad approach is preferred, ideally engaging other NSGC groups, external groups, and the public. It is at this time that a joint guideline may be considered.
2. Could consider these types of guidelines: Therapeutic intervention; Diagnostic/prognostic accuracy; Population-based screening. PICOTS (Population, Intervention, Comparison group, Outcomes, Time, Setting) is used to develop question.
3. PGC assembles inter-disciplinary groups (GCs, PhDs, MDs, medical librarians, biostatisticians, advocacy groups, other). Conflict of Interest in the groups is assessed, along with attempt to objectively determine best lead guideline authors, roles for members.
4. Review author group does this. Can engage medical librarian for help.
5. Review author group does this. Ultimately, creates table of evidence summaries (evidence table). Systematic reviews can be published on their own.
6. Review author Group does this. PGC recommends the GRADE system to evaluate strength of evidence for each target outcome. Will ultimately create an evidence profile for each.
7. Review author group does this. PGC can keep BOD in the loop. Alternative documents may also be explored here and going forward.

8. Guideline author group does this. Develops succinct, actionable recommendations that summarize evidence in answer to the specific question and submits to PGC. If the evidence base is lacking and there are compelling reasons to develop recommendations, the Guideline author group will use a systematic and transparent approach for developing consensus on what recommendations to put forth. Guidelines developed using this approach will also use “Evidence-Based Practice Guidelines” in the title because a systematic review was conducted.

9. PGC reviews, keeps BOD in the loop.

10. Guideline author Group does this. Writes and assesses guideline; can use the AGREE II instrument for assessment. Could consider external review for own purposes. PGC also reviews guideline.

11. PGC has several required steps: draft reviews and revisions, ethics, legal, NSGC member open comment period, NSGC BoD approval. Will involve external organization’s process if a joint guideline.

12. Author Group submits guideline for publication.

(And over time – a guideline’s actual use should be assessed.)
Hypothetical Timeline to an NSGC Evidence-Based Guideline

January, Year 1: Topic is approved/PICOTS question is developed, Recruitment for both Author Groups
- Step 3 of Process

February, Year 1: PGC reviews CVs, approves author groups, charges Review Author Group to generate Evidence Report, due Feb., Year 2
- Review Author Group does Steps 4-7 of Process (systematic review, synthesize data, grade evidence, write Evidence Report)
- Monthly updates to PGC Liaison

February, Year 2: Guideline Author Group drafts plan for guideline with recommendations
- Steps 8 and 9 of Process

March, Year 2: PGC reviews plan (2 weeks), BOD reviews plan (2 weeks)
- Step 9 of Process

April, Year 2: Guideline Author Group responds to feedback/initiate writing guideline
- Steps 9/10 of Process

May, Year 2: If authors choose to respond to feedback, they are given an additional 4 weeks to initiate writing
- Steps 9/10 of Process

November, Year 2: Guideline draft is submitted to PGC; PGC reviews
- Step 11 of Process

December, Year 2: Guideline goes to NSGC Ethics, Member Open Comment
- Step 11 of Process

January, Year 3: Authors have 2 months to revise based on feedback
- Step 11 of Process

March, Year 3: Guideline goes to NSGC attorney, NSGC BOD
- Step 11 of Process

April, Year 3: Guideline goes to Journal of Genetic Counseling (and/or other journal)
- Step 12 of Process

Summer Year 3: Guideline is published
**STEP 1: TOPIC GENERATION**

Evidence-Based Practice Guideline topics are generated from a variety of sources, including the NSGC Board, the PGC, NSGC SIGs and committees, NSGC members and external groups. Topics may be submitted at any time to the PGC using the Topic Proposal Form (see Appendix C).

Using the Topic Proposal Form, submitters are asked to describe the topic area and questions to be covered by the proposed guideline. The PGC encourages submitters to apply the PICOTS framework (see Step 2: Identify the Question for explanation), where appropriate, in submitting their ideas. Key references should also be listed, particularly if there are systematic reviews that have already been published or are underway on which recommendations could potentially be based (could shorten the process for developing the evidence report for the Guideline author group).

The PGC will prioritize guideline topics received on a regular (annual/biannual) basis, based upon timeliness, relevance to the profession and estimates of the evidence-base to inform the topic in question. In special circumstances, due to timeliness of a particular topic, guidelines may be prioritized for advancement outside of the typical decision making window.

Guideline topics of highest priority will be forwarded to the NSGC Board of Directors for review and approval. To facilitate generation of topics of highest priority, the PGC may engage the membership or other experts, by for example, posting key questions and outcomes on the NSGC website for public comment for a period of time, e.g., 30 days.

In the course of topic review, the PGC will also consider whether a guideline might make a suitable joint guideline. If this is the case, this will also be proposed to the NSGC BOD, and relevant organizations will be contacted once the BOD and PGC have decided to move forward with a systematic evidence review and/or guideline. The guideline process(es) of the co-sponsoring organization(s) will be reviewed and a joint review process will be proposed, integrating each committee’s policies, with timelines for each step. Some review processes (e.g. Board reviews) may be conducted in parallel with one another. The PGC may also consider whether the topic might be better suited to a different type of document (e.g., Practice Resource).
**STEP 2. DEVELOP THE QUESTION**

There are three types of questions that clinical practice guidelines can address: (a) questions about a therapeutic intervention, (b) questions regarding diagnostic or prognostic accuracy, and (c) questions regarding population screening. Each of these categories is discussed in more detail below.

*Category A.*

**Questions about a therapeutic intervention.** This question is important when genetic counselors need to decide whether or not to use a specific intervention.

For determining if this is the type of question to pursue, it helps to frame as: *Intervention for population with condition.* This is also known as the PICOT(S) format: Patient, Intervention, Comparison group/Comparator, Outcomes, Time, (Setting). Relevant outcomes of interest are usually in terms of the effectiveness, safety, and tolerability of the intervention.

Note: outcomes is plural, this is important. During the development phase, it will become important to prioritize the outcomes as critical for decision-making, important for decision-making, not important for decision-making. Ideally the guideline would focus on patient important outcomes. Questions about the value of a therapeutic intervention are often best answered using a comparative methodology (comparing against placebo, comparing against current standard practice, etc.). In this context, a randomized controlled study design is the strongest comparative methodology. For that reason, you will see in Section 3 STEP 6 on Evidence Grading that randomized controlled studies start out as providing strong evidence, though this can be downgraded if there some weaknesses in the other aspects of the study. Similarly, although other study designs are initially downgraded due to some inherent weaknesses of their study design, the evidence that they provide to the clinical question can be upgraded if there are strengths in other aspects of the study. Main message: randomized controlled studies can be important, but their absence does not preclude the creation of a clinical practice guideline.

For Category A questions, NSGC clinical practice guidelines can address questions about ways to deliver genetic counseling, people to deliver genetic counseling, types of genetic testing to offer, etc.

**Example:**

1) Can telephone-based pre-test genetic counseling for women with breast cancer be recommended?

Potential Measures of Effectiveness: enhanced knowledge, adherence to medical recommendations, etc.

Potential Measures of Safety: not harmful to patients, e.g. in terms of psychosocial outcomes

Potential Measures of Tolerability: patient satisfaction, return to clinic visits, etc.

*Category B*
Questions regarding diagnostic or prognostic accuracy. This question is important when genetic counselors need to decide whether to perform an intervention to determine the presence or prognosis of a disease, condition, or at-risk status.

Obvious questions that could be addressed include questions about whether to perform a specific genetic test to determine the presence or prognosis of a disease, condition, or at-risk status. Note that there may be other genetic counseling practice-relevant questions that could be asked, for example, about the diagnostic or prognostic accuracy of taking a pedigree or collecting family history information for a specific disease, condition, or at-risk status.

Questions of this nature are often assessed from prospective, controlled, cohort surveys of the population of interest. Relevant outcomes relate to improving the clinician's ability to predict the presence of the disease or the disease prognosis. Implication is that improving ability to diagnose and prognosticate indirectly translates to improved patient outcomes.

Example:

1) For patients with a question about their risk for inherited cancer, does the presence of 2+ affected family members accurately identify those patients with a germline mutation? If yes, then the recommendation would be for genetic counselors and other clinicians to collect family history information and identify number of family members with cancer.

Category C

Questions regarding population screening. This question is applicable to situations where a diagnostic intervention of established accuracy is employed and can be important, for example, when genetic counselors or other clinicians need to decide the scope of their patient population for a particular procedure.

For questions in this category, the relevant outcome is the yield of the procedure. If the yield is high enough then clinicians would routinely order the procedure. Studies that assess Category C questions tend to be prospective studies of a population-based cohort of patients who undergo the procedure.

For Category C questions, NSGC clinical practice guidelines can address questions about scope of patient population under different scenarios. Two examples are:

1) Should all pregnant patients routinely meet with a genetic counselor to identify potentially inherited conditions?

2) Should all primary care patients routinely meet with a genetic counselor to identify potentially inherited conditions?

In these cases, the relevant outcome would be the frequency with which genetic counselors identify potentially inherited conditions in these patient populations. It is important to keep in mind that “genetic counseling to identify potentially inherited conditions” should have an established accuracy before embarking on clinical practice guidelines to address these kinds of questions.
**STEP 3: ASSEMBLE AND ASSESS AUTHOR GROUPS**

Two author groups will be constituted for the development of an Evidence-Based Practice Guideline: (1) Review author group, and (2) Guideline author group.

Responsibilities:
- The Review author group will be responsible for performing a systematic literature review, synthesizing the evidence, grading the quality of the evidence, and writing an Evidence Report.
- The Guideline author group will be responsible for crafting recommendations based on the Evidence Report, grading the strength of the recommendations, and writing the Evidence-Based Practice Guideline.

Composition:
- Ideally, these author groups are inter-disciplinary and address relevant areas of expertise and diverse viewpoints (genetic counselors, physicians, basic scientists, medical librarians, biostatisticians, advocacy groups, other).
- At least two authors in each of the author groups must be NSGC full members, and as a group the authors must be affiliated with at least two different institutions.
- The Review author group should include at least one individual with methodology expertise (i.e., familiar with the systematic review process, synthesizing evidence, using the GRADE system for grading the quality of evidence), and at least one individual with clinical expertise. One individual may have multiple areas of expertise.
- The Guideline author group should include at least one individual with clinical expertise and at least one individual with a consumer/patient perspective.
- A PGC liaison will be assigned to the Review author group, and subsequently to the Guideline author group. The PGC liaison cannot also be a listed author.

Solicitation:
- The PGC will solicit NSGC members and non-NSGC potential candidates to submit CVs and an NSGC Disclosure Form (see Appendix C) to PGC for consideration, in response to an announcement for a specific clinical practice guideline topic/question.
- Announcements will describe the types of skill sets needed for each author group. Application could ask if willing to serve as lead author
- PGC members are not precluded from participating in an author group where it is deemed appropriate. If participating, they would be expected to recuse themselves from PGC discussions of the guideline.

Selection:
- The PGC will be responsible for identifying authors, determining the lead authors and roles for group members.
- In the case of more than one lead author, they must come from at least two different institutions.
• The NSGC Board, in consultation with the PGC, must approve any author that is not an NSGC member.
• In accordance with its Conflict of Interest policy, the PGC will evaluate any potential conflicts of interest during its review of potential author groups, as well as throughout the guideline process.
• The author groups will be voted on by the PGC and a recommendation will be forwarded to the NSGC Board for approval.

As a prerequisite to authorship of the Evidence-Based Practice Guideline, and in consideration for NSGC’s agreement to publish the proposed guideline (i.e. Contribution), authors must agree to sign an Author Agreement Form (see Appendix C). This form assigns and transfers any and all rights, titles, and interests (including all copyrights in the contribution) to NSGC.

Timeframe:
• Once the Review author group is established, the authors will have up to 12 months from the date of PGC approval to complete the activities culminating in an Evidence Report (steps 4-7). If the authors do not meet expected deadlines, the PGC and Board may withdraw its approval of pursuing a systematic review or solicit other authors to complete the document.
• The Guideline author group will have up to 6 months from the completion of the Evidence Report to complete the activities that will culminate in an Evidence-Based Practice Guideline document ready for review. If the authors do not meet expected deadlines, the PGC and Board may withdraw its approval of pursuing a practice guideline on that topic or solicit other authors to complete the document.
• Designated PGC member(s) will facilitate the guideline development process as liaisons. Authors will send all drafts to this/these individual(s) to ensure adherence to the process.
• Authors must submit a monthly update of their progress to the PGC liaison(s) and NSGC staff contact.
STEP 4. PERFORM AND DOCUMENT A SYSTEMATIC REVIEW

What is a systematic review?
For a clinical practice guideline, a **systematic literature review** is the National Guidelines Clearinghouse (NGC)-required method for gathering evidence that informs the topic of the guideline. The focus of the literature review is generally on a specific question in order to draw a specific conclusion, i.e. recommendation. Systematic review is a specific methodology and is the preferred method for developing a clinical practice guideline because it is less prone to author bias.

Note: a systematic review differs from a narrative review (also called expert review).

A narrative review can be a review of a broad topic or a narrow topic using literature to support the expert opinion, or using literature that is not comprehensive or literature search that is non-systematic or non-described. Narrative reviews can be published in peer-review journals. However, narrative reviews are a poor way to develop a Clinical Practice Guideline because the recommendations can be subject to author group bias. A Clinical Practice Guideline based on a narrative review is not NGC-compliant.

**Table 2. Comparing Systematic Review and Narrative Review**

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<thead>
<tr>
<th></th>
<th>Systematic Review</th>
<th>Narrative Review</th>
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</thead>
<tbody>
<tr>
<td>Research question</td>
<td>Strictly formulated</td>
<td>Broadly formulated</td>
</tr>
<tr>
<td>Methodology</td>
<td>Clearly defined</td>
<td>Not or insufficiently described</td>
</tr>
<tr>
<td>Search strategy</td>
<td>Clearly defined</td>
<td>Not described</td>
</tr>
<tr>
<td>Selection of studies</td>
<td>Clearly defined</td>
<td>Not described</td>
</tr>
<tr>
<td>Ranking of the studies</td>
<td>By levels of evidence</td>
<td>Not performed</td>
</tr>
<tr>
<td>Analysis of the studies</td>
<td>Clearly described</td>
<td>Not described</td>
</tr>
<tr>
<td>Interpretation of results</td>
<td>Objective</td>
<td>Subjective</td>
</tr>
</tbody>
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Performing a systematic review
A systematic review involves:

- An explicit search of specific databases using defined key words/search terms;
- Determining and applying explicit criteria for identifying which studies to include in subsequent analysis and which studies to exclude
  - Study designs (RCT, cohort, case-control, cross-sectional, other)
  - Publication status (Peer-reviewed publications only? Also include abstracts?)
  - Language (English, other languages?)
  - Other: Publication year, Study size, Minimum follow-up, other
- Data extraction into a form (usually tabular) amenable for data synthesis
Institutional librarians can play an important role in the systematic review process, in large part because they are significantly involved in assigning index terms to articles. Librarians can help an author group with the following:

- Defining the clinical question on the front end in order to get the best results to evaluate on the backend
- Translating the clinical question into searchable terminology.
- Identifying the places where the terminology needs to be searched.
- Finding literature beyond PubMed and Google Scholar databases.
  - Medline (Medical Literature Analysis and Retrieval System Online): Premier database of medical research
  - Ovid interface supported thru institutional accounts, and allows for more complex searching
  - Embase (Excerpta Medica Database)
    - Large European database similar in scope and content to Medline
    - Includes many conference proceedings
    - Up to 70% citations in Embase not in Medline
  - Cochrane Controlled Trials Registry
    - Fastest, most reliable method for determining if a controlled trial has been published on any topic
- Identifying key pieces of “gray” literature (usually outside normal publishing sources, like books or journals - includes things like technical reports, dissertations, theses, article pre-prints, conference proceedings, white papers).

Some librarians stop there and usually the librarian’s product is: “here are the search terms to use, here are the databases to search, I ran the search and here are the article titles and abstracts I found.” The author group would take this information and continue with the process, e.g., apply the inclusion/exclusion criteria to winnow down the article list to the relevant set (typically recommended to have two reviewers independently apply inclusion/exclusion criteria to the identified abstracts, compare results, and then discuss to resolve discrepancies between choices; also recommended to document inter-rater reliability at first evaluation), extract information from the included studies, synthesize the evidence from these articles, etc. (see below for more details).

Some librarians will go the next step. They will help develop a framework to organize the literature that is retrieved (knowledge management). This assistance could be as simple as recommending software or a program to use. Or if a librarian is also an expert in the subject area, e.g., genetic counseling, he/she may be included in subsequent phases. The librarian might write a paragraph in the methodology section about how the systematic search was conducted. Inclusion of librarians in the Review author Group should be considered. Or be aware that if a librarian contributes significantly to the systematic review that he/she might be added to the Review author group at a later date, pending approval from the Practice Guidelines Committee and NSGC Board.

Things to consider:
• Institutions differ in terms of (1) access to online databases (all likely have access to free databases; but some databases require subscription in order to search); (2) access to articles (all have access to open access articles, but many journals require subscription in order to access articles); (3) Fee for a librarian to conduct a systematic literature search (some institutions do not charge a fee for people affiliated with the institution). Librarians across institutions often work together to “fill in the gaps” for searching databases and accessing articles.

• Author groups should build in time to work with a librarian (PGC may be able to help identify one, if none is available to authors). Authors should build in lead time to meet with a librarian at an institution (2-3 months before evaluation of articles is a possibility).

NOTE: It is okay to do an exploratory literature search before embarking on the systematic literature search/review process. It is also okay to do more than one exploratory literature search because you may learn something important in the first exploratory search that makes you want to do another exploratory literature search. Again, the purpose is to develop a focused question that is then pursued through the systematic evidence-based process.

Documenting a systematic review
The purpose of documenting a systematic review is so that someone else could replicate the steps and come up with the same set of studies used to create a Practice Guideline. Some journals have specific requirements for how to report the process and findings of a systematic review, like PRISMA, MOOS. For the purposes of NGC-Compliant NSGC Practice Guidelines, which will typically be published in *Journal of Genetic Counseling*, the Review author group must be able to provide:

A description of the search strategy that includes a listing of database(s) searched, a summary of search terms used, the specific time period covered by the literature search including the beginning date (month/year) and end date (month/year), and the date(s) when the literature search was done.

A description of study selection that includes the number of studies identified, the number of studies included, and a summary of inclusion and exclusion criteria.

To comply with NGC criteria, we recommend that the Review author group documents the following items:

• Search Terms/Key words used;
• Databases Searched;
• Time period searched: Beginning Date (month/year) and End Date (month/year);
• Dates when literature search(es) were performed;
• Study Inclusion Criteria;
• Study Exclusion Criteria;
• Total number of studies identified
**STEP 5. EXTRACT DATA INTO EVIDENCE TABLES AND SYNTHESIZE THE DATA**

After the studies are identified, it is necessary to extract essential characteristics of each of the studies selected for inclusion. These extracted characteristics will be used to assess each study’s strength. The characteristics of each study will be included in a master (evidence) table. This table succinctly summarizes each study, including characteristics relevant to generalizability, risk of bias, and patient outcomes (harms and benefits). The point is to extract information that informs the judgment of each study’s relevance to the clinical question. Hints:

- Set priorities for data to extract
- Anticipate structure and content of final evidence tables
- Resist temptation to extract everything
- Establish quality control
- Dual extraction vs. solo extraction with checks
- Consider free electronic resources to help

Characteristics that may be important to include in the data extraction form include factors that will allow for quantitative or qualitative synthesis of the evidence and will allow for evidence grading.

**Generalizability:**

-- Relating to the patient population:
- Source of patients (*e.g.*, clinical oncologists)
- Inclusion criteria used in the study to determine the presence of the condition of interest
- Age of the patients (*e.g.*, mean and standard deviation)
- Gender of the included population (*e.g.*, proportion female)

-- Relating to the intervention and co-intervention. These will be highly dependent on the clinical question but could include the following:
- Length of telephone-based genetic counseling session
- Timing of the telephone-based genetic counseling
- Nature of the genetic counseling (*e.g.*, telephone-based vs. in person)

**Outcome Measures:**

These will also vary from question to question but could include the following:
- Scale used to determine the outcome (*e.g.*, adherence to medical recommendations)
- Duration of follow-up

**Patient Outcomes (Results, *e.g.*, Effect Size) -- could include:**
- Relative effect with 95% CI
- Best estimate of group risk

Page 19 of 61
Absolute effect (95% CI)
Sample size

During this phase it may be possible to qualitatively or quantitatively synthesize results across studies on one or more outcomes.

- Qualitative synthesis using evidence tables and written evidence summaries
- Quantitative synthesis using meta-analysis
  - Meta-Analysis:
    - Estimate a summary measure and its variance for each study
    - Weight each study according to its variance
      - Studies with larger variance (more uncertainty) get less weight
      - Statistically combine or pool results from each study to obtain a weighted average
      - Not just a simple average

It is important to note that differences in study design, populations, intervention, comparator, outcome definitions and conduct of trials can lead to differing results between studies. This phase is an opportunity to explore potential heterogeneity across the studies which could affect the overall quality of the evidence as well as help one understand the conditions most likely to yield positive or negative effects from an intervention.

Take-Home Points

Table 3.

**Key Steps for Systematic Review and Synthesizing the Evidence**

- Define question
- Establish eligibility criteria
- Search literature
- Extract data
- Evaluate individual study quality
- Synthesize data qualitatively and/or quantitatively (meta-analysis)
- Explore heterogeneity
**Table 4.**

<table>
<thead>
<tr>
<th>Systematic Review versus Meta-Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systematic Review</strong></td>
</tr>
<tr>
<td>• Literature review prepared using a systematic approach to minimize bias and random error in identification of information</td>
</tr>
<tr>
<td>• May or may not include a meta-analysis</td>
</tr>
<tr>
<td><strong>Meta-analysis</strong></td>
</tr>
<tr>
<td>• Statistical pooling of the results of individual studies</td>
</tr>
<tr>
<td>• Aims to produce a single estimate of treatment effect</td>
</tr>
<tr>
<td>• One method for synthesizing the results of a systematic review (so by itself is NOT a systematic review)</td>
</tr>
</tbody>
</table>
**STEP 6. GRADE THE EVIDENCE AND CREATE AN EVIDENCE PROFILE**

Now it is time to evaluate the quality of evidence from these studies. Think of this as an evaluation of the *body of evidence*. This is called grading the evidence. Note: Would evaluate a set of randomized controlled trial studies separately from a set of observational/cohort studies (not combine them).

*Grading Evidence*

NSGC PGC supports using the GRADE system for this activity because we (PGC) independently assessed it and preferred it; we compared GRADE to the USPTF system (see Appendix D). GRADE is also used by organizations such as the Centers for Disease Control, Agency for Healthcare Research and Quality, American College of Chest Physicians, The Cochrane Collaboration, Society for Critical Care Medicine, World Health Organization. A randomized study comparing six different evidence grading schemas found that healthcare providers were more likely to follow recommendations that used the GRADE methodology than the other methodologies (Atkins et al 2004).

When assessing the quality of evidence, make these assessments *for each outcome* across the studies. GRADE considers the following factors across the studies. Each of the first five factors is judged in terms of *no serious limitation; serious limitation* (-1), *very serious limitation* (-2). The remaining 3 factors are judged differently and can increase the quality of evidence if present. These judgments are made by considering the body of evidence across the studies. These judgments go into Worksheet 1 below.

**GRADE Factor 1.** Study design and rigor of its execution (sometimes called Risk of Bias, sometimes called Study Limitations).

First, assess Risk of Bias for each study and outcome. Use the Risk of Bias Tools (Randomized Controlled Trials use one form, developed by the Cochrane group (see Appendix D); for observational studies and cohort studies could use the Newcastle-Ottawa scales (see Appendix D). This table gives an example of what a Risk of Bias Summary could look like. ‘+’ means the answer to the question is ‘yes’; ‘-’ means the answer to the question is ‘no’. In some cases it may not be clear from the study description, in which case put a ‘?’ . Then based on a review of the entire table judge whether there is no serious limitation, serious limitation, or very serious limitation; and circle judgment in Worksheet 1, Column 2 below.
Table 5. Example: Risk of Bias Summary - Outcome 1

<table>
<thead>
<tr>
<th></th>
<th>Study 1</th>
<th>Study 2</th>
<th>Study 3</th>
<th>Study 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate sequence generation?</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Allocation concealment?</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Blinding of patients?</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Blinding of providers?</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Blinding of data collectors?</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Blinding of outcome adjudicators?</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Blinding of data analysts?</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Incomplete outcome data addressed?</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Free of selective reporting?</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Free of other bias?</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Intention to treat analysis?</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>


GRADE Factor 2. Indirectness: the extent to which available evidence can be directly applied to the target, interventions, comparisons and outcomes. Things to consider are:

a) Indirect comparison - comparison of intervention A to B not available; but A is compared to C and B is compared to C
b) Indirect population, intervention, comparator, or outcome

Indirect population
This can arise when studies pertinent to a question only include a subpopulation of patients with the disease. For example, some studies of genetic counseling sessions to discuss hereditary breast cancer may have been performed on women and not men.

Indirect intervention
For example, if all studies of patients receiving genetic counseling to discuss hereditary breast cancer genetic testing were limited to women who had prophylactic double mastectomies, the generalizability of this evidence to other patients with different surgical histories is limited.

Indirect comparator
For example, if the literature search found only studies looking at genetic counseling to offer genetic testing to patients with breast cancer and not those without breast cancer, the applicability of this evidence to the question of genetic testing is limited.

Indirect outcome
For example, a study of telephone-based genetic counseling to discuss hereditary breast cancer genetic testing may have determined outcome only at 2 months. It would be difficult to generalize this evidence to long-term outcomes.

GRADE Factor 3. Inconsistency of the results
a) Widely differing estimates of the effect size across studies suggest true differences in underlying treatment effect

b) This is the opportunity to quantify heterogeneity using a forest plot, I2 statistic

The appropriate approach to take when faced with inconsistent results in the included studies is to attempt to explain the inconsistencies. The inconsistencies can often be explained by systematic or random error. A vote counting approach is not acceptable; it ignores the potential sources of error within each study.

GRADE Factor 4. Imprecision of the results: a function of sample size

a) Wide confidence intervals include no effect, or cross the minimal important difference for benefit or harm. If a meta-analysis has been conducted and have an overall effect size, evaluate imprecision based on this confidence interval.

GRADE Factor 5. Likelihood of publication bias

a) This is a systematic underestimate or overestimate of the true effect due to selective publication of studies. Typically studies demonstrating no effect are not submitted or accepted for publication.

b) This is the opportunity to create a funnel plot from the pool of studies

The following three factors can increase the quality of evidence:

GRADE Factor 6. Magnitude of the effect
GRADE Factor 7. Demonstration of a dose-effect relationship
GRADE Factor 8. The likely direction of impact of all plausible confounding factors on the observed effect
**Worksheet 1: Assessing the quality of evidence across studies for an outcome**

<table>
<thead>
<tr>
<th>Quality Criteria</th>
<th>Rating (circle one for each criterion)</th>
<th>Footnotes (explain reasons for up- or downgrading)</th>
<th>Quality of the Evidence (Circle one per outcome)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome #1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk of bias</td>
<td>No</td>
<td>No serious (-1)</td>
<td>High (++++)</td>
</tr>
<tr>
<td></td>
<td>Serious (-1)</td>
<td></td>
<td>Moderate (+++)</td>
</tr>
<tr>
<td></td>
<td>Very serious (-2)</td>
<td></td>
<td>Low (++)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Very low (+)</td>
</tr>
<tr>
<td>Inconsistency</td>
<td>No</td>
<td>No serious (-1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Serious (-1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Very serious (-2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indirectness</td>
<td>No</td>
<td>No serious (-1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Serious (-1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Very serious (-2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Imprecision</td>
<td>No</td>
<td>No serious (-1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Serious (-1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Very serious (-2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Publication Bias</td>
<td>No</td>
<td>No serious (-1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Serious (-1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Very serious (-2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large Effect</td>
<td>Large (+1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Very large (+2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose-Response Gradient</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes (+1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plausible Confounding Would Change the Effect</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes (+1)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

From “GRADE track handout: TEACH Workshop NYAM August 7-9, 2013”

Next, produce an overall assessment of the quality of the body of the evidence for each outcome (Column 4 in Worksheet 1). In the GRADE system quality of supporting evidence is classified in four categories. The suggested terms are “high,” “moderate,” “low,” or “very low,” but some organizations prefer the use of symbols or letters to express the ranking the evidence:

- **High**: Further research is very unlikely to change certainty regarding estimate of effect
- **Moderate**: Further research is likely to change certainty regarding the estimate of effect
- **Low**: Further research is very likely to change certainty regarding the estimate of effect
- **Very low**: Any estimate of effect is very uncertain.

The GRADE system uses a point scoring method to derive an assessment of the quality of the body of evidence pertaining to each target outcome.

### Table 6. Summary of Approach

<table>
<thead>
<tr>
<th>Study design</th>
<th>Initial quality of a body of evidence</th>
<th>Lower if</th>
<th>Higher if</th>
<th>Quality of a body of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized trials</td>
<td>High</td>
<td>Risk of Bias - 1 Serious -2 Very serious</td>
<td>Large effect + 1 Large +2 Very large</td>
<td>High (++++)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inconsistency - 1 Serious -2 Very serious</td>
<td>Dose response +1 Evidence of a gradient</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Indirectness - 1 Serious -2 Very serious</td>
<td>All plausible residual confounding +1 Would reduce a demonstrated effect</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Imprecision - 1 Serious -2 Very serious</td>
<td>+1 Would suggest a spurious effect if no effect was observed</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Publication bias - 1 Likely -2 Very likely</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Observational studies</td>
<td>Low</td>
<td></td>
<td>Moderate (+++)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low (++™™)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Very low (+)</td>
<td></td>
</tr>
</tbody>
</table>

From GRADE and the Guideline Development Process” document, TEACH Workshop NYAM August 7-9, 2014

Note that randomized controlled trial studies start out as high and can be downgraded; observational studies start out as low and can be upgraded.
The overall quality of evidence is determined by the lowest quality of evidence for each of the critical outcomes (from GRADE and the Guideline Development Process, TEACH workshop NYAM August 7-9, 2014).

Example Outcome 1 = Complete response of tumor to chemotherapy. Suppose there are 5 randomized controlled trials. Factor 1 is judged as no serious limitations. Factor 2 is judged as serious inconsistency (-1). Factor 3 is judged as no serious indirectness. Factor 4 is judged no serious imprecision. Factor 5 is judged as publication bias (-1). RCTs start out as High (+++), but with these judgments, 2 stars are removed, so that the overall quality of the body of evidence for this outcome is Low (++).

Create Evidence Profile. An Evidence Profile summarizes all of the relevant information about the quality of the body of evidence and effect sizes for each outcome.

Table 7. Example: Complete response of tumor to chemotherapy

<table>
<thead>
<tr>
<th># studies</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Design</td>
<td>RCT</td>
</tr>
<tr>
<td>Limitations</td>
<td>No serious</td>
</tr>
<tr>
<td>Inconsistency</td>
<td>Serious</td>
</tr>
<tr>
<td>Indirectness</td>
<td>No serious</td>
</tr>
<tr>
<td>Imprecision</td>
<td>No serious</td>
</tr>
<tr>
<td>Other considerations</td>
<td>Publication bias</td>
</tr>
<tr>
<td># patients - intervention</td>
<td>216/344</td>
</tr>
<tr>
<td># patients – control</td>
<td>211/344</td>
</tr>
<tr>
<td>Relative risk (95% CI)</td>
<td>RR 1.0 (0.92 to 1.1)</td>
</tr>
<tr>
<td>Absolute</td>
<td>0 fewer per 1000 (from 49 fewer to 61 more)</td>
</tr>
<tr>
<td>Quality</td>
<td>Low (+++)</td>
</tr>
<tr>
<td>Importance</td>
<td>critical</td>
</tr>
</tbody>
</table>

From GRADE Track handout: TEACH Workshop NYAM August 7-9, 2013
**STEP 7. CREATE AN EVIDENCE REPORT**

The Review author group will summarize their work in a written Evidence Report. This report will fully describe the systematic review process, synthesis of the evidence, and grading of the quality of the evidence. The PGC and Guideline Author Group will review the Evidence Report, and may have in some cases have questions for the Review author group at this point. Once the Evidence Report is finalized, the NSGC BOD will receive it (with a 1-page Executive Summary cover sheet) as an informational update. Any questions or clarifications will be provided to the Review author group in writing (via the PGC liaison) and the Review author group will have **1 month** to submit written responses. Should responses necessitate a revision to the Evidence Report, the Review author group will make those revisions. It is possible that some responses will indicate that there is no strong rationale for revising the document.

Systematic reviews may also be published, and in fact, NSGC encourages their publication. In the event that NSGC fully or partially funds a systematic review, a statement acknowledging this will be included in the Systematic Review’s and related Evidence Report’s/Practice Guideline’s publications. The systematic review itself has value in informing genetic counselors and patients of the limitations/strengths of the evidence. This can be published as a stand-alone document and can provide great inspiration for future research.

Systematic reviews are not by themselves NSGC-endorsed documents and therefore **do not need** to follow the same approval process for publication.
STEP 8. CRAFT AND GRADE ACTIONABLE RECOMMENDATIONS

Ideally, the Guideline author Group will convene in person or by conference call to craft and grade their recommendations based on the Evidence Report. The Guideline author group will have up to 6 months from the date of receipt of the Evidence Report to complete the Evidence-Based Practice Guideline. If the authors do not meet expected deadlines, the PGC and NSGC BOD may withdraw its approval or solicit other authors to complete the document.

Any recommendation should be formatted in a way that clearly links it to the clinical question. The Guideline author group will use the information from the Evidence Profiles to develop recommendations. Using the GRADE system (Guyatt GH et al., 2008), author group will explicitly consider:

- Quality of evidence
- Balance of benefits and harms/burdens
- Distribution of values and preferences
- Resource implications

**Quality of evidence (as assessed by Review group).** Here develop succinct statements that summarize the evidence in answer to the specific clinical question. Ideally, these statements should indicate the magnitude of the effect and the quality of evidence on which it is based. The overall quality of evidence is determined by the lowest quality of evidence for each of the critical outcomes. The higher the quality of evidence, the more likely a strong recommendation is warranted.

**Balance of benefits and harms/burdens (or Balance between desirable and undesirable effects)** - The larger the difference between the desirable and undesirable effects, the more likely a strong recommendation is warranted. The narrower the difference, the more likely a weak recommendation is warranted.

**Distribution of values and preferences.** This refers to the relative worth or importance of a health state or consequences of a decision to follow a particular course of action (benefits, harms, burdens, treatment and resources). Individuals usually assign less value to and have less preference for more impaired health states compared to other health states. The more variability in values and preferences, or more uncertainty in values and preferences, the more likely a weak recommendation is warranted. Engagement of advocacy groups/external stakeholders will also help identify values and preferences.

**Resource implications.** The higher the costs of an intervention (that is, the more resources consumed) the less likely a strong recommendation is warranted. This may be subjective.

Based on the above factors, recommendations are classified as either “strong” or “conditional/weak.” The strength of recommendations depends on a balance between all desirable and all undesirable
effects of an intervention (i.e. net clinical benefit), quality of available evidence, values and preferences, and resource utilization (cost and others). In general, the higher the quality of the supporting evidence, the more likely it is for the recommendation to be strong. Conversely, if the quality is low or very low a conditional/weak recommendation is more likely. [Note: PGC prefers use of the word ‘conditional’ instead of ‘weak’] Strong recommendations based on low or very low quality evidence are possible, in particular if they are made against the use of new technologies that are poorly investigated (where, for example, net clinical benefit is questionable, harms are possible or probable, and the new technology is highly resource intensive). Strong recommendations may also be expressed as “we recommend” and conditional recommendations as “we suggest.” Statements about the underlying values and preferences that were used to inform the strength of the recommendation as well as the remarks are integral parts of the recommendations which serve to facilitate accurate interpretation of the recommendations and should be included.

**TIP:** When formulating evidence-based conclusions, avoid the terms *proven effective* or *established as effective.* Evidence is never definitive, and therefore conclusions derived from evidence cannot be “proven” or definitively “established.”

Table 8. Interpretation of “strong” and “conditional/weak” recommendations

<table>
<thead>
<tr>
<th>Implications</th>
<th>Strong recommendation</th>
<th>Conditional/Weak recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>For patients</td>
<td>Most individuals in this situation would want the recommended course of action and only a small proportion would not. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.</td>
<td>The majority of individuals in this situation would want the suggested course of action, but many would not.</td>
</tr>
<tr>
<td>For clinicians</td>
<td>Most individuals should be offered the intervention. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.</td>
<td>Recognize that different choices will be appropriate for individual patients, and that authors must help each patient arrive at a management decision consistent with his or her values and preferences. Decision aids may help individuals to make decisions consistent with their values and preferences.</td>
</tr>
<tr>
<td>For policy makers</td>
<td>The recommendation can be adopted as policy in most situations</td>
<td>The policy will require substantial debates and involvement of various stakeholders before adaptation</td>
</tr>
</tbody>
</table>
Example to demonstrate crafting and grading a recommendation for an Evidence-Based Genetic Counseling Practice Guideline.

Clinical question:
1) Is telephone-based genetic counseling as effective as in-person genetic counseling to identify patients appropriate for hereditary breast cancer genetic testing?

Outcome 1: (Desirable) Accurate identification of patients appropriate for genetic testing is deemed a Critical Outcome. For patients seen to discuss hereditary breast cancer genetic testing, genetic counseling delivered by phone was not statistically different in identifying patients appropriate for hereditary breast cancer genetic testing compared to that delivered in person (rate difference 5%, moderate quality of evidence).

Outcome 2: (Undesirable) Patient satisfaction is deemed a Critical Outcome. Genetic counseling delivered by phone produced lower patient satisfaction than counseling delivered in person (Cohen’s d=0.3, high quality of evidence).

Outcome 3: (Undesirable) Patient follow-up questions is deemed a Critical Outcome. Genetic counseling delivered by phone resulted in more follow-up questions by patients compared to genetic counseling delivered in person (rate difference 10%, moderate quality of evidence).

Table 9. Summary of evidence for key factors in determining the recommendation:

<table>
<thead>
<tr>
<th>Key Factors from GRADE</th>
<th>Comments for this hypothetical example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence Type for Benefits and Harms</td>
<td>Overall evidence quality for critical factors is “moderate” (based on lowest quality of evidence rating across the 3 outcomes)</td>
</tr>
<tr>
<td>Balance between benefits and harms</td>
<td>Benefits outweigh harms since patient identification does not significantly differ by counseling modality (based on Example Outcome 1); and effect sizes of potential harms are small (based on example Outcomes 2 and 3)</td>
</tr>
<tr>
<td>Values and Preferences</td>
<td>The Guideline author group placed high value on facilitating pre-test genetic counseling for individuals unable to easily attend an in person session (created to illustrate role of values and preferences of the Guideline author group in summarizing evidence to determine a recommendation). It is important to be</td>
</tr>
</tbody>
</table>
transparent about the values and preferences of the Guideline author group, if that is whose values and preferences are considered in the recommendation process.)

| Resource Implications | Cost effectiveness analysis not performed (added just to illustrate what to do if the resource implications of a recommendation are not evaluated. In some cases, resource implications may be evaluated. The point is, transparency is key.) |

From GRADE and the Guideline Development process document, TEACH Workshop NYAM August 7-9, 2014

**Conclusion:** We strongly recommend telephone-based genetic counseling be available as an option to identify patients appropriate for hereditary breast cancer genetic testing.

NB: A guideline is not excluded from National Guidelines Clearinghouse if a systematic review was conducted that identified specific gaps in the evidence base for some of the Practice Guideline's recommendations. In this case, any recommendations made must reflect this in their wording, and the identified evidence gaps must be acknowledged in a transparent manner.

**However, there may be cases when no specific recommendation is made**

- The advantages and disadvantages are equivalent
- The target population has not been identified or studied
- Insufficient evidence (for/against a clinical decision) on which to formulate a recommendation

Even when there is high-quality evidence, a recommendation need not necessarily follow. For example, there may be major concerns of generalizability or clinical applicability within the evidence base that would call into question the usefulness of any associated recommendations. In these circumstances, a formal recommendation is not required. A placeholder within the document where the recommendation would normally appear still needs to be present. This placeholder section would briefly explain why a recommendation was not made. In most circumstances, the limitations of the evidence resulting in the absence of a recommendation would be explicated in the published guideline.

Recommendations for future research. Often after formally reviewing the evidence, the guideline developers are in a unique position to suggest future research to fill in the evidence gaps. The future research section of the guideline is important for identifying areas that were found deficient on the basis of the thorough, systematic literature analysis. If such gaps exist, the Review author group would have been the ones to identify and address them in the systematic review.

**Consensus Process for Developing Recommendations**

Occasionally, after completing the systematic review and grading the evidence, practice guideline developers will realize that the evidence base is too weak to support any meaningful practice
recommendations. In these circumstances it may be appropriate to terminate the development process rather than attempt to develop an evidence-based practice guideline. However, it may be possible to develop practice recommendations (and a guideline) that are conditional and transparent about the weak evidence base, often because there is no other such resource available on the topic. The Guideline author group may determine a need for more extensive stakeholder contribution in the development of recommendations and may employ a structured approach (such as the Delphi method).
STEP 9: PGC AND NSGC BOD REVIEW

The Guideline author Group will summarize their work in a draft report. This report will briefly describe their recommendations, the rationale, and process for arriving at them. The PGC will review the draft report. Any questions or clarifications will be provided to the Guideline author group in writing and they will have one month to submit written responses. Should responses necessitate a revision to the recommendation(s) or other aspects of the report, the Guideline author group will make those revisions. It is possible that some responses will indicate that there is no strong rationale for revising the document. The PGC will vote on whether to move forward with the Evidence-Based Practice Guideline as represented in the revised draft report and forward a summary of their discussion and outcome of the vote to the NSGC BOD.
STEP 10. WRITE AND ASSESS THE EVIDENCE-BASED PRACTICE GUIDELINE

Practice Guideline Content and Format
Practice Guidelines should be well written, clear, and concise. The guideline document specifications are:

- The Practice Guideline document must at least make reference to the systematic review that took place. The systematic review documents need not be included in the guideline, but must be made available as needed by the PGC and the NGC. The systematic review may be published separately.
- The draft guideline must be double-spaced, in Times New Roman, 11 or 12-point font, following the anticipated publication journal’s author guidelines (often Journal of Genetic Counseling and another journal, if a joint guideline).

It is important to note that a Practice Guideline is not a review paper. It is a summary of key points and data from a systematic review, which then makes evidence-based recommendations to facilitate a clinical decision for the reader. It can provide references to direct the reader to more detailed information about the process used to generate, analyze, and evaluate the quality of data on which the recommendations are based.

Practice Guidelines must include the following:

Title: The title should reflect the content of the Practice Guideline document, and contain the phrase ‘NSGC Evidence-Based Practice Guideline’.

NOTE: For joint guidelines, the organization listing order in the publication should be approved by the PGC. It is preferable to alternate the order with organizations with whom multiple joint guidelines are co-authored.

Authors: Order determined by the Guideline author Group and in compliance with PGC’s Conflict of Interest Policy.

Purpose: The Practice Guideline should include a clearly articulated purpose with specific recommendations for the use of genetic information in healthcare or the methods of access to, or delivery of, genetic counseling services. This section should also specify the intended audience.

Introduction: The introduction should address:

- An explicit statement that the clinical practice guideline was based on a systematic review
- The data from the Evidence Report supporting the purpose of the guideline
- The topic’s relevance to genetic/genomic healthcare service delivery
- The reason the topic is timely (e.g. advent of new research findings and its relation to testing technologies, scientific, or practice discoveries; or correcting current inappropriate use/care
- The practice differences associated with the topic, if any, and how they will be addressed
- The way in which the practice guideline will improve or change genetic/genomic healthcare.
**Background:** The background section should summarize the key data from the Evidence Report, supporting the authors’ recommendations. This section should direct the reader to references for more extensive details regarding the data presented. Evidence tables may be useful for summarizing key information.

This section should specifically include:

a. A description of the search strategy that includes a listing of database(s) searched, a summary of search terms used, the specific time period covered by the literature search including the beginning date (month/year) and end date (month/year), and the date(s) when the literature search was done.

b. A description of study selection that includes the number of studies identified, the number of authors reviewing studies for inclusion (and how discrepancies were resolved), the number of studies included, and a summary of inclusion and exclusion criteria.

c. A synthesis of evidence from the included studies, e.g., a detailed description, meta-analysis, and/or evidence tables.

d. A summary of the evidence synthesis included in the guideline that relates the evidence to the recommendations, e.g., a descriptive summary or summary tables.

e. Review of methodology used to evaluate and incorporate benefits/harms, values/preferences, resource implications

**Practice Recommendations:** The authors’ practice recommendations should be presented in the most concise format possible to increase readability and usefulness for the intended audience. The recommendations must stem from the synthesis and grading of the evidence collected via systematic review. The recommendations must be graded or be based on a systematic and transparent consensus process, such as the AGREE II instrument (see section below). NSGC highly encourages formats that include bullet points, numbered statements, charts, tables, or diagrams. Please also note that the intended audience (outlined in the Purpose section) should be consistent and clear throughout the document.

The clinical practice guideline or its supporting documents must contain an assessment of the benefits and harms of recommended care and alternative care options.

**References:** Citations should follow the style used by the journal intended for publication of the Practice Guideline. [http://healthlinks.washington.edu/hsl/styleguides/apa.html](http://healthlinks.washington.edu/hsl/styleguides/apa.html)

Copyright Notice: The following copyright notice must appear on the bottom of the first page of each Practice Guideline:
© 20__ National Society of Genetic Counselors. All rights reserved. This document may not, in whole or in part, be reproduced, copied or disseminated, entered into or stored in a computer database or retrieval system, or otherwise utilized without the prior written consent of the NSGC.
Disclaimer: The following disclaimer should appear on each Practice Guideline:

“The practice guidelines of the National Society of Genetic Counselors (NSGC) are developed by members of the NSGC to assist genetic counselors and other health care providers in making decisions about appropriate management of genetic concerns; including access to and/or delivery of services. Each practice guideline focuses on a clinical or practice-based issue, and is the result of a systematic review and analysis of current professional literature believed to be reliable. As such, information and recommendations within the NSGC practice guidelines reflect the current scientific and clinical knowledge at the time of publication, are only current as of their publication date, and are subject to change without notice as advances emerge.

In addition, variations in practice, which take into account the needs of the individual patient and the resources and limitations unique to the institution or type of practice, may warrant approaches, treatments and/or procedures that differ from the recommendations outlined in this guideline. Therefore, these recommendations should not be construed as dictating an exclusive course of management, nor does the use of such recommendations guarantee a particular outcome. Genetic counseling practice guidelines are never intended to displace a health care provider’s best medical judgment based on the clinical circumstances of a particular patient or patient population. Practice guidelines are published by NSGC for educational and informational purposes only, and NSGC does not “approve” or “endorse” any specific methods, practices, or sources of information.”

Assessing a Practice Guideline

Once a Practice Guideline is written, it must be assessed to determine its quality and trustworthiness. This will be done by the Guideline author Group first, then by the NSGC PGC at time of review as a mechanism for quality assurance prior to publication.


The AGREE instrument is a 23-item tool comprising 6 quality-related domains that was originally released in 2003. It subsequently was adapted to the AGREE II instrument, which is the current version widely used. There are several adapted versions of this, some in electronic formats.

The following stakeholder groups can use AGREE II:

- **Health care providers** who wish to undertake their own assessment of a guideline before adopting its recommendations into their practice;
- **Guideline developers** who wish to follow a structured and rigorous development methodology, to conduct an internal assessment to ensure that their guidelines are sound, or to evaluate guidelines from other groups for potential adaptation to their own context;
• **Policy makers** who would like help on deciding which guidelines could be recommended for use in practice or to inform policy decisions; and

• **Educators** who would like help to enhance critical appraisal skills amongst health professionals and to teach core competencies in guideline development and reporting

**Number of Appraisers**

It is recommended that each guideline be assessed by at least 2 appraisers (preferably 4), as this will increase the reliability of the assessment. Reliability tests of the AGREE instrument are ongoing. **NOTE:** Depending on structure/length of guideline, using AGREE II will take 1.5 hours, on average, per appraiser.

**The 6 domains of the AGREE II instrument are (adapted from Brouwers MC et al., 2010):**

- **Scope and Purpose**
  - Overall objective(s) of guideline is/are specifically described
  - Health question(s) covered by the guideline is/are specifically described
  - Population (e.g. patients, clinicians, public, etc.) to whom the guideline is meant to apply is specifically described

- **Stakeholder Involvement**
  - Guideline development group includes individuals from all relevant professional groups
  - Target population’s views/preferences have been sought
  - Target users of the guideline are clearly described

- **Rigor of Development**
  - Systematic methods were used to search for evidence
  - Criteria for selecting the evidence are clearly described
  - Strengths/limitations of body of evidence are clearly described
  - Methods for formulating recommendations are clearly described
  - Health benefits/side effects/risks have been considered in formulating recommendations
  - Explicit link present between recommendations and supporting evidence
  - Guideline has been externally reviewed prior to publication
  - Procedure for updating the guideline is provided

- **Clarity of Presentation**
  - Recommendations are specific and unambiguous
  - Different management options of the condition/health issue are clearly presented
  - Key recommendations are easily identifiable

- **Applicability**
  - Guideline provides advice and/or tools on how recommendations can be put into practice
  - Guideline describes facilitators and barriers to its application
  - Potential resource implications of applying recommendations have been considered
  - Guideline presents monitoring and/or auditing criteria

- **Editorial Independence**
○ Views of the funding body have not influenced guideline content
○ Competing interests of guideline development group members have been recorded and addressed

Each of the AGREE II items are rated on a 7-point scale (1–strongly disagree to 7–strongly agree). A quality score is calculated for each of the six AGREE II domains. The six domain scores are independent and should not be aggregated into a single quality score. Domain scores are calculated by summing up all the scores of the individual items in a domain and by scaling the total as a percentage of the maximum possible score for that domain. More details and examples can be found at http://www.agreetrust.org/wp-content/uploads/2013/10/AGREE-II-Users-Manual-and-23-item-Instrument_2009_UPDATE_2013.pdf.

Although the domain scores are useful for comparing guidelines and will inform whether a guideline should be recommended for use, the AGREE Consortium has not set minimum domain scores or patterns of scores across domains to differentiate between high quality and poor quality guidelines. These decisions should be made by the user and guided by the context in which AGREE II is being used. Upon completing the 23 items, AGREE II users will provide 2 overall assessments of the guideline. The overall assessment requires the user to make a judgment as to the quality of the guideline, taking into account the criteria considered in the assessment process. The user is also asked whether he/she would recommend use of the guideline.

PGC members will be able to participate in the review of Practice Guidelines. Depending on the length and content of the guideline, a streamlined approach to PGC review (in which PGC members read the guideline and a subset formally appraises it, all discuss and review together, and PGC guideline liaisons send a summary with appraisal results to the authors) may occur.
**STEP 11: ADDITIONAL REQUIRED STEPS**

Once the PGC reviews and accepts an Evidence-Based Practice Guideline document, the NSGC Ethics Advisory Group will review and provide comment, and the document will simultaneously be made available to NSGC members for an open comment period of 30 days. PGC can alert Special Interest Group (SIG) Leaders or other members to make them aware the open comment period is coming for guideline review. This replaces Expert Review.

Authors will have 48 days to make any revisions based on the comments and prepare the revised draft. Once the authors make any necessary Ethics Advisory Group-related or member comment revisions, the NSGC attorney will review and provide comment. Representatives from relevant consumer or applicable professional organizations may also review the document if the Committee or the Board deems necessary. Once the review process is complete, the guideline will be submitted to the Board for final approval.
STEP 12: SUBMIT TO JOURNAL OF GENETIC COUNSELING*

Once approved, the guideline is submitted to JGC by the corresponding author for acceptance. Once JGC accepts the guideline, it will generate proofs for the corresponding author to review. Once the corresponding author secures approval from the authors on page proofs, the guideline proceeds to publication.

*There may be circumstances where an NSGC Practice Guideline is published in a different journal. For example, this might occur with guidelines that are produced jointly with another professional organization.
SECTION 4: Guideline Renewal

Evidence-Based Practice Guidelines (published January 1, 2015 or after)
To remain NGC compliant, guidelines must be reviewed every five years. The PGC will initiate the review process between 3-4 years after the original guideline has been published, and every 3-4 years thereafter, to allow ample time for revision, if necessary. For efficiency, guideline renewals may be reviewed at the same time as prior external guideline endorsements (Section 5). The review process includes the following steps:

- An updated systematic search will be performed to determine if new evidence exists which may indicate that the current document requires updating. This process will ideally be performed by an expert systematic review consultant.
- The updated systematic review report and the criteria articulated in the box below will be used by the PGC members to evaluate the guideline, who will vote on if the guideline should be revised, as provided below.

Table 10. Criteria to be used in determining the need for NSGC guideline revision/retirement

<table>
<thead>
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<th>Criteria</th>
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<tbody>
<tr>
<td>Changes in the relevance of a clinical question to the practice of genetic counseling</td>
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<td>Changes in available interventions (e.g., new drugs or devices)</td>
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<tr>
<td>Changes in evidence on the existing benefits and harms of interventions</td>
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<tr>
<td>Changes in outcomes considered important</td>
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<tr>
<td>Changes in values placed on outcomes</td>
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<tr>
<td>Changes in evidence that current practice is optimal</td>
</tr>
<tr>
<td>Changes in resources available for health care</td>
</tr>
<tr>
<td>Changes of strategic importance to NSGC</td>
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The PGC will recommend one of four options for the guideline: 1) Reaffirm guideline as originally published; 2) Reaffirm guideline with focused revisions that will be described by commentary in JGC; or 3) Retire original guideline and initiate full revision process; or 4) Retire original guideline and do not initiate a revision process.

Reaffirmation: If no substantive changes as outlined in Table 10 can be identified, the guideline will be reaffirmed by the PGC and the NSGC Board will be notified. The reaffirmation date will be posted on the NSGC website and the NGC website.

Revision: If the PGC deems focused or substantial revisions are necessary, it will recommend to the NSGC Board that the guideline be revised.
**Focused Revision:** A focused update addresses only one or a small number of points/recommendations in the guideline for which changes have been identified. This may be accomplished by publishing the focused update and simultaneously updating the previously published full guideline to include a link (electronic) to the new focused update, or publishing an e-update with a notice in the relevant journal. The revision history and date will be posted with the original guideline publication on the NSGC website and the NGC website.

**Full Revision of Guideline:** This requires a comprehensive rewrite of the guideline, which would require retiring the old version and writing a new one. A full revision is required when the PGC becomes aware of the need for an update of a large number of the recommendations in a guideline, or the need for change in scope of the guideline. The PGC may also wish to consider a full revision if 2 prior focused updates have been previously completed. The revision history and date will be posted with the original guideline publication on the NSGC website and the NGC website.

If the PGC learns that a revision is required, the authors of the original guideline may be invited to be considered a part of the new Review author group or Guideline author group. The PGC may also appoint additional authors as deemed necessary. The PGC will use the procedures for soliciting and determining authors as described in Section 3 Step 3. Authors must submit COI Disclosure Forms and PGC COI Disclosure Surveys and as described in section 3 and section 6. Author groups will use the procedures for creating an Evidence-Based Practice Guideline as described in Section 3 Steps 4-7 and Steps 8-10. Authors will have been informed prior to being involved in guideline development that they may have the opportunity to participate in the renewal process, but will have the opportunity to opt out.

If the PGC becomes aware that major publication(s) significantly impact the integrity of an established guideline, it is recommended that the renewal process would therefore begin at the time this information is brought to the attention of the guidelines committee, even if prior to the 3-4 year stated renewal process. This new information and the fact that the guidelines is being revised would be made readily available on the NSGC website.

**Retirement:** The PGC may vote that a reviewed guideline which is outdated not be revised, and will forward this recommendation to the NSGC Board for final determination. If the Board concurs, the guideline will be retired. If retired, the guideline will appear on the NSGC website in the retired document section and will be removed from the NGC website. The guideline history and retirement date will be posted on the NSGC website.

**Guidelines published before January 1, 2015**
NSGC practice guidelines published prior to January 1, 2015 do not meet NGC criteria for practice guidelines in their current format. The PGC recognizes that the content of these publications remains useful to the NSGC membership. While these publications will not remain designated as Practice Guidelines of the NSGC, each will be reclassified as a “Practice Resource” so long as the content of the guideline is deemed current at the time of reclassification based
on review by the PGC and external experts. This review and reclassification will begin in 2016 and proceed in order of necessity based upon the last date of publication/update/formal renewal of the existing guidelines. Guidelines reclassified as Practice Resources will be listed as such on the NSGC website. In the event that the content is not deemed current, the publication will be reclassified as a Retired Practice Guideline on the NSGC website. When one of these existing guidelines must be reclassified as a retired document, the feasibility of creating an Evidence-Based Practice Guideline on similar subject matter will be considered. The NSGC membership was informed in April, 2016 of this plan for reclassification.
SECTION 5: Endorsing External Practice Guidelines

Endorsement
Guideline endorsement is the process of publicly and officially supporting an external organization’s practice guideline(s). Other professional organizations may also request NSGC endorsement of their practice guidelines. The value of external guideline endorsement is to increase the number of high-quality, NSGC-vetted guidelines available to the membership to aid in clinical decision-making, and to guide clinical practice in a consistent way. Secondarily, endorsing external guidelines may increase the visibility of NSGC in the medical community.

Guideline Endorsement Process
All PGC members will participate in guideline endorsement evaluation. Endorsement is considered either upon request of an external organization or from a recommendation made by a NSGC member, Committee, Special Interest Group or other group. The PGC may also actively seek to endorse external guidelines that may be of value to the NSGC membership. External guidelines for potential endorsement must be submitted to the NSGC Executive Office (nsgc@nsgc.org), which will forward it to the Practice Guidelines Committee.

Table 11. Criteria that must be met to consider an external guideline for NSGC endorsement
- Adds value to genetic counseling practice
- Meets with National Guideline Clearinghouse standards (or at a minimum, is evidence-based)
- Is consistent with other applicable NSGC and PGC policies, and
- Is published and available in peer-reviewed literature

Endorsements are reviewed every 3-5 years and updated when appropriate. For efficiency, they may be reviewed at the same time as guideline renewals (Section 4). These criteria should be modified according to NGC or other relevant policy, NSGC’s Strategic Plan, identified knowledge gaps in the field, or other identified needs, as approved by the PGC.

The PGC may endorse published or unpublished (draft) guidelines. A decision must be returned to the external organization to be endorsed or to the endorsement requestor, as applicable, within 3 months.

While external guidelines may be accepted for endorsement after a guideline has been published, the PGC prefers to be involved in the development of an external guideline as early as possible. Early involvement increases the odds that a guideline will be endorsed by the PGC (for the NSGC). The level of involvement in the development of an external guideline may vary, and it may range from staying informed about the progress of a developing guideline to having the opportunity to suggest major content edits to a guideline draft (perhaps leading to a joint guideline).

Endorsement Process for Published and Unpublished External Guidelines
1) PGC receives a request for endorsement
2) PGC Chair(s) will ask all PGC members to evaluate the guideline against the criteria for endorsement consideration
3) PGC members will evaluate the guideline using the AGREE II instrument in blinded fashion
4) Once the review is complete, PGC members will convene to discuss results and the need, if any, for qualifications, new terminology, exceptions, clarifications, and any required enhancement to ensure applicability and appropriate use by genetic counselors
5) The PGC will proceed to vote to decide whether to:
   a) Endorse the external guideline as is
   b) Endorse the external guideline with qualifications (NOTE: PGC may choose to communicate any concerns directly back with endorsement requestor, in case those may be addressed and amendments submitted for re-review)
   c) Not endorse the external guideline
   d) Offer an “Affirmation of Value” for the external guideline – this is not an endorsement, but offers some acknowledgement of the document’s value
6) PGC will draft an Executive Summary of the external guideline evaluation (including AGREE II assessment and additional discussions). Once a decision is made, the NSGC BOD will be informed and given the Executive Summary.
7) The BOD will review the decision
8) With BOD approval, the endorsement requestor will be informed of the decision by the PGC
9) PGC can write an endorsement summary based on their findings, which could be published in the Journal of Genetic Counseling.

Endorsements shall only be made pursuant to a written agreement, in a format acceptable to NSGC in its sole discretion, which includes (i) the ability for NSGC to revoke its endorsement at any time, in its sole discretion; and (ii) an appropriate indemnification of NSGC from the endorsed or sponsoring party.
SECTION 6. Conflict of Interest Policy

National Society of Genetic Counselors (NSGC)’s mission is to advance “the various roles of genetic counselors in health care by fostering education, research, and public policy to ensure the availability of quality genetic services.” NSGC is committed to the highest standards of integrity, particularly with regard to education, research, publications, and shaping public policy. It is essential that both NSGC members and the general public trust this commitment. As such, it is crucial that all NSGC Board Members, Committee members, Special Interest Group leaders, and any agent acting on behalf of NSGC completely disclose any information that may lead to a real or perceived conflict of interest (COI). NSGC depends upon the volunteer efforts of its members and acknowledges that personal and business interests may occasionally cause a real or perceived COI. Disclosing interests that could lead to real or perceived COI should occur in timely fashion. Failure to do so will result in the individual’s removal from his or her current position.

The NSGC Practice Guidelines Committee (PGC)

As part of NSGC’s Mission, the Practice Guidelines Committee (PGC) is charged with developing practice guidelines to help promote the provision of high quality, evidence-based care. Confidence in these guidelines depends upon complete transparency in the guideline development process. Thus, the PGC is committed to minimizing any real or perceived COI for anyone involved in the guideline development process. The PGC, author groups, and expert reviewers must disclose any potential COI both for themselves and if applicable, their partner/spouse. This includes, but is not limited to, employment, consulting relationships, advisory board involvement, grants, royalties, and stock ownership. The NSGC COI Disclosure Form and PGC COI Disclosure Survey applies to all current interests as well as interests during the previous 12 months.

PGC COI Policies

1) All PGC members and authors of guidelines under PGC review must submit NSGC’s COI Disclosure Form and PGC’s COI Disclosure Survey at the beginning of each calendar year and update this form within 30 days of any changes. The PGC’s NSGC staff contact will send quarterly reminders to all authors of guidelines under PGC review.

2) The NSGC Board will make a good-faith effort to appoint a PGC Chair and a Vice Chair with no actual, potential, or apparent COI at the time of his/her appointment. In the event that a conflict arises for either the Chair or the Vice Chair during his or her term, the individual should immediately disclose the conflict to the full PGC and the NSGC Board. His or her fellow Chair, in conjunction with the NSGC Board, will appropriately manage the situation. Management may include, but is not limited to, the individual recusing him or herself from particular reviews, discussions, or votes taking place within the PGC; or the individual stepping down from his or her appointed leadership position before the end of his or her term.

3) PGC members who are co-authors of a guideline must recuse themselves from PGC discussion of that guideline.

4) Lead authors cannot have a real or perceived COI relevant to that guideline.

5) PGC will strive to minimize the number of accepted Committee members and guideline authors
with COI. An exceptional situation is one in which avoidance of members/authors with conflicts of interest is impossible, because of the important need for their expertise.

a. The PGC should publicly document that a good-faith effort was made to find experts without conflicts of interest by issuing a public call for members and other recruitment measures.

b. A majority of authors (greater than 50 percent) must not have a COI relevant to that guideline.

c. The author group’s composition of members with real or potential COI, and how this COI was managed, must be documented.

6) PGC will not accept direct funding for clinical practice guideline development from medical product companies or company foundations.

7) Authors, including those participating in guideline revisions, must each submit NSGC’s COI Disclosure Form and PGC’s COI Disclosure Survey upon submitting an application to serve as an author involved in a guideline development or revision process and update this form within 30 days of any changes to their COI with respect to the guideline.

8) The PGC will review the COI Disclosure Forms and PGC’s COI Disclosure Survey responses upon review of practice recommendations. Disclosure of COI for publication will be determined at that time.

**PGC Membership**

Because the PGC consists of a diverse cross-section of NSGC members, NSGC recognizes that occasionally, a committee member will need to recuse him or herself from discussion, review, and voting on a practice guideline if there is potential for a real or perceived COI. The individual PGC member is obligated to report such potential conflicts. A PGC member may recuse him or herself from involvement in one practice guideline while continuing to review other practice guidelines that do not directly relate to the member’s area of conflict. To promote stringent adherence to this policy, the PGC Chair and Vice Chair will also review all PGC members’ COI Disclosure Forms and PGC COI Disclosure Survey responses before the discussion and prioritization of possible practice guideline topics are submitted, to identify any members with a real or perceived COI.

If a PGC member is a part of an author group, that member will recuse him or herself from all discussions, reviews, and voting regarding the practice guideline for which he or she is an author. PGC members who fail to disclose professional interests, personal interests, or both within 30 days of any changes will be removed from the PGC for a minimum of one year.

**Practice Guidelines Author Groups**

While it is ideal for all authors in the author group of a practice guideline to be free from any financial relationship with any entity that has a commercial interest in the topic of the guideline, NSGC recognizes that such individuals may have unique knowledge and expertise in the subject and should not automatically be prevented from participating as an author after disclosing all potential conflicts. Thus, individuals who are employed by, or have a financial interest in, an entity that could potentially benefit from, or be harmed by, a practice guideline’s recommendations may not serve as the lead author of that
practice guideline. Such individuals may not constitute a majority (50 percent or more) of the author group.

Upon submitting an application to serve as an author, all applicants must also submit an NSGC COI Disclosure Form to the PGC and complete a PGC COI Disclosure Survey for review. All selected as authors must notify the PGC within 30 days of any change in COI that is relevant to that practice guideline that occurs at any time during the process. If the PGC determines that this change represents a true COI, the PGC will determine whether the author must recuse him or herself from further work on the guideline. If the newly identified conflict would increase the number of authors with a potential conflict to 50 percent or more, the author group may seek an additional author with no potential conflicts of interest relating to the guideline in order to balance the group. The author group may also request that the author in question recuse him or herself from authorship.

Authors who fail to disclose changes in their status by submitting a revised NSGC COI Disclosure Form and PGC COI Disclosure Survey within 30 days of the change will be removed from the author group and barred from authorship on future practice guidelines until the PGC Chair and Vice Chair receive his or her updated NSGC COI Disclosure Form and PGC COI Disclosure Survey. If the author group cannot reach a consensus on whether the member in question should recuse him or herself, the PGC Chair or Vice Chair will speak with the lead author and the author with the conflict to make a final determination based on the author in question’s level of contribution up to that point, as well as any other relevant factors. If the author in question is the lead author, the PGC Chair or Vice Chair will instead speak with a majority of author group members before making a final determination.

**The PGC’s COI Disclosure Form and PGC COI Disclosure Survey Review Process**

The PGC considers the following issues when evaluating potential COI:

1) The nature and content of the guideline
2) The nature of the individual’s financial and/or professional interest(s)
3) The degree to which the guideline’s recommendations may affect the individual’s interest(s)
4) The degree to which the individual’s interest(s) may affect, or be perceived to affect, the guideline’s recommendations.

**PGC members** will review NSGC COI Disclosure Forms and PGC COI Disclosure Survey responses for author groups. PGC members will treat this information as confidential, and use this information solely for the purpose of determining whether a COI exists. The decision regarding whether a COI exists for each potential author will be made by majority vote. In the event of a tie, the final decision will rest with the PGC Chair and Vice Chair, who may call upon the NSGC Board as necessary. The PGC will not invite an individual with COI relevant to the guideline to be lead author and will ensure that fewer than 50% of invited authors have COI relevant to the guideline.

COI policies from external organizations will also be considered in the case of a joint practice guideline.

**New PGC Members**
PGC members will review the NSGC COI Disclosure Forms and PGC COI Disclosure Survey responses of all PGC applicants. Having a real or perceived COI (which will be decided upon discussions during the PGC member recruitment process) does not prevent an applicant from joining the PGC, as practice guidelines cover expansive areas of practice, and a conflict in one area may not represent a conflict in other areas. If any current PGC member has a close professional or personal relationship with the applicant, he or she may contribute to the discussion regarding the applicant’s COI Disclosure Form and PGC COI Disclosure Survey, but must disclose this relationship to the group prior to the discussion and abstain from the final vote.
SECTION 7. Final Checklist for Guidelines Authors

NSGC Conflict of Interest and Disclosure form (actual form in Appendix C)

NGC Criteria Checklist
The following criteria must be met for inclusion in the National Guidelines Clearinghouse (NGC) for any guidelines with a publication date of June 2014 or after:

___ Sponsorship: Guideline must be produced under the auspices of NSGC

___ Recommendations: Guideline must contain systematically developed statements including recommendations intended to optimize patient care and assist physicians and/or other health care practitioners and patients to make decisions about appropriate healthcare for specific clinical circumstances

___ Systematic Evidence Review: Guideline is based on a systematic review of evidence as demonstrated by documenting the following features

___ An explicit statement that the guideline was based on a systematic review

___ A description of the search strategy that includes a listing of databases searched, a summary of search terms used, the specific time period covered by the literature search including the beginning date (month/year) and end date (month/year), and the date when the literature search was done

___ A description of study selection that includes the number of studies identified, the number of studies included, and a summary of inclusion or exclusion criteria

___ A synthesis of evidence from the selected studies (i.e., a detailed description or evidence tables)

___ A summary of the evidence synthesis included in the guideline that relates the evidence to the recommendations

___ Assessment of Harms and Benefits: Guideline or supporting documents contains an assessment of the benefits and harms of recommended care and alternative care options

___ Public Access: Upon submission of the guideline to NGC, it must be noted whether the systematic review or other supporting documents are available in English to the public upon request

___ Up to Date: Guideline must have been developed, reviewed or revised in past 5 years as evidenced by appropriate documentation. For guidelines more than 5 years old, the writers must demonstrate that the guideline is current using one or more of the following:

____ A new systematic literature search has been performed since the original publication of the guideline and a description of the search is provided

____ An expert committee was convened to review the currency of the guideline since the original publication of the guideline and a description of the process is provided

____ If an expert committee was convened, the committee reviewed current literature available since original publication

Contact: NSGC Executive office at nsgc@nsgc.org
SECTION 8. Resources for Authors (from Society of Obstetricians and Gynaecologists of Canada)

UPDATES

- Use free My NCBI account in PubMed and have results automatically emailed on a regular basis
- Subscription-based resources usually also allow to store and re-run search strategies
- Save and manually re-run Cochrane Library searches with each quarterly update
- Search guideline and other grey literature every 3 months or once at end of research phase

FREE RESOURCES

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</tr>
<tr>
<td><em>(via Wiley; includes CRD databases (below) but is only updated quarterly)</em></td>
<td></td>
</tr>
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<td><strong>Centre for Reviews and Dissemination (CRD) Databases</strong></td>
<td><a href="http://www.crd.york.ac.uk/crdweb/">http://www.crd.york.ac.uk/crdweb/</a></td>
</tr>
<tr>
<td><em>(critical appraisals, economic evaluations, HTA projects)</em></td>
<td></td>
</tr>
<tr>
<td><strong>EvidenceUpdates</strong></td>
<td><a href="http://plus.mcmaster.ca/EvidenceUpdates/">http://plus.mcmaster.ca/EvidenceUpdates/</a></td>
</tr>
<tr>
<td><em>(ratings and comments on articles in core clinical journals)</em></td>
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<tr>
<td><strong>Health-evidence.ca</strong></td>
<td><a href="http://health-evidence.ca/">http://health-evidence.ca/</a></td>
</tr>
<tr>
<td><em>(quality appraisals; good for public and aboriginal health issues)</em></td>
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<tr>
<td><strong>TRIP database</strong></td>
<td><a href="http://www.tripdatabase.com/">http://www.tripdatabase.com/</a></td>
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<tr>
<td><em>(Turning Research into Practice)</em></td>
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<td><strong>Latin American and Caribbean Center on Health Sciences Information</strong></td>
<td><a href="http://www.bireme.br/bvs/I/ihome.htm">http://www.bireme.br/bvs/I/ihome.htm</a></td>
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<tr>
<td><em>(LILACS) (International/Resource-Poor questions only)</em></td>
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<tr>
<td><strong>Health Sciences Online</strong></td>
<td><a href="http://www.hso.info">http://www.hso.info</a></td>
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Guidelines

<p>| Society of Obstetricians and Gynaecologists of Canada (SOGC)             | <a href="http://www.sogc.org">http://www.sogc.org</a>                                                |
| American College of Obstetricians and Gynaecologists (ACOG)             | <a href="http://www.acog.com/">http://www.acog.com/</a>                                               |
| Royal College of Obstetricians and Gynaecologists (RCOG)                | <a href="http://www.rcog.org.uk/">http://www.rcog.org.uk/</a>                                            |
| Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) | <a href="http://www.ranzcog.edu.au/">http://www.ranzcog.edu.au/</a>                                         |</p>
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<th>Resource</th>
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<td>CMA Infobase</td>
<td><a href="http://mdm.ca/cpgsnew/cpgs/index.asp">http://mdm.ca/cpgsnew/cpgs/index.asp</a></td>
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<td>eGuidelines</td>
<td><a href="http://www.library.nhs.uk/guidelinesfinder/">http://www.library.nhs.uk/guidelinesfinder/</a></td>
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<td>Guideline Check</td>
<td><a href="http://cebgrade.mcmaster.ca/guidecheck.html">http://cebgrade.mcmaster.ca/guidecheck.html</a></td>
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<td>GRADE Guideline development tool</td>
<td><a href="http://www.guidelinedevelopment.org/">http://www.guidelinedevelopment.org/</a></td>
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**SUBSCRIPTION-BASED RESOURCES**

**Databases**

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<td>Cochrane Library (via Ovid)</td>
<td><a href="http://ovidsp.ovid.com/">http://ovidsp.ovid.com/</a></td>
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<tr>
<td>Cumulative Index to Nursing &amp; Allied Health Literature (CINAHL) (via Ebscohost)</td>
<td><a href="http://search.ebscohost.com/">http://search.ebscohost.com/</a></td>
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<tr>
<td>MEDLINE (via Ovid or available free to CMA members via Ebscohost)</td>
<td><a href="http://ovidsp.ovid.com/">http://ovidsp.ovid.com/</a></td>
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**Point of Care Tools**

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<td>ACP Journal Club (or via OVID)</td>
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<td>ACP Pier (or available free to CMA members via StatRef)</td>
<td><a href="http://pier.acponline.org/index.html">http://pier.acponline.org/index.html</a></td>
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<tr>
<td>Clinical Evidence (BMJ)</td>
<td><a href="http://clinicalevidence.bmj.com/ceweb/index.jsp">http://clinicalevidence.bmj.com/ceweb/index.jsp</a></td>
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<td>DynaMed</td>
<td><a href="http://www.ebscohost.com/dynamed/">http://www.ebscohost.com/dynamed/</a></td>
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<tr>
<td>MD Consult (or available free to CMA members)</td>
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<td>UpToDate</td>
<td><a href="http://www.uptodate.com/home/index.html">http://www.uptodate.com/home/index.html</a></td>
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## SECTION 9. Appendices

### APPENDIX A: PGC MEMBERSHIP

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<tr>
<th>Committee Members</th>
<th>Years</th>
<th>Liaisons</th>
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<tr>
<td>Ana Morales</td>
<td>2015-2017</td>
<td>NSGC Board Liaison</td>
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<tr>
<td>Jaime Natoli</td>
<td>2015-2017</td>
<td>Amy Sturm</td>
<td>2014</td>
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<tr>
<td>Sarah Kalia</td>
<td>2015-2017</td>
<td>Janet Williams</td>
<td>2013</td>
</tr>
<tr>
<td>Gillian Hooker*</td>
<td>2013-2017</td>
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<tr>
<td>Ashley Parrott</td>
<td>2014-2016</td>
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<tr>
<td>Deepti Babu*</td>
<td>2014-2016</td>
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<td>Erin Carmany</td>
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<td>Stephanie Brewster</td>
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<td>Kevin Sweet</td>
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<td>Ravi Sharaf</td>
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<td>Christina Palmer*</td>
<td>2013-2015</td>
<td>Ethics Advisory Group Liaison</td>
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<td>Katie Stoll</td>
<td>2013-2015</td>
<td>Curtis Coughlin</td>
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<td>Tiffani DeMarco</td>
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<td>Laura Hercher</td>
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<td>Debbie Keelean-Fuller</td>
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<td>Adam Buchanan*</td>
<td>2012-2014</td>
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<td>Carly Siskind</td>
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<td>Catriona Hippman</td>
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<td>Heather Harris</td>
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<td>Katherine Coles</td>
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<td>Brian Strike</td>
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<tr>
<td>Margo Grady*</td>
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<td>Melanie Myers</td>
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<tr>
<td>Michelle Strecker</td>
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<td>Monica Marvin</td>
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<td>Nancy Petrucelli</td>
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<tr>
<td>Shanna Gustafson</td>
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*Chair rotation
APPENDIX B: NATIONAL GUIDELINES CLEARINGHOUSE (NGC) INCLUSION CRITERIA FOR CLINICAL PRACTICE GUIDELINES

(Excerpted verbatim from http://www.guideline.gov/about/inclusion-criteria.aspx)

Inclusion Criteria

Effective June 1, 2014, NGC employs the 2011 definition of clinical practice guideline developed by the Institute of Medicine (IOM).¹

Clinical practice guidelines are statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options.

2013 (Revised) Criteria for Inclusion of Clinical Practice Guidelines in NGC

Effective June 1, 2014: In order for NGC to accept a submitted clinical practice guideline, the guideline must meet all the criteria below. In addition to the guideline, developers must provide NGC with documentation of the underlying systematic review.*

1. The clinical practice guideline contains systematically developed statements including recommendations intended to optimize patient care and assist physicians and/or other health care practitioners and patients to make decisions about appropriate health care for specific clinical circumstances.

2. The clinical practice guideline was produced under the auspices of a medical specialty association; relevant professional society; public or private organization; government agency at the Federal, State, or local level; or health care organization or plan. A clinical practice guideline developed and issued by an individual(s) not officially sponsored or supported by one of the above types of organizations does not meet the inclusion criteria for NGC.

3. The clinical practice guideline is based on a systematic review of evidence as demonstrated by documentation of each of the following features in the clinical practice guideline or its supporting documents.
   a. An explicit statement that the clinical practice guideline was based on a systematic review.†
   b. A description of the search strategy that includes a listing of database(s) searched, a summary of search terms used, the specific time period covered by the literature search including the beginning date (month/year) and end date (month/year), and the date(s) when the literature search was done.‡
   c. A description of study selection that includes the number of studies identified, the number of studies included, and a summary of inclusion and exclusion criteria.
d. A synthesis of evidence from the selected studies, *e.g.*, a detailed description or evidence tables.

e. A summary of the evidence synthesis (see 3d above) included in the guideline that relates the evidence to the recommendations, *e.g.*, a descriptive summary or summary tables.

NB: A guideline is not excluded from NGC if a systematic review was conducted that identifies specific gaps in the evidence base for some of the guideline's recommendations.

4. The clinical practice guideline or its supporting documents contain an assessment of the benefits and harms of recommended care and alternative care options.

5. The full text guideline is available in English to the public upon request (for free or for a fee). Upon submission of the guideline to NGC, it also must be noted whether the systematic review or other supporting documents are available in English to the public upon request (for free or for a fee).

6. The guideline is the most recent version published. The guideline must have been developed, reviewed, or revised within the past five years, as evidenced by appropriate documentation (*e.g.*, the systematic review or detailed description of methodology).

*Systematic reviews are literature reviews that summarize evidence by identifying, selecting, assessing, and synthesizing the findings of similar but separate studies. They can help clarify what is known and not known about the potential benefits and harms of drugs, devices, and other healthcare services.*

‡To allow for a transition to the 2013 (revised) NGC inclusion criteria, in the scenario where the NGC inclusion team agrees that all other criteria and subcriteria are met, if an explicit statement that the clinical practice guideline was based on a systematic review is not provided, that subcriterion will be waived and the guideline included in NGC. Guideline developers will be advised of this omission and requested to correct it in future guidelines submitted to NGC.

‡To allow for a transition to the 2013 (revised) NGC inclusion criteria, in the scenario where the NGC inclusion team agrees that all other criteria and subcriteria are met, if the date(s) when the literature search was performed is not provided, that subcriterion will be waived and the guideline included in NGC. Guideline developers will be advised of this omission and requested to correct it in future guidelines submitted to NGC. Note that the specific time period covered by the literature search including the beginning date (month/year) and end date (month/year) is required and will not be waived.

References

## APPENDIX C: ADMINISTRATIVE RESOURCES FOR AUTHORS

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<tr>
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<tr>
<td>Topic Proposal Form</td>
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<td>NSGC COI Disclosure Form.doc</td>
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<td>Practice Guidelines Committee Conflict of Interest Disclosure Survey</td>
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<td>NGC Criteria Checklist</td>
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<td>CEP Trustworthy Guideline Appraisal Instrument</td>
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<td>Newcastle-Ottawa Quality Assessment Scale for Case-Control and Cohort Studies</td>
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## APPENDIX E: RETIRED PRACTICE GUIDELINES COMMITTEE DOCUMENTS FOR AUTHORS

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<td>Policy on Genetic Counseling Practice Guidelines</td>
<td>[PG Policy.pdf]</td>
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<td>Proposal for Practice Guidelines</td>
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APPENDIX F: UPDATES TO PGC GUIDELINE MANUAL

04/21/2016 - Added language regarding reclassification/retirement of guidelines created before 2015