Complete Summary

GUIDELINE TITLE

Genetic cancer risk assessment and counseling: recommendations of the National Society of Genetic Counselors.

BIBLIOGRAPHIC SOURCE(S)

Trepanier A, Ahrens M, McKinnon W, Peters J, Stopfer J, Grumet SC, Manley S, Culver JO, Acton R, Larsen-Haidle J, Correia LA, Bennett R, Pettersen B, Ferlita TD, Costalas JW, Hunt K, Donlon S, Skrzynia C, Farrell C, Callif-Daley F, Vockley CW. Genetic cancer risk assessment and counseling: recommendations of the National Society of Genetic Counselors. J Genet Counsel 2004 Apr;13(2):83-114. [104 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

- Hereditary cancer (hereditary cancer syndromes)
- Familial cancer

GUIDELINE CATEGORY

Counseling
Prevention
Risk Assessment

CLINICAL SPECIALTY

Family Practice
Gastroenterology
Internal Medicine
Medical Genetics
Nursing
Oncology
Preventive Medicine
Psychology

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Physician Assistants
Physicians
Psychologists/Non-physician Behavioral Health Clinicians
Social Workers

GUIDELINE OBJECTIVE(S)

- To present a set of practice recommendations for genetic counselors conveying cancer genetic risk assessment and counseling
- To provide background information about the process of genetic counseling and risk assessment for hereditary cancer

TARGET POPULATION

Individuals at risk for familial or hereditary cancer

INTERVENTIONS AND PRACTICES CONSIDERED

Cancer Genetic Risk Assessment and Counseling

1. Intake
    - Personal medical history
    - Family history
2. Psychosocial assessment
    - Assessment of risk perception
    - Process of psychosocial assessment
3. Cancer risk assessment
    - Determination of cancer risk
    - Communication of cancer risk
4. Molecular testing for hereditary cancer syndromes
    - Clinical, fee-for-service testing versus research testing
    - Pretest genetic counseling and obtaining informed consent
    - Sample collection
    - Results disclosure and post-test counseling
5. Follow-up
    - Medical surveillance

- Review of cancer screening guidelines and methods to reduce cancer risk
- Referral for medical management

MAJOR OUTCOMES CONSIDERED

Not stated

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The information contained in this document was derived from an extensive review of the current literature on cancer genetic risk assessment and counseling as well as the personal expertise of genetic counselors specializing in cancer genetics.

The guideline authors searched via MEDLINE the relevant English language medical and psychosocial literature between 1989 and 2002, with several key seminal articles from earlier dates. Key words included cancer genetics, genetic counseling, psychosocial assessment, and gene testing.

Published guidelines and policy statements published by American Society of Clinical Oncology (ASCO, 1996, 2003), American College of Medical Genetics (ACMG) Foundation (1999), American Society of Human Genetics (ASHG, 1994), National Action Plan on Breast Cancer (NAPBC, 1998), and genetic counseling guidelines developed by genetic counselors in the state of Washington (adaptation of Marymee et al., 1998), and the Task Force on Genetic Testing (NIH-DOE/ELSI Task Force, 1997) were also reviewed. This literature is based on clinical experience, descriptive studies, and/or reports of expert committees.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The literature was reviewed and evaluated for quality according to the categories outlined by the U.S. Preventive Services Task Force (1995):

I. Evidence obtained from at least one properly designed randomized controlled trial

II-1. Evidence obtained from well-designed controlled trials without randomization

II-2. Evidence obtained from well-designed cohort or case-control-analytic studies, preferably from more than one center or research group

II-3. Evidence obtained from multiple time series with or without the intervention

III. Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

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

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

A draft document was made available to the 2,072 members of National Society of Genetic Counselors (NSGC) for comment in October 2003. The NSGC membership includes genetic counselors, physicians, nurses, attorneys, doctors of philosophy, and students.

The revised document was reviewed by the NSGC attorney and the NSGC Ethics Subcommittee and no conflicts with the NSGC Code of Ethics or issues regarding legal liability were identified in the final document. All 20 members of the NSGC Board of Directors unanimously approved the final document in November 2003.

The authoring committee also sought expert review from genetic counselors specializing in cancer genetics; members of the American College of Medical Genetics (ACMG) and the Oncology Nursing Society; consumer groups; and the Board of Directors and Genetic Services Committee of the NSGC.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The Cancer Genetic Risk Assessment and Counseling Process

Intake

The first step of cancer risk assessment and counseling begins with collection of a client´s personal and family medical history. Intake information can be obtained via a questionnaire completed prior to a cancer risk consultation or during the consultation. Collecting information prior to the consult allows the clinician to obtain confirmatory medical records and assess the significance of the family history in advance of the session.

Personal Medical History

The table below lists the information to be collected while obtaining the client´s medical history for individuals with and without a previous cancer diagnosis. Information to be obtained includes the frequency of cancer surveillance, the date and results of recent screening examinations, and details about pertinent environmental exposures such as occupation, alcohol consumption, tobacco use, and diet.

Questions to ask all patients	Questions to ask patients who have had cancer/or regarding relatives with cancer
• Age • Personal History of benign or malignant tumors • Major illnesses • Hospitalizations • Surgeries • Biopsy history • Reproductive history[b] • Cancer surveillance • Environmental exposures	• Organ in which tumor developed • Age at time of diagnosis • Number of tumors[a] • Pathology, stage, and grade of malignant tumor • Pathology of benign tumors • Treatment regimen (surgery, chemotherapy, radiation)

[a]For patients who have developed more than one tumor, it is important to discriminate whether the additional tumor(s) was a separate primary, recurrence, or the result of metastatic disease.
[b]Especially important for women at increased risk of breast, ovarian, or endometrial cancer. Inquire about age at menarche, age at first live birth, and history of oral contraceptive use, infertility medications, or hormone replacement therapy including dosage and duration, age at menopause.

Family History

Procuring and analyzing a genetic pedigree is the cornerstone of cancer genetic risk assessment. There is a chance of underascertainment of high-risk families unless an accurate, comprehensive family history is obtained from both new and returning patients. At minimum, a three- to four-generation pedigree, including detailed medical information about the proband´s first-, second-, and, ideally, third-degree relatives should be obtained. Standardized pedigree nomenclature should be used. Gathering information about both paternal and maternal family history, ancestry/ethnicity, and consanguinity is necessary. For relatives who have had a cancer diagnosis, document health and carcinogen exposure information (see "Personal Medical History" above for information that should be collected). For relatives who are deceased, note the cause of death and age.

Erroneous cancer family history reporting has been documented in the medical literature and can affect medical management and risk assessment. Accurate family risk assessment requires medical record confirmation of key cancer diagnoses. Whenever possible, obtain confirmation of relevant cancer diagnoses in the family prior to genetic testing. In the absence of medical record confirmation, inform the client that the assessment of his/her heritable cancer risk can change substantially should records later reveal fewer, greater, or different cancer diagnoses than reported. Also, because cancer genetic risk assessment is a dynamic process, a person´s estimated cancer risk can change if additional relatives are diagnosed with cancer. Therefore, encourage individuals undergoing cancer genetic risk assessment to report any changes in their family history.

Document on the pedigree and/or in the clinical summary any pertinent information obtained through medical record review. Record information from relatives´ medical records in a manner that attempts to maintain confidentiality.

Psychosocial Assessment

An individual´s decision to seek and utilize information regarding cancer genetics is based on a variety of factors. Assessment of psychosocial issues is the optimal method for the clinician to appreciate all of the factors that affect risk perception and ultimately, utilization of cancer genetic information. This process can also enlighten the provider on the potential impact of cancer genetic information on the client´s quality of life, educational and career goals, reproductive options, and other life choices. Psychosocial issues in cancer genetic counseling can be identified and addressed by integrating the principles and practices of genetic counseling, psychology, and psycho-oncology into the evaluation.

Assessing Perception of Risk

A variety of information is collected to assess the client´s perceived estimate of personal cancer risk and the methods by which decisions are made. Such information may include but is not limited to the following:

1. Motivations for seeking a cancer risk consultation. Clarify the client´s goals for the consultation by determining what information she/he hopes to gain and guide the session based on those goals.
2. Beliefs about cancer etiology and perception of risk. Recognizing and addressing client beliefs about cancer etiology and risk is a critical component of educating and assisting the client in his/her adaptation to new cancer risk information.
3. Ethnocultural information. Awareness of the cultural background, religion, and ethnicity of the client can provide deeper understanding of how the individual may perceive and utilize the information.
4. Socioeconomic and demographic information. Knowing the client´s age, education, occupation, and so forth assists in targeting the appropriate degree of genetics information provided and helps to set the tone of the counseling session.
5. Psychosocial factors. Consider referral for additional mental health. Identify emotional reactions to cancer risk, such as feelings of anger, fear, and guilt, that may provide clues as to how the client and/or his/her family will cope with genetic information. Be aware that clients with increased levels of distress might not comprehend or cope with information as well as less distressed clients. Consider referral for additional mental health services when the client is having significant difficulty adjusting to personal circumstances or in the presence of symptoms related to a psychiatric condition. Examples might include prolonged or unresolved grief, unrealistic expectations, affective disorder, and cancer obsession, among others. Suggest that the client bring a support person (spouse, relative, friend) to their cancer genetic risk assessment sessions.
6. Cancer screening. Collect information about the client´s current screening practices and ascertain whether there are potential compliance issues.
7. Health behaviors. Identify the client´s perceptions about available preventive or risk-reducing therapies such as prophylactic surgery or chemoprevention. Prior to genetic testing, determine if the client anticipates that cancer genetic information will alter his/her health behaviors or decision to take part in risk-reduction strategies. Identify barriers to recommended health behaviors and explore methods to promote compliance.
8. Coping strategies. Assess the client´s coping mechanisms, support systems, and cancer experiences.

Process of Psychosocial Assessment

The format of cancer genetic counseling is interactive and allows time for information gathering and dissemination. This is best achieved in a face-to-face consultation to permit assessment of both the client´s verbal and nonverbal cues. A comprehensive consultation may take place over several sessions. Genetic counselors often use Carl Rogers´ client-centered approach in eliciting information from patients. Professionals performing cancer risk counseling require proficient skills in communication, critical thinking, counseling, and psychosocial assessment. In addition, they adhere to professional codes of ethics and values.

Questionnaires and standard psychological measures can provide helpful information about demographics, family history, screening practices, and the client´s psychological status. These may be sent to clients prior to their consultation, filled out at the time of the appointment, or, when relevant, completed over time (i.e., to monitor screening practices and/or psychological distress). Written or telephone correspondence are also ways of gathering psychological and other information.

Cancer Risk Assessment

The Concept of Risk

Absolute risk, which is defined as the probability that an event will occur (e.g., developing a disease) over a defined period of time, is the most beneficial way to present cancer risk information in cancer genetic counseling. Age-specific *lifetime risk* estimates are often most applicable for medical decision making. For example, a woman may have a cumulative 30% lifetime risk of breast cancer, but only have a 5% chance of developing the disease in the next 5 years. For this reason, *interval risks*, which are lifetime risks divided into defined age intervals, may be helpful for communicating immediate versus long-range risks. Such distinctions may have bearing on screening and other cancer risk management decisions that may depend on which decade of life cancer risks are most salient. Most epidemiological studies provide relative risks versus absolute risks. *Relative risks* compare the incidence of disease in people who have a certain risk factor, like family history, to those who do not have the risk factor (control group). An *odds ratio* is an approximation of relative risk derived from case-control studies. To generate an absolute risk from a relative risk or odds ratio, it is necessary to know the expected incidence of the disease in question in the population. For instance, if the incidence of cancer X in the general population without risk factor A were 1 in 1,000, a relative risk of 2.0 would mean an absolute risk of 2 in 1,000 (0.2%) in those with risk factor A. Because the specific incidence due to a particular risk factor is often not known, relative risks/odd ratios are often of limited value in counseling patients.

Conveying Risk Information

During genetic counseling, clients may be presented with several risk estimates including the risk for developing specific types of cancer and the likelihood that they have a genetic mutation associated with cancer risk. Personal experience may significantly affect the way a client interprets a numerical risk. Presenting risk information in multiple ways, such as a percentage and fraction, is helpful. As risk data often differs between studies, presenting information as ranges is often useful. It is also important to discuss the chance of never developing the cancer in question. It may be useful to establish a context for the risk estimate by pointing out how their heritable cancer risk compares to cancer risks in the general population. In addition, assessment of the potential impact of the risk estimate on the client´s health behavior is indicated.

Assessment of the client´s perception of risk and beliefs about cancer etiology is done before presenting numerical risk information. Once the information is presented, verbal and nonverbal cues are used to assess the patient´s understanding and acceptance.

Determining Cancer Risk

In cancer risk assessment, there are two aspects of risk. One is the absolute risk that the client will develop a specific type of cancer or cancers based on the family history. The second is the risk that the client carries a heritable or germline mutation in a cancer susceptibility gene. Obtaining the genetic pedigree with medical record confirmation of cancer diagnoses is an obligatory step in accomplishing both aspects of risk assessment. Once the pedigree is procured, the next step is to attempt to classify the history as hereditary, familial, or sporadic.

1. *Hereditary cancer*. Several excellent resources review the clinical features of various hereditary cancer syndromes to help the clinician identify at-risk families (see the original guideline document for suggested resources). Accurate syndrome identification is necessary to determine what types of tumors may occur in relatives, the magnitude of risk, and what gene is most likely to be involved. Even in the absence of an identifiable syndrome, any pedigree that demonstrates autosomal dominant transmission of a specific type(s) of cancer is suggestive of an inherited cancer predisposition. In families with known syndromes or dominant inheritance, first-degree relatives of affected individuals have a 50% risk of inheriting the putative cancer-predisposing gene mutation segregating in the family. Those who do not inherit the familial mutation are typically at the general population risk of cancer. Those who inherit the mutation are at increased risk of developing the associated cancers and for passing the causative gene to offspring. Most hereditary cancer syndromes are characterized by incomplete penetrance and variable expressivity. Therefore, identification of a heritable cancer susceptibility mutation generally indicates a probability that cancer will develop but not a certainty (incomplete penetrance). Furthermore, age of onset, number of primary tumors, and tumor site can vary within and among families (variable expressivity).
    a. Determining absolute cancer risk in hereditary syndromes. Cancer risk information is available for many of the defined cancer syndromes, such as hereditary breast ovarian cancer syndrome and hereditary nonpolyposis colorectal cancer syndrome. Using pedigree assessment to determine the likelihood that a client has inherited a mutation in a particular cancer-predisposing gene and data from the literature regarding cancer risk in mutation carriers, it is often possible to estimate a client´s heritable cancer risk. It is critical to utilize current risk estimates from peer-reviewed research as these numbers have changed as understanding of the conditions has increased. If there is an identifiable mutation in the family, molecular testing can determine definitively whether a person inherited the familial mutation and can refine cancer risk estimation. In families with autosomal dominant transmission of a specific type of cancer without molecular evidence of an identifiable syndrome, cancer risk estimation is provided through pedigree assessment and the use of available empiric risk models (described below).

        In families with known cancer syndromes, Bayes´ theorem can be used to refine risk estimates as long as age-specific expression information is available for the syndrome in question. For example, relatives who have lived beyond the age at which they would likely

have developed cancer if they had a mutation have a lower chance of actually carrying the mutation than is predicted by their position in the pedigree.

b. Determining the probability of identifying a mutation in hereditary cancer families. Models for determining the probability that genetic testing will reveal a mutation in a predisposition gene are currently available for the BRCA1, BRCA2, MLH1, and MSH2 genes. These models utilize factors such as age of onset of cancer, number of affected relatives, and presence/absence of associated malignancies in estimating the likelihood of a mutation in an affected member of the family. Ancestry may also affect the likelihood of a mutation in a family, as is the case for BRCA1/2 mutations in Ashkenazi individuals. Once these models have been utilized in a family, pedigree analysis can then determine the likelihood that an unaffected relative will have an identifiable mutation. Knowing the probability that genetic testing will reveal a mutation is helpful for those considering molecular analysis, as many clients will have overestimated their risk. It is an important component of informed decision-making.

2. *Familial cancer*. Histories classified as familial are those in which there are more cases of a specific type(s) of cancer than expected on the basis of chance alone, but not necessarily exhibiting the classic features of hereditary cancers (early age of onset, multifocal tumors, dominant inheritance). These histories may be the result of small family size, paucity of individuals of the higher risk gender, multifactorial influences, chance clustering of sporadic cases, underreporting of cancer history in a hereditary cancer family, a cancer syndrome with reduced penetrance, or a chance limited transmission of a cancer susceptibility gene. Genetic testing is often less likely to provide additional information about cancer risk in these cases than in hereditary ones.
    a. Determining absolute cancer risk in familial cases. Statistical models are available for estimating cancer risk in familial cases of breast cancer and, to a more limited extent, colon, ovarian, and prostate cancer (see Table V in original document). These models take into account factors such as age of onset, number of affected relatives, and the degree of relationship between the patient and the affected relatives in estimating lifetime cancer risks. One model, the Gail model, takes into account specific environmental risk factors but incorporates only limited family history information. The risks generated from such models are empiric, that is, an estimate based on average risk in a population of people with similar risk factors. For individuals whose relatives have sporadic cancer, the empiric risk calculated by the Gail model may be an overestimate of actual cancer risk. In individuals whose relatives have hereditary cancer, the empiric risk may be an underestimate of actual risk.

       Empiric risks are useful because they can demonstrate to clients that not everyone with a family history of cancer is at significantly increased risk of developing the disease. In addition, this information can be useful to clinicians in deciding how often to perform cancer screening and what interventions to offer, if any, to reduce cancer risk.

b. Determining the probability of identifying a mutation in familial cancer families. The models mentioned previously can be used to determine the likelihood of a heritable mutation in presumed familial histories. Reviewing these probabilities with clients provides them with statistical evidence as to why testing for mutations in hereditary cancer genes may have a low likelihood of further characterizing their cancer risk.

3. *Sporadic cancer*. Sporadic histories are those in which the cancer(s) in the family is mainly due to nonhereditary causes. When available, empiric risk data will further support this assessment. The likelihood that molecular testing will reveal a mutation in families such as these generally approaches the frequency in the general population. The exception lies with some rare tumors. For instance, up to 10% of patients with "sporadic" medullary thyroid cancers may have germline mutations in the RET proto-oncogene, which causes multiple endocrine neoplasia type. In addition, up to one third of cerebellar hemangioblastomas are associated with the hereditary cancer syndrome, von Hippel–Lindau. Consequently, be aware of the rare tumors that have a significant a priori likelihood of being hereditary before ruling out the possibility of increased risk to other relatives (see Table II in original document).
4. *Histories of uncertain significance*. Many families presenting for cancer risk assessment have some of the features of an inherited syndrome, such as early age of onset, but without clear evidence of single gene inheritance. Several factors can lead to difficulty in pedigree assessment, including small family size, reduced penetrance (lower cancer rates than usual in mutation carriers), a paucity of susceptible gender for sex-influenced or sex-limited cancers like prostate or breast cancer, prophylactic surgeries in at-risk members, and lack of information/inaccurate information regarding key relatives in the pedigree, as can be the case with adoption. When available, providing empiric estimates of cancer risk and mutation probabilities can be useful in such families. Encourage families with histories of uncertain significance to report any new cancer diagnoses so that the pedigree can be reassessed in the future.

   Given the potential complexity of pedigree interpretation, some centers have established multidisciplinary case review conferences, where pedigrees can be discussed and assessed for clues about possible inherited susceptibility. The multidisciplinary format can also facilitate discussion of the appropriate cancer risk management strategies.

Molecular Testing for Hereditary Cancer Syndromes

Consider offering molecular testing for hereditary cancer susceptibility only when a client has a significant personal and/or family history of cancer as previously described, the test can be adequately interpreted, the results will affect medical management, the clinician can provide or make available adequate genetic education and counseling, and the client can provide informed consent. With regard to BRCA gene testing specifically, an updated American Society of Clinical Oncology (ASCO) statement recommends evaluation by a health care professional experienced in cancer genetics to determine the appropriateness of genetic testing. A previous recommendation to offer genetic testing only if the client has a greater than 10% prior probability of carrying a mutation has been deleted in 2003 by ASCO. American College of Medical Genetics (ACMG) Foundation, in their

1999 document "Genetic Susceptibility to Breast and Ovarian Cancer: Assessment, Counseling, and Testing Guidelines" does not establish a numerical cutoff for when cancer genetic testing should or should not be offered. However, the guideline states that testing is not recommended in situations where there is a low probability of carrying a mutation, given the financial cost of cancer genetic testing as well as the potential psychological ramifications. Furthermore, the ACMG states that to offer genetic testing is to take the responsibility, either personally or through referral to appropriate professionals, for adequate pretest education, the process of informed consent, and posttest counseling.

Regulation of Genetic Testing

1. *Clinical testing*. Molecular analysis is available on a clinical, fee-for-service basis, for an increasing number of genes implicated in hereditary cancer syndromes. The Clinical Laboratory Improvement Act (CLIA) establishes standards for these clinical testing laboratories. Medicare and many third-party insurance carriers require CLIA certification for reimbursement of molecular analysis. For this reason, as well as for quality control, clinical genetic tests should be ordered from CLIA-approved laboratories.
2. *Research testing*. Molecular analysis may be available within the context of a research study. Such studies must have an institutional-review-board-approved protocol and a written informed consent form that research participants are required to sign.

When both clinical and research testing are available to a client, the pros and cons of each approach should be discussed in detail. Unlike clinical laboratories, research laboratories do not have to be CLIA-approved. Therefore, the research laboratory may not be able to release results to the client unless a CLIA-approved laboratory confirms them. The turnaround time for results, if and when they are released, is generally longer for research versus clinical tests. However, a potential benefit of research testing is that tests are performed at reduced or no cost.

Pretest Genetic Counseling and Informed Consent

Prior to beginning an in-depth discussion of the benefits, risks, and limitations of genetic testing, inquire about the client´s motivations and expectations for pursuing cancer genetic testing.

Informed consent is a necessary component of molecular testing for hereditary cancer syndromes whether in a clinical or research setting. The process of informed consent includes a thorough discussion of the possible outcomes of testing, a review of the possible benefits, risks, and limitations, and a discussion of alternatives to molecular testing. Basic elements of informed consent in cancer genetic risk assessment and genetic counseling have been reviewed in the medical literature and are described below. In general, genetic cancer susceptibility testing is not performed on persons under the age of 18, as minors may not be able to give informed consent. The exception includes cases where medical intervention is warranted in childhood such as with familial adenomatous polyposis (*APC* testing) and multiple endocrine neoplasia type II (*RET* testing).

Elements of Informed Consent for Cancer Genetic Testing

1. *Purpose of the test and who to test*. Explain why the test is being offered, if and how the results might alter the client´s cancer risk, and how the results might affect medical management. For clients who are seeking presymptomatic genetic testing, in the absence of a known mutation in their family, discuss the importance of testing an affected relative first. This approach helps determine whether there is an identifiable mutation in the gene(s) in question for which unaffected relatives can be tested. The best relative with whom to initiate genetic testing is generally one who had an early age of onset of the cancer in question and/or multifocal cancer. In some cases, an affected relative may not be available (deceased or out of contact with the family), willing, or financially able to proceed with testing. In such situations, discuss the limitations of presymptomatic testing without an identified mutation in detail with the client (see below).
2. *General information about the gene(s)*. Review cancer risks associated with gene mutations including the concepts of penetrance and variable expressivity and the possibility of genetic heterogeneity.
3. *Possible test results*. Explain the implications of all possible test results and the likelihood that the test will be informative.
    a. *Positive result: A functionally significant mutation that indicates an increased cancer risk*. The likelihood of developing various cancers depends upon the gene in which the mutation is detected and sometimes where in the gene the mutation is located. Epigenetic factors (other genes and environmental risk factors) may also modify cancer risk. In the case of presymptomatic testing, results indicate a probability of developing cancer, not a certainty, and do not indicate when cancer may develop or the tumor site.
    b. *Negative result: No mutation identified*. In the absence of a known mutation in a family, a negative result in an unaffected person with a strong family history of cancer is generally considered uninformative. The family may have a mutation in the gene tested that is not detectable with current technology. Alternatively, because many cancer syndromes are genetically heterogeneous, the family may carry a mutation in a different gene. It is important to stress the nature of an uninformative negative test result in this setting. Failure to understand the significance of an uninformative negative result may lead to failure to comply with recommended cancer screening or cancer risk reduction practices. The interpretation of the significance of a negative result in an affected person depends on the sensitivity of the genetic test, the family history, and the a priori likelihood that the individual would have had a positive result.
    c. *Negative result: Known mutation in family*. If a functionally significant mutation has been previously identified in a close biological relative and the client tests negative for the mutation, he/she is not at increased risk of developing cancer based on the family history and is instead at general population risk. Testing the client for the familial mutation only is usually sufficient. An exception may be the cases where the client belongs to an ethnic group in which common, recurrent mutations have been identified. For instance, in Ashkenazi families that carry one of the three common *BRCA1/2* mutations, relatives electing to have molecular analysis should be tested for all three mutations, not just the one identified in the family
    d. *Variant of uncertain significance: An alteration in a gene has been identified but it is unknown whether the alteration will affect gene*

function. Examples of variants of unknown significance can include missense mutations of unknown functional significance or alterations in intronic sequences not known to be involved with messenger ribonucleic acid (mRNA) processing. Further studies involving the client and his/her relatives as well as an improved understanding of gene function may be necessary to establish the clinical significance of a variant. Unless the variant is determined to be significant (i.e., affecting gene function), predictive genetic testing cannot be performed in other relatives. If significant family history is present, such a result does not rule out a hereditary cancer syndrome in the family, and appropriate medical management should be based on family history alone.

4. *Likelihood of positive result*. When available, use statistical models, pedigree assessment, and/or Bayes´ theorem to provide the client with information about the chance that testing will reveal a mutation in the gene(s) in question. Provide clients with qualitative and/or quantitative information about the likelihood of a positive rest result (see the section Determining the probability of identifying a mutation in hereditary cancer families).
5. *Technical aspects and accuracy of the test*. Review method(s) that will be used for mutational analysis and the likelihood of a false-positive or false-negative result (sensitivity and specificity).
6. *Economic considerations*. Apprise the client of the cost of genetic testing and that some insurance plans may not provide reimbursement for such tests. Because of the high costs of many genetic tests, it may be useful to determine insurance coverage before proceeding. Inform the client of the benefits and risks associated with pursuing reimbursement for a genetic test (see below).
7. *Risks of genetic discrimination*. Persons considering genetic testing for cancer susceptibility need to be aware of (1) the potential consequences on insurability, (2) whether the results will be disclosed to any third party (including the referring physician), and (3) whether the center initiating the testing has any confidentiality safeguards. Encourage clients to review their insurance policies prior to testing.

   Inform clients about the status and limitations of state and federal legislation providing protection against genetic discrimination in health insurance, life insurance, and employability. At the federal level, the Health Insurance Portability and Accountability Act (HIPAA) of 1996 provides some protection against genetic discrimination with regard to health insurance for individuals with group policies (http://www.hhs.gov/ocr/hipaa/). Information about genetic discrimination, current legislation, and bills up for consideration can be found at the following websites: http://thomas.loc.gov, and http://www.nationalpartnership.org/. In addition, be familiar with the current legislation in your state to be able to explain the protections or lack of protections it affords clients seeking genetic testing (see http://www.genome.gov/PolicyEthics/LegDatabase/pubsearch.cfm).

   Life and disability insurance are generally considered separately from health insurance. Some life/disability insurers now include questions regarding genetic testing on the application form. Persons who do not already have life/disability insurance at the time they are tested may jeopardize their chances of obtaining such policies if they are found to have a gene mutation.

The possibility of employment discrimination was addressed in 1995 when the Equal Employment Opportunity Commission (EEOC) issued a guideline interpreting the Americans with Disabilities Act (ADA) to prohibit workplace discrimination of healthy persons based on genetic tests.

8. *Psychosocial aspects*. The components of psychosocial assessment regarding testing to be addressed include but are not limited to the following:
    a. *Anticipated reaction to results*. Discuss with the client his/her anticipated reactions to positive, negative, uninformative, or ambiguous results, and explore anticipated coping strategies. Failure to anticipate reactions accurately can lead to increased emotional distress months after testing.
    b. *Timing and readiness for testing*. Ascertain the client´s readiness to proceed with testing and reassure him/her that testing can be performed at a later date if preferable. Discuss the option of deoxyribonucleic acid (DNA) banking when applicable.
    c. *Family issues*. Explore whether the client has discussed testing with his/her spouse or partner and family members, their reactions to obtaining genetic information, and how their reactions might influence relationships with the client. Discuss client´s plans for sharing results.
    d. *Preparing for results*. Prepare the client for how results will be provided. Discuss who will be present at the session, the language used to share results, and what will happen following the results session. Refer to mental health professional if indicated.
9. *Confidentiality issues*. Prior to testing, discuss confidentiality with the client as it pertains to how or if information will be released to his/her insurer, referring physician, and other family members.
10. *Utilization of test results: medical surveillance and preventative measures*. Review recommendations for cancer screening, available preventive measures, and the limitations of such approaches. Discuss how or if these recommendations would change in the event of a negative versus positive genetic test result. Ascertain how the client anticipates test results will affect his/her medical management and health behaviors.
11. *Alternatives to genetic testing*. Review methods of cancer risk estimation and options for medical management in the absence of genetic testing. Not all family members will choose genetic testing as an appropriate option. Discuss the availability of DNA banking.
12. *Storage and potential reuse of genetic material*. Inform the client of the testing laboratory´s policy for storage or potential reuse of genetic material.

Sample Collection

If or when a client has decided to proceed with molecular testing, coordinate sample collection and shipment. Provide the client with an estimated turnaround time for completion of genetic test results and establish a plan for disclosing results. Encourage the client to bring a support person to the results disclosure session. Inform the client that he/she has the option to withdraw from the testing process or delay results disclosure.

Results Disclosure and Post-test Counseling

This is a multi-step process, optimally done during a face-to-face meeting.

1. *Results disclosure*. After client´s consent, inform him/her of the result.
2. *Significance of test results*. Review the specificity and sensitivity of the test and discuss how the client´s result affects his/her cancer risk.
3. *Impact of test results*. Assess the emotional impact of the result on the client and his/her support person through verbal and nonverbal cues; provide support as needed.
4. *Medical management*. Review screening recommendations and options of cancer risk reduction, such as chemoprevention or prophylactic surgery, if available, including benefits, risks, and limitations of these options. Provide referrals to other medical professionals for additional discussions of these topics and strongly encourage compliance with screening recommendations.
5. *Informing other relatives*. Discuss cancer risks to other relatives and importance of informing family members about family history/genetic test results. Written documentation that the client can share with relatives may be provided, safeguarding confidentiality as desired by client. If a high-risk client refuses to contact at-risk relatives, an ethics consult is an option
6. *Future contact*. If follow-up care will be managed elsewhere, encourage the client to maintain contact with the cancer risk assessment center for updates about their family history, the genetics of familial cancer disorders, and the management of inherited predisposition to cancer. The same applies to high-risk families with negative test results who may be candidates for future genetic tests. When available, offer clients the option of participating in long-term follow-up studies.
7. *Resources*. Provide the client with resources about cancer genetics (see Table VI in the original guideline document) and contacts with other willing clients, if desired and available. Serve as a psychosocial support resource for the client or refer to other qualified individuals if additional support is needed.

Surveillance/Treatment/Follow-Up

Follow-up for all clients seeking cancer genetic risk assessment and genetic counseling services, regardless of cancer risk category, should include a discussion of cancer screening guidelines, reviewing limitations when relevant, methods for reducing cancer risk if known, and referrals to appropriate medical professionals for long-term medical management if needed.

Summary

Cancer genetic risk assessment and genetic counseling is a multistep process. The process begins by collecting information about the client´s personal medical history and family history to assess heritable cancer risk. A psychosocial assessment is also performed to determine the client´s perception of risk and ability to cope with risk information. Once this information is collected, a counseling model is used to discuss risk, facilitate adjustment to risk, provide informed consent for genetic testing when applicable, and review options for medical management. Genetic counseling is an integral part of cancer genetic risk assessment that enhances clients´ ability to cope with and understand the genetic information presented.

Special Cases/Exceptions to Practice Recommendations

Genetic testing of at-risk individuals during childhood: Because minors may not be able to give informed consent, in general, genetic cancer susceptibility testing is not performed on persons under the age of 18 years. The exception includes cases where medical intervention is warranted in childhood such as with familial adenomatous polyposis (*APC* testing) and multiple endocrine neoplasia type II (*RET* testing).

Adopted proband: Individuals with early-onset cancer who have no details regarding family history will be evaluated on the basis of personal medical and psychosocial history alone.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

All supporting evidence is class III, opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees. No supporting literature of categories I and II was identified.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Early detection of heritable cancers
- Prevention of heritable cancers by alerting at-risk individuals to make appropriate lifestyle or environmental changes

POTENTIAL HARMS

- Economic considerations
- High costs of many genetic tests
- Uncertainty of insurance reimbursement
- Risks of genetic discrimination.
- Potential consequences on insurability
- Risk of unwanted third party disclosure
- Potential for confidentiality breach
- Possibility of illegal employment discrimination

QUALIFYING STATEMENTS

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The genetic counseling recommendations of the National Society of Genetic Counselors (NSGC) are developed by members of the NSGC to assist practitioners and patients in making decisions about appropriate management of genetic

concerns. Each practice recommendation focuses on a clinical or practice issue and is based on a review and analysis of the professional literature. The information and recommendations reflect scientific and clinical knowledge current as of the submission date and are subject to change as advances in diagnostic techniques, treatments, and psychosocial understanding emerge. In addition, variations in practice, taking 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, or procedures alternative to the recommendations outlined in this document. Therefore, these recommendations should not be construed as dictating an exclusive course of management, nor does use of such recommendations guarantee a particular outcome. Genetic counseling recommendations are never intended to displace a health care provider´s best medical judgment based on the clinical circumstances of a particular patient.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

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

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GUIDELINE DEVELOPER(S)

National Society of Genetic Counselors - Medical Specialty Society

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GUIDELINE COMMITTEE

Genetic Services Committee of the National Society of Genetic Counselors

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Not available at this time.

Print copies: Available from the National Society of Genetic Counselors, 233 Canterbury Drive, Wallingford, PA 19086-7608; Web site: www.nsgc.org.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on September 21, 2004. The information was verified by the guideline developer on September 23, 2004.

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