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PROFESSIONAL ISSUES

Essential Elements of Genetic Cancer Risk Assessment, Counseling, and Testing: Updated Recommendations of the National Society of Genetic Counselors

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Abstract Updated from their original publication in 2004, these cancer genetic counseling recommendations describe the medical, psychosocial, and ethical ramifications of counseling at-risk individuals through genetic cancer risk assessment with or without genetic testing. They were developed by members of the Practice Issues Subcommittee of the National Society of Genetic Counselors Familial Cancer Risk Counseling Special Interest Group. The information contained in this document is derived from 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 recommendations are intended to provide information about the process of genetic counseling and risk assessment for hereditary cancer disorders rather than specific information about individual syndromes. Essential components include the intake, cancer risk assessment, genetic testing for an inherited cancer syndrome, informed consent, disclosure of genetic test results, and psychosocial assessment. These recommendations should not be construed as dictating an exclusive course of management, nor does use of such recommendations guarantee a particular outcome. These recommendations do not displace a health care provider's professional judgment based on the clinical circumstances of a client.

Keywords Cancer genetic counseling · Risk assessment · Genetic testing · Family history · Psychosocial assessment · Hereditary cancer · Informed consent

Purpose The National Society of Genetic Counselors (NSGC) is the primary leader for the genetic counseling profession. Its 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. To that end, the Society promotes the development of practice guidelines for genetic counselors and others who provide genetic counseling services. The purpose of this document is to present a current and comprehensive set of practice recommendations for effective genetic cancer risk assessment, counseling, and testing. These guidelines were developed by the NSGC's Familial Cancer Risk Counseling Special Interest Group which includes NSGC members providing cancer genetics services.

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Introduction

In 2004, the NSGC published its first cancer risk assessment guideline (Trepanier et al. 2004). Since 2004, the number of clinically available genetic tests for

inherited cancer predisposition has increased substantially, as has the identification of conditions associated with an increased cancer risk. More evidence regarding the natural history of common cancer syndromes and the effectiveness of management strategies is available. Legal protection against genetic discrimination at both the state and federal level has improved. In addition, service delivery models that go beyond the traditional face-to-face pre-test and post-test counseling model are being utilized by genetic counselors (Trepanier et al. 2011; Wham et al. 2010). These developments call for an update of the existing guidelines for genetic cancer risk assessment.

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Background

Hereditary Cancer

The term "hereditary cancer" refers to cancer that develops due to a germline mutation in a cancer predisposition gene (s). Hereditary cancer accounts for an estimated 5–10% of cancer occurrences. More than 45 hereditary cancer syndromes have been described. These syndromes predispose individuals to common cancers such as breast, ovarian, colon, and endometrial cancers, as well as rare cancers such as medullary thyroid and diffuse gastric cancers (Lindor et al. 2008). Individuals with a hereditary cancer syndrome are usually at increased risk for more than one type of cancer or tumor.

Cancer risks associated with hereditary cancer syndromes are significantly elevated in comparison to general population risks, and there is both an increased risk of developing more than one primary cancer, and of having an earlier age of onset than is typical. Consequently, for unaffected, at-risk individuals, cancer screening is usually indicated at an earlier age, and may include different and/or more frequent screening tests than those used in average risk populations (NCCN 2011). Individuals with cancer syndromes who are diagnosed with cancer may also be offered different surgical and treatment options. Therefore, identification of individuals at increased risk for hereditary cancer has implications for screening and clinical management.

A growing body of evidence supports the benefits of genetic risk assessment, genetic testing, and the efficacy of clinical management in those with certain hereditary cancer syndromes. For example, in 2009, the Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group found sufficient evidence to recommend that individuals who have a newly diagnosed colorectal cancer be offered genetic testing for Lynch syndrome for the purpose of reducing morbidity and mortality in their relatives (EGAPP Working Group 2009). Evidence also indicates that colonoscopic surveillance is efficacious in individuals with an inherited susceptibility to Lynch syndrome (Lindor et al. 2006). The United States Preventive Services Task Force recommended genetic risk assessment and evaluation for *BRCA1/2* testing for unaffected individuals at elevated risk of hereditary breast ovarian cancer syndrome based on specific family history criteria (USPSTF 2005). A survival analysis of *BRCA1/2* mutation carriers revealed that prophylactic surgery confers a substantial survival probability (Domchek et al. 2010). The American Thyroid Association recommends pre- and post-test genetic counseling and genetic testing for *RET* mutations to all patients with medullary thyroid cancer to facilitate optimal

management for patients and relatives with multiple endocrine neoplasia type 2A (Kloos et al. 2009). As a result, establishing best practices for those providing genetic cancer risk assessment, counseling, and testing has become even more important to make sure that those who have an inherited predisposition are appropriately identified and managed.

Genetic Counseling, Testing and Risk Assessment

Genetic counseling and risk assessment is the process of identifying and counseling individuals at increased risk of developing cancer, and distinguishing between those at high risk (highly penetrant hereditary cancer syndrome), those at a modestly increased risk (multifactorial etiology or low penetrance allele), and those at average risk. Using a combination of pedigree analysis, genetic testing, risk modeling, biochemical tests and imaging, and sometimes consideration of physical features, potential hereditary cancer syndromes are identified and cancer risks are quantified for patients and their biological relatives. The information is then used to develop a management plan for cancer screening, prevention, and risk-reduction as well as notification of at-risk family members. Genetic counseling also includes patient education about hereditary cancer syndromes and assistance coping with the psychological responses that can occur in families at increased cancer risk (Trepanier et al. 2004). A referral for genetic cancer risk assessment is appropriate for patients with a personal and/or family history suggestive of an increased cancer risk. While the process of cancer risk assessment often includes genetic testing, many patients may benefit from risk assessment and counseling even though they may not ultimately be candidates for genetic testing or choose not to pursue testing for personal or financial reasons. General referral criteria have been published to help identify families who may benefit from a referral to genetic counseling (Hampel et al. 2004; NCI 2010; NCCN 2011).

Identification of genetic cancer risk through genetic counseling and testing can also have an impact on treatment decisions and the associated outcomes for patients with cancer. For example, patients with early stage breast cancer who are *BRCA* mutation carriers may decide to have a bilateral mastectomy and salpingo-oophorectomy over lumpectomy and radiation to reduce their inherently increased risk of developing a second breast cancer (Domchek et al. 2010; Metcalfe et al. 2004). Patients with later stage breast cancer may be eligible for trials of targeted therapies such as a Poly (ADP-Ribose) Polymerase-1 (PARP) inhibitor which targets the homologous recombination DNA repair pathway affected by *BRCA* mutations (Audeh et al. 2010; Byrski et al. 2010; Fong et al. 2009; Tutt et al. 2010). Patients with breast cancer or other cancers who are *TP53* mutation carriers may be offered surgical treatment options over radiotherapy to reduce the increased risk of a radiation-induced cancer that is a consequence of their mutation status (Evans et al. 2006). Additionally, patients with colorectal cancers that demonstrate defective mismatch repair (dMMR), as determined by microsatellite instability or the absence of MMR proteins, might not be prescribed a fluorouracil (FU)-based chemotherapy treatment given a potential lack of benefit in tumors with such defects (Sargent et al. 2010). In all of these ways, cancer risk assessment and testing contributes not only to risk identification but also to personalizing therapies based on mutation status for the purpose of improving treatment outcomes over strategies that do not incorporate genomic information.

The recommendations below delineate the essential elements of genetic cancer risk assessment, counseling and testing. The elements are similar to those described in the first such NSGC guideline (Trepanier et al. 2004). However, some of the recommendations have changed in response to changes in cancer genetics knowledge, demand for services, and public policy.

Recommendations

Recommendation 1

The information collected at intake should include a thorough personal medical history and a 3–4 generation family medical history (pedigree), both of which are crucial for effective cancer risk assessment.

Standardized human pedigree nomenclature should be used (Bennett et al. 2008) and targeted questions should serve to elicit the information necessary for risk assessment. Information should be sought about ancestry/ethnicity and consanguinity. Since family medical history changes over time, the pedigree should be updated as additional information becomes available. Table 1 lists the information to be collected while obtaining patients' medical history for individuals with and without a previous cancer diagnosis (Bennett 2010, 1999; Schneider 2002).

Attention should be paid to cancer screening and surgical interventions such as oophorectomy in young women or colorectal polypectomies, which can reduce cancer incidence. As with any patient-reported information, inaccuracies in reporting (Qureshi et al. 2007) may occur and documentation may provide more accurate cancer risk assessment. Education level, gender, and degree of relatedness can all have an impact on reporting accuracy (Schneider et al. 2004). Acceptable forms of documentation include pathology reports, medical consultation notes, and death certificates.

Table 1 Collecting a personal medical history: questions to ask patients with/without cancer

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

[a] Especially important for women at increased risk of breast, ovarian, or endometrial cancer. Inquire about age of menarche, age at first live birth, and history of oral contraceptive use, infertility medications, or hormone replacement therapy, (including dosage and duration), and age at menopause.

[b] For patients who have developed more than one tumor, it is important to discriminate whether additional tumors were separate primaries, a recurrence of the initial primary cancer, or the result of metastatic disease

Several limitations may be encountered while taking a family history. For example, one can encounter limited family structure due to unknown family history (including adoptions), small family size, or the presence of family members who have died at a young age from non-cancer related conditions/situations (Weitzel et al. 2007). These limitations can "mask" the presence of a hereditary cancer genetic syndrome, and should be taken into account during the assessment and counseling session.

There are electronic tools for gathering and recording pedigree information, such as the United States Surgeon General's Family Health Portrait tool (http://www.hhs.gov/familyhistory/). Commercial software is also available (e.g. Progeny, Hughes Risk Apps). These publicly available tools may be valuable to the clinician as they can often engage the patient in collecting the necessary family health information.

Recommendation 2

The genetic cancer risk assessment process should include using personal and family medical history information to determine whether an individual/family has an average, modest or increased cancer risk. This information can then be used to generate a list of hereditary cancer syndromes to consider in the differential diagnoses.

There are a number of family history factors that can be indicative of increased cancer risk and can guide risk assessment. These include multiple close relatives with similar or related cancers, early age at diagnosis, an individual having more than one primary tumor or bilateral cancers in paired organs, the presence of rare cancers or tumors, ethnicity, and individuals with unusual or excessive benign lesions (such as colon polyps, dysplastic moles, or rare adrenal tumors) (Bennett 2010). When pedigree analysis is suggestive of an inherited predisposition to cancer, reviewing one of the many resources available that describe the malignant and benign clinical features of various cancer syndromes can be helpful in establishing differential diagnoses (Lindor et al. 2008). As new genes associated with hereditary cancer predisposition are discovered, the list of differential diagnoses may expand, and patients who have previously had negative genetic testing results may benefit from additional testing. This is aptly illustrated by the discovery of mutations in the *EPCAM/TACSTD1* gene, which is a causal gene of Lynch syndrome (Ligtenberg et al. 2009). Staying abreast of clinically relevant genetic discoveries and the features of the associated syndromes is essential in providing an accurate, up-to-date risk assessment.

Physical examinations can be vital in determining the appropriate clinical diagnosis and genetic testing options. In the absence of a clinical geneticist who may perform physical exams, referral to an appropriate health care provider to evaluate the presence or absence of physical features of a suspected cancer syndrome is recommended. For example, patients suspected of having PTEN Hamartoma syndrome or Birt-Hogg-Dubé syndrome warrant a referral to a dermatologist for evaluation of benign skin findings associated with these syndromes (Pilarski 2009).

Many family histories collected during the genetic cancer risk assessment process will lack features of

hereditary cancer, and consequently, the likelihood of identifying a mutation in a cancer-predisposition gene in such families will be low given the current state of technology. In these cases, a cancer risk assessment can be performed, using family history information without genetic testing, to quantify the patient's empiric cancer risk.

Several empiric cancer risk models are available to aid in risk assessment. Models for breast cancer risk estimation include the Gail, Claus, BRCAPRO, Tyrer-Cuzick, and BOADICEA models (Gail et al. 1989; Claus et al. 1993; Parmigiani et al. 1998; Tyrer et al. 2004; Antoniou et al. 2004) All of these models incorporate family history of breast cancer in first degree relatives; some include substantial amounts of family history while others include hormonal factors. These models and their limitations have been reviewed in detail elsewhere (Amir et al. 2010; Culver et al. 2006). Several published tools are also available to assess risk of colon, ovarian, lung, melanoma and many other cancers. (http://riskfactor.cancer.gov/cancer_risk_prediction/about.html).

The identification of patients with empirically increased risks allows for tailored screening and other interventions. For example, the American Cancer Society recommends breast MRI screening for women who have an approximately ~20–25% or greater lifetime breast cancer risk (Saslow et al. 2007) as calculated by the Claus, BRCAPRO, Tyrer-Cuzick or BOADICEA models. The FDA has approved the use of tamoxifen for chemoprevention in women with a 5 year breast cancer risk of >1.66% as calculated by the Gail model (Fisher et al. 1998). The National Comprehensive Cancer Network recommends colonoscopy screening every 5 years, beginning at age 40 years, for patients with a first degree relative with colorectal cancer diagnosed between 50 and 60 years of age (NCCN 2011). As such recommendations demonstrate, identifying patients at increased risk of cancer, even in the absence of a suspected hereditary cancer syndrome, can be important in tailoring screening and preventive measures.

Recommendation 3

Genetic testing should be offered when the following conditions apply:

- An individual has a personal or family history suggestive of an inherited cancer syndrome. (ASCO 2003; Robson et al. 2010)
- The genetic test can be adequately interpreted. (ASCO 2003; Robson et al. 2010)
- Testing will influence medical management of the patient or other relatives. (ASCO 2003; Robson et al. 2010)
- The potential benefits of testing outweigh the potential risks.
- Testing is voluntary.
- The individual seeking testing or their legal proxy can provide informed consent.

Various probability models and clinical criteria are available to estimate the likelihood that an individual carries a mutation related to a hereditary cancer syndrome. These tools can help distinguish between average, modest, and high risk family histories and drive clinical decision-making about the suitability of genetic testing in further assessing risk. Insurance companies may also use such tools in determining eligibility for coverage of genetic testing. The positive and negative predictive values of genetic testing can be strongly influenced by prior probability (e.g. positive family history) (Rich et al. 2004).

A number of *BRCA* gene mutation probability models are available. The Myriad and Couch models can be accessed with published tables; Penn 2 and BOADICEA are web-based programs; and BRCAPRO and Tyrer-Cuzick models are used via software download (Frank et al. 1998; Couch et al. 1997; Lindor et al. 2010; Antoniou et al. 2004; Parmigiani et al. 1998; Tyrer et al. 2004). These models incorporate the presence of certain types of cancer in the patient and first- and second-degree relatives, ages of cancer onset, and Ashkenazi Jewish ancestry. Beyond that, each model incorporates different factors to determine likelihoods and should be utilized selectively based on the characteristics of the patient's personal and family history. Some of these assess absolute risk of breast and ovarian cancer in addition to mutation probabilities.

There are also several models available that calculate Lynch-syndrome mutation probabilities (Weissman et al. 2011). However, recommendations for genetic testing for Lynch syndrome are more often based on specified criteria, for example the Revised Bethesda Guidelines in individuals with colon cancer (Umar et al. 2004). As mentioned previously, the EGAPP Working Group found sufficient evidence to recommend offering genetic testing for Lynch syndrome to all individuals with a new diagnosis of CRC (EGAPP Working Group 2009). Clinical criteria also exist for other syndromes including Cowden syndrome (PTEN Hamartoma syndrome) and Li-Fraumeni syndrome (NCCN 2011). Finally, the various mutation probability models may underestimate risk in certain situations such as a limited family structure (Weitzel et al. 2007). Therefore, reliance on probabilities predicted by a model should not supersede sound clinical judgment.

Cancer genetic predisposition testing should not typically be offered to persons under the age of 18 who have not previously been diagnosed with cancer unless screening and/or risk-reduction strategies are available for this age group and

there is an increased probability of developing cancer during childhood (Stultiens et al. 2006; ACMG 1995). Examples of syndromes for which childhood cancer risk is increased and testing minors may be considered include but are not limited to: familial adenomatous polyposis, multiple endocrine neoplasia type 2, and von Hippel-Lindau syndrome (ASCO 2003; ASHG 1998; Nelson et al. 2001). In such cases, parents have to weigh the benefits and risks of screening a child who may or may not have inherited a familial mutation against definitively determining risk in childhood through genetic testing. Parents should also be cautioned that there are little published data regarding the long-term impact on children who test positive for cancer predisposition genes. Genetic counseling can help the parents identify and consider the impact of such decisions.

In addition to cancer management options, various reproductive options are available for patients with a molecularly confirmed hereditary cancer syndrome: assisted reproduction with or without egg or sperm donation, prenatal diagnosis, and preimplantation genetic diagnosis (PGD). Prenatal diagnosis and selective pregnancy termination are feasible but may not be personally, socially or ethically acceptable to some individuals. PGD involves testing embryos conceived via in vitro fertilization (IVF) for the familial mutation and implanting only unaffected embryos (Konstantopoulou et al. 2009; Offit et al. 2006; Spits et al. 2007). When offering genetic testing for prenatal diagnosis or for use in PGD, the above considerations should be taken into account while recognizing that "medical management" issues will be different compared to testing an adult.

Recommendation 4

An informed consent process is a necessary, and in some states legally required, component of genetic testing for hereditary cancer susceptibility and should precede genetic testing.

The process of informed consent should include a discussion of the precise gene(s) being tested, the possible outcomes of such testing, medical management issues specific to the test results, and a review of the possible benefits, risks, and limitations, and alternatives to genetic testing. This information should be presented in a way that is easily understandable to the patient. Assessing educational level and prior knowledge of medical genetics can be important in determining how to most effectively provide informed consent.

Direct to consumer (DTC) genetic testing has recently gained momentum, and many companies that offer DTC testing do not require a physician's order to obtain testing or pre-test counseling with a trained health care professional. Proponents of DTC testing argue that it will increase access to genetic testing services. However, DTC testing may not allow for adequate informed consent. Therefore, it is strongly encouraged that appropriately trained clinical genetics professionals be involved in the genetic testing process from the beginning (Hudson et al. 2007; NSGC 2007).

Basic elements of informed consent as part of the cancer genetic counseling process have been reviewed in detail in the medical literature (ASCO 2003; Geller et al. 1997) and are described below.

Elements of Informed Consent for Cancer Genetic Testing

1. **Purpose of the test and who to test**. An explanation should be provided that covers why the test is being offered, how the results might alter the individual's or their family members' cancer risk and the medical or surgical options to manage this risk. In the absence of an identified mutation in a family, the importance of first testing an affected relative should be discussed. If this is not an option, the limitations of testing an unaffected individual in the absence of an identified familial mutation should be described in detail with the patient (see below).
2. **General information about the gene(s)**. Cancer risks associated with the gene mutation(s) in question, including the mode of inheritance and the concepts of genetic heterogeneity, incomplete penetrance and variable expressivity, should be reviewed.
3. **Possible test results**. The implications of all possible test results should be explained:

    a. Positive Result (a deleterious mutation was identified): The identification of a known deleterious mutation guides management. In addition, it provides an opportunity for other at-risk relatives in the family (whether affected or unaffected with cancer) to undergo genetic counseling and testing for the identified familial mutation.
    b. Negative Result (no deleterious mutations were identified):

        i. Uninformative Negative: In the absence of a known deleterious mutation in a family, a negative result is generally considered uninformative and must be interpreted with caution. It is important to stress the meaning of an uninformative test result to the patient, as failure to understand the significance of such a result may lead to the patient's non-adherence to recommended cancer screening or cancer risk reduction practices.
        ii. True negative: If a patient tests negative for a known deleterious mutation that has been previously

identified in a close biological relative, the patient is generally not considered to be at a significantly increased risk of developing cancer.

c. Variant of Uncertain Significance (VUS): In this case, a DNA change in a gene has been identified, but it is unknown whether the DNA change affects gene function or if it represents normal variation. Genetic testing for the VUS should not be offered to other relatives on a clinical basis. Research studies involving the patient's relatives may help establish the clinical significance of the variant. Various online mutation evaluation programs may provide information to help interpret the significance of VUS (e.g. MAPP-MMR, http://mappmmr.Blueankh.com/Impact.php; Polyphen, http://genetics.bwh.harvard.edu/pph/; Leiden Open Variation Database; BIC Database). The practitioner should be aware that there are notable limitations in the accuracy of such models and variant databases.

4. **Technical aspects and accuracy of the test**. The method(s) used for mutational analysis and the likelihood of a false-positive or false-negative result (sensitivity and specificity) should be reviewed (Eng et al. 2001). The turn-around-time for results and method of disclosure should also be addressed.
5. **Economic considerations**. Patients should be apprised of the cost of genetic testing, and informed that their particular insurance plan(s) may not provide coverage or reimbursement for such tests.
6. **Possibility of genetic information discrimination**. Although there has been significant concern, there has been limited evidence of genetic discrimination in health insurance. Over the last two decades, new state and federal statutes in the United States have reduced the potential risk of genetic discrimination in health insurance and employment for a majority of citizens. Nonetheless, the status and limitations of legislation not only in health insurance and employment but also life, long-term, and disability insurance should be discussed with persons considering genetic testing for cancer predisposition.
7. **Psychosocial aspects**. A psychosocial assessment regarding testing should be performed. The assessment should include but not be limited to 1) anticipated reaction to results and coping strategies (Baum et al. 1997; Croyle et al. 1997; Lerman et al. 1997); 2) timing and readiness for testing; 3) family issues; and 4) preparing for result disclosure. Failure to anticipate reactions accurately can lead to increased emotional distress months after testing (Dorval et al. 2000). See the original recommendations (Trepanier et al. 2004) for an expanded discussion of these aspects.
8. **Confidentiality**. Genetic counselors have an ethical responsibility and legal obligation to maintain patient confidentiality. Federal Health Information Portability and Accountability Act (HIPAA) regulations require health providers to protect the privacy of all medical information, including genetic information. As a consequence, genetic counselors should share genetic testing results, pedigree and other medical information only as the patient directs (Gallo et al. 2009). Patients should also be made aware whether the results will be disclosed to any third party (including the referring physician), and whether the center initiating the testing has any confidentiality safeguards. Several organizations have addressed the challenges of maintaining confidentiality in the genetic counseling setting (ASCO 2003; ASHG 1998; Robson et al. 2010; Schneider et al. 2006). Because the results of genetic testing may be valuable to family members even if the patient is deceased, it is important to establish in advance which individual or individuals should have access to the patient's test results in their absence.
9. **Utilization of test results**. Options for cancer risk reduction and surveillance based on the patient's: level of risk for specific cancers, genotype, family history, medical history, dietary, and social habits should be presented. Patients should be encouraged to seek additional information from their referring physicians.
10. **Alternatives to genetic testing**. Patient decisions about genetic testing should be free from coercion. Patients may decide against genetic testing for cancer susceptibility for a variety of reasons including: 1) lack of interest, 2) indecision, 3) inadequate insurance coverage, and 4) uninformative results in an affected family member. When genetic testing is not done, risk assessment and related recommendations should be made based on the family and medical history. When appropriate and feasible, an affected patient's DNA should be banked allowing designated at-risk family members the opportunity to seek genetic testing in the future (Brown et al. 2006; Quillin et al. 2010).

Recommendation 5

Disclosure of genetic test results should include personalized interpretation of results, cancer risk re-assessment, and identification of at-risk family members, regardless of whether the result is positive, negative, or inconclusive.

Given the complexity of result interpretation and emotional responses elicited by all types of results, the disclosure of test results in person is often very helpful.

However, a randomized comparison of telephone versus in-person disclosure of *BRCA1/2* results did not identify any statistically significant differences in anxiety or general well-being between the two groups (Jenkins et al. 2007). Furthermore, new data suggest that telephone disclosure for select patients is frequently being used (Wham et al. 2010).

Elements of Disclosure:

- Address questions and concerns prior to disclosure of results
- Disclose test results with interpretation
- Assess patient reaction to and understanding of results, and provide emotional support
- Review medical and psychological impact of results on patient and family members
- Explain specificity, sensitivity and limitations of the specific genetic test performed
- Provide cancer risk re-assessment and medical management guidelines/recommendations (see below)
- Refer patient to appropriate health care providers
- Identify at-risk family members and provide patient with tools to inform and educate family members (i.e. family contact letter, website information, referrals to genetic professionals) (Brown et al. 2006; Gaff and Bylund 2010; Trepanier et al. 2004).

– If a patient refuses to share information with relatives, the genetic counselor should evaluate his/her potential legal and/or ethical duty to warn (Offit et al. 2004). This evaluation should include a consultation with their institution's HIPAA compliance officer and/or ethics committee.

Cancer screening and prevention options should be provided for the patient and at-risk relatives based on specifics of risk assessment and genetic testing, including their position in the pedigree, genetic testing results for the patient and family members, and related medical history.

Patients who test positive for a specific gene mutation associated with cancer susceptibility should be informed about management options specific to their genetic syndrome. For many syndromes, guidelines for management have been developed after rigorous clinical research prompting consensus statements from professional and advocacy groups. Sources of consensus statements include the National Comprehensive Cancer Network (NCCN), American Cancer Society (ACS), American College of Obstetrics and Gynecology (ACOG), Society of Gynecologic Oncologists (SGO), American Gastroenterological Association (AGA), and the American Thyroid Association (ATA). If consensus management guidelines do not exist for a patient's specific hereditary cancer syndrome, providers should present available options for treatment and prevention as detailed in the medical literature, and look for options for research participation for the family. In some situations, the specific mutation found may alter management guidelines. For instance, the recommended timing of preventive thyroidectomy varies from early infancy to after 5 years old depending on the specific *RET* mutation identified (Kloos et al. 2009).

Patients with a positive test result should be urged to notify at-risk relatives who may benefit from genetic testing. There is some evidence that suggests implementing a follow-up counseling program after test results are revealed, will increase the proportion of relatives informed of their genetic risk. This can include telephone conversations with the patient verifying which family members have been contacted and offering assistance in sharing this result information (Forrest et al. 2008).

For patients with negative genetic testing results, counseling unaffected individuals about their empiric risk of cancer requires careful consideration of the patient's personal and family history, often using empiric risk models, as discussed in detail under Recommendation 2. One should also consider testing another affected family member for mutations in the same gene, as the patient initially tested could be presenting with a phenocopy of the disease. Finally, additional diagnoses within the differential may need to be considered. Genetic testing is a powerful tool for establishing genetic diagnosis but, because many hereditary causes are still unknown and the sensitivity of existing tests is typically less than100 percent, patients with uninformative results may still be at increased risk for developing cancer. Individuals with negative test results should be encouraged to reconnect with the program over time to discuss changes in the family history information and advances in gene testing options.

Recommendation 6

Psychosocial assessment is critical and should be part of both the pre-test and post-test genetic counseling process.

The assessment begins by identifying the patient's primary reason for seeking the consultation and inquiring about the patient's current understanding of cancer genetics risk assessment and testing process. Any misconceptions should be addressed in a sensitive manner. Psychosocial issues that should be assessed include cancer worry, anxiety, intrusive thoughts, depression, anger, fear, guilt, family experiences with cancer, perception of risk for self and others, competence for giving informed consent, social stressors and supports and networks, family communications, and readiness for testing. Much of this information can be gained through the process of collecting the family medical history and discovering the impact cancer has had on the

family. Assessing the psychosocial impact often provides clues about how the counselee and family may understand and cope with disclosure of genetic testing information (Edwards et al. 2008; Pieterse et al. 2005; Pieterse et al. 2007). Expanded discussions about each of these elements have been published in great detail (Chivers-Seymour et al. 2010; Gaff and Bylund 2010; Koehly et al. 2009; Patenaude and Julien-Reynier 2008; Trepanier et al. 2004).

The psychological impact of genetic testing amongst individuals who have never been affected by cancer demonstrates that many people with negative test results derive significant psychological benefits from genetic testing. While no adverse effects have been observed among most people with positive test results, a select subset of people will be vulnerable to testing distress and require more professional assistance (Braithwaite et al. 2006; Meiser 2005). Sivell et al. (2007) suggest that cancer genetic risk assessment services help to reduce distress, improve the accuracy of the perceived risk of, and increase knowledge about, cancer and genetics.

If available, referral to support groups and research studies investigating the psychological impact of hereditary cancers should be considered. Other sources of support may include peer support, internet-based support organizations, and patient-focused gatherings focused on hereditary cancer (Kenen et al. 2007; McKinnon et al. 2007).

Conclusion

The above recommendations are considered essential for enhancing the quality of patient care. Procuring an accurate, targeted family and medical history is a critical component of effective cancer risk assessment. Developing a differential diagnosis allows the genetic professional not only to determine the nature of risk but also to accurately assess available genetic testing options. Selecting the appropriate genetic test informs clinical decision making and facilitates the prevention of adverse health outcomes (Robson et al. 2010) while reducing healthcare costs. Securing informed consent prior to genetic testing respects patient autonomy. Effective disclosure of genetic test results facilitates patient understanding, communication to at-risk family members, and appropriate clinical management. Finally, incorporating a psychosocial assessment throughout the genetic counseling and testing process assists in evaluating the patient's understanding and responses to risk information, support resources, and coping mechanisms. Utilization of these guidelines by professionals providing cancer risk assessment and counseling will help ensure that patients and their families gain the most from the preventive benefits of genetic medicine.

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