



## Complete Summary

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### GUIDELINE TITLE

Neurofibromatosis type 1 in genetic counseling practice: recommendations of the National Society of Genetic Counselors.

### BIBLIOGRAPHIC SOURCE(S)

Radtke HB, Sebold CD, Allison C, Haidle JL, Schneider G. Neurofibromatosis type 1 in genetic counseling practice: recommendations of the National Society of Genetic Counselors. *J Genet Counsel* 2007 Aug;16(4):387-407. [160 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  
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QUALIFYING STATEMENTS  
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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES  
IDENTIFYING INFORMATION AND AVAILABILITY  
DISCLAIMER

## SCOPE

### DISEASE/CONDITION(S)

Neurofibromatosis Type 1 (NF1)

### GUIDELINE CATEGORY

Counseling  
Risk Assessment

### CLINICAL SPECIALTY

Dermatology  
Family Practice

Internal Medicine  
Medical Genetics  
Neurological Surgery  
Neurology  
Nursing  
Obstetrics and Gynecology  
Oncology  
Orthopedic Surgery  
Pediatrics  
Psychology  
Surgery

### **INTENDED USERS**

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

### **GUIDELINE OBJECTIVE(S)**

To serve as a comprehensive resource for health care professionals providing genetic counseling to patients and families undergoing evaluation for neurofibromatosis type 1 (NF1) or who have received a diagnosis of NF1

Specifically,

- To review the history, epidemiology, and genetics of NF1
- To summarize the current understanding of the natural history of NF1
- To provide a framework for the genetic counseling sessions of individuals and families with NF1
- To present a list of resources for patients and families with NF1

### **TARGET POPULATION**

Patients and families undergoing evaluation for neurofibromatosis type 1 (NF1) or who have received a diagnosis of NF1

### **INTERVENTIONS AND PRACTICES CONSIDERED**

1. Genetic counseling
2. Medical and developmental history
3. Family history
4. Psychological assessment and counseling, including unique psychosocial concerns
5. Risk assessment

6. Patient and family education addressing clinical features and natural history of neurofibromatosis Type 1 (NF1), inheritance pattern and recurrence risk, prenatal testing and reproductive options, alternate risk reduction, and signs and symptoms that warrant immediate referral and evaluation
7. Obtaining informed consent for DNA testing
8. Aiding patients in identifying additional support services

#### **MAJOR OUTCOMES CONSIDERED**

- Establishment of patient/counselor rapport in the neurofibromatosis (NF) counseling process
- Accuracy of NF risk assessment

### **METHODOLOGY**

#### **METHODS USED TO COLLECT/SELECT EVIDENCE**

Searches of Electronic Databases

#### **DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE**

MEDLINE, PubMed and Internet databases were searched (using the key words neurofibromatosis type 1, NF1, neurofibromin) to locate relevant English language medical papers published between 1966 and 2007.

#### **NUMBER OF SOURCE DOCUMENTS**

Not stated

#### **METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE**

Expert Consensus  
Subjective Review  
Weighting According to a Rating Scheme (Scheme Given)

#### **RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE**

- 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. The 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**

The literature was reviewed and evaluated according to categories outlined by the US Preventive Services Task Force (1995) (see "Rating Scheme for the Strength of the Evidence"). Particular attention was paid to genetic counseling issues.

## **METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Expert Consensus

## **DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS**

These recommendations are the opinions of a multi-center working group of genetic counselors with expertise in the care of individuals with neurofibromatosis type 1 (NF1). These recommendations are based on the committee's clinical experiences, a review of pertinent English language medical articles, and reports of expert committees.

The NF1 Working Group was composed of genetic counselors with experience in various NF1 Clinics throughout the United States.

## **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**

Following the completion of the initial draft of the guidelines, the Neurofibromatosis Type 1 (NF1) Working Group elicited opinions and feedback from noted medical experts in the field, as well as representatives of NF1 support and advocacy organizations. These recommendations were approved by the National Society of Genetic Counselors Board of Directors in March, 2007.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

#### Genetic Counseling

##### **Contracting**

As with other genetic counseling indications, ascertaining the family's understanding of the reason for the visit as well as their primary questions and concerns, and mutually developing a plan to address these concerns, are key components of establishing rapport in the neurofibromatosis (NF) counseling process.

##### **Medical and Developmental History**

See Figure 1 in the original guideline document for a sample clinic intake form.

##### **Family History**

To identify additional family members who may be affected with NF, obtain at least a three generation, targeted pedigree from the consultand or proband using standardized pedigree symbols. When possible, verify positive or questionable family history with medical records.

Suggestions for a targeted family history (these targeted questions may also aid in differential diagnosis):

- Birthmarks or other targeted skin findings
- Benign growth or tumors
- Malignant tumor or cancer
- Significant hearing problem such as hearing loss or ringing of the ears
- Significant vision problem such as tumor, poor vision, or blindness
- Bone or joint problems (fractures, dislocations, curved spine)
- Developmental delay, learning disability, attention deficit hyperactivity disorder (ADHD) or mental retardation (MR)
- Seizures, epilepsy or other nervous system problems
- Macrocephaly

##### **Psychosocial Assessment and Counseling**

Similar to genetic counseling for other conditions, obtaining a thorough psychosocial history and assessment is critical to the NF counseling process.

*Suggestions for a Targeted Psychosocial History/Assessment*

- Level of education
- Possible barriers to communication, including cultural/language diversity or the presence of learning disabilities

- Current level of knowledge regarding diagnosis of neurofibromatosis Type 1 (NF1)
- Family's understanding and perception of medical information
- Previous experiences with NF1, if any
- Family's perception of the etiology of NF1
- Emotional reaction to the diagnosis of NF1
- Family structure and functioning
- Family and community support systems
- Coping skills
- Meaning of a genetic diagnosis for the family, including implications for family planning and parenting

In addition to topics that are covered during a typical genetic counseling session, individuals with NF1 may have some unique psychosocial concerns that need to be addressed.

- a. Realize that many individuals have received information about NF1 from other sources (Internet, physicians, etc.), and that this information may be inaccurate, outdated, or only representative of the most severe cases of NF1.
- b. Recognize that the list of potential complications associated with NF1 is extensive. Appreciate that the information may be overwhelming for some individuals. The genetic counselor should use his or her clinical judgment in gauging the appropriate amount of information discussed during a session and may wish to continue discussions at subsequent appointments.
- c. Assess perception of the risk for malignancy. The term "tumors" can be especially frightening and it should be stressed that most NF tumors are benign. Malignancy risks should be discussed in the context of the general population's cancer risk, which is approximately 41%.
- d. Address concerns and fears regarding the variable and unpredictable natural history of NF1. Explain that the majority of individuals lead productive lives, meaning that they are able to attend school, be employed, and live independently. Providing the family with a list of concerning symptoms (See "Education," below) can be helpful in giving the family a sense of control when they are experiencing anxiety about the unpredictable nature of NF1.
- e. Assess perception of the impact of NF1 on the individual's daily life, with a focus on cosmetic and medical concerns.
- f. Discuss family's concerns regarding labeling and self-fulfilling prophecies. Many parents are concerned that the diagnosis of a genetic condition will lower a child's self-expectations or the expectations of others for the child.
- g. Assess the family's knowledge and perception of the Elephant Man. Despite the current belief that "The Elephant Man" did not have NF1, older literature and resources often refer to NF1 as the disease of "The Elephant Man." Families of patients with NF1 may still be affected by the association of NF1 with the difficult life of Joseph Merrick.
- h. Elicit the individual's experiences at school, work and other social situations. In addition to the learning disabilities, many NF1 patients have difficulty with social skills. This may also be impacted by the co-occurrence of ADHD.
- i. Be aware of issues regarding counseling an individual with a learning disability. In familial cases of NF1, a parent may also have a learning disability. This may affect an individual's understanding and perception of the disorder, their ability to recognize or cope with the potential medical issues, and their comprehension of the genetic implications for future offspring. In

- these families, it is particularly important to determine the level of understanding and adjust the counseling session to reflect the family's comprehension level. It is also important to keep in mind that individuals with learning disabilities may prefer alternate methods of receiving information and may benefit from reinforcement at follow-up visits.
- j. As indicated, assist the family in navigating the complexities of special education and/or other interventional services. Many individuals with NF1 require additional services in school, and obtaining these services may prove challenging and frustrating.

### **Risk Assessment**

In order to complete an accurate risk assessment, it is crucial to determine whether the disease and/or mutation was inherited or de novo. This can often be accomplished through physical and ophthalmologic examination of the proband's parents. Alternatively, if a DNA mutation has been identified in the patient, molecular genetic testing can be performed.

#### *If the Mutation is De Novo*

Risk for siblings of proband is low (thought to be less than 1%), but remains increased due to the possibility of germline mosaicism (see "Special Considerations," below).

#### *If the Mutation is Familial*

Apply principles of autosomal dominant inheritance to pedigree. All offspring of an affected parent have a 50% risk to inherit the mutation. As indicated, identify nearest genetics/NF clinic for affected relatives not living in the area.

### **Education**

#### **Clinical Features and Natural History**

Review the main features of the condition, its natural history, and the typical timeline for the development of features. See "Natural History" in the original guideline document.

#### **Inheritance Pattern and Recurrence Risk**

NF1 is an autosomal dominant condition. Approximately 50% of NF1 cases are inherited from a parent. The remaining 50% of cases of NF1 are due to a de novo mutation in the proband. This is felt to be due, in part, to the large size of the NF1 gene, which makes it more susceptible to mutation. Penetrance is essentially 100%, but expressivity is variable, even amongst family members. If neither parent of the proband has NF1, the chance of recurrence is low. However, because of the possibility of germline mosaicism, the recurrence risk is likely somewhat higher than the general population risk (see "Special Considerations" below).

Please see "Variants of NF1" in the original guideline document for recurrence risks for segmental NF.

### **Prenatal Testing and Reproductive Options**

Prenatal molecular genetic testing is available for families in which the mutation has been identified in the proband. Alternatively, if there are multiple affected family members, and linkage has been established within the family, linkage analysis is an option. In these situations, prenatal diagnosis is possible via chorionic villus sampling (CVS) or amniocentesis. In the vast majority of cases, ultrasound is not useful in the prenatal diagnosis of NF1. There are some reports of prenatal identification of NF1-related abnormalities. These abnormalities included cardiac and craniofacial anomalies as well as tumors. However, the abnormalities included in these reports were atypical for NF1, and in only one instance was the diagnosis of NF1 considered before birth.

Given the variability and unpredictable nature of the condition, genetic counseling is critical for a couple considering prenatal testing for NF1. Genetic counseling informs a couple about the signs, course, and genetics of NF1. It also facilitates the discussion of personal, moral, and ethical issues they need to explore in order to make an autonomous decision that meets their needs.

### **Alternate Risk Reduction Options**

In families where a parent is affected and the risk to offspring is 50%, various options can reduce the risk in a future pregnancy. The use of assisted reproductive technology with a donor gamete from an unaffected individual in place of the gamete from the affected parent can greatly reduce the risk to future children. Alternatively, preimplantation genetic diagnosis (PGD) may be available for couples in which the causative NF1 mutation has been identified or if linkage phase has been established.

### **Signs and Symptoms that Warrant Immediate Referral and Evaluation**

Parents and patients often find it helpful to be informed of what types of symptoms warrant an immediate referral and evaluation.

#### *Signs/Symptoms Warranting Immediate Referral*

- Pain of unknown etiology
- Weakness, numbness, tingling in the extremities
- Change in balance or coordination
- Change in vision
- Change in intensity or frequency of headaches
- Neurofibromas that change rapidly in size and/or color, or cause pain
- Abnormal neurologic exam
- Sudden onset of hypertension
- Regression of cognitive skills or loss of developmental milestones
- Significant deviation from individual's established pattern of growth

### **Follow-up**

## **Management**

Management recommendations for patients with NF1 vary between centers and must be tailored to the individual. It is not the intention of this guideline to address specific management recommendations. It should be noted, however, that management of these patients typically requires a multidisciplinary team. Disciplines that may be involved in the care of a patient with NF1 are listed in Table VIII in the original guideline document.

## **Documentation**

Providers are encouraged to thoroughly document all patient interactions. This may be done via a patient summary letter and/or a physician note. In many centers, these two forms of documentation are combined. Please see Table IX in the original guideline document for a list of suggested items to be included.

## **Special Considerations**

### **Germline Mosaicism**

Germline mosaicism is a recognized phenomenon occurring in a number of dominant genetic disorders and has been observed in NF1. Therefore, caution must be used when discussing recurrence risks with the parents of a child with an apparently de novo case of NF1, even if parental lymphocyte analysis is negative following mutation identification in the proband. Nevertheless, it is estimated that the risk for recurrence due to germline mosaicism is less than 1%.

### **Consent for DNA Testing**

Informed consent for molecular analysis should be obtained from the patient or legal guardian prior to the acquisition of a sample for DNA testing. A consent form from the clinical testing laboratory should be reviewed with the family. Typically, this form describes the limitations and benefits of testing, how results will be reported, and any other potential uses of the specimen.

### **Patient Resources**

It is important to aid the family in identifying additional sources of supports, such as advocacy and support groups, and other families. A list of patient resources is listed in Table X in the original guideline document.

## **CLINICAL ALGORITHM(S)**

None provided

## **EVIDENCE SUPPORTING THE RECOMMENDATIONS**

## **TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS**

The rating of supporting literature for the recommendations is Class III (opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees).

## **BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS**

### **POTENTIAL BENEFITS**

- Effective genetic counseling for neurofibromatosis type 1 (NF1)
- Accurate risk assessment for NF1
- Effective education of patients and families with NF1

### **POTENTIAL HARMS**

Not stated

## **QUALIFYING STATEMENTS**

### **QUALIFYING STATEMENTS**

- These recommendations are not intended to dictate an exclusive course of management, nor does the 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 an individual patient.
- This document is not intended to replace the judgment of an individual genetic counselor with respect to particular patients or special clinical situations and cannot be considered inclusive of all practices or exclusive of other practices reasonably directed at obtaining the same results. In addition, the practice of genetic counseling is subject to regulation by federal, state and local governments. In a subject jurisdiction, any such regulations will take precedence over this statement. The National Society of Genetic Counselors (NSGC) expressly disclaims any warranties or guarantees, express or implied, and shall not be liable for damages of any kind, in connection with the information set forth in this document or for reliance on its contents.

## **IMPLEMENTATION OF THE GUIDELINE**

### **DESCRIPTION OF IMPLEMENTATION STRATEGY**

An implementation strategy was not provided.

### **IMPLEMENTATION TOOLS**

Chart Documentation/Checklists/Forms

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Living with Illness

### IOM DOMAIN

Effectiveness  
Patient-centeredness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Radtke HB, Sebold CD, Allison C, Haidle JL, Schneider G. Neurofibromatosis type 1 in genetic counseling practice: recommendations of the National Society of Genetic Counselors. *J Genet Counsel* 2007 Aug;16(4):387-407. [160 references]  
[PubMed](#)

### ADAPTATION

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

### DATE RELEASED

2007 Aug

### GUIDELINE DEVELOPER(S)

National Society of Genetic Counselors - Medical Specialty Society

### SOURCE(S) OF FUNDING

This project was supported by the National Society of Genetic Counselors, Inc.

### GUIDELINE COMMITTEE

NF1 Working Group

### COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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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 available from the [National Society of Genetic Counselors, Inc. Web site](#).

Print copies: Available from the National Society of Genetic Counselors, 401 N. Michigan Avenue, Chicago, IL 60611; Web site: <http://www.nsgc.org/>.

## **AVAILABILITY OF COMPANION DOCUMENTS**

A sample intake form for a neurofibromatosis type 1 (NF1) clinic visit is available in the [original guideline document](#).

## **PATIENT RESOURCES**

None provided

## **NGC STATUS**

This NGC summary was completed by ECRI Institute on May 30, 2008. The information was verified by the guideline developer on June 23, 2008.

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