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Awareness and Agreement with Neurofibromatosis Care Guidelines among Neurofibromatosis Specialists

Running Title: Awareness and Agreement with NF Care Guidelines

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Abstract

Background: Given the wide range of neurofibromatoses (NF) symptoms and medical specialties involved in NF care, we sought to evaluate the level of awareness of, and agreement with, published NF clinical guidelines among United States NF specialists.

Methods: An anonymous, cross-sectional online survey was distributed to attendees of a large NF research conference. Respondents self-reported demographics, practice characteristics, awareness of seven NF guideline publications, and level of agreement with up to 40 individual guidelines using a 5-point Likert scale. We calculated the proportion of guidelines that each clinician rated “strongly agree”, and assessed for differences in guideline awareness and agreement by respondent characteristics.

Results: Sixty-three clinicians (49% female; 80% academic practice) across >8 medical specialties completed the survey. Awareness of each guideline publication ranged from 53%-79% of respondents; specialists had higher awareness of publications endorsed by their medical professional organization (p<0.05). The proportion of respondents who “strongly agree” with individual guidelines ranged from 17%-83%; for 16 guidelines, less than 50% of respondents “strongly agree”. There were no significant differences in overall agreement with guidelines based on clinicians’ gender, race, specialty, years in practice, practice type (academic/private practice/other), practice location (urban/suburban/rural), or involvement in NF research (p>0.05 for all).

Conclusions: We identified wide variability in both awareness of, and agreement with, published NF care guidelines among NF experts. Future efforts should focus on evidence-based, consensus-driven methods to update and disseminate guidelines across this multi-specialty group. Patients and caregivers should also be consulted to anticipate barriers to accessing and implementing guideline-driven care.

Keywords: neurofibromatosis 1, neurofibromatosis 2, schwannomatosis, practice guidelines,
Introduction

The neurofibromatoses (NF) - neurofibromatosis 1 (NF1), neurofibromatosis 2 (NF2) and schwannomatosis - are rare genetic disorders that predispose patients to develop multiple nerve sheath tumors and many other physical, neurocognitive, and psychosocial symptoms. Given the varied clinical spectrum of these diseases, physicians from multiple medical specialties provide care for NF patients. For example, patients with NF1 may visit pediatricians for initial evaluations; neurologists or neuro-oncologists for brain tumors, learning disabilities, headaches, or focal neurological deficits; plastic surgeons or dermatologists for cutaneous neurofibromas; orthopedic surgeons for scoliosis or pseudoarthrosis; and various other specialists for their complex disease. The need for specialty care for the wide range of manifestations of NF may lead to fragmented care, highlighting the critical importance of disseminating clinical best practices.

Clinical practice guideline publications provide clinicians with collated recommendations based on systematic evidence reviews, while expert review documents provide recommendations where evidence-based data is more limited. Currently there are seven peer-reviewed publications providing clinical care recommendations for NF, hereafter referred to collectively as ‘NF guidelines’. Prior work has shown the importance of clinicians’ knowledge and attitudes - including their familiarity and agreement with guidelines – in predicting implementation of clinical guidelines. However, to date, there is no evidence of how broadly NF guidelines have been disseminated across the various specialties caring for NF patients, nor is there data on the agreement with or use of these guidelines. Therefore, we sought to evaluate the awareness of, and agreement with, NF guidelines among NF clinicians as a first step to developing consensus on NF clinical best practices.
**Materials and Methods:**

**Participant Recruitment**

United States based clinicians (including physicians, advanced practice providers, and other health care providers) who currently care for neurofibromatosis patients were eligible to participate in the survey. Potentially eligible participants were identified using registration lists for the 2016-2018 Children’s Tumor Foundation NF conferences, the largest NF-specific research conference in the U.S. Registration lists did not reliably differentiate whether conference attendees were clinicians or non-clinicians nor their country of residence, so all potentially eligible participants (n=358) were included in the recruitment process and we relied on screening questions at the start of the survey to filter out non-clinicians and those residing outside the U.S. An invitation to complete the survey was emailed to this cohort by the chair of the Children’s Tumor Foundation Clinical Care Advisory Board in September 2019, with a follow-up reminder email two weeks later. Participation in the survey was voluntary and anonymous. Participants read a short fact sheet about the study and indicated their consent to participate by completing the survey. The study protocol was reviewed by the Mass General Brigham Institutional Review Board and was deemed to meet criteria for exemption.

**Survey Design**

This cross-sectional survey was administered online using REDCap, a secure online data collection platform. Respondents were asked to self-report demographic data and practice characteristics [i.e. gender, race, ethnicity, medical specialty, years in practice, practice type (academic practice/private practice/other), practice location (urban/suburban/rural), involvement in NF research, affiliation with the Children’s Tumor Foundation NF Clinic Network, and whether their practice
currently included pediatric and adult NF1, NF2, and schwannomatosis patients.] The research team identified six relevant NF guideline publications3-8 via literature review to include in the survey (as French guidelines from Bergqvist et al. (2020) were published after this survey was administered). All respondents were asked to identify whether they were previously aware, unaware, or unsure about each publication [which were identified by first author, title, journal, publication year, PubMed ID and primary topic area (i.e. pediatric NF1)]. Respondents were asked about their awareness of all six NF guideline publications, even if their practice did not currently include the specific NF patient population addressed by the publication, under the assumption that clinicians should have broad knowledge of these resources to remain current with the field, to be prepared to coordinate care for new patients, and to help pediatric patients transition to adult care.

One author (JTJ) extracted 40 individual guidelines from five guideline publications4-8 for assessment of guideline agreement (as pediatric NF1 guidelines from Miller et al. (2019) were published after this section of the survey was finalized). Guidelines were largely extracted verbatim, with minor changes in wording to combine nearly identical guidelines from multiple publications or to improve grammar (see Table 1 for full list of guidelines). All guidelines were assessed by two authors (JTJ and VLM) to determine the relevant patient population addressed (i.e. pediatric or adult; NF1, NF2, or schwannomatosis). Respondents were asked to rate their agreement with each individual guideline relevant to their practice population using a 5-point Likert scale (strongly agree to strongly disagree, with neutral as the midpoint). The study size was determined by the number of eligible respondents who completed at least one guideline agreement rating.

Data Analysis

Descriptive data on all variables are reported as frequencies and percentages. Only questions assessing study eligibility and determining the subpopulations of NF included in each clinicians’
practice were mandatory; all other questions were optional, and percentages are reported out of the sample size of non-missing responses unless otherwise noted. Due to the risk of acquiescence bias (the tendency for some survey respondents to select positive response options)\textsuperscript{13}, we focused our reporting of clinicians’ agreement with NF guidelines on the percentage of respondents who selected “strongly agree”, thus actively indicating a strong preference in favor of each guideline. As clinicians’ level of support for a clinical practice guideline is associated with their adherence to guidelines is practice\textsuperscript{14,15}, this type of top-box analysis (used often in patient experience surveys)\textsuperscript{16-18} may best predict clinicians’ real-world behavior.

We examined whether clinician demographics or practice characteristics were correlated with level of agreement with NF clinical guidelines. Given the large number of individual guidelines and respondent subgroups of interest (and concomitant risk of Type 1 error from performing multiple comparisons), we assessed clinicians’ overall agreement with all clinical guidelines relevant to their own practice populations. To do this, we calculated the proportion of guidelines to which each clinician ‘strongly agreed’ as a proportion of the total number of guidelines for which they completed ratings. This proportion could range from 0 (does not strongly agree with any guidelines) to 1 (strongly agrees with all guidelines). This proportion was compared across respondent subgroups used t-tests or ANOVA as appropriate.

Finally, two NF1 guidelines publications were endorsed by U.S. medical societies – Miller et al. guidelines for pediatric NF1 published by the American Academy of Pediatrics (AAP) and endorsed by the American College of Medical Genetics and Genomics\textsuperscript{3} (ACMG) and Stewart et al. guidelines for adult NF1 published by ACMG\textsuperscript{4}. To better understand guideline dissemination patterns, we assessed whether clinicians in these professions (pediatrics and medical genetics, respectively) were more likely
to report being aware of guideline publications than clinicians in other specialties using Fisher’s exact test. A p-value of $\leq 0.05$ was considered statistically significant for all tests.

**Results:**

Eighty-two U.S. based clinicians accessed the survey; twelve did not complete any questions beyond eligibility screening and an additional seven did not complete any guideline agreement questions, resulting in a final analytic sample of 63 people [63/358 (17.6%) of potentially eligible respondents, 63/82 (76.8%) of eligible respondents who accessed the survey]. Clinician demographics, practice characteristics, and type of NF specialization are shown in Table 2. Clinicians represented >8 medical or surgical specialties, with one-third (n=21) of respondents in neurology or neuro-oncology. Clinicians were located across the U.S., representing 26 U.S. states with the greatest number of respondents from New York, California, Florida, Massachusetts, and Minnesota (respectively). Most respondents (n=50, 79.4%) provided clinical care as part of a specialized neurofibromatosis clinic affiliated with the Children’s Tumor Foundation NF Clinic Network\(^{19}\) and the majority were involved in NF research (n=39 for clinical trials and n=47 for non-treatment research studies such as tumor banks, natural history studies or questionnaire-based research).

**Guideline Awareness**

Clinicians self-reported their awareness of publications containing NF clinical care guidelines (Table 3). The percentage of respondents who were aware of each guideline set ranged from 53.2% (for schwannomatosis guidelines within Evans et al. 2017) to 79.4% (for pediatric NF1 guidelines published by Ferner et al. 2007). Among only those respondents who reported currently seeing the relevant patient population, awareness was only marginally increased (by 1.1 to 5.1 percentage points), with the
exception of adult NF2 guidelines by Evans et al. 2005, in which awareness increased 11.6 percentage points to 65.7% of respondents. Overall, 26-36% of respondents were unaware of recently published guideline documents (2017-2019). Medical geneticists were significantly more likely to report awareness of adult NF1 guidelines endorsed by the ACMG than clinicians of other specialties (100% of medical geneticists vs. 56.1% of other specialists, p=0.0008). Pediatricians and medical geneticists were also more likely to report awareness of pediatric NF1 guidelines endorsed by the AAP and the ACMG (87.0% of pediatricians and medical geneticists vs. 55.6% of other specialists, p=0.021).

Guideline Agreement

Overall, less than half of survey respondents had strong agreement with 16/40 (40%) of NF guidelines. Clinicians’ level of agreement with NF1 guidelines are presented in Figure 1. Total number of respondents eligible to respond was n=55 for pediatric NF1 guidelines, n=51 for adult NF1 guidelines; and n=61 for NF1 guidelines applicable across both age cohorts. Level of strong agreement with individual guidelines ranged from 17% to 83%. Strong agreement was highest for the preference of MRIs over CT scans to reduce exposure to ionizing radiation exposure (83%); annual blood pressure checks (80%); education about signs and symptoms of malignant peripheral nerve sheath tumors (76%); and annual check-ins on development and school progress for pediatric patients (76%). For 9/26 (34.6%) of NF1 guidelines, less than half of respondents selected ‘strongly agree’. These guidelines addressed breast cancer screening, counseling regarding family planning, vitamin D supplementation, evaluation of hypertension, pregnancy management, assessment of glomus tumors, and use of whole-body MRI.

Clinicians’ level of agreement with NF2 and schwannomatosis guidelines are presented in Figure 2. Total number of respondents eligible to respond was n=48 for pediatric NF2 guidelines; n=53 for
guidelines applicable to pediatric and adult NF2; and n=36 for schwannomatosis guidelines. Level of strong agreement with individual NF2 guidelines ranged from 36% to 73%. Strong agreement was highest for receiving care at specialized NF clinics (73%) and for receiving care annually at an NF clinic (72%). For 4/11 (36.4%) of NF2 guidelines, less than half or respondents selected ‘strongly agree’. These guidelines addressed the frequency of spinal MRIs in all patients and the timing of brain MRIs for pediatric patients. Agreement was noticeably lower for pediatric imaging recommendations including the provision to start surveillance at age 10 when compared to identical adult guidelines (absolute difference of 15.4 percentage points for brain MRIs and 9.3 percentage points for spinal MRIs). Level of strong agreement with three schwannomatosis guidelines addressing genetic testing for younger patients with potential schwannomatosis and the timing of brain and spine MRIs (including age at baseline scan and frequency of imaging) ranged from 27-38%.

The median proportion of guidelines with which each clinician strongly agreed was 0.55 (range, 0-1; 25th-75th percentile, 0.35 to 0.73). There were no statistically significant differences in guideline agreement proportion based on clinicians’ gender, race, specialty, years in practice, practice type, practice location, participation in the NF Clinic Network, involvement in NF treatment trials, or involvement in non-treatment NF research. Medical geneticists were no more likely to than other specialists to strongly agree with adult NF1 guidelines endorsed by the ACMG (agreement index 0.52 vs. 0.53, p=0.89). As guidelines were not systematically extracted from the pediatric NF1 guidelines endorsed by the AAP and ACMG, a parallel test of pediatricians’ agreement with these guidelines was not performed.

Discussion

We evaluated NF specialists’ agreement with NF clinical guidelines to assess the efficacy of guideline dissemination and identify any areas of disagreement regarding best practices for NF clinical
care. We identified wide variability in both awareness of, and agreement with, NF published guidelines among NF experts. While many respondents were aware of relevant guideline publications, and most guidelines did not have large proportions of disagreement, our findings highlight areas warranting further attention as the multidisciplinary NF community strives to reach consensus on optimal care recommendations. Approximately one-quarter to one-third of respondents were unaware of recently published NF guideline documents, and the majority of survey respondents did not strongly agree with 40% of assessed guidelines. While clinician’s primary specialty appears to be related to awareness of NF guidelines, no demographic or practice characteristics were associated with clinicians’ overall level of agreement with NF guidelines.

Clinicians’ awareness of and familiarity with clinical guidelines is the first step in providing guideline-driven care, but can be inhibited by the large volume of information each clinician must process and the limited time they have available to stay informed with literature. Our findings suggest that clinicians may be more aware of guidelines published by their affiliated medical professional organization (although we could not demonstrate whether they were also more likely to agree with these guidelines). Given the multi-system manifestations of NF and diverse array of specialists involved in NF care, the field should evaluate strategies for broader dissemination of existing guidelines across specialties. Prior research suggests a multifaceted dissemination approach using both written materials (e.g. journal articles, checklists, educational materials, etc.) and personal appeals (e.g. via local discussion forums or one-on-one contacts from peers) may be most effective. Rather than duplicate prior guideline creation efforts, medical societies relevant to NF may also want to review, endorse, and republish relevant guidelines with high agreement to facilitate multidisciplinary collaboration in NF patient care.
However, there remains a number of NF guidelines lacking strong agreement. Potential sources of this reduced enthusiasm for certain guidelines are several-fold. First, perceived lack of evidence on efficacy or utility of a guideline-recommended assessments may limit agreement. For example, the utility of whole body MRI is under study and routine use is increasing; however, the optimal use, timing and interpretation of this technology is not yet known.\(^4\) Furthermore, not all medical centers have this imaging capability nor do all insurance plans cover whole body MRI for this indication. This inability to reliably implement a guideline-recommended assessment may also lead to lower levels of strong agreement. Another informative example is guidelines on the preferred timing and modality for breast cancer screening in adult women with NF1. There may be lower community agreement on guidelines where additional prospective research evidence is needed (such as comparative effectiveness research on breast MRI vs. mammography) or where standardized guidelines may conflict with individualized patient preferences (such as when personalized shared-decision making is needed to determine optimal screening schedules)\(^4\) Finally, response to guideline agreement may be impacted by lack of clarity as to which population or clinical context is intended.

This empirical data on agreement with NF clinical guidelines among U.S. specialists can inform discussions on the value of, evidence base for, and implementation of NF clinical guidelines. For guidelines with weaker agreement, consensus-based methods across medical specialties should be used to review guidelines, understand opposition to recommended health services, and propose any necessary clarifications and revisions. Any updated guidelines should adhere to best practices for guideline development.\(^22\) For example, the Appraisal of Guidelines, Research and Evaluation (AGREE II) instrument can be used to assess the quality of existing clinical guidelines and provide guidance on appropriate development and reporting of revised guidelines.\(^23\) Many sources emphasize writing clear, unambiguous guidelines that are explicitly and transparently linked to the underlying evidence base.\(^24,25\)
For guidelines with insufficient evidence to support widespread agreement and adoption, funders could prioritize systematic evidence reviews and/or additional prospective studies on the value of recommended interventions.

Recent research also emphasizes the need to incorporate patient perspectives in guideline development. Interdisciplinary teams that include clinicians across multiple specialties and methodologists in implementation science, guideline development, and qualitative research may be best poised to meaningfully incorporate patient preferences into guidelines and address real-world barriers to implementation. It is important to address external barriers such as patients preferences that conflict with guideline recommendations and environmental factors (such as lack of time, resources, or insurance approval) to ensure widespread implementation of guidelines. Input from clinicians, patients, and family members from diverse practice settings and geographic locations should be sought to understand access and barriers to receiving guideline-driven care. A survey of patients and their family members/caregivers to assess receipt of guideline-concordant care is currently being developed for an NF patient registry for this purpose.

There are several limitations to this study. As we desired to get broad input from the NF community on current guidelines, our recruitment email was sent to a large distribution list and the exact number of eligible clinicians approached and their response rate is unknown. While the exact percentage of NF clinicians who are aware of or agree with guidelines in our cross-sectional sample may vary from the overall population of U.S. NF specialists, our findings highlight important areas of disagreement that likely need to be addressed. Our target population was clinicians attending NF-specific research conferences, who likely specialize in NF and see a high volume of NF patients. This population is likely more aware of NF guideline publications and possibly more likely to agree with guidelines than the larger group of clinicians who care for NF patients. Future work should seek to
understand how primary care clinicians find and use guidelines for patients with rare diseases who may be unique in their practice, and how specialists and primary care clinicians can share responsibilities for providing guideline-concordant care for such patients (especially for routine monitoring and surveillance). Finally, due to the large number of guidelines relative to our sample size, we did not statistically test for demographic or practice factors that may influence agreement with individual guidelines. Qualitative work exploring clinicians’ reasons for not strongly agreeing with specific NF guidelines would be informative in revising guidelines and developing additional interventions to promote guideline use.

In conclusion, our study demonstrates that there is significant variation in levels of strong agreement with NF clinical guidelines. For guidelines with strong agreement, future efforts to enhance guideline use should prioritize broad dissemination of guidelines across medical specialties. A focus on implementation of guidelines in routine care – for example, by providing multiple versions of guidelines adapted for different users and purposes, and organizing and formatting content to make it easy to understand and use – will enhance the success of dissemination efforts. For guidelines with weak or mixed agreement, future efforts to improve guideline relevance and use should prioritize evidence-based, consensus-driven approaches to reviewing and updating guidelines. An international Delphi panel, such as that used recently to revise NF diagnostic criteria, may be an efficient approach to gather widespread input from all relevant stakeholders, including patients and their family members. Together these initiatives could help combat common barriers to guidelines awareness, agreement, and implementation, maximizing the chances for guideline adherence and the delivery of high-quality NF care in the future.
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Figure 1. NF Clinician Agreement with Neurofibromatosis 1 Guidelines

Figure 1 Legend: Stacked bar charts displaying the percentage of clinicians who “strongly agreed” (dark blue), “agreed” (orange), were “neutral” (gray), “disagreed” (yellow), or “strongly disagreed” (light blue) with each guideline. Overlaid boxes display the percentage of clinicians who “strongly agreed” (dark blue) and “agreed” (orange) to each guideline, rounded to the nearest percentage point. Guidelines are presented with short descriptions for reference; for full guideline text and citations please refer to Table 1, where all guidelines are presented in the same rank order. Abbreviations: CT = computerized tomography; HTN = hypertension; NF = neurofibromatosis; MPNST = malignant peripheral nerve sheath tumor; MRA = magnetic resonance angiography; MRI = magnetic resonance imaging; WBMRI = whole body magnetic resonance imaging.

Figure 2: NF Clinician Agreement with Neurofibromatosis 2 and Schwannomatosis Guidelines

Figure 2 Legend: Stacked bar charts displaying the percentage of clinicians who “strongly agreed” (dark blue), “agreed” (orange), were “neutral” (gray), “disagreed” (yellow), or “strongly disagreed” (light blue) with each guideline. Overlaid boxes display the percentage of clinicians who “strongly agreed” (dark blue) and “agreed” (orange) to each guideline, rounded to the nearest percentage point. Guidelines are presented with short descriptions for reference; for full guideline text and citations please refer to Table 1, where all guidelines are presented in the same rank order. Abbreviations: NF = neurofibromatosis; MRI = magnetic resonance imaging; PTA = pure tone average; WRS = word recognition score. SMARCB1 and LZTR1 refer to gene variants known to cause schwannomatosis.
Table 1. NF Clinical Guidelines Assessed in the Current Study

| Neurofibromatosis 1 (NF1) Guidelines |
|--------------------------------------|
| MRI is preferred over CT scanning to reduce ionizing radiation exposure in patients with NF1.⁴ |
| Blood pressure should be recorded at least annually in patients with NF1 from early childhood through adulthood.⁴, ⁵, ⁷ |
| Patients with NF1 should be educated about malignant peripheral nerve sheath tumor (MPNST) signs and symptoms at initial and follow up visits.⁴, ⁷ |
| Development and progress at school should be recorded at each annual visit for pediatric patients with NF1.⁵ |
| For hypertensive patients with NF1 who are under 30 years of age, pregnant and/or have abdominal bruits, causes of renovascular hypertension should be evaluated.⁴ |
| Height and weight should be recorded for patients with NF1 at every visit until one year old, then at least annually until adulthood.⁵ |
| Patients with NF1 under 8 years old should have annual testing of visual acuity and fundoscopy to assess for optic disc pallor and elevation.⁵ |
| Neurologic examination should be performed routinely for patients with NF1 from one month to one year of age, then annually until adulthood.⁵ |
| Pubertal development should be recorded for patients with NF1 at each annual visit from early childhood through puberty.⁵ |
| Evaluation of the skin of patients with NF1 should be recorded at each visit until 1 year old, and then at least annually thereafter.⁵ |
| From birth to 8 years old, patients should have ophthalmologic exams every 6-12 months including objective and quantitative visual acuity testing, visual fields, pupillary reflexes, and fundus exam.⁷ |
| Head circumference should be recorded for pediatric patients with NF1 at each visit until puberty.⁵ |
| Patients with NF1 should be referred to orthopedics if there is concern about scoliosis.⁴ |
| Patients with NF1 should be seen at least annually at an NF clinic.⁴ |
| Patients with NF1 should be followed at a specialized NF clinic.⁴ |
| All individuals with NF1 should have annual clinical evaluation of the back with Adam's forward bend test.⁴, ⁵ |
| Adult patients with NF1 should be screened for depression.⁴ |
| Women with NF1 should have annual mammogram starting at age 30 years, and consideration of contrast-enhanced breast MRI between ages 30 and 50 years.⁴ |
| Family planning should be revisited annually for patients of child bearing age who have NF1.⁴ |
| Patients with NF1 should be supplemented with vitamin D to reach serum 25-hydroxyvitamin D concentrations in the sufficient range.⁴ |
| For hypertensive patients with NF1 who are under 30 years of age, pregnant and/or have abdominal bruits, concomitant screening for pheochromocytoma with plasma free metanephrines is recommended.⁴ |
| MRA is the preferred imaging modality for evaluation of renovascular hypertension. However, for patients with impaired renal function, spiral CT and CT angiography may be used.⁵ |
| Pregnant women with NF1 should be referred to a high-risk obstetrician.⁴ |
Adults with NF1 should be asked about chronic fingertip and toe pain in the assessment of possible glomus tumors.4

Because the risk of MPNST being associated with high internal tumor burden, whole-body MRI should be considered between ages of 16 and 20 years to assess this in patients with NF1.7

Preanesthesia neuraxial imaging to evaluate for spinal or paraspinal neurofibromas is probably not needed. If there are concerns, spinal anesthesia may be considered.4

| Neurofibromatosis 2 (NF2) Guidelines |
|-------------------------------------|
| Patients with NF2 should be followed at a specialized NF clinic.6 |
| Patients with NF2 should be seen at least annually at an NF clinic.8 |

Ophthalmologic examination by a specialized ophthalmologist is recommended in children with NF2.8

Annual audiology with measurement of pure-tone thresholds and word recognition scores is recommended for patients with NF2.8

All children presenting with either clear diagnostic criteria for NF2, or those with an NF2 tumor (any schwannoma or meningioma) presenting in childhood should undergo genetic testing of NF2.8

Patients with NF2 should be informed that follow-up for life with interval scanning is necessary.6

Annual brain MRI is recommended for patients with NF2, unless no tumors are seen on first scan in which case frequency may reduce to every 2 years.8

Surveillance spinal MRI is recommended for patients with NF2 at 24- to 36-month intervals, unless there are no tumors in which case the frequency can be decreased.8

Surveillance spinal MRI is recommended for patients with NF2 at 24- to 36-month intervals beginning at 10 years of age.8

The interval between spinal surveillance MRI scans may be increased in patients with NF2 if there is no disease detected on baseline imaging.8

Annual brain MRI is recommended for patients with NF2 starting at 10 years of age, unless no tumors are seen on first scan in which case frequency may reduce to every 2 years.8

Schwannomatosis Guidelines

Test for pathogenic variants ('mutations') in SMARCB1 and LZTR1 genes should be performed in children and young adults with one or more non-intradermal schwannoma, including those with vestibular schwannoma negative for NF2.8

Baseline MRI of the brain should be obtained at diagnosis, then every 2-3 years, beginning at age 10 for SMARCB1-mutant patients and at age 15-19 for LZTR1-mutant patients with schwannomatosis.8

Baseline MRI of the spine should be obtained at diagnosis, then every 2-3 years, beginning at age 10 for SMARCB1-mutant patients and at age 15-19 for LZTR1-mutant patients with schwannomatosis.8
Table 2. Respondent Demographics and Practice Characteristics (n=63)

| Clinician Demographics          | N (%)          |
|---------------------------------|----------------|
| Gender                          |                |
| Female                          | 31 (49.2%)     |
| Male                            | 27 (42.9%)     |
| Non-binary                      | 1 (1.6%)       |
| Prefer not to answer or missing | 4 (6.3%)       |
| Race                            |                |
| White                           | 53 (84.1%)     |
| Black or African American       | 1 (1.6%)       |
| Asian                           | 6 (8.4%)       |
| American Indian or Alaska Native| 0 (0.0%)       |
| Native Hawaiian or other Pacific Islander | 0 (0.0%) |
| Other                           | 2 (3.2%)       |
| Missing                         | 1 (1.6%)       |
| Ethnicity                       |                |
| Hispanic or Latino              | 3 (4.8%)       |
| Not Hispanic or Latino          | 56 (88.9%)     |
| Missing                         | 4 (6.3%)       |
| Primary Specialty               |                |
| Medical Genetics                | 18 (28.6%)     |
| Neuro-Oncology                  | 11 (17.4%)     |
| Neurology                       | 10 (15.9%)     |
| Pediatrics                      | 5 (7.9%)       |
| Hematology/Oncology or Medical Oncology | 5 (7.9%) |
| Dermatology                     | 2 (3.2%)       |
| Neurosurgery                    | 1 (1.6%)       |
| Orthopedic Surgery              | 0 (0.0%)       |
| Other                           | 8 (13.7%)      |
| Missing                         | 3 (4.8%)       |
| Years in Post-Training Practice |                |
| <5 years                        | 11 (17.4%)     |
| 5-10 years                      | 14 (22.2%)     |
| 10-20 years                     | 21 (33.3%)     |
| >20 years                       | 17 (27.0%)     |
| Practice Characteristics        |                |
| Practice Type                   |                |
| Academic medical practice       | 50 (79.4%)     |
| Private Practice                | 5 (7.9%)       |
| Other                           | 7 (11.1%)      |
| Missing                         | 1 (1.6%)       |
| Location of Primary Office      |                |
| Urban                           | 49 (77.8%)     |
| Suburban                        | 12 (19.0%)     |
| Rural                           | 1 (1.6%)       |
|                                |       |
|--------------------------------|-------|
| Missing                        | 1 (1.6%) |
| **Primary Language of Patients in Practice** |       |
| English                        | 61 (96.8%) |
| Spanish                        | 2 (3.2%) |
| **Neurofibromatosis Specialization** | N (%) |
| **Affiliation with Children’s Tumor Foundation** |   |
| **NF Clinic Network**         |       |
| Yes                            | 50 (79.4%) |
| No                             | 11 (17.4%) |
| Unsure                         | 1 (1.6%) |
| Missing                        | 1 (1.6%) |
| **Clinician Involvement in NF Treatment Trials** |   |
| Yes                            | 39 (61.9%) |
| No                             | 23 (36.5%) |
| Missing                        | 1 (1.6%) |
| **Clinician Involvement in NF Non-Treatment Research** |   |
| Yes                            | 47 (74.6%) |
| No                             | 16 (25.4%) |
| **Clinicians Seeing Each Patient Population** |   |
| Pediatric Neurofibromatosis 1 | 55 (87.3%) |
| Adult Neurofibromatosis 1     | 51 (81.0%) |
| Pediatric Neurofibromatosis 2 | 48 (76.2%) |
| Adult Neurofibromatosis 2     | 36 (57.1%) |
| Schwannomatosis                | 36 (57.1%) |
Table 3. Clinicians’ Self-Reported Awareness of NF Clinical Guideline Publications

| Neurofibromatosis 1 Guidelines | Total Number of Respondents (N) | Aware of Guideline Document N (%) | Unaware of Guideline Document N (%) | Unsure N (%) |
|-------------------------------|---------------------------------|-----------------------------------|-------------------------------------|-------------|
| Stewart et al. (2018)         | 62                              | 43 (69.4%)                        | 16 (25.8%)                         | 3 (4.8%)    |
| Ferner et al. (2007)          | 63                              | 50 (79.4%)                        | 11 (17.5%)                         | 2 (3.2%)    |
| Evans et al. (2017a)          | 63                              | 47 (58.7%)                        | 21 (33.3%)                         | 5 (7.9%)    |
| Miller et al. (2019)          | 62                              | 43 (69.4%)                        | 17 (27.4%)                         | 2 (3.2%)    |

| Neurofibromatosis 2 Guidelines | Total Number of Respondents (N) | Aware of Guideline Document N (%) | Unaware of Guideline Document N (%) | Unsure N (%) |
|--------------------------------|---------------------------------|-----------------------------------|-------------------------------------|-------------|
| Evans et al. (2005)            | 61                              | 33 (54.1%)                        | 26 (42.6%)                         | 2 (3.3%)    |
| Evans et al. (2017b)*          | 61                              | 40 (65.6%)                        | 18 (29.5%)                         | 3 (4.9%)    |

| Schwannomatosis Guidelines     | Total Number of Respondents (N) | Aware of Guideline Document N (%) | Unaware of Guideline Document N (%) | Unsure N (%) |
|--------------------------------|---------------------------------|-----------------------------------|-------------------------------------|-------------|
| Evans et al. (2017b)*          | 62                              | 33 (53.2%)                        | 22 (35.5%)                         | 7 (11.3%)   |

Table Legend: *Respondents were asked to rate their awareness of the neurofibromatosis 2 guidelines and schwannomatosis guideline within Evans et al. 2017b separately.
Neurofibromatosis 1 Guidelines

MRI preferred over CT scan: 83% Strongly Agree, 15% Agree, 2% Neutral, 0% Disagree, 0% Strongly Disagree
Blood pressure at least annually: 80% Strongly Agree, 19% Agree, 1% Neutral, 0% Disagree, 0% Strongly Disagree
Educate about MPNST: 76% Strongly Agree, 19% Agree, 5% Neutral, 0% Disagree, 0% Strongly Disagree
Renovascular HTN screening: 74% Strongly Agree, 19% Agree, 7% Neutral, 0% Disagree, 0% Strongly Disagree
Height/weight annually: 71% Strongly Agree, 20% Agree, 9% Neutral, 0% Disagree, 0% Strongly Disagree
Annual eye testing <8yrs: 67% Strongly Agree, 22% Agree, 11% Neutral, 0% Disagree, 0% Strongly Disagree
Routine neurological exams annually: 65% Strongly Agree, 20% Agree, 15% Neutral, 0% Disagree, 0% Strongly Disagree
Pubertal development check-in annually: 65% Strongly Agree, 24% Agree, 11% Neutral, 0% Disagree, 0% Strongly Disagree
Skin exams annually: 64% Strongly Agree, 24% Agree, 12% Neutral, 0% Disagree, 0% Strongly Disagree
Eye exams Q6-12 month until 8 years old: 62% Strongly Agree, 31% Agree, 17% Neutral, 0% Disagree, 0% Strongly Disagree
Head circumference each visit til puberty: 53% Strongly Agree, 25% Agree, 22% Neutral, 0% Disagree, 0% Strongly Disagree
Orthopedics referral for scoliosis: 53% Strongly Agree, 36% Agree, 11% Neutral, 0% Disagree, 0% Strongly Disagree
NF clinic visit at least once per year: 53% Strongly Agree, 34% Agree, 13% Neutral, 0% Disagree, 0% Strongly Disagree
Followed at specialized NF clinic: 53% Strongly Agree, 34% Agree, 13% Neutral, 0% Disagree, 0% Strongly Disagree
Annual clinical check for scoliosis: 53% Strongly Agree, 24% Agree, 23% Neutral, 0% Disagree, 0% Strongly Disagree
Screen adults for depression: 52% Strongly Agree, 33% Agree, 15% Neutral, 0% Disagree, 0% Strongly Disagree
Breast cancer screening ≥ age 30: 48% Strongly Agree, 31% Agree, 21% Neutral, 0% Disagree, 0% Strongly Disagree
Family planning annually: 47% Strongly Agree, 39% Agree, 14% Neutral, 0% Disagree, 0% Strongly Disagree
Vitamin D supplementation: 44% Strongly Agree, 24% Agree, 32% Neutral, 0% Disagree, 0% Strongly Disagree
Pheochromocytoma screening: 40% Strongly Agree, 36% Agree, 24% Neutral, 0% Disagree, 0% Strongly Disagree
Prefer MRA screen for renovascular HTN: 34% Strongly Agree, 37% Agree, 29% Neutral, 0% Disagree, 0% Strongly Disagree
High-risk obstetrician referral: 34% Strongly Agree, 27% Agree, 40% Neutral, 0% Disagree, 0% Strongly Disagree
Glomus tumor screening: 33% Strongly Agree, 22% Agree, 45% Neutral, 0% Disagree, 0% Strongly Disagree
WBMRI screen at 16-20 years old: 22% Strongly Agree, 32% Agree, 46% Neutral, 0% Disagree, 0% Strongly Disagree
Preanesthesia neuroimaging not needed: 17% Strongly Agree, 32% Agree, 51% Neutral, 0% Disagree, 0% Strongly Disagree
Neurofibromatosis 2 Guidelines

- Followed at specialized NF clinic: 73% strongly agree, 25% agree, 26% neutral
- Specialized ophthalmologist for children: 67% strongly agree, 29% agree
- Annual audiology with PTA and WRS: 65% strongly agree, 31% agree
- Genetic testing for children: 64% strongly agree, 22% agree
- Inform of need for lifelong imaging: 63% strongly agree, 29% agree
- Annual brain MRI; biannual if no tumors: 51% strongly agree, 33% agree
- Surveillance spine MRI Q24-36 months; can be reduced if no tumors: 47% strongly agree, 33% agree
- Surveillance spine MRI Q24-36 months beginning at age 10: 38% strongly agree, 42% agree
- Spine MRI interval may be increased if no tumors: 36% strongly agree, 47% agree
- Annual brain MRI beginning at age 10; biannual if no tumors: 36% strongly agree, 44% agree

Schwannomatosis Guidelines

- Genetic testing for children/young adults: 38% strongly agree, 47% agree
- Brain MRI Q24-36 month, beginning at age 10 for SMARCB1 or age 15-19 for LZTR1: 30% strongly agree, 52% agree
- Spine MRI Q24-36 month, beginning at age 10 for SMARCB1 or age 15-19 for LZTR1: 27% strongly agree, 58% agree

Legend:
- Strongly Agree
- Agree
- Neutral
- Disagree
- Strongly Disagree