AD_____

Award Number: W81XWH-11-1-0255

TITLE: Comprehensive Quality of life (QoL) in Neurofibromatosis type II (NF2): Development, refinement and standardization of a multi-dimensional metric

PRINCIPAL INVESTIGATOR: Maura Cosetti, MD

CONTRACTING ORGANIZATION: New York University
New York, NY 10016

REPORT DATE: April 2012

TYPE OF REPORT: Annual Summary

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
01-04-2012	Annual Summary report	1 Apr 11-31 Mar 12

4. TITLE AND SUBTITLE

Comprehensive Quality of life (QoL) in Neurofibromatosis type II (NF2): Development, refinement and standardization of a multi-dimensional metric

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-11-1-0255

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Maura Cosetti

E-Mail: mkcosetti@yahoo.com, Maura.cosetti@nyumc.org

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

New York University
New York, NY 10016

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Neurofibromatosis Type 2 (NF2), a genetic disorder with highly penetrant autosomal dominant transmission, is characterized by the predictable development of bilateral vestibular schwannomas (VS), intracranial and spinal schwannomas, meningiomas, gliomas and ependymomas, cataracts and multiple skin tumors. Tumor progression, as well as therapeutic intervention, may lead to significant cranial, spinal and peripheral nerve dysfunction, resulting in global impairment across of variety of domains. Management of NF2 disease is challenging, complex and controversial. International consensus recommendations and expert panels have described the importance of quality of life (QoL) measurements in clinical decision making and research trials. However, few studies have examined the QoL in patients with neurofibromatosis and NF2-specific, validated metrics for this population are not currently available. The objective of this research was to develop, refine and validate a multi-dimensional metric for assessment of QoL in patients with NF2. Progress toward this goal has thus far has included generation and ongoing structured interviews with NF2 patients, multidisciplinary health care providers, as well as initial operationalization of this content into a provisional module. Continued work on the additional project aims (as specified in the initialstatement of work and annual report) is ongoing and will continue until the project termination in October 2012.

15. SUBJECT TERMS
Quality of life, neurofibromatosis type 2

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
U	U	U	UU	17	19b. TELEPHONE NUMBER *(include area code)*

Table of Contents

INTRODUCTION

Neurofibromatosis Type 2 (NF2), a genetic disorder with highly penetrant autosomal dominant transmission, is characterized by the predictable development of bilateral vestibular schwannomas (VS), intracranial and spinal schwannomas, meningiomas, gliomas and ependymomas, cataracts and multiple skin tumors. Tumor progression, as well as therapeutic intervention, may lead to significant cranial, spinal and peripheral nerve dysfunction, resulting in global impairment across of variety of domains. Currently, ideal management of NF2 disease is challenging, complex and controversial. International consensus recommendations and expert panels have described the importance of quality of life (QoL) measurements in clinical decision making and research trials. At present, however, there are few studies examining the QoL in patients with neurofibromatosis and NF2-specific, validated metrics for this population are not widely available. The aim of the current study is to develop, refine and validate a multi-dimensional metric for assessment of QoL in patients with NF2.

BODY

Research accomplishments as well as challenges encountered in methodology are described in detail below and are based on the previously outlined Statement of Work (SOW). Task 1 of the SOW involved the development of a NF2-specific QoL module. Task 1A involved generation of an exhaustive list of NF2-specific QoL issues and assessment of content validity using the following methods:

(i) literature review of existing QoL metrics
(ii) structured interviews with members of multidisciplinary NYU Neurofibromatosis Center
(iii) structured patient interviews with NF2 patients
(iv) Operationalization of content into a set of questionnaire items using the EORTC item bank and generation of novel items.

Complete bibliography of the literature review is included in Appendix A. As described previously, research examining QoL in NF2 patients is currently lacking. NF2 is a genetic disorder with highly penetrant autosomal dominant transmission that characterized by the predictable development of bilateral vestibular schwannomas (VS), intracranial and spinal schwannomas, meningiomas, gliomas and ependymomas, cataracts and multiple skin tumors. Tumor progression, as well as therapeutic intervention, may lead to significant cranial, spinal and peripheral nerve dysfunction. The unique complexity of the intra-cranial and extra-axial tumor burden in this population leads to a diverse constellation of symptoms and impairments across a wide variety of functional domains. Therefore, a systematic literature review was performed targeting QoL metrics applied to patient populations with brain, skull base, intracranial, spinal, ocular, or head and neck disease. Additionally, given the eventual development of profound sensorineural hearing loss in this population, research examining QoL metrics in populations with deafness as well as those receiving auditory brainstem

implants were included. Lastly, studies investigating QoL in patients with genetic diseases affecting reproduction and family planning were also reviewed.

Literature search was performed using PUBMED and MEDLINE. Relevant articles were reviewed for additional references and then systematically categorized by affected organ system, ie brain, skull base, intracranial, spinal, ocular, and head and neck disease (Appendix A.) A preliminary list of QoL domains applicable to patients with NF2 was generated and used in the structured interview portion of the module development.

Structured interviews were performed with patients with NF2 (Appendix B) and members of multidisciplinary NYU Neurofibromatosis Center (Appendix C). Interviews followed the guidelines outlined in the EORTC Guidelines for Module Development[1] and included both open-ended and semi-structured questions. Interviews lasted 30 minutes – 1 hour. Notes were taken throughout the interviews and were clarified with the interviewee at the end of the session, if necessary.

Structured interviews of patients are detailed in Appendix B and consisted of 3 parts: general, relevance of domains and breadth of coverage. Patients were asked to identify and rank 5 domains which they valued particularly highly and those in which they experienced significant challenges. Neutral probes were used to obtain more specific details about each experience. Open-ended questions were used to query the patients regarding breadth of identified QoL domains as well as additional issues missing or incompletely addressed in the provided list.

Structured interviews of health care providers are detailed in Appendix C and similarly consisted of 3 parts: relevance of domains, relative importance within each domain and breadth of coverage. Providers were asked to rate each domains on a 4-point Likert scale from (1) “not at all relevant” to (4) “very relevant.” For instances in which the individual responded with a (1) “not at all relevant,” additional follow-up questions were asked to clarify the basis of the response. To identify which issues affect NF2 patients most profoundly, providers were asked to identify and rank the top 5 domains they felt had the greatest impact on QoL in NF2. For assessment of the relative importance of each issue (and ultimately pare down the QoL questionnaire), providers were asked to indicate whether each item should be included on the final questionnaire. Lastly, providers were asked to identify additional issues that were missing or incompletely addressed in the list.

Once completed, responses were analyzed for deletion or addition of issues. Domains were considered for deletion if they 1) were not included in the top 5 of any patient responses to challenges or positive experiences; 2) were not included in the top 5 of any provider response; or 3) had a low mean relevance score (mean < 2) in provider evaluation. New areas were considered for addition if 1) they were mentioned by at least 2 patients or providers or 2) mentioned by 1 patient or provider with significant plausible motivation.

To date, interviews with both patients and providers are ongoing. Among patients interviewed thus far (N=5), areas of hearing, balance/ambulation and oral intake have the highest rank order for importance, while hearing, balance/ambulation and facial weakness represent the areas with highest rank for difficulty. For

breadth of coverage, 2 patients noted difficulty related to writing or typing due to peripheral neurofibromas. Additionally, 2 suggested that internet based survey (rather than a paper format) would be an easier format to complete given their level of functioning. Among provider responses, hearing, balance/ambulation and facial weakness have the highest rank order and mean relevance score (4.0). Areas with low relevance score (2-3) include sexual activity and future uncertainty. No area has yet received a relevance score of 1.

Following completion of structured interviews, items will be added or deleted based on the guidelines above. This will then be refined into provisional module and pre-tested to a small group of patients. All patients will be de-briefed following pre-testing using a structured interview (Appendix D.)

KEY RESEARCH ACCOMPLISHMENTS

- Initiation of phase 1-3 of module development
- Completion of literature review of existing QoL metrics and generation of relevant QoL domains (Appendix A)
- Generation and ongoing administration of structured
    - Patient interviews (Appendix B)
    - Provider interviews (Appendix C)
- Operationalization of content into a set of questionnaire items using the EORTC item bank and generation of novel items (ongoing)
- Generation of structured patient interview following pre-testing (Appendix D)
- Initiation of IRB application for administration of provisional module

REPORTBALE OUTCOMES – pending

CONCLUSION

At present, there are few studies examining the QoL in patients with neurofibromatosis and NF2-specific, validated metrics for this population are not widely available. The present study to develop, refine and validate a multi-dimensional metric for assessment of QoL in patients with NF2 is in progress. Once completed, this will provide further insight into areas of functioning affected by of NF2. Additionally, as novel treatment options for NF2 emerge, the ability to accurately assess the impact of these therapies on QoL will be a crucial component of treatment decision-making.

REFERENCES

1. Sprangers MAG, Cull A, Groenvold M, Bjordal K, Blazeby J, Aaronson NK for the EORTC Quality of life Study Group. The European Organization for Research and Treatment of Cancer approach to developing questionnaire modules: an update and overview. *Qual Life Res* 1998; 7: 291-300.

APPENDICES: A-D

Appendix A: Literature Review- Quality of Life and Neurofibromatosis Type 2

1. Gauden A, Weir P, Hawthorne G, Kaye A. Systematic review of quality of life in the management of vestibular schwannoma. J Clin Neurosci. 2011 Dec;18(12):1573-84. Epub 2011 Oct 19. Neary WJ, Hillier VF, Flute T, Stephens SD, Ramsden RT, Evans DG. The relationship between patients' perception of the effects of neurofibromatosis type 2 and the domains of the Short Form-36. Clin Otolaryngol. 2010 Aug;35(4):291-9.
2. Evans DG, Baser ME, O'Reilly B, Rowe J, Gleeson M, Saeed S, King A, Huson SM, Kerr R, Thomas N, Irving R, MacFarlane R, Ferner R, McLeod R, Moffat D, Ramsden R. Management of the patient and family with neurofibromatosis 2: a consensus conference statement. Br J Neurosurg. 2005 Feb;19(1):5-12.
3. Neary WJ, Hillier VF, Flute T, et al. Use of a closed set questionnaire to measure primary and secondary effects of neurofibromatosis type 2. Journal of laryngology and otology 2010; 124:720 -728.
4. Neary WJ, Stephens D, Ransden RT, Evans G. Psychosocial effects of Neurofibromatosis type 2: effects on specific systems. Audiol Med 2006; 4: 211-219.
5. Neary WJ, Stephens D, Ransden RT, Evans G. Psychosocial effects of Neurofibromatosis type 2 (Part 1): general effects. Audiol Med 2006; 4: 202-210.
6. Benjamin CM, Colley A, Donnai D, Kingston H, Harris R, Kerzin-Storrar L. Neurofibromatosis type 1 (NF1): knowledge, experience, and reproductive decisions of affected patients and families. J Med Genet. 1993 Jul;30(7):567-74.
7. Terzi YK, Oguzkan-Balci S, Anlar B, Aysun S, Guran S, Ayter S. Reproductive decisions after prenatal diagnosis in neurofibromatosis type 1: importance of genetic counseling. Genet Couns. 2009;20(2):195-202.
8. Brandberg Y, Damato B, Kivelä T, Kock E, Seregard S; EORTC Ophthalmic Oncology Task Force; EORTC Quality of Life Group. The EORTC ophthalmic oncology quality of life questionnaire module (EORTC QLQ-OPT30). Development and pre-testing (Phase I-III). Eye (Lond). 2004 Mar;18(3):283-9.
9. Park SS, Grills IS, Bojrab D, Pieper D, Kartush J, Maitz A, Martin A, Perez E, Hahn Y, Ye H, Martinez A, Chen P. Longitudinal assessment of quality of life and audiometric test outcomes in vestibular schwannoma patients treated with gamma knife surgery. Otol Neurotol. 2011 Jun;32(4):676-9.
10. Lloyd SK, Kasbekar AV, Baguley DM, Moffat DA. Audiovestibular factors influencing quality of life in patients with conservatively managed sporadic vestibular schwannoma. Otol Neurotol. 2010 Aug;31(6):968-76.
11. Grauvogel J, Kaminsky J, Rosahl SK. The impact of tinnitus and vertigo on patient-perceived quality of life after cerebellopontine angle surgery. Neurosurgery. 2010 Sep;67(3):601-9; discussion 609-10.
12. Shaffer BT, Cohen MS, Bigelow DC, Ruckenstein MJ. Validation of a disease-specific quality-of-life instrument for acoustic neuroma: the Penn Acoustic Neuroma Quality-of-Life Scale. Laryngoscope. 2010 Aug;120(8):1646-54.
13. Brooker JE, Fletcher JM, Dally MJ, Briggs RJ, Cousins VC, Smee RI, Malham GM, Kennedy RJ, Burney S. Quality of life among acoustic neuroma patients managed by microsurgery, radiation, or observation. Otol Neurotol. 2010 Aug;31(6):977-84.

14. Gouveris HT, Mann WJ. Quality of life in sporadic vestibular schwannoma: a review. ORL J Otorhinolaryngol Relat Spec. 2010;72(2):69-74.
15. Iyer AP, Gunn R, Sillars H. Quality of life after vestibular schwannomas surgery: does hearing preservation make a difference? J Laryngol Otol. 2010 Apr;124(4):370-3.
16. Cheng S, Naidoo Y, da Cruz M, Dexter M. Quality of life in postoperative vestibular schwannoma patients. Laryngoscope. 2009 Nov;119(11):2252-7.
17. Godefroy WP, Kaptein AA, Vogel JJ, van der Mey AG. Conservative treatment of vestibular schwannoma: a follow-up study on clinical and quality-of-life outcome. Otol Neurotol. 2009 Oct;30(7):968-74.
18. Di Maio S, Akagami R. Prospective comparison of quality of life before and after observation, radiation, or surgery for vestibular schwannomas. J Neurosurg. 2009 Oct;111(4):855-62.
19. Wackym PA, Hannley MT, Runge-Samuelson CL, Jensen J, Zhu YR. Gamma Knife surgery of vestibular schwannomas: longitudinal changes in vestibular function and measurement of the Dizziness Handicap Inventory. J Neurosurg. 2008 Dec;109 Suppl:137-43.
20. Browne S, Distel E, Morton RP, Petrie KJ. Patients' quality of life, reported difficulties, and benefits following surgery for acoustic neuroma. J Otolaryngol Head Neck Surg. 2008 Jun;37(3):417-22.
21. Brooker J, Burney S, Fletcher J, Dally M. A qualitative exploration of quality of life among individuals diagnosed with an acoustic neuroma. Br J Health Psychol. 2009 Sep;14(Pt 3):563-78.
22. Vogel JJ, Godefroy WP, van der Mey AG, le Cessie S, Kaptein AA. Illness perceptions, coping, and quality of life in vestibular schwannoma patients at diagnosis. Otol Neurotol. 2008 Sep;29(6):839-45.
23. Guntinas-Lichius O, Straesser A, Streppel M. Quality of life after facial nerve repair. Laryngoscope. 2007 Mar;117(3):421-6.
24. Lee J, Fung K, Lownie SP, Parnes LS. Assessing impairment and disability of facial paralysis in patients with vestibular schwannoma. Arch Otolaryngol Head Neck Surg. 2007 Jan;133(1):56-60.
25. Lassaletta L, Alfonso C, Del Rio L, Roda JM, Gavilan J. Impact of facial dysfunction on quality of life after vestibular schwannoma surgery. Ann Otol Rhinol Laryngol. 2006 Sep;115(9):694-8.
26. Nicoucar K, Momjian S, Vader JP, De Tribolet N. Surgery for large vestibular schwannomas: how patients and surgeons perceive quality of life. J Neurosurg. 2006 Aug;105(2):205-12.
27. Myrseth E, Møller P, Wentzel-Larsen T, Goplen F, Lund-Johansen M. Untreated vestibular schwannomas: vertigo is a powerful predictor for health-related quality of life. Neurosurgery. 2006 Jul;59(1):67-76; discussion 67-76.
28. Tufarelli D, Meli A, Alesii A, De Angelis E, Badaracco C, Falcioni M, Sanna M. Quality of life after acoustic neuroma surgery. Otol Neurotol. 2006 Apr;27(3):403-9.
29. Baumann I, Polligkeit J, Blumenstock G, Mauz PS, Zalaman IM, Maassen MM. Quality of life after unilateral acoustic neuroma surgery via middle cranial fossa approach. Acta Otolaryngol. 2005 Jun;125(6):585-91.
30. Ryzenman JM, Pensak ML, Tew JM Jr. Facial paralysis and surgical rehabilitation: a quality of life analysis in a cohort of 1,595 patients after acoustic neuroma surgery. Otol Neurotol. 2005 May;26(3):516-21; discussion 521.
31. Myrseth E, Møller P, Pedersen PH, Vassbotn FS, Wentzel-Larsen T,Lund-Johansen M. Vestibular schwannomas: clinical results and quality of life after microsurgery or gamma knife radiosurgery. Neurosurgery. 2005 May;56(5):927-35; discussion 927-35.
32. Ryzenman JM, Pensak ML, Tew JM Jr. Headache: a quality of life analysis in a cohort of 1,657 patients undergoing acoustic neuroma surgery, results from the acoustic neuroma association. Laryngoscope. 2005 Apr;115(4):703-11.
33. Sandooram D, Grunfeld EA, McKinney C, Gleeson MJ. Quality of life following microsurgery, radiosurgery and conservative management for unilateral vestibular schwannoma. Clin Otolaryngol Allied Sci. 2004 Dec;29(6):621-7.
34. Pritchard C, Clapham L, Davis A, Lang DA, Neil-Dwyer G. Psycho-socio-economic outcomes in acoustic neuroma patients and their carers related to tumour size. Clin Otolaryngol Allied Sci. 2004 Aug;29(4):324-30.
35. MacAndie C, Crowther JA. Quality of life in patients with vestibular schwannomas managed conservatively. Clin Otolaryngol Allied Sci. 2004 Jun;29(3):215-8.

36. Ryzenman JM, Pensak ML, Tew JM Jr. Patient perception of comorbid conditions after acoustic neuroma management: survey results from the acoustic neuroma association. Laryngoscope. 2004 May;114(5):814-20.
37. Kelleher MO, Fernandes MF, Sim DW, O'Sullivan MG. Health-related quality of life in patients with skull base tumours. Br J Neurosurg. 2002 Feb;16(1):16-20.
38. Salo J, Niemelä A, Joukamaa M, Koivukangas J. Effect of brain tumour laterality on patients' perceived quality of life. J Neurol Neurosurg Psychiatry. 2002 Mar;72(3):373-7.
39. Magliulo G, Zardo F, Damico R, Varacalli S, Forino M. Acoustic neuroma: postoperative quality of life. J Otolaryngol. 2000 Dec;29(6):344-7.
40. Inoue Y, Ogawa K, Kanzaki J. Quality of life of vestibular schwannomas patients after surgery. Acta Otolaryngol. 2001 Jan;121(1):59-61.
41. Martin HC, Sethi J, Lang D, Neil-Dwyer G, Lutman ME, Yardley L. Patient-assessed outcomes after excision of acoustic neuroma: postoperative symptoms and quality of life. J Neurosurg. 2001 Feb;94(2):211-6.
42. da Cruz MJ, Moffat DA, Hardy DG. Postoperative quality of life in vestibular schwannoma patients measured by the SF36 Health Questionnaire. Laryngoscope. 2000 Jan;110(1):151-5.

Appendix B: Structured Interview with NF2 patients

Patient Name:_____

We are asking your help to devise a questionnaire which will be used to better understand the experiences of patients with Neurofibromatosis Type 2.

1. General

   A. I would like to ask you a few questions about your health and daily life. Can you tell me about the experiences you have had as a result of NF2?

   B. (Neutral probes to follow their response): *Can you tell me more about that? Can you give me an example? In what way?*

2. Relevance of domains

   Below is a list of experiences that patients with NF2 may have. You may have had positive and/or negative experiences with each of these. These issues may not be equally important to you and you may consider some areas to be more important than others.

   A. Can you please identify and rank the 5 areas that you value the most highly or are most important to you?

Domains	**Rank Order**
Hearing	
Balance/Ambulation	
Facial weakness	
Vision	
Speaking	
Psychosocial	
Oral intake	
Cognition	
Pain	
Sexual activity	
Future uncertainty	

   B. Can you please identify and rank the 5 areas that cause you the most difficulty?

Domains	**Rank Order**
Hearing	
Balance/Ambulation	
Facial weakness	
Vision	
Speaking	
Psychosocial	
Oral intake	
Cognition	
Pain	
Sexual activity	
Future uncertainty	

   C. For each area, please describe the experiences you have had in more detail.

D. For areas you did not rank in either A or B above, have you had any experiences in this area that you would like to share?

3. Breadth of coverage

A. Can you think of anything else which you have experienced or had to cope with that we have not discussed?

B. For each issue mentioned in A, can you tell me more about that?

C. Any additional comments?

Appendix C: Structured Interview with NF2 Providers

Provider Name and degree:_____

The following is an attempt to get your input on issues affecting the quality of life in patients with Neurofibromatosis Type 2.

I. Relevance of domains

A. Please answer with the extent to which each of these domains is relevant to patients with NF2. "Relevance" refers to the frequency with which a specific symptom/issue occurs and the degree to which you believe this issue affects their quality of life. (The more frequently a complaint occurs and greater the implications for quality of life, the more "relevant" it will be.)

Domains	**Not relevant**	**A little relevant**	**Quite relevant**	**Very relevant**
Hearing	1	2	3	4
Balance/Ambulation	1	2	3	4
Facial weakness	1	2	3	4
Vision	1	2	3	4
Speaking	1	2	3	4
Psychosocial	1	2	3	4
Oral intake	1	2	3	4
Cognition	1	2	3	4
Pain	1	2	3	4
Sexual activity	1	2	3	4
Future uncertainty	1	2	3	4

B. For each issue in which a "1" or a "2" was circled, please expand upon why this is not or only partially relevant for patients with NF2?

C. In an attempt to identify which issues affect NF2 patients most profoundly, please identify the top 5 domains that you feel are most important to assess. Please rank these from 1-5.

Domains	**Rank Order of Relevance**
Hearing	
Balance/Ambulation	
Facial weakness	
Vision	
Speaking	
Psychosocial	
Oral intake	
Cognition	
Pain	
Sexual activity	
Future uncertainty	

II. Relative importance within each domain (sub-set identification)

Although NF2 affects a many domains, we can only include a sub-set of items. Please give your opinion regarding whether the items under each domain should be included in the final questionnaire. All items will begin with "In the past week…"

Hearing

Item (Begins with "In the past week…")	Yes	No	Unsure
Have hearing problems stopped you from performing your usual activities?			
Have hearing problems stopped you from performing your professional duties?			
Have you had difficulty communicating with others because of hearing loss?			
Have you been able to use the telephone?			
Have tinnitus or "ringing" or noises in the ear stopped you from performing your usual activities?			
For patients with ABIs or Cochlear implants: Has the implant improved your ability to communicate with others?			
For patients with either ABIs or CIs: Has the implant improved your ability to perform your usual activities?			
For patients with either ABIs or CIs: Has the implant improved your ability to perform your professional activities?			

Balance/Ambulation

Item (Begins with "In the past week…")	Yes	No	Unsure
Have balance problems stopped you from performing your usual activities?			
Did you have any trouble doing strenuous activities, like carrying a heavy shopping bad or suitcase?			
Did you have any trouble taking a long walk?			
Did you have any trouble taking a short walk?			
Did you need to stay in bed or a chair during the day?			
Did you need help with eating, dressing, washing yourself or using the toilet?			
Did you have weakness on one side of your body?			
Did you have weakness of both legs?			
Did you have trouble with your coordination?			
Did you feel off balance?			
Did you feel unsteady on your feet?			
Did you feel drowsy in the daytime?			
Have you worried about loss of mobility because of NF2?			
Have you worried about becoming dependent on others because of your illness?			

Facial weakness

Item (Begins with "In the past week…")	Yes	No	Unsure
Has facial weakness or paralysis stopped you from performing your usual activities?			
Has facial weakness or paralysis caused you difficulty with eating?			
Has your appearance bothered you?			
Have you felt physically less attractive as a result of NF2 or the treatment for NF2?			

Vision

Item (Begins with "In the past week…")	Yes	No	Unsure
Did you have double or blurred vision?			
Did you have difficulty reading because of your vision?			
Did you have difficulty pouring (ie tea or coffee?)			
Did problems with your sight stop you from performing your usual activities?			

Oral intake

Item (Begins with "In the past week…")	Yes	No	Unsure
Have you had trouble eating?			
Have you had trouble eating in front of your family?			
Have you had trouble eating in front of other people?			
Have you had trouble enjoying your meals?			
Have you had problems swallowing food?			
Have you had problems with your sense of smell?			
Have you had problems with your sense of taste?			
Have you gained weight?			
Have you lost weight?			

Cognition

Item (Begins with "In the past week…")	Yes	No	Unsure
Has tinnitus or "ringing" or noises in the ear affected your concentration?			
Did you have seizures?			
Did you have trouble finding the right words to express yourself?			
Have you had difficulty concentrating on things?			
Have you had difficulty remembering things?			

Pain

Item (Begins with "In the past week…")	Yes	No	Unsure
Did you have headaches?			
Have you used pain medication?			
Have you felt hopeful your pain will get better?			
Has pain interfered with your daily activities?			

Speaking

Item (Begins with "In the past week…")	Yes	No	Unsure
Did you have difficulty speaking?			
Have you been hoarse?			
Have you coughed?			
Has you had trouble talking to other people?			

Psychosocial

Item (Begins with "In the past week…")	Yes	No	Unsure
Have you felt calm and peaceful?			
Have you felt happy?			
Have you had trouble having social contact with your family?			
Have you had trouble having social contact with friends?			
Have you had trouble going out in public?			
Have you worried about becoming dependent on others because of your illness?			
Has your physical condition or medical treatment caused you financial difficulties?			

Future uncertainty

Item (Begins with "In the past week…")	Yes	No	Unsure
Did you feel uncertain about your future?			
Did your outlook on the future improve?			
Have you felt positive about your health?			

Sexual activity

Item (Begins with "In the past week…")	Yes	No	Unsure
Have you felt more interest in sex?			
Have you felt more sexual enjoyment?			

Other

Item (Begins with "In the past week…")	Yes	No	Unsure
Did you have difficulty controlling your bladder?			

III. Breadth of coverage

A. Can you identify any issues that may be relevant to patients with NF2 and are not included above? Please expand on the details of each issue, including the frequency and severity with the NF2 population.

B. Any additional comments on the relevance or breadth of coverage?

Appendix D: Structured debriefing of NF2 patient after pre-testing of the provisional module

Patient Name:_____

Thank you for your help in devising a questionnaire about patient experiences with NF2. I want to make sure that we asked the right questions in the right way and that we cover the issues most important to patients with NF2.

*For items in which the patient indicated they **HAVE** difficulty (3 "quite a bit" or 4 "very much" on the Likert scale):*

1. I see you have this problem, is that correct?
2. Do you think this problem is related to NF2?
3. Can you tell me more about your experience with this?
4. Did you have any difficulty responding to this question?
5. Did you find this question
    a. Annoying?
    b. Confusing?
    c. Upsetting?
6. How would you have asked this question?

*For items in which the patient indicated they **DO NOT HAVE** difficulty (1 "not at all" or 2 "a little" on the Likert scale):*

1. I see you have not had this problem during the previous week? Is that correct?
2. Have you experienced this problem before?
3. If yes, do you think it was related to NF2?
    a. Can you tell me more about this problem?
    b. Did you have difficulty responding to this question?
4. Did you find this question
    a. Annoying?
    b. Confusing?
    c. Upsetting?
5. How would you have asked this question?

With respect to the entire questionnaire:

1. Were their questions you found intrusive?
2. Can you think of anything else that you have had to cope with that was not included on the questionnaire?