ARTIGO ORIGINAL/ORIGINAL ARTICLE

# Translation and Validation of the European Portuguese Version of the Quality of Life in Neurofibromatosis 1 Patients Scale (INF1-QoL)

## Tradução e Validação da Versão em Português Europeu do Questionário Sobre o Impacto da Neurofibromatose Tipo 1 na Qualidade De Vida (INF1-QoL)

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## Abstract

**Introduction:** The INF1-QoL questionnaire is an essential tool for assessing patients' perceptions of their illness and its impact on their daily lives. This study aimed to obtain and validate the European Portuguese version of this questionnaire.

**Methods:** The English version of INF1-QoL was translated using the "forward-backward" procedure. The questionnaire was administered to 78 adult patients with neurofibromatosis type 1.

**Results:** The Portuguese-translated version of INF1-QoL showed good internal consistency (Cronbach's alpha: 0.86); the mean total INF1-QoL score was 9.11 (SD 6.35), the median was 8.00, with a range of 0–31, and no significant correlations with age, gender or education were found. The mean total EuroQol score was 6.6 (SD: 1.55), the median was 6. Total INF1-QoL score correlated with total EuroQol score (r=0.839, $p$<0.001. The highest impact on QoL were moderate or severe problems with anxiety and depression (28%) and the negative effects of NF1 on role and outlook on life (49%).

The mean clinical severity score was 2.96 (SD: 0.987) correlating with the total INF1-QoL score (r=0.279, $p$=0.019) and correlated with the total EuroQol score (r=0.251, $p$=0.036). The clinical severity was mild in 34 (49%), moderate in 22 (31%), and severe in 14 (20%) of individuals.

**Conclusion:** Based on a detailed analysis of the results obtained, we found that the translated version of INF-QoL is a reliable and valid self-assessment screening tool for the Portuguese population with neurofibromatosis type 1.

## Resumo

**Introdução:** O questionário INF1-QoL é uma importante ferramenta usada para avaliar a perceção dos doentes quanto à sua doença e respetivo impacto quotidiano.

O objetivo deste estudo consistiu na tradução e validação do questionário INF1-QoL para português europeu.

**Métodos:** A versão inglesa do INF1-QoL foi traduzida utilizando o método de tradução-retroversão. O questionário foi aplicado em 78 doentes com neurofibromatose tipo 1.

**Resultados:** A tradução portuguesa do INF1-QoL revelou uma boa consistência interna (alfa de Cronbach: 0,86), uma pontuação média total da INF1-QoL de 9,11

(DP= 6,35), uma mediana de 8 com um intervalo de valores situado entre 0-31, não havendo correlação com idade, sexo ou escolaridade. A pontuação média total do EuroQol foi de 6,6 (DP=1,55), a mediana de 6. A correlação do total INF1-QoL com o total EuroQol foi de r=0,839, *p*<0,001. O maior impacto na QoL foi a ansiedade e depressão (28%) e efeitos negativos da NF1 na perspetiva de vida (49%) foram os itens com maior impacto na qualidade de vida desta população. A pontuação média de gravidade clínica foi 2,96 (DP=0,987) correlacionada r=0,279 com pontuação total INF1-QOL (*p*=0,019) e correlacionada r=0,251 com pontuação total do EuroQol (*p*=0,036). Quanto à pontuação de gravidade clínica, 34 (49%) participantes apresentavam NF1 ligeira, 22 (31%) NF1 moderada e 14 (20%) foram classificados como severos.

**Conclusão:** A análise detalhada dos resultados permite-nos concluir que a versão traduzida do questionário INF-QoL é uma valiosa ferramenta na avaliação de doentes portugueses com neurofibromatose tipo 1, fiável e válida para a população portuguesa.

## Introduction

Neurofibromatosis type 1 (NF1) is an inherited disease primarily affecting the nervous system, eyes, skin, and bones. It is associated with an increased risk of benign and malignant tumors, the most common being neurofibromas, benign tumors of the peripheral nerve sheath.[1] Complications are multisystemic and unpredictable, varying in severity, ranging from minor cosmetic issues, such as *café au lait* spots to life-threatening conditions like glioblastoma.[1] These complications can affect both the central and peripheral nervous system, leading to serious consequences such as central nervous system tumors; spinal cord and nerve root compression; and hypertension arising from vascular complications.[1] Additionally, NF1 can cause significant deformities, bone problems, and neurocognitive and learning disabilities.[1]

These aspects can negatively impact patients' mental health, leading to sleep disturbances, social isolation, and potential psychiatric comorbidities. In addition to the individual impact of an NF1 diagnosis, patients may also experience psychological distress due to the genetic risk of transmitting the disease to their offspring. This genetic disorder carries an autosomal dominant inheritance pattern, meaning that each child of an individual with NF1 has a 50% chance of inheriting the mutated gene and thus developing the disorder. Furthermore, having family members who are severely disabled or experiencing the loss of loved ones due to complications related to NF1 may also cause psychological anguish.[2-4]

Assessing the impact of NF1 on an individual's quality of life (QoL) is challenging. Thus, specific questionnaires are needed for this purpose. QoL is recognized as an important marker of disease progression and as an outcome measure following interventions. Various semi-structured interviews and generic questionnaires such as the Short-Form 36 (SF-36) and the EuroQoL have been conducted in previous studies to evaluate QoL in NF1 patients.[5-9] However, none of these questionnaires specifically address NF1-related symptoms and their time-consuming nature can be a problem in this population, due to sustained attention deficits.

In 2017, R. Ferner *et al*[10] developed and validated a disease-specific QoL assessment questionnaire for adults with NF1, called the Impact of NF1 on Quality-of-Life Questionnaire (INF1-QoL). This self-completion questionnaire is simple, reliable, and can be completed in 10 minutes, with results obtainable in just one minute. It covers the wide phenotypic variability of NF1 in 14 questions and evaluates various domains that can be affected by NF1, with a good correlation with clinician-related severity. These domains were chosen from a comprehensive list of symptoms and social and emotional difficulties related to NF1 using a literature review; qualitative interviews with patients; input from practitioners with expertise in NF1; and patient focus group sessions. The items were clustered into six groups: physical problems; emotions and feelings; activities of daily living and leisure activities; relationships with employers, family, and friends; school difficulties; and work issues. Using simple questions, easily understandable by patients, the questionnaire evaluates the different parameters that can be impaired in NF1. The questions assess the following items, reflecting the six groups previously mentioned: vision, cosmetic appearance, pain intensity and quality, learning problems, behavioral and personality, mobility and walking, hand function, speech, bone health, breathing, sleeping, role and outlook on life, depression, and anxiety. The questionnaire uses a 4-point Likert scale, ranging from 0 to 3, with higher scores indicating a greater impact on the quality of life. After adding all items, the questionnaire has a maximum potential score of 42, with higher scores indicating a greater impact on quality of life. The results of the original study[10] showed good internal reliability, a moderate correlation with the severity of the disease, with role and outlook on life, anxiety, and depression having the most significant impact on QoL, reflecting both the severity and unpredictability of NF1.

The translation of the INF1-QoL questionnaire into different languages can provide valuable tools to identify NF1 patients at risk and assess their QoL. Given the lack of a European Portuguese version of the scale for assessing the QoL in NF1 patients, this study aimed to translate and validate the INF1-QoL questionnaire to the Portuguese population.

## Methods

The Neurology Department of Instituto Português de Oncologia Francisco Gentil (IPOLFG) serves as a center for the diagnosis, treatment, and follow-up of NF1 patients in Portugal. It is the largest NF1 center in the country, providing care to both pediatric and adult patients. This study was approved by the Scientific and Ethics Committees of IPOLFG.

In this study, we conducted the translation and validation of the INF1-QoL scale into European Portuguese. Permission to use the questionnaire was obtained from the original authors, and authorization to translate the original version and validate it to the European Portuguese clinical context and language was also secured. Semantic equivalence was achieved through translation, back-translation, back-translation validation, and obtaining a final consensus version by a panel of experts from different NF1 centers in Portugal, composed of 7 doctors and 1 psychologist.

All patients who agreed to participate in the study met the following criteria: age over 18 years; ability to provide informed consent; fluency in Portuguese; known diagnosis of NF1, and regular follow-up at the Neurology Department of IPOLFG. Participants were approached during their previously scheduled Neurofibromatosis outpatient visit. They were given information stating the aims of this project and were invited to participate. A staff nurse provided help in case impairment or disability hindered the fulfillment of the questionnaire, such as visual impairment. Patients who were under 18 years of age; unable to provide informed consent, for example, due to cognitive disability; not fluent in Portuguese; did not have an established medical diagnosis of NF1, and/or were otherwise unavailable to engage in the research, were not included.

Using standard sample size recommendations,[11] of which 5 participants should be recruited for each question, 74 adult participants with NF1 being followed up at the Neurology Department of IPOLFG were recruited.

After obtaining written informed consent, participants completed a brief demographic questionnaire, the INF1-QoL scale, and the EuroQoL scale (EQ 5D-3L).

The EQ-5D questionnaire was employed to investigate concurrent validity both in this study and in the original study, where its results correlated highly with the INF1-QoL. It was considered by the authors of INF1-QoL as the gold standard to assess QoL in the NF1 population. Although a previous questionnaire to assess QoL in the adult NF1 population already existed,[12] the authors of INF1-QoL pointed out its extended length, the lack of assessment in some important domains of NF1 such as bone health and sleep disorders, and the small sample included in its development. Plus, there was no translated or validated version in European Portuguese. As such, the best instrument to assess QoL in NF1, and the one that could be considered a gold standard, was the EQ-5D. It is a standardized measure of health-related quality of life, widely used in both clinical practice and research. It has been in the public domain since 1990 and it was intended for the instrument to add to other QoL measures, making it easier to collect a common data set for reference purposes.[13] The EQ-5D consists of a descriptive system and visual analogue scale (VAS). The EQ-5D comprehends five dimensions such as mobility; self-care; usual activities; pain or discomfort; anxiety and depression. Each dimension can be graded as no problems, some problems, and extreme problems; recognized as a three-dimension version (EQ-5D-3L) and in a newer version (EQ-5D-5L) in five grades. It is worth noting that the EQ 5D-3L scale is so far the only one validated for the Portuguese population. It results in a 1-digit number that represents each one of those five dimensions.[14] The EQ visual analogue scale (VAS) measures the patient's self-rated health on a vertical visual analogue scale of 0 to 100, where the endpoints are labeled 'best imaginable health state' (100) and 'worst imaginable health state' (0). It offers a global health score that reflects the patient's judgment.[14] The Portuguese version of the EQ 5D-3L scale, finalized in 1998, followed the guidance standards defined by the EuroQoL group, including translation and back-translation procedures.[15]

The two main authors of the paper, with expertise in NF1, rated the patient clinical problems listed according to Riccardi's NF1 severity classification, where grades 1 and 2 corresponded to mild disease, grade 3 to moderate disease and grade 4 to severe disease.[16] Similarly to the original article, severity grades 1 and 2 were merged.

In summary, the assessment of the INF1-QoL scale was performed by evaluating internal consistency using Cronbach's alpha, and concurrent validity using Spearman's rank correlation coefficient. Subsequent correlation between the INF1-QoL scale and Riccardi's classification of NF1 severity and the EQ-5D scale was studied. An exploratory factor analysis was also performed. The statistical significance was set at 0.05 (alpha value) and the statistical analysis was performed using RStudio version 2024.04.0+735.[17]

## Results

A total of 74 out of 78 adult patients with NF1 participated in the study. Only 4 participants did not fully complete at least 1 of the questionnaires and hence were excluded from the study. In the study, 37% of the participants were male and 63% female. The mean age was 41.99 years (SD 16.81), and the age range was between 18 and 80 years. In terms of education, 7 (10.14%) of the participants had completed the 4th year of primary school; 15 (21.74%) had completed middle school, 33 (47.83%) had completed secondary school, and 14 (20.29%) had completed higher education. The aim was to obtain a representative sample of NF1. These results show that the European Portuguese version of the INF1-QoL questionnaire is suitable for the NF1 population, as it was easily understandable by patients and most participants completely fulfilled the questionnaire.

The final version of the translation of the INF1-QOL revealed a good internal consistency (Cronbach alpha: 0.86). The mean total score of the INF1-QOL was 9.11 (SD: 6.35), and the median was 8, with a range of values

**Table 1.** Responses to the 14 items of the INF1-QoL in the sample of participants with NF1.

| Question of the INF1-QoL questionnaire | No Problems n (%) | Slight Problems n (%) | Moderate Problems n (%) | Severe Problems n (%) | Pearson Correlation with Total INF1-QoL Score (*p* 2-tailed) | | Spearman Correlation with Total INF1-QoL Score (*p* 2-tailed) | |
|---|---|---|---|---|---|---|---|---|
| Q1 Vision | 28 (40) | 29 (41) | 11 (16) | 2 (3) | .516 | <0.001 | .536 | <0.001 |
| Q2 Cosmetic appearance | 42 (60) | 21 (30) | 6 (9) | 1 (1) | .487 | <0.001 | .419 | <0.001 |
| Q3 Pain quality | 25 (36) | 31 (44) | 12 (17) | 2 (3) | .719 | <0.001 | .752 | <0.001 |
| Q4 Pain intensity | 21 (30) | 24 (34) | 19 (27) | 6 (9) | .626 | <0.001 | .675 | <0.001 |
| Q5 Learning problems | 36 (51) | 23 (33) | 10 (14) | 1 (1) | .572 | <0.001 | .473 | <0.001 |
| Q6 Behaviour and personality | 52 (74) | 13 (19) | 5 (7) | 0 (0) | .573 | <0.001 | .502 | <0.001 |
| Q7 Mobility and walking | 45 (64) | 21 (30) | 4 (6) | 0 (0) | .591 | <0.001 | .518 | <0.001 |
| Q8 Weakness, numbness, clumsiness in hands | 46 (66) | 21 (30) | 3 (4) | 0 (0) | .630 | <0.001 | .570 | <0.001 |
| Q9 Speech | 57 (81) | 12 (17) | 0 (0) | 1 (1) | .505 | <0.001 | .377 | 0.001 |
| Q10 Bones | 42 (60) | 20 (29) | 7 (10) | 1 (1) | .706 | <0.001 | .623 | <0.001 |
| Q11 Breathing | 53 (76) | 13 (19) | 2 (3) | 2 (3) | .526 | <0.001 | .529 | <0.001 |
| Q12 Sleep | 23 (33) | 33 (47) | 13 (19) | 1 (1) | .537 | <0.001 | .571 | <0.001 |
| Q13 Role and outlook on life | 26 (37) | 15 (21) | 20 (29) | 9 (13) | .735 | <0.001 | .770 | <0.001 |
| Q14 Depression and anxiety | 26 (37) | 31 (44) | 10 (14) | 3 (4) | .704 | <0.001 | .686 | <0.001 |

The number and percentage of individuals with no problems, mild, moderate or severe problems for each of the 14 questions are detailed. The numbers inside the brackets correspond to the percentage. Values of $p < 0.05$ were considered statistically significant.

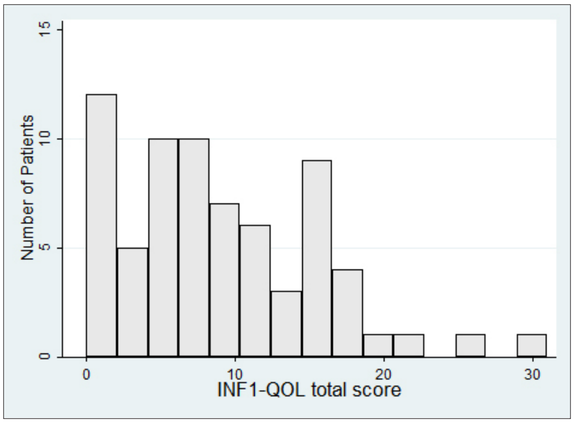


**Figure 1.** Distribution of the total score of the INF1-QoL in the sample of participants with NF1.

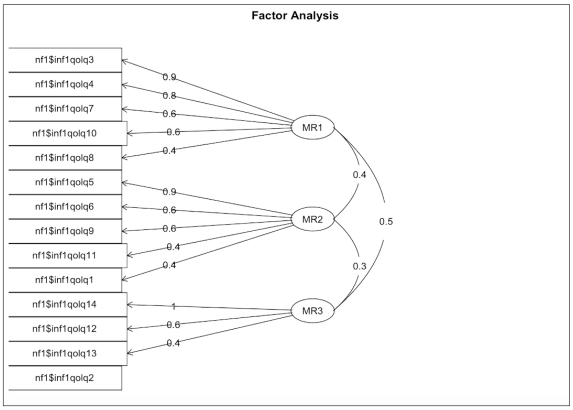


**Figure 2.** Exploratory factor analysis performed in the sample of participants with NF1. The sample was best divided with three factors with no cross-loading pattern.

between 0-31 (**Fig. 1**). The floor effect was 5.7% and the ceiling effect 1.4%, with no association with age (*p*-value = 0.167), gender (*p*-value = 0.143) or education (*p*-value = 0.321).

The answers to the individual items are shown in **Table 1**, where the number and percentage of individuals with no problems, mild, moderate, or severe problems for each of the 14 questions are detailed. Similarly to the previous research conducted, by Ferner *et al*[10] and Bicudo *et al*,[18] question 13 (Q13), which assesses the impact of NF1 on the role and outlook on life, achieved the highest score. In our sample, 49% of participants revealed that the diagnosis of NF1 had a negative impact on their outlook on life. About 28% of participants reported moderate and/or severe problems related to anxiety and depression (Q14). As in the original article,[10] the quality of pain correlates better with the INF1-QoL score than its intensity. However, both have a significant impact on the quality of life of patients. The visibility of dermatological lesions by third parties and the consequent impact on self-image was reported by 30% of participants as mild-to-moderate and by 10% of participants as severe. In the remaining domains, the results showed only mild problems, such as respiratory pathology, learning and speech difficulties.

As performed by Bicudo *et al*,[18] we proceeded to assess an exploratory factor analysis (EFA). Our sample showed a Kaiser-Meyer-Olkin index (0.785) and Bartlett's sphericity test ($\chi^2(91) = 406.08$, $p<0.001$) both supported the EFA. The division in two factors defended by Bicudo *et al*. presented a cross-loading pattern. Our sample was best divided with three factors that presented no cross-loading pattern (**Fig. 2**). Our model showed goodness-of-fit indices of: root mean square error of approximation (RMSEA)=0.091; $\chi^2=83.08$, df=70, $p=0.004$; comparative fit index (CFI)=0.96; Tucker–Lewis's index (TLI)=0.82. Our H-Observed index was <0.35 and may indicate greater complexity or multidimensionality in our sample, compared to Bicudo *et al*.[18]

The mean total EuroQol score was 6.6 (SD 1.55), the median was 6, and the range of values observed was between 5-12. The EQ-VAS score (mean global score) was 71.36 (SD 20.53), the median was 70, and the range of values observed was between 10-100. Individual responses to the five questions (no problems, moderate problems, or extreme problems) are presented in **Table 2**.

**Table 2.** Responses to the EQ-5D-3L in the sample of participants with NF1.

| EQ-5D | Questions | No Problem n (%) | Moderate Problems n (%) | Extreme Problems n (%) |
|---|---|---|---|---|
| Mobility | Q1 | 55 (79) | 15 (21) | |
| Self-care | Q2 | 68 (97) | 2 (3) | |
| Usual activities | Q3 | 57 (81) | 11 (16) | 2 (3) |
| Pain/Discomfort | Q4 | 33 (47) | 36 (51) | 1 (1) |
| Anxiety/Depression | Q5 | 34 (49) | 30 (43) | 6 (9) |

The correlation between the total INF1 and the total EuroQol was $r=0.839$, $p<0.001$, which indicates a strong positive correlation between the total scores of the INF1 questionnaire and the EuroQol questionnaire (**Fig. 3**). This suggests that the INF1 QoL is a valid instrument to assess the QoL in the Portuguese NF1 population.

The clinical severity score according to the Riccardi's scale was 2.96 (SD 0.987) correlated $r=0.279$ with the total INF1-QoL score ($p=0.019$) and correlated $r=0.251$ with the total EuroQol score ($p=0.036$). On the clinical severity scale, 34 (49%) participants had mild NF1, 22 (31%) moderate NF1, and 14 (20%) severe NF1.

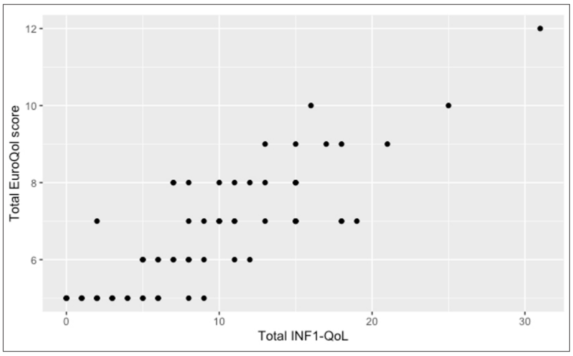


**Figure 3.** Correlation of the total EuroQol score with the total INF1-QoL score in the sample of participants with NF1.

## Discussion

The sample used was considered representative of the adult Portuguese population of patients with NF1 and was well distributed by age and gender. These results agree with the wide range and phenotypic variability of patients with NF1 and with the previous research by Ferner *et al*.[10] We emphasize that NF1 can greatly impact quality of life, with varying severity across different aspects of the condition.

Questions 13 (Q13) and 14 (Q14), represented in **Table 1**, revealed that anxiety, depression, and outlook on life were the items with the most significant impact on quality of life in this population, which is concordant with the literature.[19] In this study, 28% of participants reported moderate and/or severe problems related to anxiety and depression and 49% revealed that the diagnosis of NF1 had a negative impact on their outlook on life. This impact may be particularly significant in patients with family members affected with severe forms of the disease. These values overlap with those obtained in the original article, which is explainable given the chronicity, genetic transmissibility, and unpredictability regarding individual evolution and survival.

Our H-Observed index was <0.35 and it may indicate greater complexity or multidimensionality in our sample compared to Bicudo *et al*.[18] Our results represent a clear difference from their work and further studies are needed to understand and clarify the factors.

The strong positive correlation of $r=0.839$, $p<0.001$ between the total INF1-QoL and EuroQoL suggests a robust alignment between the measures of quality of life as captured by the two instruments within the Portuguese NF1 population. This finding is significant as it supports the concurrent validity of the newly translated INF1-QoL questionnaire. In this instance, the high correlation with the EuroQoL- a well-established tool in health-related quality of life measurement - reinforces the validity of the INF1-QoL as an effective tool for assessing quality of life in individuals with NF1. These results imply that the translated version of the INF1-QoL is not only capable of capturing the quality of life impacts specific to NF1, but also aligns closely with broader, more generalized measures of health-related quality of life. This alignment is crucial for ensuring that the INF1-QoL can be reliably used, in both clinical and research settings, to monitor the well-being of NF1 patients, facilitate comparisons across different studies, and integrate findings into larger datasets or meta-analyses.

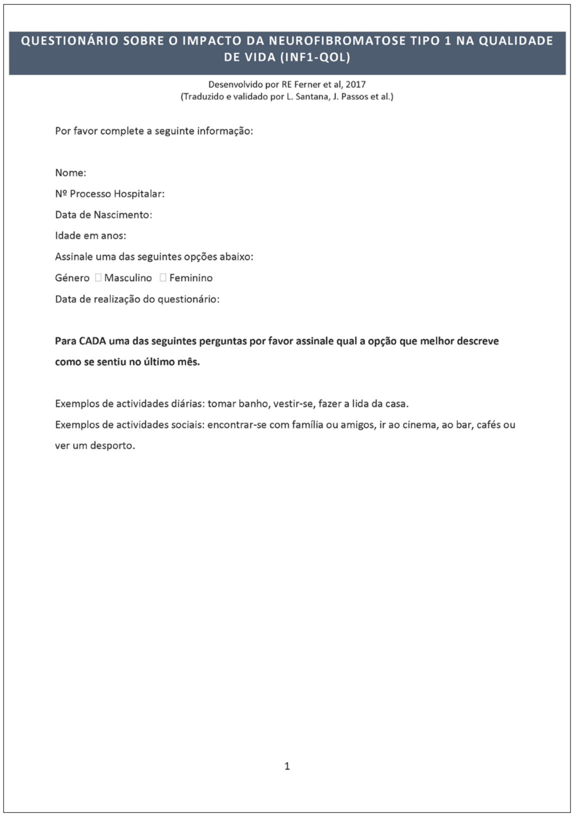
The moderate correlation between clinical severity and INF1-QOL score implies that the severity of the condition as experienced by the individual and assessed by the clinicians may not directly correspond to their reported quality of life scores on the questionnaire. This could be explained by the fact that the patient's perception of their illness is not only impacted by the direct effect of their illness, but also in an indirect way: by the impact NF1 has on family members; their perception of life outcomes; their coping mechanisms and, as previously stated, by the hereditary component of this illness.

Regarding its strengths, this paper employed a rigorous methodology, utilizing standardized assessment tools and appropriate statistical analyses. It also benefits from a sizable and varied sample, improving the applicability of the results to the NF1 adult population. As for its limitations, although the size of the simple followed standard recommendations, the total number of 74 participants could be considered small for generalizing our findings, especially given the diverse manifestations of NF1. We also point out the fact that a convenience sample was included, gathered in a single urban center in the country's capital, which may misrepresent some cultural or geographical sub-groups of the Portuguese population. With this being said, the IPOLFG is the largest center for the diagnosis, treatment, and follow-up of NF1 patients in Portugal which should help mitigate eventual bias. Another limitation we believe existed in our study was the absence of data regarding an inter-rater agreement.

## Conclusion

We conclude that the European Portuguese-translated version of the INF1-QoL questionnaire is both a valid and reliable tool for assessing the Portuguese population of patients with NF1. We believe that it can be a tool with high applicability both in the characterization of patients with NF1 and in the screening of disease-related comorbidities. It may also be useful in the monitoring of long-term therapeutic interventions used regarding the possible improvement in the quality of life of this population. ■

**Annex 1.** Questionnaire.



**QUESTIONÁRIO SOBRE O IMPACTO DA NEUROFIBROMATOSE TIPO 1 NA QUALIDADE DE VIDA (INF1-QOL)**

Desenvolvido por RE Ferner et al, 2017
(Traduzido e validado por L. Santana, J. Passos et al.)

Por favor complete a seguinte informação:

Nome:
Nº Processo Hospitalar:
Data de Nascimento:
Idade em anos:
Assinale uma das seguintes opções abaixo:
Género ☐ Masculino ☐ Feminino
Data de realização do questionário:

**Para CADA uma das seguintes perguntas por favor assinale qual a opção que melhor descreve como se sentiu no último mês.**

Exemplos de actividades diárias: tomar banho, vestir-se, fazer a lida da casa.
Exemplos de actividades sociais: encontrar-se com família ou amigos, ir ao cinema, ao bar, cafés ou ver um desporto.

1

**QUESTIONÁRIO SOBRE O IMPACTO DA NEUROFIBROMATOSE TIPO 1 NA QUALIDADE DE VIDA (INF1-QOL)**

Desenvolvido por RE Ferner et al, 2017
(Traduzido e validado por L. Santana, J. Passos et al.)

**Q1 Sente que problemas com a sua visão interferem com estudar, trabalhar, actividades diárias ou actividades sociais?**

Sem quaisquer problemas com a visão ☐0
Problemas ligeiros mas tenho capacidade de realizar estas actividades ☐1
Problemas moderados com a visão causam dificuldades em realizar estas actividades ☐2
Problemas graves com a visão impedem de realizar estas actividades ☐3

**Q2 A aparência cosmética dos seus neurofibromas (o seu aspecto) interfere com estudar, trabalhar, actividades diárias ou actividades sociais?**

Sem quaisquer dificuldades com a aparência dos meus neurofibromas ☐0
Dificuldades ligeiras mas tenho capacidade de realizar estas actividades ☐1
A aparência dos meus neurofibromas causa problemas moderados em realizar estas actividades ☐2
A aparência cosmética dos meus neurofibromas impede estas actividades ☐3

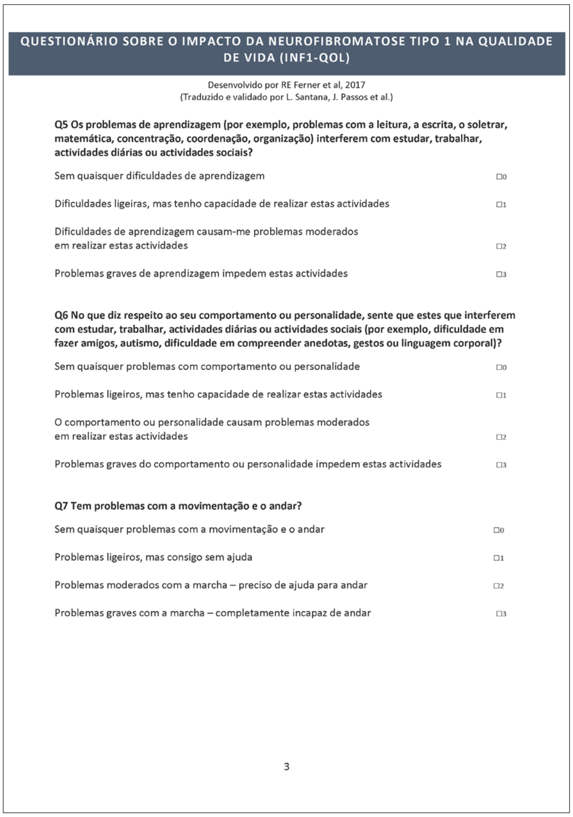
**Q3 Dor - Sofre de dor que interfira com estudar, trabalhar, actividades diárias ou actividades sociais?**

Sem quaisquer problemas com dor ☐0
Dificuldades ligeiras mas tenho capacidade de realizar estas actividades ☐1
A dor causa problemas moderados em realizar estas actividades ☐2
Dor intensa impede estas actividades ☐3

**Q4 Quão forte é a sua dor habitualmente?**

0 = sem dor ☐0
1-4 = dor ligeira ☐1
5-7 = dor moderada ☐2
8-10 = dor severa ☐3

2



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**Q5 Os problemas de aprendizagem (por exemplo, problemas com a leitura, a escrita, o soletrar, matemática, concentração, coordenação, organização) interferem com estudar, trabalhar, actividades diárias ou actividades sociais?**

Sem quaisquer dificuldades de aprendizagem ☐0

Dificuldades ligeiras, mas tenho capacidade de realizar estas actividades ☐1

Dificuldades de aprendizagem causam-me problemas moderados em realizar estas actividades ☐2

Problemas graves de aprendizagem impedem estas actividades ☐3

**Q6 No que diz respeito ao seu comportamento ou personalidade, sente que estes que interferem com estudar, trabalhar, actividades diárias ou actividades sociais (por exemplo, dificuldade em fazer amigos, autismo, dificuldade em compreender anedotas, gestos ou linguagem corporal)?**

Sem quaisquer problemas com comportamento ou personalidade ☐0

Problemas ligeiros, mas tenho capacidade de realizar estas actividades ☐1

O comportamento ou personalidade causam problemas moderados em realizar estas actividades ☐2

Problemas graves do comportamento ou personalidade impedem estas actividades ☐3

**Q7 Tem problemas com a movimentação e o andar?**

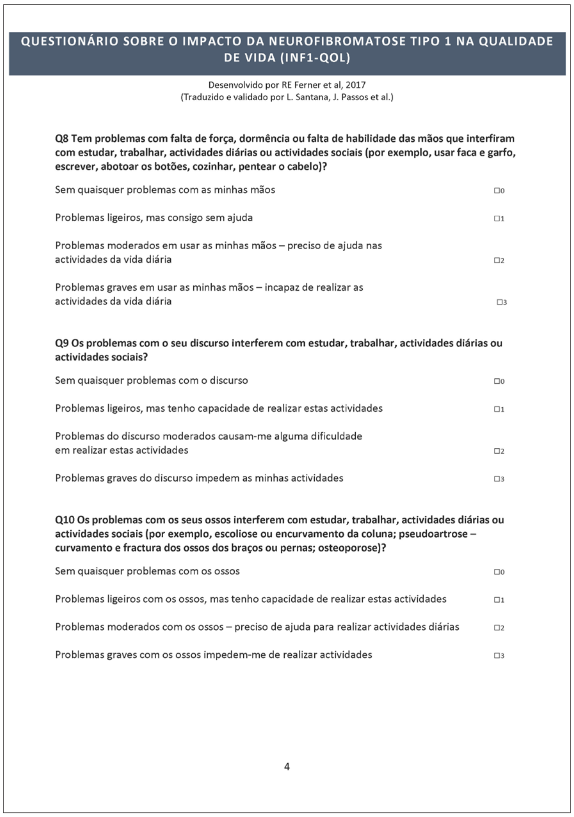
Sem quaisquer problemas com a movimentação e o andar ☐0

Problemas ligeiros, mas consigo sem ajuda ☐1

Problemas moderados com a marcha – preciso de ajuda para andar ☐2

Problemas graves com a marcha – completamente incapaz de andar ☐3

3



**QUESTIONÁRIO SOBRE O IMPACTO DA NEUROFIBROMATOSE TIPO 1 NA QUALIDADE DE VIDA (INF1-QOL)**

Desenvolvido por RE Ferner et al, 2017
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**Q8 Tem problemas com falta de força, dormência ou falta de habilidade das mãos que interfiram com estudar, trabalhar, actividades diárias ou actividades sociais (por exemplo, usar faca e garfo, escrever, abotoar os botões, cozinhar, pentear o cabelo)?**

Sem quaisquer problemas com as minhas mãos ☐0

Problemas ligeiros, mas consigo sem ajuda ☐1

Problemas moderados em usar as minhas mãos – preciso de ajuda nas actividades da vida diária ☐2

Problemas graves em usar as minhas mãos – incapaz de realizar as actividades da vida diária ☐3

**Q9 Os problemas com o seu discurso interferem com estudar, trabalhar, actividades diárias ou actividades sociais?**

Sem quaisquer problemas com o discurso ☐0

Problemas ligeiros, mas tenho capacidade de realizar estas actividades ☐1

Problemas do discurso moderados causam-me alguma dificuldade em realizar estas actividades ☐2

Problemas graves do discurso impedem as minhas actividades ☐3

**Q10 Os problemas com os seus ossos interferem com estudar, trabalhar, actividades diárias ou actividades sociais (por exemplo, escoliose ou encurvamento da coluna; pseudoartrose – curvamento e fractura dos ossos dos braços ou pernas; osteoporose)?**

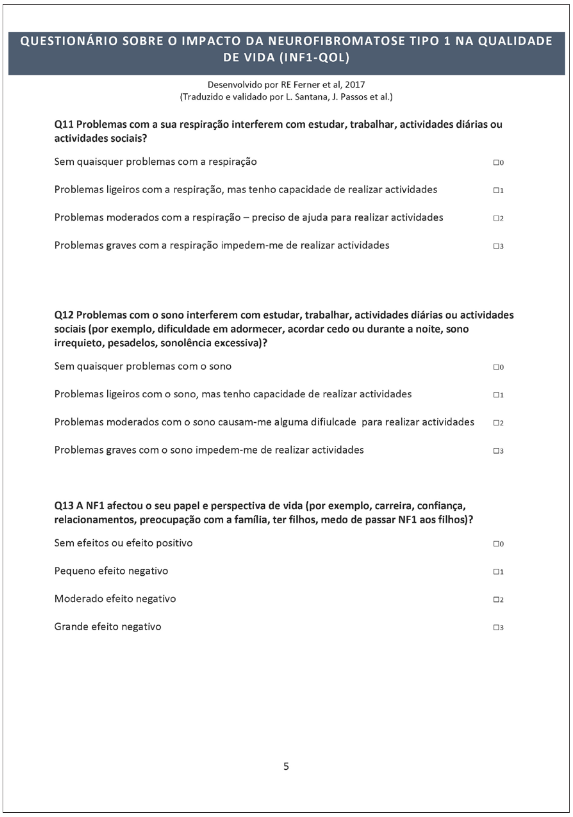
Sem quaisquer problemas com os ossos ☐0

Problemas ligeiros com os ossos, mas tenho capacidade de realizar estas actividades ☐1

Problemas moderados com os ossos – preciso de ajuda para realizar actividades diárias ☐2

Problemas graves com os ossos impedem-me de realizar actividades ☐3

4



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**Q11 Problemas com a sua respiração interferem com estudar, trabalhar, actividades diárias ou actividades sociais?**

Sem quaisquer problemas com a respiração ☐0

Problemas ligeiros com a respiração, mas tenho capacidade de realizar actividades ☐1

Problemas moderados com a respiração – preciso de ajuda para realizar actividades ☐2

Problemas graves com a respiração impedem-me de realizar actividades ☐3

**Q12 Problemas com o sono interferem com estudar, trabalhar, actividades diárias ou actividades sociais (por exemplo, dificuldade em adormecer, acordar cedo ou durante a noite, sono irrequieto, pesadelos, sonolência excessiva)?**

Sem quaisquer problemas com o sono ☐0

Problemas ligeiros com o sono, mas tenho capacidade de realizar actividades ☐1

Problemas moderados com o sono causam-me alguma difiulcade para realizar actividades ☐2

Problemas graves com o sono impedem-me de realizar actividades ☐3

**Q13 A NF1 afectou o seu papel e perspectiva de vida (por exemplo, carreira, confiança, relacionamentos, preocupação com a família, ter filhos, medo de passar NF1 aos filhos)?**

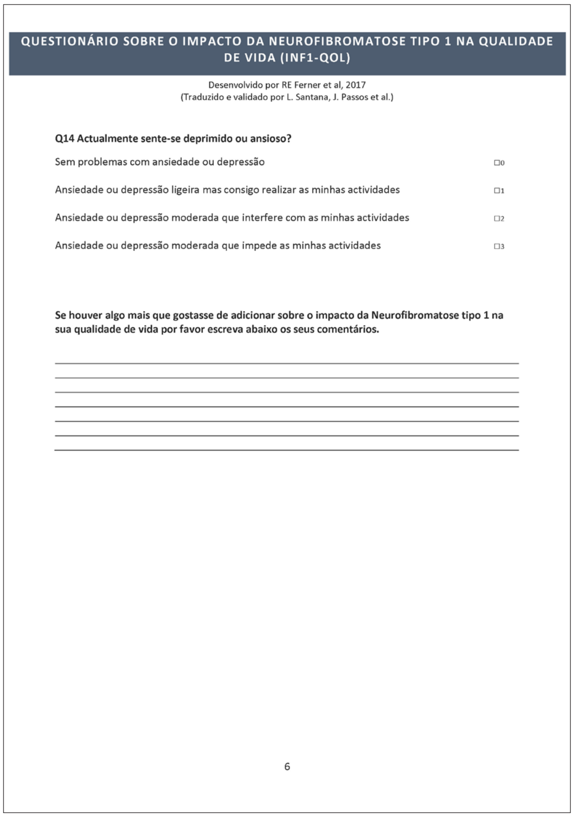
Sem efeitos ou efeito positivo ☐0

Pequeno efeito negativo ☐1

Moderado efeito negativo ☐2

Grande efeito negativo ☐3

5



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**Q14 Actualmente sente-se deprimido ou ansioso?**

Sem problemas com ansiedade ou depressão ☐0

Ansiedade ou depressão ligeira mas consigo realizar as minhas actividades ☐1

Ansiedade ou depressão moderada que interfere com as minhas actividades ☐2

Ansiedade ou depressão moderada que impede as minhas actividades ☐3

**Se houver algo mais que gostasse de adicionar sobre o impacto da Neurofibromatose tipo 1 na sua qualidade de vida por favor escreva abaixo os seus comentários.**

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### Contributorship Statement / Declaração de Contribuição

LBS, JP: Study design; data acquisition and analysis; writing, edition and revision of the last versions of the article prior to publication.

DJ: Data analysis; writing, edition and revision of the last versions of the article prior to publication.

FA: Study design; writing, edition and revision of the last versions of the article prior to publication.

DN: Statistical treatment and data analysis;writing, edition and revision of the last versions of the article prior to publication.

DS: Study design; supervised and reviewed the last versions of the article prior to publication.

All authors discussed and reviewed the final manuscript and agreed with it before submission.

LBS, JP: Conceptualização do artigo; recolha e análise dos dados; redação, edição e revisões finais do manuscrito prévias à publicação.

DJ: Análise de dados; redação, edição e revisões finais do manuscrito prévias à publicação.

FA: Conceptualização do artigo; redação, edição e revisões finais do manuscrito prévias à publicação.

DN: Tratamento estatístico de dados; análise dos dados; revisões finais do manuscrito prévias à publicação.

DS: Conceptualização do artigo; supervisão e revisão final do manuscrito.

Todos os autores avaliaram e concordaram com o manuscrito final prévio à publicação..

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Proteção de Pessoas e Animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pela Comissão de Ética responsável e de acordo com a Declaração de Helsínquia revista em 2013 e da Associação Médica Mundial.

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## References / Referências

1. Ferner RE. Neurofibromatosis 1 and Neurofibromatosis 2: a twenty-first century perspective. Lancet Neurol. 2007;6:340–51.
2. Ferner RE. Psychological impact of the Neurofibromatoses. In: Ferner RE, Huson SM, Evans DG, editors. Neurofibromatoses in clinical practice. Berlin: Springer; 2011. p. 129-140.
3. Belzeaux R, Lançon C. Neurofibromatose de type 1. Troubles psychiatriques et altération de la qualité de vie. Presse Med. 2006;35:277-80.
4. Vranceanu AM, Merker VL, Park E, Plotkin SR. Quality of life among adult patients with neurofibromatosis 1, neurofibromatosis 2 and schwannomatosis: a systematic review of the literature. J Neurooncol. 2013;114:257-62. doi: 10.1007/s11060-013-1195-2.
5. Jenkinson C, Coulter A, Wright L. Short form 36 (SF36) health survey questionnaire: normative data for adults of working age. BMJ. 1993;306:1437–40.
6. The EuroQol Group. EuroQol—a new facility for the measurement of health-related quality of life. Health Policy. 1990;16:199–208.
7. Crawford HA, Barton B, Wilson MJ, Berman Y, McKelvey-Martin VJ, Morrison PJ et al. The impact of neurofibromatosis type 1 on the health and wellbeing of australian adults. J Genet Couns. 2015;24:931–44. doi: 10.1007/s10897-015-9829-5.
8. Bicudo NP, de Menezes Neto BF, da Silva de Avó LR, Germano CM, Melo DG. Quality of life in adults with neurofibromatosis 1 in Brazil. J Genet Couns. 2016;25:1063–74. doi: 10.1007/s10897-016-9939-8.
9. Granstrom S, Lanagenbruch A, Augsutin M, Mautner VF. Psychological burden in adult neurofibromatosis type 1 patients: impact of disease visibility on body image. Dermatology. 2012;224: 60–77. doi: 10.1159/000337548.
10. Ferner RE, Thomas M, Mercer G, Williams V, Leschziner GD, Afridi SK, et al. Evaluation of quality of life in adults with neurofibromatosis 1 (NF1) using the Impact of NF1 on Quality Of Life (INF1-QOL) questionnaire. Health Qual Life Outcomes. 2017;15:34.  doi: 10.1186/s12955-017-0607-y.
11. Tsang S, Royse CF, Terkawi AS. Guidelines for developing, translating, and validating a questionnaire in perioperative and pain medicine. Saudi J Anaesth. 2017;11:S80-9. doi: 10.4103/sja.SJA_203_17.
12. Nutakki K, Hingtgen CM, Monahan P, Varni JW, Swigonski NL. Development of the adult PedsQL™ neurofibromatosis type 1 module: initial feasibility, reliability and validity. Health Qual Life Outcomes. 2013;11:21. doi: 10.1186/1477-7525-11-21.
13. Brooks R. EuroQol: the current state of play. Health Policy.1996;37:53–72. doi: 10.1016/0168-8510(96)00822-6
14. EuroQoL. EQ-5D. 2023. [Accessed July 27, 2023] Available at: https://euroQoL.org/eq-5d-instruments
15. Ferreira PL, Ferreira LN, Pereira LN. Contributos para a Validação da Versão Portuguesa do EQ-5D. Acta Med Port. 2013;26:664-75.
16. Riccardi VM, Kleiner B. Neurofibromatosis: a neoplastic birth defect with two age peaks of severe problems. Birth Defects Orig Artic Ser. 1977;13:131-8.
17. Posit team. RStudio: Integrated Development Environment for R. [Accessed May 11, 2024] Available at: http://www.posit.co
18. Bicudo NP, de Menezes Neto BF, da Silva de Avó LR, Germano CM, Melo DG. Quality of Life in Adults with Neurofibromatosis 1 in Brazil. J Genet Couns. 2016;25:1063–74.
19. Brar KS, Trivedi C, Kaur N, Adnan M, Patel H, Beg U, et al. Prevalence of psychiatric comorbidities in patients with neurofibromatosis. Prim Care Companion CNS Disord. 2023;25:23m03514. doi: 10.4088/PCC.23m03514.