

## Main Article

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## Abstract

**Objectives.** In decision making regarding the management of vestibular schwannomas, alongside clinical outcomes, an understanding of patient reported health-related quality of life measures is key. Therefore, the aim of this research is to compare health-related quality of life in vestibular schwannoma patients treated with active observation, stereotactic radiotherapy and microsurgical excision.

**Methods.** A cross-sectional study of patients diagnosed with unilateral sporadic vestibular schwannomas between 1995 and 2015 at a specialist tertiary centre was conducted. Patients completed the Penn Acoustic Neuroma Quality of Life questionnaire and handicap inventories for dizziness, hearing and tinnitus.

**Results.** Of 234 patients, 136 responded (58.1 per cent). Management modality was: 86 observation, 23 stereotactic radiotherapy and 25 microsurgery. Females reported significantly worse dizziness; males reported significantly worse physical disability. Patients less than 65 years old reported significantly worse tinnitus and pain scores. Overall, quality of life was higher in the observation group.

**Conclusion.** Conservative management, where appropriate, is favourable with higher quality-of-life outcomes in this cohort. This must be weighed against the risks of a growing tumour.

## Introduction

### Background

Decision making regarding the optimal management of vestibular schwannomas is multifactorial taking into consideration tumour size, rate of growth, tumour location, hearing, facial function, patient factors, and institutional expertise. Management modalities for vestibular schwannoma include microsurgical excision, radiation therapy (stereotactic radiosurgery and stereotactic radiotherapy), and active observation with serial magnetic resonance imaging (MRI).

Their often-indolent nature is now better recognised and observational studies have demonstrated that once detected, many vestibular schwannomas undergo minimal or no growth, remaining unchanged over long-term follow up.<sup>1</sup> A review of over 4000 cases found one-third of vestibular schwannomas grew in the three years after diagnosis, that the average growth rate was 0.99–1.11mm/year and progression in the first year was a predictor of the likelihood of tumour growth.<sup>2</sup>

There has been a rise in the incidence and early detection of vestibular schwannomas, potentially due to the availability, widespread use and improved sensitivity of MRI, in addition to the implementation of guidelines for the investigation of asymmetric sensorineural hearing loss.<sup>3,4</sup> A proportion of those diagnosed present with small to medium-sized vestibular schwannomas and few or no audio-vestibular symptoms.<sup>5</sup> Vestibular schwannoma mortality rates are extremely low whilst treatment-associated morbidity can be significant. Subsequently, there has been a shift toward an emphasis on function preservation and quality-of-life (QoL) outcomes, in addition to tumour control, in the management of vestibular schwannomas.<sup>6,7</sup>

Shaffer et al. published the first validated disease-specific health-related quality-of-life (QoL) instrument for vestibular schwannomas in 2010: the Penn Acoustic Neuroma QoL scale.<sup>8</sup> The availability of a disease-specific measure has provided a reliable instrument to study health-related QoL in vestibular schwannoma management. The Penn Acoustic Neuroma QoL assesses seven disease-specific domains: anxiety, balance, general health, hearing, energy, pain and facial function.

Early studies showed that balance symptoms have the most detrimental effect upon long-term health-related QoL (more so than hearing loss and tinnitus).<sup>9–12</sup> Although even a modest drop in hearing has been shown to still adversely affect QoL.<sup>13</sup>

## Objective

The aim of this study is to investigate patient-reported, health-related QoL associated with the three main treatment modalities, with particular focus on the effect of symptoms of dizziness, hearing and tinnitus.

## Materials and methods

### Ethical considerations

Approval for the study was granted by the Liverpool University Hospitals NHS Foundation Trust's Audit & Research Department.

### Participants

This was a cross-sectional study conducted retrospectively at a single tertiary referral centre in Liverpool, UK. All patients over the age of 18 diagnosed with a sporadic unilateral vestibular schwannoma between 1995 and 2015 on the skull base register were included. Those with neurofibromatosis type-2 were excluded.

### Study design and setting

Patients were categorised by treatment modality: active observation, stereotactic radiotherapy or microsurgical excision. Management decisions were made by a multidisciplinary team in collaboration with the patient. Generally, for smaller tumours (< 3 cm), patients had MRI at six months after initial diagnosis to assess for growth. If negative, patients were observed with an annual MRI for five years, two yearly for six years and then three yearly for life. If patients reported new or a change in existing symptoms, the scan was expedited. Patients with small to medium-sized tumours (1–3 cm) with evidence of growth were offered microsurgery or stereotactic radiotherapy. Large tumours (> 3 cm) were usually managed with microsurgical excision (translabrynthine (75 per cent) or retrosigmoid (25 per cent) approaches). The data were analysed to compare the three management modalities and patient-reported outcomes by gender, age, tumour size and length of follow up.

### Instruments

Patients were surveyed using the Penn Acoustic Neuroma QoL, dizziness handicap inventory, hearing handicap inventory and tinnitus handicap inventory.

#### *Penn Acoustic Neuroma Quality of Life (QoL)*

The Penn Acoustic Neuroma QoL comprises 26 questions on a 5-point Likert scale with 1 signifying strong disagreement and 5 strong agreement. It assesses seven disease-specific domains: anxiety, balance, general health, hearing, energy, pain and facial function. Domain scores are added to give a total score from 0 to 100 with a higher score representing a higher QoL.

#### *Hearing handicap inventory*

The hearing handicap inventory consists of 25 questions grouped into two subscales that assess the emotional and social effects of hearing loss. It was designed as an instrument to evaluate patients' perception of the effect of their hearing

loss on daily life and psychosocial function not represented in audiological testing.<sup>14</sup>

#### *Dizziness handicap inventory*

The dizziness handicap inventory consists of 25 questions grouped into three subscales that assess the functional, emotional and physical effects of vestibular dysfunction upon daily life. It was developed as a measure to assess patients' perception of the handicap caused by their vestibular disorder.<sup>15</sup>

#### *Tinnitus handicap inventory*

The tinnitus handicap inventory consists of 25 questions grouped into three subscales that assess the functional, emotional and catastrophic response to tinnitus. It was developed to classify patients' perceived effect of tinnitus on their daily life.<sup>16</sup>

The handicap inventories are robust tools with high internal consistency, high test–retest reliability and its repeatability detects differences in patient-perceived handicap.<sup>17</sup> Each of the handicap inventories consist of 25 self-assessment questions to which the respondent chooses to answer “yes, maybe or no” denoting 4, 2 and 0 points respectively. A total score is calculated (0–100) with a high score representing a worse handicap, which notably is opposite to the Penn Acoustic Neuroma QoL scoring system.

### Statistical analysis

The variables examined for each cohort were gender, age, tumour size at diagnosis, Penn Acoustic Neuroma QoL, and hearing handicap inventory, dizziness handicap inventory and tinnitus handicap inventory questionnaire scores. Descriptive statistics were performed to study the relationships among these variables. Not all the continuous variables were normal, therefore non-parametric tests were performed. Wilcoxon–Mann–Whitney and Kruskal–Wallis tests were used to examine the independent data series. A statistical significance level of 5 per cent ( $p$ -value  $\leq 0.05$ ) was applied.

## Results

### *Patient demographics*

Of the 234 patients that met the inclusion criteria, 136 completed the questionnaires (response rate 58.1 per cent). Two were excluded due to incomplete data. There were 65 males and 69 females. Categorised by management modality, 86 patients were managed with active observation, 23 with radiotherapy and 25 underwent microsurgical excision. In line with current literature, those with smaller tumours (< 15 mm) were more likely to be observed ( $p = 0.001$ ), compared to those with larger tumours (> 15 mm), who were more likely to undergo treatment in the form of radiotherapy or microsurgical excision ( $p = 0.001$ ).

### *Comparison by gender*

A Wilcoxon–Mann–Whitney test was selected to assess between the male ( $n = 65$ ) and female ( $n = 69$ ) subgroups as an effective test for comparing independent subsets of data with low sample numbers. Female patients reported significantly worse dizziness compared to male patients when answering the Penn Acoustic Neuroma QoL questionnaire ( $p = 0.036$ ). According to the dizziness handicap inventory, male patients reported significantly worse physical disability than reported by female patients ( $p = 0.013$ ). There were no

significant differences between genders in any of the other subdomains.

### Comparison by age

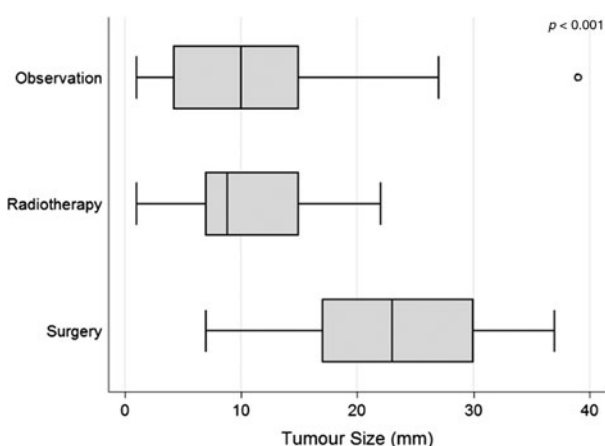
Because the two data series were independent, a Wilcoxon–Mann–Whitney test was performed to compare patients less than 65 years old ( $n = 58$ ) or 65 years old and older ( $n = 69$ ). The younger-aged group complained of significantly more pain according to the Penn Acoustic Neuroma QoL questionnaire ( $p = 0.013$ ). There was also a trend towards worse facial function on the Penn Acoustic Neuroma QoL questionnaire in younger patients, but this was not significant ( $p = 0.063$ ). All three tinnitus handicap inventory subgroup scores differed between age categories, with patients less than 65 years old reporting worse functional ( $p = 0.009$ ), emotional ( $p = 0.006$ ) and catastrophic outcomes ( $p = 0.011$ ) than patients 65 years old or older.

### Comparison by tumour size

Patients were categorised by tumour size (155 m mm or less, including intracanalicular lesions, and tumours greater than 155 m mm) at time of diagnosis. Tumour size across the three management groups was assessed and  $p$ -values obtained performing Fisher's exact and Kruskal–Wallis tests. As expected, tumour size was significantly smaller in the observation cohort ( $p < 0.001$ ) (Figure 1). Questionnaire scores did not differ between tumour sizes, except for Penn Acoustic Neuroma QoL facial-function scores, which showed that patients with a larger tumour complained of significantly worse facial symptoms ( $p = 0.039$ ) (Table 1).

### Comparison by treatment modality

Table 2 and Figure 2 display questionnaire scores (subgroups and total) by management group with the median and interquartile range. Because subgroups were being compared with total score the Kruskal–Wallis test was selected. Overall, the Penn Acoustic Neuroma QoL score demonstrated a better QoL in patients who were managed conservatively ( $p = 0.001$ ). Interestingly, anxiety and energy were not affected by treatment modality. The observation group had significantly lower dizziness handicap inventory total scores, indicating a better outcome in terms of dizziness handicap compared to



**Figure 1.** Comparison of vestibular schwannoma size (mm) at time of diagnosis in patients managed with active observation ( $n = 86$ ), stereotactic radiotherapy ( $n = 23$ ) or microsurgical excision ( $n = 25$ ).

microsurgery and radiotherapy. Assessed by dizziness handicap inventory subdomains there was statistical difference for the physical domain ( $p = 0.002$ ) but not for the functional and emotional domains. Importantly though, the dizziness handicap inventory questionnaire was designed for vertigo, not for general unsteadiness usually caused by a vestibular schwannoma. The tinnitus handicap inventory scores showed a significantly worse QoL in patients who underwent radiotherapy ( $p = 0.018$ ). Finally, the hearing handicap inventory score was not found to be different across the three treatment modality groups, reflecting that hearing reduces regardless of the management. However, the Penn Acoustic Neuroma QoL did identify better hearing QoL in the observation group.

### Comparison by follow-up duration

Length of follow up, calculated as time from diagnosis to date of completing the questionnaire, was analysed for 122 patients. Those who had surgery or radiotherapy were combined to form two groups: observation and a joined-treatment group. Length of follow up was categorised into 0–3 and  $\geq 4$  years. Total mean length of follow up was four years (interquartile range 2, 5). Table 3 shows the total QoL scores by follow-up period and group.

## Discussion

### Discussion of results

Understanding and informing patients about health-related QoL outcomes is crucial to conveying risk, projecting long

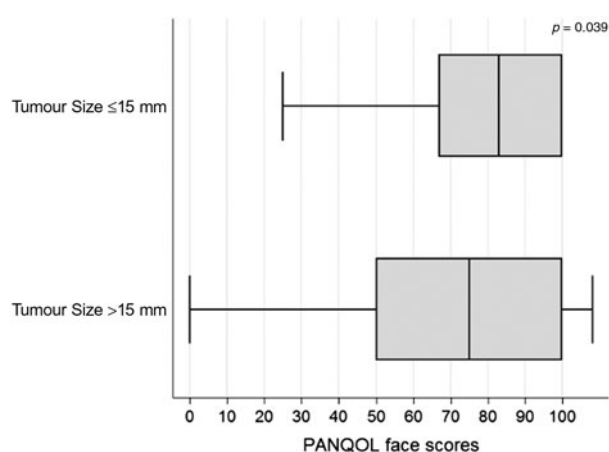
**Table 1.** Comparison of subdomain and total scores for Penn Acoustic Neuroma Quality of Life (PANQOL), hearing handicap inventory (HHI), dizziness handicap inventory (DHI) and tinnitus handicap inventory (THI) with vestibular schwannoma size of  $\leq 155$  m mm (including intracanalicular (IC)) or  $> 155$  m mm at the time of diagnosis. Values shown with median and interquartile range

	Tumour Size		$p$
	$\leq 15$ mm (IC included)	$> 15$ mm	
PANQOL, $n$	79	38	
– Anxiety	75(56,100)	66(38,94)	0.129
– Face	83(67,100)	75(50,100)	0.039
– General	50(50,63)	50(50,63)	0.942
– Balance	71(38,92)	67(29,79)	0.283
– Hearing	56(31,69)	44(31,75)	0.395
– Energy	63(42,83)	58(33,75)	0.332
– Pain	80(60,100)	80(40,100)	0.613
HHI, $n$	79	37	
– Social	18(10,28)	18(12,32)	0.457
– Emotional	16(8,30)	24(10,32)	0.191
DHI, $n$	79	38	
– Functional	2(0,12)	6(0,12)	0.097
– Emotional	2(0,10)	5(0,14)	0.080
– Physical	4(0,10)	7(0,14)	0.202
THI, $n$	79	38	
– Functional	8(0,18)	10(0,20)	0.814
– Emotional	0(0,8)	5(0,12)	0.209
– Catastrophic	4(0,8)	5(0,8)	0.704

**Table 2.** Comparison of subdomain and total scores for Penn Acoustic Neuroma Quality-of-Life (PANQOL), hearing handicap inventory (HHI), dizziness handicap inventory (DHI) and tinnitus handicap inventory (THI) questionnaires in patients managed with active observation ( $n = 86$ ), stereotactic radiotherapy ( $n = 23$ ) or microsurgery ( $n = 25$ ). Values shown with median and interquartile range

	Management Groups			<i>p</i>
	Observation	Radiotherapy	Surgery	
PANQOL, <i>n</i>	86	23	25	
- Anxiety	75(56,100)	63(38,100)	75(50,88)	0.194
- Face	96(75,100)	83(67,100)	58(33,75)	< 0.001
- General	50(38,63)	50(50,63)	50(50,63)	0.912
- Balance	75(46,100)	50(29,75)	50(29,67)	< 0.001
- Hearing	56(44,75)	31(19,56)	38(31,69)	0.014
- Energy	67(46,83)	46(25,83)	50(33,71)	0.075
- Pain	80(60,100)	60(40,100)	60(40,80)	0.005
- Total	69(61,83)	57(44,75)	56(45,68)	0.001
HHI, <i>n</i>	85	24	24	
- Social	16(8,26)	23(12,34)	18(11,29)	0.077
- Emotional	16(6,28)	27(12,41)	18(10,30)	0.055
- Total	32(14,54)	48(25,74)	37(24,64)	0.055
DHI, <i>n</i>	86	23	25	
- Functional	2(0,8)	4(0,20)	8(4,18)	0.023
- Emotional	2(0,10)	8(2,14)	6(4,14)	0.054
- Physical	2(0,10)	8(2,16)	12(4,16)	0.002
- Total	9(0,28)	18(8,54)	24(12,46)	0.005
THI, <i>n</i>	87	23	24	
- Functional	4(0,16)	16(8,22)	9(1,17)	0.020
- Emotional	0(0,8)	6(2,12)	3(0,9)	0.034
- Catastrophic	2(0,8)	6(4,10)	4(0,8)	0.036
- Total	10(0,32)	26(12,44)	15(3,37)	0.018

term morbidity and for informed decision making. In this study, the overall Penn Acoustic Neuroma QoL score was significantly higher in the observation cohort ( $p = 0.001$ ). This is



**Figure 2.** Comparison of facial function subdomain scores for Penn Acoustic Neuroma Quality-of Life (PANQOL) questionnaire for vestibular schwannoma size of  $\leq 155$  mm (including intracranial) or  $> 155$  mm at time of diagnosis.

consistent with some studies,<sup>18</sup> whilst others have reported no significant difference between treatment modalities.<sup>19–21</sup> Interestingly, in a longitudinal study comparing Penn Acoustic Neuroma QoL scores in observation versus stereotactic radiosurgery groups, the baseline Penn Acoustic Neuroma QoL score was higher in the observation group, but the scores were equivalent at the end of follow up.<sup>22</sup> Conversely, another longitudinal study reported that Penn Acoustic Neuroma QoL scores remained consistent with no effect of time since diagnosis, irrespective of the initial management modality.<sup>17</sup>

Comparison of questionnaire scores by tumour size identified that larger tumours showed a significantly lower score for the facial function domain of the Penn Acoustic Neuroma QoL only ( $p = 0.039$ ). This is anticipated for two reasons. Firstly, larger tumours are more likely to affect the facial nerve causing compression and weakness. Secondly, large tumours are more likely to be managed with microsurgery or radiotherapy, which is associated with a higher risk of facial dysfunction.

Penn Acoustic Neuroma QoL subdomain scores demonstrated perceived pain being significantly lower in the observation group. The disease process in vestibular schwannomas is not characterised by pain and very rarely associated with



**Table 3.** Total QoL scores by follow up period and group. Values shown with median and interquartile range

	Observation		Treatment (Surgery or Radiotherapy)	
	0–3 years (n = 31)	4 or more years (n = 45)	0–3 years (n = 18)	4 or more years (n = 28)
Follow-up (years)	2(1, 3)	5(4, 6)	2(2, 3)	5(4, 5)
PANQOL score	67(58, 86)	72(64, 79)	53(42, 63)	59(45, 75)
HHI score	30(14, 48)	34(14, 59)	36(24, 50)	51(25, 71)
DHI score	13(0, 31)	6(0, 24)	18(9, 31)	16(9, 51)
THI score	14(0, 33)	8(0, 28)	11(5, 27)	28(17, 41)

trigeminal neuralgia.<sup>23</sup> In contrast, protracted headache and neuralgia is a recognised sequela of microsurgery and stereotactic radiosurgery.<sup>24,25</sup>

The Penn Acoustic Neuroma QoL balance subdomain was significantly lower in the microsurgery and radiotherapy groups, demonstrating less favourable outcome. The overall dizziness handicap inventory score was significantly worse in patients who underwent surgery compared to observation and radiotherapy ( $p = 0.005$ ). It may be expected that the patient would centrally compensate over time from the initial imbalance due to a unilateral vestibular loss after tumour removal, however this is not reflected in our patient cohort. Alternatively, it could be that a higher proportion of the microsurgery group had vestibular complaints (compounded by other patient factors) prior to treatment and thus were more likely to have intervention. Importantly, long term vertigo and balance symptoms have repeatedly been shown to have the most detrimental effect on health-related QoL over other domains such as hearing loss or tinnitus, making them key considerations.

The hearing handicap inventory score was not found to be different across the three treatment modality groups, reflecting that regardless of the management, hearing reduces which is well recognised. Interestingly though, the Penn Acoustic Neuroma QoL did identify a difference in hearing among the management groups. The hearing subdomain score was significantly higher in the observation group, indicating a more favourable outcome, compared with the stereotactic radiotherapy and microsurgery groups ( $p = 0.014$ ).

Operating to preserve hearing has variable success rates. Only patients with good hearing (American Academy of Otolaryngology Head and Neck Surgery class A or B) with tumours up to 2.5 cm in size usually considered for hearing preservation.<sup>26</sup> In this study, hearing-preservation surgery was attempted in few patients. In a meta-analysis of hearing preservation after vestibular schwannoma resection, immediate post-operative usable hearing (classified as American Academy of Otolaryngology Head and Neck Surgeons class A and B or Gardner Robinson grade 1 and 2) was preserved in 50–70 per cent of patients.<sup>27</sup> Of these, 70 per cent retained usable hearing after five years post-surgery. There was no

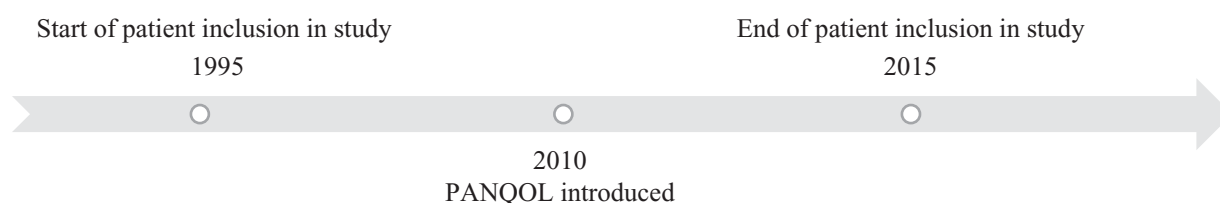
difference in hearing preservation between a middle-cranial fossa or retrosigmoid approach. In a meta-analysis of long-term hearing preservation after stereotactic radiosurgery, preservation was achieved in almost 60 per cent more than six years post treatment.<sup>28</sup> In 100 per cent of patients with speech discrimination at presentation that were managed with observation, 69 per cent continued to have good hearing more than 10 years post treatment.<sup>29</sup>

- The Penn Acoustic Neuroma Quality of Life questionnaire is a validated disease-specific health-related quality-of-life instrument for vestibular schwannomas
- Comparing questionnaire scores by tumour size identified that patients with larger tumours had a significantly lower Penn Acoustic Neuroma Quality of Life facial-function score
- The Penn Acoustic Neuroma Quality of Life balance score was significantly lower in the microsurgery and radiotherapy groups
- The Penn Acoustic Neuroma Quality of Life scores for anxiety and energy were not affected by treatment modality, suggesting that once recovered from microsurgery or radiotherapy, energy levels return to normal
- The hearing handicap inventory score did not differ across treatment modalities, reflecting that hearing reduces regardless of management
- When suitable, depending on tumour size and symptoms, conservative management with active observation allows a better health-related quality of life, although this must be weighed against the risks of a growing tumour

Interestingly the Penn Acoustic Neuroma QoL scores for anxiety and energy were not affected by treatment modality. This may indicate that once patients have recovered from microsurgery or radiotherapy their energy levels return to normal. One study reported better anxiety outcomes in patients managed with microsurgery, which the authors attributed to the tumour having been removed.<sup>18</sup> Conversely, another study identified worse anxiety outcomes over time in patients managed with microsurgery.<sup>19</sup> It is well recognised that, regardless of treatment modality, at the time of diagnosis patients report increased anxiety and a temporary reduction in QoL.<sup>30</sup>

### Study limitations

There are some limitations of this study. This study has taken a cross-sectional view of health-related QoL at one point in time, however patients' symptoms are likely fluid and change with

**Figure 3.** Study-inclusion timeline (from date of diagnosis) and introduction of the Penn Acoustic Neuroma Quality-of Life (PANQOL) instrument.

time, thus a longitudinal study would be needed to capture this. The study inclusion time was from 1995 to 2015, which included some time prior to the introduction of the Penn Acoustic Neuroma QoL questionnaire in 2010 (Figure 3). The inclusion length was decided upon to capture a sufficient number of vestibular schwannoma cases for meaningful analysis, taking into account their low incidence, and to allow for some comparison by follow-up duration. To the authors' knowledge, this is the first study to use the Penn Acoustic Neuroma QoL questionnaire together with the handicap inventories. Whilst these have never been formally compared in the literature and it is beyond the scope of this paper, this would be an interesting area to investigate.

### Future work

Following on from the Penn Acoustic Neuroma QoL, Carlson et al. published a validated disease-specific quality-of-life instrument for sporadic vestibular schwannoma: the Mayo Clinic vestibular schwannoma QoL index.<sup>31</sup> This puts more emphasis on previously underrepresented domains that affect QoL such as cognition, occupational limitations and management satisfaction. It would be interesting to assess these other QoL domains using this instrument in the vestibular schwannoma group.

### Conclusion

When suitable, depending on tumour size and symptoms, conservative management with active observation allows a better health-related QoL than treatment with stereotactic radiotherapy or microsurgery. This must be weighed against the risks of a growing tumour.

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**Ethical standards statement.** Approval for the study was granted by the Liverpool University Hospitals NHS Foundation Trust's Audit & Research Department.

**Competing interests statement.** The authors declare none.

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