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# Quality of life outcomes in acoustic neuroma: systematic review (2000–2021)

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#### **Abstract**

**Background:** The majority of acoustic neuroma (AN) outcome studies examine medical outcomes. An alternative is to examine how AN, its treatment, and complications impact patients' quality of life (QOL). A systematic review for AN was conducted using MEDLINE, PUBMED, and EMBASE.

Manuscripts were limited to human participants, written in English, and published from 2000 to 2021. Of 426 unique citations, only 48 examined QOL outcomes. Risk of bias was assessed using Downs and Black's Quality Assessment Index.

**Results:** Sixteen studies (33.3%) compared AN patients to normative/control data, 15 (31.25%) compared QOL outcomes between treatment groups, 8 (16.7%) examined changes in QOL over time within a treatment modality, 7 (14.6%) examined QOL in relation to a specific sample characteristic, and 2 (4.2%) used non-standard methods to describe patients experiences. QOL was worse post-surgery and/or radiotherapy compared with healthy controls and active surveillance and tied to symptoms experienced. Study quality was reasonable despite expectable limitations due to the nature of the population.

**Conclusions:** AN treatments, particularly surgical, may result in pain and nerve damage. Whilst not common, these can significantly impact QOL domains, including social and emotional wellbeing and social participation. Surgical teams should prepare patients for this possibility and ensure adequate community follow-up with specialist physical therapies, audiology, ophthalmology, and psychology to mitigate these effects should they occur.

Keywords: Acoustic neuroma, Quality of life, Review

#### **Background**

Acoustic neuroma (AN), also known as vestibular schwannoma, is a benign tumour arising from the Schwann cells of the vestibular division of the eighth cranial nerve [1]. AN accounts for approximately 6% of all intracranial tumours [2]. Recent incidence rates across ages range between 3.0 and 5.2 per 100,000 person-years, with highest incidence reported in those aged > 70 years (peak 20.6/100,000 person-years) [3]. Treatment options include surgical excision, stereotactic radiosurgery (SRS)

or stereotactic radiotherapy (SRT), and conservative management/active surveillance. Individual patient management depends on various factors including age, medical comorbidities, size and location of the tumour, and hearing status [4].

Surgical excision is widely used [5]. The surgical procedure used is selected based upon the size and location of the tumour and hearing status. Surgical removal does carry the risk of complications (e.g. facial or cochlear nerve injury) [6]. Preserving facial nerve function is an important outcome, as facial nerve injury can have physical and psychological consequences for the patient [7].

SRS or SRT are an alternative to surgery, particularly in patients at increased risk of perioperative complications due to comorbidities or increased age [8, 9]. Generally, SRS/SRT is managed without inpatient admission and

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there is little postoperatively recovery time [8, 10]. However, there are also short- and long-term risks of SRS/SRT including radiation toxicity, which can damage neural structures resulting in facial weakness, facial numbness or dysesthesia, and impaired hearing and balance [11–13]. Hydrocephalus can also occur as a late complication post-radiosurgery and may require ventricular shunting [14].

Conservative management (i.e. active surveillance) involves serial imaging to monitor growth and is seen as suitable in patients with smaller tumours (< 20 mm), in older patients, or those with comorbidities that preclude more invasive treatment [15–18]. This treatment protocol is based on ANs slow growth rate and static presentation in many patients with minimal symptoms [19, 20].

Most AN outcome studies focus on medical outcomes such as cranial nerve function and recurrence rates. Whilst important, these do not reflect how AN diagnosis, or its treatment/s, impact the lives of those affected. An alternative approach is to examine impact upon patients' quality of life (QOL). The World Health Organization's defines QOL as an individual's perception of their position in life in the context of their own culture and value systems which spans physical health, psychological state, level of independence, social relationships, and their relationships to their environment [21].

In a systematic review on QOL outcomes of AN, Gauden et al. [22] concluded, based upon 47 studies published until 2010, that (1) patients with AN experience reduced QOL compared to population norms, (2) those with larger tumours may experience lower QOL than those with smaller tumours, (3) surgery may improve QOL in patients with large tumours after a temporary decline in physical dimensions of QOL and, (4) conservative treatment and radiosurgery have no effect on QOL. Furthermore, comparison indicated that whilst QOL did not differ significantly between those who had surgery and conservative management, more mixed results were found when comparing surgical and SRS treatment, though these results were confounded by differential tumour size.

A further systematic review [4] compared QOL in relation to treatment options and control populations in 39 studies (1980–2015). Microsurgery in retrospective studies had a negative effect on QOL, but this improved in prospective studies, though never to the degree of controls. Most studies suggest that SRT had little or no negative impact on QOL. The authors note few studies allowed "fair" comparison between treatments as the microsurgical group had immediate morbidity from surgery and recovery, whilst SRT has insignificant immediate effects but may develop toxicities over time. Importantly, allocation to treatment takes into account

tumour size and patient demographics and wishes, introducing bias.

#### Aim

Surgical and non-surgical AN treatments have continued to improve over the last 10 years. The aim of this paper was to provide an updated systematic review of literature on QOL outcomes in patients with AN, with a focus on recent publications (i.e. 2000–2021).

#### Search strategy

This review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The systematic review involved searches of databases MEDLINE, PUBMED, and EMBASE with search term Acoustic Neuroma as a keyword. Inclusion criteria comprised adults with AN where QOL was a study's outcome variables. The search was limited to publications with human participants, original research (both observational and experimental), in English, and published from 2000 to 2021.

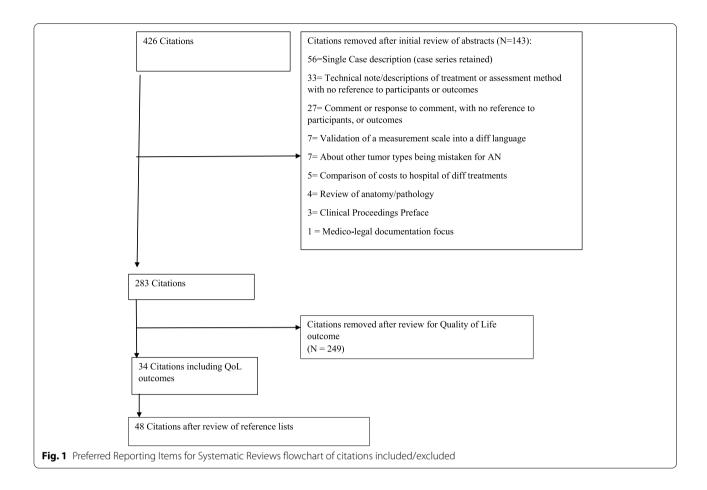
Four hundred twenty-six unique citations were identified after duplicates were removed (see Fig. 1). Titles and abstracts of each citation was screened by the first author. Of those remaining, a further148 were removed as the abstracts indicated the papers did not measure QoL, leaving 284 papers. Review of full manuscripts revealed that only 34 papers referred to QOL as an outcome variable. After reviewing reference lists of these 34 papers, an additional 14 papers not identified in the original search (as they contained Schwannoma rather than AN as key words) were identified which met inclusion criteria, leading to final inclusion of 48 papers. Any conflicts that arose during eligibility assessment were resolved through consensus with the authors. Each of the included papers obtained participant consent and was approved by an appropriate ethics committee.

#### Risk of bias

Risk of bias was assessed using Downs and Black's [23] Quality Assessment Index which was designed to assess quality in randomised and non-randomised studies of health care interventions. Scores range from 0 to 31 with higher scores indicating better quality. Scores are calculated from nine items on reporting, three on external validity, seven on bias in measurement, six on bias in subject selection, and one on statistical power. Scores are described as "excellent" (score 24-28), "good" (score 19-23), "fair" (14-18), or "poor" ( $\leq 13$ ).

#### Main findings

Whilst some overlap between groups was present, overall, 16 studies (33.3%) made comparisons of AN patients



to normative/control data, 15 (31.25%) studies compared QOL outcomes of various treatment groups, 8 (16.7%) studies examined changes in QoL over time within a particular treatment modality, 7 (14.6%) studies examined QOL in relation to a specific sample characteristic (e.g. AN association membership) or symptom, and the remaining 2 (4.2%) studies used non-standard methods to obtain a description of patients experiences. Characteristics of studies within each grouping are presented in Table 1.

#### Measures of QOL

The most commonly used measure of QOL was the Short Form-36 (SF-36; n=34/48, 70.8%), with one additional study using the SF-12. This was followed by the Glasgow Benefit Inventory (GBI; n=12, 25%) and the Penn Acoustic Neuroma QOL scale (PANQOL; n=6, 12.5%). Other measures related to QOL included the Beck Depression Inventory, Rosenberg Self-Esteem Scale and a visual analogue rating of QOL used in one study; the European Quality of Life–5 dimensions in one study; and the Zung Self-Rating Anxiety and Depression scales that were used in another study. Four studies did not use

standardised assessment but reflected on QOL using a survey of patients' overall experiences [25], conducted thematic analysis of patient focus group transcripts [70], invited responses to questions tied to the WHO framework of impairments, disability and Handicap [71], or administered a survey developed to capture post-operative QOL [31].

#### Comparison to norms/controls

Of the 16 studies which compared AN to a non-AN comparison group, the AN group comprised post-surgical patients in 12 studies (one limited to post-surgical vertigo and one to translabyrinthine approach), active surveillance patients in one study, and mixed treatment groups in the remaining studies (1=surgical vs SRS, 2=surgical vs SRS vs active surveillance). The majority (10/16) of studies examined AN in relation to normative data, with one comparing to three different normative data sets. An additional study also compared to three normative data sets alongside two sets of surgical data. Of the remaining studies, one compared AN to age- and gender-matched controls, one to a non-patient control group who visited the same hospital, and the remaining three studies made

Table 1 Summa	ıry of charac	Table 1         Summary of characteristics of studies included in	in review ( $N = 48$ )			
Author	Quality Index (QI) <sup>a</sup>	Sample	Measure/s of QoL	Timing	Grouping factors	Finding
Relation to Sample Prummer [24]	: Characteristi	Relation to Sample Characteristic/Symptoms ( $N = 7$ ; mean QI= 15.14)  Prummer [24] 17 $N = 802$ , Acoustic Neuroma PAI Association members $N = 258$ , non-ANA from a single clinical site	PANQOL	Not explicitly stated Presentation January 2015– March 2017, so within 2 years	ANA membership	ANA members significantly:  Younger (59 vs 60 years), larger tumour size, and Sig more women (72 vs 55%), microsurgery (57 vs 21%), radiation (21 vs 8%), hearing loss (95 vs 88%), tinnitus (80 vs 73%), dizziness (78 vs 64%), headache (56 vs 45%), and facial paralysis (37 vs 12%).  Sig less watch and wait (16 vs 65%) ANA Sig lower PANQOL scores for: hearing (OR: 0.47, 95% CI: 0.35–0.64), pain (OR: 0.51, 95% CI: 0.38–0.70), pain (OR: 0.63, 95% CI: 0.42–0.80), energy (OR: 0.54, 95% CI: 0.42–0.80), anxiety (OR: 0.54, 95% CI: 0.40–0.74), general QoL (OR: 0.72, 95% CI: 0.50–0.99), anxiety (OR: 0.54, 95% CI: 0.53–0.99), Total QOL (OR: 0.72, 95% CI: 0.53–0.99),

Table 1 (continued)

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Author	Quality Index (QI) <sup>a</sup>	Sample	Measure/s of QoL	Timing	Grouping factors	Finding
Broomfield [25]	01	N = 598 BANA members	Online survey of: overall experience of diagnosis and/or treatment	78.9%—since 2000, 17.2%—in 1990s 3.1%—1980s 0.9%—pre-1980 10—not reported	₹ Ž	Most common symptoms at diagnosis: hearing loss (84%), unilateral tinnitus (40%), imbalance (51%).  Information neceived: 39% just the right amount of information about all 'management options', 32% 'not enough information'.  Treatment after-effects (QoLoverall): 'a lot better' (11%), 'a little better' (7%), unchanged' (25%), a little worse' (19%).  G1% respondents continued in the same job. G5% return to social life, hobbies, sports impaired. Overall experience: Treatment as 'much better than expected' (20%), 'a little better' (15%), 'about the same' (27%), a little worse' (22%) and 'much worse' (16%).
Oddon [26]	91	N = 26 active surveillance 14 tumour growth 12 no growth 0 tumour shrinkage	Pangol SF-36	Mean 25 months (range 6–72) Presence of vertigo	Presence of vertigo	Vertigo or dizziness = poorer OoL on SF-36 (Social Function- ing, Role-Emotional) and PAN- OoL scale (Balance, Energy) Psychological factors (QoL, depression, and self-esteem) do not seem to influence decision-making in this patient population

Author	Quality Index (QI) <sup>a</sup>	Sample	Measure/s of QoL	Timing	Grouping factors	Finding
AL-Shudifat [27]	8	N = 395 surgically treated	SF-36	Range 11 to 32 years	Age (<64, ≥ 65) Gender Tumour size	All SF-36 domains (except pain) showed moderate decrease, reaching a 30% reduction postoperatively in comparison with Swedish norms. The pain score was showed an increase (mean= 1.0169) compared to norms. No significant differences were shown between age groups. Only tumour diameter and taste loss showed significant correlations with both physical and mental component scores.
lyer [28]	<u>4</u>	N = 83 surgically treated 19 middle cranial fossa 64 translabyrinthine	SF-36 GBI	Not reported	Hearing preservation	QoL reduced in both surgery groups. Mean GBI score for translabyrinthine group was – 7.5 (95% CI: – 2.5 to – 13.5) and middle fossa group – 4 (CI: 213.5 to 5.5). GBI domains: general aspects reduced, social improved, physical no change. GBI scores if hearing preserved were similar SF-36 sig reduction in social function scores vs norms (p=0.035). Translabyrinthine similar as social function only domain to show sig deterioration (p=0.007). Middle fossa no sig reductions. SF-36 scores no sig difference between groups, apart from social function (p=0.015; better in middle fossa group)
Lassaletta [29]	15	N = 70 surgically treated	GBI	Up to 7 years post	Facial functioning	No sig differences found in GBl between those with and those without facial dysfunction Reduced QoL was associated with post-operative pain

Table 1 (continued)	ned)					
Author	Quality Index (QI) <sup>a</sup>	Sample	Measure/s of QoL	Timing	Grouping factors	Finding
Lloyd [30]	91	N = 165 active surveillance	SF-36	Up to 19 years	Hearing and dizziness	Physical component scores signower than norms. Mental component scores sig above norms. Dizziness and age were strong predictors of physical component ( $p$ 's= 0.0001) Dizziness and tinnitus were signomedictors of mental component ( $p$ = 0.0004 and 0.027). However, ( $p$ = 0.0004 and 0.027). However, explained
Comparisons to nc	ormative data	Comparisons to normative data and/or controls (N = 16; mean Q	QI= 18.38)			
Broomfield [31]	71	N = 34 (SF-36) (369 QoL-2) surgically treated Translabyrinthine approach	SF-36 Generic postoperative QoL scale (Qol-2)	Minimum 5 years	Comparison to normative data	SF-36 all scores diff sig from norms except'role emotional' Largest difference was physical function, followed by role-physical, body pain, and general health Mental component score: tumour size $\geq 4$ cm likely to have $3.4$ less score than tumour o< 1 cm ( $\rho$ =0.037). Little evidence for effect of small tumour sizes. No evidence for tumour size effect on the physical component score associated with increased time since surgery (age an tumour size accounted for) QOL-2: patients reported an improvement ("a lot" or "a little" better) in their ("a lot" or "a little" better) in their
						overall quality of life (24%) and overall health (20.4%)

Table 1 (continued)

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Author	Quality Index (QI) <sup>a</sup>	Sample	Measure/s of QoL	Timing	Grouping factors	Finding
Cheng [32]	15	N = 98 surgically treated	SF-36	Minimum 6-months	Comparison to normative data Also by gender, age, tumour size, operative approach	Compared to norms: Lower physical function, role- physical, general health, vitality, social function, role-emotional, and mental health Higher for body pain (i.e. less pain reported by patients) Only role-physical significant No sig diffs for gender, age, turnour size or surgical approach
Tufarelli [33]	21	N = 386 surgically treated	SF-36	Mean 4.01 years SD 2.39 years post-op	Comparison to normative data	231 (59.8%) = asymptomatic post-surgery. 155 (40.15%) = very disabling symptom/s Hearing loss as most disabling symptom SF-36 scores lower than normal population particularly for role physical, role emotional, and physical function (differentials all > 10) Women produced sig lower scores than men age had sig impact on physical functioning (≤45 years had sig inther score than patients > 45 years) Time interval from surgery did not influence QoL
Baumann [34]	19	N = 42 surgically treated	SF-36	Median 3.1 years (range 1.0–5.3)	Comparison to normative data	Significantly lower SF-36 scores than normative sample on all scales with exception of vitality and mental health scales
Sun [35]	51	N = 24 surgically treated	SAS SDS SF-36	1 year post-op	Comparison to normative data	No sig difference to norms for anxiety or depression; 2 (9.5%) patients scores > cut-offs for each Sig higher scores on general health and vitality dimensions of the SF-36 compared to norms No significant differences in other dimensions observed

Author	Quality	Sample	Measure/s of QoL	Timina	Grouping factors	Finding
	Index (QI) <sup>a</sup>					
Godefroy [36]	61	N = 17 surgically treated with rotatory vertigo	SF-36	Pre-operative and 3 and 12-month post-operative	Comparison to normative data	All SF-36 scores below norms at pre, 3-month and 12-month follow-up across scales Improvements though none sig pre-op to 3 months Sig improved scores 12 months post-op for all except body pain and vitality
Browne [37]	<u></u>	N = 119 AN surgically treated	SF-36	Not reported	Comparison to normative data Comparison to illness group controls (e.g. diabetes, der- matitis)	AN report impaired overall QoL compared to general population controls and other chronic illness groups AN patients reported better physical and general health outcomes Hearing was the most frequent difficulty post-surgery, and this impacted social functioning Most AN patients named at least one positive outcome from their illness AN patients who had facial difficulties following surgery were less likely to report positive outcomes outcomes outcomes
Betchen [38]	6	N = 101 surgically treated	SF-36	Mean 3.2 years (range 6 months to 7 years)	Comparison to normative data (x3 sets)	Compared to Ware's norms: Lower scores on all scales except vitality Sig lower role physical, role emotional, and body pain Compared to Jenkinson norms: Significant lower in current study for physical function, role physical, social function, and body pain Compared with McDowell norms: Sig lower score on body pain, but sig higher scores for general, physical functioning, role physical, role emotional, and vitality

Table 1 (continued)

Author	Quality Index (QI) <sup>a</sup>	Sample	Measure/s of QoL	Timing	Grouping factors	Finding
daCruz [39]	5	N = 72 surgically treated	SF-36	> 18 months	Comparison to healthy sex- and age-matched controls	SF-36 scores were lower than controls for physical function, role-physical, body pain, general health, social functioning, role emotional, mental health higher than that of controls. Significance of differences not reported.  Gender, age, turnour size, and surgical approach did not sig impact QoL scores
Scheich [40]	91	N = 86 surgically treated	SF-36	>6 months post-op	Comparison to normative data Comparison to those with hearing loss	Norms: Sig lower scores all categories except bodily pain. Hearing loss: Sig lower scores for social function and roleemotional; Sig higher score for body pain
Nicoucar [41]	21	N = 72 surgically treated	SF-36	Mean 7.6 years (range 6 months–19 years)	Comparison to normative data (x3 sets) Comparison to surgical controls (x2 sets)	Sig lower scores than all three normative data sets for role- emotional, physical functioning, social functioning, and vitality Sig lower than one study on body pain and 2 studies for mental health. Compared to surgical norms: Lower vitality compared to both surgical groups, whilst compared to one study also showed higher body pain, but worse mental health, physical function, and social functioning

Author Q	Quality Index (QI) <sup>a</sup>	Sample	Measure/s of QoL	Timing	Grouping factors	Finding
Martin [42]	50	N = 76 surgically treated	SF-36	Mean 18 months Interquartile range 19 months	Comparison to normative data	Sig lower scores than norms for General health, vitality, role-physical, physical functioning, social functioning.  Time post-op (< 12 months > 12 months) all on timpact findings Larger tumours = lower physical function  Older patients= lower physical and role-physical  Women = lower vitality, physical functioning, body pain  Number postoperative symptom was associated with all SF-36 scales except vitality and physical functioning (scores lower if more symptoms)
Kelleher [43]	21	N = 54 29 active surveillance 19 surgery 6 SRS 2 died (unrelated)	SF-36	Median 36.8 months (range 14–176)	Comparison to normative data	Active surveillance vs norms: No sig difference Surgery vs norms: Sig worse social function and role-physical
Myrseth [44]	∞_	<ul><li>N = 189 (140 for analysis)</li><li>86 surgery</li><li>103 SRS</li></ul>	SF-36 GBI	Mean 6.7 years range, 1.5–13.0	Comparison to normative data	GBI: Overall score for surgery sig- lower than SRS Sig higher for SRS than surgery on "general and psychosocial health" No sig diffs for "social support" and "physical health status" SF-36: patients sig lower than norms for role-physical and social functioning Sig greater deviations below norms for surgery than SRS for physical functioning, role-physi- cal, and role-emotional SRS means > surgical means all other categories, but not sig

Table 1 (continued)

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Author	Quality Index (QI) <sup>a</sup>	Sample	Measure/s of QoL	Timing	Grouping factors	Finding
Myrseth [45]	50	N = 199 45 surgery 63 SRS 91 active surveillance	SF-36 GBI	Not reported	Comparison to non-patient controls	SF-36 sig below norms range 0.006 (bodily pain) to less than 0.001 (remaining categories) GBI negative benefit in general and physical sections and positive benefit in the social section Vertigo, sig assocd with reduced QOL across all SF-36 scales and general and physical parts of GBI.  Tinnitus was associated with body pain, and unsteadiness with role physical and physical function
MacAndie [46]	20 eatment mode	MacAndie [46] 20 N = 42 Active surveillance Controls from clinic Changes within a treatment modality (N = 8: mean Ol = 19.25)	SF-36	Not reported	Comparison to matched controls from same clinic	OoL was comparable with an age- and sex-matched control group presenting with similar symptoms
Turel [47]	6	N = 100 Surgically treated	SF-36 GBI	Pre versus 1 and 2 year follow- ups	Pre vs 1 and 2 years post	Preoperative—decrease in all SF-36 domains, then improved at 1 year in all cases 63–85% patients show minimum clinically important difference (MCID) in various SF-36 domains At 2 years SF-36 improvement sustained with further improvement in some domains. On GBI, 87% of patients reported improvement, 1% felt no change, and 12% reported deterioration
Timmer [48]	6	N = 97 SRS (Gamma Knife)	SF-36 GBI	Pre vs post	Hearing and dizziness	SF-36 similar to norms (role physical and general health sig lower) and not correlated to age, gender, tumour size or radiation dose. Audio vestibular symptoms post-SRS correlated with decreased GBI and SF-36 scores Slight reduced GBI pre to post

Table 1 (continued)

Author	Quality Index (QI) <sup>a</sup>	Sample	Measure/s of QoL	Timing	Grouping factors	Finding
Varughese [49]	17	N = 45 SRS (Gamma Knife) Large tumour	SF-36	Pre vs post treatment (mean 30.2 and 50 months post diag)	Diagnosis and Pre vs post	Significant improvements in body pain and general health, whilst social function was significantly reduced from pre to post treatment.  Mental health reduced significant from diagnosis to treatment and then increased (non sigh) post treatment
Wangerid [50]	17	N = 98 SRS (Gamma Knife) Small to medium tumour	EQ-5D	Median 104 months (11–165)		At end of the follow-up, mean QQL was calculated to 0.77 and median to 0.91 (1.0= best possible health state).  Median score was 1.0 for each subcategories (mobility, selfcare, daily activities, pain/discomfort, anxiety/depression)
Godefroy [51]	23	N = 41 Active surveillance	SF-36	Mean 40 months (range 11–73 Diagnosis vs follow-up months)	Diagnosis vs follow-up	SF-36 scores slightly deteriorated except for social functioning, which was slightly improved Follow-up scores did not differ sig from baseline

Table 1 (continued) Author Q	nued) Quality Index	Sample	Measure/s of QoL	Timing	Grouping factors	Finding
Breivik [52]	23 S	N = 186 Active surveillance (74 treated during follow-up)	SF-36 GBI	Medan 43 months (range 9–115 months; SD = 21 48	Pre vs post treatment	Active surveillance: slight but sig trend to improved SF-36 vitality and role-emotional, and GBI general and physical dimensions Sig worse SF-36 Social function- ing and GBI social dimension Treatment: small but sig worse SF-36 physical functioning and role-emotional; and improved GBI total, general, and physical aspects Examining symptoms, tumour volume, sex, age, and QOL: INCREASED vertigo related to reduced QOL through all dimen- sions in both questionnaires Tinnitus was associated with 1 GBI and 4 SF-36 subscales Females had sig lower values in both SF-36 and GBI (all scales)
Fahy [53]	<u>†</u>	N = 51 surgically treated	GBI derivative	1–3 years post-surgery	Pre vs post-op Relation to tinnitus	than men over time  There was no statistically significant association of changes in tinnitus status and changes in the QoL post-op (P>0.05).
Park [54]	22	N = 59 Post-SRS	SF-36	1-, 3-, 6-, 12-, and 18-month post-treatment	$\geq$ 6 months, $n = 46$ $\geq$ 12 months, $n = 35$ $\geq$ 18 months, $n = 16$	No sig decline in QOL observed from baseline to any follow-up period SF-36 overall at baseline was 73, with range 70–77 across follow-ups
Comparison betw	veen Treatmen 18	Comparison between Treatment Modalities ( $N=15$ , mean QI= 2 Nellis [55] 18 $N=216$ 98 surgery 118 active surveillance	= 20.07) RSES BDI VRQOL Overall QoL on a visual analogue scale (0–100, higher rating as more positive).	Post-diagnosis, pre-treatment decision	Choice to undergo resection vs active surveillance	No significant association between psychological factors (Qol, voice-related Qol depression, self-esteem) and decision to undergo surgery or pursue active surveillance VRQoL sig lower in patients with hearing loss, difficulty swallowing liquids or solids, change in voice, and headache $(p < 0.05)$

Table 1 (continued)

Author	Quality Index (QI) <sup>a</sup>	Sample	Measure/s of QoL	Timing	Grouping factors	Finding
Lodder [56]	71	N = 359 BANA members 185 surgery 94 SRS or SRT 17 surgery + SRT 63 active surveillance	PANQOL	Up to > 10 years follow-up	Treatment approach Length of follow-up	Composite QoL scores no significant group diff ( $\rho = 0.532$ : microsurgery 58 (SD=35), radiotherapy 56 (SD=18), surgery and radiotherapy 49 (SD=14), observation only group 54 (SD 20) Composite QOL score different sig ( $\rho < 0.001$ ) by follow-up: $< 6$ years= $52$ (SD=18), $6$ –10 years = $55$ (SD=20)
Robinett [57]	75	N=279 157 surgery 79 active surveillance 43 SRT	PANQOL	Mean follow-up 7.9 years	Surgery, SRT, active surveil- lance Years follow-up (0–5, 6–10, > 10)	Composite QoL scores highest in SRT and lowest in active surveil-lance (means, 71, 73, 82), with SRT sig higher than the other two groups When time interval included, sig diff was only present at 0–5 years Within groups QoL sig reduced from 0–5 year to 6–10 years in SRT
McLaughlin [58]	73	N= 186 98 active surveillance 49 SRS 39 surgery	PANQOL	Mean follow-up = 2.6 years	surgery vs SRS vs surveillance	Tumour size (mm) sig diff between groups: surveillance (8 $\pm$ 4.8), gamma (18 $\pm$ 5.9), surgery (22 $\pm$ 8.3) groups ( $p$ < 0.001) Speech recognition threshold and speech discrimination % sig better for surveillance vs gamma or surgery ( $p$ < 0.001) Hearing domain scores better for surveillance (62 $\pm$ 26) than surgery (47 $\pm$ 25) General and total domain scores were similar across groups, QoL scores for gamma and surgery

Table 1 (continued)

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Author	Quality Index (QI) <sup>a</sup>	Sample	Measure/s of QoL	Timing	Grouping factors	Finding
DiMaio [59]	<u>∞</u>	N = 205 134 surgery 48 SRS or SRT 47 active surveillance	SF-36		Pre vs post Surgery vs SRS/SRT vs active surveillance	SF-36 not sig diff between groups at baseline except for surgical with tumour > 3 cm, where scale scores were sig lower on role physical, vitality, social functioning, role-emotional, and the two dimensional scores (emotional and physical) SF-36 no change baseline to follow-up for surveillance and radiation groups SF-36 sig improved for surgical group (> 3 cm tumour) at 1.5 months and 24 months on composite mental and at 24 months on composite mental and at 24 dimension Asked: "the single most important factor affecting QOL right now"—roughly one third (across all groups) reported hearing to be the most important factor
Myrseth [60]	52	<ul><li>N = 88</li><li>28 surgery</li><li>63 SRS</li><li>3 withdrew</li></ul>	SF-36 GBI	1- and 2-year post-tx follow-up Surgery vs SRS	Surgery vs SRS	SF-36 and GBI no sig diffs bw groups at baseline SF-36 did not change sig from baseline within any group nor did the groups differ sig. GBI non-sig trend to better scores in SRS group at 1 year Sig better GBI outcomes for gamma knife at 2 years on general, physical, and total scores (latter 2 positive for SRS and negative for surgery group)

Table 1 (continued)	5					
Author	Quality Index (QI) <sup>a</sup>	Sample	Measure/s of QoL	Timing	Grouping factors	Finding
Pollock [61]	54	N = 82 36 surgery 46 SRS	SF-36 (refer to as HSQ)	Mean 42 months range 12–62 Assessed 3 and 12 months, and final follow-up	Surgery vs SRS	Sig changes in SF-36 for surgery group only 3 months: sig decline in SF-36 Physical function, role-physical, body pain, and physical composite Sig increases in social function and vitality 1 year: sig declines from baseline for physical function and body pain for physical function and body pain Final: Sig increase in mental tal health scale and mental composite score from 1 year, sig decrease in body pain from baseline
Sandooram [62]	50	N = 33 15 surgery 18 active surveillance	SF-36 GBI	One- and 6-month post-op follow-up	Surgery vs active surveillance	SF-36: microsurgery signircreased vitality and health perception, and trend to better role-emotional from baseline to 6 months than active surveillance GBI: surgery signircrease in social support Score from baseline to 6 months compared to active surveillance
Sandooram [63]	21	N = 165 102 surgery 42 active surveillance (AS) 10 SRS 6 AS then Surgery 5 AS then surgery	GBI	Range 0.2–15 years	Pre vs post Comparison of Tx groups	Surgical deteriorated in QoL post- treatment Active surveillance QoL maintain life they had at initial presentation Trend towards poorer QoL post-surgery compared to active surveillance (p = .070) Slightly poorer QoL in SRS compared to active surveillance (p=0.121) There was no statistically significant difference SRS vs surgery Delayed surgery GBI total scores similar to surgical group Delayed SRS had better QoL compared to SRS

Table 1 (continued)

Author Index (%)   (Outling)		,					
21         N = 180         5F-12         ≤5 years post-op but > 6           4.2 SRT         so active surveillance         F-36         I month post-discharge           23         N = 100         N = 101         Mean 5.9 years           50 translabyrinthine approach         S0 translabyrinthine approach         SF-36         Mean 11.5 years           51         N = 101         S9 translabyrinthine approach         SF-36         Mean 11.5 years           52         N = 25 complete facial paralysis         SF-36         Mean 11.5 years           54 facial newe repair during initial Answer repair during linitial Answer repair during linitial Answer repair during linitial Answer repair during linitial Answer greater auriculan newe of interprosition greater auriculan newe of interprosition anastomosis, with hyperglossal anastomosis with hyperglossal nerve         SF-36         Mean 11.5 years	Author	Quality Index (QI) <sup>a</sup>	Sample	Measure/s of QoL	Timing	Grouping factors	Finding
5] 23 N=100 SF-36 I month post-discharge 50 translabyrinthine approach. 50 retrosigmoid approach. 51 SP-36 Mean 5.9 years sugically treated 59 translabyrinthine approach 42 retrosigmoid approach 42 retrosigmoid approach 42 retrosigmoid approach 42 retrosigmoid approach 43 retrosigmoid approach 44 retrosigmoid approach 45 retrosigmoid approach 46 retrosigmoid approach 47 retrosigmoid approach 48 retrosigmoid approach 49 retrosigmoid approach 49 retrosigmoid approach 40 retrosigmoid approach 4	Brooker [64]	23	N = 180 102 surgery 42 SRT 36 active surveillance	SF-12 GBI	≤ 5 years post-op but > 6 months post	Surgery vs radiation vs surveillance	No sig diff SF-12 across microsurgery, radiation, and observation patients  More deterioration GBI general well-being in microsurgery vs radiation patients More improvement in the GBI social support scale in microsurgery vs observation patients No sig group diffs on GBI total or physical health scores Number symptoms consistently predicts SF-12 and GBI scores
15   N = 101   SF-36   Mean 5.9 years surgically treated 59 translabyrinthine approach 42 retrosigmoid approach 42 retrosigmoid approach 42 retrosigmoid approach 43 retrosigmoid approach 44 retrosigmoid approach 52   N = 25 complete facial paralysis   SF-36   Mean 11.5 years post-surgery 4 facial nerve repair during initial AN surgery 7 end-to-end nerve to hypoglossal anastomosis, 7 end-to-side with sural nerve, greater auricular nerve or interposition graft, 7 end-to-side facial nerve anastomosis with hyperglossal nerve	Ning [65]	23	<ul><li>N = 100</li><li>50 translabyrinthine approach</li><li>50 retrosigmoid approach.</li></ul>	SF-36	1 month post-discharge	Surgical approach	retrosigmoid approach: sig higher social functioning, role- emotional, and mental health Translabyrinthine approach: sig higher body pain and vitality
22 N=25 complete facial paralysis SF-36 Mean 11.5 years post-surgery 4 facial nerve repair during initial AN surgery 7 end-to-end nerve to hypoglossal anastomosis, 7 end-to-end nerve or interposition graft, 7 end-to-side diacial nerve anastomosis with hyperglossal nerve	Rameh [66]	15	N = 101 surgically treated 59 translabyrinthine approach 42 retrosigmoid approach	SF-36	Mean 5.9 years	Surgical approach	Both groups sig lower scores than norms Pain correlated most with poorer QoL but was the least frequent symptom reported Facial weakness not correlated with a poorer QOL
	Lin [67]	22	N = 25 complete facial paralysis post-surgery 4 facial nerve repair during initial AN surgery 7 end-to-end nerve to hypoglossal anastomosis, 7 end-to-side with sural nerve, greater auricular nerve or interposition graft, 7 end-to-side facial nerve anastomosis with hyperglossal nerve	SF-36	Mean 11.5 years Range 1–25 years	Comparison of nerve repair groupings	Patients in end-to-side interposition group had sig better QoL than those in end-to-end group for physical function $(p=0.04)$ and role-physical $(p=0.05)$ No other sig differences found

Table 1 (continued)

Author	Quality Index (QI) <sup>a</sup>	Sample	Measure/s of QoL	Timing	Grouping factors	Finding
Carlson [68]	50	N = 1288 229 no treatment selected 303 active surveillance 185 SRS 507 surgery 64 surgery + SRS	PANQOL	Mean = 5 years (SD= 7.3)	surgery vs radiation vs surveil- lance vs no treatment yet selected	Adjusted for covariates PANQOL total: highest for AS (65; 95% C: 62–68), lowest surgery + SRS (56; 51–61) or no treatment selected (58; 55–62), intermediate for single treatment (microsurgery 60; 58–62); radiosurgery 61; 57–64) ( $\rho$ = 0.001). No sig differences between SRS + surgery and single treatment in total PANQOL scores for short (0–5 years), intermediate (6–10 years), or long-term (> 11 years) after adjust for baseline covariates ( $\rho$ 's > 0.05)
Henzel [69]	51	Henzel [69] 15 <i>N</i> = 74 35 SRS 39 SRT	SF-36	Median 50 months	SRS vs SRT in relation to tumour volume shrinkage	No sig differences observed after SRS/SRT. Previous operations and gender did not affect QoL (p > 0.05) Compared to German norms, all QoL domains were worse except for mental health

Alternative approaches to QoL measurement (N=2; mean QI= 12.0)

Table 1 (continued)

Author	Quality Index (QI) <sup>a</sup>	Sample	Measure/s of QoL	Timing	Grouping factors	Finding
Brooker [70]	5	N = 21 8 surgery 4 SRS 5 SRT 2 Surgery + SRS 1 Surgery + SRT 1 active surveillance	Focus groups with thematic analysis	Mean = 3.7 years Range 1–11 years	₹ Z	Themes (subthemes):  1) Physical symptoms (hearing loss, balance problems, fatigue, tinnitus, fatigue assoc'd with hearing, balance and facial paralysis).  2) Psychological wellbeing (anger/frustration, depression, anxiety/uncertainty, body image, gratitude relief and psychological benefit). Higher psychological wellbeing assoc'd with less severe physical symptoms, and "received a good treatment outcome"  3) Social wellbeing (social interactions were negatively impacted by hearing impairment and balance disturbance, but not facial paralysis)  4) Functional status (activities of daily living and occupational status)  5) Psychosocial factors influencing adjustment (individual differences and social support)
Bateman [71]	0	N=53 Post- surgical	Questions tied to WHO framework on impairment disability, handicap	>1 year Range 1—3 years		For handicap, social isolation emerged as a strong theme 15/43 (35%) were reluctant to attend large social gatherings Employment was also important with 7/43 (16%)

AN acoustic neuroma, BD/ Beck Depression Inventory, EQ-5D European Quality of Life-5 dimensions, GB/ Glasgow Benefit Inventory, HSQ Health Status Questionnaire, PANQOL Penn Acoustic Neuroma QOL, RSES
Rosenberg Self-Esteem Scale, SAS Zung Self-Rating Anxiety Scale, SDS Zung Self-Rating Depression Scale, SF-36 Short form 36, SF-12 Short form 12, Sig significant, SRS stereotactic radiosurgery, SRT stereotactic radiation therapy, VRQOL Voice-Related Quality of Life, WHO World Health Organisation

<sup>a</sup> Quality Index Scores [23] range from 0 to 31 with higher scores indicating better quality; comprised of 9 items on reporting, 3 on external validity, 7 on bias in outcomes measurement, 6 on bias in subject selection, and 1 on power to detect real effects

comparisons to both normative/controls and another patients group (i.e. with illness, with hearing loss, surgical controls).

In the only study to compare active surveillance to ageand gender-matched controls (patients at the same clinic with similar symptoms but not AN), QOL scores were comparable [46]. Two additional studies included active surveillance participants, one of which [43] also reported no difference between this group and controls. The final study did not report comparisons based upon treatment group [45].

Of those studies which included various treatment groups, Kelleher [43] found worse QOL in those who underwent surgery than norms for social function and physical role limitations (SRS group was too small to conduct analyses). Myrseth [44] also found significantly lower SF-36 social functioning and physical role limitation scores than norms, with deviations below norms significantly greater for surgery than SRS for physical functioning, physical role limitations, and emotional role limitations. Overall, GBI score and scale scores for general and psychosocial health were significantly lower post-surgery than post-SRS. As noted previously, Myrseth [45] did not report findings by treatment group.

Of the remaining studies, which contrasted post-surgical AN patients to normative data, the most consistent finding was of patients having lower QOL than normative data, often across all SF-36 scales [36, 40]. Of particular note, physical role limitations were lower than controls in five studies [31–33, 39, 42], and in comparison to two out of three normative data sets by a final study [38]. A few studies also reported patients producing higher SF-36 scores than norms, particularly for vitality [34, 35, 38], emotional role limitations [31, 38], and general health [35, 38]; one particular study reported all three [38].

#### Links to patient characteristics

Of the seven studies that linked QOL to specific patient characteristics, two described participants in relation to membership in local AN associations, two studies examined QOL in those under active surveillance, and the remaining three examined QOL in relation to symptom outcomes and demographics post-surgery.

In the two studies reporting on QOL in members of local AN associations, Prummer et al. [24] report that members were younger, had larger tumours, included more women, were more likely to have had surgery or radiation, and to report symptoms (hearing loss, tinnitus, dizziness, headache, facial paralysis) than non-members. As would then be expected, members had significantly lower scores on the PANQOL. In a description of QOL in British AN association members, Broomfield and colleagues [25] found that the most common symptoms at

diagnosis were hearing loss, tinnitus, and imbalance. In asking about overall life quality related to treatment, the largest proportion felt a little worse, followed by those who were unchanged, a lot worse, a lot better, and a little better.

In the studies of active surveillance, Oddon et al. [26] examined the impact of vertigo or dizziness on QOL and found poorer QOL on SF-36 (Social Functioning, Role- Emotional) and PANQOL scale (Balance, Energy) when either of these was present. Lloyd [30] also found that dizziness alongside increased age predicted physical QOL in those under active surveillance. Vertigo was also linked to reduced QOL in the treatment comparison study by Breivik [52].

In the remaining three studies looking at QOL within surgically treated groups, all authors reported worse QOL than norms [27–29]. Al-Shudifat [27] found that age and gender did not impact QOL, but tumour size correlated significantly with physical and mental aspects of QOL, whilst Lasseletta [29] linked worse QOL to post-operative pain but not facial functioning.

#### QOL change within treatment modality

Eight studies examined changes in QOL over time within a particular treatment modality; two examined changes from diagnosis to follow-up in those under active surveillance (one included those treated during follow-up), two examined changes with surgical intervention, and four examined changes pre versus post-SRS.

The two studies of active surveillance had contrasting results. Godefroy et al. [51] reported non-significant decreases in QOL to follow-up except for social function which had a non-significant improvement; whereas Breivick et al. [52] reported slight but significant improvements in vitality and emotional role limitation over time but reductions in social functioning. This later study also reported reduced QOL was related to presence of vertigo and tinnitus.

In those who underwent surgery, Fahy et al. [53] report no statistically significant association pre versus post-surgery or in relation to changes in tinnitus. Turel [47] found reductions in all areas of QOL (compared to norms) preoperatively, followed by improvements in these at 1 year and again at 2 years post-surgery.

Across the four studies of changes in QOL with SRS treatment, two [48, 50, 54] report QOL similar to norms, with no changes up to 18 months post-treatment [54]. One of these specified no relation of QOL to age, gender, tumour size, or radiation dose but a significant relationship between auditory and vestibular symptoms and reduced QOL [48]. The remaining paper [49] found increased mental health issues between diagnosis and pre-treatment, which were not present post-treatment,

and an increase in pain related QOL and decreases in general health and social functioning from pre to post-SRS.

#### Comparison between treatments

Of the 15 studies that compared QOL outcomes between treatment modalities, six compared surgery, SRT, and/ or SRS and active surveillance; two compared surgery and SRS; two compared surgery and active surveillance; one compared surgery, SRS or SRT, surgery +SRT, and active surveillance; and one compared surgery, active surveillance, SRS, active surveillance+SRS, and active surveillance+surgery. Finally, two studies compared translabyrinthine and retrosigmoid surgical approaches, and the final study compared four approaches to facial nerve repair.

Examining these last three studies, on the SF-36, whilst one study reported no differences in QOL in relation to surgical approach [66], the other reported that retrosigmoid surgery resulted in significantly higher social functioning, role limitations due to emotional issues and mental health, whilst translabyrinthine surgery was associated with better outcomes in terms of body pain and vitality [64]. Whilst Lin [67] reported only two significant findings, with patients who underwent end-to-side interposition nerve repair reporting significantly better QOL than those in end-to-end group for physical function and role limitations due to physical difficulties.

One of the studies with surgery and active surveillance groups [55] did not look at QOL post-treatment but whether QOL impacted treatment decision making, finding no significant association with QOL, voicerelated QOL, depression, or self-esteem. Of those studies which contrasted QOL following different treatments, four reported no significant differences. All four studies included surgical and SRS/SRT groups, with three including active surveillance and one also including surgery followed by SRS. The one study to contrast SRS to SRT [69] noted no significant differences in QOL. In the only study which included those diagnosed but with treatment not allocated as a group [68], those in active surveillance had the best QOL. Of note, those who had undergone both surgery and SRS and those who had not yet had treatment allocated had the worst QOL scores.

In the remaining studies, there was a trend towards significantly worse QOL post-surgery compared to active surveillance, whose QOL was maintained over time [63]. Another pre-post comparison study similarly reported that whilst QOL did not change for active surveillance and SRT groups; post-surgery, there was a significant improvement in QOL [59]. This difference possibly reflects use of different measurement tools (SF-36 vs GBI) and in timing of measurement with the latter being

assessed on average <3 years post, whilst the former had a delay of up to 15-years post-treatment.

The remaining studies had mixed findings, though active surveillance generally had better outcomes. Pollock [12] reports that only surgery related to significant reductions in QOL scores at 3 (Physical function, Role-Physical, Body pain) and 12 months (Physical and Body pain), whilst there was no change in those who had SRS. Robinette [57] reported that those post-SRT had significantly better QOL than those post-surgery or remained in active surveillance, but that QOL in the SRT group reduced as time elapsed post-treatment. In contrast, Sandooram [63] reported that those undergoing SRS had similar QOL to those undergoing surgery (whose QOL reduced post-treatment), which was poorer QOL than those in active surveillance whose QOL remained about the same.

#### Alternative OOL measurement

The final two studies examined QOL in AN samples using unstandardized methods of measurement. Brooker et al. [70] conducted the only qualitative study which spoke specifically to QOL. The thematic analysis of focus groups of patients with various treatments (surgery with/ without SRS/SRT and active surveillance) and from 1 to 11 years post-treatment revealed that individuals were most concerned about physical symptoms (hearing loss, balance, fatigue, tinnitus, facial paralysis); they presented with anger/frustration, depression, anxiety/uncertainty, and issues with body image but also reflected gratitude, relief, and psychological benefit associated with less severe physical symptoms and having a 'good treatment outcome.' Social interactions were seen as being impacted by balance and hearing impairments and social factors were important to overall adjustment.

In contrast, Bateman and colleagues [71] used a questionnaire to ask about impairment, handicap, and disability as defined by the WHO framework 1–3 years post-surgery. In relation to handicap, social isolation emerged as a strong theme, with over one third of individuals expressing reluctance to attend large social gatherings, and a smaller proportion finding impacts on employment outcomes important.

#### Study quality

As can be seen in Table 1, the Quality Index (QI) for the studies ranged from 9 to 24 with an average QI of 17.81 across all of the studies. One study was of excellent quality, whilst the largest proportion of studies were of good quality (n = 26; 54.17%), 16 (33.3%) were of fair quality, and the remaining five (10.42%) were of poor quality. As might be expected given differences in design, studies within different areas produced different QIs. The

lowest mean QI (12.0; poor range) was produced by the studies which used alternative approaches to measurement of QOL. This is not unexpected given that both studies were exploratory in nature, did not contain control groups, and did not group participants in terms of either treatment received or explore confounders. This was followed by studies looking at sample characteristics (15.14; fair), comparisons to norms (18.38; fair to good), changes within a treatment (19.25; good), and comparisons between treatments (20.07; good).

Characteristics of the population contributed to lowered scores across study types. For example, as would be expected, none of the studies provided power calculations (which contributes 5 points to the total), involved randomisation to treatments, or blinding of participants to treatment. Across the board, studies had good levels of reporting, provided good descriptions of their samples and treatments of interest, used appropriate statistics, and showed no evidence of data dredging.

#### Discussion

This study demonstrates continued interest in AN outcomes beyond physical symptoms but also QOL and provides an update to previous systematic reviews [4, 22]. Study quality was generally good despite expected limitations due to the nature of the population, which does not allow randomisation or blinding or participants. To summarise the present findings: (1) when compared to normative controls, QOL of those with AN is similar if they are under active surveillance. This group typically produced significantly better QOL scores than those who underwent surgery, and there was some indication of improvements in QOL from diagnosis to follow-up. (2) Whilst the greatest proportion of studies comparing QOL between treatment modalities found no significant differences, across study types, those who underwent surgery tended to produce worse QOL than normative data, or those undergoing SRT/SRS or active surveillance, and also show reductions in QOL pre- to post- surgery which were not present in those undergoing SRT/SRS or active surveillance. Evidence for changes in QOL following SRT/SRS was mixed. (3) There was consistency across study types that presence of vertigo and dizziness negatively impacts on QOL regardless of treatment received and that pain (whilst uncommon) also reduces QOL post-surgery; however, the findings for demographic factors such as age, gender, and tumour characteristics were variable across studies. (5) Those who belong to local AN associations may not be representative of AN as a whole, being less likely to remain in active surveillance and more likely to report symptoms and have poorer QOL.

#### Quality of life and AN

Whilst active AN treatments can have positive outcomes, they can result in a wide range of long-term deficits including reduced hearing, vision, facial movements, vertigo, dizziness and imbalance, and pain. Whilst these are uncommon, for those that are impacted, they significantly impact on self-perception, identity, well-being, social participation, and QOL. As noted above, when compared to normative controls, QOL of those with AN is similar if they are under active surveillance, whilst those who undergo surgery tend to produce lower QOL scores. This is not unexpected given these individuals have undergone major surgical intervention and often a lengthy recovery. Patients should be prepared prior to treatment initiation for the possibility of these symptoms and supported postoperatively should they arise. It should be noted here that in addition to the possibility of major surgery with potential for complications driving reduced QOL, the factors contributing clinical treatment decisions will likely have resulted in between group differences pre-treatment. For example, those in active surveillance tend to have smaller tumours and fewer symptoms than those who undergo surgery. In one study reviewed, Breivik et al. [52] followed 186 patients under active surveillance, 74 of whom underwent treatment during the follow-up period, reporting that treatment resulted in small but significant worsening in QOL related to physical functioning and emotional role limitations. Sandooran [63] found surgery after surveillance led to QOL scores similar to surgery without an initial surveillance period, whilst in contrast delayed SRS had better QOL outcomes compared to SRS.

#### **Treatment differences**

Whilst differences between treatments, particularly between surgery and active surveillance, are present, the findings are inconsistent. Those who underwent surgery tended to produce worse QOL scores than other group (i.e. norms, SRT/SRS, surveillance) and also show reductions in QOL pre- to post-surgery. It is important to recognise the difference in patient diagnostics, characteristics, and comorbidities across groups. For example, decision-making between treatment modalities needs to consider long-term benefits and risks as well as posttreatment QOL. Whilst those with active surveillance were spared worsening QOL, as is noted above, this group differs significantly, and up to 40% of patients will eventually require surgery or other active treatment [47]. Indeed, the most consistent finding was that, regardless of treatment received (i.e. surgical, SRS, surveillance), the presence of auditory and vestibular symptoms negatively impacted QOL.

#### Clinical implications

For many, active AN treatments are necessary and result in good physical and QOL outcomes. Whilst validated QOL questionnaires offer useful normative comparisons, more qualitative research is needed to provide an in-depth, richer understanding of the post-treatment services needed by AN patients who have residual deficits. Brooker et al. [70], for example, identified a number of factors not covered by typical QOL measures, such as presence of anger/frustration, body image, gratitude/relief, and impact of perceptions of treatment outcomes. In addition, Prummer and colleagues [24] suggest patients do not access peer support in the UK unless they have significant impairments, with a trend towards younger patients with larger tumours and more physical symptoms seeking support. It is well established in cancer care that treatment burden, outcomes and QOL can be improved by social supports [72]. Peer support, either 1:1, support groups, online support, or national associations can offer social, emotional, and practical assistance and contribute to improved QOL long-term. This systematic review suggests patients should be offered peer support to maximise QOL post-diagnosis and treatment.

#### Limitations and future directions

Whilst a systematic database search was conducted, it is possible that some papers of relevance were missed. Whilst we accepted all observational and experimental studies available with a QOL outcome, our ability to draw conclusions on QOL between treatment modalities is limited by the non-randomisation to treatments due to clinicians' need to make clinical decisions for patient's best outcomes. Future studies should focus on qualitative studies asking patient opinions on their OOL, its relationship to physical symptoms, and what support they would like from healthcare providers. Also, quality of the research could be improved by blinding assessors to treatment allocation, which was reported by only two studies.31,61 Whilst the impact of potential confounders (age, tumour size) were addressed in many studies, as seen in Table 1, the length of follow-up was often variable. The impact of this potential confounder should be addressed in future either statistically or through initiating regular assessments post-diagnosis (e.g. alongside annual scans), regardless of treatment allocation. This would allow comparisons of patients diagnosed across time but with more uniform follow-up periods post-treatment.

#### **Conclusions**

Active AN treatments, whilst necessarily to preserve health, can leave some patients with long-term physical deficits. These can have a significant impact across a wide range of

QOL domains beyond the physical impairment and into social and emotional wellbeing and participation in society. Surgical teams should adequately prepare patients for this prior to treatment and ensure patients receive adequately community follow-up in terms of specialist physical therapies, audiology, ophthalmology, and psychological follow-up as well as encouraging patients to join support groups and AN associations to learn from and engage the support of peers. Quality-of-life should be a consideration in treatment decisions in view of the differences across modalities.

#### Abbreviations

AN: Acoustic neuroma; BDI: Beck Depression Inventory; EQ-5D: European Quality of Life–5 dimensions; GBI: Glasgow Benefit Inventory; HSQ: Health Status Questionnaire; PANQOL: Penn Acoustic Neuroma QOL; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; QOL: Quality of life; RSES: Rosenberg Self-Esteem Scale; SAS: Zung Self-Rating Anxiety Scale; SDS: Zung Self-Rating Depression Scale; SF-36: Short form 36; SF-12: Short form 12; SRS: Stereotactic radiosurgery; SRT: Stereotactic radiation therapy; VRQOL: Voice-Related Quality of Life; WHO: World Health Organization.

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#### Authors' contributions

SB contributed to developing the concept for the paper and methods, she conducted the literature and synthesis alongside validity analysis and produced the first draft of the paper. AM contributed to developing the concept for the paper and methods, made considerable contributions to the written manuscript, particularly in the drafting of the discussion and in presenting the validity analysis. JG contributed to developing the concept for the paper and contributed significant insights into the final draft. The author(s) read and approved the final manuscript.

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#### Competing interests

The authors declare that they have competing interests.

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