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Multi-disciplinary evidence-based consensus statements on salvage surgery for recurrent head and neck cancer (IReC)

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1. Abstract

1.1 Background

Recurrent head and neck squamous cell carcinomas (rHNSCC) are an understudied subgroup, lacking high quality evidence and thus gold standard management recommendations, resulting in significant variations in practice. The aim of this project was to deliver a national multi-disciplinary expert consensus on patients with rHNSCC managed by curative salvage surgery.

1.2 Methods

The AGREEII protocol guided the Delphi process. Best practice statements were developed after literature review on the perioperative management and surgical salvage of major rHNSCC subsites. Members of the International centre for Recurrent head and neck cancer (IREC) network, and other UK based professional stakeholder organisations were invited into an online Delphi study. Participants voted upon statements over three rounds, with items modified in response to vote thresholds and comments.

1.3 Results

Twenty-eight experts participated including 11 otolaryngologists, 7 oncologists, 9 oral and maxillofacial surgeons, and 1 speech and language therapist. Consensus was achieved on 73 statements, with 29 (39.7%) achieving unanimous (threshold: 100%) and 25 (34.2%) (threshold >90%) agreement.

1.4 Conclusions

Salvage surgery for rHNSCC are challenging cases that require intensive multidisciplinary input to achieve cure while balancing impact on function and quality-of-life. In this article, we provide a large series of statements based on UK-wide expert consensus, that will guide clinicians through the complex intra- and perioperative management of patients undergoing surgical salvage.

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2. Introduction

Despite advances in surgical and oncological treatments over the last three decades, patients with a history of head and neck squamous cell carcinoma (HNSCC) are at a substantially elevated risk of recurrent and residual disease (rHNSCC). When combined with a rising incidence of HNSCCs internationally[1], this has produced a large patient cohort requiring further investigations and treatment after primary management. The reported rates of rHNSCC are conflicting, with studies such as the recent ARTDECO trial of intensity-modulated radiotherapy finding a 2-year locoregional control rate of 74.7% in laryngeal and hypopharyngeal cancers[2], whilst a 2021 update of the MACH-NC systematic review reported a pooled locoregional failure rate as high as 42%[3].

Radiotherapy can induce several post-treatments changes to the head and neck mucosa including scarring, diminished blood supply, and radio-resistance. As a result, the Royal College of Radiologists cautions against reirradiation of recurrent cancers with a short latency of 6-12 months, in addition to recommending avoidance of elective cervical nodes and aiming for a narrow clinical tumour volume of <50cm^3[4]. Salvage surgery is commonly the only curative option for many patients; however, compared to primary resections, salvage procedures are associated with a higher risk of post-operative complications and treatment failure[5]. Unfortunately, due to a lack of effective alternative treatments, difficulties in standardising surgical techniques, and a low number of patients eligible for recruitment, there are few high-quality prospective trials in salvage surgery on which to base treatment recommendations. Moreover, there is a shortage of clinical practice guidelines specific to rHNSCC, and those that do exist are hampered by their methodological quality[6]. Accordingly, there is little evidence to support multidisciplinary team (MDT) decision making, and resultantly, many rHNSCC patients are deemed ineligible for salvage surgery at diagnosis, with one series showing only 47.4% of recurrences undergo salvage surgery, with considerable variations noted across subsites[7].

Members of our institution, in partnership with ENT UK, recently conducted a UK-wide Delphi study, producing best practice statements on the management of unknown primary HNSCC (HNSCCUP), which ultimately influenced recommendations in the 6th edition of the UK head and neck cancer guidelines[8]. This project clearly demonstrated the efficacy of national multidisciplinary consensus studies in producing best practice statements for uncommon tumours with complex management pathways and a weak evidence base. Consequently, the aim of this project was to use a modified Delphi methodology to produce comprehensive best practice statements on curative salvage surgery for rHNSCC, to guide head and neck MDT decision making in patients being considered for salvage surgical intervention. Specifically, the statements concern pre-operative

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optimisation, surgical intervention of recurrent laryngeal, hypopharyngeal, oropharyngeal and oral cavity tumours, and post-operative management and follow-up.

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3. Methods

3.1 Project oversight

The Delphi methodology was adapted from a previous consensus study, the details of which are published elsewhere[9]. Project oversight was provided by the scientific committee of the International centre for Recurrent head and neck Cancer (IReC), consisting of a panel of clinicians and researchers with an interest in rHNSCC. IReC is a network of nine high volume centres, led by the Royal Marsden Hospital, London, to accelerate research and improve outcomes for patients with rHNSCC and set international standards in the curative treatment, palliation, and supportive care of this disease. The AGREE II protocol was used to prepare this process (**table S1**)[10], with the methodology shared in advance with Delphi participants.

3.2 Literature search

Topic themes on management of rHNSCC were identified by review of existing international guidelines and consensus recommendations[8,11–14]. Following this, multiple English language literature searches were performed using a systematic review and meta-analysis filter of articles published between 2003-2023. Literature searches were performed on Pubmed on 01/04/2023 and updated on 31/10/2023. Search criteria are provided in **methods S1**, in summary, phrases relating to head and neck subsites and surgeries including “laryngectomy”, “neck dissection” and “transoral robotic surgery” were combined with terms such as “recurrence”, “recurrent”, and “salvage”. In addition, two bespoke systematic reviews were commissioned[15,16], and additional targeted searches of randomised trials and case series were undertaken where no systematic review evidence existed.

3.3 Statement generation

Draft statements were produced according to the NICE guidance for recommendation language[17]. This recommends directive language (e.g., “offer”) is used for treatments that should be performed, and less commanding phrasing, (e.g., “consider”) is advised for recommendations where there is less clarity on the risks and benefits. Statements were authored by an otolaryngology research fellow and resident surgeon (AW), a senior HNC surgeon (VP), with input from a specialist HNC speech and language therapist (SLT) and dietician (GB/NH). The statements identified points in the patient pathway that necessitates decision making to proceed to the next step in management.

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Where available, statements were mapped to existing literature, and the quality of the evidence was graded by the research fellow using the Strength Of Recommendation Taxonomy (SORT)[18]. SORT is a grading scale that evaluates the quality and consistency of evidence and rates research on a simple 3 point scale of A (consistent and good quality patient-orientated evidence), B (inconsistent and limited-quality patient-orientated evidence), and C (based on consensus, usual practice, opinion, disease-oriented evidence, or case series).

3.4 Participant selection

After steering committee review, statements were distributed to nominated representatives from units across the UK. Each centre was asked to nominate a consultant Otolaryngologist, Oncologist, and Oral and Maxillofacial surgeon (OMFS). In addition, representatives from UK-based professional stakeholder organisations including ENT UK, the British Association of Head and Neck Oncologists (BAHNO), and the British Association of Oral and Maxillofacial Surgeons (BAOMS) were invited to participate.

3.5 Delphi process

Representatives were sent a weblink to a three-stage, online modified Delphi process hosted on Survey Monkey (San Mateo, USA). Statements were answered with agree/disagree/unsure options. Each statement was accompanied by a free text box to facilitate comments and feedback. Results were single blinded, with only two authors (AW/VP) able to review voting and comments between rounds. Participants were provided with summary documents of the best practice guidelines and research articles used to generate statements before voting (**tables S2 & S3**). Each round was conducted over two weeks, with reminder emails sent on days 5 and 10.

The Delphi was split into two phases. The first, covering pre-operative management and salvage surgery of the larynx and hypopharynx was conducted between 6th November 2023 until 19th December 2023, with the second, concerning salvage oral and oropharyngeal surgery and post-operative management and follow-up, occurring between 12th February 2024 and 5th April 2024.

3.6 Voting thresholds

Thresholds were modified from the Royal College of Radiology consensus statements[4] (**table S4**). “Unsure” or unanswered statements were discarded, and thresholds were calculated from

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agree/disagree responses. Statements achieving “unanimous” (100%), “very strongly supported” (90-99%) and “strongly supported” (80-89%) thresholds were removed from future voting rounds. After round 1, statements were modified in line with participant comments. Most modifications involved toning down the statement to allow more latitude in management choice. The original and modified questions were both presented in follow-up rounds. If both statements reached the same threshold, but one attained a higher percentage level of agreement, then it was accepted. Additionally, if the “offer” and “consider” statements reached the same percentage of agreement, then the former was accepted. Finally, the agreed-upon statements were graded with the Flesch reading ease score and reviewed by IReC’s Patient and Public Involvement (PPI) team, and where possible minor adjustments were made to recommendation language to enhance readability. The Delphi leads (AW/VP) retained the concluding remarks on statements between voting and on the final arrangement of the consensus document.

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4. Results

4.1 Delphi process

Phase 1 involved 19 experts (11 Otolaryngologists, 7 Oncologists, 1 SLT) including representatives from ENT UK (n=2) and BAHNO (n=1). Phase 2 added 9 OMFS experts, including BAHNO (n=4) and BAOMS (n=1) representatives. **Figure 1** summarises both Delphi phases. Phase 1 consisted of 31 statements (9 pre-operative management, 22 laryngeal and hypopharyngeal salvage surgery), whilst phase 2 contained 42 statements, (24 oral and oropharyngeal salvage surgery, 18 post-operative management). Response rates were 19/19 (100%), 17/19 (89.5%), and 16/19 (84.2%) in phase 1, and 23/28 (82.1%), 23/28 (82.1%), and 24/28 (85.7%) in phase 2. After final arrangement of statements, the mean Flesch reading ease level was 8.9 (range 0-52.87).

4.2 Delphi results

All 73 statements achieved consensus, with agreement thresholds reached as follows: 29 (39.7%) unanimous, 25 (34.2%) very strongly supported, 17 (23.3%) strongly supported, and 2 (2.7%) majority agreement (**figure 2**). Reported rates of agreement describe when a statement first met a pre-determined agreement threshold, and does not report the number of rounds or revisions a particular item underwent. A full summary of statements, voting thresholds across rounds, SORT criteria, supporting evidence, and participant comments are provided in **tables 1-4** and **tables S5-S8**.

4.3 Pre-operative management and evaluation

Full statements, voting thresholds, references[15,19–23] and comments on pre-operative management are summarised in **table 1** and **table S5**. The Delphi cohort agreed unanimously (n=19/19, 100%, SORT: C) that all aspects of pre-habilitation, surgical management, and rehabilitation should be undertaken in an MDT environment. Pre-operative imaging with contrast enhanced CT and/ or MRI reported by a specialist head and neck radiologist (n=17/17, 100%, SORT: A), and assessment with whole-body 18-FDG-PETCT (n=15/15, 100%, , SORT: A) also reached unanimous agreement. The cohort had very strong agreement (n=18/19, 94.7%, SORT: C) that patients should receive a full discussion of all appropriate salvage techniques and be offered a choice of treatment where multiple options exist.

There was very strong agreement (n=18/19, 94.7%, SORT: C) that specialist SLT examination and counselling should be offered to all pre-salvage patients. Strong agreement was achieved for

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offering instrumental assessment with videofluoroscopy and/or flexible endoscopic evaluation of swallowing (FEES) (n=12/14, 85.7%, SORT: C). Screening with validated nutrition tools, with referral to specialist dieticians where a risk of malnourishment and malnutrition is identified (as defined by NICE Clinical Guideline 32[24]), had very strong consensus (n=15/16, 93.8% , SORT: C). The Delphi cohort had very strong agreement on the use of supplemental feeding with prophylactic gastrostomy in those with poor swallowing prognosis, prolonged (>4 weeks) swallow rehabilitation, undernutrition (defined as <30kcal/kg/day) or nasogastric tube feeding, and those at risk of malnutrition (n=17/18, 94.4%, SORT: B). Use of nasogastric feeding in patients with short term (<4 weeks) swallow impairment or undernutrition was again very strongly supported (n=15/16, 93.8%, SORT: C).

4.4 Salvage surgery for recurrent laryngeal and hypopharyngeal squamous cell carcinoma

Statements, voting thresholds, sources[15,16,25–58], and comments relating to salvage surgery for laryngeal and hypopharyngeal rHNSCC are available in **table 2** and **table S6**. There was unanimous agreement (n=19/19, 100%, SORT: C) that all patients should undergo rigid endoscopic evaluation under general anaesthetic to determine quality of transoral access and tumour resectability.

4.4.1 Organ preservation salvage surgeries

On organ-preserving salvage surgeries, there was unanimous consensus that all patients should be counselled on the risk of completion laryngectomy (n=19/19, 100%, SORT: B). Unanimous agreement was attained for the following procedures: transoral laser microsurgery (TLM) for T1-T2 glottic recurrence with limited anterior commissure involvement (n=17/17, 100%, SORT: B) and TLM and transoral robotic surgery (TORS) in T1-T2 recurrent supraglottic (n=18/18, 100%, SORT: B) and hypopharyngeal (n=14/14, 100%, SORT: B) cancers with sufficient transoral access. Experts unanimously agreed that partial laryngectomy can be offered in both T1-2 and T3-4 recurrent laryngeal disease where adequate respiratory and laryngeal function exists (both n=12/12, 100%, SORT: B).

4.4.2 Salvage total laryngectomy and laryngopharyngectomy

There was unanimous agreement that salvage total laryngectomy and laryngopharyngectomy may be used in patients with adequate an ECOG performance status and T1-2 laryngeal (n=17/17, 100%, SORT: B) and hypopharyngeal (n=18/18, 100%, SORT: B) cancers where there is a high risk of

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involved surgical margins or laryngeal dysfunction. Experts also had unanimous agreement on treatment of T3-4 rHNSCC of the larynx (n=18/18, 100%, SORT: B) and hypopharynx (n=17/17, 100%, SORT: B) with total laryngectomy and laryngopharyngectomy. When considering margins, strong agreement (n=13/16, 81.3%, SORT: C) was achieved on a >5mm cut-off in open laryngeal and hypopharyngeal procedures.

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4.4.3 Neck dissection for recurrent laryngeal and hypopharyngeal squamous cell carcinoma

When considering management of cervical nodes during salvage laryngectomy and laryngopharyngectomy, there was strong agreement (n=8/9, 88.9%, SORT: B) that observation of the cervical lymph nodes in lieu of planned neck dissection may be appropriate in T1-T2 laryngeal and hypopharyngeal node-negative disease. However, for T3-4 recurrence with N0 nodes, there was majority agreement (n=8/11, 72.7%, SORT: B) that at least ipsilateral selective (IIa, III, IV) or super-selective neck dissection (IIa, III) would be appropriate in well-lateralised disease, whilst bilateral dissection should be performed in midline cancers (n=14/17, 82.4%, SORT: B). For node positive disease, there was strong agreement (n=14/17, 82.4%, SORT: B) that patients should undergo either selective (IIa, IIb, III, IV) or super-selective (IIa, IIb, III) neck dissection.

4.4.4 Surgical margins in recurrent laryngeal and hypopharyngeal cancers

On margin status in transoral procedures, there was very strong agreement (n=13/14, 92.9%(both n=12/12, 100%, SORT: C) on a >1mm threshold for early glottic disease. In open laryngeal and hypopharyngeal procedures, there was strong agreement (n=13/16, 81.3%, SORT: C) was achieved on a >5mm margin cut-off.

4.4.5 Adjunct procedures in salvage laryngectomy and laryngopharyngectomy

For adjunct procedures performed during salvage laryngectomy and laryngopharyngectomy, there was very strong agreement on performing ipsilateral hemithyroidectomy (n=10/11, 90.9%, SORT: B), considered use of salivary bypass tubes (SBT) in those at high risk of post-operative pharyngocutaneous fistula (PCF) and stricture (n=11/12, 91.7%, SORT: B), and avoidance of primary tracheoesophageal puncture (TOP) (n=10/11, 90.9%, SORT: B). There was unanimous agreement on use of secondary TOP procedures (n=8/8, 100%, SORT: B). Delphi participants had strong agreement (n=12/14, 100%, SORT: B) on use of free and pedicled flaps in patients undergoing salvage

laryngectomy and laryngopharyngectomy, and unanimous (n=13/13, 100%, SORT: B) agreement on their use in laryngopharyngectomy with circumferential defects.

4.5 Salvage surgery for recurrent oral cavity and oropharyngeal squamous cell carcinoma

Full statements, thresholds, resources[21,33,37,41–43,59–76] and participant feedback on salvage oral cavity and oropharyngeal surgery are summarised in table 3 and table S7. Pre-operatively, there was a strong consensus in recurrent oropharyngeal tumours for rigid endoscopic assessment under anaesthetic to assess tumour extent and resectability (n=20/21, 95.2%, SORT: C).

4.5.1 Transoral resections for recurrent oral cavity and oropharyngeal squamous cell carcinoma

Unanimous agreement was seen in statements supporting transoral resection of T1-2 oral (n=21/21, 100%, SORT: B) and oropharyngeal recurrence (n=22/22, 100%, SORT: A), whereas agreement was strong on the use of TORS and TLM in select T3-4 oropharyngeal rHNSCC (n=13/15, 86.7%, SORT: A). There was unanimous agreement that salvage TORS should only be offered by units who have first developed experience of robotic resections in primary cancers (n=22/22, 100%, SORT: C). To mitigate bleeding after salvage TORS, there was very strong agreement (n=13/14, 92.9%, SORT: B) on prophylactic arterial ligation, and strong agreement (n=16/18, 88.9%, SORT: B) on using vascularised tissue flaps to cover exposed vessels.

4.5.2 Open resections for recurrent oral cavity and oropharyngeal squamous cell carcinoma

It was agreed unanimously (n=23/23, 100%, SORT: C) that salvage open oral and oropharyngeal resections should be treated by teams experienced with managing recurrent cancers and flap reconstruction. Unanimous agreement (n=18/18, 100%, SORT: B) was documented for open resections in patients with T1-2 recurrent oral and oropharyngeal cancers with poor transoral access, whilst very strong agreement (n=16/17, 94.1%, SORT: B) was reached for open procedures in T3-4 disease. Agreement was unanimous (n=23/23, 100%, SORT: B) for use of salvage glossolaryngectomy in locally advanced, low oropharyngeal cancers, and on performing prophylactic tracheostomy in procedures where post-operative airway obstruction was anticipated (n=23/23, 100%, SORT: C).

4.5.3 Neck dissection for recurrent oral cavity and oropharyngeal squamous cell carcinoma

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In recurrent oropharynx cancer with cN0 disease, there was strong agreement for (n=18/21, 85.7%, SORT: B) selective (IIa, IIb, III, IV) or super-selective (IIa, IIb, III) neck dissection for well-lateralised tumours, and bilateral clearance for midline disease (n=18/21, 85.7% , SORT: B). Very strong agreement was accomplished in node positive recurrent oropharyngeal cancers for selective (IIa, IIb, III, IV) neck dissection, again incorporating unilateral lymph node removal in well-lateralised disease (n=22/23, 95.7%, SORT: B), and bilateral for midline tumours (n=22/23, 95.7%, SORT: B).

In the oral cavity, it was decided unanimously (n=18/18, 100%, SORT: B) that T2-4 N0 disease may be managed by ipsilateral level I, IIa, and III dissection, whilst strong consensus (n=14/17, 82.4%, SORT: B) supported neck dissection in T1 N0 cancers. In node positive disease, unanimous agreement was obtained for dissection of levels I, IIa, and III (and level IV in oral tongue disease), once again demarcated as ipsilateral in well-lateralised (n=21/21, 100%, SORT: C), and bilateral in midline disease (n=21/21, 100%, SORT: C).

4.5.4 Surgical margins in recurrent oral cavity and oropharyngeal squamous cell carcinoma

Margin status was difficult to define in the oropharynx, with a >5mm margin achieving strong agreement (n=20/23, 87%, SORT: C) in salvage cases for T3-4 disease. A statement asserting clinicians may consider salvage surgery for recurrent T1-2 cancers even if <5mm margins are anticipated, achieved very strong consensus (n=18/19, 94.7%, SORT: B) in the tonsil, but majority agreement (n=13/18, 72.2%, SORT: B) in the tongue base. A >5mm margin was met with very strong approval (n=18/20, 90%, SORT: B) in oral cavity resections of any stage.

4.6 Post-operative management, rehabilitation, and follow-up

Full statements, consensus thresholds, references[20,22,77–94], and comments for post-operative rehabilitation and follow-up are provided in **table 4** and **table S8**.

4.6.1 Immediate post-operative management

Post-procedure, use of 24-48 hours of antibiotics was strongly supported after clean contaminated salvage surgery (n=16/18, 88.9%, SORT: B) and flap reconstruction (n=16/18, 88.9%, SORT: B). Commencement of enteral feeding within 24 hours received very strong consensus (n=18/19, 94.7%, SORT: C), while regular specialist dietetic assessment was met with unanimous agreement (n=20/20, 100%, SORT: C). Consideration of early oral feeding (<5 days after salvage) had

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strong agreement for oral and oropharyngeal resections (n=17/20, 85%. SORT: B), whereas a statement advising against early oral feeding after salvage laryngectomy had very strong support (n=15/16, 93.8%, SORT: A).

Participants unanimously agreed (n=21/21, 100%, SORT: C) to ongoing post-operative evaluation by specialist SLTs, whilst post-operative instrumental assessment including video fluoroscopy and FEES had very strong agreement (n=20/21, 95.7%, SORT: C). There was unanimous agreement (n=17/17, 100%, SORT: B) on use of water-soluble contrast swallow assessment prior to commencing feeding after salvage laryngectomy.

4.6.2 Long term follow-up after salvage head and neck surgery

On follow-up, there was very strong agreement on maintaining existing 5-year follow-up schedules (n=20/22, 90.9%, SORT: C), with 1-2 monthly reviews for the first two years, and broadening timeframes thereafter (n=17/18, 94.4%, SORT: C). At each follow-up, there was very strong agreement (n=18/20, 90%, SORT: B) on performing a full head and neck examination, including assessment with flexible nasolaryngoscopy and narrow band imaging where available.

4.6.3 Imaging recommendations in recurrent head and neck cancer

Performing baseline cross-sectional imaging to facilitate comparison with future scans at 3-4 months post-salvage had very strong consensus (n=19/20, 95%, SORT: C), and reporting of all post-operative imaging by a specialist head and neck radiologist had a unanimous response (n=22/22, 100%, SORT: C). Very strong agreement (n=19/21, 90.5%, SORT: C) was achieved in consideration of annual cross-sectional imaging surveillance to facilitate detection of early recurrent and oligometastatic disease.

After primary chemo-radiotherapy, there was very strong agreement (n=22/23, 95.7%, SORT: A) on offering 18-FDG-PETCT instead of planned neck dissection at 3-4 months. There was strong agreement on offering CT and/or MRI imaging with a view to conducting salvage neck dissection when unequivocal FDG-avidity is identified at 3-4 months (n=18/21, 85.7%, SORT: C), and performing an interval 3–4-month 18-FDG-PETCT in cases of equivocal FDG-uptake (n=16/19, 84.2%, SORT: A).

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5. Discussion

5.1 Overview of results

This article summarises the results of a modified Delphi study that produced best practice statements on salvage surgery for rHNSCC, modified from IReC and ENT UK's previous experience on generating consensus on the management of HNSCCUP[9]. The outcome is one of most expansive group of recommendations on salvage rHNSCC surgery to date, providing a strong foundation of practice for operations where little high-quality literature exists. Participants reached agreement on 73 items covering numerous themes, with a high rate of unanimous (n=29/73, 39.7%) and very strongly supported statements (n=25/73, 34.2%). A further advantage is the quality of the Delphi cohort, consisting of 28 expert ENT, OMFS, oncology, and SLT consultants from high volume centres. This reflects the structure of many cancer MDTs, and provides a broad range of opinions relevant to the varying patient populations around the UK.

5.2 Results in context

The Delphi demonstrated broad support for salvage surgery across a host of recurrent tumour subsites and staging. This is strengthened by a recent meta-analysis comparing surgical and non-surgical salvage treatments, which demonstrated 5-year overall survival (OS) of 26%-67% and 0%-32% respectively, strongly favouring surgical intervention[33]. The challenging post-operative course following salvage laryngectomy should not be underestimated however, as complication occur in around 67.5% of patients[49], with PCF identified as a particularly common (19-37%) and troublesome to manage[49]. By comparison, survival is more varied after salvage oropharyngeal surgeries, with a review of 776 resections finding a 2-year OS of 52%, falling to 30% at 5 years[62]. As with the larynx, outcomes are superior to nonsurgical management, with a review of studies comparing operative and non-operative interventions finding statistically significantly improved 5-year OS in those receiving surgery (26% vs 16%, p= 0.001)[61].

Transoral procedures including TORS and TLM were well supported by the Delphi experts across several cancer subsites and staging. There is growing evidence that transoral procedures can achieve encouraging survival in difficult-to-access recurrent tumours with fewer complications than open resections. For example, a systematic review of salvage TORS found 2-year OS and disease-free survival of 73.8% and 74.8%[59]. Results are slightly less reassuring in salvage TLM, with a review by Russo et al of recurrent laryngeal cancer noting local control rates of 74.2% and 39.1% at 1 and 5 years respectively, with a laryngeal preservation rate of 73.5%[29]. Nonetheless, this consensus process

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strongly favours transoral and open salvage procedures as an effective curative treatment for many rHNSCCs, and future iterations of this Delphi may benefit from a focus on novel strategies such as adjuvant immunotherapy to enhance survival following these surgeries.

There was clear harmony on the importance of multidisciplinary input in the perioperative management and rehabilitation of salvage surgery patients, which has previously demonstrated survival benefits on meta-analysis[96]. In particular, MDTs can expediate early intervention for malnutrition and swallow dysfunction by SLTs and dieticians, which can have a considerable impact on post-operative quality-of-life and function. Salvage patients, who often carry extensive treatment histories and fibrosed tissues, are at a higher risk of swallowing impairment and malnutrition than primary disease, with pooled long-term feeding tube dependency after salvage procedures being 18%, increasing to 41% after open oral and oropharyngeal resections[15]. Unfortunately, the literature review found a paucity of research in speech and swallow rehabilitation after salvage surgery, and many Delphi comments mentioned a lack of availability of SLT and instrumental swallow assessments across departments. Despite robust consensus over the import of these interventions, the applicability of these statements may be highly dependent on local resource provision.

Numerous controversies arose during the Delphi, in particular surgical margins in recurrent oropharyngeal tumours, which may be due to inconsistent definitions in the literature. The Royal College of Pathologists recommends a 5mm margin in the oropharynx[97], however this is not replicated in the wider literature, where definitions vary from 1-5mm[74]. The RECUT study recently found that margins >1mm were associated with a 2-year local control rate of 80.9%, compared to 54.2% in those of ≤1mm[60], suggesting salvage TORS may be safely attempted even when margins <5mm are anticipated. However, another study of salvage TORS by GETTEC, who defined involved margins as ≤2mm, found R1 resections were associated with an increased mortality risk on univariate analysis[60], leaving margins in this cohort as a major area of debate.

Numerous minor disagreements also arose concerning procedures adjunct to salvage laryngectomy, including SBTs and timing of TOP, necessitating alterations to use less instructive language. Systematic reviews report improved rates of PCF in laryngectomy procedures with SBTs (15.8-22.2% vs 35.3-38.3%)[52,54]. Nevertheless, participants preferred more judicious use of SBTs, commenting SBTs are poorly tolerated and troublesome to manage, and only advocated for their use in select procedures including circumferential resection and reconstruction. Concerning TOP, systematic reviews of primary and salvage laryngectomy have shown an elevated risk of PCF in primary compared to secondary puncture[55,56]. In salvage laryngectomy, a small cohort study of 30 patients found a statistically significant difference in post-operative PCF in the primary TOP group (0%

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vs 50%, p<0.05)[98]. Certain Delphi comments reported successful local experience with primary TOP in post-radiotherapy cases, which may indicate an area of future prospective research.

Finally, although HPV status has a considerable impact on primary oropharyngeal cancers, this was not incorporated into our statements for oropharyngeal salvage. Recent evidence suggests superior survival in HPV positive compared to negative rHNSCC, however the former is associated with more frequent distant metastasis, precluding many patients from salvage surgery[99]. Furthermore, this survival disparity does not translate to the salvage cohort, and there is little evidence to recommend differing surgical approaches between these two groups. For instance, RECUT found no difference in OS (p=0.36), disease-free (p=0.45), and disease-specific survival (p=0.24), or local control (p=0.43) between HPV positive and negative rHNSCC undergoing TORS[60]. This was replicated in an oropharyngeal cancer series by GETTEC, where there was no difference in OS (p=0.3) or relapse-free survival (p=0.4) following first recurrence according to p16 status[100].

5.3 Applying recommendations to clinical practice

While this project aimed to provide extensive recommendations on salvage surgery for rHNSCC, they cannot consider every clinical permutation in this complex patient cohort. As such, management plans need to account for the difficulties and ambiguity surrounding the various patient, tumour, and healthcare factors that influence the suitability of surgery as a curative treatment. This complexity therefore demands shared multi-disciplinary decision-making and judicious implementation of these recommendations, and clinicians must understand that certain recommendations may have to be altered or disregarded in certain cases.

Moreover, rHNSCC treatment is an evolving space, for example, recent phase II trials suggest adjuvant or neoadjuvant immunotherapy may have a large impact disease-free survival[101], whilst adjuvant reirradiation with proton therapy has been well tolerated in small cohorts[102]. Although these treatments show promise, they have not undergone randomised phase III trials and are not commonplace oncological practice. In the future, this consensus methodology may have to be reapplied to incorporate these adjuvant therapies should they show widespread efficacy and become standard of care.

5.4 Limitations

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This Delphi carries some limitations. Although the consensus statements cover a widespread array of practice, they are not exhaustive, and as a result there may be patient subsets and treatment nuances that may not have been considered. Additionally, by trying to not burden the cohort with a high number of items, the Delphi was limited by its division over two phases, in particular by the later addition of OMFS participants and low representation from allied health professionals, who may have provided valuable insight into reconstruction and peri-operative statements respectively.

A limitation common to many Delphi studies is their generalisability and applicability to real-world practice, which are subject to funding and staffing constraints. By inviting specialists from various UK regions where practice is relatively homogeneous for primary HNSCC, we aimed to embody a wider spectrum of UK practice that considered each unit's unique challenges and resources. For the same reasons, this renders international consensus more difficult and less applicable, as differences in disease aetiology, epidemiology, and historical healthcare systems and practices between countries are often too great to create single unified recommendations. Nevertheless, it is our aim that the lessons learnt from this national process will be used to deliver future international consensus.

While this study can be criticised for a lack of input from key multidisciplinary stakeholders involved in diagnostics (radiologists, histopathologists) and supportive care (dietetics), the selected professionals are the key decision makers in delivering salvage surgical service. Ultimately, the level of consensus attained is a reflection of the participating cohort's attitudes, experience, clinical background and interpretation of available evidence, and we believe this study has accrued a sufficiently wide spectrum of professionals to do this robustly.

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6. Conclusion

In conclusion, this Delphi has produced one of the largest collections of best practice statements on salvage surgery for rHNSCC, consisting of 73 statements voted upon by 28 multidisciplinary experts. Participants represented 4 national organisations and 14 hospitals, and thus encompasses a wide selection of UK practice. In the future, there is a need to assess if these consensus statements are reflected in real-world management. To this end, IReC is currently undertaking RESCUE (NCT05808920), which prospectively studies survival, quality-of-life, and variations in standards of salvage surgical care, thus providing essential information on the relevancy and applicability of these statements.

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Data Availability: The data that support the findings of this study are available from the corresponding authors (AW/ VP), upon reasonable request.

Funding: Funding for this study was provided by a £1,000 award from the ENTUK Foundation Research Grant (Grant number 000231). The salary of Mr Andrew Williamson (Head and Neck Research fellow) is provided through a grant from the Royal Marsden Cancer Charity/ International centre for Recurrent head and neck Cancer (IReC). The funder had no role in the design of the study; the collection, analysis, or interpretation of the data; or the writing of the manuscript and decision to submit it for publication.

Conflict of interest: The authors of this article have consulted the JNCI author guidelines and declare no relevant conflict of interest.

Acknowledgements: We would like to thank the team and network collaborators at the International Centre for Recurrent Head and Neck Cancer (IReC) for their ongoing support with this article and our wider programme of research, Mr Ahmad Abou-Foul for providing help with figures 1 and 2 and committee members of ENT UK, the British Association of Head and Neck Oncologists (BAHNO), and the British Association of Oral and Maxillofacial Surgeons who participated in this study. We would also like to thank ENT UK, whose foundation grant helped fund access to Survey Monkey for this project. This article was presented as an oral presentation at the annual IReC scientific day 16th May 2024 (London), and BAHNO annual scientific meeting on 17th May 2024 (London).

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9. Tables

Table 1: Consensus statements on the pre-operative management of patients undergoing salvage procedures for recurrent head and neck squamous cell carcinoma.

Number	Statement	Round 1 (%)	Round 2 (%)	Round 3 (%)	Level of Agreement	SORT	References
	Pre-operative management and evaluation						
1	Plan all aspects of multimodal prehabilitation, pre-operative assessment, surgical care, reconstruction, and rehabilitation with a multi-disciplinary team that has experience in managing recurrent head and neck cancers.	100.0	-	-	Unanimous	C	Expert consensus or existing best practice guidelines
2	Offer contrast-enhanced CT and/or MRI reported by a specialist head and neck radiologist in all patients with suspected recurrent cancer who are being considered for salvage surgery with curative intent.	100.0	-	-	Unanimous	A	Zhu (2023)[19]
3	Offer whole-body 18-FDG-PETCT scans in patients with suspected recurrent head and neck cancer who are being considered for salvage surgery with curative intent.	100.0	-	-	Unanimous	A	Gao (2014)[20], Gupta (2011)[88], Isles (2008)[22], Zhu (2023)[19]
4	Offer patients a full preoperative discussion of all appropriate surgical techniques including the likely post-operative functional outcomes and rehabilitation and identify any patient preferences if a choice of surgical procedure exists.	94.7	-	-	Very strong agreement	C	Expert consensus or existing best practice guidelines
5	Offer patients a full preoperative multidisciplinary evaluation of communication, voice, and swallowing using clinician and patient reported outcome measures, and pre-treatment counselling by a speech & language therapist.	94.7	-	-	Very strong agreement	C	Expert consensus or existing best practice guidelines
6	Offer patients a preoperative instrumental evaluation of swallowing using videofluoroscopy and/or Flexible Endoscopic Evaluation of Swallowing (FEES)	85.7	-	-	Strong agreement	C	Expert consensus or existing best practice guidelines

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7	Offer nutritional screening using a validated tool, with urgent referral to a specialist dietitian for assessment and treatment in any patient identified to have, or be at risk of malnourishment* or malnutrition**	93.8	-	-	Very strong agreement	C	Expert consensus or existing best practice guidelines
8	Offer specialist dietician review and prophylactic nutritional support via an endoscopic or radiologically guided gastrostomy in patients undergoing salvage surgical procedures with; • Poor prognosis for swallowing recovery or prolonged (>4 weeks) swallow rehabilitation • At risk of prolonged (>4 weeks) undernutrition (<30kcal/kg/day) • At risk of prolonged (>4 weeks) nasogastric tube feeding • At risk of malnutrition**	94.4	-	-	Very strong agreement	B	Wang (2014)[23], Williamson (2023)[15]
9	Offer prophylactic nutritional support via a nasogastric tube to patients at risk of short term (<4 weeks) impaired swallowing or undernutrition (<30kcal/kg/day).	93.8	-	-	Very strong agreement	C	Expert consensus or existing best practice guidelines

- denotes a round where the statement was not voted upon due to previous acceptance or introduction in later rounds

* Patient at risk of malnourishment defined as per NICE Clinical guideline 3232: body mass index <18.5kg/m2, unintentional weight loss of >10% within the last 3 to 6 months, a BMI of <20kg/m2 and unintentional weight loss of >5% within the last 3 to 6 months

** Patient at risk of malnutrition defined as per NICE Clinical guideline 3232: eaten little or nothing for more than 5 days and/or are likely to eat little or nothing for 5 days or longer, a poor absorptive capacity and/or high nutrient losses and/or increased nutritional needs from causes such as catabolism

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Table 2: Consensus statements on the surgical management of patients undergoing salvage procedures for recurrent head and neck squamous cell carcinoma of the larynx and hypopharynx.

Number	Statement	Round 1 (%)	Round 2 (%)	Round 3 (%)	Level of Agreement	SORT	References
10	Offer direct examination under anaesthetic to assess tumour extent, accessibility, cord mobility, and resectability in patients being considered for curative salvage surgery of recurrent laryngeal and hypopharyngeal cancers.	100.0	-	-	Unanimous	C	Expert consensus or existing best practice guidelines
	Organ preservation salvage surgeries						
11	Inform patients undergoing transoral and partial salvage laryngeal and hypopharyngeal procedures of the risk of requiring completion salvage laryngectomy or laryngopharyngectomy for recurrence or dysfunction.	100.0	-	-	Unanimous	B	De Virgilio (2018)[25], Leone (2016)[26], Paleri (2011)[27], Ramakrishnan (2013)[28], Russo (2023)[29], Williamson (2023)[15]
12	Offer transoral laser microsurgery in select T1-T2 recurrent glottic cancer with normal cord mobility and laryngeal function, limited anterior commissure involvement, and appropriate transoral access.	100.0	-	-	Unanimous	B	Ramakrishnan (2013)[28], Russo (2023)[29], Zhong (2015)[30]
13	Offer transoral laser microsurgery or transoral robotic surgery in select T1-T2 recurrent supraglottic cancer with normal vocal fold mobility and laryngeal function, and adequate transoral access.	100.0	-	-	Unanimous	B	Lechien (2020)[31], Ramakrishnan (2013)[28], Russo (2023)[29]
14	Offer open partial laryngectomy in cases of T1-T2 and smaller T3-4 recurrent laryngeal cancers with good pre-operative respiratory function and no laryngopharyngeal dysfunction.	100.0	-	-	Unanimous	B	De Virgilio (2018)[25], Leone (2016)[26], Paleri (2011)[27], Saraniti (2022)[32]
	Salvage total laryngectomy and laryngopharyngectomy						
15	Offer open partial laryngectomy in T1-T2 and small T3-4 recurrent laryngeal cancers with good pre-operative respiratory and function and no laryngopharyngeal dysfunction.	100.0	-	-	Unanimous	B	Bulbul (2022)[33]

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16	Offer salvage total laryngectomy in patients with adequate ECOG performance status scores and T3-4 recurrent laryngeal tumours.	100.0	-	-	Unanimous	B	Bulbul (2022)[33]
17	Offer endoscopic resection techniques including transoral laser microsurgery and transoral robotic surgery in select T1-T2 recurrent hypopharyngeal cancer with adequate transoral access and no laryngopharyngeal dysfunction.	100.0	-	-	Unanimous	B	Lai (2022)[34], Lane (2020)[35]
18	Offer salvage laryngopharyngectomy in patients with adequate ECOG performance status scores and T1-T2 recurrent hypopharyngeal cancers where there is an increased risk of significant laryngopharyngeal dysfunction or involved surgical margins.	100.0	-	-	Unanimous	B	Bulbul (2022)[33]
19	Offer salvage laryngopharyngectomy in patients with adequate ECOG performance status scores and T3-4 recurrent hypopharyngeal tumours.	100.0	-	-	Unanimous	B	Bulbul (2022)[33]
Neck dissection for recurrent laryngeal and hypopharyngeal squamous cell carcinoma							
20	Consider clinical and radiological observation of the cervical lymph nodes instead of planned neck dissection in T1-T2 recurrent laryngeal and hypopharyngeal tumours with clinically and radiographically N0 disease.	76.9	88.9	-	Strong agreement	B	Davies-Husband (2020)[36], Finegersh (2020)[37], Gross (2020)[38], Lin C (2019)[39], Lin D (2019)[40]
21	Consider at least ipsilateral selective (levels IIa, III, IV) or super-selective (IIa, III) neck dissection T3-T4, well lateralised, recurrent laryngeal and hypopharyngeal tumours with a history of radiotherapy treatment to the neck, and clinically and radiologically N0 cervical lymph nodes.	-	75.0	72.7	Majority	B	Davies-Husband (2020)[36], Finegersh (2020)[37], Gross (2020)[38], Lin C (2019)[39], Lin D (2019)[40]
22	Consider bilateral selective (levels IIa, III, IV) or super-selective (IIa, III) neck dissection in midline T3-T4 recurrent laryngeal and hypopharyngeal tumours with a history of radiotherapy treatment to the neck, and clinically and radiologically N0 cervical lymph nodes.	82.4	-	-	Strong agreement	B	Davies-Husband (2020)[36], Finegersh (2020)[37], Gross (2020)[38], Lin C (2019)[39], Lin D (2019)[40]
23	Offer selective (levels II-IV) or super-selective (II-III) neck dissection in all recurrent laryngeal and hypopharyngeal cancers with clinically and radiologically node positive cervical lymph nodes.	82.4	-	-	Strong agreement	B	Bovenkamp (2017)[41], Bovenkamp (2018)[42], Robbins (2005)[43], Van der Putten (2009)[44]

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Surgical Margins in recurrent laryngeal and hypopharyngeal squamous cell carcinoma							
24	Surgeons should aim for a >1mm margin when performing salvage transoral surgery for early glottic recurrent cancer.	92.9	-	-	Very strong agreement	C	Expert consensus or existing best practice guidelines
25	Surgeons should aim for a >5mm margin when performing salvage open partial laryngectomy, total laryngectomy, and laryngopharyngectomy.	81.3	-	-	Strong agreement	C	Expert consensus or existing best practice guidelines
Adjunct procedures in salvage laryngectomy and laryngopharyngectomy							
26	Consider ipsilateral hemithyroidectomy and sparing the contralateral thyroid lobe in salvage total laryngectomy and laryngopharyngectomy when there is no radiological or macroscopic evidence of direct invasion of the thyroid, thyroid cartilage lamina, or subglottis.	-	90.9	-	Very strong agreement	B	Kumar (2013)[45], Xie (2022)[46]
27	Offer reinforcement with vascularised tissue from outside the radiation field, including pedicled or free flaps, in all patients undergoing salvage total laryngectomy and laryngopharyngectomy to promote wound healing and reduce post-operative fistulae and pharyngeal stricture.	85.7	-	-	Strong agreement	B	Cabrera (2020)[47], De Virgilio (2022)[25], Guimaraes (2016)[51], Hasan (2016)[49], Paleri (2014)[50], Sayles (2013)[58], Williamson (2023)[16]
28	Offer reconstruction with vascularised tissue from outside the radiation field in all patients undergoing salvage laryngopharyngectomy with circumferential defects or where only a narrow section of pharyngeal mucosa remains.	100.0	-	-	Unanimous	B	Guimaraes (2016)[51], De Virgilio (2022)[48], Paleri (2014)[50], Williamson (2023)[16]
29	Consider using salivary bypass tubes in salvage total laryngectomy or laryngopharyngectomy cases at high risk of post-operative fistula or pharyngeal stricture, for example in those requiring circumferential reconstruction.	-	91.7	-	Very strong agreement	B	Costantino (2022)[52], Kamhieh (2018)[53], Marijic (2021)[54]
30	Consider avoiding primary tracheoesophageal puncture in salvage laryngectomy and laryngopharyngectomy patients to reduce the risk of pharyngocutaneous fistula	-	90.9	-	Very strong agreement	B	Barauna Neto (2017)[55], Chakravarty (2018)[56], (2018)[57]

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31	In patients without existing speech valve rehabilitation, consider secondary tracheoesophageal puncture after salvage laryngectomy and laryngopharyngectomy in those deemed suitable after multidisciplinary surgical and speech and language therapist review.	-	100.0	-	Unanimous	B	Barauna Neto (2017)[55], Chakravarty (2018)[56], (2018)[57]

- denotes a round where the statement was not voted upon due to previous acceptance or introduction in later rounds

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Table 3- Consensus statements on the surgical management of patients undergoing salvage procedures for recurrent head and neck squamous cell carcinoma of the oral cavity and oropharynx.

Number	Statement	Round 1 (%)	Round 2 (%)	Round 3 (%)	Level of Agreement	SORT	References
32	Offer direct examination under anaesthetic to assess for tumour anatomy, accessibility, and trismus in all patients being considered for salvage surgery of recurrent oropharyngeal tumours.	95.2	-	-	Very strong agreement	C	Expert consensus or existing best practice guidelines
Transoral resections for recurrent oral cavity and oropharyngeal squamous cell carcinoma							
33	Offer minimally invasive resection techniques such as transoral robotic and transoral laser salvage surgery in T1-2 recurrent oropharyngeal cancer with favourable tumour anatomy and adequate transoral access.	100.0	-	-	Unanimous	A	Hardman (2020)[59], Hardman (2022)[60], Jayaram (2016)[61], Kao (2017)[62]. Turner (2023)[63]
34	Offer transoral resection techniques in recurrent T1-2 oral cavity cancer with favourable tumour anatomy and transoral access.	100.0	-	-	Unanimous	B	Chen (2021)[64], Nandy (2022)[65], Weckx (2019)[66]
35	Offer minimally invasive techniques such as transoral robotic and transoral laser salvage surgery in select T3-4 recurrent oropharyngeal cancer with favourable tumour anatomy and transoral access.	86.7	-	-	Strong agreement	A	Hardman (2020)[59], Hardman (2022)[60], Jayaram (2016)[61], Kao (2017)[62]. Turner (2023)[63]
36	Salvage transoral robotic surgery should be offered by units who have first developed extensive experience of transoral robotic surgery for primary head and neck cancers.	100.0	-	-	Unanimous	C	Expert consensus or existing best practice guidelines
37	Offer prophylactic transcervical arterial ligation to mitigate the risk of post-operative haemorrhage in salvage transoral robotic surgery of the oropharynx.	92.9	-	-	Very strong agreement	B	Bollig (2020)[67]
38	Offer use of vascularised pedicled or free tissue to cover exposed vessels to mitigate the risk of post-operative haemorrhage in salvage transoral robotic surgery of the oropharynx.	88.9	-	-	Strong agreement	B	Turner (2023)[63]

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Open resections for recurrent oral cavity and oropharyngeal squamous cell carcinoma							
39	Patients being evaluated for open salvage oral and oropharyngeal resections should be treated by a surgical team with experience of managing recurrent head and neck cancers and reconstruction with vascularised tissue flaps.	100.0	-	-	Unanimous	C	Expert consensus or existing best practice guidelines
40	Offer open salvage resections via trans-mandibular or mandible-sparing transcervical approaches in patients with adequate ECOG performance status scores with T1-2 recurrent oral and oropharyngeal cancers where there is inadequate access for transoral procedures.	100.0	-	-	Unanimous	B	Bulbul (2022)[33], Jayaram (2016)[61], Kao (2017)[62], Pang (2018)[68]
41	Offer open salvage resections via trans-mandibular or mandible-sparing transcervical approaches in patients with adequate ECOG performance status scores and T3-4 recurrent oral and oropharyngeal cancers.	94.1	-	-	Very strong agreement	B	Bulbul (2022)[33], Jayaram (2016)[61], Kao (2017)[62], Pang (2018)[68]
42	After pre-operative counselling and speech and swallow assessment, offer salvage total glossolaryngectomy in highly selected patients with adequate ECOG performance status scores and low T3-4 oropharyngeal tumours with or without gross laryngeal involvement.		100.0	-	Unanimous	B	Kamhieh (2018)[69], Mazerolle (2022)[70], Sinclair (2011)[71]
43	Offer perioperative tracheostomy in patients undergoing salvage oral cavity and oropharyngeal surgery who are at high risk of post-operative airway oedema or obstruction.	100.0	-	-	Unanimous	C	Expert consensus or existing best practice guidelines
Neck dissection for recurrent oral cavity and oropharyngeal squamous cell carcinoma							
44	Offer at least ipsilateral selective (levels IIa, III, and IV) or super-selective (IIa, III) neck dissection with clinically and radiologically N0 cervical lymph nodes in well lateralised recurrent oropharyngeal cancers of any stage.	85.7	-	-	Strong agreement	B	Bovenkamp (2017)[41], Bovenkamp (2018)[42], Finegersh (2020)[37], Gupta (2022)[21], Malik (2023)[72], Robbins (2005)[43]
45	Offer at least bilateral selective (levels IIa, III, and IV) or super-selective (IIa, III) neck dissection with clinically and radiologically N0 lymph nodes in midline recurrent oropharyngeal cancers of any stage.	85.0	-	-	Strong agreement	B	Bovenkamp (2017)[41], Bovenkamp (2018)[42], Finegersh (2020)[37], Gupta (2022)[21], Malik (2023)[72], Robbins (2005)[43]

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46	Offer at least ipsilateral selective (levels IIa, IIb, III, and IV) neck dissection with clinically and radiologically positive cervical lymph nodes in well lateralised recurrent oropharyngeal cancers of any stage.	95.7	-	-	Very strong agreement	B	Malik (2023)[72]
47	Offer at least bilateral selective (levels IIa, IIb, III, and IV) neck dissection with clinically and radiologically positive cervical lymph nodes in midline recurrent oropharyngeal cancers of any stage.	95.7	-	-	Very strong agreement	B	Malik (2023)[72]
48	Offer at least ipsilateral selective (levels I, IIa, and III to all subsites, and include IV in oral tongue) neck dissection in clinically and radiologically N0 recurrent T1 oral cavity cancer. In particular, in those with no previous history of neck dissection.	82.4	-	-	Strong agreement	B	Finegersh (2020)[37], Gupta (2022)[21], Hutchison (2019)[73]
49	Offer at least ipsilateral selective (levels I, IIa, and III to all subsites, and include IV in oral tongue) neck dissection in clinically and radiologically N0 recurrent T2-4 oral cavity cancer. In particular in those with no previous history of neck dissection.	100.0	-	-	Unanimous	B	Finegersh (2020)[37], Gupta (2022)[21], Hutchison (2019)[73]
50	Offer at least ipsilateral selective (levels I, IIa, IIb, and III to all subsites, and include IV in oral tongue) neck dissection with clinically and radiologically positive cervical nodes in well lateralised recurrent oral cavity cancer of any stage. In particular, in those with no history of neck dissection	100.0	-	-	Unanimous	C	Expert consensus or existing best practice guidelines
51	Offer at least bilateral selective (levels I, IIa, IIb, and III to all subsites, and IV in oral tongue) neck dissection with clinically and radiologically positive cervical lymph nodes in midline recurrent oral cavity cancer of any stage. In particular, in those with no history of neck dissection.	100.0	-	-	Unanimous	C	Expert consensus or existing best practice guidelines
Surgical margins in recurrent oral cavity and oropharyngeal squamous cell carcinoma							
52	Multi-disciplinary teams should consider salvage transoral surgery for recurrent T1-T2 tonsil cancers deemed resectable after clinical and radiological assessment, even if <5mm pathological margins are anticipated.	-	94.7	-	Very strong agreement	B	Hardman (2022)[60], Williamson (2023)[74]
53	Multi-disciplinary teams should consider salvage transoral surgery for recurrent T1-T2 tongue base cancers deemed resectable after clinical and radiological assessment, even if <5mm pathological margins are anticipated.	-	-	72.2	Majority agreement	B	Hardman (2022)[60], Williamson (2023)[74]

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54	Multi-disciplinary teams should aim for a >5mm margin when performing open salvage surgery for T3-4 recurrent oropharyngeal cancer.	87.0	-	-	Strong agreement	C	Expert consensus or existing best practice guidelines
55	Multi-disciplinary teams should aim for a >5mm margin when performing salvage transoral and open surgery for recurrent oral cavity cancer of any stage.	90.0	-	-	Very strong agreement	B	Bungum (2020)[75], Young (2023)[76]

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Table 4

Consensus statements on the post-operative management and follow-up of patients who have undergone salvage procedures for recurrent head and neck squamous cell carcinoma.

Number	Statement	Round 1 (%)	Round 2 (%)	Round 3 (%)	Level of Agreement	SORT	References
	Immediate post-operative management						
56	Offer 24 to 48 hours of post-operative broad-spectrum intravenous antibiotics following all clean contaminated salvage surgical procedures.	88.9	-	-	Strong agreement	B	Vander Poorten (2020)[77]
57	Offer 24 to 48 hours of post-operative broad-spectrum intravenous antibiotics following all salvage procedures requiring vascularised tissue transfer for reconstruction or reinforcement.	88.9	-	-	Strong agreement	B	Haidar (2018)[78]
58	Begin enteral feeding within 24 hours following salvage surgery where patients will be nil by mouth for greater than 72 hours or are have pre-operatively undernutrition.	94.7	-	-	Very strong agreement	C	Expert consensus or existing best practice guidelines
59	Offer regular specialist dietetic intervention to assist post-salvage patients in meeting their nutritional needs. Teams should aim for 80% (but not exceeding 110%) of estimated requirements via enteral and/or oral routes within 7 days, which should continue until patients are meeting their nutritional goals.	100.0	-	-	Unanimous	C	Expert consensus or existing best practice guidelines
60	Consider early oral feeding (within 5 days post-operatively) in selected patients undergoing salvage oral and oropharyngeal resections with defects reconstructed by vascularised tissue transfer following assessment of swallowing by a speech & language therapist.	-	85.0	-	Strong agreement	B	Brady (2022)[79], Kerawala (2021)[80], Stramiello (2021)[81]

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61	Early oral feeding is not recommended in patients undergoing salvage laryngectomy and laryngopharyngectomy procedures with and without free flap reconstruction.	93.8	-	-	Very strong agreement	A	Milinis (2021)[82], Singh (2020)[83]
62	Offer ongoing post-operative speech and language therapist evaluation including provision of speech, voice, and swallowing rehabilitation.	100.0	-	-	Unanimous	C	Expert consensus or existing best practice guidelines
63	Offer instrumental evaluation of swallowing using videofluoroscopy and/or Flexible Endoscopic Evaluation of Swallowing (FEES) to guide swallowing rehabilitation in patients with pre- and post-salvage swallowing difficulties.	95.2	-	-	Very strong agreement	C	Expert consensus or existing best practice guidelines
64	Offer using water soluble contrast swallow in salvage laryngectomy and laryngopharyngectomy patients to assess for fistulae before commencing oral feeding.	100.0	-	-	Unanimous	B	Leroy (2023)[84], Narayan (2020)[85]
	Long term follow-up after salvage head and neck surgery						
65	Offer post-salvage patients follow-up for a minimum of 5 years, or longer if deemed to have an elevated risk of further recurrence.	90.9	-	-	Very strong agreement	C	Expert consensus or existing best practice guidelines
66	Offer post-salvage patients follow up every 1-2 months for the first two years, and every 3-6 months in years three to five, or more frequently if deemed to have an elevated risk of further recurrence.	94.4	-	-	Very strong agreement	C	Expert consensus or existing best practice guidelines
67	Offer all post-salvage patients regular head and neck examination including visualisation of the upper aerodigestive tract with flexible or rigid nasolaryngoscopy augmented by narrow band imaging (where available) to assess for further recurrence.	90.0	-	-	Very strong agreement	B	Cosway (2016)[86]
	Imaging recommendations in recurrent head and neck cancer						
68	Offer baseline MRI and/ or contrast enhanced CT scanning 3-6 months following salvage surgery in patients deemed to be at high risk of further recurrence, to facilitate comparison with future imaging studies.	95.0	-	-	Very strong agreement	C	Expert consensus or existing best practice guidelines
69	Consider annual MRI and/or contrast enhanced CT surveillance imaging following salvage surgery in high-risk patients to facilitate early detection and	-	-	90.5	Very strong agreement	C	Expert consensus or existing best practice guidelines

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	implementation of systemic therapy for low volume recurrent/metastatic cancer.						
70	Cross-sectional imaging including MRI and/ or contrast enhanced CT imaging should be reported by a specialist head and neck radiologist in all patients with suspected further head and neck cancer recurrence.	100.0	-	-	Unanimous	C	Expert consensus or existing best practice guidelines
71	Offer 18-FDG-PETCT instead of planned salvage neck dissection at 3-to-4 months after radical (chemo)radiotherapy treatment for all primary mucosal squamous head and neck cancers.	-	95.7	-	Very strong agreement	A	Cheung (2016)[87], Gao (2014)[20], Gupta (2011)[21], Isles (2008)[22], Javidnia (2010)[89], Mehanna (2016)[90], Sheikhbahaei (2015)[91]
72	Offer cross-sectional MRI or CT imaging prior to salvage neck dissection for all primary mucosal squamous head and neck cancers when unequivocal FDG-avidity is demonstrated in cervical lymph nodes 3-to-4 months after radical (chemo)radiotherapy treatment.	-	85.7	-	Strong agreement	C	Expert consensus or existing best practice guidelines
73	Offer interval 3-to-4-month 18-FDG-PETCT in cases of equivocal cervical lymph node FDG-avidity, followed by cross-sectional CT or MRI imaging and salvage neck dissection in cases of persistent FDG-avidity.	84.2	-	-	Strong agreement	A	Mehanna (2016)[90], Liu (2019)[92], Rulach (2019)[93], Wong (2019)[94]

- denotes a round where the statement was not voted upon due to previous acceptance or introduction in later rounds

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10. Figure Legends

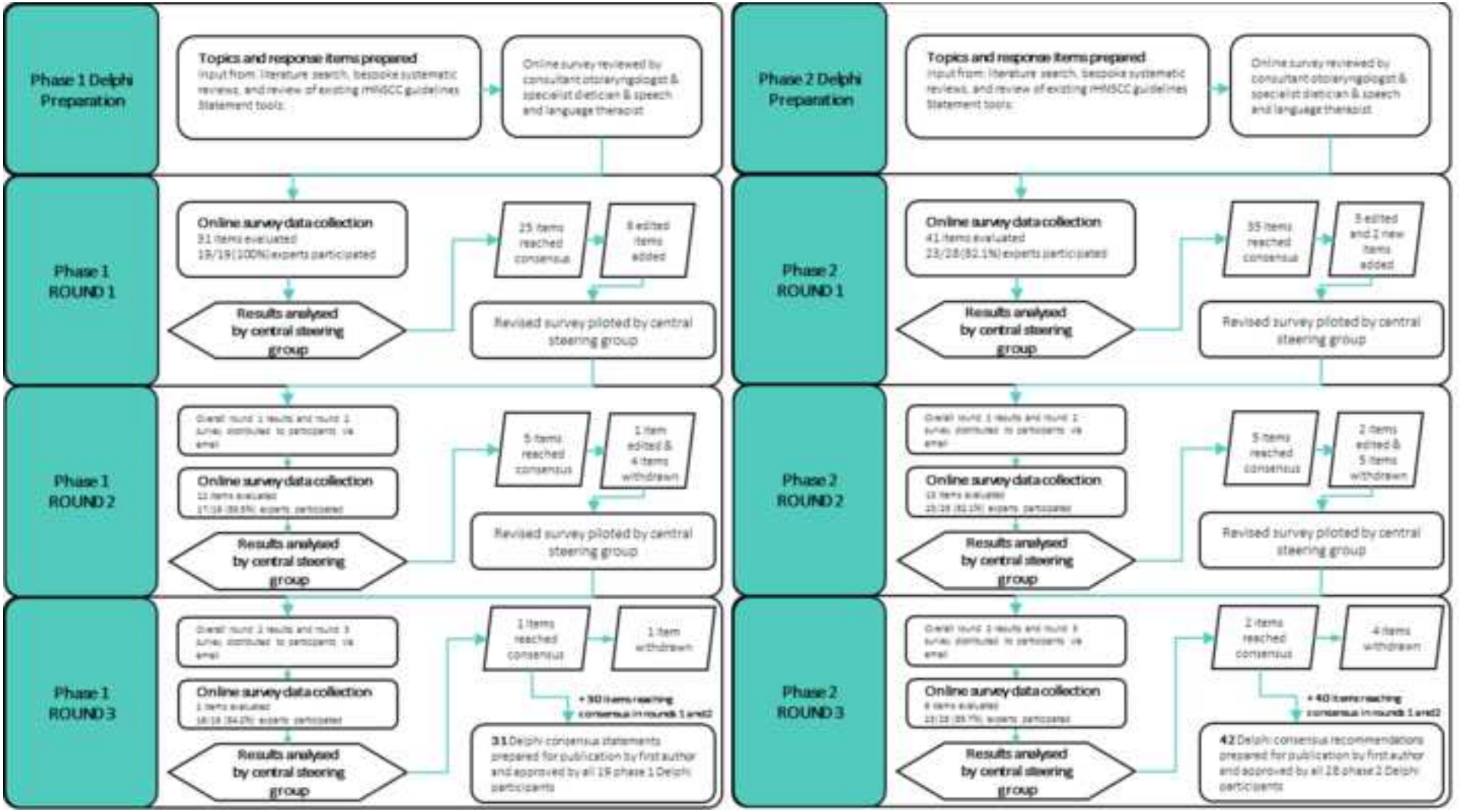
Figure 1- Summarises the Delphi process in phase 1 (**Figure 1A**- pre-operative management and salvage laryngeal and hypopharyngeal surgery) phase 2 (**Figure 1B**- salvage oral cavity and oropharyngeal surgery, and post-operative management and follow-up)

Figure 2- Chart summarising the number of statements with unanimous, very strong, strong, majority, and equipoise agreement across the four major themes (pre-operative management, laryngeal and hypopharyngeal salvage surgery, oral cavity and oropharynx salvage surgery, post-operative management).

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Figure 1

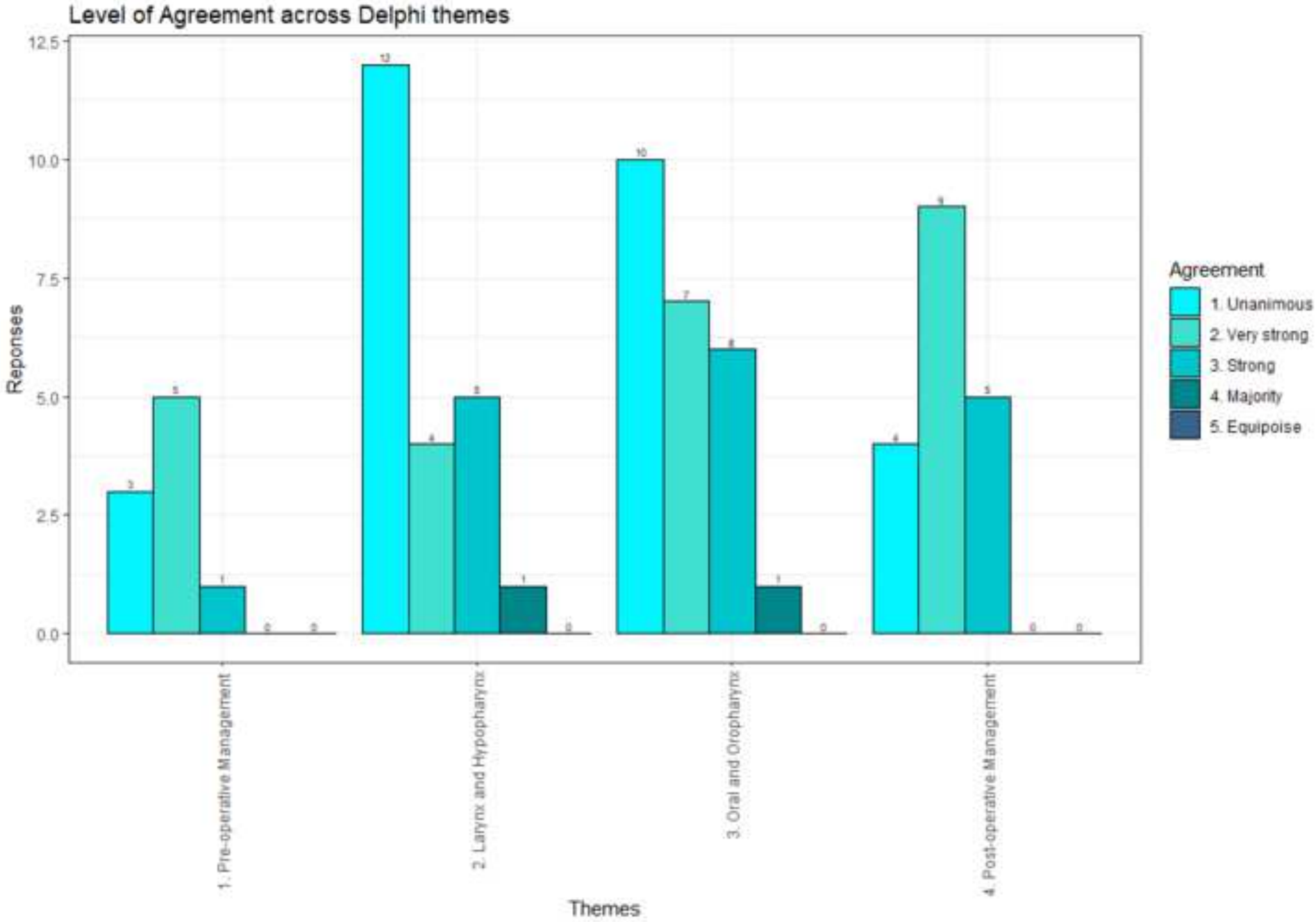
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Figure 2

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