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REVIEW ARTICLE

# Physiological Changes to the Swallowing Mechanism Following (Chemo)radiotherapy for Head and Neck Cancer: A Systematic Review

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**Abstract** Emerging research suggests that preventative swallowing rehabilitation, undertaken before or during (chemo)radiotherapy ([C]RT), can significantly improve early swallowing outcomes for head and neck cancer (HNC) patients. However, these treatment protocols are highly variable. Determining specific physiological swallowing parameters that are most likely to be impacted post-(C)RT would assist in refining clear targets for preventative rehabilitation. Therefore, this systematic review (1) examined the frequency and prevalence of physiological swallowing deficits observed post-(C)RT for HNC, and (2) determined the patterns of prevalence of these key physiological deficits over time post-treatment. Online databases were searched for relevant papers published between January 1998 and March 2013. A total of 153 papers were identified and appraised for methodological quality and suitability based on exclusionary criteria. Ultimately, 19 publications met the study's inclusion criteria. Collation of reported prevalence of physiological swallowing deficits revealed reduced laryngeal excursion, base-of-tongue (BOT) dysfunction, reduced pharyngeal contraction, and impaired epiglottic movement as most frequently reported. BOT dysfunction and impaired epiglottic movement showed a collective prevalence of over 75 % in the majority of patient cohorts, whilst reduced laryngeal elevation and pharyngeal contraction had a prevalence of over 50 %. Subanalysis suggested a trend that the prevalence of these key deficits is dynamic although persistent over time. These findings can be used by clinicians to inform preventative intervention and support the use of specific, evidence-based therapy tasks explicitly selected to target the highly prevalent deficits post-(C)RT for HNC.

**Keywords** Deglutition · Deglutition disorders · Head and neck neoplasms · Swallow pathophysiology

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## Introduction

Dysphagia is recognised as a common, multifactorial, and debilitating sequela for patients who undergo definitive (chemo)radiotherapy ([C]RT) for head and neck cancer (HNC). Whilst acute toxicities, including oedema, mucositis, pain, and altered/thickened salivary flow, impair the swallowing mechanism in the short-term [1–4], radiation-induced tissue fibrosis and chronic oxidative stress perpetuate impairment to the deglutition musculature long after treatment has been completed [5–7]. These long-term swallowing complications can contribute to significant survivorship burden for HNC patients [8–10], resulting in detrimental impacts on the psychosocial aspects of and participation in everyday life [11, 12] and ultimately reduced quality of life [13, 14].

In light of the mounting evidence documenting the persistent and deleterious effects of (C)RT on the swallowing mechanism, optimal treatment methods for the management of dysphagia in this population have come into question. Historically, treatment approaches have been reactive, with rehabilitation administered after medical intervention (either surgical or nonsurgical). However, emerging evidence [15–19] has instigated a shift towards the use of preventative dysphagia rehabilitation, based on the premise that proactively exercising swallowing structures known to be negatively impacted by radiation may limit the extent of (C)RT-induced dysfunction [20].

A number of recent studies have reported the early benefits of preventative swallowing exercises for patients undergoing curative-intent (C)RT for HNC. In particular, the findings of three randomized controlled trials (RCTs) [16, 17, 19] have demonstrated that patients who underwent prophylactic swallowing rehabilitation protocols before and/or during (C)RT had superior outcomes across a range of swallowing indexes following treatment, including improved functional swallowing outcomes; significantly less deterioration in head and neck muscle composition; less decline in mouth opening, taste, and smell; better preservation of salivary flow; and fewer patients requiring or dependent on gastrostomy tube feeding. However, despite each RCT reporting some degree of positive findings for prophylactic swallowing exercises in the (C)RT-HNC population, examination of the study protocols reveals wide variability in the exercises employed, with each study reporting the use of different groups of therapy tasks. In each, a range of between two and five therapy tasks had been implemented, which included batteries of stretch and strengthening techniques, including tongue-base strengthening, range of motion and retraction exercises, Masako, effortful swallow, super-supraglottic swallow and Mendelsohn manoeuvres, falsetto, jaw range of motion, and jaw resistance training using the Therabite Jaw Rehabilitation System (Atos Medical AB, Hörby, Sweden) [16, 17, 19]. Great diversity in prophylactic exercise protocols has also been revealed in the clinical domain. Surveys of usual practice in HNC management have demonstrated that whilst there is a percentage of clinicians who administer dysphagia therapy proactively [21, 22], the nature of therapy provided is highly variable, with most survey respondents administering a range of exercises to address a range of potential swallowing impairments. This broad, nonspecific approach is responsive to the lack of strong evidence for any one or a particular set of manoeuvre(s) to accomplish positive swallowing outcomes [21].

In order to inform the formation of a core set of swallowing exercises that may be most beneficial to apply proactively with HNC patients undergoing (C)RT, there is a need to clarify exactly (1) what are the predominant physiological changes to the swallowing mechanism associated with (C)RT treatment, (2) which of these changes occur with the highest prevalence, and (3) which remain long-standing issues for patients in the months and years post-treatment. Whilst a number of excellent systematic and critical reviews have already been published which discuss what is known about the characteristics of dysphagia following (C)RT for HNC and the clinical and functional implications for this population [3, 12, 23–27], no review to date has explicitly focused on the patterns of key physiological or anatomical disorders underlying these difficulties and compared their reported prevalence. Furthermore, no investigation has attempted to longitudinally analyse whether trends exist in the collective prevalence of swallowing impairments post-(C)RT. Therefore, the purpose of this systematic review is to (1) review the current evidence for the underlying physiological swallowing deficits observed post-(C)RT for HNC in order to determine which deficits are highly frequent and prevalent, and (2) determine the patterns of prevalence of these key physiological deficits over time post-treatment.

## Methods

### Search Strategy

PubMed, Medline, ScienceDirect, SpringerLink, CINAHL, and Wiley databases were searched for electronic publications in English that were published in peer-reviewed journals between January 1998 and March 2013. The following medical subject headings (MeSH) search terms were used: deglutition, deglutition disorders, radiotherapy, chemoradiotherapy, and head and neck neoplasms. Additional search terms included head and neck cancer, dysphagia, swallowing, videofluoroscopy, and fiberoptic endoscopic evaluation of swallowing (FEES). Subsequently, the reference lists of identified studies and selected review papers were manually searched for additional relevant publications.

### Selection Criteria

Studies were included if: (1) participants were adults diagnosed with HNC, (2) participants received (C)RT treatment regimens, and (3) objective dysphagia outcomes were reported utilising instrumental assessment (videofluoroscopy or FEES) at one or more time points post-treatment. The following material was excluded: (1) review papers and editorials, (2) studies reporting data pertaining to mixed cohorts (including primary surgical, postoperative RT, or recurrence populations), (3) studies only reporting dysphagia toxicity (i.e., CTCAE or RTOG), (4) studies only using swallow assessments other than instrumental measures (i.e., swallowing-related or general quality of life, patient-reported swallowing function, dependence on alternative feeding), and (5) studies only reporting pre-treatment outcomes. Those publications that reported data exclusively on participants with nasopharyngeal

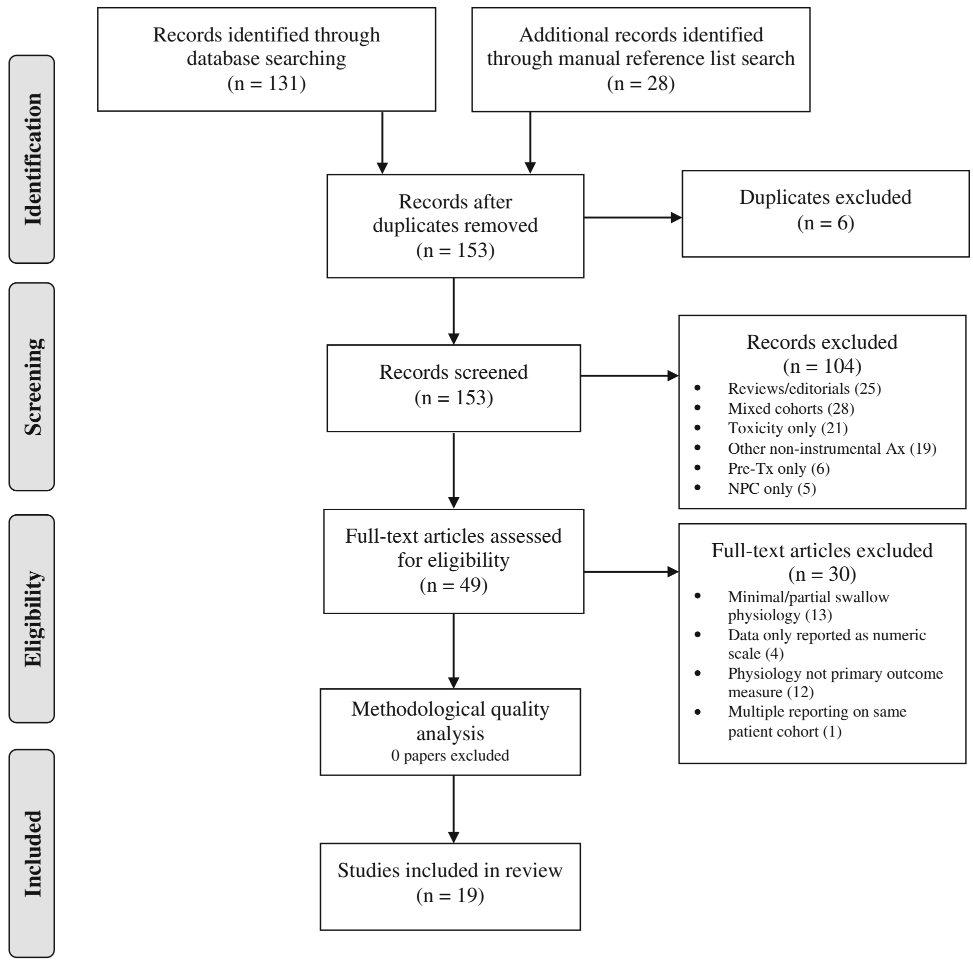


**Fig. 1** PRISMA flow diagram detailing search strategy and selection criteria

carcinomas were also excluded because of the disparities in pathology and treatment regimens that often accompany this population.

In total, 153 papers were identified, 49 of which were deemed relevant after perusal of their abstracts (Fig. 1). Three researchers reviewed these selected papers independently. Upon analysis of the full text, 29 studies were subsequently rejected based on a second set of exclusionary criteria: (1) studies only reporting minimal or partial information relating to swallow physiology (i.e., penetration/aspiration, residue, stasis, or oropharyngeal swallow efficiency only), (2) studies which collapsed instrumental swallow assessment results into a numeric scale and reported no descriptive physiological data, and (3) studies in which swallow physiology was not the primary outcome measure (including dosimetric analyses). This yielded a provisional cohort of 20 papers eligible for review [28–47]. Of these, two sets of articles by Cartmill et al. [29, 30] and Kendall et al. [38, 39] were identified as successive publications reporting data on the same respective groups of participants. To reduce the risk of publication bias, the first article by Cartmill et al. [29] was excluded in favour of the authors' subsequent paper [30], which included a larger number of participants and thus demonstrated greater statistical power and methodological rigour. Conversely, the outcome measurements of the Kendall et al. [38, 39] studies were deemed sufficiently different to warrant the inclusion of both papers, with the earlier research reporting exclusively on structural physiological data (e.g., distance of hyoid displacement and degree of pharyngeal constriction), and the subsequent study focusing on temporal physiological measures (e.g., pharyngeal transit time and timing of laryngeal vestibule closure). This left a total of 19 publications eligible for inclusion (Table 1) [28, 30–47].

## Methodological Quality

The methodological quality of eligible studies was also evaluated in detail to determine their suitability for inclusion in the final analysis. As all publications were a variety of nonrandomised designs, this evaluation was performed using the Transparent Reporting of Evaluations with

**Table 1** Studies included for review detailing study design, the number of participants, site of disease, treatment regimens, and swallow physiology evaluation method

| First author | Year | Study design | $N^a$ | Site of disease | Treatment | Ax time point(s) | Formal outcome measure (if applicable) |
|---|---|---|---|---|---|---|---|
| Bleier et al. [28] | 2007 | Retrospective case series | 49 | Mixed (>2 sites) | conRT: 45<br>IMRT: 4<br>CCT: 36 | 22.7 Months[b] | |
| Cartmill et al. [30] | 2012 | Prospective cohort study | 31 | Oropharynx | AFRT-CB: 14<br>CRT: 17 | 6 Months | NZIMES<br>PAS |
| Eisbruch et al. [31] | 2002 | Descriptive case series: post-test | 26 | Mixed (>2 sites) | CRT | Pre-Tx<br>1–3 Months<br>6–12 Months | |
| Eisbruch et al. [32] | 2004 | Prospective cohort study | 26 | Mixed (>2 sites) | IMRT: 20<br>RADPLAT: 6 | Pre-Tx<br>1–3 Months<br>6–12 Months | |
| Feng et al. [33] | 2007 | Descriptive case series: pre-test/post-test | 36 | Oropharynx<br>Nasopharynx | CRT | Pre-Tx<br>3 Months | |
| Goguen et al. [34] | 2006 | Descriptive case series: post-test | 23 | Mixed (>2 sites) | CRT | 3.5 Months[b] | Swallow Performance Scale |
| Graner et al. [35] | 2003 | Descriptive case series: pre-test/post-test | 11 | Mixed (>2 sites) | accRT + CCT | 19 Weeks[b] | |
| Hutcheson et al. [36] | 2008 | Retrospective case series | 32 | Larynx | conRT: 16<br>accRT: 24<br>IMRT: 3<br>CCT: 30 | <6 Months or<br>6–11 Months or<br>12+ months | |
| Hutcheson et al. [37] | 2012 | Descriptive case series: post-test | 29 | Mixed (>2 sites) | RT: 11<br>CRT: 18 | 9 Years[b] | PAS<br>NIH-SSS<br>MBSImp |
| Kendall et al. [38] | 1998 | Prospective cohort study | 20 + 60 Controls | Mixed (>2 sites) | NR | 12+ Months | |
| Kendall et al. [39] | 2000 | Prospective cohort study | 20 + 60 Controls | Mixed (>2 sites) | conRT | 12 Months | |
| Kotz et al. [40] | 1999 | Descriptive case series: post-test | 15 | Mixed (>2 sites) | accRT + CCT | 3–45 Weeks | |
| Kotz et al. [41] | 2004 | Descriptive case series: pre-test/post-test | 12 | Mixed (>2 sites) | CRT: 7<br>accRT + CTT: 5 | Pre-Tx<br>8 Weeks[c] | |
| Lal et al. [42] | 2009 | Descriptive case series: post-test | 56 | Mixed (>2 sites) | accRT + CCT | 3 Months | |
| Logemann et al. [43] | 2006 | Prospective cohort study | 53 + 140 Controls | Mixed (>2 sites) | CRT | Pre-Tx<br>3 Months | |
| Logemann et al. [44] | 2007 | Prospective case series | 48 | Mixed (>2 sites) | RT: 12<br>CRT: 36 | Pre-Tx<br>3 Months<br>12 Months | |

**Table 1** continued

| First author | Year | Study design | $N^a$ | Site of disease | Treatment | Ax time point(s) | Formal outcome measure (if applicable) |
|---|---|---|---|---|---|---|---|
| Newman et al. [45] | 2002 | Prospective cohort study | 30 | Mixed (>2 sites) | RADPLAT: 14<br>CRT: 16 | Pre-Tx<br>1 Month | |
| Pauloski et al. [46] | 2006 | Prospective case series | 170 | Mixed (>2 sites) | RT: 22<br>CRT: 147 | Pre-Tx<br>1, 3, 6, and 12 months | |
| Smith et al. [47] | 2000 | Prospective case series | 10 | Mixed (>2 sites) | CRT | 9 Weeks[b]<br>70 Weeks[b] | |

*ConRT* conventional radiotherapy, *IMRT* intensity-modulated radiotherapy, *CCT* concomitant chemotherapy, *AFRT-CB* altered fractionation radiotherapy with concomitant boost, *NZIMES* New Zealand Index for Multidisciplinary Evaluation of Swallowing, *CRT* chemoradiotherapy, *PAS* penetration-aspiration scale, *RADPLAT* radiotherapy and concomitant intra-arterial cisplatin, *accRT* accelerated radiotherapy, *RT* radiotherapy alone, *NIH-SSS* National Institutes of Health Swallowing Safety Scale, *MBSImp* MBS impairment profile, *NR* not reported

[a] Refers to number of participants who underwent at least one instrumental swallow assessment

[b] Median follow-up point

[c] Mean follow-up point

Nonrandomized Designs (TREND) checklist [48], developed to be consistent with the Consolidated Standards of Reporting Trials (CONSORT) statement for RCTs [49]. The 22 criteria specified by TREND were given a rating of 1 (satisfies the criteria) or 0 (does not satisfy the criteria), yielding a maximum quality rating of 22. Three researchers rated the papers independently then subsequently met to compare their ratings and an agreed consensus was reached. A summary of the consensus TREND ratings for quality of methodology is shown as a modified harvest plot in Fig. 2. This method was pioneered by Ogilvie et al. [50] and more recently utilised by Crowther et al. [51] to provide a visual display of synthesised evidence, where lack of homogeneity between studies has precluded the traditional use of a forest plot. The average TREND score was 13.8 (range 10–18). Despite the variable scorings, studies were deemed to have sufficiently comparable quality in their methodology and reported findings, hence none warranted exclusion from the final cohort.

### Data Synthesis

Sources of heterogeneity (population, treatment protocols, research design) in the studies included in this review prohibited a meta-analysis of the data. Therefore, the reported frequencies of physiological swallowing deficits (most commonly expressed as percentages) are presented descriptively. The prevalence of aspiration, penetration, residue, and stasis was also compiled due to their inextricable interactions with swallow physiology and frequent reporting in the literature. A second stage of subanalysis explored the reported prevalence of these physiological and associated swallowing impairments over time. Percentage data were extracted from the papers that used specified evaluation points (i.e., baseline, 1, 3, 6, and 12 months post-[C]RT). Those studies that reported only means [41], medians [28, 34, 35, 37, 47], or ranges [31, 32] for follow-up assessments (Table 1) were excluded from this subanalysis. The availability of comparable data points allowed longitudinal investigation up to 12 months post-(C)RT.

## Results

Of the 19 publications that met the study criteria (Table 1), most were prospective studies (89 %, $n = 17$) reporting on participant cohorts with heterogeneous disease sites (84 %, $n = 16$), including the oral cavity, oropharynx, hypopharynx, and larynx. Participants in the included studies underwent varied RT regimens of differing dose levels (mean $=$ 70.95 Gy, range $=$ 65–79.2 Gy), often accompanied by a

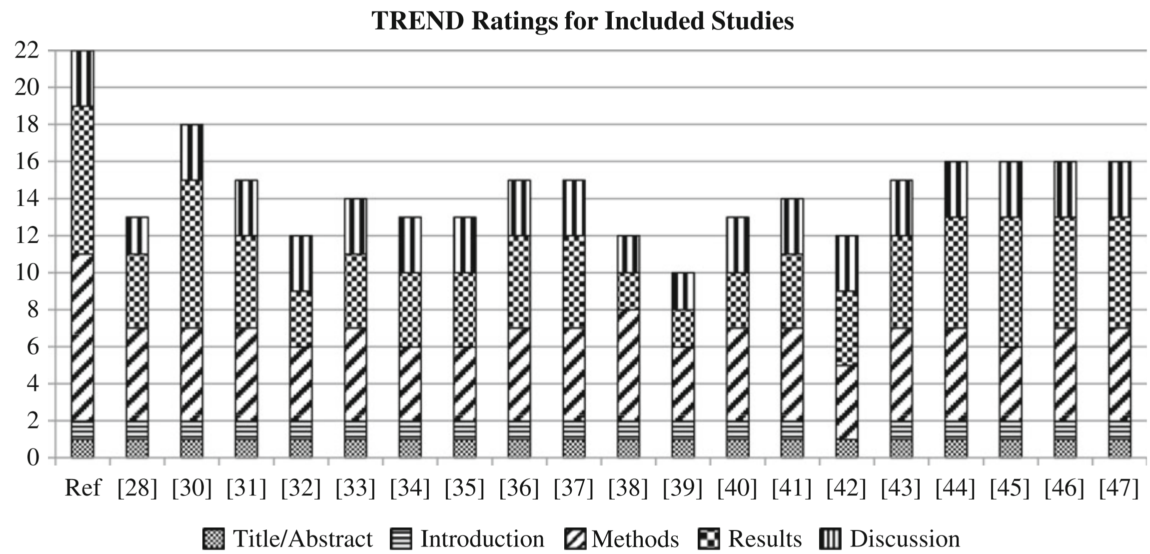


**Fig. 2** Harvest plot of consensus ratings given for each included study reviewed using the TREND checklist

range of concomitant chemotherapy agents (cisplatin, gemcitabine, carboplatin, paclitaxel, docetaxel, hydroxyurea, and 5-fluorouracil). All publications used videofluoroscopic swallow studies to evaluate patients' physiological swallowing impairments. Almost half the studies (45 %, $n = 9$) reported baseline data and the mean follow-up assessment point was at 5.38 months (range 1 month–9 years) post-treatment. Only four studies reported multiple post-treatment assessment points.

## Reported Prevalence of Physiological Swallowing Deficits

The reported prevalence of physiological swallowing deficits observed post-(C)RT for HNC is summarised in Table 2. For those parameters that had three or more studies reporting percentage data, overall prevalence ranges are provided. Abnormalities in the pharyngeal phase predominated the data extracted from the reviewed papers. Dysfunction in the hyolaryngeal complex, namely, reduced laryngeal elevation/excursion, was the most frequently reported physiological parameter, with 15 studies (79 %) demonstrating deficits following (C)RT. An additional four studies reported deficits in hyoid movement. Of those studies specifying percentages, 75 % ($n = 6/8$) reported reduced laryngeal elevation to occur in more than 50 % in their respective patient cohorts.

Dysfunction in the base-of-tongue–posterior pharyngeal wall (BOT–PPW) complex was also frequently documented. Specifically, deficits relating to the BOT (i.e., BOT weakness, reduced BOT retraction, reduced BOT–PPW contact) were reported in 14 of the 19 studies (74 %). Reported percentages indicated high prevalence, with the majority recording BOT dysfunction in over 75 % of patients. Three papers cited BOT weakness or reduced BOT retraction as the most [41, 43] or one of the most [36] common swallowing abnormalities observed at all assessment intervals. Newman et al. [45] determined BOT dysfunction to be the most common across all bolus types. Absent or non-functional BOT retraction was reported in two studies. Correspondingly, reduced pharyngeal contraction and/or pharyngeal weakness was also reported with high frequency in the included studies (68 %, $n = 13$). Where percentage data was specified, 75 % ($n = 6/8$) of the studies reported pharyngeal dysmotility occurred in more than 50 % of patient cohorts. Two studies [40, 47] reported detailed analysis of pharyngeal constrictor dysmotility using Leopold and Kagel's [52] videofluoroscopic descriptors of pharyngeal transport abnormalities, whereby dysfunction to a specific pharyngeal constrictor is inferred from persistent residue on the appropriate segment of the posterior pharyngeal wall. These data revealed that the function of all three constrictor muscles deteriorated following (C)RT [40]; however, the highest frequency of impairment was to the middle pharyngeal constrictor [47].

The next most frequently reported physiological swallowing deficit was again within the hyolaryngeal complex, with ten studies documenting a reduction in epiglottic deflection following (C)RT. Of those studies that specified percentages, 89 % ($n = 8/9$) reported epiglottic dysfunction in more than 50 % of patients and over half (56 %, $n = 5/9$) reported it in more than 75 % of patients. Similar to BOT dysfunction, decreased epiglottic movement was cited by two studies as the most [34] or among the most [36] prevalent pharyngeal phase abnormalities at all evaluation intervals. Absent or nonfunctional epiglottic

**Table 2** Reported prevalence of physiological swallowing deficits in papers included for review

| Deficit | Reported prevalence in reviewed papers |
|---|---|
| *Oral phase* | |
| Impaired mastication | 50 % or more [30] |
| Reduced tongue strength/movement | Overall prevalence range: <5–60 % |
| | 57–60 % [44][a] |
| | 51 % Reduced strength |
| | <5 % Reduced lateral/anterior stabilisation and vertical movement [43] |
| | 11 % [42] |
| | Reported, but no percentage data provided [45, 46] |
| *Pharyngeal phase* | |
| Impaired velopharyngeal closure | 14 % Palatal kink; 12.5 % loss of nasopharyngeal seal [42] |
| | <5 % [43] |
| BOT-PPW complex | |
| Premature spill | Overall prevalence range: 26.5–36 % |
| | 36 % [42] |
| | >30 % [30] |
| | 26.5 % [28] |
| BOT weakness/reduced BOT retraction | Overall prevalence range: 55–100 % |
| | 100 % Abnormal retraction, 17 % absent [37] |
| | 89 % Reduced function, 3 % nonfunctional [33] |
| | 89 % [43] |
| | 85–100 % [32] |
| | 85–90 % [44] |
| | 84.7–94 % [46] |
| | 82 % [35] |
| | 80–100 % [36] |
| | 55–85 % [31] |
| | Reported, but no percentage data provided [38, 45] |
| Reduced BOT–PPW contact | 100 % [41] |
| | Reported, but no percentage data provided [34] |
| Reduced pharyngeal contraction/pharyngeal weakness | Overall prevalence range: 21–100 % |
| | 100 % [32] |
| | 100 % Abnormal, 34 % absent [37] |
| | 80 % [40] |
| | 79.6 % [28] |
| | 60–100 % [47] |
| | 50 % or more [30] |
| | 29 % Unilateral impairment [42] |
| | 21–23 % [44] |
| | Reported, but no percentage data provided [38, 39, 41, 43, 45] |
| Hyolaryngeal complex | |
| Impaired epiglottic inversion | Overall prevalence range: 46–100 % |
| | 100 % Abnormal, 86 % absent [37] |
| | 100 %; 93 % Enlarged epiglottis [40] |
| | 100 % Abnormal or absent [47] |
| | 86.7–100 % [36] |
| | 85.7 %; 57.1 % Bulbous epiglottis [28] |
| | 61 % Reduced function, 22 % nonfunctional [33] |
| | 50–54 % [31] |
| | 50–83 % [32] |
| | 46 % [42] |
| | Reported, but no percentage data provided [34, 41] |
| Reduced laryngeal elevation/excursion | Overall prevalence range: 31–100 % |
| | 100 % Abnormal, 17 % absent [37] |
| | 82 % [35] |
| | 78.3–85.7 % [36] |
| | 67 % [33] |
| | 50–83 % [32] |
| | 50 % or more [30] |
| | 36 % [43] |
| | 31–35 % [44] |
| | Reported, but no percentage data provided [34, 38, 40, 41, 45–47] |
| Reduced hyoid movement | 97 % Abnormal, 38 % absent [37] |
| | 41 % [42] |
| | Reported, but no percentage data provided [38, 39] |
| Impaired laryngeal vestibule closure | Overall prevalence range: <5–83 % |
| | 50–83 % [32] |
| | 66 % Absent closure [37] |
| | 54–60 % [44] |
| | 31 % Slowed/delayed, <5 % incomplete closure [43] |
| | Reported, but no percentage data provided [39, 41, 45, 46] |
| Delayed swallow reflex | 42–56 % [44] |
| | 30–62 % [31] |
| | Reported, but no percentage data provided [45, 46] |
| *Oesophageal phase* | |
| Decreased opening of UES | Overall prevalence range: 17–100 % |
| | 100 % [32] |
| | 50 % or more [30] |
| | 28.3 % [43] |
| | 21–23 % [44] |
| | 17 % [41] |
| | Reported, but no percentage data provided [46] |

[a] Data reported for multiple time points, bolus types, or treatment groups are indicated as ranges

**Table 3** Reported prevalence of penetration, aspiration, residue, and stasis in papers included for review

| Deficit | Reported prevalence in reviewed papers |
|---|---|
| Penetration | Overall prevalence range: 7–95.9 % |
| | 95.9 % [28] |
| | 82 % [35] |
| | 67 % [40] |
| | 17 % [34] |
| | 7–35 % [30][a] |
| | Reported, but no percentage data provided [41] |
| Aspiration | Overall prevalence range: 0–100 % |
| | 100 %, 82 % Silent [37] |
| | 78 %, 35 % Silent [34] |
| | 73.3–85.7 %, 44 % Silent [36] |
| | 68 % [31] |
| | 65.3 % [28] |
| | 64 %, 86 % Silent [35] |
| | 52 % [42] |
| | 44 % [33] |
| | 40 % [47] |
| | 33 % [41] |
| | 23 % [43] |
| | 10 % [38] |
| | 10 % [39] |
| | 7–41 % [30] |
| | 0–40 % [45] |
| | Reported, but no percentage data provided [40] |
| Combined P/A reporting | 60–100 % [32] |
| Pharyngeal residue | Overall prevalence range: 33–100 % |
| | 100 % [37] |
| | 94 % [33] |
| | 90 % [35] |
| | 80 % [40] |
| | 75–100 % [32] |
| | 75–77 % [31] |
| | 70–88 % Vallecular residue; 38–50 % pyriform residue [47] |
| | 54 % [42] |
| | 33 % [41] |
| | Reported, but no percentage data provided [39, 43, 45] |
| Stasis | 80–100 % Pharyngeal stasis [47] |
| | 80 % Supraglottic laryngeal and pharyngeal stasis [40] |
| | 57.1 % Pyriform stasis [28] |
| | 45 % Vallecular stasis; 19 % pyriform stasis [33] |

[a] Data reported for multiple time points, bolus types, or treatment groups are indicated as ranges

movement was reported in three papers and enlarged epiglottic structure in two papers. Impaired laryngeal vestibule closure was the final pharyngeal phase deficit of notable frequency, with seven studies (37 %) reporting dysfunction in this parameter. However, the prevalence among patient cohorts was variable, ranging from <5 % incomplete closure to 66 % completely absent closure of the glottis following (C)RT.

Compared with the pharyngeal phase, oral phase impairments were reported less frequently in the included literature. The most frequently reported oral phase parameters were reduced tongue strength and range of movement, which were documented in five studies. However, the prevalence varied across papers, ranging from <5 to 60 %. With regards to the upper esophageal phase, decreased opening of the upper esophageal sphincter (UES) was reported in six studies. However, it is unclear whether this frequency of UES dysfunction stemmed from core impairment to the cricopharyngeal muscle or as a comorbidity of reduced laryngeal movement, observed in many of the studies. The following physiological deficits had low prevalence in the literature, reported in less than 25 % of the included studies: delayed triggering of the pharyngeal swallow (4 studies), premature spillage over the BOT (3 studies), velopharyngeal dysfunction (2 studies), and impaired mastication (1 study).

## Reported Prevalence of Penetration/Aspiration, Residue, and Stasis

The reported prevalence of penetration/aspiration, residue, and stasis observed post-(C)RT for HNC is summarised in Table 3. For those parameters with three or more studies reporting percentage data, overall prevalence ranges are provided. All but two papers [44, 46] reported on penetration and/or aspiration which allowed a total of 17 studies for analysis. Of these studies, 16 (94 %) documented aspiration specifically and 6 (35 %) documented penetration specifically, with one paper [32] presenting a combined penetration/aspiration finding. The prevalence of penetration and aspiration associated with (C)RT varied considerably among the included studies, ranging from 7 to 95.9 % and from 0 to 100 %, respectively. Four studies (21 %) also documented cases of silent aspiration, the frequencies of which were also variable (range 35–86 %). Pharyngeal residue following (C)RT was reported by 12 studies (63 %). Of those that specified percentages, 89 % ($n = 8/9$) observed residue in more than 50 % of patients and two-thirds (67 %, $n = 6/9$) did so in over 75 % of patients. Stasis in the pharynx was also reported in four studies; however, the location of stasis and its prevalence was variable.

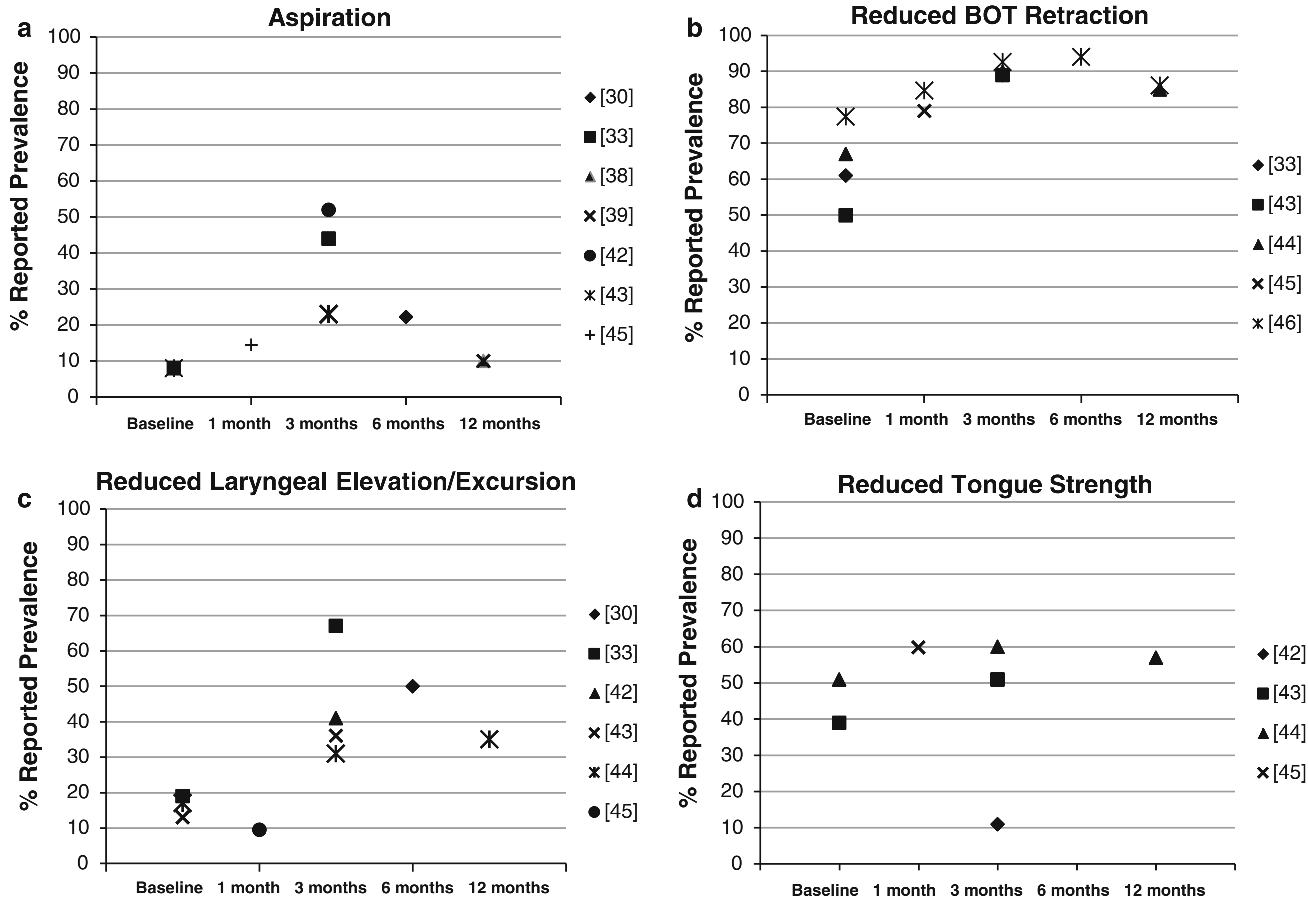


**Fig. 3** **a–d** Reported prevalence of aspiration and core oral and pharyngeal phase physiological swallowing deficits at varying follow-up points over time

### Changes in Prevalence of Physiological Swallowing Deficits Over Time

The articles that contributed to the subanalysis of physiological swallowing deficits over time consisted of four studies reporting data pre-(C)RT [33, 43, 44, 46], two studies reporting at 1 month post-treatment [45, 46], five studies at 3 months post-treatment [33, 42–44, 46], two studies at 6 months post-treatment [30, 46], and four studies at 12 months post-treatment [38, 39, 44, 46]. Percentages from applicable studies were collated and plotted to allow longitudinal examination from pre- to 12 months post-(C)RT. Graphical representations of the prevalence of aspiration and the most frequently reported oral phase (reduced tongue strength) and pharyngeal phase (reduced laryngeal elevation/excursion and reduced BOT retraction) deficits are shown in Fig. 3a–d. These figures are demonstrative of the general trends observed across all of the physiological and associated swallowing deficits documented in Tables 2 and 3.

## Discussion

The purpose of this systematic review was to coalesce the evidence for the frequency and prevalence of physiological swallowing deficits observed post-(C)RT for HNC. The most frequently reported physiological deficits were those to the hyolaryngeal and BOT–PPW complexes, including reduced laryngeal excursion, BOT dysfunction, reduced pharyngeal contraction, and impaired epiglottic movement. BOT dysfunction and impaired epiglottic movement exhibited a collective prevalence of over 75 % in the majority of applicable patient cohorts, whilst reduced laryngeal elevation and pharyngeal contraction had a prevalence of over 50 % in the majority of applicable cohorts.

Dosimetric response studies are a new avenue of research seeking to ascertain how physiological swallowing parameters are differentially affected by (C)RT. Eisbruch et al. [32] were the first to postulate a set of dysphagia/aspiration-related structures (DARS), i.e., deglutitive structures whose damage was deemed likely to cause dysphagia and aspiration, as observed on videofluoroscopy, and demonstrated radiation-induced structural changes in post-treatment CT scans. Recent review papers have reported that these DARS included the superior, middle, and inferior pharyngeal constrictors; glottic and supraglottic larynx and its adductor muscles; UES; and mucosal/submucosal surfaces of the BOT [53, 54]. Examination of dose-volume correlates for the DARS [54] have also revealed that the mean dose to the pharyngeal constrictor muscles was the most important dosimetric predictor of late swallowing complications (>3 months post-[C]RT). Whilst the notion of general resistance of skeletal muscle to RT is well accepted [55], it has been postulated that the pharyngeal constrictor and laryngeal adductor muscles and epiglottic walls, which are situated in close proximity to the submucosa, may be secondarily affected by the acute radiation-induced inflammatory response of these mucosal layers, culminating in the loss of elasticity and therefore dysfunction of the laryngeal and oropharyngeal musculature [32, 56]. Further research is still required to ratify the relationship between these anatomical changes and functional impacts on the swallowing mechanism; however, these findings may explain why deficits in the BOT–PPW and hyolaryngeal complexes demonstrated the highest reported frequencies and prevalence in this review. Whilst abnormalities in the pharyngeal phase were the most prominent, the current review still observed deterioration across a myriad of physiological parameters, including those in the oral and upper esophageal phases. This appears to reflect the impact of the large treatment fields required for definitive (C)RT in HNC patients, with similar oral and pharyngeal deglutitive structures targeted irrespective of lesion site to ensure adequate coverage of macroscopic disease [29, 43, 57, 58]. The small proportion of oral cavity primary sites in the included studies may also have contributed to the comparatively low prevalence of oral-phase physiological deficits, relative to the pharyngeal phase.

Exploratory subanalysis demonstrated that the collective prevalence of physiological swallowing deficits following (C)RT is dynamic over time post-treatment. This finding is not unexpected, as clinical manifestations of radiation-induced side effects at different points along the treatment continuum are well differentiated in the literature [3]. Overall, the general trends observed across the physiological and associated deficits indicated a degree of impairment at baseline, deterioration of function following (C)RT that peaked at 3–6 months post-treatment, and some degree of improvement in function 6–12 months post-treatment. However, the nature and extent of this amelioration in function in the later months post-treatment is inconsistent across the parameters examined, as discussed further below.

Whilst aspiration (Fig 3a) exhibited the most bell-shaped distribution, with prevalence peaking at 3 months post-(C)RT, Fig. 3b, c demonstrated ongoing deficits in the pharyngeal phase post-(C)RT, with function not improving in comparable magnitude by 12 months post-treatment. Similarly, in the oral phase (Fig. 3d), the prevalence of reduced tongue strength remained fundamentally static across the 12 months post-(C)RT. This is consistent with research findings which establish that although acute radiation-induced toxicities improve substantially in the months following (C)RT in the majority of patients, chronic fibrosis, neuropathy, and atrophy of the oral, pharyngeal, and laryngeal musculature endures long after the completion of treatment [37, 47, 59, 60]. Thus, persistent impairment to the range of motion of the BOT–PPW and hyolaryngeal complexes and muscle power of the tongue up to 12 months post-(C)RT is indicative of these chronic sequelae. It has also been postulated that these ongoing oral and pharyngeal phase deficits may be attributable to consequential late reactions, phenomena caused by unhealed acute responses, which allow for additional mechanical or chemical damage distinct from true generic chronic impairments [61, 62].

The fact that the prevalence of aspiration improved despite these ongoing deficits also suggests that the irradiated swallowing mechanism may, in some capacity, physiologically adapt over time to improve swallow safety. Whether this is by means of conscious changes orchestrated by the patient, with or without assistance from post-(C)RT dysphagia rehabilitation, or by progressive unconscious changes to the underlying physiology of the involved structures is difficult to extrapolate. It should be noted that this statement of improvement was based on the results of one study and therefore requires further research to corroborate these findings. Nevertheless, that the most prevalent physiological swallowing deficits (that of the hyolaryngeal and BOT–PPW complexes) remained highly prevalent up to 12 months post-(C)RT confirms the need for ongoing rehabilitation of these parameters well in to the survivorship phase.

With the clinical use of prophylactic swallowing intervention still at a relatively nascent stage of implementation, the current investigation helps to refine which deficits may be best targeted in preventative exercise protocols. UK clinicians surveyed by Roe et al. [22] were reported to most commonly target oral tongue range of motion (ROM), resistance, and strength, hyolaryngeal movement, UES opening, BOT ROM and strength (using the effortful swallow and gargle techniques), and pharyngeal contraction (using the Masako manoeuvre). Less common prophylactic treatment foci included neck stretching, ROM exercises for the facial muscles, lips, and jaw, and the super-supraglottic swallow manoeuvre. In the US, clinicians' dysphagia intervention strategies during (C)RT included (in decreasing order of frequency) compensatory techniques, nonswallow exercises (BOT, laryngeal, and pharyngeal exercises, Shaker manoeuvre), swallow manoeuvre exercises (Mendelsohn, effortful swallow, and super-supraglottic swallow), stretching (neck, jaw, and tongue), or other therapies [21]. Therefore, research examining practice patterns for the management of the (C)RT-HNC population suggests that clinicians *are* targeting the most prevalent physiological deficits identified in this review; however; they are also targeting a number of ancillary deficits and utilising a myriad of treatment strategies to rehabilitate them.

This current multiplicity of exercises, in conjunction with the already intensive nature of researched prophylactic protocols, raises concerns regarding the clinical feasibility of, and patient adherence to, preventative dysphagia therapy in the (C)RT-HNC population. To contest such concerns, current exercise protocols need to be optimised. This requires the derivation and prioritisation of a core set of swallowing therapy targets, thus providing the precursor for consistent implementation into mainstream clinical practice. The authors acknowledge the importance of individualising treatment programs to achieve maximum functional and salient outcomes for patients. However, the findings of this review provide a preliminary set of core physiological swallowing parameters that are likely to become particular sources of deficit for this population, based on their documented prevalence over time post-treatment. Further research is subsequently required to validate the impact of such core therapy targets on long-term patient outcomes.

Whilst this was the first study to specifically elucidate the collective prevalence and patterns of physiological swallowing deficits following (C)RT for HNC, limitations are recognised. First, the heterogeneity of the study cohort limited detailed inferential analysis in this review. There was considerable methodological variance in the number and types of physiological parameters assessed under videofluoroscopy, which created the potential for bias. It is acknowledged that the reported frequency of a particular deficit may have been influenced by how common the deficit was featured in the studies' outcome measurements. Second, there was an absence of comprehensive reporting of physiological changes to the swallowing mechanism over multiple time points, with only four studies achieving this. Consequently, the percentage of data extracted for exploratory longitudinal analysis was sporadic and the findings should therefore be considered only preliminary at this stage. More systematic, longitudinal following and recording of physiological swallowing parameters in HNC patients is needed to allow better understanding of the trends dictating prevalence over time.

## Conclusion

This is the first investigation to systematically review the frequency and prevalence of physiological swallowing deficits following (C)RT for HNC and analyse the prevalence patterns of these deficits over time. Collective analysis has demonstrated that reduced laryngeal excursion, BOT dysfunction, reduced pharyngeal contraction, and impaired epiglottic movement are the most frequently reported and prevalent physiological swallowing deficits exhibited by HNC patients following (C)RT. Preliminary evidence suggests that the prevalence of key deficits is dynamic though persistent over time. The current findings can be used to inform preventative intervention by identifying key, persistent deficits that are highly prevalent for HNC patients. However, these findings are only one part of the bigger question regarding prophylactic swallowing therapy. Ultimately, to fully understand (1) what parameters of the swallowing mechanism need to be targeted, (2) when is the optimal time to target these parameters, and (3) what are the most effective therapy tasks and methods of service delivery to habilitate them, ongoing research is required to validate and progress the results of the current study to optimise preventative swallowing exercise protocols in the future.

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