

Physiological changes to the swallowing mechanism following (chemo)radiotherapy for head and neck cancer: A systematic review

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Running head: Physiological swallowing deficits following (C)RT for HNC

Abstract

Emerging research suggests that preventative swallowing rehabilitation, undertaken pre- 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 which 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. In total, 153 papers were identified and appraised for methodological quality and suitability based on exclusionary criteria. Ultimately, nineteen 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%. Sub-analysis suggested a trend that the prevalence of 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.

Key words: deglutition, deglutition disorders, head and neck neoplasms, swallow pathophysiology

Introduction

Dysphagia is recognised as a common, multifactorial and debilitating sequela for patients undergoing 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 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 non-surgical). 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 RCTs [16,17,19] have demonstrated that patients who underwent prophylactic swallowing rehabilitation protocols pre- 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 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 use of different groups of therapy tasks. In each, a range of between two and five therapy tasks have been implemented, which have 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 are a percentage of clinicians administering 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, non-specific approach is responsive to the lack of strong evidence for any one or particular set of manoeuvre(s) to accomplish positive swallowing outcomes [21].

In order to inform the formation of a core set swallowing exercises which may be most beneficial to apply proactively with HNC patients undergoing (C)RT, there is a need to clarify exactly (a) what are the predominant physiological changes to the swallowing mechanism associated with (C)RT treatment, (b) which of these changes occur with the highest prevalence, and (c) 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 physiologic 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.

Method

Search Strategy

PubMed, Medline, ScienceDirect, SpringerLink, CINAHL and Wiley databases were searched for electronic publications in English 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, post-operative RT or recurrence populations); 3) studies only reporting dysphagia toxicity (i.e.,

CTCAE or RTOG); 4) studies only utilising 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 reporting data exclusively on participants with nasopharyngeal carcinomas were also excluded, due to 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 (Figure 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 this risk of publication bias, [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. studies [38,39] were deemed sufficiently different to warrant the inclusion of both papers, with the earlier research exclusively reporting 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].

[Insert Figure 1 & Table 1 near here]

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 was performed using the Transparent Reporting of Evaluations with Nonrandomized Designs (TREND) checklist [48], developed to be consistent with the Consolidated Standards or Reporting Trials (CONSORT) statement for randomized controlled trials [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 possible total 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 (Figure 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.

[Insert Figure 2 near here]

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 were also compiled due to their inextricable interactions with swallow physiology and frequent reporting in the literature. A second stage of sub-analyses explored the reported prevalence of these physiological and associated swallowing impairments over time. Percentage data was extracted from the papers which used specified evaluation points (i.e., baseline, 1-, 3-, 6-, and 12-months post (C)RT). Those studies which only reported means [41], medians [28,34,35,37,47] or ranges [31,32] for follow-up assessments (Table 1) were excluded from this sub-analysis. 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 70.95Gy, range 65-79.2Gy), often accompanied by a 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 median 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 are summarised in Table 2. For those parameters with 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 this parameter 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 studies reported pharyngeal dysmotility to occur 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. This 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 10 studies documenting a reduction in epiglottic deflection following (C)RT. Of those studies specifying percentages, 89% (n = 8/9 studies) reported epiglottic dysfunction in more than 50% of patients, and over half (56%, n = 5/9) in over 75% of patients. Similar to BOT dysfunction, decreased epiglottic movement was cited by two studies as the most [34] or among the most prevalent pharyngeal phase abnormalities at all evaluation intervals [36]. Absent or non-functional epiglottic movement was reported in three papers and enlarged epiglottic structure by 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 less frequently reported in the included literature. The most frequently reported oral phase parameter was reduced tongue strength and/or range of movement, documented in five studies. However, the prevalence was variable across papers, ranging from <5% - 60%. With regards to the upper esophageal phase, decreased opening of the 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).

[Insert Table 2 near here]

Reported prevalence of penetration/aspiration, residue and stasis

The reported prevalence of penetration, aspiration, residue and stasis observed post-(C)RT for HNC are 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 allowing a total of 17 studies for analysis. Of these studies, 16 (94%) documented aspiration specifically and six (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 7-95.9% and 0-100% respectively. Four studies (21%) also documented cases of silent aspiration, the frequencies of which were also variable (range: 35-86%). Pharyngeal residue was reported following (C)RT by 12 studies (63%). Of those specifying percentages, 89% (n = 8/9) observed residue in more than 50% of patients, and two-thirds (67%, n = 6/9) 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.

[Insert Table 3 near here]

Changes in prevalence of physiological swallowing deficits over time

The literature pool contributing to the sub-analysis of physiological swallowing deficits over time consisted of: four studies reporting data pre-(C)RT [33,43,44,46], two studies reporting at one month post-treatment [45,46], five studies at three months post-treatment [33,42-44,46], two studies at six 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 Figures 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.

[Insert Figure 3 near here]

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) – 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 these DARS to include the: superior, middle and inferior pharyngeal constrictors, glottic and supraglottic larynx and its adductor muscles, upper esophageal sphincter 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 the 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 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 sub-analysis demonstrated 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 peaking 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 three months post-(C)RT, Figures 3b and 3c 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, persisting impairment to the range of motion of the BOT-PPW and hyolaryngeal complex 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 improvement was based on the results of one study, and therefore requires further research to corroborate these findings. Nevertheless, the fact that the most prevalent physiological swallowing deficits (that of hyolaryngeal and BOT-PPW complexes) continued to remain 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 USA, clinicians' dysphagia intervention strategies during (C)RT included (in decreasing order of frequency): compensatory techniques, non-swallow exercises (BOT, laryngeal and pharyngeal exercises, Shaker manoeuvre), swallow manoeuvre exercises (Mendelsohn, effortful swallow and super supraglottic swallow), stretches (neck, jaw, tongue) or other therapies [21]. Therefore, research examining practice patterns for the management of the HNC-(C)RT 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. In order 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 which 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. Firstly, 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 featured in the studies' outcome measurements. Secondly, 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 data extracted for the exploratory longitudinal analysis was sporadic and the findings should therefore only be considered 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 which are highly prevalent for HNC patients. This data is however only one part to 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.

Conflict of Interest

The authors declare that they have no conflict of interest.

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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 [^]	Site of disease	Treatment	Ax time point(s)	Formal outcome measure (if applicable)
Bleier [28]	2007	Retrospective case series	49	Mixed (>2 sites)	conRT ^a : 45 IMRT ^b : 4 CCT ^c : 36	22.7 months [#]	
Cartmill [30]	2012	Prospective cohort study	31	Oropharynx	AFRT-CB ^d : 14 CRT ^f : 17	6 months	NZIMES ^e PAS ^g
Eisbruch [31]	2002	Descriptive case series: post-test	26	Mixed (>2 sites)	CRT	Pre-Tx 1-3 months 6-12 months	
Eisbruch [32]	2004	Prospective cohort study	26	Mixed (>2 sites)	IMRT: 20 RADPLAT ^h : 6	Pre-Tx 1-3 months 6-12 months	

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Feng [33]	2007	Descriptive case series: pre-test/post-test	36	Oropharynx Nasopharynx	CRT	Pre-Tx 3 months	
Goguen [34]	2006	Descriptive case series: post-test	23	Mixed (>2 sites)	CRT	3.5 months [#]	Swallow Performance Scale
Graner [35]	2003	Descriptive case series: pre-test/post-test	11	Mixed (>2 sites)	accRT ⁱ + CCT	19 weeks [#]	
Hutcheson [36]	2008	Retrospective case series	32	Larynx	conRT: 16 accRT: 24 IMRT: 3 CCT: 30	<6 months or 6-11 months or 12+ months	
Hutcheson [37]	2012	Descriptive case series: post-test	29	Mixed (>2 sites)	RT ^j : 11 CRT: 18	9 years [#]	PAS NIH-SSS ^k MBSImp ^l
Kendall [38]	1998	Prospective cohort study	20 + 60 controls	Mixed (>2 sites)	NR	12+ months	
Kendall [39]	2000	Prospective cohort study	20 + 60 controls	Mixed (>2 sites)	conRT	12 months	

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Kotz [40]	1999	Descriptive case series: post-test	15	Mixed (>2 sites)	accRT + CCT	3-45 weeks
Kotz [41]	2004	Descriptive case series: pre-test/post-test	12	Mixed (>2 sites)	CRT: 7 accRT + CTT: 5	Pre-Tx 8 weeks ^{\$}
Lal [42]	2009	Descriptive case series: post-test	56	Mixed (>2 sites)	accRT + CCT	3 months
Logemann [43]	2006	Prospective cohort study controls	53+140	Mixed (>2 sites)	CRT	Pre-Tx 3 months
Logemann [44]	2007	Prospective case series	48	Mixed (>2 sites)	RT: 12 CRT: 36	Pre-Tx 3 months 12 months
Newman [45]	2002	Prospective cohort study	30	Mixed (>2 sites)	RADPLAT: 14 CRT: 16	Pre-Tx 1 month
Pauloski [46]	2006	Prospective case series	170	Mixed (>2 sites)	RT: 22 CRT: 147	Pre-Tx 1, 3, 6 and 12 months
Smith [47]	2000	Prospective case series	10	Mixed (>2 sites)	CRT	9 weeks [#]

^aconventional radiotherapy; ^bintensity modulated radiotherapy; ^cconcomitant chemotherapy; ^daltered fractionation radiotherapy with concomitant boost;

^eNew Zealand Index for Multidisciplinary Evaluation of Swallowing; ^fchemoradiotherapy; ^gPenetration Aspiration Scale; ^hradiotherapy and

concomitant intra-arterial cisplatin; ⁱaccelerated radiotherapy; ^jradiotherapy alone; ^kNational Institutes of Health Swallowing Safety Scale; ^lMBSImp =

MBS impairment profile

*Based on the NHMRC Guidelines (NHMRC, 2000; 2005)

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

[#] denotes median follow-up point

^{\$} denotes mean follow-up point

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	<p><i>Overall Prevalence Range: <5% - 60%</i></p> <p>57 - 60%^{[44]*}</p> <p>51% reduced strength; <5%: reduced lateral/anterior stabilisation and vertical movement^[43]</p> <p>11%^[42]</p> <p>Reported, but no percentage data provided^{[45], [46]}</p>
PHARYNGEAL PHASE	
Impaired Velopharyngeal closure	<p>14% palatal kink; 12.5% loss of nasopharyngeal seal^[42]</p> <p><5%^[43]</p>
BOT-PPW Complex	
Premature spill	<p><i>Overall Prevalence Range: 26.5% - 36%</i></p> <p>36%^[42]</p> <p>>30%^[30]</p> <p>26.5%^[28]</p>
BOT weakness/ reduced BOT retraction	<p><i>Overall Prevalence Range: 55% - 100%</i></p> <p>100% abnormal retraction, 17% absent^[37]</p> <p>89% reduced function, 3% non-functional^[33]</p> <p>89%^[43]</p>

	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/	<i>Overall Prevalence Range: 21% - 100%</i>
	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	<i>Overall Prevalence Range: 46% - 100%</i>
	100% abnormal, 86% absent ^[37]
	100%; 93% enlarged epiglottis ^[40]
	100% abnormal or absent ^[47]
	86.7 - 100% ^[36]

	<p>85.7%; 57.1% bulbous epiglottis^[28]</p> <p>61% reduced function, 22% non-functional^[33]</p> <p>50 – 54%^[31]</p> <p>50 - 83%^[32]</p> <p>46%^[42]</p> <p>Reported, but no percentage data provided^{[34], [41]}</p>
Reduced laryngeal elevation/excursion	<p><i>Overall Prevalence Range: 31% - 100%</i></p> <p>100% abnormal, 17% absent^[37]</p> <p>82%^[35]</p> <p>78.3 - 85.7%^[36]</p> <p>67%^[33]</p> <p>50 - 83%^[32]</p> <p>50% or more^[30]</p> <p>36%^[43]</p> <p>31 - 35%^[44]</p> <p>Reported, but no percentage data provided^{[34], [38], [40], [41], [45], [46], [47]}</p>
Reduced hyoid movement	<p>97% abnormal, 38% absent^[37]</p> <p>41%^[42]</p> <p>Reported, but no percentage data provided^{[38], [39]}</p>
<hr/>	
Impaired Laryngeal Vestibule closure	<p><i>Overall Prevalence Range: <5% - 83%</i></p> <p>50 - 83%^[32]</p> <p>66% absent closure^[37]</p> <p>54 - 60%^[44]</p> <p>31% slowed/delayed, <5% incomplete closure^[43]</p> <p>Reported, but no percentage data provided^{[39], [41],}</p>

	[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	<i>Overall Prevalence Range: 17% - 100%</i>
	100% ^[32]
	50% or more ^[30]
	28.3% ^[43]
	21 - 23% ^[44]
	17% ^[41]
	Reported, but no percentage data provided ^[46]

*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	<i>Overall Prevalence Range: 7% - 95.9%</i>
	95.9% ^[28]
	82% ^[35]
	67% ^[40]
	17% ^[34]
	7 - 35% ^{[30]*}
	Reported, but no percentage data provided ^[41]
Aspiration	<i>Overall Prevalence Range: 0% - 100%</i>
	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	<i>Overall Prevalence Range: 33% - 100%</i>
	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]

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

Figure 1

PRISMA Flow Diagram detailing search strategy and selection criteria.

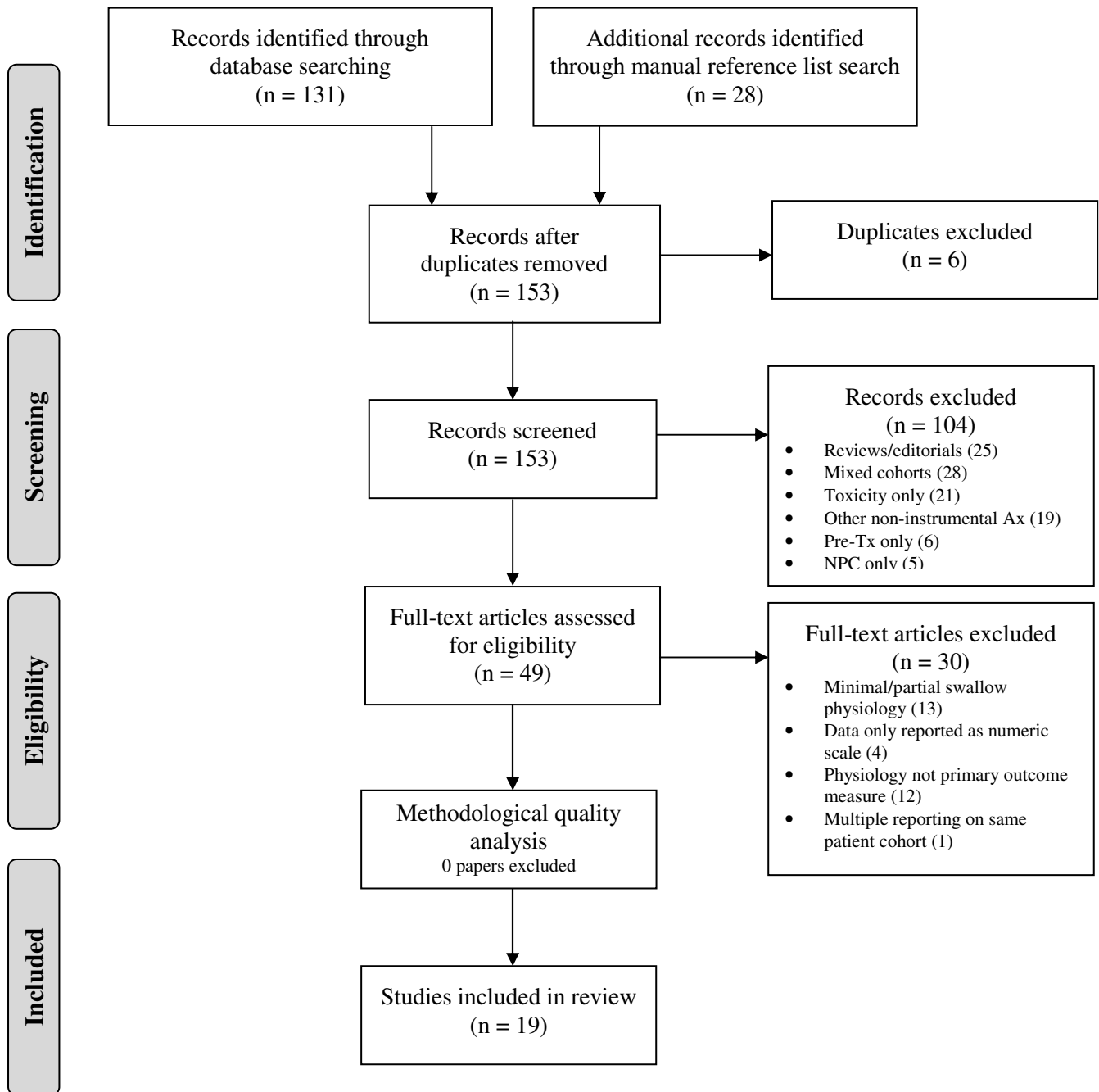
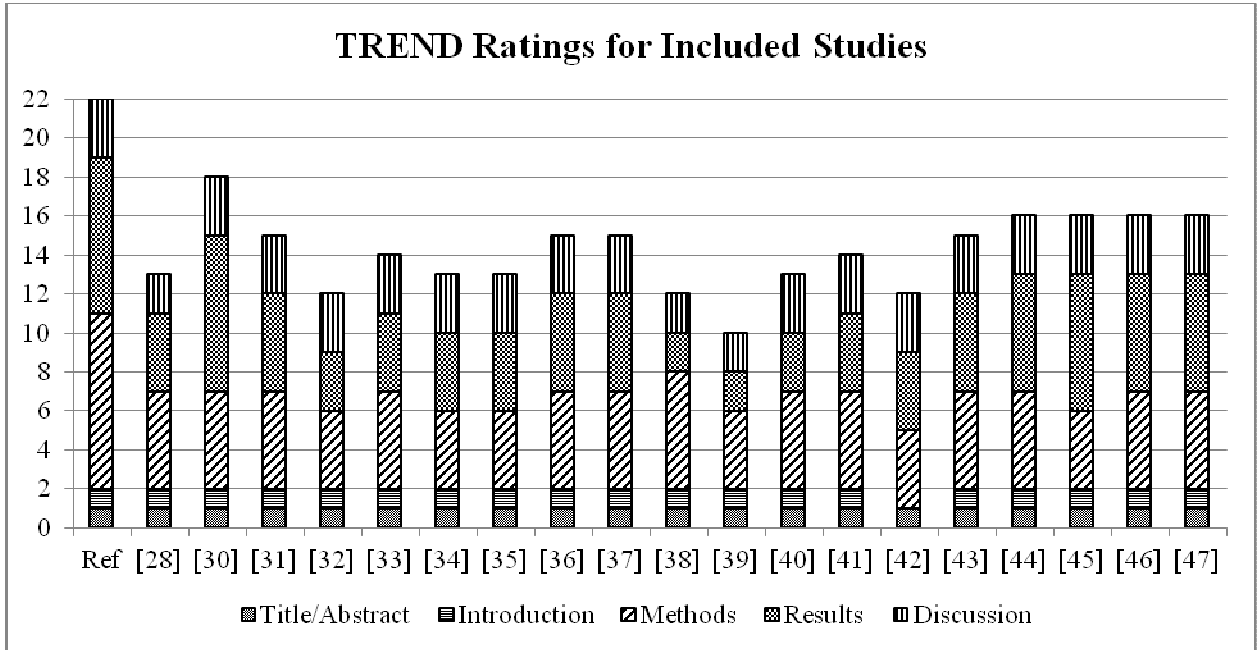


Figure 2

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



Figures 3a – d

Reported prevalence of aspiration and core oral and pharyngeal phase physiological swallowing deficits at varying follow-up points over time.

Fig 3a

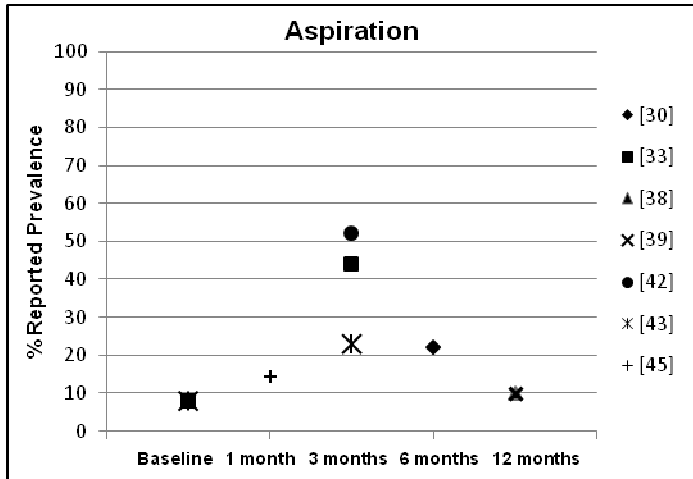


Fig 3b

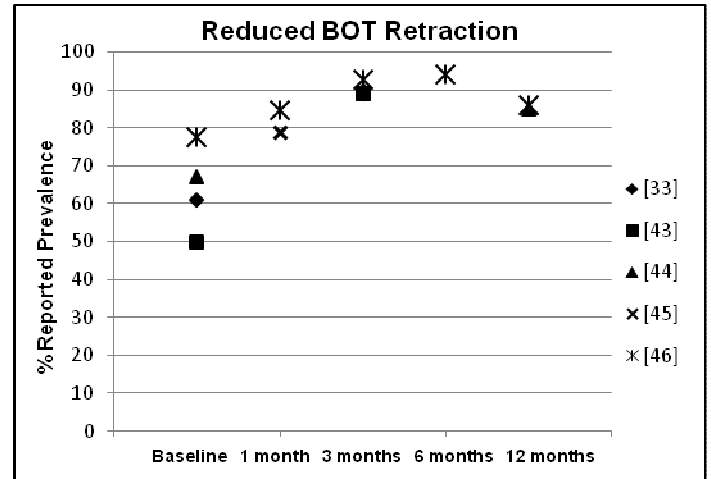


Fig 3c

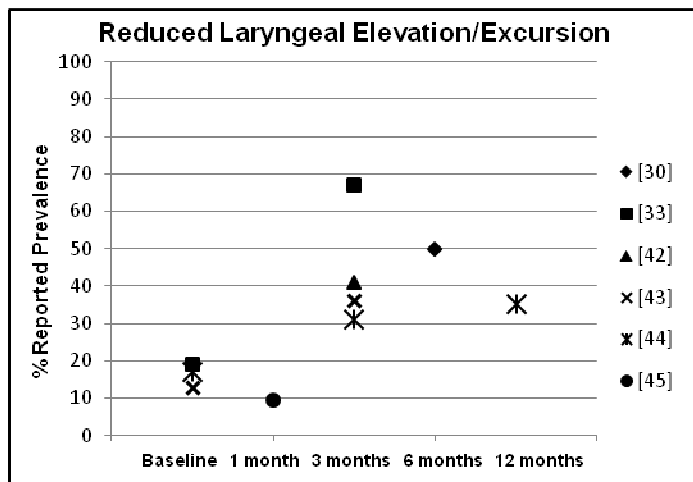


Fig 3d

