



Canadian Agency for
Drugs and Technologies
in Health

RAPID RESPONSE REPORT: SUMMARY WITH CRITICAL APPRAISAL

TITLE: Nasogastric Feeding Tubes versus Percutaneous Endoscopic Gastrostomy for Patients with Head or Neck Cancer: A Review of Clinical Effectiveness and Guidelines

DATE: 13 August 2014

CONTEXT AND POLICY ISSUES

Cancer of the head and / or neck (HN) describes malignant tumours that broadly include cancers of the lip, oral cavity, tongue, salivary glands, pharynx, larynx, nasal cavity, ear and skull base; 80% to 90% are squamous cell carcinomas (SCCs).¹ Although not a complete match and an underestimate of the entire group of HN cancers, Canadian Cancer Society statistics report 3675 cases of oral cancer in 2007, the majority being cancer of the mouth or tongue; 68% occurred in men.² Cigarette smoking and alcohol misuse are risk factors for HN SCC.³ Although historically most of these cancers have occurred in people over age 50, the affected age is dropping with recent increases in the incidence of human papillomavirus.^{1,4}

For many patients with advanced stages of HN cancer, oral nutrition does not provide enough nourishment during treatment with chemoradiotherapy (CT) and / or radiotherapy (RT) due to the acute toxicity of treatment, obstruction caused by the tumour, or both.⁵⁻⁸ It has been reported that these patients are more likely to experience nutritional depletion than patients with any other cancer during all illness phases.⁹ Many patients enter treatment with weight loss and up to 80% lose additional weight during treatment; poor nutrition is linked with poor prognoses.^{1,6,10,11} In these cases, enteral nutrition (i.e., delivered straight to the intestine) is considered the best option.^{3,12}

Non-oral / enteral supply of nutrients can be delivered directly into the stomach via a nasogastric (NG) feeding tube inserted through the nose into the stomach, or via a percutaneous endoscopic gastrostomy (PEG) inserted through the skin of the abdomen directly into the stomach. The latter can be inserted prophylactically before treatment starts or reactively when the patient needs it.⁶ The optimal method of non-oral feeding is controversial.^{1,9,13-15} Although several groups have developed predictive models to determine which patients will benefit from feeding tubes and when,^{3,6} others believe the situation is too complex and multifactorial to make this type of tool usable.¹³

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The purpose of this report is to assess the literature reporting on NG feeding tubes versus PEG for this patient group, including the guidance contained in relevant evidence-based CPGs.

RESEARCH QUESTIONS

1. What is the clinical effectiveness of nasogastric feeding tubes compared with percutaneous endoscopic gastronomy for patients with head or neck cancer?
2. What are the evidence-based guidelines regarding the use of nasogastric feeding tubes in an outpatient setting for patients with head or neck cancer?

KEY FINDINGS

Patients with advanced head and neck (HN) cancer may not receive adequate nutrition orally. Non-oral (enteral) alternatives include feeding via a nasogastric (NG) tube when the issue becomes a problem (the traditional approach) or via percutaneous endoscopic gastronomy (PEG) prophylactically or when needed (a more recent approach). Due to a lack of RCTs, there is limited evidence to support one treatment method over the other. In part, the issue has been lack of willingness of these very ill and vulnerable patients to be randomized. It also appears that individualized treatment is optimal as patients' preferences vary. An RCT to test the feasibility of a larger comparative RCT has been launched in England with results expected mid-2016. In clinical practice guidelines, there was little distinction between outpatient and inpatient treatment in the guidance and also little distinction between NG tube versus PEG feeding.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2014, Issue 7), the University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2009 and July 14, 2014.

Selection Criteria and Methods

For the clinical review (research question 1), publications were selected if they assessed the comparative clinical effectiveness and safety of NG tube use versus PEG for the enteral delivery of nutrients for patients with HN cancer. For the CPG review (research question 2), CPGs were included if they mentioned the use of enteral feeding for patients with HN cancer. One reviewer screened the titles and abstracts of the retrieved publications and evaluated the full-text publications for the final article selection. Table 1 summarizes selection criteria. Appendix 1 illustrates document selection flow.

Table 1: Study Selection Criteria

Population	Patients with HN cancer requiring enteral delivery of nutrients.
Intervention	NG feeding tubes
Comparator	PEG
Outcomes	Q1: Comparative clinical effectiveness and safety Q2: Duration of use, consequence of misuse/overuse, discontinuation criteria, etc.
Study Designs	Q1: HTAs / SRs / MAs, RCTs, non-randomized studies Q2: CPGs with evidence of rigorous development (guided by the AGREE II CPG quality tool)

CPG=clinical practice guideline; HTA=health technology assessment; HN=head and neck; MA=meta-analysis; NG=nasogastric; PEG=percutaneous endoscopic gastronomy / gastrostomy; RCT=randomized controlled trial; SR=systematic review

Exclusion Criteria

References were excluded if they did not meet the criteria outlined in Table 1, if they were published prior to 2009, or if they were duplicate publications of a selected study. CPGs were excluded if their methodology was not documented as rigorous or was not clear.

Critical Appraisal of Individual Studies

The AMSTAR instrument (“**A Measurement Tool to Assess Systematic Reviews**”) was used to critically appraise the methodological quality of the included SRs.¹⁶ For the one RCT currently in progress, attention was paid to study design and size, potential for blinding, planned outcome measures, and funding source. For the CPGs, the AGREE II tool¹⁷ was used as a guide with particular attention paid to CPG scope (including specific patient population and intended users); aspects of CPG methodology such as extent and reporting of the literature search, types of included evidence, types of clinical outcomes tracked, and grading of evidence and recommendations; and potential conflicts of interest of the developers and funders.

SUMMARY OF EVIDENCE

Quantity of Research Available

The literature search identified 480 citations of which 28 citations were deemed potentially relevant upon review of titles and abstracts. An additional seven potentially relevant references were identified in the grey literature, primarily CPGs. From these 35 references, nine were included following full text review: five for the clinical review (4 SRs and one RCT in progress) and four CPGs. The evidence for each research question is reported separately. Appendix 1 illustrates the document selection flow.

Summary of Study Characteristics

What is the clinical effectiveness of NG feeding tubes compared with PEG for patients with HN cancer?

Four SRs^{1,9,18,19} were identified. No additional published RCTs beyond those included in the SRs were identified although one RCT in progress was found.¹⁵ Table 2 presents overviews of the four SRs and Appendix 2 provides greater SR detail. The lead authors of the SRs were from Canada,¹⁹ the Netherlands,¹⁸ the UK¹ and China.⁹ Two SRs limited their analyses to RCTs which were rare, with one meeting inclusion criteria in the Cochrane review¹ and two different trials in the SR from the Netherlands.¹⁸ The other two SRs included less rigorous evidence, primarily cohort studies (seven in one and eight in the other).^{9,19} Patient groups varied from very specific (e.g., one SR included only studies on adults with stage III or IV HN SCC receiving curative CT plus RT¹⁹) to quite general (e.g., the most recent SR from China included studies on adults with HN cancer receiving CT and / or RT⁹). This may explain the variation in numbers and types of included studies in the four SRs.

Table 2: Overview of Included SRs

First Author, Year, Country	Patient group and intervention		Literature search well described?; end of search	Studies included	COI declaration
	Patients & CA treatment	Intervention & comparators			
Orphanidou, 2011, Canada ¹⁹	Adults with stage III or IV HN SCC receiving curative CT plus RT	Prophylactic PEG versus alternatives	Yes; October 2009	No RCTs; included seven studies of comparative (2) and cohort (5) designs	Declared no COI
Languis, Netherlands, 2013 ¹⁸	Adults with HN SCC receiving CT or RT	Prophylactic PEG versus alternatives (other interventions and comparisons were also covered)	Yes; January 2012	Two studies they considered to be RCTs	Lead author partly funded by nutrition company
Nugent (Cochrane review), UK, 2013 ¹	Adults with HN CA receiving CT and / or RT	One method of enteral feeding with another, e.g. NG or PEG	Yes; February 2012	One RCT	Declared no COI
Wang, 2014, China ⁹	Adults with HN CA receiving CT and / or RT	NG versus PEG	Yes; 2013 (month NR)	Included eight cohort or case-control	NR

CA=cancer; COI=conflict-of-interest; CT=chemotherapy; HN= head & neck; NR=not reported; PEG=percutaneous endoscopic gastrostomy RCT=randomized controlled trial; RT=radiotherapy; SCC=squamous cell carcinoma

Detail about an RCT in progress:

*NIHR-NETSCC, the "TUBE trial" (ISRCTN48569216 in "Controlled Clinical Trials"):*¹⁵ A three-center study in England will examine whether a definitive RCT is feasible in patients with Stage III and IV HN SCC undergoing CT and RT. The objective is to compare prophylactic PEG (or percutaneous fluoroscopic gastrostomy [PFG]) versus oral feeding plus as-needed NG tube feeding. It is hoped that about 60 patients will be randomized and the trial will run from June to December 2014. Randomization will be administered centrally by the Newcastle Clinical Trials Unit internet-accessed secure web-based system. Due to the obvious visual differences in the technologies being studied, blinding of patients and providers is not possible. Funding is from the HTA programme of the National Institute for Health Research. The study protocol was

published May 1, 2014 and the estimated date of study publication is July 2016. Planned outcomes for this feasibility RCT are to:

- Assess willingness to be randomized
- Assess retention and drop-out rates from each arm
- Refine interventions and study processes to inform definitive trial design
- Estimate parameters to inform sample size for a definitive trial

What are the evidence-based guidelines regarding the use of NG feeding tubes in an outpatient setting for patients with HN cancer?

Four CPGs were identified that provided enough methodological detail to assure the reader that fairly rigorous processes had been followed (Table 3).²⁰⁻²³ The four CPGs originated from Australia,²³ Ontario, Canada,²¹ the United Kingdom,²⁰ and the United States²² and publication years spanned 2009 to 2014. Processes for the very recent United States National Comprehensive Cancer Network (NCCN) were not completely clear in the 190-page CPG but the guidance was included here as another author described NCCN cancer CPGs as “*the most comprehensive and widely used oncology standard in clinical practice in the world...recommendations are now accepted by the Centers for Medicare and Medicaid Services and most private insurance companies.*” (p.187)²⁴

Table 3: Overview of Included CPGs

Author / Organization, Year; Country	Patient population	Literature search well described?	Grading of evidence	Grading of recommendations	COI declarations for experts & funders
Gilbert et al (CCO), 2009; Canada ²¹	Adult patients with HN cancer	Yes – to January 2008; adapted from CPGs issued by NICE (2004) & SIGN (2006)	Unclear	Yes; used the system employed by the CPG being adapted, i.e., primarily NICE & SIGN	Declared no COI for developers; funder was Ontario MOHLTC through CCO
ENT UK, 2011; UK ²⁰	Patients with HN cancer	No – references at end of each section	Described use of SIGN system but not evident in CPG body	Yes; used the system employed by SIGN	Unclear
Cancer Council Australia, 2014; Australia ²³	Adult patients with HN cancer	Yes – ended January 2011	Yes; used the NHMRC system	Yes, used the NHMRC system	Declared no COI for developers; funder was Cancer Institute NSW Oncology Group (Head & Neck)
NCCN, 2014; USA ²²	Patients with HN CA	Not in CPG document but many citations and extensive reference list	The CPG states that all evidence is considered 2A (defined as low quality evidence but uniform consensus) unless otherwise noted	Not evident	Panel members' COI reported; extensive industry funding for NCCN also detailed

CA=cancer; CCO=Cancer Care Ontario; CPG=clinical practice guideline; HN=head and/or neck; MOHLTC=Ministry of Health & Long-term Care; NCCN= National Comprehensive Cancer Network; NHMRC=National Health and Medical Research Council (Australia); NICE=National Institute for Health & Care Excellence; NSW= New South Wales; SIGN=Scottish Intercollegiate Guidelines Network; UK=United Kingdom; USA=United States of America

Summary of Critical Appraisal

What is the clinical effectiveness of NG feeding tubes compared with PEG for patients with head or neck cancer?

The AMSTAR quality assessment tool for SRs¹⁶ was used to assess SR quality and scores were assigned (Table 6 in Appendix 2). All SRs were based on extensive and well documented literature searches. All SRs employed at least two independent data extractors. Despite these efforts, the evidence base is limited as there have been very few RCTs. For example, one RCT of 33 randomized patients²⁵ was included in the recent Cochrane review,¹ the RCT being switched to a prospective non-randomized study as few patients would consider randomization¹² and two others were included in an SR from the Netherlands (although these were considered by the Cochrane reviewers and ultimately did not meet their inclusion criteria).¹⁸ The other two SRs included more studies but these were of less rigorous designs.^{9,19} Of these two SRs, the earlier review¹⁹ commented that the available studies were not of high quality but did not report using a tool to assign scores, whereas the more recent SR⁹ used the Newcastle-Ottawa scale to assess study quality and assigned scores of 5 to 9 with a mean value of 6.5 (median 6) out of a maximum score of nine.

What are the evidence-based guidelines regarding the use of NG feeding tubes in an outpatient setting for patients with HN cancer?

The AGREE II instrument for CPG quality¹⁷ was used as a general guide with particular attention paid to CPG scope; CPG methodology, i.e., extent and reporting of the literature search, types of included evidence, grading of evidence and recommendations; and developer and funder potential conflicts-of-interest (COI). See Table 4 for CPG strengths and limitations.

Cancer Care Ontario (CCO) CPG²¹ developers sought the highest quality CPGs available from other groups upon which to base their work. They determined that a CPG from the Scottish Intercollegiate Guidelines Network (SIGN) best addressed questions about clinical management and a CPG from the National Institute of Health & Care Excellence (NICE) in the United Kingdom best addressed questions about organization of care. These two base CPGs were assessed by three independent reviewers for quality, currency, content, consistency, and acceptability/applicability using the Appraisal of Guidelines Research and Evaluation (AGREE) instrument. Information was updated via a Medline literature review to late 2007 (details are provided). This material was used to develop 177 recommendations. A 40-person working group from seven professions involved in the care of patients with HN cancer reviewed the recommendations via a modified Delphi survey process. Recommendations were marked according to degree of consensus (i.e., complete or not).

The ENT UK CPG document²⁰ is extensive and was developed by the input of members of 10 professions; 128 experts are credited for their contributions. Unfortunately, there is little detail about the actual methodology of CPG development including how literature was chosen. Recommendations were graded using the SIGN system of A to D based on a grading system of the evidence ranging from 1++ (high quality meta-analyses, SRs of RCTs, or RCTs with a very low risk of bias) to 4 (expert opinion). The methods used to develop the CPG are not included in the document.

A CPG developed by the Cancer Council of Australia in 2014²³ includes a detailed description of the methodology. The Cochrane Database of Systematic Reviews, CENTRAL, MEDLINE, EMBASE, CINAHL and AMED databases were searched in December 2009 with the search repeated in January 2011 (limited to English language). The search terms are provided. Two researchers reviewed the literature to select included materials and the strength of the evidence was assessed (Levels I to IV) using the level of evidence rating system recommended by Australia’s National Health and Medical Research Council (NHMRC). Study quality was assessed via a tool supported by the American Dietetic Association that includes four relevance questions and ten validity questions to assess the strength of the study design. Recommendations were graded using the NHMRC Grades of Recommendation (A to D). The CPG is published on a wiki website and it is anticipated that it will continually be reviewed as new literature is published and based on input from other stakeholders.

Finally, the very recent CPG developed by the National Comprehensive Cancer Network (NCCN)²² is extensive and involved the input of many experts (predominantly physicians). The 190-page CPG focusses on many aspects of treating patients with HN cancer but there is no description of the methods used to develop the guidance. There are two pages of advice on principles of nutrition, supported by three references, but no assessment of the evidence or grading of evidence or recommendations.

Table 4: Strengths and Limitations of Included CPGs

Author / Organization, Year; Country	Strengths	Limitations
Gilbert et al (CCO), 2009; Canada ²¹	Adapted (using ADAPTE tool) from NICE and SIGN CPGs plus information added from a literature search; clear description of methodology; no COI; public sector funding	Original documents published 8 and 10 years ago, although literature search was updated using SIGN search strategy (to January 2008); evidence grading scheme described but unclear how it was employed; limited guidance on our topic of interest
ENT UK, 2011, UK ²⁰	Extensive document (382 pages) with input of many multidisciplinary experts; recommendations graded (using SIGN system)	Literature search not described (unclear what its methodology was); COI of developers and funders not described
Cancer Council Australia, 2014; Australia ²³	Detailed description of studies used as evidence; evidence and recommendations graded using NHMRC system; no COI declared; public sector funding	Search limited to English language
NCCN, 2014; USA ²²	Very recent; extensive document (190 pages) with input of many multidisciplinary members of an advisory panel; detailed coverage of a vast number of aspects of care for patients with HN cancer	Document not user-friendly; literature search not described (unclear what its methodology was); evidence and recommendations not graded; NCCN supported by many industry partners.

COI=conflict-of-interest; HN=head and / or neck; NHMRC=National Health and Medical Research Council; NICE=National Institute for Health & Care Excellence; SIGN=Scottish Intercollegiate Guidelines Network; UK=United Kingdom; USA=United States of America

Summary of Findings

What is the clinical effectiveness of NG feeding tubes compared with PEG for patients with head or neck cancer?

Four SRs were identified that included from one to eight primary studies.^{1,9,18,19} One of the SRs was a recently updated Cochrane review¹ that included one study – a small (n=33) RCT published in 2009. Another SR also limited itself to RCTs and included two studies. Individual review findings are reported in Table 7 of Appendix 2 and demonstrate that not one of the four SRs was able to conclude that the newer technology, PEG, was definitely superior to the traditional use of NG tube feeding employed on an as-needed basis. For example, the most recent SR⁹ included eight studies of less rigorous design and the authors were tentative in their conclusions. They noted that the evidence did not illustrate differences between groups in maintenance of weight or survival, though several differences between groups were noted (Table 7). From the perspective of PEG superiority: tube dislodgement was lower, PEG was more suitable for long-term feeding (> 30 days), and PEG allowed greater mobility, enhanced cosmesis and improved QOL. However, on the negative side, the included studies suggested that PEG is associated with delay in return to oral diet, prolonged duration of RT, increased incidence of pain, increased incidence of dysphagia and markedly increased cost.

What are the evidence-based guidelines regarding the use of NG feeding tubes in an outpatient setting for patients with head or neck cancer?

The CPGs were reviewed for advice on the use of NG tube feeding in outpatients with HN cancer (Table 5); however, recommendations were seldom specific to the outpatient versus the inpatient setting and also gave little guidance about use of NG tube versus PEG feeding (rather using a generic “tube feeding” description). Where there was specific detail about NG tube or PEG feeding, this is included in Table 5.

Table 5: Summary of CPG Content Related to Tube Feeding for Adults with HN Cancer

Author / Organization, Year; Country	Specific Guidance
Gilbert et al (CCO), 2009; Canada ²¹	Feeding tube insertion [no distinction regarding type] should be considered for individuals initially presenting with one or more of the following: significant weight loss (> 5% in one month or > 10% in 6 months), BMI < 18.5, dysphagia, anorexia, dehydration, pain, or any other symptoms that interfere with the ability to eat. (There was no grading of associated evidence or recommendations although degree of consensus was noted for each individual recommendation.)
ENT UK, 2011, UK ²⁰	<ul style="list-style-type: none"> • Patients should be offered intensive dietary advice during treatment to prevent weight loss, increase intake and reduce interruption to radiotherapy (Grade A, i.e., at least one SR or RCT directly applicable to target population) • Tube feeds should be considered if cancer interferes with swallowing and if mucositis is expected or thought to affect swallowing (Grade C, i.e., studies rated as 2++ (well conducted cohort or case-control) directly applicable to the target population, and demonstrating overall consistency of results) • Tube feeding can be given by either nasogastric or gastrostomy routes (Grade C)

Author / Organization, Year; Country	Specific Guidance
Cancer Council Australia, 2014; Australia ²³	<ul style="list-style-type: none"> • Tube feeding [technology not specified] may reduce unplanned hospital admissions and reduced disruptions to treatment compared to oral intake alone. (Grade C, i.e., body of evidence provides some support for recommendation(s) but care should be taken in its application) • Nutrition intervention (dietary counselling and/or supplements and/or tube feeding) improves patient-centred outcomes (QOL, physical function and patient satisfaction). (Grade B, i.e., body of evidence can be trusted to guide practice in most situations)
NCCN, 2014; USA ²²	<ul style="list-style-type: none"> • Monitor patient closely if weight loss > 10% or difficulty swallowing due to obstruction or pain; should have counselling from an RD and / or feeding tube management (NG or PEG); ensure pre- and post-treatment evaluation using a recognized scale; ensure regular follow-up until nutritionally stable post-treatment. • Prophylactic placement of NG tube or PEG not recommended if patient has good performance status and no significant pre-treatment weight loss, dysphagia or airway obstruction.

BMI=body mass index; CCO=Cancer Care Ontario; HN=head and / or neck; NCCN= National Comprehensive Cancer network; NG=nasogastric; NICE=National Institute for Health & Care Excellence; OP=outpatient; PEG=percutaneous endoscopic gastrostomy; QOL=quality of life; RD=registered dietitian; UK=United Kingdom; USA=United States of America

Limitations

A significant limitation for this report, and indeed for researchers in this field, is the lack of high quality evidence. Very few RCTs have been conducted, despite the apparently fairly common use of NG tube or PEG feeding for patients with HN cancer. This lack of evidence may be addressed by a feasibility RCT recently launched in England,¹⁵ although the initial trial will only test the feasibility of conducting an RCT on the competitive technologies. This deficit meant it was not possible to answer the research question related to NG tube feeding versus PEG as even recent articles continue to point out the evidence void.^{1,9,13-15} Similarly, although the challenges related to enteral nutrition for patients with HN cancer are addressed in several recent CPGs, it was not possible to specifically address the research question as there was little distinction made between management of outpatients versus inpatients, nor the advantages or disadvantages related to NG tube versus PEG feeding.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

Although HN cancer is not common, those affected with advanced forms are often malnourished due to the disease, the treatment, or both. The oral route for nutrients is not feasible for many and therefore enteral routes are employed, either prophylactically or on an as-needed basis. Historically, NG tube feeding was initiated for malnourished patients but PEG is a more recent alternative¹⁰ as it overcomes some of the disadvantages of NG tube feeding (e.g., narrow calibre that can prolong feeding times, nasal and sinus inflammation and cosmetic issues)⁵ PEG feeding is also viable for a longer period of use (i.e., > 30 days) and has other advantages such as easier feeding due to wide tube diameter, low maintenance and improved cosmesis.⁵ However, PEG is also associated with a number of drawbacks including risk of major and minor complications.²⁶⁻²⁸ Information on the safety of PEG can be found in a prospective analysis of 121 patients with HN cancer in England²⁷ which reported one death (1%); four major

complications (3%, major hemorrhage or major wound infection); and 35 minor complications (29%), mainly infection or inflammation at the tube entry point, tube leaks and abdominal pain. Three long-term studies (2 years, 2.5 years, and 6 years) showed that PEG-dependence may lead to adverse swallowing ability in post-irradiated HN cancer patients possibly due to decreased use of the swallowing musculature,^{26,28,29} although another small 2-year follow up study did not show a difference between groups.³⁰ Through case reports, concern has been expressed that PEG could lead to cancer metastasis via direct implantation of tumor cells through instrumentation.³¹

The current evidence is unable to demonstrate superiority of one method over another and this lack of evidence is reflected in CPGs that provide advice about use of nutritional feeding but not specific to a preferred method. Few RCTs have been conducted, in part because these very ill patients will not consider randomization.^{15,25} A feasibility RCT underway in England may address the controversy, although not for several years.

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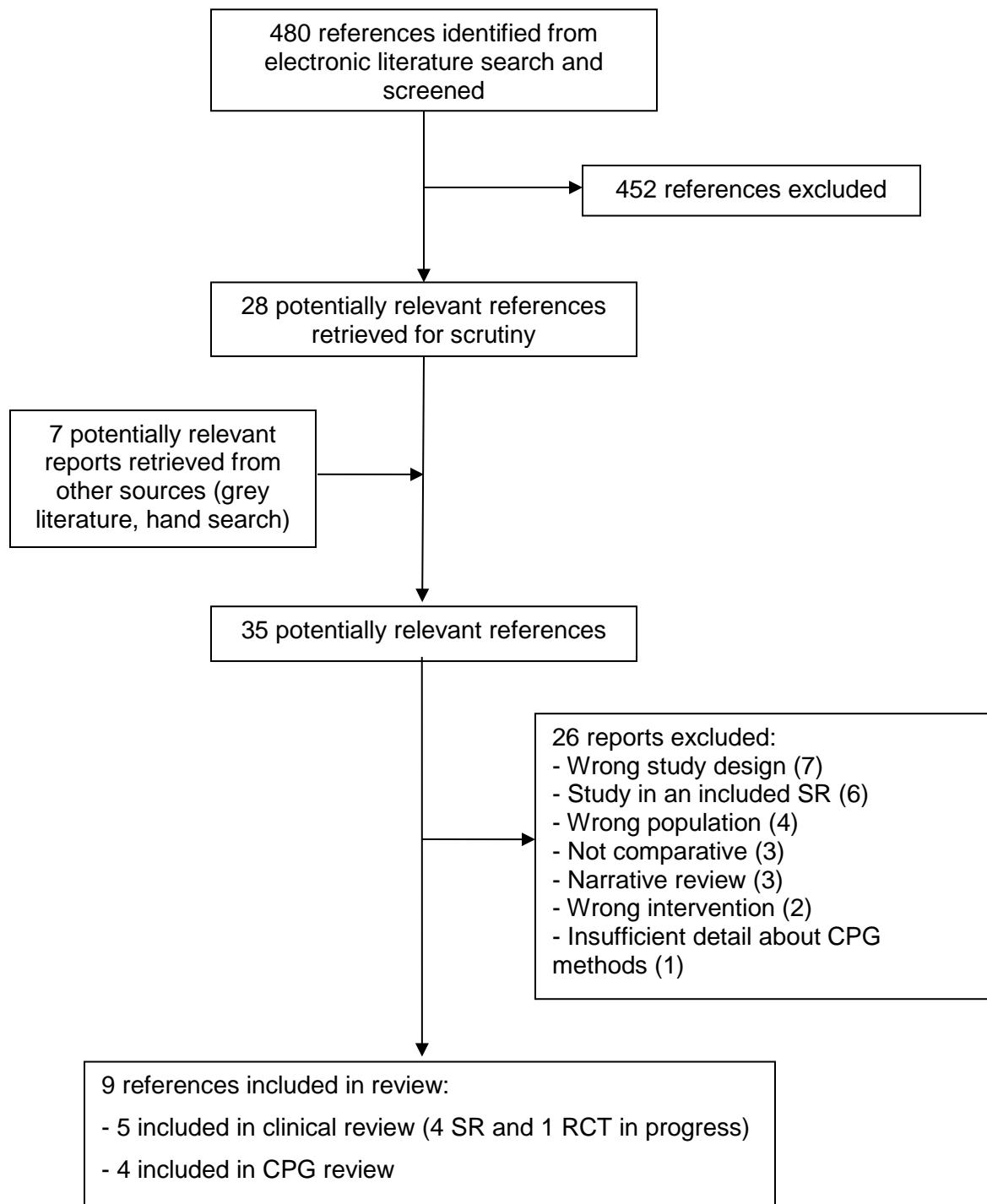
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APPENDIX 1: Selection of Included Studies



APPENDIX 2: EVIDENCE TABLES

Table 6: Summary of Critical Appraisal of Included Clinical Reviews

First Author, Pub. Year	AMSTAR score (max. 11)	Strengths	Limitations
Orphanidou, 2010 ¹⁹	7	<ul style="list-style-type: none"> Comprehensive literature search including conference abstracts and search of bibliographies; no language restrictions. Three independent study reviewers. Data extracted by one reviewer and checked by two others. Public sector funding. 	<ul style="list-style-type: none"> Not clear that research questions and inclusion criteria were established <i>a priori</i>. Evidence to 2009 – now 5 years old. No RCTs available and evidence considered low quality. Excluded studies not mentioned. Characteristics of included studies not reported, e.g., age and sex of patients. Basically no conclusions drawn due to low quality of evidence.
Languis, 2013 ¹⁸	8	<ul style="list-style-type: none"> Research question and inclusion criteria established <i>a priori</i>. Comprehensive literature search (limited to Dutch and English). Contacted corresponding authors if data were incomplete. Two independent data extractors. Limited their evidence to RCTs. Assessed risk of bias. 	<ul style="list-style-type: none"> Only two included studies (both RCTs) and these were small (Salas et al., 2009³² and Silander et al., 2012⁷) List of excluded studies not provided although PRISMA diagram provided. Some funding received from a nutrition company, including support for lead author.
Nugent (Cochrane review), 2013 ¹	10	<ul style="list-style-type: none"> Followed Cochrane methodology. Research question and inclusion criteria established <i>a priori</i>. Comprehensive literature search with no restrictions based on language or type of publication; authors were also contacted. Limited evidence to RCTs. Identified many potential outcomes to track. Two independent data extractors. Risk of bias assessed by two reviewers. 	<ul style="list-style-type: none"> Included only one RCT of 33 patients (Corry et al, 2009)²⁵ – the study was planned for 150 but accrual was poor so recruitment ceased. Planned analyses such as heterogeneity and sensitivity analysis not possible with only one included study.
Wang, 2014 ⁹	4	<ul style="list-style-type: none"> Comprehensive literature search. Two independent data extractors. Study quality assessed via the Newcastle-Ottawa scale. 	<ul style="list-style-type: none"> Studies limited to English language. Included only one RCT (same as in Nugent et al.) plus 7 cohort and case-control studies (3 prospective & 4 retrospective). Unclear whether combining of data was appropriate. One included study assessed NG tube versus PFG (a related procedure using fluoroscopic guidance), not PEG.

CPG=clinical practice guideline; NG=nasogastric; PEG=percutaneous endoscopic gastronomy; PFG=percutaneous fluoroscopic gastronomy; RCT=randomized controlled trial

Table 7: Summary of Study Findings and Authors' Conclusions for Included Reviews

Author, Year	Main Study Findings	Authors' Conclusions
Orphanidou, 2010 ¹⁹	<ul style="list-style-type: none"> • Seven included studies, all low quality. • <i>A priori</i> outcomes: completion of CT & RT, weight loss, treatment interruption, unplanned hospitalization, AEs, length of feeding tube dependency, incidence of stenosis and stricture, and QOL. • Most outcomes NR. • Authors aimed to provide an evidence base for CPG and concluded this was not possible. 	<p><i>The available evidence was insufficient to draw definitive conclusions about the effectiveness of prophylactic feeding tubes in the target patient population (or to support an evidence-based practice guideline).</i>(p. E191)</p>
Languis, 2013 ¹⁸	<ul style="list-style-type: none"> • Analysis of tube feeding was only one part of a larger review of nutrition interventions. • In prophylactic PEG versus no PEG studies, there was no difference in patient weight post-surgery by study's end (6 months and 2 years post-RT). • However, when only patients who lost weight were considered, patients in PEG group lost less. • QOL was generally not influenced by PEG versus no PEG. • Mortality was not different between groups. 	<p><i>"... prophylactic PEG feeding ... showed no beneficial effects on nutritional status compared to tube feeding if required. No differences were found for mortality. Effects on QOL were inconsistent."</i> (p. 675)</p>
Nugent (Cochrane review), 2013 ¹	<ul style="list-style-type: none"> • 6 weeks post-treatment, PEG patients gained weight versus NG patients (P=0.001); however, the benefit was not seen at 6 months. • AEs: no difference in chest infection rates (33% for NG, 33% for PEG); 12 NG patients had feeding tube dislodgement versus 0 for PEG; 0 NG patients had site infection versus 4 for PEG. • Patient satisfaction did not differ between groups. • 2 NG and 4 PEG patients required unscheduled treatment breaks of a median of 6 and 2 days, respectively. • NG duration significantly shorter than PEG feeding (range 23-136 days versus 56-488 days; P=0.0006). • NG cost 10% of the cost of PEG (AUS 76 versus 736). 	<p><i>"There is not sufficient evidence to determine the optimal method of enteral feeding for patients with head and neck cancer receiving CT and / or RT."</i> (p. 2)</p>
Wang, 2014 ⁹	<ul style="list-style-type: none"> • No difference between groups in maintenance of weight or survival. • Some differences: <ul style="list-style-type: none"> – Tube dislodgement higher in NG group (but technique has improved). – PEG advantages: more suitable for long-term feeding (> 30 days); allows greater mobility, enhanced cosmesis & improved QOL <u>but</u> associated with delay in return to oral diet, prolonged duration of RT, increased incidence of pain, increased incidence of dysphagia & increased cost. 	<p><i>NG and PEG feeding have both been found to be effective in maintaining nutritional status; however, due to the limited scope and small number of studies, the review was unable to definitively identify the optimal method of enteral feeding for patients with HN cancer.</i> (p. 565)</p>

AE=adverse event; CPG=clinical practice guideline; CT=chemotherapy; NR=not reported; QOL=quality of life; RT=radiotherapy