Region Västra Götaland, HTA-centrum

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Prophylactic insertion of a gastrostomy for nutritional support in patients with head and neck cancer

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Prophylactic insertion of a gastrostomy for nutritional support in patients with head and neck cancer
[Nutrition via profylaktiskt inlagd gastrostomi hos patienter med cancer i huvud- och halsregionen]

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1. Abbreviations

ARR	Absolute Risk Reduction
BMI	Body Mass Index
EORTC	European Organisation of Research and Treatment of Cancer
H&N	Head and Neck
HPV	Human papilloma virus
Non-rand.	Non-randomised
NA	Not Applicable
PEG	Percutaneous endoscopic gastrostomy
pPEG	Prophylactic percutaneous endoscopic gastrostomy
RIG	Radiologically inserted gastrostomy
pRIG	Prophylactic radiologically inserted gastrostomy
QoL	Quality of life
HRQoL	Health related quality of life
MDADI	M.D. Anderson Dysphagia Inventory
NG	Nasogastric tube
RCT	Randomized controlled trial
RR	Relative Risk.
SF-36	Short Form -36
TNM	Tumor, nodes, metastasis
VGR	Västra Götalands Regionen (in English: Region Västra Götaland)

2. Summary of the Health Technology Assessment

Background

Head and neck (H&N) cancer is the common term for nine different tumour locations in the upper aero-gastric pathway. Advanced tumours that affect lymph nodes can be treated with a combination of surgery and radiation, or in the most advanced cases with a combination of chemo- and radiotherapy. A major side effect of radiotherapy that occurs after approximately three weeks is a pronounced mucositis with pain, difficulties with oral food intake, loss of taste, dry mouth and an increased risk of weight loss. Patients with dysphagia and the need of nutritional support during treatment routinely receive a nasogastric tube (NG) or a gastrostomy. A gastrostomy could either be a percutaneous endoscopic gastrostomy (PEG) or a radiological inserted gastrostomy (RIG). A PEG or a RIG can be placed prior to the start of chemoradiotherapy, i.e. prophylactic PEG or RIG, or once the patient start to develop dysphagia or other nutritional symptoms. The latter is called a therapeutic PEG or RIG.

Objective

To assess whether prophylactic placement of a PEG or a RIG can improve survival, malnutrition and health related quality of life, and reduce hospital admissions in patients with H&N cancer undergoing curative treatment compared to patients who are given a therapeutic NG, PEG or RIG.

Search methods and study selection criteria

Systematic searches were performed in Medline, EMBASE, CINAHL, the Cochrane Library, and a number of HTA-databases. Reference lists of relevant articles were scrutinized for additional references. Studies were required to be a systematic review, a controlled trial of prophylactic gastrostomy, or a case series of more than 100 patients. The latter was used only to analyse adverse effects. The certainty of evidence was assessed using the GRADE system.

Main results

Two randomised, controlled trials and 14 non-randomised, controlled studies met the inclusion criteria. In comparison to oral nutrition or a therapeutic PEG or RIG the treatment strategy of a prophylactic PEG probably results in little or no difference in survival and health related quality of life (Low certainty of evidence, GRADE ⊕⊕OO), and may result in little or no difference in the degree of malnutrition and need for hospitalisation (GRADE ⊕⊕OO). The procedure related mortality in patients with prophylactic gastrostomy is 0 - 2 %, and any major complication can occur in up to 13 % of the patients.

Concluding remarks

The insertion of a prophylactic PEG probably results in little or no difference in survival and health related quality of life in patients with H&N cancer. Since, autonomy, independence and integrity of the patient will all be affected by a prophylactic gastrostomy it is of utmost importance to inform the patient thoroughly, and correctly, about this type of nutritional support. It is equally important that the patient is fully aware that his or her opinion is crucial in the final decision to accept prophylactic placement of the gastrostomy.

3. Svensk sammanfattning – Swedish summary

Bakgrund
Avancerad cancer i huvud och halsregionen behandlas vanligen med en kombination av kirurgi, kemoterapi och strålning. En svår biverkan av strålningen mot halsregionen som vanligen uppkommer efter cirka 3 veckors behandling är en uttalad mucosit. Den leder till smärta, svårigheter att svälja mat, smakförlust, torra slemhinnor och en ökad risk för viktförlust. Patienter med svåra sväljningsbesvär som behöver näringstillskott behandlas idag antingen med extra näringstillförsel via en sond som läggs från näsan genom matstrupen ned till magsäcken (nasogastrisk sond) eller via en sond som läggs in via bukväggen direkt in i matsäcken (PEG= percutaneous endoscopic gastrostomy, eller RIG= radiological inserted gastrostomy). Patienten kan ges en PEG eller RIG innan kemo- och strålningsbehandlingen inleds. Detta kallas för en profylaktisk gastrostomi. Om patienten ges en PEG eller RIG först när de utvecklat sina besvär med att svälja och försörja sig adekvat med näring benämns detta en terapeutisk gastrostomi.

Frågeställning
Leder profylaktiskt inlagd gastrostomi hos patienter som behandlas med kemo-och radioterapi för huvud-eller halscancer till en ökad överlevnad, förbättrad livskvalitet, mindre malnutrition och mindre sjukhusvård jämfört med vanligt näringsstöd givet peroralt eller via en terapeutisk gastrostomi som anläggs först när patienten får symtom på försvårat näringsintag?

Resultat
Litteratursökningen identifierade två randomiserade kontrollerade studier, och 14 icke-randomiserade, kohort-studier som uppfyllde inklusionskriterierna. I de studier som jämfört profylaktisk gastrostomi med PEG med terapeutisk gastrostomi eller bara peroralt näringsstöd fann man att profylaktisk gastrostomi resulterar i ingen eller i endast i en liten skillnad i mortalitet och livskvalitet (Begränsad vetenskaplig dokumentation, GRADE ⊕⊕OO). Samma slutsatser gäller malnutrition och behovet av sluten sjukhusvård (Begränsat vetenskapligt underlag, GRADE ⊕⊕OO).
I de studier som jämfört profylaktisk gastrostomi med PEG eller RIG med terapeutisk gastrostomi eller bara peroralt näringsstöd var resultatet att det är osäkert om profylaktisk gastrostomi resulterar i någon skillnad i mortalitet, livskvalitet, malnutrition och behovet av sluten sjukhusvård (Otillräckligt vetenskapligt underlag, GRADE ⊕OOO).
En allvarlig komplikation i direkt anslutning till en profylaktisk inläggning av en gastrostomi uppträder i upp till 13 % av alla patienter och en dödlig komplikation har rapporterats inträffa hos 0 - 2 %.

En viktig etisk aspekt är att noga informera patienten om hur en profylaktisk gastrostomi kan vara till fördel för patienten då hans eller hennes autonomi, oberoende och fysiska integritet påverkas av gastrostomin. Patienten måste därför vara delaktig i beslutet om att en gastrostomi ska anläggas före behandlingsstart eller först när bieffekterna av behandlingen uppkommer.

Sammanfattande bedömning
För patienter med avancerad huvud- eller halscancer som behandlas med kemo- och strålterapi resulterar profylaktisk inläggning av gastrostomi troligen i ingen eller endast en liten skillnad i mortalitet, livskvalitet, malnutrition och behov av sluten sjukhusvård.

The above summaries were written by HTA-centrum and approved by the Regional board for quality assurance of activity-based HTA. The Regional Health Technology Assessment Centre (HTA-centrum) Region Västra Götaland, Sweden has the task to make statements on HTA reports carried out in VGR. The English summary is a concise summary of similar outline as the summaries in the Cochrane systematic reviews. The Swedish summary addresses the question at issue, results and quality of evidence regarding efficacy and risks, and economical and ethical aspects of the particular health technology that has been assessed in the report, and is ended with a final statement/concluding remark from HTA-centrum.

Christina Bergh, Professor, MD
Head of HTA-centrum of Region Västra Götaland, Sweden, 2015-04-14

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4. Summary of Finding (SoF-table)

Prophylactic percutaneous endoscopic gastrostomy (pPEG) for nutritional support compared to oral nutritional support or therapeutic gastrostomy for nutritional support in patients with head and neck cancer. PICO 1. (NA = not applicable).

Outcomes	Study design Number of studies	Relative effect	Absolute effect	Certainty of evidence GRADE
Mortality	2 RCT	RR = 0.74 (95% CI: 0.44 to 1.24)	ARR = - 7 % (95 % CI: - 0.19 to + 0.05)	⊕⊕◯◯ Low [1]
	4 Non-rand. controlled studies	RR = 1.41 (95% CI:0.71 to 2.81)	ARR = + 7 % (95 % CI: - 0.05 to + 0.19)	⊕◯◯◯ Very low [2,3,4]
Malnutrition	2 RCT	No significant difference in any of the RCTs	At 6 months: Difference in BMI: 0.7 kg/m^2 Difference in no. of patients with < 10% weight loss: + 9%	⊕⊕◯◯ Low [5,6]
	9 Non-rand. controlled studies	5/9 studies reported significantly less "malnutrition" in pPEG treated patients	NA	⊕◯◯◯ Very low [2]
Health Related Quality of Life	2 RCT	NA	1 RCT reported a significant difference in a global health score of 12 points at 6 months in favour of pPEG, but no significant difference at 12 months.	⊕⊕◯◯ Low [7]
Hospitalisation	1 RCT	NA	Difference in hospital days: + 1 Non-significant	⊕⊕◯◯ Low [8]
	2 Non-rand. controlled studies	NA	ARR = -0.5 days (95 % CI: -1.5 to 0.5)	⊕◯◯◯ Very low [2]

[1] Very serious imprecision. Few fatal events.
[2] Serious study limitations. Selection of intervention by physician's and patient's preference.
[3] Serious inconsistency.
[4] Uncertain precision. Few events in each study.
[5] Serious inconsistency. Malnutrition was differently defined and the results of the studies were contradictory.
[6] Uncertain precision. Few patients in one of the RCTs.
[7] Uncertain precision. Few patients in one of the RCTs. Multiple statistical inference testing.
[8] Very serious imprecision. Few patients in only one RCTs.

Summary of Findings (SoF)-table
Prophylactic percutaneous endoscopic or radiological inserted gastrostomy (pPEG or pRIG) for nutritional support compared to oral nutritional support or therapeutic gastrostomy for nutritional support in patients with head and neck cancer. PICO 2. (NA = not applicable).

Outcomes	Study design Number of studies	Relative effect	Absolute effect	Certainty of evidence GRADE
Mortality	1 Non-randomised controlled study	3-year survival: RR = 0.98 (95 % CI: 0.52 to 1.8)	3-year survival: ARR = - 0.7 %	⊕◯◯ ◯ Very low[1,2]
Malnutrition	2 Non-randomised controlled studies	NA	Difference in weight at 6 months: ± 0 to +1.8 kg Non-significant	⊕◯◯◯ Very low[1,2,3]
Health Related Quality of Life	2 Non-randomised controlled studies	NA[3]	NA	⊕◯◯◯ Very low[3]
Hospitalisation	1 Non-randomised controlled study	Percentage patients in need of hospitalisation: RR = 0.77 (95 % CI: 0.59 – 1.0)	Percentage patients in need of hospitalisation: ARR = -18 %	⊕◯◯◯ Very low[1]

[1] Serious study limitations. Study groups not balanced at baseline.
[2] Uncertain precision. Small study groups with few events.
[3] Serious study limitations. No baseline data.

5. Participants in the project

The question was posed by

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Conflicts of interest for the proposer or any of the participants

Jan Nyman is a co-author of one of the included articles.

Project time

HTA was accomplished during the period 2014-02-19 – 2015-04-29
Literature searches were made in March 2014 and August 2014.

6. Head and neck cancer

Head and neck (H&N) cancer is the common term for nine different tumour locations in the upper aero-gastric pathway (ICD code C00-14, C30-32 and C77.0). The dominating histology of the malignant tumours is squamous cell carcinoma. Most patients are diagnosed at a locally advanced stage, although distant metastases are uncommon. The risk factors vary with the particular subsites. Smoking, alcohol abuse and viral infections with human papilloma virus (HPV) are the most well-known.

Head and neck cancer can affect several vital functions such as eating and breathing, and also impair the patient's ability to communicate with negative effects on speech, sight and hearing. A H&N cancer may also negatively affect the patient's body image and appearance. The challenge when treating these malignancies is to achieve loco-regional tumour control with preserved vital functions and a good health related quality of life.

Prevalence and incidence of head and neck cancer

The incidence of H&N cancer in Sweden is approximately 1300 patients per year. This amounts to 2.3 % of the total cancer incidence. The age-adjusted incidence is slightly increasing in women. Oro-pharyngeal cancer is increasing due to HPV. Lip cancer, however, is decreasing. In the Region Västra Götaland of Sweden (VGR) the current incidence is approximately 260 new cases per year.

Head and neck cancer is twice as common in men as in women. The median age at diagnosis is 66 years. The long term survival varies in the different subsites. In the whole group of H&N cancer the disease specific survival is about 60 %.

Present treatment of head and neck cancer

Small oral tumours are often treated with surgery, whereas small laryngeal tumours are commonly treated with radiotherapy. More advanced tumours that affect lymph nodes are preferably treated with a combination of surgery and radiation. The most advanced cases that are inoperable are treated with a combination of chemo- and radiotherapy.

A typical treatment protocol of chemoradiotherapy includes a pre-treatment preparation and examinations with dental care, renal clearance, audiogram, nutritional advice, fixation and CT-scanning for dose-planning of the radiotherapy. The primary tumour and the affected lymph nodes will be irradiated with a higher dose, and a lower prophylactic dose will be used for non-affected lymph nodes. The total dose of radiation is divided into 34 fractions during six weeks. A weekly administration of chemotherapy is given intravenously for patients with locally advanced tumour who are in a general good condition.

The side effect of radiotherapy is a pronounced mucositis with pain, difficulties with oral food intake, loss of taste, dry mouth and risk of weight loss. This occurs after approximately three weeks. The chemotherapy can cause nausea and vomiting, and increases the risk of serious infections.
The chemoradiotherapy often starts on an out-patient basis, but approximately half of the patients have to be hospitalised for more intensive care and nutritional support after a few weeks.

The number of patients per year who undergo chemoradiotherapy for head and neck cancer

Currently, approximately 170 patients with carcinoma of the head and neck region are treated with radiotherapy each year in the Region Västra Götaland of Sweden. Seventy of these also in

combination with chemotherapy. A few of the patients have dysphagia even before they start treatment due to symptoms from the tumour.

In 2014, 30 patients with H&N cancer received a percutaneous endoscopic gastrostomy (PEG) at the Sahlgrenska University Hospital. Most of them had their gastrostomy inserted due to the development of a radiation mucositis, i.e. as a therapeutic gastrostomy. Only a minority of the patients received a prophylactic PEG or a prophylactic radiologically inserted gastrostomy (RIG).

The normal pathway of a patient through the health care system

Patients with H&N cancer normally seek a general practitioner for local symptoms from the head or neck region or for a lump in the neck. They are referred to an Ear, Nose and Throat clinic in Region Västra Götaland for diagnostic work-up. The diagnosis and treatment is thereafter discussed and decided at the weekly multidisciplinary board at Sahlgrenska University Hospital.

Actual wait time for medical assessment and treatment

The median time from referral to the treatment decision is one month, and two months to the start of treatment, according to the Swedish National Registry for H&N cancer. These long lead times are considered unsatisfactory.

Prophylactic gastrostomy in patients with head and neck cancer undergoing curative treatment

Patients with dysphagia who need nutritional support during treatment for H&N cancer routinely receive a nasogastric tube (NG) or a gastrostomy. A gastrostomy could either be a PEG or a RIG.

A NG is a fine tube inserted through the nose via pharynx down into the stomach. The insertion is performed in the outpatient clinic or at the ward. The procedure takes about 15 minutes.

A PEG tube is placed by the Pull-through method. The procedure is usually performed in a gastro-endoscopic unit. The patient is sedated during the whole procedure which takes about 30 min. An esophagogastroscopy is performed with a standard upper endoscope. After local anesthesia and a small skin incision a guide wire is brought into the stomach through the abdominal wall via a cannula. In the stomach the wire is grasped by an endoscopic snare. The endoscope with the secured wire is withdrawn through the mouth. The PEG tube is attached to the wire and pulled through the oral cavity, oesophagus, stomach and through the abdominal wall out onto the skin. Occasionally, an additional deeper skin incision is needed to cut the hypodermis in order to pull the PEG tube through the abdominal wall.

A RIG tube is placed by the aid of ultrasound. The procedure is performed in a radiological unit. The patient is sedated and the whole procedure takes approximately 30 min. The stomach is filled with air, for better visualization, either by a temporary NG or by inserting a thin needle through the abdominal wall into the stomach. After a small skin incision the gastrostomy tube is pushed through the abdominal wall into the stomach.

The reported complication rates associated with PEG and RIG vary in different studies, and many studies and reviews have not reported the incidence rates separately for prophylactic and therapeutic gastrostomies Fatal complications in these patient series and reviews have been reported to occur between 1-12 %, and major complications between 7 – 26 % (Ehrsson 2004, Grant 2009, McAllister 2013)..

Most patients today are given a NG or a gastrostomy once dysphagia and food intake have become a clinical problem. This is referred to a ***therapeutic NG*** or a ***therapeutic PEG or RIG***. However, it has been proposed that the patient may benefit by the placement of a PEG or RIG prior to the occurrence of reduced food intake. The benefits of such a ***prophylactic gastrostomy (PEG or RIG)*** have been discussed in several systematic reviews (Langius 2013, Nugent 2013). It has been argued that PEG may have advantages over NG (Gibson 1992, Piquet 2002), and, moreover, that prophylactic PEG may further reduce weight-loss and hospital admissions (Lee 1998, Rutter 2011).

The maintenance of an adequate nutritional status of the patient has been shown to have a positive impact on the outcome of treatment and to improve the quality of life (Liu 2006, Ravasco 2005). It is therefore reasonable to expect that interventions that prevent malnutrition will be beneficial, and that prophylactic placement of a gastrostomy will be efficient in this regard. If prophylactic PEG does affect QoL and survival in H&N cancer patients it should be included routinely in the curative treatment of these patients.

The central question for the current HTA project

Does prophylactically inserted PEG and/or RIG for nutrional support improve survival, malnutrition and health related quality of life and reduce hospital admissions in patients with head and neck cancer undergoing curative treatment compared to therapeutic enteral nutritional support?

PICO 1 and PICO 2

(P= Patients, I= Intervention, C= Comparison, O=Outcome)

P = Adult patients with head and neck cancer (gingival, palatal, tongue, laryngeal and pharyngeal neoplasm) treated with curative chemotherapy or chemo-radiotherapy

I_1 = Prophylactic PEG

I_2 = Prophylactic PEG or RIG

C_1 = Oral nutritional support or therapeutic PEG or RIG

C_2 = Oral nutritional support or therapeutic PEG or RIG

O = <u>Critical for decision making</u>
Survival
Malnutrition

<u>Important but not critical for decision making</u>
Health related quality of life

<u>Not important</u>
Hospitalisation

7. Review of Certainty of Evidence

Search strategy, study selection and references (Appendix 1)

During February 2014, with an update in August 2014, two librarians (AL, TS) performed systematic searches in Medline, Embase, Cinahl, the Cochrane Library, and a number of HTA-databases. Reference lists of relevant articles were also scrutinised for additional references. Search strategies, eligibility criteria and a graphic presentation of the selection process are presented in Appendix 1. The librarians conducted the literature searches, selected the studies and independently of one another assessed the obtained abstracts. They made a first selection of full-text articles for inclusion or exclusion. Any disagreements were resolved in consensus. The remaining articles were sent to the participants of the project group, who read the articles independently of one another, and then decided in a consensus meeting the studies that fulfilled the PICO criteria. These were included in the final assessment.

The literature search identified a total of 1049 articles (after removal of duplicates). The librarians excluded 925 of them after reading their abstracts. Another 42 were excluded by the librarians after reading them in full text. The remaining 82 articles were sent to the participants of the project group, and 27 articles were finally included in the report (Appendix 2). Three of the publications reported results from two randomised controlled trials, and 14 were non-randomised controlled studies. These were critically appraised using checklists from SBU (Swedish Council on Health Technology Assessment). Ten articles reported results from case series.

The included studies are presented in Appendix 2. The excluded studies and the reasons for exclusion are presented in Appendix 3.

The certainty of evidence was graded according to the GRADE system.

The present knowledge of prophylactic percutaneous endoscopic gastrostomy compared to oral nutritional support or therapeutic gastrostomy (PICO 1)

Survival (Appendices 4:1 and 4:2)

Two RCTs and four non-randomised, controlled studies reported survival rates. The RCTs were of good scientific quality, whereas the non-randomised, controlled studies all had some study limitations. Both RCTs and two of the non-randomised, controlled studies showed no differences in survival rates at six months up to three years follow-up. One cohort study reported a significantly lower survival in the pPEG group, whereas another reported the opposite. The latter also reported an increase in the disease-free survival in the control group. However, after controlling for TNM stage and HPV status, this difference was no longer significant.
Conclusion: There is probably little or no difference in survival in H&N cancer patients undergoing chemoradiotherapy who have a prophylactically inserted PEG compared to those who are treated with only oral nutritional support or a therapeutic gastrostomy. Low certainty of evidence (GRADE ⊕⊕OO).

Malnutrition (Appendix 4:3)
Two RCTs and 10 non-randomised, controlled studies reported on weight or body mass index (BMI). The RCTs were of good scientific quality, whereas the non-randomised, controlled studies all had some study limitations and some had low precision. One RCT showed no significant difference in the reduction of BMI between pPEG and therapeutic nutritional support. The other RCT did not observe any significant differences in the frequency of patients with malnutrition, defined as a weight loss of more than 10 %, during a follow-up period of up to 24 months after start of treatment. Six of the nine non-randomised, controlled studies reported that the weight-loss in patients with pPEG was significantly less in comparison to the patients with oral nutrition or therapeutic gastrostomy.
Conclusion: There is probably little or no difference in nutritional status in H&N cancer patients undergoing chemoradiotherapy who have a prophylactically inserted PEG compared to those who are treated with only oral nutritional support or a therapeutic gastrostomy. Low certainty of evidence (GRADE ⊕⊕OO).

Health related quality of life (Appendix 4:4)
Health related quality of life (HRQoL) was analysed only in the two RCTs. The Swedish study (Silander 2012, 2013) included 134 patients. It used two different HRQoL questionnaire's (EORTC QLQ-C30 and QLQ-HN35) at baseline and after 3, 6 12 and 24 months. There were no significant differences in the great majority of all the analysed variables during follow-up. The other RCT included 39 patients. It used three QoL questionnaire's (EORTC QLQ-C30, QLQ-HN35 and SF36). The changes in global health status were not different between the study groups.
Conclusion: There is probably little or no difference in health related quality of life in H&N cancer patients undergoing chemoradiotherapy who have a prophylactically inserted PEG compared to those who are treated with only oral nutritional support or a therapeutic gastrostomy. Moderate certainty of evidence (GRADE ⊕⊕⊕O).

Hospitalisation (Appendix 4:5)
One RCT and two non-randomised, controlled studies reported on hospitalisation. There was no difference between the study groups in days of hospitalisation or in the frequency of hospital admissions in any of the studies
Conclusion: There may be little or no difference in the need for hospitalisation in H&N cancer patients undergoing chemoradiotherapy who have a prophylactically inserted PEG compared to those who are treated with only oral nutritional support or a therapeutic gastrostomy. Low certainty of evidence
(GRADE ⊕⊕OO).

The present knowledge of prophylactic percutaneous endoscopic or radiologically inserted gastrostomy compared to oral nutritional support or therapeutic gastrostomy (PICO 2)

Survival (Appendix 4:6 and 4:7))
One non-randomised, controlled study reported overall survival and disease-free survival after 3 years follow-up. It had severe study limitations. After adjusting for covariates there were no significant differences between the study groups.
Conclusion: It is uncertain whether there is little or no difference in survival in H&N cancer patients undergoing chemoradiotherapy who have a prophylactically inserted PEG or RIG compared to those who are treated with oral nutritional support or a therapeutic gastrostomy. Very low certainty of evidence (GRADE ⊕OOO).

Malnutrition (Appendix 4:8)
Two non-randomised, controlled studies analysed weight-loss after chemoradiotherapy. Both studies had severe study limitations and some uncertainties in precision. There were no significant differences in weight-loss between the study groups.
Conclusion: It is uncertain whether there is little or no difference in nutritional status in H&N cancer patients undergoing chemoradiotherapy who have a prophylactically inserted PEG or RIG compared to those who are treated with oral nutritional support or a therapeutic gastrostomy. Very low certainty of evidence (GRADE ⊕OOO).

Health related quality of life (Appendix 4:9)
Two non-randomised, controlled studies analysed health related quality of life. Both studies had severe study limitations and uncertainties in precision. The MDADI questionnaire, which addresses dysphagia, was used in both studies. One of the studies observed significantly less symptoms in all domains of the swallowing questionnaire in the pPEG study group, whereas the other did not find any significant differences between the groups in either domain of the MDADI questionnaire
Conclusion: It is uncertain whether there is little or no difference in swallowing in H&N cancer patients undergoing chemoradiotherapy who have a prophylactically inserted PEG or RIG compared to those who are treated with oral nutritional support or a therapeutic gastrostomy. Very low certainty of evidence (GRADE ⊕OOO).

Hospitalisation (Appendix 4:10)
One non-randomised, controlled study reported on hospitalisation. There was no statistical significant difference between the study groups in the need for hospitalisation.
Conclusion: It is uncertain whether there is little or no difference in the need for hospitalisation in H&N cancer patients undergoing chemoradiotherapy who have a prophylactically inserted PEG or RIG compared to those who are treated with oral nutritional support or a therapeutic gastrostomy. Very low certainty of evidence (GRADE ⊕OOO).

Complications in patients with a prophylactic gastrostomy (Appendix 4:11 and 4:12)
The procedure related mortality reported in the patients with prophylactically inserted gastrostomy was 0 - 2 %, and any major complication occurred in 3 – 13 % (Appendix 4:11). Common complications were local minor infections, leakage around gastrostomy tube and local pain with incidence rates between 1 – 26 % (Appendix 4:12).

Ongoing research
A search in ClinicalTrials database (www.clinicaltrials.gov), 141105, using the search term ”gastrostomy” identified 95 studies. One study was considered relevant for the PICOs in this report. It is a randomised, controlled trial from Pakistan (NCT01985438). The purpose is to compare the effect of prophylactic enteral feeding tube placement (either PEG or NG) in patients undergoing treatment for H&N cancer on nutritional status, QoL, mental and emotional health, rates of clinical complications, and cost of care. The study is estimated to be completed in June 2015.

Medical societies or health authorities that recommend prophylactic gastrostomy

In the recommendations of the European Society for Parenteral and Enteral nutrition (ESPEN) it is concluded that PEG tubes may be placed prior to surgery, radiotherapy or chemotherapy in patients with H&N cancer, and that it should be removed when the patient has recovered and has a reliable and adequate oral intake (Löser C 2005).

In 2011, a national multidisciplinary panel in Canada made a consensus-based recommendation including the statement: ”Prophylactic feeding tube insertion should be seriously considered for individuals who present one or more of the following symptoms: significant weight loss (more than 5% in 1 month or more than 10% in 6 months), body mass index below 18,5, dysphagia, anorexia, dehydration, pain, or any other symptom that interferes with the ability to eat” (Orphanidou, 2011).

The American National Comprehensive Cancer Network (NCCN) state in their guidelines that “factors in support of prophylactic PEG for nutrition in H&N cancer patients are severe weight loss prior to treatment (5% in past month, 10% in past 6 months), symptoms including ongoing dehydration, severe dysphagia, anorexia, odynophagia that interferes with oral intake, significant comorbidities requiring good oral intake, severe aspiration in any patient, any aspiration in an elderly patient or patients with comprised cardiopulmonary function, and finally patients anticipating high-dose radiation” (NCCN Guidelines for Head and Neck cancer 2, 2013).

8. Ethical consequences (Appendix 5)

The autonomy, independence and integrity of a patient with head or neck cancer undergoing chemoradiotherapy will all be affected by a prophylactic gastrostomy. Therefore, it is of utmost importance to inform the patient thoroughly, and correctly, about this type of nutritional support. It is equally important that the patient is fully aware that his or her opinion is crucial in the final decision to accept, or not accept, prophylactic placement and later use of the gastrostomy.
A percutaneous gastrostomy is less visible and most probably affects the autonomy of the patient less than a nasogastric tube. The nutrition solutions are delivered to the patient’s doorstep. This will probably compromise the patient’s personal integrity (regardless of whether it is a gastrostomy or a nasogastric tube).

9. Organisation

When can prophylactic placement of PEG or RIG be put into practice

The PEG technique is already in practice in all hospitals in Region Västra Götaland. The RIG technique is in practice at Sahlgrenska University Hospital and Södra Älvsborgs Hospital.

Consequences of the implementation of prophylactic PEG or RIG for personnel

If more patients with advanced H&N cancer than today would accept prophylactic placement of PEG or RIG more personnel need to be trained in handling these gastrostomies.

Consequences for other clinics or supporting functions at the hospital or in the whole Region Västra Götaland of Sweden

There would need to be a regional routine for follow-up and removal or replacement of the PEG/RIG.

10. Economy aspects

Present costs of percutaneous or radiological insertion of a gastrostomy

The cost of a PEG insertion for the oncology department at Sahlgrenska University Hospital is currently 22 000 SEK per patient. This includes material and two days of hospitalisation. The corresponding cost for a RIG insertion is 17 000 SEK (also including two days of hospital stay). The total annual cost for 30 patients who in the majority of cases received a therapeutic gastrostomy (20 out of 30) was 600 000 SEK in 2014.

Expected costs of prophylactic gastrostomy

The number of patients with locally advanced head and neck cancer (stage III-IV) in need of chemoradiotherapy with a curative intent with an indication for a prophylactic gastrostomy during the next coming years is estimated to be 40 per year. Of these it is estimated that 30 would be suitable for PEG and 10 for RIG. The total annual cost for 40 patients will then be 830 000 SEK (30 x 22 000 SEK + 10 x 17 000 SEK).

Total change of cost

The cost of insertion of a prophylactic gastrostomy is the same as the cost of the insertion of a therapeutic gastrostomy. However, it may be that patients in need of a therapeutic gastrostomy will require a longer stay in hospital due to malnutrition. Therefore, it is difficult to estimate a possible change in total cost.

Can the use of prophylactic gastrostomy be adopted and used within the present budget (clinic budget/hospital budget)?

Yes.

Are there any available analyses of health economy?

There are no cost-effectiveness analyses of prophylactic PEG.

11. Unanswered questions

Important gaps in scientific knowledge

There are several studies and two Cochrane analyses on the use of gastrostomy during treatment in patients with H&N cancer. The majority of publications concern complications and survival. There are some studies addressing HRQoL. However, data on long-term effects on HRQoL is still lacking. This will hopefully change as a five year follow-up study is currently being performed at Sahlgrenska University Hospital (Silander and Hammerlid).
One question is of particular interest since different specialists have conflicting opinions. The question is if gastrostomy reduces the patient´s ability to swallow after the curative treatment is finished?

Interest in the own clinic to start studies of the effects on prophylactic gastrostomy

Currently, we do not see any apparent need to start any new studies on the use of gastrostomy in patients with H&N cancer.

Appendix 1

Question at issue:
Does prophylactically inserted PEG and/or RIG improve survival, malnutrition and health related quality of life and reduce hospital admissions in patients with head and neck cancer undergoing curative treatment compared to therapeutic enteral nutritional support?

PICO 1

P = Adult patients with head and neck cancer (gingival, palatal, tongue, laryngeal and pharyngeal neoplasm) treated with curative chemotherapy or chemo-radiotherapy

I = Prophylactic PEG

C = Oral nutritional support or therapeutic PEG or RIG

PICO 2

P = Adult patients with head and neck cancer (gingival, palatal, tongue, laryngeal and pharyngeal neoplasm) treated with curative chemotherapy or chemo-radiotherapy

I = Prophylactic PEG or RIG

C = Oral nutritional support or therapeutic PEG or RIG

O = <u>Critical for decision making</u>
Survival
Malnutrition

<u>Important but not critical for decision making</u>
Health related quality of life

<u>Not important</u>
Hospitalisation

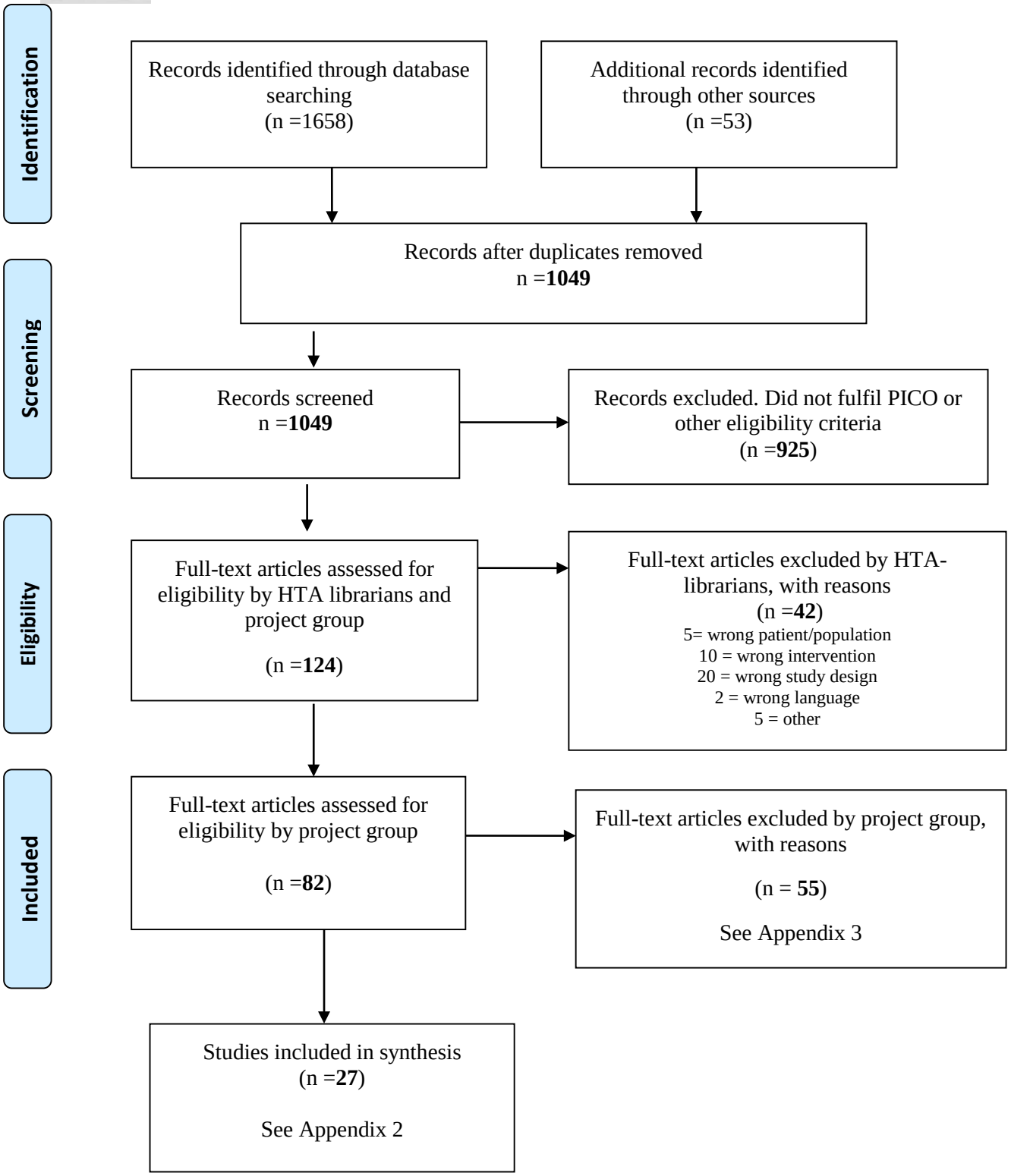
<u>Eligibility criteria</u>

Study design:
Systematic reviews
RCT
Non-randomized controlled studies
Case series if ≥100 patients
Qualitative studies if ≥10 patients

Language:
English, Swedish, Danish, Norwegian

Publication date:
2000-

Selection process – flow diagram



Search strategies

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present
Date: 2014-02-27
No of results: 610
Search updated: 2014-08-01, 52 results

#	Searches	Results
1	(Head or neck or oropharyn* or pharyn* or laryn* or throat or ear or glotti* or nasopharyn* or hypopharyn* or otorhino* or oral* or squamous or esophag* or mouth or tongue or nose or parathyroid* or thyroid* or trachea*).ab,ti.	1312790
2	(cancer* or carcinom* or tumor or tumors or tumour* or neoplas* or malignan* or metasta*).ab,ti.	2189523
3	((Head or neck or oropharyn* or pharyn* or laryn* or throat or ear or glotti* or nasopharyn* or hypopharyn* or otorhino* or oral* or squamous or esophag* or mouth or tongue or nose or parathyroid* or thyroid* or trachea*) adj5 (cancer* or carcinom* or tumor or tumors or tumour* or neoplas* or malignan* or metasta*)).ab,ti.	199237
4	exp "Head and Neck Neoplasms"/	235197
5	(hnscc or hnc or scchn or "head and neck squamous cell carcinoma" or "head and neck carcinoma" or "head and neck cancer" or "squamous cell carcinoma of the head and neck").ab,ti.	20231
6	3 or 4 or 5	309832
7	exp Gastrostomy/	6336
8	"gastrostom*".ab,ti.	6464
9	7 or 8	9113
10	(enteral or feed or feeding or nutrition* or tube or tubes or tubing or percutaneous or endoscopic or radiological* or prophylactic* or proactive or pro-active or pre-treatment).ab,ti.	799502
11	exp Enteral Nutrition/	15382
12	10 or 11	802012
13	9 and 12	6294
14	(PEG or RIG or PPEG or "Percutaneous endoscopic gastrostomy" or "Radiologically inserted gastrostomy" or "prophylactic percutaneous endoscopic gastrostomy").ab,ti.	27381
15	13 or 14	31163
16	6 and 15	1076
17	limit 16 to (yr="2000 -Current" and (danish or english or norwegian or swedish))	650
18	(animals not (animals and humans)).sh.	3791961
19	17 not 18	638
20	(comment or editorial or letter).pt.	1302700
21	**19 not 20**	**610***

Database: EMBASE 1980 to Present
Date: 2014-02-27
No of results: 686
Search updated: 2014-08-01, 55 results

#	Searches	Results
1	exp "head and neck tumor"/	226568
2	(Head or neck or oropharyn* or pharyn* or laryn* or throat or ear or glotti* or nasopharyn* or hypopharyn* or otorhino* or oral* or squamous or esophag* or mouth or tongue or nose or parathyroid* or thyroid* or trachea*).ti,ab.	1597034
3	(cancer* or carcinom* or tumor or tumors or tumour* or neoplas* or malignan* or metasta*).ti,ab.	2760646
4	((Head or neck or oropharyn* or pharyn* or laryn* or throat or ear or glotti* or nasopharyn* or hypopharyn* or otorhino* or oral* or squamous or esophag* or mouth or tongue or nose or parathyroid* or thyroid* or trachea*) adj5 (cancer* or carcinom* or tumor or tumors or tumour* or neoplas* or malignan* or metasta*)).ti,ab.	249844
5	(hnscc or hnc or scchn or "head and neck squamous cell carcinoma" or "head and neck carcinoma" or "head and neck cancer" or "squamous cell carcinoma of the head and neck").ti,ab.	27510
6	1 or 4 or 5	392537
7	exp gastrostomy/	7510
8	"gastrostom*".ti,ab.	8677
9	7 or 8	11949
10	exp enteric feeding/	20561
11	(enteral or feed or feeding or nutrition* or tube or tubes or tubing or percutaneous or endoscopic or radiological* or prophylactic* or proactive or pro-active or pre-treatment).ti,ab.	1022828
12	10 or 11	1026548
13	9 and 12	8380
14	exp percutaneous endoscopic gastrostomy/	3527
15	(PEG or RIG or PPEG or "Percutaneous endoscopic gastrostomy" or "Radiologically inserted gastrostomy" or "prophylactic percutaneous endoscopic gastrostomy").ti,ab.	37919
16	13 or 14 or 15	43819
17	6 and 16	1622
18	limit 17 to (embase and (danish or english or norwegian or swedish) and yr="2000 -Current")	1083
19	**limit 18 to (article or conference paper or note or "review")**	**686**

Database: The Cochrane Library
Date: 2014-02-27
No of results: 53
Cochrane reviews 5
Other Reviews 1
Trials 44
Economic Evalutaions 3
Search updated: 2014-08-01, 5 results

ID	Search	Hits
#1	Head or neck or oropharyn* or pharyn* or laryn* or throat or ear or glotti* or nasopharyn* or hypopharyn* or otorhino* or oral* or squamous or esophag* or mouth or tongue or nose or parathyroid* or thyroid* or trachea*:ti,ab,kw (Word variations have been searched)	121813
#2	cancer* or carcinom* or tumor or tumors or tumour* or neoplas* or malignan* or metasta*:ti,ab,kw (Word variations have been searched)	84126
#3	#1 and #2	16504
#4	hnscc or hnc or scchn or "head and neck squamous cell carcinoma" or "head and neck carcinoma" or "head and neck cancer" or "squamous cell carcinoma of the head and neck":ti,ab,kw (Word variations have been searched)	2805
#5	#3 or #4	16534
#6	PEG or RIG or PPEG or "Percutaneous endoscopic gastrostomy" or "Radiologically inserted gastrostomy" or "prophylactic percutaneous endoscopic gastrostomy":ti,ab,kw (Word variations have been searched)	1492
#7	gastrostom*:ti,ab,kw (Word variations have been searched)	303
#8	#6 or #7	1636
#9	**#5 and #8 from 2000**	**53**

Database: Cinahl
Date: 2014-02-28
No of results: 167
Search updated: 2014-08-01, 13 results

#	Search	Hits
S18	**S6 AND S16 Avgränsare - Publiceringsdatum: 20000101-; Språk: Danish, English, Norwegian, Swedish**	**167**
S17	S6 AND S16	179
S16	S13 OR S14 OR S15	2,618
S15	TI (PEG or RIG or PPEG or "Percutaneous endoscopic gastrostomy" or "Radiologically inserted gastrostomy" or "prophylactic percutaneous endoscopic gastrostomy") OR AB (PEG or RIG or PPEG or "Percutaneous endoscopic gastrostomy" or "Radiologically inserted gastrostomy" or "prophylactic percutaneous endoscopic gastrostomy")	1,663
S14	(MH "Gastrostomy Tubes")	435
S13	S9 AND S12	1,461
S12	S10 OR S11	108,460
S11	TI (enteral or feed or feeding or nutrition* or tube or tubes or tubing or percutaneous or endoscopic or radiological* or prophylactic* or proactive or pro-active or pre-treatment) OR AB (enteral or feed or feeding or nutrition* or tube or tubes or tubing or percutaneous or endoscopic or radiological* or prophylactic* or proactive or pro-active or pre-treatment)	107,280
S10	(MH "Enteral Nutrition")	5,752
S9	S7 OR S8	1,790
S8	TI gastrostom* OR AB gastrostom*	1,306
S7	(MH "Gastrostomy")	1,177
S6	S1 OR S4 OR S5	32,425
S5	TI (hnscc or hnc or scchn or "head and neck squamous cell carcinoma" or "head and neck carcinoma" or "head and neck cancer" or "squamous cell carcinoma of the head and neck") OR AB (hnscc or hnc or scchn or "head and neck squamous cell carcinoma" or "head and neck carcinoma" or "head and neck cancer" or "squamous cell carcinoma of the head and neck")	3,862
S4	S2 N5 S3	19,765
S3	TI (cancer* or carcinom* or tumor or tumors or tumour* or neoplas* or malignan* or metasta*) OR AB (cancer* or carcinom* or tumor or tumors or tumour* or neoplas* or malignan* or metasta*)	228,014
S2	TI (Head or neck or oropharyn* or pharyn* or laryn* or throat or ear or glotti* or nasopharyn* or hypopharyn* or otorhino* or oral* or squamous or esophag* or mouth or tongue or nose or parathyroid* or thyroid* or trachea*) OR AB (Head or neck or oropharyn* or pharyn* or laryn* or throat or ear or glotti* or nasopharyn* or hypopharyn* or otorhino* or oral* or squamous or esophag* or mouth or tongue or nose or parathyroid* or thyroid* or trachea*)	145,733
S1	(MH "Head and Neck Neoplasms+") OR (MH "Esophageal Neoplasms") OR (MH "Facial Neoplasms+") OR (MH "Mouth Neoplasms+") OR (MH "Otorhinolaryngologic Neoplasms+") OR (MH "Thyroid Neoplasms")	26,227

Database: CRD
Date: 2014-02-28
No of results: 17
Search updated: No

Line	Search	Hits
1	(Head or neck or oropharyn* or pharyn* or laryn* or throat or ear or glotti* or nasopharyn* or hypopharyn* or otorhino* or oral* or squamous or esophag* or mouth or tongue or nose or parathyroid* or thyroid* or trachea*) AND (cancer* or carcinom* or tumor or tumors or tumour* or neoplas* or malignan* or metasta*)	1907
2	(hnscc or hnc or scchn) OR (head and neck squamous cell carcinoma) OR (head and neck carcinoma)	32
3	(head and neck cancer) OR (squamous cell carcinoma of the head and neck)	177
4	#1 OR #2 OR #3	1907
5	(PEG or RIG or PPEG) OR (Percutaneous endoscopic gastrostomy) OR (Radiologically inserted gastrostomy)	89
6	(prophylactic percutaneous endoscopic gastrostomy) OR (gastrostom*)	62
7	#5 OR #6	120
8	**#4 AND #7**	**17**

The web-sites of **SBU, Kunnskapssenteret** and **Sundhedsstyrelsen** were visited
2014-03-20
Three references relevant to the question at issue was found

Reference lists
A comprehensive review of reference lists brought 50 new records

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Appendix 2: **Included studies – Design and patient characteristics**.
Abbreviations: pPEG = prophylactic percutaneous endoscopic gastrostomy. tPEG = therapeutic PEG (or reactive PEG). RIG = radiological inserted percutaneous gastrostomy. pRIG = prophylactic RIG. CT = conventional therapy (includes patients who had a gastrostomy after initiation of chemoradiotherapy if this was deemed clinically necessary for nutritional reasons).

Author, Year, Country	Study design	Follow-up	Study groups; Intervention vs control	Patients (n)	Mean Age (years)	Men (%)	Outcome variables
Salas 2009 France	Randomised controlled trial	6 months	pPEG vs CT	21 18	59 60	100 83	Quality of life
Silander 2012 & 2013 Sweden	Randomised controlled trial	51 months	pPEG vs CT	73 72	63 60	68 71	Survival Malnutrition Quality of life Hospitalisation
Anwander 2004 Germany	Non-randomised controlled study	3 weeks after surgery	pPEG vs CT	15 15	57 60	60 93	Malnutrition
Assenat 2011 France	Non-randomised controlled study	Mean: 2.9 years	pPEG vs CT	61 78	<60 years: 87% <60 years: 74%	84 82	Malnutrition
Chang 2009 New Zealand	Non-randomised controlled study	64 months	pPEG vs CT	7 64	60 58	71 69	Malnutrition Hospitalisation

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Author, Year, Country	Study design	Follow-up	Study groups; Intervention vs control	Patients (n)	Mean Age (years)	Men (%)	Outcome variables
Chen 2010 USA	Non-randomised controlled study	Median: 30 months	pPEG vs CT	67 53	59	58	Survival Malnutrition
Kramer 2014 USA	Non-randomised controlled study	27 months	pPEG vs CT	56 30	58 59	75 83	Survival Malnutrition
Mercuri 2009 UK	Non-randomised controlled study	7 weeks	pPEG vs CT	10 10	65 70	80 80	Malnutrition
Nugent 2010 UK	Non-randomised controlled study	Not reported	pPEG vs CT	27 169	Not reported	76	Malnutrition

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Abbreviations: pPEG = prophylactic percutaneous endoscopic gastrostomy. tPEG = therapeutic PEG (or reactive PEG). RIG = radiological inserted percutaneous gastrostomy. pRIG = prophylactic RIG. CT = conventional therapy (includes patients who had a gastrostomy after initiation of chemoradiotherapy if this was deemed clinically necessary for nutritional reasons).

Author, Year, Country	Study design	Follow-up	Study groups; Intervention vs control	Patients (n)	Mean Age (years)	Men (%)	Outcome variables
Oozeer 2011 Canada	Non-randomised controlled study	> 24 months	pPEG or pRIG vs CT	16 15	65 60	56 60	Quality of life (Functional outcome in swallowing after treatment)
Peerwong 2012 Thailand	Non-randomised controlled study	4 months	pPEG vs CT	77 142	51 49	68 70	Malnutrition
Prestwich 2014 UK	Non-randomised controlled study	> 24 months	pPEG or pRIG vs CT	43 13	54 58	77 54	Quality of life (Functional outcome in swallowing after treatment)
Romesser 2012 USA	Non-randomised controlled study	3 months	pPEG vs CT	325 75	56 61	87 87	Malnutrition Hospitalisation
Rutter 2011 USA	Non-randomised controlled study	36 months	pPEG vs CT	53 58	58	83	Survival Malnutrition
Scolapio 2001 USA	Non-randomised controlled study	Not specified	pPEG or pRIG vs CT	41 13	69	74	Malnutrition

Appendix 2: **Included studies – Design and patient characteristics**.
Abbreviations: pPEG = prophylactic percutaneous endoscopic gastrostomy. tPEG = therapeutic PEG (or reactive PEG). RIG = radiological inserted percutaneous gastrostomy. pRIG = prophylactic RIG. CT = conventional therapy (includes patients who had a gastrostomy after initiation of chemoradiotherapy if this was deemed clinically necessary for nutritional reasons).

Author, Year, Country	Study design	Follow-up	Study groups; Intervention vs control	Patients (n)	Mean Age (years)	Men (%)	Outcome variables
Williams 2012 UK	Non-randomised controlled study	Median: 30 months	pPEG or pRIG vs CT	71 33	54 57	79 66	Survival Malnutrition Hospitalisation
Avery 2008 UK	Case series	30 days – 6.2 years	tPEG	223 tPEG 2 RIG	62	58	Complications
Bäck 2014 Finland	Case series	1 week – 37 months Mean: 17 months	PEG	292	62	73	Complications
Baschnagel 2013 USA	Case series	2 years	pPEG or tPEG	161 32	62 64	84 84	Complications
Chan 2010 China	Case series	>150 days	RIG	110	65	85	Complications
Foster 2007 UK	Case series	>18 months	pPEG	149	63	-	Complications

Appendix 2: **Included studies – Design and patient characteristics**.
Abbreviations: pPEG = prophylactic percutaneous endoscopic gastrostomy. tPEG = therapeutic PEG (or reactive PEG). RIG = radiological inserted percutaneous gastrostomy. pRIG = prophylactic RIG. CT = conventional therapy (includes patients who had a gastrostomy after initiation of chemoradiotherapy if this was deemed clinically necessary for nutritional reasons).

Author, Year, Country	Study design	Follow-up	Study groups; Intervention vs control	Patients (n)	Mean Age (years)	Men (%)	Outcome variables
Lawson 2009 USA	Case series	Until feeding tube removal, death, or end of study period (3 years).	pPEG or pRIG	27 pPEG 75 pRIG	< 40: 7% 41-50: 23% 51-60: 34% 61+: 36%	75	Complications
McAlister 2013 UK	Case series	3 years	pPEG or pRIG	21 pPEG 89 pRIG	Not reported	Not reported	Complications
Nguyen 2006 USA	Case series	Median: 19 months	pPEG	104	59	99	Complications
Pulkkinen 2014 Germany	Case series	Not reported	pPEG	194	64	74	Complications
Raykher 2009 USA	Case series	Not reported	pPEG or tPEG	161 pPEG 2 tPEG	58	74	Complications

Appendix 3. **Excluded articles**. Prophylactic gastronomy in patients with head and neck cancer.

Study (author, publication year)	Reason for exclusion
Beaver 2001	Not correct PICO (Prophylactic and therapeutic PEG combined)
Blanchford 2014	Not correct PICO (Prophylactic and therapeutic PEG combined)
Brown TE 2013	Comparison of guidelines
Beer 2005	Not correct PICO (Includes also patients with esophagus cancer, an not clear if all patients in PEG group were given prophylactic PEG))
Brown T 2014 Support Care Cancer	Not correct PICO (Wrong outcome)
Brown T 2014 BMC Nurs	Study protocol. No results.
Canis 2014	Not correct PICO (Study of microsurgery)
Cappel 2007	Not correct PICO (Prophylactic and therapeutic PEG combined)
Corry 2008	Not clear that all patients had prophylactic PEG.
Corry 2009	Not correct PICO (Prophylactic and therapeutic PEG combined)
Cruz 2005	Not correct PICO (Prophylactic and therapeutic PEG combined)
de Mones 2014	Case report.(two patients)
De Souza 2009	Not correct PICO (Prophylactic and therapeutic PEG combined)
Deurloo 2001	Not correct PICO (Prophylactic RIG and therapeutic RIG combined)
Dobrosotskaya 2014	Not correct PICO (Study of radiation and cisplatin)
El-Deiry 2009	Not correct PICO (Not clear if all patients were given prophylactic PEG)
Eley 2012	Not correct PICO (Unclear whether all patients received postoperative radiochemotherapy)
Fietkau 2013	Not correct PICO. All patients pPEG but no data on complications.
Gomes 2012	Not correct PICO (Studies included neurological patients were included in the review)
Grant 2009	Not correct PICO (Prophylactic and therapeutic PEG combined)
Gurney 2008	Not correct PICO (Patients without PEG were also included)
Habib 2014	Not correct PICO (Prophylactic and therapeutic PEG combined)
Hiki 2008	Not correct PICO (Includes also other malignancies than head and neck cancer)
Huang 2013	Not correct PICO (Includes only patients with metastasis)
Hughes 2013	Not correct PICO (Prophylactic PEG and RIG combined)
Jack 2012	Not correct PICO (Prophylactic and therapeutic PEG combined). Case series with n < 100
Koyfman 2012	A “non-systematic” review.

Appendix 3. **Excluded articles**. Prophylactic gastronomy in patients with head and neck cancer.

Study (author, publication year)	Reason for exclusion
Kwong 2014	Case series with less than 100 patients.
Köhler 2014	Not correct PICO (Prophylactic PEG and therapeutic PEG combined)
Langmore 2012	Not correct PICO (Prophylactic PEG and therapeutic PEG combined
Lee 2008	Not correct PICO (Prophylactic PEG and therapeutic PEG combined)
Langius 2013	A systematic review of RCTs examining different nutritional interventions in patients with head and neck cancer. It did find any other RCT than both RCTS included in the present health technology assessment. The results/conclusions were not graded.
Leeds 2010	Not correct PICO (Prophylactic PEG and therapeutic PEG combined)
Locher 2012	Not correct PICO (Wrong outcome)
Masgne 2001	Not correct PICO (Prophylactic PEG and therapeutic PEG combined)
Mansoor 2014	Not correct PICO (Prophylactic PEG and therapeutic PEG combined)
Martin 2012	Not correct PICO (Mixed population also including non-malignant diagnoses)
Mekhail 2001	Not correct PICO (Prophylactic and therapeutic PEG or NG combined)
Merrick 2012	Not correct PICO (Wrong outcome variables)
Nevler 2014	Case report.
Nugent 2013	A systematic review of RCTs examining different nutritional interventions in patients with head and neck cancer. The inclusion criteria were very strict and no RCT was found that fulfilled the criteria of the present health technology assessment.
Olson 2013	Not correct PICO (Prophylactic PEG and therapeutic PEG combined
Osborne 2012	Case series with less than 100 patients (n = 51)
Paleri 2010	Review of case series with each include study had less than 100 patients
Piquet 2002	Not correct PICO (Intervention group included also patients with only dietary counselling)
Rogers 2007	Not correct PICO (Not clear if all patients in PEG group were given prophylactic PEG)
Sabir 2014	Not correct PICO (Mixed cancer population)
Sadasivan 2012	Not correct PICO (Not clear if all patients in PEG group were given prophylactic PEG)
Sanguineti 2013	Not correct PICO (Wrong outcome)
Schneider 2014	Not correct PICO (Not clear if all patients in PEG group were given prophylactic PEG)
Schurink 2001	Not correct PICO (Prophylactic and therapeutic PEG combined)
Sobani 2011	Not correct PICO (Not clear if all patients in PEG group were given prophylactic PEG)
Terrel 2004	Not correct PICO (Patients with or without PEG combined)

Appendix 3. **Excluded articles**. Prophylactic gastronomy in patients with head and neck cancer.

Study (author, publication year)	Reason for exclusion
Wang 2014	A systematic review of RCTs examining PEG with nasogastric tube feeding in patients with head and neck cancer. No RCT was included. Both non-randomised controlled studies and case series were included
Zuercher 2011	Not correct PICO (Prophylactic and therapeutic PEG combined)

* + No problem
? Some problems
- Major problems

Appendix 4:1 **Prophylactic endoscopic gastrostomy compared to conventional nutritional support.**
Outcome variable: Overall survival
Abbreviations: RCT = randomised controlled trial. NS = non-significant. pPEG = prophylactic percutaneous endoscopic gastrostomy. CT = conventional therapy (includes patients who had a gastrostomy after initiation of chemoradiotherapy if this was deemed clinically necessary for nutritional reasons).

Author, year	Country	Study design	Number of patients	With-drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Prophylactic PEG	Conventional therapy				
Salas 2009	France	RCT	pPEG = 21 CT = 18	pPEG = 2 CT = 2	At 6 months: 89 % NS between study groups	At 6 months: 90 %		+	+	+
Silander 2012/2013	Sweden	RCT	pPEG = 73 CT =72	pPEG = 18 CT = 13	At 1 year: 84 % At 2 years: 77 % NS between study groups	At 1 year: 79 % At 2 years: 69 %		+	+	+
Chen 2010	USA	Non-randomised controlled study	pPEG = 67 CT =53		At 3 years: 66 % NS between groups	At 3 years: 69 %		+	?	+
Kramer 2014	USA	Non-randomised controlled study	pPEG = 56 CT =30	Not reported	At 1 year: 80 % p= 0.02 between study groups	At 1 year: 100 %		+	?	?

* + No problem
? Some problems
- Major problems

Appendix 4:1 **Prophylactic endoscopic gastrostomy compared to conventional nutritional support.**
Outcome variable: Overall survival
Abbreviations: RCT = randomised controlled trial. NS = non-significant. pPEG = prophylactic percutaneous endoscopic gastrostomy. CT = conventional therapy (includes patients who had a gastrostomy after initiation of chemoradiotherapy if this was deemed clinically necessary for nutritional reasons).

Author, year	Country	Study design	Number of patients	With-drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Prophylactic PEG	Conventional therapy				
Romesser 2012	USA	Non-randomised controlled study	I =325 C = 75*	3	2 years: 86.5 % p = 0.028 between study groups	2 years: 80.0 %	* Of the 75 nonPEG patients who refused prophylactic PEG placement 26 patients (34.7%) required acute PEG placement at a mean of 4.9 weeks from the start of IMRT (radiotherapy). NonPEG group is really 49 patients!	+	?	+
Rutter 2011	USA	Non-randomised controlled study	pPEG = 53 CT = 58	Not reported	2 years: 71 % NS between study groups	2 years: 81 % *	* Only patients with therapeutic PEG. The rate of survival in nonPEG group is not presented. The timing of PEG placement did not have a statistically significant effect on overall survival.	+	-	-

* + No problem

Appendix 4:2 **Prophylactic endoscopic gastrostomy compared to conventional nutritional support.**
Outcome variable: Disease-free survival
Abbreviations: RCT = randomised controlled trial. NS = non-significant. pPEG = prophylactic percutaneous endoscopic gastrostomy. CT = conventional therapy (includes patients who had a gastrostomy after initiation of chemoradiotherapy if this was deemed clinically necessary for nutritional reasons).

Author, year	Country	Study design	Number of patients	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Prophylactic PEG	Conventional therapy				
Kramer 2014	USA	Non-randomised controlled study	pPEG = 56 CT = 30	12	At 12 months: 80 % p = 0.02 between study groups	At 12 months: 100%	Disease free survival at 12 months before controlling for TNM stage and HPV status.	+	?	?

* + No problem
? Some problems
- Major problems

Appendix 4:3. **Prophylactic endoscopic gastrostomy compared to conventional nutritional support.**
Outcome variable: Malnutrition.
Abbreviations: RCT = randomised, controlled trial. BMI = body mass index. pPEG = prophylactic percutaneous endoscopic gastrostomy. RIG = radiological inserted percutaneous gastrostomy. CT = conventional therapy (includes patients who had a gastrostomy after initiation of chemoradiotherapy if this was deemed clinically necessary for nutritional reasons). Δ = Change between baseline and end of follow-up. NS = non-significant

Author, year	Country	Study design	Number of patients	With-drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Prophylactic PEG	Conventional therapy				
Salas 2009	France	RCT	pPEG = 21 CT = 18	pPEG = 2 CT = 2	<u>BMI</u> At 6 months: Δ = - 2.5 kg/m^2 (sd 1.8) NS between study groups	<u>BMI</u> At 6 months: Δ = -1.8 kg/m^2 (sd 1.4)		+	+	+
Silander 2012/2013	Sweden	RCT	pPEG = 73 CT = 72	pPEG = 18 CT = 13	<u>Frequency of malnutrition*:</u> At 2 months: 6 % At 6 months: 62 % At 12 months: 52 % At 24 months: 48 % NS between study groups at all occasions of follow-up	<u>Frequency of malnutrition*:</u> At 2 months: 19 % At 6 months: 71 % At 12 months: 56 % At 24 months: 37 %	Malnutrition was defined as >10% unintended weight loss during the last 6 months.	+	+	+
Anwander 2004	Germany	Non-randomized control study	pPeg = 15 CT = 15	-	<u>Weight</u> (Percentage of optimal body weight) At 3 weeks after surgery: 93% NS between study groups	<u>Weight</u> (Percentage of optimal body weight) At 3 weeks after surgery: 89%	Both groups underwent preoperative chemotherapy and radiation followed by radical tumour surgery.	+	-	-
Assenat 2001	France	Non-randomized control study	I=61 C=78	-	<u>Weight</u> At the end of treatment: Δ = -1,0 kg (-10 to +7) p < 0.001 between study groups	<u>Weight</u> At the end of treatment: Δ = -5,0 kg (-20 to +2)	1998-2001 the patients did not receive PEG= control group. 2001-2003 the patients received PEG=intervention group.	-	-	-

* + No problem
? Some problems
- Major problems

Appendix 4:3. **Prophylactic endoscopic gastrostomy compared to conventional nutritional support.**
Outcome variable: Malnutrition.
Abbreviations: RCT = randomised, controlled trial. BMI = body mass index. pPEG = prophylactic percutaneous endoscopic gastrostomy. RIG = radiological inserted percutaneous gastrostomy. CT = conventional therapy (includes patients who had a gastrostomy after initiation of chemoradiotherapy if this was deemed clinically necessary for nutritional reasons). Δ = Change between baseline and end of follow-up. NS = non-significant

Author, year	Country	Study design	Number of patients	With-drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Prophylactic PEG	Conventional therapy				
Chang 2009	New Zealand	Non-randomised controlled study	pPEG = 7 CT = 64	-	Weight At the end of treatment: Δ = -1,6 kg (range -1,3--4,5) NS between study groups	Weight At the end of treatment: Δ = - 4,4 kg (range -2,4—7,8)	.	+	-	-
Chen 2010	USA	Non-randomised controlled study	I =67 C =53	9?	Weight At the end of treatment: Δ = -8.6 kg (0—23) p < 0.001 between study groups	Weight At the end of treatment: Δ = -19.5 pounds (0—34.5)		+	?	+
Kramer 2014	USA	Non-randomised controlled study	I =56 C =30	12?	Weight At 12 months: Δ = -17.1 % NS between study groups	Weight At 12 months: Δ = -16.3 %		+	?	?
Mercuri 2009	UK	Non-randomised controlled study	pPEG =10 CT =10	-	Weight At weeks 6-7: Δ = -1.8 % (range 0—10) p < 0.04 between study groups	Weight At weeks 6-7: Δ = -4,9 % (range-3—11)	The CT (=non-PEG) group losing an average of 2.6 kg more than the PEG group.	+	-	-

* + No problem
? Some problems
- Major problems

Appendix 4:3. **Prophylactic endoscopic gastrostomy compared to conventional nutritional support.**
Outcome variable: Malnutrition.
Abbreviations: RCT = randomised, controlled trial. BMI = body mass index. pPEG = prophylactic percutaneous endoscopic gastrostomy. RIG = radiological inserted percutaneous gastrostomy. CT = conventional therapy (includes patients who had a gastrostomy after initiation of chemoradiotherapy if this was deemed clinically necessary for nutritional reasons). Δ = Change between baseline and end of follow-up. NS = non-significant

Author, year	Country	Study design	Number of patients	With-drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Prophylactic PEG	Conventional therapy				
Nugent 2010	UK	Non-randomised controlled study'	pPEG =27 CT =139	-	Radio-therapy: Weight Δ = -1.4 % Chemo- and radio-therapy: Weight Δ = -4.6 % Induction with chemo-therapy: Weight Δ = -3.0 % NS between all study groups	Radio-therapy: Weight Δ = -3.0 % to -5.4 % Chemo- and radio-therapy: Weight Δ = -6.1 % to - 8.7 % Induction with chemo-therapy: Weight Δ = -3.5 % to -9.4 %	The length of follow-up was not reported. Conventional therapy was presented in three different groups; Nasogastric tube, PEG inserted during treatment and oral feeding only.	+	-	-
Peerawong 2012	Thailand	Non-randomised controlled study	pPEG =72 CT =142	-	<u>Weight</u> At 17 weeks: Δ = -9.0 % <u>Weight loss >10%</u> At 17 weeks: 49 % p < 0.01 between study groups	<u>Weight</u> At 17 weeks: Δ = -15.3 % <u>Weight loss >10%</u> At 17 weeks: 74 %		?	-	?
Romesser 2012	USA	Non-randomised controlled study	pPEG = 325 CT =75*	3	<u>Weight</u> At 3 months: Δ = -11.1 kg p = 0.04 between study groups	<u>Weight</u> At 17 weeks: Δ = -13.1 kg		+	?	+

* + No problem
? Some problems
- Major problems

Appendix 4:3. **Prophylactic endoscopic gastrostomy compared to conventional nutritional support.**
Outcome variable: Malnutrition.
Abbreviations: RCT = randomised, controlled trial. BMI = body mass index. pPEG = prophylactic percutaneous endoscopic gastrostomy. RIG = radiological inserted percutaneous gastrostomy. CT = conventional therapy (includes patients who had a gastrostomy after initiation of chemoradiotherapy if this was deemed clinically necessary for nutritional reasons). Δ = Change between baseline and end of follow-up. NS = non-significant

Author, year	Country	Study design	Number of patients	With-drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Prophylactic PEG	Conventional therapy				
Rutter 2011	USA	Non-randomized control study	pPEG = 53 CT = 58	-	<u>Weight</u> At 6 weeks: Δ = -6.7 kg At 6 months: Δ = -5.5 kg p < 0.05 between study groups at both times of follow-up	<u>Weight</u> At 6 weeks: Δ = -11.9 kg At 6 months: Δ = -12.1 kg	Among the 90 patients who received a PEG a correlation of timing of the PEG tube placement with the percentage weight-loss revealed that the patients who received a tube earlier in the course of therapy had a significantly lower percentage weight-loss.	+	-	-

* + No problem
? Some problems
- Major problems

Appendix 4:4. **Prophylactic endoscopic gastrostomy compared to conventional therapy.**
Outcome variable: Quality of life
Abbreviations: RCT = randomised controlled trial. NS = non-significant. pPEG = prophylactic percutaneous endoscopic gastrostomy. CT = conventional therapy (includes patients who had a gastrostomy after initiation of chemoradiotherapy if this was deemed clinically necessary for nutritional reasons).
EORTC = European Organisation for Research and Treatment of Cancer questionnaire.

Author, year	Country	Study design	Number of patients	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Prophylactic PEG	Conventional therapy				
Salas 2009	France	RCT	pPEG = 21 CT =18	pPEG = 2 CT = 2	<u>EORTC Global</u> Baseline: 63.0 (sd 24.1) At 6 months: Δ = + 15.9 (sd 30.6) NS between study groups	<u>EORTC Global</u> Baseline: 57.8 (sd 25.8) At 6 months: Δ = - 4.5 (sd 36.4)	Scale 0-100. An increase indicates improvement.	+	+	+
Silander 2012/2013	Sweden	RCT	pPEG = 73 CT = 72	pPEG =18 CT =13	<u>EORTC Global</u> Baseline: 67 At 6 months: 64 p = 0.02 between study groups	<u>EORTC Global</u> Baseline: 63 At 6 months: 52	Scale 0-100.An increase indicates improvement. The quality of life deteriorated significantly in both groups but returned to the baseline level at the 12 month follow-up.	+	+	+

* + No problem
? Some problems
- Major problems

Appendix 4:5**. Prophylactic endoscopic gastrostomy compared to conventional nutritional support.**
Outcome variable: Hospitalisation
Abbreviations: RCT = randomised controlled trial. NS = non-significant. pPEG = prophylactic percutaneous endoscopic gastrostomy. CT = conventional therapy (includes patients who had a gastrostomy after initiation of chemoradiotherapy if this was deemed clinically necessary for nutritional reasons).

Author, year	Country	Study design	Number of patients n=	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Prophylactic PEG	Conventional therapy				
Silander 2012/2013	Sweden	RCT	pPEG = 73 CT = 72	pPEG =18 CT = 13	<u>Days</u> Mean: 26 (range 3-66) NS between study groups	<u>Days</u> Mean: 25 (range 6-90)	Hospital stay during tumour treatment. During the period from treatment completion until the 6-month follow-up the average hospital stay was another 8 days for both groups.	+	+	+
Chang 2009	New Zealand	Non randomised controlled study	pPEG = 7 CT = 64	Not reported	<u>No of patients:</u> 2/7 (29 %) <u>Days of hospitalisation:</u> 4.3 (sd 9.7) NS between study groups for both variables	<u>No of patients:</u> 31/64 (48 %) Days of hospitalisation: 5.1 (sd 7.5)	Hospital admissions for nutritional reasons	+	-	-
Romesser 2012	USA	Non-randomised controlled study	pPEG =325, CT =75	3.	<u>No of patients:</u> 49/325 (15 %) p = 0.026 between study groups <u>Days of hospitalisation:</u> 5.2 (sd 5.0) NS between study groups	<u>No of patients:</u> 20/75 (27 %) <u>Days of hospitalisation:</u> 5.7 (sd 3.7)	CT (nonPEG) group is really 49 patients. The hospital admission in this subgroup is not clear.	+	?	+

* + No problem
? Some problems
- Major problems

Appendix 4:6. **Prophylactic percutaneous endoscopic or radiological inserted gastrostomy compared to conventional nutritional support.**
Outcome variable: Survival
Abbreviations: pPEG = prophylactic percutaneous endoscopic gastrostomy. pRIG = prophylactic radiological inserted gastrostomy. NGT = nasogastric tube. tPEG = therapeutic percutaneous endoscopic gastrostomy. CT = conventional therapy (includes patients who had a gastrostomy after initiation of chemoradiotherapy if this was deemed clinically necessary for nutritional reasons). NS = non-significant.

Author, year	Country	Study design	Number of patients	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Prophylactic gastrostomy	Conventional therapy				
Williams 2012	UK	Non-randomised controlled study	pPEG or pRIG = 71 CT = 33	Not reported	At 3 years: 71 % NS between study groups	At 3 years: tPEG=42 % NGT=86 %		+	-	?

* + No problem
? Some problems
- Major problems

Appendix 4:7. **Prophylactic percutaneous endoscopic or radiological inserted gastrostomy compared to conventional nutritional support.**
Outcome variable: Disease-free survival
Abbreviations: pPEG = prophylactic percutaneous endoscopic gastrostomy. pRIG = prophylactic radiological inserted gastrostomy. NGT = nasogastric tube. tPEG = therapeutic percutaneous endoscopic gastrostomy. CT = conventional therapy (includes patients who had a gastrostomy after initiation of chemoradiotherapy if this was deemed clinically necessary for nutritional reasons). NS = non-significant. = change between baseline and end of follow-up.

Author, year	Country	Study design	Number of patients	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Prophylactic gastrostomy	Conventional therapy				
Williams 2012	UK	Non-randomised controlled study	pPEG or pRIG = 71 CT = 33	Not reported	At 3 years: 78.0% NS between study groups	At 3 years: tPEG=50.9% NGT=90.0%		+	-	?

* + No problem
? Some problems
- Major problems

Appendix 4:8. **Prophylactic percutaneous endoscopic or radiological inserted gastrostomy compared to conventional nutritional support.**
Outcome variable: Malnutrition
Abbreviations: pPEG = prophylactic percutaneous endoscopic gastrostomy. pRIG = prophylactic radiological inserted gastrostomy. NGT = nasogastric tube. tPEG = therapeutic percutaneous endoscopic gastrostomy. CT = conventional therapy (includes patients who had a gastrostomy after initiation of chemoradiotherapy if this was deemed clinically necessary for nutritional reasons). NS = non-significant. = change between baseline and end of follow-up.

Author, year	Country	Study design	Number of patients	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Prophylactic gastrostomy	Conventional therapy				
Scolapio 2001	USA	Non-randomised controlled study	pPEG = 41 CT = 13	Not reported	<u>Weight:</u> Δ = -2.7 kg	<u>Weight:</u> Δ = -4.5 kg	The time of follow-up was not reported. No statistica presented.	?	-	-
Williams 2012	UK	Non-randomised controlled study	pPEG/pRIG = 71 CT = 33	Not reported	<u>Weight</u> At 6 months post radiotherapy: Δ = -11.7 %. At end of treatment: Δ = -6.1 % NS between study groups for both times of follow-up	<u>Weight</u> At 6 months post radiotherapy: NGT: Δ = -14.3 % tPEG: Δ = -8.9 %. At end of treatment: NGT: Δ = -7.1 %, tPEG: Δ = -6.2 %.		+	-	?

* + No problem
? Some problems
- Major problems

Appendix 4:9. **Prophylactic percutaneous endoscopic gastrostomy or radiological inserted gastrostomy compared to conventional nutritional support**
Outcome variable: Quality of life
Abbreviatons:. MDADI = MD Anderson Dysphagia Inventory. Scale 0 – 100. The higher score the better. NS = non-significant. pPEG = prophylactic percutaneous endoscopic gastrostomy. RIG = radiological inserted percutaneous gastrostomy. CT = conventional therapy (includes patients who had a gastrostomy after initiation of chemoradiotherapy if this was deemed clinically necessary for nutritional reasons).

Author, year	Country	Study design	Number of patients	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Prophylactic gastrostomy	Conventional therapy				
Oozeer 2011	UK	Non-randomised controlled study	pPEG/pRIG=16 CT=15	13	<u>MDADI scores:</u> > 2 years after treatment: Functional: 36.5 Emotional: 34.6 Physical: 36.1 Global: 35.0 p < 0.001 between study groups for all scores	<u>MDADI scores:</u> > 2 years after treatment: Functional: 84.3 Emotional: 61.5 Physical: 61.2 Global: 60.0	No baseline data with regard to MDADI score.	+	-	-
Prestwich 2014	UK	Non-randomised controlled study	pPEG/pRIG =43 CT =13	7	<u>MDADI scores:</u> > 2 years after treatment: Functional: 70 Emotional: 68 Physical: 55 Global: 40 NS between study groups for all scores	<u>MDADI scores:</u> > 2 years after treatment: Functional: 48 Emotional: 50 Physical: 53 Global: 40	No baseline data with regard to MDADI score. .	+	-	-

* + No problem
? Some problems
- Major problems

Appendix 4:10. **Prophylactic percutaneous endoscopic or radiological inserted gastrostomy compared to conventional therapy.)**
Outcome variable: Hospitalisation.
Abbreviations: pPEG = prophylactic percutaneous endoscopic gastrostomy. pRIG = prophylactic radiological inserted gastrostomy. NGT = nasogastric tube. tPEG = therapeutic percutaneous endoscopic gastrostomy. CT = conventional therapy (includes patients who had a gastrostomy after initiation of chemoradiotherapy if this was deemed clinically necessary for nutritional reasons). NS = non-significant.

Author, year	Country	Study design	Number of patients	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Prophylactic gastrostomy	Conventional therapy				
Williams 2012	UK	Non-randomised controlled study	pPEG or pRIG = 71 CT = 33	Not reported	<u>No of patients</u> 43/77 (61 %) <u>Days of hospitalisation</u> Median 6 NS between stud groups for all outcomes	<u>No of patients</u> NGT: 18/21 (86 %) tPEG: 8/12 (67 %) <u>Days of hospitalisation</u> NGT: Median 14 tPEG: Median 7		?	-	-

Appendix 4:11: **Major complications associated with prophylactic gastrostomy in patients with with head-and-neck cancer undergoing chemoradiotherapy.**

Author, Year, Country	Study design	Follow-up	Procedure related mortality	Major infection (Septicemia Abscess Peritonitis)	Bleeding	Inserted-site metastasis	Other major complication	Any major complication
Silander 2012/ 2013 Sweden	RCT	51 months	2 % (1/64)	2 % (1/64)				3 % (2/64)
Romesser 2012 USA	Non-randomised controlled study	3 months			4 % (2/51)	1 % (1/51)		
Avery 2008 UK	Case series	30 days – 6.2 years			1 % (2/218)		2 % (5/218)	3 % (6/218)
Bäck 2014 Finland	Case series	1 week – 37 months Mean: 17 months	1 % (1/114)	2 % (2/114)	0%		6 % (7/114)	8 % (9/114)
Baschnagel 2013 USA	Case series	2 years		3% (5/144)			2% (3/144)	9%

Appendix 4:11: **Major complications associated with prophylactic gastrostomy in patients with with head-and-neck cancer undergoing chemoradiotherapy.**

Author, Year, Country	Study design	Follow-up	Procedure related mortality	Major infection (Septicemia Abscess Peritonitis)	Bleeding	Inserted-site metastasis	Other major complication	Any major complication
Chan 2010 China	Case series	>150 days	0%	1% (1/108)	1% (1/108)			2% (2/108)
Foster 2007 UK	Case series	>18 months	0%	1% (1/148)				1% (1/148)
Lawson 2009 USA	Case series	Up to3 years.			1% (1/102)			
McAlister 2013 UK	Case series	3 years	0%				PEG: 10% (2/21) RIG: 13% (12/89)	PEG: 10% (2/21) RIG: 13% (12/89)
Nguyen 2006 USA	Case series	Median: 19 months	0%					0%
Pulkkinen 2014 Germany	Case series	Not reported		7% (14/194)			1% (1/194)	8% (15/194)

Appendix 4:11: **Major complications associated with prophylactic gastrostomy in patients with with head-and-neck cancer undergoing chemoradiotherapy.**

Author, Year, Country	Study design	Follow-up	Procedure related mortality	Major infection (Septicemia Abscess Peritonitis)	Bleeding	Inserted-site metastasis	Other major complication	Any major complication
Raykher 2009 USA	Case series	Not reported		1% (1/161)	1% (1/161)	0%		

Appendix 4:12: **Minor complications associated with prophylactic gastrostomy in patients with with head-and-neck cancer undergoing chemoradiotherapy.**

Author, Year, Country	Study design	Follow-up	Tube leakage	Tube obstruction	Tube dis-lodgement	Minor infection	GI disorder	General disorder	Pain	Mild skin necrosis	Other minor compli-cation	Any mild complication
Silander 2012/ 2013 Sweden	RCT	51 months				Frequency not specified						Frequency not specified
Romesser 2012 USA	Non-randomised controlled study	3 months	2 % (7/325)			6 % (21/325)			6 % (9/325)	1 % (2/325)		
Avery 2008 UK	Case series	30 days – 6.2 years	3 % (4/218)	3 % (6/218)		7 % (15/218)						12 % (26/218)
Bäck 2014 Finland	Case series	1 week – 37 months				19 % (22/114)						26 % (30/114)
Baschnagel 2013 USA	Case series	2 years	1% (2/144)		1% (1/144)				1% (2/144)			
Chan 2010 China	Case series	>150 days	6% (7/108)	4% (4/108)	6% (7/108)	3% (3/108)						19% (21/108)
Foster 2007 UK	Case series	>18 months	1% (2/148)		3% (4/148)	3% (5/148)			1% (2/148)		2% (3/148)	

Appendix 4:12: **Minor complications associated with prophylactic gastrostomy in patients with with head-and-neck cancer undergoing chemoradiotherapy.**

Author, Year, Country	Study design	Follow-up	Tube leakage	Tube obstruction	Tube dis-lodgement	Minor infection	GI disorder	General disorder	Pain	Mild skin necrosis	Other minor compli-cation	Any mild complication
Lawson 2009 USA	Case series	Up to 3 years.		1% (1/102)	11% (11/102)	9% (9/102)			6% (6/102)		4% (4/102)	
McAlister 2013 UK	Case series	3 years	PEG: 5% (1/21) RIG: 2% (2/89)	PEG: 5% (1/21) RIG: 1% (1/89)							PEG: 5% (1/21) RIG: 0%	PEG: 14% (3/21) RIG: 3% (3/89)
Nguyen 2006 USA	Case series	Median: 19 months	2% (2/103)			1% (1/103)						3% (3/103)
Pulkkinen 2014 Germany	Case series	Not reported				21% (42/194)	2% (4/194)		10% (20/194)		1% (2/194)	
Raykher 2009 USA	Case series	Not reported	13% (21/161)			7% (12/161)	1% (1/161)		12% (20/161)		2% (3/161)	

Appendix 5

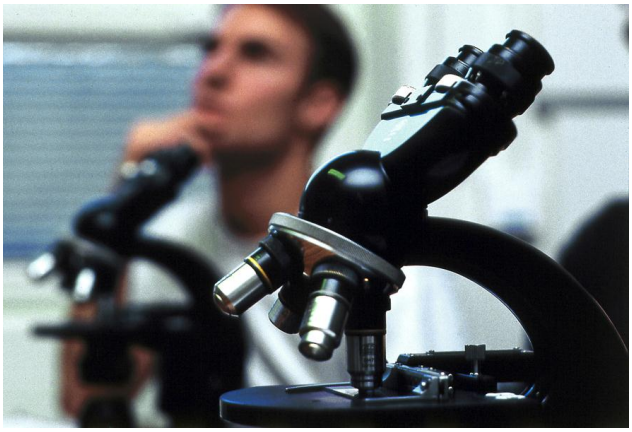
ETHICAL ANALYSIS OF PROPHYLACTIC GASTROSTOMY

Question	Answer/ comment
1. From the patient's perspective, how does this prophylactic gastrostomy affect the patient's quality of life and life expectancy?	It may initially negatively affect the quality of life before the chemoradiotherapy has caused dysphagia and malnutrition. However, many patients may prefer a percutaneous gastrostomy to a nasogastric tube since it is not visible to other people. In is not shown that the life expectancy is improved in comparison to other nutritional support..
2. How severe is the patient's need that the prophylactic gastrostomy must meet?	Very severe. Malnutrition secondary to chemoradiotherapy is a risk factor for mortality.
3. Does prophylactic gastrostomy have any influence on how others view the patient (concerning humanity and human dignity), or on how the patient views himself or herself (concerning humanity and human dignity)?	Compared to a nasogastric tube a percutaneous gastrostomy does not affect how other people view the patient, since it is not visible when the patient is dressed. Most patients do not report the presence by a percutaneous gastrostomy per se change their view on themselves.
4. Can prophylactic gastrostomy affect the patient’s ability and possibility to be independent?	A patient with head or neck cancer is always dependent on the health care system. A percutaneous gastrostomy decreases this independence to some degree, since it will reduce the need for hospitalisation for total parenteral nutrition.
5. If implemented, does this prophylactic gastrostomy require any special steps to not compromise the patient's autonomy?	The autonomy of a patient with head or neck cancer undergoing chemoradiotherapy is always compromised. The patient has a potential lethal condition, and the chemoradiotherapy is associated with adverse effects. The use of a prophylactic percutaneous gastrostomy will decrease this negative effect on the autonomy to some extent since it will enable the patient to stay longer at home. The feeding process will also be faster than feeding via a nasogastric tube.
6. How does prophylactic gastrostomy affect the patient’s physical, moral and personal integrity?	The physical integrity is negatively affected by the placement of an extracorporeal device into the body. The personal integrity can be negatively affected by the delivery of nutrional solutions to the home of the patient. Currently, these are delivered by postal services that put the boxes with the nutritional solutions outside the patient’s door. Thereby, neighbours will become aware of that the person is sick.
7. Is prophylactic gastrostomy cost-effective?	Not known.
8. How does this prophylactic gastrostomy affect resources?	Only to a minor extent since the number of patients of this particular patient category patient is limited.

9. Is this prophylactic gastrostomy in conflict with professional values?	No.
10. Does prophylactic gastrostomy change the role of the professional in relation to the patient?	No.
11. Does prophylactic gastrostomy affect, or does it put any new demands on, a third party?	Yes. Some patients will need the assistance of their spouse or other relatives to connect the nutrional solution to the gastrostomy. This does not differ from the situation of the usage of a nasogastric tube.
12. Is there any legislation of relevance with regard to prophylactic gastrostomy?	No.
13. Is there any risk of conflict between the use of prophylactic gastrostomy and values of the society, or values of different groups?	The prophylactic placement and later use of gastrostomy is optional. By thorough information of the patient he /she will make the final decision whether it will be accepted to him/her based on their cultural heritage or religious beliefs.
14. Is there a risk that an introduction of prophylactic gastrostomy will cause a conflict with particular interests?	Probably not.
15. Can an introduction of prophylactic gastrostomy influence the trust of the health care system?	If the patient has been thoroughly, and correctly, informed of the benefits and risks involved in the use of a gastrostomy the risk of forthcoming mistrust of the health care system should be minimised. However, without such information it is a definite risk thet the trust in the health care system will be negatively affected.
CONCLUSIONS	The autonomy, independence and integrity of a patient with head or neck cancer will all be affected by a prophylactic gastrostomy. Therefore, it is of utmost importance to inform the patient thoroughly, and correctly, about this type of nutritional support. It is equally important that the patient is fully aware that his or her opinion is crucial in the final decision to accept, or not accept, prophylactic placement and later use of the gastrostomy. A percutaneous gastrostomy is less visible and most probably affects the autonomy of the patient less than a nasogastric tube. Since the nutrition solutions are delivered to the patient's doorstep the use of a gastrostomy (regardless of whether it is a gastrostomy or a nasogastric tube) will compromise the patient's personal integrity.

Region Västra Götaland, HTA-centrum

Health Technology Assessment
Regional activity-based HTA



HTA

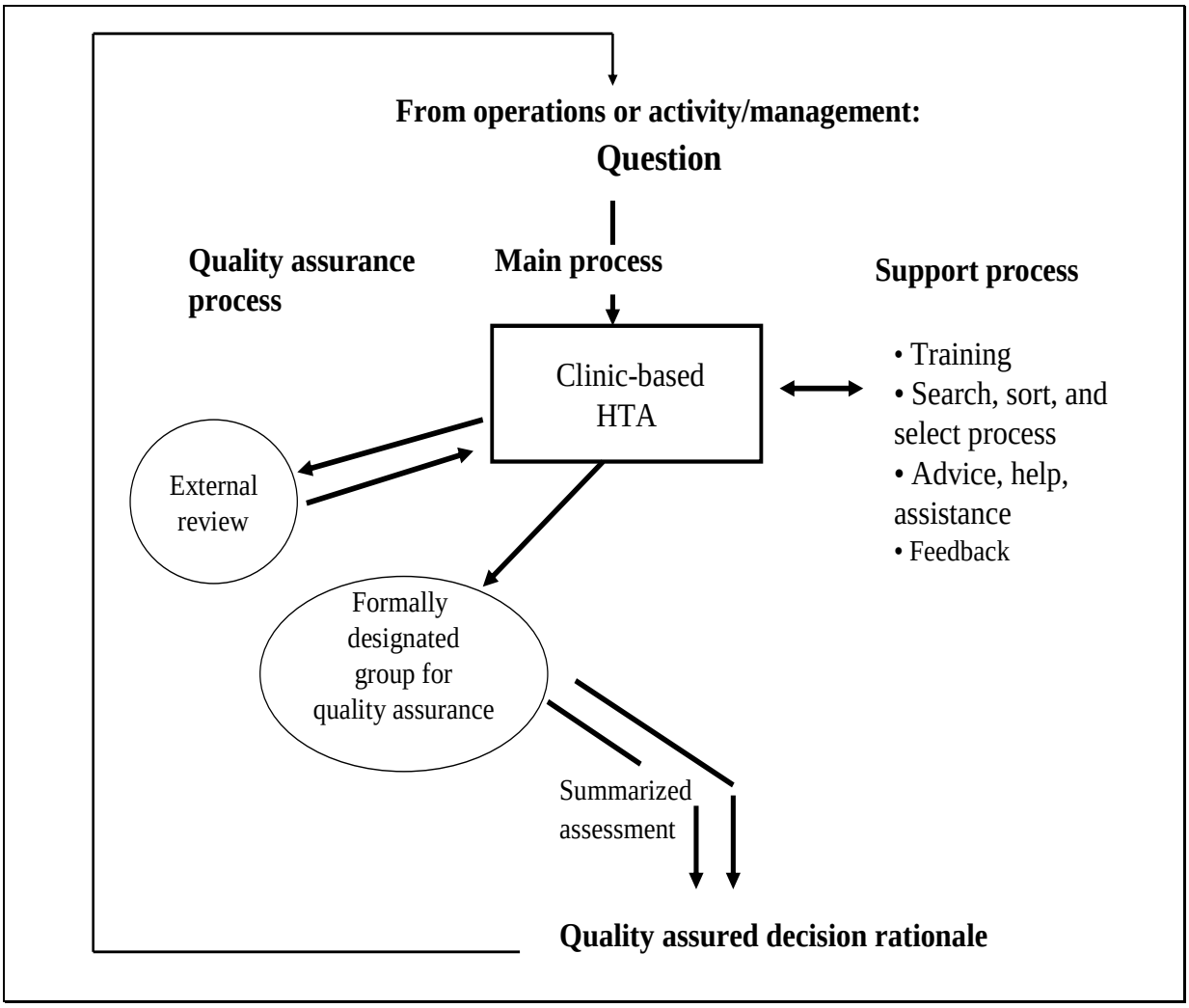
Health technology assessment (HTA) is the systematic evaluation of properties, effects, and/or impacts of health care technologies, i.e. interventions that may be used to promote health, to prevent, diagnose or treat disease or for rehabilitation or long-term care. It may address the direct, intended consequences of technologies as well as their indirect, unintended consequences. Its main purpose is to inform technology-related policymaking in health care.

To evaluate the quality of evidence the Centre of Health Technology Assessment in Region Västra Götaland is currently using the GRADE system, which has been developed by a widely representative group of international guideline developers. According to GRADE the level of evidence is graded in four categories:

High quality of evidence	= (GRADE⊕⊕⊕⊕)
Moderate quality of evidence	= (GRADE ⊕⊕⊕O)
Low quality of evidence	= (GRADE ⊕⊕OO)
Very low quality of evidence	= (GRADE ⊕OOO)

In GRADE there is also a system to rate the strength of recommendation of a technology as either “strong” or “weak”. This is presently not used by the Centre of Health Technology Assessment in Region Västra Götaland. However, the assessments still offer some guidance to decision makers in the health care system. If the level of evidence of a positive effect of a technology is of high or moderate quality it most probably qualifies to be used in routine medical care. If the level of evidence is of low quality the use of the technology may be motivated provided there is an acceptable balance between benefits and risks, cost-effectiveness and ethical considerations. Promising technologies, but a very low quality of evidence, motivate further research but should not be used in everyday routine clinical work.

Christina Bergh, Professor, MD.
Head of HTA-centrum


From operations or activity/management:
Question
Quality assurance process
Main process
Support process
Clinic-based HTA
• Training
• Search, sort, and select process
• Advice, help, assistance
• Feedback
External review
Formally designated group for quality assurance
Summarized assessment
Quality assured decision rationale

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