

# Gastrostomy versus nasogastric tube feeding for chemoradiation patients with head and neck cancer: the TUBE pilot RCT

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**Disclaimer:** This report contains transcripts of interviews conducted in the course of the research and contains language that may offend some readers.

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## Scientific summary

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# Scientific summary

## Background

Each year the NHS treats 9000 new patients with head and neck squamous cell cancers (HNSCCs). Stage III and IV HNSCC can be treated non-surgically by chemoradiation therapy (CRT). This treatment offers an overall 60% chance of cure, but at the cost of significant side effects, which have an impact on basic functions of eating, drinking, communication and breathing. Eating and drinking problems are a top concern for HNSCC survivors. Specifically, CRT leads to loss of taste, dry mouth, pain on swallowing and difficulties with swallowing mechanics secondary to fibrosis, which can result in decreased efficiency and a high risk of aspiration of material. A small proportion of patients may never eat or drink again following treatment. Recent work has shown that aspiration pneumonia is responsible for 19% of non-cancer-related deaths in HNSCC at 5 years post treatment.

Over 90% of patients undergoing this treatment require nutritional support to prevent substantial weight loss during and after CRT. There are two options for nutritional support: (1) to have a gastrostomy tube placed prior to the onset of CRT and for patients to start feeding when their nutritional intake becomes compromised; or (2) to have a nasogastric tube fitted, if and when it becomes necessary, as advised by clinical staff. There is no agreed practice across the UK and no national guidelines, with each centre adopting its own practice in accordance with local policies.

Each feeding method has advantages and disadvantages. Nasogastric tube feeding has lower rates of morbidity associated with placement of the tube than gastrostomy tube feeding alone. However, the former is associated with a greater negative effect on body image, is considered more inconvenient and uncomfortable for patients and requires patients to be hospitalised during treatment. Feeding via gastrostomy tube is faster, but it requires a pre-CRT hospital admission and is costlier than a nasogastric tube. Gastrostomy feeding has been identified as a predictor of poorer diet scores at 1 year and of late-onset dysphagia following radiotherapy. This is thought to be because the duration of dependency on alternative feeding is longer than is required for nasogastric tube feeding, giving rise to 'disuse atrophy' and, thus, a dysfunctional swallowing mechanism. Systematic reviews have highlighted the lack of evidence regarding the impact of a gastrostomy on swallowing outcomes, which has resulted from methodological flaws and significant selection bias. One randomised controlled study (RCT) from Australia aimed to address this question, but the study closed early, as the number of patients recruited was insufficient. Limited information was available on the problems associated with recruitment. Findings on which feeding tube route resulted in better swallowing outcomes were inconclusive.

The purpose of this study was to explore the feasibility of conducting a RCT comparing the two feeding tube options, with particular emphasis on patient willingness to be randomised and clinician willingness to approach eligible patients.

## Aim and objectives

Our aim was to determine whether or not a definitive RCT of head and neck cancer patients with minimal swallowing problems undergoing CRT comparing prophylactic gastrostomy tube feeding with oral feeding plus as-needed nasogastric tube feeding was feasible (the TUBE trial). The TUBE trial feasibility phase is a necessary prelude to a full trial of these complex interventions, to assess whether or not an adequate proportion of eligible patients can be recruited into the trial, according to both quantitative and qualitative data parameters.

The objectives were to:

1. identify recruitment and retention rates and explore barriers to, and facilitators of, trial implementation and reasons for attrition
2. carry out a preliminary estimation of key parameters to inform design and study processes
  - i. refine power/sample size for the definitive trial primary outcome
  - ii. test subsidiary quality-of-life outcomes
  - iii. monitor nutritional parameters
3. provide preliminary health economics metrics
  - i. assess the economic value of information derived from the feasibility study
  - ii. provide a preliminary estimate of the costs, effects and relative cost-effectiveness.

## Methods/design

This was a mixed-methods multicentre study to establish the feasibility of a RCT comparing oral feeding plus pre-treatment gastrostomy with oral feeding plus as-required nasogastric tube feeding in patients with HNSCC.

We aimed to randomise 60 participants to the two arms of the study (using a 1 : 1 ratio). The eligibility criteria were patients with advanced-staged HNSCC who were suitable for primary CRT with curative intent and who presented with no swallowing problems.

The primary outcome was the willingness to be randomised and recruited to the trial. A qualitative process evaluation investigating patient, family and friends and staff experiences of trial participation was conducted. Patient interviews were conducted within 2 weeks of recruitment discussions. The focus of these interviews was on the patients' experiences and understanding of trial processes and the intervention (i.e. feeding tube options). When possible, follow-up interviews were conducted approximately 8 months after recruitment to explore the acceptability of assessment tools and patients' experiences of the intervention.

Clinicians (medical, nursing, dietetic and speech and language specialists) were interviewed to allow us to understand and map existing processes of care in relation to tube feeding in this patient group, and to explore experiences of, and perspectives on, the TUBE trial and the study interventions.

Baseline data included patient demographics, disease characteristics and the treatment plan. Questionnaires included the MD Anderson Dysphagia Inventory, the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – C30 (EORTC QLQ-C30), the EORTC QLQ – Module for Head and Neck Cancer (EORTC QLQ-H&N35) and the Short Form questionnaire-36 items. Clinical assessments included body mass index and usual weight, Performance Status Scale (normalcy of diet subscale) and data from oral health assessment. Questionnaires and assessments were collected again at 3 months, 6 months and 12 months.

A within-trial economic evaluation was conducted. Data on the use of hospital and primary care services and patient/family/carer costs were collected. A bespoke decision-analytic economic model was also developed to estimate the costs, effects and relative cost-effectiveness of the two feeding tube options. The clinical pathways of patients within the feasibility study were used to help inform the model structure. An economic value-of-information analysis was performed to identify if further research would be cost-effective.

## Results

The trial was conducted across five head and neck cancer centres, with the period of recruitment ranging from 3 to 11 months. In total, 75 patients were identified as fitting the eligibility criteria, of whom 17 agreed to being randomised [0.23, 95% confidence interval (CI) 0.13 to 0.32]. Retention rates were high at completion of treatment (0.94, 95% CI 0.83 to 1.05). Data completeness was excellent.

The qualitative substudy identified a collection of factors that had an impact on recruitment to the trial, many of which were potentially amenable to change. Clinical and organisational contexts were critical to the implementation of the TUBE trial. Variation in clinician preferences and practices was apparent. Operational contexts concerning the set-up and conduct were identified as extrinsic factors that had an impact on the study. The eligibility criteria and the interpretation of these were seen as potential barriers. Integrating research and clinical pathways required additional work. There was over-riding support for identifying best practice for feeding tube selection.

A key issue explaining the differential recruitment between sites was the degree to which the whole multidisciplinary team gave a consistent demonstration of equipoise at all patient interactions at which supplementary feeding was discussed. Patients described their decision-making regarding randomisation. Some had strong preferences, whereas others were ambivalent over feeding tube selection. There were concerns regarding whether or not participation in the TUBE trial could affect the timing of the patients' care pathways in the lead-up to treatment. The importance of feeding tube placement and its perceived problems became more obvious to patients during and after CRT. Patients described managing their feeding tube. Patients with a nasogastric tube reported its insertion as being very unpleasant, and there were concerns over dislodgement.

The economic model, based on published evidence and expert opinion, suggests that pre-treatment gastrostomy tube feeding is not a cost-effective option over a 6-month time horizon. However, more work is required to substantiate this finding. The economic value-of-information analysis indicates that conducting additional research to eliminate uncertainty around all model parameters is highly likely to be cost-effective.

## Conclusions

The TUBE trial identified a range of issues that affected recruitment to the feasibility of randomising patients with HNSCC being treated with CRT to either pre-treatment gastrostomy or reactive nasogastric tube placement. Our process evaluation identified organisational and operational issues that need to be overcome to improve recruitment for such a trial, when multiple professionals have a stake in deciding recruitment, driven by clinical experience and personal views. At least one-third of patients could be recruited to a future trial to address this important treatment decision if appropriate measures are implemented to address these issues. The health economic argument is reasonably compelling to warrant the need for a further study, the design for which will need to take into consideration the results from the TUBE trial.

## Trial registration

This trial is registered as ISRCTN48569216.

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