A pragmatic randomised controlled trial of the cost-effectiveness of palliative therapies for patients with inoperable oesophageal cancer

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Executive summary

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Background
Inoperable oesophageal cancer is a devastating diagnosis. Without treatment, swallowing deteriorates with dramatic effects on quality of life. There is no evidence for using one dysphagia-relieving palliative treatment over another. Self-expanding metal stents (SEMS) may be most effective, but are expensive and the NHS burden of palliation is escalating. A prospective, randomised controlled trial (RCT) is essential for informed, cost-effective treatment choice.

Objectives
The primary objective of this study was to compare whether treatment with SEMS is more cost-effective than treatment with conventional modalities in patients with inoperable oesophageal cancer.

The secondary objectives were also included as part of the study. The first was to determine whether metal stents provide a better quality of swallowing, require fewer follow-up interventions and provide a greater number of quality-adjusted life-years. The second was to determine quality of life effects associated with all treatment and health outcomes.

Methods
Design
A multicentre pragmatic RCT with health economic analysis.

Setting
Seven NHS hospitals were selected to represent a cross-section of UK hospitals in terms of facilities and staffing.

Subjects
All patients attending the centres with oesophageal cancer deemed unsuitable for surgery were assessed for inclusion in the main trial; 217 patients were randomised. A health state utilities substudy was also performed in 71 patients who had previously received curative surgery for oesophageal cancer.

Interventions
Eligible patients were randomised to one of four treatment groups within two study arms. Assessments were performed by research nurses at enrolment, 1 week following treatment and thereafter at 6-weekly intervals until death, with prospective data collection on complications and survival. Structured interviews to elicit patient preferences to health states and treatments were performed in a substudy, using one of two randomly assigned techniques.

Main outcome measures
The main outcome measures were: dysphagia grade at 6 weeks; quality of life at 6 weeks; survival; resources consumed from randomisation to death; and quality-adjusted life-years.

Results
It was found that there was no difference in cost or effectiveness between SEMS and non-SEMS therapies. It was also found that the 18-mm SEMS had equal effectiveness to, but less associated pain than, 24-mm SEMS. Rigid intubation was associated with a worse quality of swallowing and increased late morbidity. Bipolar electrocoagulation and ethanol-induced tumour necrosis were found to be poor in primary palliation. A survival advantage for non-stent therapies was evident, but with a significant delay to treatment. The length of hospital stay accounts for the majority of the cost to the NHS. Patients were found also to have distinct individual treatment preferences.

Conclusions
It was concluded that rigid tubes and 24-mm SEMS should no longer be recommended. Similarly, bipolar electrocoagulation and ethanol-induced tumour necrosis should not be used for primary palliation.

Implications for healthcare
It is suggested that the choice in palliation should be between non-stent and 18-mm SEMS treatments, and that non-stent therapies should be made more
available and accessible to reduce delay. A multidisciplinary team approach to palliation may be appropriate, with consideration also being given to length of stay in order to reduce the NHS burden of palliation, with due regard to quality of life and costs.

**Recommendations for further research**
A randomised controlled clinical trial of 18-mm SEMS versus non-stent therapies considering survival and quality of life end-points would be valuable. An audit of palliative patient admissions is also suggested in order to determine the reasons and need for inpatient hospital care, with a view to implementing cycle-associated change to reduce inpatient stay. Delay in palliative radiotherapy treatment should also be studied, with a view to implementing cycle-associated change to reduce waiting time.

**Publication**
The research findings from the NHS R&D Health Technology Assessment (HTA) Programme directly influence key decision-making bodies such as the National Institute for Clinical Excellence (NICE) and the National Screening Committee (NSC) who rely on HTA outputs to help raise standards of care. HTA findings also help to improve the quality of the service in the NHS indirectly in that they form a key component of the ‘National Knowledge Service’ that is being developed to improve the evidence of clinical practice throughout the NHS.

The HTA Programme was set up in 1993. Its role is to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and provide care in the NHS. ‘Health technologies’ are broadly defined to include all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care, rather than settings of care.

The HTA programme commissions research only on topics where it has identified key gaps in the evidence needed by the NHS. Suggestions for topics are actively sought from people working in the NHS, the public, consumer groups and professional bodies such as Royal Colleges and NHS Trusts. Research suggestions are carefully considered by panels of independent experts (including consumers) whose advice results in a ranked list of recommended research priorities. The HTA Programme then commissions the research team best suited to undertake the work, in the manner most appropriate to find the relevant answers. Some projects may take only months, others need several years to answer the research questions adequately. They may involve synthesising existing evidence or designing a trial to produce new evidence where none currently exists.

Additionally, through its Technology Assessment Report (TAR) call-off contract, the HTA Programme is able to commission bespoke reports, principally for NICE, but also for other policy customers, such as a National Clinical Director. TARs bring together evidence on key aspects of the use of specific technologies and usually have to be completed within a limited time period.

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