An investigation into
the perioperative nutritional status of patients
with oesophagogastric carcinoma
and
the effect of hospital food fortification
and supplementary home enteral feeding on
nutritional status and nutritional intake

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Declaration

This work has not previously been accepted in substance for any degree and is not concurrently submitted in candidature for any degree.

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Summary

Patients who undergo surgery for upper gastrointestinal carcinoma are at high risk of inadequate nutritional intake and deterioration in nutritional status postoperatively. Early postoperative enteral feeding though widely used in this patient population is rarely continued throughout hospitalisation and patients become dependent on hospital food to meet nutritional requirements. The provision of energy dense foods has been found to improve voluntary energy intake and attenuate weight loss in institutionalised elderly patients. The first part of this thesis (study 1) was undertaken to evaluate the effects of energy and protein dense food provision to patients following upper gastrointestinal surgery for carcinoma.

A control group, comprising forty-four consecutive admissions with oesophagogastric carcinoma that underwent upper gastrointestinal surgery and received standard postoperative care, was compared with thirty-eight consecutive admissions that received fortified foods following surgery.

The provision of fortified foods resulted in a significant improvement in individual energy and protein intakes (p<0.003) but no difference was found in energy and protein intake between control and intervention groups. Maximum oral energy and protein intake during hospitalisation did not exceed 60% overall. Gastric and oesophageal carcinoma patients were well nourished preoperatively indicated by a median preoperative weight loss of less than 10% and a body mass index within the normal or overweight range. A large proportion of patients experienced weight loss during hospitalisation and following discharge home with no difference between control and intervention groups. The follow-on to this study (study 2) involved twenty-one consecutive patients who following oesophagogastrectomy for oesophageal carcinoma were discharged home with supplementary enteral feeding. Nutritional intake and nutritional status was compared with matched patients from the previous study who following oesophagogastrectomy were discharged home with dietary advice alone.

This patient group (enteral feeding group) was also found to be well-nourished preoperatively. Total energy and protein intake was significantly higher in the patients receiving supplementary enteral feeding four weeks following discharge (p<0.001 and p<0.011 respectively). Serum albumin levels were also significantly higher four weeks following discharge (p=0.021). The supplementary feeding was not found to affect oral intake. Perioperative weight loss up to four weeks post discharge was less in the enteral feeding group (p=0.04).

The study highlights the difficulties these patients experience with oral intake post operatively despite intensive dietary monitoring, support and food fortification during hospitalisation. It suggests that continued enteral feeding following discharge home may attenuate weight loss and improve nutritional intake. The effect on patient centred outcomes and quality of life warrants further research.
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Chapter one

Introduction and literature review
1.0 Introduction

Although there is no universally accepted definition of malnutrition, the following has been suggested (Elia 2000):

Malnutrition is a state of nutrition in which a deficiency or excess (or imbalance) of energy, protein, and other nutrients causes measurable adverse effects on tissue/body form (body shape, size and composition) and function, and clinical outcome.

It is well documented that malnutrition affects many cancer patients. A particularly high incidence has been reported among upper gastrointestinal (GI) cancer patients (DeWys et al 1980, Bozzetti et al 1981, Saito et al 1990). In oesophageal carcinoma, dysphagia and anorexia are considered to be the main cause of malnutrition (Belghiti et al 1987, Saito et al 1991). In the case of gastric carcinoma, delays in diagnosis are common and as a result patients frequently present with advanced disease and poor nutritional status (Wastell 1992). In both cases tumour type and stage of disease have been shown to affect nutritional status (Saito et al 1991, Bozzetti et al 1981).

Oesophagogastrectomy and total gastrectomy performed for the treatment of oesophageal and gastric carcinoma respectively are extensive surgical procedures and may have a significant impact on nutritional status (Sitges-Serra et al 1990, Bozzetti et al 1990). These operations necessitate a prolonged period of ‘nil by mouth’ postoperatively until the integrity of the anastomosis is established. Progressive weight loss following surgery has, been demonstrated (Johansson and Walther 2000, Ludwig et al 2001, Sategna-Guidetti and Bianco 1989). Nonetheless the nutritional management of these patients remains an area of controversy with some studies showing evidence of benefit of perioperative nutritional support (Bozzetti et al 2001, Braga et al 2002, Gianotti et al 2002) whilst others do not (Watters et al 1997).
The inadequacies of hospital catering systems and their failure to meet the needs of patients have recently been highlighted (Allison 1999). It has been recommended that the provision of food suitable for the sick should not be considered a hotel function but a treatment (Allison 1999). Studies examining the use of more individualised food prescriptions on nutritional intake of elderly, orthopaedic, medical and surgical patients have found it to be of benefit in removing patients from energy but not protein deficit (Olin et al 1996, Gall et al 1998, Barton et al 2000b).

Patients who undergo the extensive surgical procedures of oesophagogastrrectomy or gastrectomy become dependent on hospital food and oral dietary supplements (if offered) to sustain them during illness once artificial nutrition support (if provided) is withdrawn. In the current hospital climate where hospital menus are institutionalised, this is likely to put them in a vulnerable position for further deterioration of their nutritional status. Once discharged home they become dependent on home prepared foods and oral dietary supplements (if tolerated) to meet their nutritional requirements. With the introduction of oral intake following gastrectomy or oesophagogastrrectomy, the frequently encountered problems of early satiety, anorexia and nausea associated with lack of the stomach reservoir capacity and altered intestinal motility may compromise nutritional intake (Braga et al 1988, Braga et al 1990, Tabira et al 2000). These problems may continue for an indeterminate length of time (McLarty et al 1997, Johansson and Walther 2000, Tabira et al 2002). Even in the absence of pre-existing malnutrition it seems reasonable to infer that these patients are at considerable nutritional risk postoperatively).

Little published material exists on the provision of fortified foods to patients following upper GI surgery or the use of jejunostomy feeding to supplement oral intake following discharge home. The aims of the present study were to determine if the provision of normal foods enriched with protein and energy during hospitalisation, in conjunction with
intensive dietetic support, may be of benefit to this patient group in improving their nutritional intake and nutritional status during hospitalisation and also to determine if continuing supplementary jejunostomy feeding following discharge home may facilitate an improved nutritional intake and consequently prevent deterioration in nutritional status.
1.1 Oesophageal Carcinoma

1.1.1 Epidemiology

Studies have revealed a wide geographical variation in incidence of carcinoma of the oesophagus. The highest incidence in the world is the Linxian province in China where it is commonest single cause of death with more than 100 cases per 100,000 population per annum (Bancewicz 2000). Elsewhere incidence varies from less than five per 100,000 in whites in the USA to 26.5 per 100,000 in some regions of France (Bancewicz 2000). In the UK it represents 1.9% of all cancers (Doll and Peto 1987) but incidence is rising both in the UK and worldwide (Guillou and Monson 2001). It is more common in men than in women and incidence rises with age (Watson 1999).

1.1.2 Aetiology

In the Western world alcohol and smoking are important risk factors for cancer of the oesophagus (Watson 1999). These two factors account for the great majority of cases of squamous cell carcinoma. The mechanism by which alcohol increases the risk of cancer is not known, however the poor diet associated with increased alcohol consumption may be a factor as well as the irritation of the mucosal lining leading to increased cell division and spontaneous mutation. Alcohol and tobacco appear to act in synergy to increase the rate of carcinogenesis (Watson 1999). There is little evidence that either is implicated in adenocarcinoma of the oesophagus which is supplanting squamous cell carcinoma as the predominant histologic type of oesophageal carcinoma in the western world (Bancewicz 2000). The established risk factors for adenocarcinoma of the oesophagus are Barrett’s oesophagus, gastro-oesophageal reflux and obesity (Bancewicz 2000). Medications that relax the lower oesophageal sphincter might contribute to increasing the risk as well as the decreasing prevalence of *Helicobacter pylori* infection (Lagergren 2005).
1.1.3 Pathology

(i) Squamous cell carcinoma

Squamous cell carcinoma originates in the stratified flat epithelium in any part of the oesophagus. It appears as three types (Watson 1999).

1. Fungating carcinomas have a large polypoid intraluminal growth.
2. Ulcerating tumours have a large central ulcer with raised everted edges.
3. Infiltrative carcinomas are uncommon. Usually there is a small central ulcer but the bulk of the disease is in the submucosa and muscularis mucosa (Watson 1999).

(ii) Adenocarcinoma

Adenocarcinoma originates in the glandular epithelium, mostly Barrett’s epithelium. Ninety percent occur in the distal third of the oesophagus (Beers and Berkow 1999).

1.1.4 Clinical Features

Early oesophageal cancer may go unnoticed (Beers and Berkow 1999). When the lumen of the oesophagus becomes constricted to <14mm, dysphagia is the most common symptom. Difficulty is experienced on swallowing solids first, then semi-solids and finally liquids (Beers and Berkow 1999). Most cancers involve at least a 4cm length of the oesophagus before diagnosis, and the typical patient will have had 3-6 months of dysphagia before first contacting a physician (Riccardi and Allen 1999). An inevitable consequence is a reduced dietary intake and subsequent weight loss (Watson 1999). The metabolic effects of the tumour itself may exacerbate weight loss. Pain is uncommon and if it occurs is a late manifestation (Watson 1999).

1.1.5 Investigations

1. Upper gastrointestinal endoscopy provides tissue for diagnostic biopsy and should be performed in all patients in whom a diagnosis of oesophageal cancer is suspected (Watson 1999).
2. Computed tomographic (CT) scanning of the neck, chest, abdomen and pelvis may help stage the tumour by identifying enlarged lymph nodes, metastasis to distant organs, and malignant fluid collections (pleural effusions, ascites) and may help determine respectability (Watson 1999).

3. Endoscopic ultrasonography is more widely used in recent years and may enable more accurate staging than CT scanning (Watson 1999). It comprises a rotating ultrasonic transducer built into the tip of a dedicated endoscope. The ability to scan in close proximity to the oesophageal wall, gland fields and contiguous structures confers advantages over other staging methods in that the individual layers of the oesophageal wall are clearly discernible and a distinction can be made between normal and metastatic lymph nodes (Watson 1999).

4. Laparoscopy enables a tissue diagnosis to be made and the diagnosis of peritoneal metastases and liver and nodal metastases (Watson 1999).

1.1.6 Treatment

Treatment depends on the tumour stage, exact tumour size, location and the patient's wishes (Beers and Berkow 1999). Curative treatment should be attempted providing the patient is fit enough to withstand a major surgical procedure and there is no evidence of spread to the supraclavicular glands, tracheo-bronchial tree or liver (Watson 1999). The choice of operation depends on the location and size of the tumour and the experience of the surgeon (Beers and Berkow 1999). The principles of resection with cure in mind are wide resection margins and radical lymph node clearance within the chest and for distal growths at the oesophagogastric junction also in the upper abdomen (Guillou and Monson 2001). The conventional method of resection is by open operation, which may involve opening the abdomen and thorax (Guillou and Monson 2001). Transhiatal removal is now also possible (without thoracotomy) where the abdomen alone is opened and the oesophagus alone is freed in the chest by blunt dissection through the diaphragmatic hiatus
(Guillou and Monson 2001). Stomach or colon for reconstruction is then passed through the posterior mediastinum to the neck where it is anastomosed to the upper oesophagus through a cervical incision (Guillou and Monson 2001).

Other operations

1. If surgery is undertaken for carcinoma of the middle third of oesophagus a partial oesophagogastrectomy is performed. Only about one fifth of the stomach is removed and this is best carried out by a right thoracotomy (Ivor Lewis) operation (Guillou and Monson 2001).

2. Carcinoma of the lower third oesophagus may be resected by a partial oesophagogastrectomy with a larger portion of the stomach removed, about three fifths, often together with the spleen (Guillou and Monson 2001).

Oesophageal resection is a major elective procedure and the potential for complications is high (Watson 1999). Complications include: haemorrhage, infection, thromboembolic disease and cardiovascular problems. Pulmonary complications may range from a simple chest infection to pneumonia, pulmonary collapse, persistent pneumothorax, haemothorax or damage to the trachea or bronchus (Watson 1999).

1.1.7 Prognosis

With improvements in preoperative preparation, operative and anaesthetic technique and postoperative management, there has been a significant decline in postoperative mortality and morbidity. Stage of disease is the overriding factor affecting survival (Guillou and Monson 2001). As the degree of wall penetration increases so does the likelihood of nodal metastases. Other factors that may affect survival include the type of resection performed and the use of adjuvant therapy: chemotherapy, radiotherapy or both (Wenz and Mamon 2001).
Multinodal therapy (surgery, radiotherapy, and chemotherapy in the same treatment plan) has been used to control both local disease and distant metastasis. Preoperative radiotherapy and chemotherapy have been used to reduce tumour bulk and enhance the respectability (Wenz and Mamon 2001). However it is not established if preoperative therapy improves the cure rate. Various combinations of preoperative radiotherapy with cisplatin and 5-fluorouracil (5-FU) or preoperative chemotherapy alone have been studied (Bancewicz 2000, Wenz and Mamon 2001).

There is some data that multimodality treatment may result in prolonged disease free and overall survival in patients (Walsh et al 2002, Medical Research Council Oesophageal Cancer Working Party 2002). In these studies benefit has been found in patients with squamous cell or adenocarcinoma and is superior to that achieved with surgery alone.
1.2 Gastric Carcinoma

1.2.1 Epidemiology

Gastric cancer is one of the most common causes of death from malignant disease (Fielding 1999). There are wide international variations in incidence (Fielding 1999). It is common in Japan, South America and Eastern Europe, occurs with intermediate frequency in Western Europe and is uncommon in the USA (Fielding 1999). In addition to international variations, the incidence varies within countries. In the UK areas of high incidence include South Wales, Scotland and the Midlands. The mortality ratio in Wales exceeds that of the UK as a whole at 34 deaths per 100,000 males compared with 23 deaths per 100,000 (Fielding 1999). Delays in diagnosis are common and as many as one in three patients in Britain continue to present with advanced incurable disease. The incidence is twice as high in males as females and highest incidence is in those over 60 years (Fielding 1999).

1.2.2 Aetiology

There are a few definite premalignant conditions and risk factors (Primrose 2000). These include: a gastric polyp, pernicious anaemia, autoimmune and environmental gastritis, gastric surgery for benign conditions, gastric mucosal dysplasia, cigarette smoking, longstanding dyspepsia and genetic factors. Dietary factors may also be important, in particular dietary nitrates and nitrites, excessive salt intake and deficiency of antioxidants (Primrose 2000). In 1994, the WHO declared Helicobacter pylori to be a grade 1 carcinogen for gastric adenocarcinoma and mucosa associated lymphoid tumours of the stomach (Beers and Berkow 1999).
1.2.3 Pathology

Gastric adenocarcinoma accounts for 95% of malignant tumours of the stomach (Beers and Berkow 1999). Gastric adenocarcinomas can be classified according to gross appearance (Beers and Berkow 1999).

(1) Protruding. The tumour is polypoid or fungating.
(2) Penetrating. The tumour has a well circumscribed border and may be ulcerated.
(3) Spreading. The tumour shows superficial spread along the mucosa or infiltration within the wall.
(4) Miscellaneous. The tumour shows characteristics of two of the other types.

1.2.4 Staging

A number of staging systems have been devised, the most popular of which are the Union International Contra Cancer (UICC) stage and the TNM system (Table 1). The TNM system is the most appropriate system for staging gastric cancer (Sobin and Wittekind 1997).

T- The extent of the primary tumour

N-The absence or presence and extent of regional lymph node metastasis

M-The absence or presence of distant metastasis

The addition of numbers to these three components indicates the extent of the malignant disease, thus:

T0, T1, T2, T3, T4     N0, N1, N2, N3    M0, M1 (Table 1).

In effect the system is a ‘shorthand notation’ for describing the extent of a particular malignant tumour (Sobin and Wittekind 1997). Early gastric cancer is when the disease is confined to the mucosa and submucosa with or without lymph node involvement (T1, any N) (Fielding 1999). Advanced gastric cancer involves the muscularis (Fielding 1999). Early gastric cancer is eminently curable and even early gastric cancers associated with lymph node involvement have five-year survival rates in the region of 90% (Primrose
2000). However in the UK it is uncommon to detect gastric cancers at this stage (Primrose 2000).

Table 1.0 Staging, treatment and survival in carcinoma of the stomach (Guillou and Monson 2001)

<table>
<thead>
<tr>
<th>UICC stage</th>
<th>TMN stage</th>
<th>Treatment</th>
<th>5-year survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>T₁N₀M₀</td>
<td>Radical resection</td>
<td>70</td>
</tr>
<tr>
<td>11</td>
<td>T₂N₀M₀</td>
<td>Radical resection</td>
<td>30</td>
</tr>
<tr>
<td>111</td>
<td>T₀-4N₁-₃M₀</td>
<td>Radical resection</td>
<td>10</td>
</tr>
<tr>
<td>1V</td>
<td>T₄N₃M₀-₁</td>
<td>Palliation</td>
<td>1-2</td>
</tr>
</tbody>
</table>

1.2.5 Clinical features

It is a difficult disease to diagnose early because of the time lag between the commencement of the growth and the appearance of symptoms and also because of diversity in its presentation (Wastell 1992). Yet the key to improving the outcome of gastric cancer is early diagnosis (Primrose 2000).

Typical presenting symptoms include: gastric distension with inability to eat a normal meal, vomiting, anorexia with associated weight loss, anaemia with associated tiredness, weakness and pallor and persistent epigastric or abdominal pain (Wastell 1992).

1.2.6 Investigations

1. Fibreoptic endoscopy permits macroscopic assessment of the gastric mucosa and enables biopsies and direct brush cytology to be obtained (Fielding 1999).

2. Endoscopic ultrasonography is a relatively new technique that has the ability to define intramucosal or submucosal tumours and is useful in assessing resectability of oesophagogastric malignancies (Fielding 1999).
3. Laparoscopy allows direct visual assessment of the peritoneal cavity (Fielding 1999).
   The technique is associated with minimal morbidity and may avoid unnecessary laparotomy by its ability to detect small liver or peritoneal metastases (Fielding 1999).

1.2.7 Treatment

Excision of the tumour offers the only hope of cure (Fielding 1999). A curative resection is defined as a surgical resection with no macroscopic disease remaining.

The two most appropriate operations for gastric cancer are a radical subtotal distal gastrectomy and a total gastrectomy (Fielding 1999). For carcinoma of the lower one third of the stomach, a subtotal distal gastrectomy is the surgery of choice (Fielding 1999). For lesions of the middle third and upper third of the stomach the most appropriate resection is a total gastrectomy. In all resections, at least 5 cm clearance of the primary lesion should be achieved (Fielding 1999).

Total Gastrectomy

The extent of resection is a subject of debate. In Japan, where the best results are obtained, the stomach is removed together with the nodes within 3 cm of the tumour (N1) and the regional nodes (N2), and sometimes even more radical resections (N3) (Mine 1970, Maruyana 1987). D2 gastrectomy (removal of the second tier of nodes) at least is performed on all operable gastric cancer and the results of surgical treatment, stage for stage, in Japan are much better than commonly reported in the West (Kinoshita et al 1993). It is suggested that the main reasons for the successful Japanese results are technical skills and strict respect to the treatment schedule (Degiuli et al 1998). However the build of the average Japanese patient favours the performance of more radical procedures compared to the average patient in the West (Sue-Ling et al 1993). In the UK and Europe randomised trials have been set up to compare D1 and D2 gastrectomy (Bonenkamp 1995, Cushieri et al 1996). Overall it seems that a D2 gastrectomy is associated with a better oncological
outcome but higher operative morbidity and mortality. This may be related to the en bloc removal of the spleen and distal pancreas with the stomach (Bonenkamp 1995, Cushieri et al 1996) whereas in Japan the spleen and pancreas is preserved. Nonetheless many western surgeons prefer partial resections of the N1/N2 nodes only because of the lack of randomised controlled trials to show benefit.

**Subtotal Gastrectomy.**

This operation is similar to a total gastrectomy except the proximal stomach is preserved (Primrose 2000). After a partial gastrectomy, gastrointestinal continuity is restored either by a modification of the Biliroth I anastomosis or by a Biliroth II anastomosis (Fielding 1999). In the former, the whole of the divided end of the stomach is anastomosed end to end to the duodenum (Fielding 1999). For a Biliroth II reconstruction the duodenal stump is closed in two layers (Fielding 1999). After a gastrectomy the best reconstruction is a Roux-en-Y (Fielding 1999). This procedure is valuable because it prevents regurgitation of bile and pancreatic juice into the oesophagus (Guillou and Monson 2001).

**1.2.8 Prognosis**

Prognosis is poor. Examining the survival statistics from the UK some series demonstrate overall five year survival in the region of 5% (Primrose 2000). However it is an eminently curable disease provided that it is detected at an appropriate stage and treated adequately. Gastric cancer rarely disseminates widely before it has involved the lymph nodes and therefore there is an opportunity to cure the disease prior to dissemination (Primrose 2000). Early diagnosis is the key to success. Lymph node status is also an important factor and the Japanese have demonstrated that extensive lymphadenopathy increases survival (Mine 1970, Maruyana 1987).
Long-term complications of surgery

Most patients will have a reduced capacity particularly in the short term and need to be given nutritional advice emphasising the need for small, frequent, nutrient dense meals while the jejunum or small gastric remnant adapts (Primrose 2000). There is little functional difference between patients who have a total and subtotal gastrectomy (Primrose 2000). It is surprising but these patients rarely suffer from complications of gastric surgery such as dumping syndrome and diarrhoea (Primrose 2000). The loss of the parietal cell mass leads to vitamin B12 deficiency and replacement should be given routinely (Primrose 2000). Other nutritional deficiencies may occur and patients should be monitored with this in view (Primrose 2000).
1.3 Nutrition screening and assessment

Nutrition screening refers to a rapid, often initial evaluation undertaken by nurses, medical or other staff to detect significant risk of malnutrition. Nutrition assessment is a more detailed, more specific and more in-depth evaluation of nutritional status by an ‘expert’ (Elia 2003).

Many anthropometric, biochemical and immunological tests and body compositional analyses have been developed for nutrition assessment of patients. However, no single nutrition index can fully characterise the extent of malnutrition. There is currently no anthropometric measurement that is considered to be completely accurate as well as practical for use in the clinical setting (Charney 1995). More precise techniques such as measurements of total body potassium or sodium or dual energy x-ray absorptiometry may be too cumbersome for use outside the research setting. (Charney 1995).

1.3.1 Anthropometric parameters

Body weight and height

The simplest and oldest measure of nutritional status is body weight compared with previous or ideal body weight (Carney and Meguid 2002). The accuracy of this simple technique is dependent on regular calibration and maintenance of equipment. However, body weight can be measured simply and accurately and therefore weight loss is easily determined if weight is established before and after the occurrence of the loss. A limitation of using body weight alone is that no information is provided as to the components of weight lost or gained (Carney and Meguid 2002).

It is well established that unintentional weight loss is an indicator for poor prognosis. As early as 1936, Studley et al reported 33% mortality in patients with 20% weight loss admitted for ulcer surgery. More recently, Roy et al (1985) found that loss of >6% of usual body weight more accurately predicted morbidity and mortality in surgical patients
than several prognostic indices. The accuracy of the result however depends on the accuracy of the original weight estimation before the onset of weight loss. Many patients can give some estimate of their weight when well but the accuracy of the reported weight is questionable. Weight loss as determined by history has been found to be limited by poor predictive power (Morgan et al 1980). Nonetheless various national reports, organisations and individual workers have provided a range of cut off values, which generally fall within the 5-10% range of weight loss over the previous 3-6 months (or 10% of pre-illness weight), (Allison 1995, Detsky et al 1987, American Society for Parenteral and Enteral Nutrition 1989, Elia 2000). There is a paucity of information as to why these cut off values were chosen but it seems that clinical judgement was important.

Height measurement is another simple measure that is frequently neglected in the clinical setting (McWhirter and Pennington 1994). The accuracy of measurement may be improved when subjects are measured without shoes or headwear and maintain appropriate posture when standing (Charney 1995).

**Body mass index (BMI)**

The BMI provides a relation between body weight and body height and is defined as:

Body weight (kg) / height\(^2\) (m). It aims to overcome the limitations of changes in body weight and the need to compare it with expected normal values (Carney and Meguid 2002). It has been recorded in a wide range of studies in relation to mortality and body function in a variety of circumstances (De Wys 1980, Meguid et al 1988). This makes possible a comparison of data obtained from different parts of the world and different settings. A BMI of less than 15kg/m\(^2\) is associated with a significant increase in morbidity (DeWys et al 1980). In hospitalised patients, a BMI less than 18.5 kg/m\(^2\) is associated with longer intensive care unit stay, increased frequency of postoperative complications and delays in resumption of oral intake (Meguid et al 1988). Its usefulness is limited by poor
sensitivity with respect to baseline assessment, particularly for overweight patients who can undergo significant change in nutritional status prior to estimation of having an abnormal status or being nutritionally depleted (Carney and Meguid 2002). Furthermore, comorbid conditions that promote underhydration, oedema or ascites will confound the calculation (Carney and Meguid 2002).

**Arm anthropometry**

Mid arm circumference (MAC) provides a measure of muscle mass while triceps and subscapular skinfold thickness provides a measure of subcutaneous fat (Carney and Meguid 2002). Triceps skinfold (TSF) is the most frequently used method for estimation of fat stores and is a relatively inexpensive and easily performed test (Charney 1995). Measurements obtained are compared to various standards. However no standard tables exist for use in hospitalised patients (Charney 1995). The most commonly used standards for triceps skinfold thickness and midarm circumference are those reported by Jelliffe (1966), which are based on measurements of European male military personnel and low-income American women, and those reported by Frisancho (1981), which are based on measurements of white men and women participating in the 1971-1974 US Health and Nutrition Survey. The use of these standards in many patients to identify malnutrition is problematic because of the restrictive database and the absence of correction factors for age, hydration status and physical activity. Furthermore, these measurements have been found to be poor in specificity and accuracy. Studies have demonstrated that 20-30% of healthy control subjects would be considered malnourished based on these standards (Harries et al 1982, Thuluvath and Triger 1995). Interpretation of the data may be further limited by inter-rater variability. Hall et al (1980) found considerable inconsistencies when anthropometric measurements were performed by three different observers. The coefficient of variation was 4.7% for arm circumference and 22.6% for triceps skinfold
thickness. Also, the time frame needed before changes in measurements are seen must be considered.

**Functional capacity and muscle power**

Klidijian et al (1980) reported that reduction in muscle power, as indicated by weak handgrip strength and respiratory muscle strength, was a better predictor of complications in postoperative patients than weight loss or arm muscle circumference. Similarly, other studies have found that measurement of grip strength is accurate in predicting postoperative morbidity and mortality in patients (Hunt et al 1985, Kalfarentzos et al 1989). Its usefulness is limited however by the need for patient cooperation and the need to avoid use of analgesics and sedatives which impair patient response (Carney and Meguid 2002).

### 1.3.2 Biochemical parameters

The serum proteins albumin, prealbumin and transferrin have been used in the assessment of nutritional status (Charney 1995). These proteins have transport functions separate from their use in nutrition assessment (Charney 1995). Serum levels reflect a balance between synthesis, distribution and degradation. Hepatic protein synthesis is influenced by factors such as hepatic protein function, amino acid availability and acute injury/stress (Charney 1995). Alteration in distribution may also occur in acute stress and during uncomplicated starvation. For these reasons serum levels should be evaluated with respect to the clinical condition and its impact on hepatic protein metabolism (Charney 1995).

In the hospital setting many reports have related serum albumin to in-hospital morbidity, length of stay and mortality. Harvey et al (1981) investigated the prognostic value of nutritional and immunological parameters in 282 hospitalised patients and found hypoalbuminemia to be the best single indicator of ongoing sepsis and the best predictor of
mortality during hospitalisation. Leite et al (1987) studied 117 patients undergoing major abdominal procedures and showed that serum albumin levels of less than 32g/l were associated with a five-fold increase in the incidence of major postoperative complications. More recently, Hermann et al (1992) examined 15,511 medical and surgical patients and recorded serum albumin concentrations within 48 hours of admission. Patients with hypoalbuminemia had higher mortality, longer hospital stay and were more likely to be readmitted after discharge. Gibbs et al (1999) in a study of 54,215 noncardiac surgery patients found preoperative serum albumin was the strongest predictor of mortality and morbidity compared with 61 other preoperative risk parameters. Heys et al (1998) reported pre-treatment serum albumin to be an independent predictor of five-year survival rate in patients with colorectal cancer.

Because of a half-life of 18-20 days, changes in albumin levels are rarely due to nutrition related factors making albumin more a marker of injury severity than nutritional status (Charney 1995). Hypoalbuminaemia is associated with a series of physiological derangements that may lead to complications and death. For instance, extracellular water expansion has been associated with hypoalbuminemia. Interstitial oedema is detrimental to organ function, particularly the lung (Franch-Arcas 2001). Hypervolaemia and oedema may induce heart failure with further impairment of respiratory function (Franch-Arcas 2001). Wound healing may also be impaired by the presence of oedema (Holte et al 2002). Hypoalbuminaemia therefore appears to be a predictor of poor prognosis in a number of different situations (Carney and Meguid 2002).

In certain situations serum albumin may not be a marker of malnutrition. An example is in anorexia nervosa where serum albumin is maintained despite an extreme loss of weight (Charney 1995). It may be more appropriate therefore to consider hypoalbuminemia as a
predictor of risk rather than a parameter for identifying or quantifying malnutrition (Franch-Arcas 2001).

Other short lived proteins

Short-lived proteins such as prealbumin, retinol binding protein (RBP), transferrin and insulin-like growth factor-1 (IGF-1) are sensitive to quick changes in nutrient availability (Lopez-Hellin et al 2002). Their synthesis is altered by a deficiency in nutritional intake. However both prealbumin and albumin are catabolised in the kidney leading to elevated levels in patients with renal failure (Jeejeebhoy 1998). Transferrin levels must be evaluated in the context of iron stores as iron deficiency leads to an increase in transferrin levels (Charney 1995). The usefulness of these proteins as indicators to assess the nutritional support given to patients during the metabolic stress phase produced by surgery was examined in a study by Lopez-Hellin et al (2002). Twenty-four patients receiving four different nutritional regimens for seven days after surgery were examined. Prealbumin and RBP were found to be sensitive to nutritional intake but their usefulness in nutritional assessment was limited as they were strongly affected by the stress response. Insulin like growth factor-1 (IGF-1) was not influenced by the stress response and was sensitive to the nutritional supply closely matching the nitrogen balance response to nutritional intake. Although these markers may have a potential use in nutrition assessment, the high cost of testing and the fact that they are not currently readily available, make them unsuitable for universal application as clinical markers of nutritional status (Carney and Meguid 2002).

Cholesterol

Serum cholesterol levels have not been frequently studied in hospital patients. Hypocholesterolaemia has been found to be a predictor of death in geriatric patients and in patients with acute renal failure (Obliao et al 1999, Sacks et al 2000). In a study of 2989 consecutive admissions to a general surgery unit, serum albumin and HDL-C levels
exhibited an inverse relationship with the risk of dying: mortality increased when these variables diminished (Delgado-Rodriguez et al 2002).

The authors recommend routine measurement of albumin and cholesterol fractions on hospital admission to provide a better prediction of nosocomial infection, in hospital death and hospital stay.

Other markers including urinary urea nitrogen, creatinine height index (CHI), and delayed cutaneous hypersensitivity have attributes that correlate well with nutritional state; however, they do not improve on the sensitivity and universal familiarity of albumin during recovery from illness (Carney and Meguid 2002). Creatinine excretion is enhanced in acute illness and is therefore not a good index for assessment of malnutrition in this situation (Jeejeebhoy 1998).

Immune competence as measured by delayed cutaneous hypersensitivity (DCH) is affected by severe malnutrition (Jeejeebhoy 1998). A number of factors nonspecifically alter DCH in the absence of malnutrition: infections, uraemia, cirrhosis, hepatitis, trauma, burns, drugs including steroids, immunosuppressants, cimetidine, warfarin, and other factors including general anaesthesia and surgery. Hence in the critically ill patient, many factors can alter DCH and render it valueless in assessing the state of nutrition (Jeejeebhoy 1998).

1.3.3 Nutrition screening and assessment tools
There are well over 50 published nutrition screening tools and many more unpublished tools that are used in clinical practice, but they may give widely different results for a variety of reasons (Elia 2003). The number and type of criteria used to detect malnutrition may vary considerably (Elia 2003). Cut-off points for malnutrition may vary even when the same criteria are used (Elia 2003). Many tools have not been adequately tested for validity and reliability (Elia 2003).
Recently the ‘Malnutrition Universal Screening Tool’ (MUST) has been launched by the British Association for Enteral and Parenteral Nutrition (BAPEN), (2003). MUST is a reliable and valid tool that can be used to screen for malnutrition in different groups of adult patients in different healthcare settings (Elia 2003). It is linked to a care plan, which may be modified according to local policy. It is hoped that the use of a single tool such as ‘MUST’ across different healthcare settings will improve the detection and management of malnutrition (Elia 2003). The tool is based on BMI and weight loss cut-off points but also gives consideration to acute disease effects that result in no dietary intake and rapid weight loss (Elia 2003).

A carefully performed history and physical examination has been proposed as the best available nutrition-assessment tool (Baker et al 1982, Detsky et al 1984). The subjective global assessment (SGA) relies solely on clinical assessment in determining nutritional status. Weight changes, dietary intake, gastrointestinal symptoms, functional capacity and diagnosis are assessed and patients categorised as well nourished, suspected or moderately malnourished or severely malnourished on the basis of this evaluation (Detsky et al 1987). The SGA was tested preoperatively in 59 general surgical patients. A significant association was found between the severity of malnutrition as judged by the physicians and that assessed by the nutrition assessment techniques (Baker et al 1982). Detsky et al (1984) evaluated the SGA in 202 patients admitted for major GI surgery. Patients at highest risk were detected by a combination of SGA and admission albumin level.

The Prognostic Nutrition Index (PNI) is a tool developed to identify patients at risk of developing nutrition-related complications (Buzby et al 1980). A model was developed using assessment variables in 161 patients undergoing major intra-abdominal or intra-thoracic surgical procedures. It was subsequently validated in 100 consecutive patients undergoing major non-emergency gastrointestinal surgery. Patients were assessed at least
48 hours before surgery and monitored until death or discharge. Values < 40% are classified as low risk, while those > 50% signify high risk (Buzby et al 1980). The PNI requires that serum albumin and transferrin levels as well as delayed hypersensitivity skin test results and triceps skinfold measurements are available therefore limiting its use in the clinical setting. When tested in 29 patients with head and neck cancer higher PNI values were associated with increased risk for complications (Hooley et al 1983). However patients with PNI > 30% who were randomised to receive total parenteral nutrition (TPN) had no difference in complications and death when compared with patients who did not receive TPN in spite of improved PNI results after ten days of preoperative TPN (Smith and Hartemink 1988). 

In a review paper of nutrition assessment techniques (Charney 1995) it is concluded that there is no method of assessment that is universally accepted, easily applicable, can accurately predict prognosis and can forecast a patient’s response to treatment. It is therefore recommended that a combination of thorough clinical evaluation with readily available inexpensive laboratory tests, such as serum albumin be performed as part of the initial nutrition assessment.

1.3.4 Nutrition assessment in the cancer patient

Malignant diseases are now among the leading causes of premature death in Western countries. Malnutrition is a common complication, affecting patients with advanced neoplastic disease (DeWys 1980). Nutrition assessment of cancer patients is important to discover mild or moderate states of malnutrition before patients become overtly wasted and thus enabling attempts to be made to prevent further deterioration (Thoresen et al 2002). In 2002, Thoresen et al conducted a study comparing the nutritional status of 46 patients with advanced cancer assessed by objective criteria including anthropometry and assays of serum proteins and a modification of the original SGA questionnaire produced by Detsky et al (1987). Twenty-eight patients overall were classified as malnourished by the
objective criteria and 30 patients were considered moderately or severely malnourished according to the SGA rating. Thus the sensitivity for the SGA method was 96% and its specificity was 83%. The SGA method correlated highly to the objective nutritional criteria and the mean values of TSF, MAMC, BMI and weight were all significantly different between the SGA groups. This study is not considered a formal validation in that the objective method may not be considered as a ‘gold standard’ for assessment of nutrition status. However the high sensitivity and good specificity of the SGA method suggest that it is as valid as the objective method. The SGA method has advantages over the objective method in that it is easily performed and separates the group into moderate and severely malnourished.

Interestingly, a weaker correlation was found between the results of the serum albumin and prealbumin assays and those of the classification of the patients in the SGA groups than what was observed for the anthropometric variables. It is suggested that this may indicate that serum proteins may not be such a sensitive marker of nutritional status as TSF, MAMC, and body weight in this patient group. As previously mentioned, serum albumin level may be affected by the disease process itself, or by inflammatory reactions, liver disease or hydration status and may therefore be considered more an indicator of illness or as a prognostic factor predicting complications and mortality and not a major indicator of nutritional status.

Another validated assessment tool that has been developed to detect malnutrition in elderly patients is the Mini Nutritional Assessment (MNA (Guigoz et al 1994). It includes anthropometric measurements, a global assessment, a dietary questionnaire and a subjective assessment. In a study examining the reliability and practicality of this tool in cancer patients, complete scores were available for only 10% of patients (Zulian et al 1999). The assessment was found to be time consuming and limited by cognitive
impairment of the subjects as well as lack of motivation on the part of the professionals performing the assessment. A similar nutritional status was found in the cancer and non-cancer groups. However the type or stage of cancer is not taken into account. This study highlights the problems associated with long and complicated nutrition assessment procedures. In a climate where time is limited and the knowledge of medical staff on nutrition issues is insufficient for them to recognise the value of time spent performing a nutritional assessment on admission, simple and short assessment procedures are essential.

1.3.5 Dietary intake assessment

According to Burke (1947) in an article entitled ‘The Dietary History as a Tool in Research’, ‘A much more detailed and accurate dietary history is necessary (for research) than is needed for corrective teaching. The type of history used in corrective clinical work should never be used for research purposes, unless it was originally taken with that purpose in mind and all safeguards observed to ensure its accuracy’. Measurement of dietary intake may seem a simple matter. For accuracy however, techniques require a high degree of skill, care and dedication on behalf of the observer (Garrow 1974).

Errors incurred in the measurement of food intake may be random or systematic (Bingham 1987). Random errors affect the precision of the method and can be reduced by increasing the number of observations (Bingham 1987). Systematic errors remain regardless of the number of observations made. Sources of error include food tables, coding errors, incorrect food weight, reporting error, response and sampling bias. Studies conducted in an attempt to quantify the error in dietary assessment methods have found that most estimates using the 24-hour recall are accurate to ±10% (Chattaway et al 1946, Mc Henry et al 1945, Bransby et al 1948).
Food Tables

All results from food intake surveys are ultimately dependent on the quality of the food tables used unless the foods eaten by subjects are analysed independently (Bingham 1987). Random errors are introduced by the use of food tables because the values are based on analytical averages of representative food samples (Bingham 1987). These can be reduced by increasing the number of observations. Another source of error with the use of food tables may occur in the coding stage due to mistakes or difficulties in interpretation.

Estimation of food weight.

Errors introduced by incorrect measurement of the weight of food consumed have been reduced with the use of electronic scales (Bingham 1987). Alternatively weights may be estimated using standard household measures e.g. spoons or cups or using replica models of food (Bingham 1987). In research, records with weights of food are recommended for individuals.

Reporting error

In recall methods of dietary assessment there is the problem that subjects need to remember what they ate. In a review of dietary assessment techniques, a negative bias for the 24-hour recall was reported (Bingham 1987).

Response bias

When subjects are asked to record everything they eat or are made aware that what they are eating is being recorded there is a risk that they will alter their dietary habits. Interview methods have been criticised however because it is said that it is easier for subjects to make incorrect statements about food intake during an interview than it is to alter actual consumption during the course of a record (Keys 1965).
There are considerable errors involved in many methods of dietary assessment, probably far greater than is generally acknowledged. Quantitative estimates of the errors incurred in the standard methods of dietary assessment are limited but when subjects are asked to estimate the weight of food consumed rather than weighing it, the coefficients of variation may regularly be in the 50% range for foods and 20% for nutrients (Bingham 1987).
1.4 Nutritional status of patients with carcinoma

1.4.1 Incidence of malnutrition in patients with carcinoma

The rate and frequency of malnutrition in cancer patients varies widely and depends largely on the type and site of the tumour, stage of disease, and to a lesser extent the treatment performed (Bozzetti et al 1981, Saito et al 1991). If solid tumours are considered in an initial stage when the disease is manageable with surgery, malnutrition has been observed to be present only in oesophageal and stomach cancer patients (Bozzetti et al 1981). In these patients an inadequate intake of nutrients, a result of anorexia, mechanical impairment in swallowing and/or digestion, as well as increased energy expenditure are the determinants of malnutrition.

Bozzetti et al (1981) reported no significant alteration of the nutritional status of patients with radically resectable cancer of the colon-rectum, head-neck, oat cell carcinoma and lymphoma. However patients with oesophageal and stomach cancer had significant depletion of body weight, triceps skinfold, total protein and serum albumin. Patients typically present with malnutrition at the time of diagnosis while the severe side effects of multimodality treatments contribute further risks for nutritional deficits.

In a study of the Eastern Cooperative Oncology Group (ECOG) on 3047 patients with 11 different tumour types, DeWys et al (1980) reported the highest frequency of weight loss to be in pancreatic and gastric cancer patients: 83% and 87% respectively. The incidence of malnutrition in gastric carcinoma was found to be approximately 65%. The criteria used to define malnutrition was weight loss >5% in six months. The patients included were considered at a stage when the extent of disease was beyond the scope of surgery or radiation therapy.
In a study by Ray-Ferro et al (1997), the incidence of mild, moderate and severe malnutrition in gastric carcinoma was 5%, 42.5% and 15% respectively. The Nutrition Risk Index (an index derived from serum albumin and the ratio of actual to usual body weight according to an equation) was used in this case to define malnutrition (NRI>97.5, NRI 83.5-97.5, NRI <83.5 for mild, moderate and severe malnutrition).

Saito et al (1990) examined the nutritional status of 59 patients with squamous cell carcinoma of the oesophagus and 52 with adenocarcinoma of the stomach. The frequency of protein calorie malnutrition (PCM) was 81.3% in the oesophageal cancer patients and 63.8% in the gastric cancer patients, with PCM defined as abnormal levels of at least one of: body weight, TSF, arm muscle circumference (AMC) and albumin. In a later study possible factors contributing to PCM in oesophageal cancer patients were examined (Saito 1991). Four factors: sex, age, stage of cancer and degree of dysphagia were found to be associated with PCM. The degree of dysphagia contributed to a depletion of albumin and transferrin, body weight and arm muscle circumference. Thus simple starvation contributed to a depletion of muscle protein and visceral protein. In those patients with gastric cancer, nutritional status was negatively contributed to by age and stage of cancer.

These results are consistent with the findings of Larrea et al (1992) who reported that when compared with other digestive and extradigestive neoplasia the highest incidence of malnutrition was found in those with oesophageal cancer (78.9%).

Sitges-Serra et al (1990) prospectively analysed the nutritional status of 84 patients with oesophageal carcinoma and found that 58% of patients had body weight and/or triceps skinfold measurements below the 5th percentile, albumin concentrations below 35g/l or both.
Riccardi and Allen (1999) in a review of 30 oesophageal cancer patients reported marasmus (defined as weight loss > 10%) in 70% of cases. In most cases, weight loss occurred rapidly over a period less than four months as a result of progressive dysphagia and/or anorexia with intolerance to regular diet. Other studies quote incidence of malnutrition based on the presence of any involuntary weight loss. Martin et al (1999) in a study of 143 patients following oesophagogastrectomy for carcinoma reported preoperative weight loss in 58% of cases. Daly et al (2000) reported involuntary weight loss in 57% of oesophageal carcinoma patients.

In a study examining 46 patients with advanced cancer, two thirds were rated as malnourished (Thoresen et al 2002). Unintentional weight loss was found in 83% of patients (n=38). Of these 63% (n=24) had lost more than 10% of their body weight. As defined by BMI, 30% (n=14) of patients were underweight, 35% (n=16) were overweight and 35% (n=16) were normal weight. Serum albumin was < 30g/l in 13% of patients (n=15), The type of cancer studied is not documented however.

Comparison of the incidence of malnutrition across different studies and different patient groups is difficult as it is hindered by the absence of a standard method to define malnutrition.

1.4.2 Diagnosis of malnutrition

The actual incidence of malnutrition depends on the method used to identify it and the cut-off values used to distinguish between normality and abnormality (Stratton et al 2003). The U-shaped BMI mortality curves suggest that a BMI of 20-25kg/m² is acceptable and associated with the lowest mortality. Mortality is increased below a BMI of 20kg/m² and above a BMI of 25kg/m². BMI cut-off values of < 20 kg/m² and > 25 kg/m² have consequently been agreed to classify underweight and overweight respectively (Office of
Population Censuses and Surveys 1993, 1994). BMI is easy to obtain, minimally invasive and has been found to correlate closely with mid upper arm circumference (Powell-Tuck and Hennessy 2003).

There is little information on normal unintentional weight variability in weight loss over three to six months but the available information suggests that it is approximately 5% for middle aged to elderly subjects (-2SD) (Stratton et al 2003). Although there are limitations to using a single cut-off value for detecting clinically relevant weight loss, there is general agreement that unintentional weight loss of >10% over 3-6 months is significant (Studley 1936, DeWys et al 1980, Windsor and Hill 1988). Weight loss in excess of the normal intra-individual variation (suggested to be 5% over 3-6 months) may be used as a warning signal for the development of malnutrition (Stratton et al 2003).

A combination of BMI and weight loss may be effective in identifying malnutrition and has been used in a number of recent studies (Bruun et al 1999, Tessier et al 2000, Edington et al 2000).

1.4.3 Cancer cachexia

In a large series of cancer patients, DeWys et al (1980) reported that 15% of patients had lost more than 10% of their pre-illness weight with greatest prevalence of weight loss in patients with GI tumours. Other essential features of cancer cachexia include anorexia, early satiety and chronic nausea. Anorexia has been found to be the main determinant of malnutrition (Belghiti et al 1987) and present in 15-40% of cases at presentation and in 80% of patients with advanced disease.

Anorexia in patients with cancer has several causes. The production of appetite-depressing factors by tumour cells and immune cells of the host, changes in taste and smell
perception, psychological factors, uncontrolled pain and therapy-induced side effects all play a role (Body 1999). Various metabolic abnormalities have been described in cancer patients. An important difference between chronic starvation and cancer cachexia is the preferential mobilisation of fat and sparing of skeletal muscle in starvation compared with an equal mobilisation of fat and skeletal muscle in cancer patients (Brennen 1997). An increase in basal energy expenditure has also been reported. In a series of surgical patients investigators found that cancer patients had increased basal energy expenditures compared with non-cancer patients before surgery whether or not they had lost weight (Hyltander et al 1991).

Other studies have reported that changes in metabolic rate depend on the type of tumour. Increases in resting energy expenditure (REE) have been seen in patients with sarcomas, leukaemia, lymphoma, lung, head and neck tumours, small cell lung carcinoma and gastric tumours; decreases in REE in pancreatic tumours; and metabolically normal rates with colon cancers. Increases in REE seem to parallel advanced disease and decreased food intake (Bloch 1999).

Cytokines play an essential role in these abnormalities. They may act on the brain to induce anorexia, on adipose tissue to reduce fat synthesis and increase catabolism, on peripheral muscles to decrease the synthesis and increase catabolism of proteins and on the liver to increase glucose production and the synthesis of acute phase proteins (Gelin et al 1991).

Hormones may also have a contributory role in the pathogenesis of cancer cachexia. Catecholamines and cortisol levels have been found to be increased which could account for the increase in energy expenditure. Also a decreased ratio of insulin and glucagon has been reported with increased insulin resistance (Body 1999).
1.4.4 Effects of hospitalisation and surgery on nutritional status

Various patient groups show deterioration in nutritional status during hospital stay. In particular, a substantial proportion lose weight including those who are undernourished or well nourished on admission to hospital (McWhirter and Pennington 1994, Martin et al 1999, Corish et al 2000a, Arnold et al 2001). Malnutrition can develop rapidly in hospitalised patients partly because of the catabolic effects of the surgery (Maxfield et al 2001) and partly because of the effects of partial or total starvation (Bruun et al 1999). Starvation (water only) for 5 days, even when uncomplicated by disease produces a weight loss between 5% of body weight, which typically occurs in obese individuals with a BMI of 35kg/m², and 10% of body weight, which occurs in individuals with a BMI of 18kg/m² (Stratton et al 2003). In the presence of severe disease weight loss can be even faster.

Bruun et al (1999) in a survey of orthopaedic and GI surgical patients reported that 83% lost weight. Fifty percent lost up to 5% of their admission weight, 25% lost between 5% and 10% of body weight and 8% lost 10%-15%. This is consistent with the findings of Christensen and Kehlet, (1984) where average weight loss 10 days postoperatively in a group of GI surgical patients was found to be almost 5%. Martin et al (1999) examining patients following oesophagogastrectomy reported postoperative weight loss in 87% of cases, of which 21% had weight loss >10% of immediate preoperative weight. Gianotti et al (2002) examined patients with carcinoma of the gastrointestinal tract following elective surgery. Mean weight loss at eight days postoperative with respect to admission weight was 4.8% in those given no perioperative nutrition support, 5.2% in those given preoperative nutrition support only and 3% in those given both pre- and postoperative nutrition support suggesting that perioperative nutrition support may attenuate loss of body weight. Another more recent study reported 33% of patients experienced weight loss >5% body weight during hospitalisation following elective GI surgery (Fettes et al 2002). The
majority of patients in this study underwent surgery for colorectal cancer and inflammatory bowel disease with only a small number undergoing upper GI surgery.

In a prospective study conducted by Wang et al (1998), 37 patients who underwent en bloc oesophagectomy with radical lymph node dissection for epidermoid carcinoma of the oesophagus, underwent a nutritional and immune status assessment preoperatively and at regular intervals thereafter. The preoperative nutritional and immune status of all patients with resectable carcinoma was within the normal range. Biochemical parameters and not weight loss or other anthropometric measures were considered however. Nutritional status was found to deteriorate in the initial three days after resection. The most severe degradation was found in serum iron, transferrin, Total Iron Binding Capacity (TIBC), cholesterol and zinc. Thereafter, the nutritional parameters improved most returning to preoperative levels within two-three weeks. However serum levels of iron, transferrin and TIBC needed a longer period (>one month) to return to normal (Wang et al 1998).

1.4.5 Nutritional status and outcome in oesophageal and gastric carcinoma

Malnutrition has long been considered to adversely affect outcome of patients with benign and malignant disease. As early as 1936, Studley demonstrated the harmful effect of weight loss on clinical outcome. He found 33% mortality in patients undergoing operation for chronic peptic ulcer disease who had lost greater than 20% of their body weight, compared to 4% mortality in those who had lost less than 20%. Antibiotics were not available at this time and it could be argued that mortality would have been lower had they been available.

Since then numerous other studies have been conducted examining the impact of nutritional status on surgical outcome.
Oesophagogastrectomy and total gastrectomy performed for treatment of oesophageal and gastric carcinoma respectively are extensive surgical procedures and are likely to have a significant impact on nutritional status (Sitges-Serra et al 1990, Bozzetti et al 1990). Prognosis has improved recently probably due to more accurate tumour staging and superior locoregional control of the disease by a complete resection (Muller et al 1990). Conti et al (1977) demonstrated a higher morbidity and mortality rate in patients undergoing oesophagogastrectomy with a weight loss greater than 15% compared to those with less than 15%. Sepsis was the main cause of morbidity and mortality in this study. The authors suggest that this may be related to the effect of malnutrition on the immune status of the patient. Infectious complications continue to be the major cause of postoperative mortality in patients with oesophageal carcinoma (Sitges-Serra et al 1990) Nutritional status is an important determinant of immunocompetence and therefore may have an impact on the frequency of these complications (Jeejeebhoy 1998).

DeWys et al (1980) demonstrated that median survival was significantly shorter in patients with a variety of malignancies with weight loss prior to chemotherapy compared to those with no weight loss even when corrected for stage. The greatest difference was between no weight loss and 0.5% weight loss categories.

Contrary to these findings, an investigation of the nutritional status of 65 patients who underwent surgery for epidermoid oesophageal carcinoma found no nutritional differences between the survivors and the non-survivors (Sitges-Serra et al 1990). Preoperative nutritional status was not found to have a significant impact on postoperative mortality and infection rates. Although malnutrition may be a contributory factor to a poor surgical outcome, other factors linked to the surgical procedure itself are also of utmost prognostic importance. These patients had epidermoid cancer and while they are often malnourished their protein visceral status and their skin responses are fairly well preserved. Both groups
had a preoperative serum albumin within the normal range but had experienced weight loss of 15%.

Saito et al (1990) examined the nutritional status of 59 patients with squamous cell carcinoma of the oesophagus and 52 with adenocarcinoma of the stomach. Patients underwent oesophagectomy and gastrectomy respectively. Of the patients studied and the controls, those patients with oesophageal carcinoma were found to have the lowest mean values and highest frequency of abnormal values in all nutritional measures except serum albumin which were the same for the gastric and oesophageal cancer patients. As previously quoted, the frequency of protein calorie malnutrition was 81.3% in the oesophageal cancer patients and 63.8% in the gastric cancer patients, with protein calorie malnutrition defined as depletion of at least one of body weight TSF, AMC and albumin. In the gastric cancer group there were no severe postoperative complications leading to death and as for non fatal septic complications the frequency and grade were significantly less than in those with oesophageal cancer. Average admission body weight, triceps skinfold thickness (TSF), arm muscle circumference (AMC), creatinine height index (CHI), and retinal binding protein (RBP) were lower in those patients with oesophageal carcinoma with fatal septic complications than in those without. This suggests that the risk of fatal septic complications postoperatively is higher than in those without such depletion.
1.5 Nutritional support for upper gastrointestinal malignancies

It has previously been shown that patients with upper GI cancer are frequently malnourished on presentation and that malnutrition is a risk factor in patients undergoing major surgical resection (Saito et al 1991). Malnutrition in addition to the major trauma of surgery leads to a severe catabolic state. A delay in the achievement of an adequate nutrient intake postoperatively will inevitably lead to further compromise of the nutritional status. The time taken for resumption of adequate oral intake postoperatively has been found to be associated with preoperative nutritional status, age, nature of disease and incidence of complications: the occurrence of which is influenced by preoperative nutritional status (Meguid et al 1988). It seems reasonable therefore to suggest that patients at high risk of a prolonged period of inadequate oral intake postoperatively should be given nutritional support preoperatively and continued postoperatively. The high incidence of malnutrition in patients with malignancies and higher incidence in the over 40yr category puts this patient group in a high-risk category. Consequently, the provision of adequate nutrition perioperatively to allow for an improvement in nutritional status and avoidance of wound and septic complications should be given just consideration.

1.5.1 Preoperative parenteral nutrition

Preoperative parenteral nutrition has been reported to have an impact on wound healing and wound infections (Heatley et al 1979, Haydock and Hill 1987). A significant reduction in the incidence of wound infections was noted by Heatley et al (1979) in those patients with oesophageal or gastric cancer who underwent surgical resection and who were given 7-10 days of preoperative parenteral nutrition. Patients were randomised to receive preoperative parenteral nutrition (n=38) and 36 patients served as controls. A greater number of patients with low serum albumin levels on admission (less than 35g/l) developed wound infections in the control group than in the treated group. The authors
feel that the small level of benefit achieved is insufficient to justify the routine use of this type of regime given the cost and morbidity associated with it.

Muller et al (1982) examined patients with carcinoma of the oesophagus, stomach, colon, rectum and pancreas and the impact of ten days of preoperative parenteral nutrition on postoperative complications. Patients were randomised to treatment and control groups (66 and 59 respectively). They were not subdivided by nutritional status and both groups received the same postoperative treatment. A significant difference was found only for major complications and mortality. Weight gain was achieved between admission and surgery in the treatment group whilst the controls lost weight during the same time. This finding is unsurprising as the preoperative nutritional status of cancer patients may be difficult to improve by oral feeding because of anorexia, malabsorption or physical obstruction.

Haydock and Hill (1987) reported an improved wound healing response in surgical patients requiring parenteral nutrition compared with normally nourished patients. Improvements were reported after one week of therapy and before recognised indices of nutritional status were significantly changed.

Saito et al (1990) recommends that preoperative total parenteral nutrition (TPN) be given to oesophageal cancer patients with abnormal admission AMC, body weight and serum RBP. If the repletion of these nutritional deficiencies is poor then further perioperative treatment should be considered as postoperative complications were found to be more frequent in those with lower average admission levels of these parameters. However preoperative TPN did little to correct these measures in those who later suffered fatal septic complications.
1.5.2 Perioperative parenteral nutrition

Thompson et al (1981) examined the impact of a perioperative course of parenteral nutrition in 21 patients with gastrointestinal cancer (five of whom had an oesophagogastrrectomy). Patients with significant weight loss were randomised to receive parenteral nutrition or standard treatment. Twenty patients without weight loss served as controls. No difference was found between the groups in complication rate or in serum albumin levels. However postoperative weight loss was less in the TPN supplemented group. The authors suggest a longer period of perioperative nutritional therapy may be justified. Further studies of the time period for parenteral nutrition and the efficacy of enteral nutrition are necessary.

In a retrospective review, Daly et al (1982) examined the impact of perioperative TPN in patients with oesophageal carcinoma. Patients given TPN (n=72) were compared with 43 non-TPN patients treated over the same period (1973-1980). Mean age, sex distribution, site and stage of disease were similar in both groups. TPN was offered when possible to malnourished patients for 1-2 weeks preoperative and then postoperative until patients were able to ingest adequate nutrients orally. No details of the TPN regime or the treatment offered to the non-TPN patients is provided by the authors. The TPN group had more complications present on admission (10% versus 5%) and body weight was significantly lower, but serum albumin was not. The provision of TPN was found to be associated with a reduction in major infections, wound and anastomotic complications. Major postoperative complications occurred in 10% of TPN patients and 23% of non-TPN patients. Also there was a difference in major postoperative complications between the pre- and postoperative TPN group (4%) and the postoperative TPN (24%) or non TPN group (23%) suggesting that preoperative nutritional support in malnourished patients may be associated with lower morbidity.
Mueller et al (1982) found postoperative morbidity to be lower in patients with upper GI malignancy undergoing major operative procedures given preoperative TPN (17%) compared with the control group (32%). Mortality was 11% in the TPN group and 22% in the control group.

Another prospective randomised controlled study of perioperative parenteral nutrition in patients undergoing major gastrointestinal surgery examining only malnourished patients, was conducted by Bellantone et al (1990). Patients underwent colorectal and upper gastrointestinal resections. Fifty-four and 68 patients considered to be malnourished by two different criteria were included. While no significant difference was found in the mortality rates between those receiving perioperative TPN and those receiving standard treatment, a significant reduction in septic complications was found in those who received nutritional support.

The Veterans Affairs TPN Cooperative Study Group conducted a multihospital study (1991). This study is the largest of its kind and one of the most important of perioperative nutrition of the past 20 years. A total of 459 patients were randomised either to receive TPN for seven to fifteen days before and three days after non-emergent laparotomy or to receive no perioperative TPN. Patients were stratified according to severity of malnutrition. The study showed a clinical benefit of TPN in severely malnourished patients but no benefit in borderline or mildly malnourished patients where an increased rate of infections was found. This study did not specifically involve cancer patients but showed a reduction in postoperative complications from 42.9% to 5.3% (p=0.03). The value of this study is that it defined limits on the benefits of perioperative nutrition support and suggested a means of identifying patients where the benefits of parenteral nutrition may outweigh the risks. The results are consistent with a more recent study by Bozzetti et al (2000). This study randomised 90 patients with gastric or colorectal carcinoma
requiring surgical treatment in addition to weight loss of 10% or more to receive TPN for ten days perioperatively and nine days postoperatively (n=43) or to undergo surgery without preoperative nutrition support and to undergo standard treatment subsequently (n=47). A significantly lower incidence of non-infectious complications but no difference in infectious complications was found in the TPN group compared with the standard treatment group. The authors feel that their evidence is sufficient to recommend perioperative TPN in cancer patients where weight loss is at least 10% and where urgent surgery is not required.

1.5.3 Postoperative parenteral nutrition

A prospective trial of 117 patients randomised postoperatively to receive or not to receive postoperative TPN was conducted by Brennen et al (1994). Patients underwent pancreatic resection for pancreatic malignancy. The majority of patients showed preoperative nutritional impairment with approximately 6% body weight loss in both groups and a serum albumin level below normal. No significant difference was found in minor complications but there was a significant increase in intra-abdominal abscess formation in the TPN group, a trend towards increased incidence of peritonitis and intestinal obstruction also in the TPN group. However there was a significant crossover of ten patients into the TPN group because of complications. It is suggested that the increase in non-catheter related infections might be due to the absence of enteral feeding which has been associated with bacterial translocation.

Thus studies performed to date have produced varying results.

In a meta-analysis evaluating 18 trials examining effectiveness of perioperative TPN, Detsky et al (1987a), points out that failure of trials to exclude patients who were not malnourished limit their ability to show effectiveness of TPN. TPN is of no benefit to
mildly malnourished patients and may even be harmful because of the finding of increased infectious complications in this group. Detsky and colleagues conclude that routine use of TPN in unselected patients having major surgery is not justified however patients at high risk may benefit. Studies conducted since 1987 further support these conclusions.

1.5.4. Enteral feeding and the acute phase response

After injury the liver increases production of acute phase proteins such as C-reactive protein (CRP) and alpha 1-antitrypsin while decreasing production of constitutive proteins such as albumin and transferring (Elia 2001). Levels return to baseline within several days unless the post-injury course is complicated by sepsis, which prolongs the acute phase protein response (Elia 2001). This response to injury is very important to recovery because these proteins defend against bacterial invasion while limiting damage to normal tissue induced by leukocyte responses to bacteria and necrotic tissue (Elia 2001).

Moore et al (1989) randomised 75 patients to receive enteral (n=39) or parenteral (n=36) nutrition post emergency laparotomy. A total of 59 patients were evaluated. A significant difference was found with respect to major infections: 3% in the total enteral nutrition (TEN) group compared with 20% in the TPN group. By day 10, albumin and transferrin were significantly higher in the TEN patients. The reprioritisation of hepatic protein synthesis was attenuated with enteral nutrition. This was shown earlier by Peterson et al (1988). In Moore’s study enteral nutrition provided a significant advantage in reducing major septic complications in patients following blunt abdominal trauma.

Kudsk et al (1994) examined the impact of the route of nutrient delivery on the development of septic morbidity and visceral protein response after severe injury. Patients with trauma (n=68) requiring an emergency laparotomy were randomised to early enteral (n=34) or parenteral (n=34) feeding. The incidence of pneumonia and line sepsis was
significantly higher with parenteral than with enteral nutrition (p<0.05 and p<0.03). Infection resulted in significantly lower levels of serum albumin, transferrin, prealbumin and fibronectin and higher levels of the acute phase proteins in the parenterally and enterally fed patients. It was the presence of significantly fewer infected patients in the enteral group than the parenteral group that was the major factor in the higher levels of constitutive proteins and the lower acute phase protein response in this group.

These studies have demonstrated that TPN is associated with an exaggerated acute phase protein response and consequently a higher rate of infectious complications when compared with enteral nutrition.

It has also been suggested that the nutritional supply route may alter the metabolic responses after surgical injury (Lin et al 1996). Cytokines, among them interleukin-6 and interleukin-10, play important roles in host responses under a stressed state. Interleukin-6 (IL-6) is considered an integral mediator of the acute phase response to injury but excessive and prolonged post-injury elevations of circulating IL-6 levels have been associated with higher morbidity and mortality (Schluter et al 1991). Interleukin-10 (IL-10) counteracts inflammatory responses and can downregulate cellular immunity; thus causing an immunosuppressive state in surgically stressed individuals (Klava et al 1997).

The effect of feeding route on systemic IL-6 and IL-10 responses and gut barrier functions was examined by Takagi et al (2000). Twenty-nine patients who underwent oesophagectomy for oesophageal carcinoma were divided into two groups to receive perioperative enteral (n=11) or parenteral (n=18) nutrition. Both IL-6 and IL-10 significantly increased during and after the operation in both groups. Serum concentrations of IL-6 were significantly higher during the operation on postoperative day 3 and day 7 in the TPN group compared with those in the enteral group. Similarly
significant differences were observed in the serum IL-10 during the operation and at two hours after the operation between the TPN and EN groups. The ratio of serum IL-6 to IL-10 increased in both groups however it remained high in the TPN group and was significantly higher on postoperative days 3 and 7 when compared with those in the EN group. This prolonged higher ratio of IL-6 to IL-10 in the TPN group indicated the promoted systemic release of proinflammatory cytokine rather than the reduced production of anti-inflammatory cytokine. Serum endotoxin level increased significantly in the TPN group from the intraoperative period, which was not observed in the enterally fed group. It is suggested that the postoperative elevated serum endotoxin seen in the TPN group may play a role in the augmented inflammatory response. Consequently EN is recommended for its attenuation of excessive systemic cytokine responses and reduction of endotoxin translocation. This study was retrospective and non-randomised with the attending physician selecting TPN or EN at his discretion. There was no significant difference in age, operative time, intraoperative blood loss or serum concentrations of albumin, prealbumin or transferrin preoperatively or on postoperative days 3, 7 and 21 between the two groups. No details are given of other markers of nutritional status such as weight loss.

The effect of enteral and parenteral nutritional support on protein metabolism in cancer patients was further investigated by Burt et al (1983). Patients with squamous cell carcinoma of the distal oesophagus were randomised according to their percentage of pre-illness body weight loss and their ability to swallow liquids. The stage of disease is not recorded but patients were excluded if evidence of metastases was demonstrated. Those with < 20% loss of their pre-illness weight and able to swallow liquids safely were then randomised to either continue eating or to receive TPN (group 1 and 2 respectively) and those unable to swallow liquids with > 20% loss of pre-illness body weight were randomised to receive either jejunostomy feeding or TPN (group 3 and 4). After a two-week period of nutritional repletion the TPN groups (groups 2 and 4) demonstrated a
significant increase in body weight and a significant improvement in nitrogen balance. However, group 4 did receive more nitrogen than the jejunostomy group. No group demonstrated a significant change in the serum level of the proteins measured (serum total protein, albumin, transferrin and ceruloplasmin). During the control (basal) period, whole body protein catabolism was significantly higher than synthesis for all groups. During the period of nutritional repletion whole body protein synthesis tended to be greater than that of catabolism for all groups but group 1. While TPN was found to be better able to promote weight gain compared with isocaloric jejunal feeding, this discrepancy may be attributed to the lower nitrogen intake in the jejunally fed group. As neither group demonstrated a significant increase in total body potassium the gain in weight may have been due to water or fat accrual. Overall, both TPN and jejunostomy feeding was found to stabilise nutritional state and whole body protein economics. However TPN appeared to be slightly more efficacious as judged by an increase in body weight and increased positive nitrogen balance.

A randomised prospective study to determine whether early enteral feeding may improve protein kinetic parameters in postoperative upper GI cancer patients was conducted by Hochwald et al (1997). Preoperative diagnosis and procedures were similar in the two groups and no difference reported in preoperative weight loss or serum albumin levels. Patients undergoing curative resections only were included (n=29) and were randomised intraoperatively to standard postoperative IV fluids (n=17) or early enteral nutrition (n=12). Net balance of whole body protein was significantly higher in the fed group compared with the IV fluid group (p<0.001). A significant reduction in protein catabolism was demonstrated but little effect on protein synthesis. This supports the findings of Burt et al (1983). By positively impacting protein loss the provision of enteral nutrition support in these patients may contribute to a reduction in postoperative morbidity and mortality.
1.5.5 Enteral feeding and gut barrier integrity

The gut barrier hypothesis suggests that substances can cross the gut mucosal lining and initiate or amplify a systemic inflammatory response. While enteral nutrition may have a trophic effect on gut structure and integrity which contributes to the maintenance of gut barrier function and protects against invasions of bacteria and toxins, many studies have reported that TPN may induce alterations in gut integrity, leading to mucosal atrophy and an increased rate of translocation of luminal bacteria into the systemic blood flow; (Deitch et al 1987, Alverdy et al 1988, Buchman et al 1995).

A randomised controlled trial comparing enteral and parenteral nutrition on gut barrier integrity was conducted by Reynolds et al (1997). Sixty-seven patients undergoing major upper GI surgery were randomised prospectively to receive either seven days postoperative enteral (n=33) or parenteral nutrition (n=34). The groups were matched for age, sex, nutritional status, surgical procedure and blood transfusions. The mean energy and nitrogen intake over the seven days was not significantly different between the two groups. The results show no significant difference in the incidence of non-infective complications or the number of total infection episodes between the two groups. Enteral nutrition was not found to be associated with a reduced incidence of infections. Neither was it found to significantly modulate gut barrier function determined by the lactose/mannitol test. Intestinal permeability was increased after surgery but returned to normal by day seven in both groups. This study therefore does not support the hypothesis that enteral nutrition may positively modulate host defences by supporting gut barrier function. Neither does it corroborate the findings of Peterson et al (1998) or Kudsk et al (1994) that suggested that enteral feeding modulates the acute-phase response while reprioritising visceral protein synthesis. Median CRP remained high in both groups after seven days. It is possible that enteral feeding is less effective after hypermetabolism is established and if enteral feeding had been instituted earlier the findings may have been altered. For example, Muller et al
(1986) reported a reduced rate of major complications in patients with upper GI cancer who received pre and postoperative TPN compared with no nutritional supplementation. Alternatively, it may be that it is only in critically ill multiple trauma patients that enteral nutrition confers advantages over parenteral nutrition in terms of infectious complications. In this study 80% of patients were malnourished and there were a high number of severely malnourished patients in both treatment arms, 33% TEN and 22% TPN, making it consistent with the findings of the Veterans Affairs Total Parenteral Nutrition Cooperative Study Group (1991) and Von Meyenfeldt et al (1992). Here a similar rate of reduction in infective complications was achieved in patients receiving preoperative enteral nutrition or total parenteral nutrition compared with depleted patients who were not repleted in the perioperative period. These studies have reported that TPN after major surgery may be of benefit only to severely malnourished patients.

Brooks et al (1999) randomised patients after complete resection of upper GI malignancy to receive enteral nutrition via a jejunostomy tube or standard care with IV fluids. A nonoperative healthy control group was also included. Twenty-six patients participated in the intestinal permeability test (eight received EN and 11 standard care). An increase in intestinal permeability in the immediate postoperative period was demonstrated, however it normalised in both groups by postoperative day five suggesting that enteral nutrition may not be necessary for recovery of intestinal barrier function. These patients were well nourished preoperatively however with normal serum albumin and a low level of weight loss (1.7kg and 1.0 kg for the fed and non-fed groups respectively) and no significant difference in these parameters or nutrition risk index between the two groups.

In a randomised trial of patients undergoing intestinal resection, 14 were allocated to receive enteral feeding and 14 were managed conventionally with IV fluids. While no difference was demonstrated in overall clinical outcomes there appeared to be fewer
complications in the enterally fed group. Also a significant attenuation in gut permeability was demonstrated \((p<0.05)\) in comparison to the conventionally fed group (Carr et al 1996). No information is provided on the type of operation or preoperative nutritional status of the patients making it difficult to make a direct comparison between the two studies.

### 1.5.6 Early enteral nutrition following GI surgery


A randomised double blind prospective trial to examine the effect of early postoperative enteral nutrition compared with no nutrition on the postoperative course in patients after major abdominal surgery was conducted by Beier-Holgersen and Boesby (1996). Thirty patients were included in each group. Malnourished patients were randomised separately. Most of the patients underwent lower GI surgery. The study found a significantly lower incidence of postoperative infectious complications \((P<0.0009)\) in the treated group \((7\%)\) compared with the control group \((47\%)\). The study group included nine malnourished patients. Three of the five malnourished allocated to the control group had a severe complication whereas none of the malnourished allocated to the feeding group had any complications. This study therefore suggests that the malnourished patient may benefit from nutritional support and also that enteral feeding may confer benefits to patients who are not malnourished. Previous studies have suggested that only severely malnourished patients may benefit from perioperative TPN (Veterans Affairs Total Parenteral Nutrition Cooperative Study Group 1991). The study also confirms that enteral nutrition can be given safely within a few hours of surgery. A systematic review and meta-analysis of
randomised controlled trials comparing any type of enteral feeding started after surgery with nil by mouth management in elective gastrointestinal surgery was carried out by Lewis et al (2001a). Early feeding was associated with a shorter length of hospital stay and reduced frequency of infection, the greatest reduction being in wound infections. While the trials included were heterogeneous in clinical terms, the effect of early nutrition seemed to be homogenous. The authors conclude that there is little evidence that keeping patients 'nil by mouth' is beneficial.

Early enteral nutrition following upper GI surgery

Jejunostomy feeding as a method of nutrition support was first described in 1858 by Busch and since its initial use in a patient with inoperable gastric malignancy it has gained wide acceptance in particular over the last decade. Jejunostomy feeding has been found to give a safe and effective access for postoperative enteral feeding (Cade 1990, Gerndt and Orringer 1994, De Gottardi et al 1999). Minor technical complications have been reported (De Gottardi et al 1999, Braga et al 2002, Date and Gilliland 2004) but these may be reduced by a good insertion technique and careful postoperative management (De Gottardi et al 1999).

In a large study recently carried out by Braga et al (2001) patients undergoing curative surgery for upper GI cancer (n=257) were randomised to receive early postoperative enteral (n=126) or parenteral nutrition (n=131). The two groups were similar for baseline characteristics: age, sex, body weight, serum albumin, haemoglobin, and % malnourished and surgical variables. At any time point no significant differences were found between the two groups in all the nutritional variables, immune function variables and inflammatory response indices. Early enteral nutrition was not found to improve outcome compared with parenteral nutrition in the overall population. When a separate analysis was performed in the subgroup of malnourished patients, a tendency to a lower overall complication rate was
noted in the enterally fed group (37.1%) compared with the TPN group (52%) (p=0.23). A significantly shorter length of hospital stay was found in the enteral nutrition group compared with the TPN group (p=0.042). This was a relatively large sample size of malnourished patients (n=91) and suggests for the first time that for depleted cancer patients undergoing major upper GI tract surgery early enteral nutrition may reduce postoperative infectious morbidity compared with TPN. Furthermore, while a lowering of oxygen tension was observed in both groups, patients receiving enteral nutrition had a significant faster recovery of oxygen tension from postoperative day five, suggesting that full enteral regimen may be needed to enhance intestinal blood supply.

Given the feasibility and safety of enteral nutrition, the low prevalence of metabolic adverse effects, the improved gut oxygenation and the low cost of enteral feeding, the authors recommend its use in this patient group. Enteral feeding is also favoured in an Italian Multicentre trial (Bozzetti et al 2001). More than 300 malnourished patients with GI cancer (weight loss of at least 10%) were randomly assigned to receive enteral or parenteral isocaloric and isonitrogenous feeding regimens. The incidence of postoperative complications was significantly lower at 34% in enterally fed patients compared with 49% in those parenterally fed (p=0.005). Length of postoperative stay was also reduced in enterally fed patients (p=0.009).

Results of early jejunal feeding over a nine-year period after digestive surgery has recently been reported by Braga et al 2002. A total of 650 patients were studied of which 270 underwent gastrectomy. All patients received jejunal feeding postoperatively. The majority of patients (70%) did not experience any adverse effects related to jejunal feeding and nutritional goals were met in 91% of cases by enteral nutrition. Adverse GI effects were reported in 30% of cases with abdominal cramps and bloating being the most frequently occurring symptoms. In most cases this was resolved by reduction of the
infusion rate or by administration of appropriate drugs. No detrimental effect of enteral nutrition on the anastomosis healing process was observed. In fact in the gastrectomised patients no leak in the jeuno-ileal anastomosis was observed which was distal to the tip of the NJ tube. The study also compared nasojejunal administration of nutrients with a feeding jejunostomy tube. Although the two groups were not randomised, the rate of GI side effects was similar for the two techniques. The NJ tube had a higher rate of displacement and clogging than the jejunostomy catheter (p=0.0005 and p=0.0007 respectively).

Studies reported to date have found early postoperative feeding to either reduce the incidence of infectious complications or to have no effect. A study conducted by Watters et al (1997) however found immediate postoperative enteral feeding to have a negative effect. Patients undergoing major elective abdominal or thoracic surgery were assigned to receive enteral feeding postoperatively (n=13) or no feed (n=15). Most of the patients were well nourished preoperatively (as determined by Subjective Global Assessment). The two groups were similar in terms of preoperative biochemical and clinical variables likely to influence postoperative strength. Handgrip strength, vigour and fatigue decreased postoperatively in both groups. Vital capacity, which in part reflects the strength of the respiratory muscles, was significantly lower in the fed group compared to the unfed group throughout the postoperative period of study. This impairment is most likely due to the abdominal distension experienced with the enteral feed, which would influence diaphragm function. Abdominal distension was experienced in 62% of cases. This may be related to aggressive feeding regimen a maximum of 2500mls/d to be achieved by the second postoperative morning. Daily postoperative maximal activity levels were higher (p<0.01) and tended to recover more rapidly in the unfed group. The reason for this is unclear but total postoperative lengths of stay did not differ between the groups. In view of these findings the authors do not recommend routine postoperative enteral feeding in well-nourished patients.
1.5.7 Enteral feeding formulas

Most of the studies examining enteral feeding in postoperative patients have used standard formulas. Recently there have been studies using formulas believed to have immune enhancing properties.

*Immune enhancing formulas*

Studies have been conducted where standard enteral formulas have been compared with formulas supplemented with arginine, fish oil and RNA believed to have immune enhancing effects. Daly et al (1992) examined a formula supplemented with arginine, RNA, and omega-3 fatty acids in patients with upper GI malignancies. Patients (n=85) were randomised to receive either a supplemented enteral formula or a standard enteral formula. Both groups had a similar energy intake but nitrogen intake was significantly greater in the supplemented group. A lower incidence of infectious and wound complications was found in the supplemented group (11% vs 37%) and length of stay was shorter. However there were no control arms that did not receive nutritional support in the study design. Also the study was not designed with separate randomisation according to nutritional status of the patients. McCarter et al (1997) conducted a prospective study of 167 patients undergoing upper GI surgery for carcinoma of the oesophagus, stomach and pancreas. Patients received a standard or supplemented formula via a jejunostomy postoperatively. The authors did not examine the occurrence of complications in the two groups but instead examined the tolerance of the enteral feeds. The majority of symptoms experienced were mild and included abdominal cramping, abdominal distension, nausea and diarrhoea. This is not attributed to the use of different formulas as no significant difference was found in tolerance of feed between the standard and immune enhanced formula group. A direct correlation between jejunal feeding and the occurrence of symptoms is not clear due to the absence of a control group without an enteral feed.
Heslin et al (1997) examined the effect of an immune-enhancing formula on morbidity, mortality and length of stay in upper GI cancer patients when given early postoperatively. After curative resection patients were randomised to receive either enteral feeding (n=97) or conventional intravenous fluids (n=98) (Intent-to-treat analysis). There was a 5-6% preoperative weight loss suggesting some degree of malnutrition however serum albumin levels were within the normal range. Symptoms of abdominal cramping, distension, nausea, vomiting or diarrhoea were experienced by 20-53% of the patients during the postoperative period but this was not significantly different between the groups. The incidence of symptoms was found to be related to the initiation of feeding in both groups, occurring earlier in the enterally fed group. No significant difference was found between the groups in the incidence of major or minor complications, mortality rates or length of stay. One potentially confounding factor was that the patients randomised to immunonutrition received a small amount of key substrates (approximately 30% of the planned goal in the first week).

Previous studies have reported that nutritional status is an important factor influencing the incidence of postoperative infections. These patients were not malnourished which may explain the absence of benefit of the enteral feeding formula. The authors recommend further study to investigate the subset of patients with upper GI cancer who may benefit from early enteral nutritional support.

Braga et al (1998) used an immune enhancing formula in 166 patients who underwent abdominal surgery for gastric or pancreatic cancer. Patients were randomised to TPN, standard enteral feeding or enteral feeding with the enriched formula. Greater than 10% weight loss in the preceding 6 months occurred in 78 patients. There was a trend towards fewer infections in the enteral group; it did not reach statistical significance, and the
severity of infection was lower with the enhanced formula than with the TPN or standard enteral formula.

A series of more recent studies from Italy, (Braga et al 1999, Braga et al 2002a, Braga et al 2002b, Gianotti 2002), have provided more evidence of the benefits of perioperative enteral feeding. Preoperative oral feeding with an immune enhancing formula combined with postoperative jejunal feeding with the same formula in patients with GI cancer resulted in a significantly reduced incidence of postoperative infectious complications (Braga et al 1999, Braga et al 2002a). Further studies were then conducted in malnourished and well-nourished patients. In malnourished patients the greatest benefit on the reduction of complications was achieved with an immune enhancing formula given perioperatively (Braga et al 2002b). In well-nourished patients the provision of an immune enhancing formula preoperatively alone was sufficient to significantly reduce infectious complications and length of postoperative stay (Gianotti et al 2002).

1.5.8 Enteral tube feeding and appetite

Enteral tube feeding is unphysiological; therefore it is possible that disturbances in appetite sensations may occur in patients receiving enteral tube feeding (Stratton and Elia 1999). Studies on animal and healthy human subjects suggest that the sole provision of nutrients by enteral tube feeding does not fully satisfy hunger or the desire to eat (Stratton and Elia 1999). In disease states few studies have documented the effect of tube feeding on energy intake or appetite sensations in patients able to eat.

Yeung et al (1979) found no difference in voluntary oral intake in a control group and a group given jejunostomy feeding following colorectal surgery. Total energy intake was found to more than double in the jejunostomy fed group compared with the control group. Bastow et al (1985) observed that overnight nasogastric feeding was associated with a
doubling of voluntary oral intake. Other controlled trials that have been conducted in a hospital environment suggest that overnight enteral tube feeding suppresses oral energy intake by less than 20% compared with control groups (Bastow et al 1983, McWhirter and Pennington 1996).

1.5.9 Prolonged postoperative enteral feeding

It is feasible to continue jejunostomy feeding at home as an adjunct to oral intake in patients failing to meet their nutritional requirements. Few studies have examined its use beyond the early postoperative period and a recent questionnaire to major cancer centres in England suggests prolonged jejunostomy feeding is not widespread (Murphy et al 2005). The mean duration of jejunostomy feeding in patients following oesophagectomy for oesophageal carcinoma reported by Yagi et al (1999) was 69 days. Gerndt and Orringer (1994) in a series of 378 patients with malignant disease reported jejunostomy feeding to be continued for more than three weeks in 12% of patients and more than two months in 7.7% but no details of the impact on nutritional status or nutritional intake is recorded. There is some evidence for the benefit of enteral tube feeding in patients in the community with malignancy, however all trials have been undertaken in patients with head and neck cancer mostly during or after radiotherapy (Shike et al 1989, Fietkau et al 1991). There is a need for a well-designed trial to examine the impact of continuing enteral feeding in the community in patients following surgery for upper GI malignancy.
1.6 Oral dietary supplements

Several studies have found evidence of clinical benefits of supplementation of ward diet with oral supplements following surgery. Rana et al (1992) conducted a randomised controlled trial to determine the clinical efficacy of dietary supplements postoperatively in patients undergoing moderate to major gastrointestinal surgery. 40 patients completed the trial (20 control, 20 treatment group). The treatment group was offered oral dietary supplements ad libidum as well as standard diet once free fluids and/or light diet was allowed. Control patients received the standard hospital diet. Baseline preoperative anthropometric values, serum albumin, prealbumin, retinol binding protein and grip strength dynamometry were not significantly different between the two groups. Neither group was malnourished at the onset of the study with a mean preoperative weight loss <10% (range 7.1-7.6%) and serum albumin 33-35g/l. The treatment group was found to have a significantly higher energy and protein intake, accounted for by an increased intake of hospital diet as well as the dietary supplements. Those patients in the treatment group suffered no significant weight loss and maintained muscle function, evidenced by dynamometric data in contrast to the control group. Furthermore a significant reduction in the incidence of postoperative chest and wound infections was found in the treatment group. This supports the findings of Delmi et al (1990) where patients following surgery for fractured neck of femur when given dietary supplements, had a lower rate of complications than the unsupplemented group.

Keele et al (1997) in a randomised controlled trial, examined patients undergoing elective moderate to major gastrointestinal surgery. During the inpatient phase of the study, control patients (n=53) received standard hospital diet and the treatment group (n=47) received the standard diet supplemented ad libidum with an oral dietary supplement. There were no significant differences in the baseline nutritional variables between the two groups. On admission to the study the patients were marginally nutritionally depleted with a mean
weight loss of 4% usual body weight and mean serum albumin of 35.4g/dl. A general decline in nutritional status was found during hospital stay. Patients in both groups lost weight and serum albumin concentrations fell. Control patients lost significantly more weight than treatment patients at study day three and discharge. Skeletal muscle function was preserved to a greater extent in the treatment group, indicated by hand grip dynamometry measurements. A reduced incidence of postoperative complications was found in the treatment group (p<0.05). Clinically significant benefits were thus demonstrated with the administration of oral dietary supplements postoperatively to patients who had undergone elective moderate to major gastrointestinal surgery irrespective of their preoperative nutritional status. The study continued for four months after discharge from hospital but no evidence was found to support the use of dietary supplements after discharge.

A systematic review of randomised controlled trials of oral protein supplementation in adults was conducted by Potter et al (1998). A total of 30 trials were included in the analysis, twenty of which evaluated oral supplementation. In almost all trials a greater percentage weight gain, (or smaller percentage weight loss), and improved anthropometric measures were found in the supplemented groups compared with the controls. An unequivocal effect of nutritional supplementation in reducing case fatality was not found.

In a prospective randomised controlled trial conducted by Beattie et al (2000), an improvement in nutritional status with postoperative nutritional supplementation is also reported. This was a large study, including 101 malnourished elective GI and vascular surgical patients of 450 examined. The treatment group (n=52) was encouraged to take 400ml of an oral dietary supplement from the initiation of oral diet up to 10 weeks postoperative; the control group (n=49) received standard hospital diet. From the point of intervention, the control group lost more weight than the treatment group (9.8% vs 5.6%).
The risk of chest and wound infections was found to be lower in the treatment than in the control group but the trend did not reach statistical significance. The treatment group showed more evidence of improving nutritional status four weeks after surgery; the control group demonstrated progressive weight loss for eight weeks following surgery.

In a more recent randomised controlled trial (Smedley et al 2004) involving 152 patients undergoing moderate to major lower GI surgery, significantly less postoperative weight loss was found in those patients receiving supplements ad libidum pre- and postoperatively compared with those receiving no supplements or those receiving supplements postoperatively only. Patients included had a good nutritional status preoperatively (as indicated by BMI). Fewer minor complications were found in those receiving supplements pre- and postoperatively and in those receiving supplements only postoperatively compared with the controls. No difference in major complications was found.

The findings of Beattie et al (2000) and Smedley et al (2004) are not supported by MacFie et al (2000) where perioperative oral dietary supplements failed to achieve a demonstrable effect on clinical outcome. One hundred patients undergoing major elective gastrointestinal surgery were randomised to receive oral dietary supplements either pre-and postoperatively, preoperatively or postoperatively alone or no supplements. All groups demonstrated significant weight loss from preoperative randomisation to outpatient review four weeks post discharge and a fall in mean serum albumin. The incidence of postoperative complications, mortality and duration of hospital stay were similar for all groups. Possible explanations for the discrepancy in these results and those previously reported include the duration of supplement provision, the nature of the patients studied, the sample size and the degree of severity of pre-existing malnutrition. Patients in this study received a significantly greater mean energy and protein intake from the oral dietary supplements in the preoperative period than the postoperative phase (p<0.001). Only 15%
underwent upper GI surgery compared with 43% in the trial by Beattie et al (2000). Following upper GI surgery problems of early satiety and discomfort on eating are more common. Dietary supplements may be easier to take than solid food and may therefore be an effective way of enhancing nutrient intake in this patient group. In the patients receiving postoperative oral dietary supplements, although > 30% of total energy intake was derived from the supplements, the observed increase in total intake was modest compared to the patients not receiving oral dietary supplements (252kcal±195). The increase did not reach statistical significance and could not be expected to achieve a significant change in body weight or muscle function. The patient population in this study was largely well nourished with only six patients included with a BMI < 19 and 17 patients with ≥10% pre-illness weight loss. As in the MacFie study the majority of the patient population included by Smedley et al underwent elective lower GI surgery and had a good preoperative nutritional status. However different postoperative management protocols were employed. The authors concede that the routine practice of early postoperative feeding with the introduction of oral nutritional supplements and voluntary food on the first postoperative day and avoidance of the use of nasogastric tubes may explain the failure to demonstrate benefit of oral dietary supplements (MacFie et al 2000). They propose that this may result in the perceived benefits of supplements being proportionately less than in the previously quoted studies where initiation of feeding is delayed until resumption of bowel sounds.

Results of a recent systematic review examining the benefits of nutritional supplements in patients with illness-related malnutrition suggest a positive impact on body weight (Baldwin and Parsons 2004). The studies included involved patients from varied clinical backgrounds and all patients included were below their usual weight at entry or at risk of nutritional problems.
In summary, the use of oral dietary supplements does appear to limit the loss of body weight that typically accompanies surgery. The attenuation of weight loss was found to be statistically significant in three of the five randomised controlled trials examined (Keele et al 1997, Beattie et al 2000, Smedley et al 2004). In the study by MacFie et al (2000), weight loss was reduced in those receiving supplements preoperatively but the changes did not reach clinical significance. Complication rates have also been shown to be reduced in patients given supplements postoperatively (Rana et al 1992, Keele et al 1997, Beattie et al 2000, Smedley et al 2004). In the study by Keele et al (1997) the reduction in complications was clinically significant. Smedley et al found a significant reduction in minor but no difference in major complications. In the other two studies there was a trend towards supplemented patients receiving fewer antibiotic prescriptions postoperatively but the trend was non significant. No significant difference was found by MacFie et al (2000), however the dietary supplements failed to significantly improve total energy intake in his patient group and also the patients were better nourished than in the other trials.

Poor compliance appears to be the most difficult problem in patients offered liquid dietary supplements. Ovensen et al (1991) reported poor compliance in one third of patients despite an enthusiastic approach and offerings of several choices of flavour. A more recent study of unselected postoperative nutritional supplementation in orthopaedic patients found median compliance to be 14.9% with supplements taken for a median of only 4 days (Lawson et al 2003).

1.6.1 Oral dietary supplements and food intake

It has been postulated that the ingestion of oral dietary supplements in between meals may compromise food intake. This has not been confirmed in the literature: Rana et al (1992), McWhirter and Pennington (1996), Keele et al (1997), McCarthey and Weihofen (1999), Lawson et al (2003).
In the study by Rana et al (1992), energy and nitrogen intakes were found to be significantly greater in the supplemented group. The increased protein intake is accounted for by protein ingested from the oral supplements. The increase in energy intake was associated with energy ingested from the supplements but also an increased intake of standard hospital diet. Thus energy intake from food was actually stimulated. Keele et al (1997) reported no significant difference in nutrient intakes from ward diet between those offered supplements and those not offered them. There was no reduction in voluntary food intake in those offered supplements but energy and protein intakes were significantly higher in the first four days of the study period. Supplements were not found therefore to be substitutes for food intake.

The study by McWhirter and Pennington (1996) was designed to determine if patients with cancer undergoing radiotherapy reduced their daily food intake if encouraged to consume oral dietary supplements. A significant increase in total daily energy and protein intake was found in the group who ingested the supplements, compared with those not offered the supplements.

1.6.2 Oral dietary supplements at home
Keele et al (1997) found no evidence of benefit in continuing nutritional supplementation on discharge. Smedley et al (2004) found that following discharge the supplemented groups maintained enhanced intake at two weeks but by four weeks total nutritional intakes were similar in all groups. A study where elective and acute GI surgery patients were randomised to receive dietary advice and four months of protein rich nutritional supplements or not on discharge was conducted by Jensen and Hessov (1997). This study differs from the other two in that patients did not receive any nutritional advice or supplementation whilst inpatients. The intervention group was found to have an increased
energy and protein intake and achieved a gain in lean body mass and fat mass (control 1.7kg LBM and 0.2kg fat versus intervention 3.1kg LBM and 1.5kg fat LBM p=0.029 and fat p=0.056).
1.7 Food intakes in hospital patients

Although there are still areas of disagreement, there are a growing number of studies showing that nutritional support improves outcome in certain groups of patients. Most studies have focused on artificial nutrition support however the majority of patients could receive their nourishment from hospital food.

The simplest, safest and cheapest way to provide nutritional care and support is to get patients to eat more of hospital food. Many barriers to adequate food intake have been identified (Association of Community Health Councils Document 1997). Patients who have undergone major upper GI surgery experience problems of early satiety, nausea and anorexia, which compromise intake. This is compounded by hospital specific factors: lack of clearly formulated descriptions of responsibilities, absence of a powerful voice for food service systems, lack of involvement from hospital management and lack of cooperation between different staff groups (Association of Community Health Councils Document 1997).

While many ‘at risk’ patients can be managed by simple means such as nursing help with meals, appropriate meal size and presentation, other patients require a more individualised approach with an assessment of nutritional needs and a plan to achieve nutritional goals (Kondrup 1998). Current catering systems are modelled on hotels or institutions catering for large numbers and are not targeted to sick patients with particular needs. Despite a recommended meal pattern of six meals per day, patients are served only three meals per day. Meals are inflexible with long gaps between some meals eg. 14 hours between evening meal and breakfast and short gaps between others (Allison 1999). Even when sufficient food is available a high wastage rate has been reported. Barton et al (2000a) reported a food wastage rate of approximately 40%. A recent Danish study reported a wastage rate of up to 60% with patients consuming only 40-45% of food produced (Almdal
et al 2003). Factors contributing to high rates of food wastage include poor palatability and presentation of food as well as inappropriate volumes of food compared to appetite. In a study of 1416 hospitalised patients (Dupertuis et al 2003) 43% had a total food intake below their minimum nutritional needs. The number with an inadequate nutritional intake increased to 70% when recommended needs were considered. Of these 97% did not eat all the food served. While disease and/or treatment was attributable to the reduced intake in 26% of cases, at least 59% of the underfed patients did not meet their nutritional needs because of other reasons, namely inadequate meal service.

Numerous studies have examined the actual food consumed by hospital patients, (Hackett et al 1979, Todd et al 1984, Simon 1991, Rana et al 1992, Keele et al 1997, Barton et al 2000a). Hackett et al (1979) examined voluntary food intake in 12 patients over a two-week period, following elective colectomy. In this study energy intake averaged 949 kcal/day. Up until day seven the intake of only two patients exceeded 1000 kcals/day. The energy balance data showed that the patients with the greatest need for energy i.e. those with the highest energy output had proportionately least chance of meeting this need from voluntary food intake. These patients do not appear to be able to compensate for their higher energy needs by increasing voluntary food intake.

Todd et al (1984) examined 55 patients (12 of whom were surgical) over a two-month period. Patients were free to choose their own food from the hospital menu. Mean energy and protein intake of the general surgical patients was 1411 kcal ±75 and 57.2g ±3.8 respectively. No significant differences were found between the groups examined. 24% of the patients had energy intakes below their predicted BMR. 16% had protein intakes less than 0.8g/kg body weight. Only those patients who could eat three meals a day for five consecutive days were included in this study. If these patients could not meet baseline
energy and protein requirements it is undoubtable that the total number of surgical patients failing to meet their nutritional requirements is far greater.

Mughal and Meguid (1987) reported the length of inadequate oral intake after surgery for benign gastrointestinal disease to be 11.9 ±1.9 days in the well-nourished group and 30.5 ±3.7 days in the malnourished group because of the higher morbidity in this group. Inadequate oral intake was considered to be an inability to take at least 60% of estimated requirements orally.

Rana et al (1992) reported mean daily energy intake for the first seven postoperative days to be 1108kcal ±56 and protein intakes of 52.9g ±29. This is comparable with results reported by Hackett et al (1979). Eastwood (1997) reported more than a quarter of all meals were missed on a surgical unit with postoperative fasting accounting for three quarters of these missed meals. In a study investigating nutritional intake and nutritional status of cancer patients in palliative care, energy intake was on average 1300kcal/d and protein intake on average 43g/d. The food records showed that patients ate no more than 2-4 times / day, snack meals included (Osterberg 1997). Poor intake was related to eating problems. Vomiting, nausea and loss of appetite was reported in 80% of patients, 60% had mouth dryness and 30% reported taste disorders.

Keele et al (1997) in a study of surgical patients reported an optimum energy and protein intake from ward diet of 1425-1481 kcal and 45.5-53.5g protein achieved on the seventh postoperative day. Intakes of energy and protein remained below estimated requirements for the entire hospital stay.

More recently, in an attempt to investigate the cause of reported continuing weight loss in hospitalised patients, Barton et al (2000a) examined the nutritional intake of medical, surgical, orthopaedic and elderly hospital patients. The mean total daily energy and
protein intakes of surgical patients were estimated to be 1348 kcal and 41g protein. This is 75% of the minimum energy (1800kcal) recommended by the Department of Health. The low protein intakes also fall short of ideal: the requirements of the sick being in the region of 1.25-2.5g protein /kg/day (Elia 1996). A food wastage rate of greater than 30% was found overall. Interpretation of this study in relation to postoperative patients is difficult as it is not clear if the surgical patients included were examined pre-or post-operatively. No details of the patients’ nutritional status are documented. Neither is there any information on the clinical condition at the time of assessment.

It is clear from these studies that the standard hospital diet is inadequate and is failing to meet the needs of surgical patients.

1.7.1 Fortified hospital food

Studies have examined the impact of more individualised and nutrient dense food prescriptions on nutritional intake. The use of energy and protein dense menus is not very widespread in Europe (Beck et al 2002). The general hospital menu in the majority of European hospitals has a low nutrient density. Yet studies have shown that eating an energy dense menu increases energy and protein intake and reduces the wastage of food (Olin et al 1996, Gall et al 1998, Barton et al 2000b). Several well-controlled studies have demonstrated energy intake to be directly related to changes in energy density (Rolls and Bell 1999). When individuals consumed foods of low energy density they felt satisfied, despite reductions in energy intake. This suggests that foods of high energy density may be useful in situations of energy deficit or malnutrition since a small volume or weight of food would contain a significant amount of energy (Rolls and Bell 1999).

Kondrup et al (1998) examined patients referred to their nutrition unit and found 10% of those referred could not be managed by normal food and supplements as they were judged
to be at special risk requiring more intensive management. A ‘special diet’ was designed as an alternative to regular lunch and dinner each serving supplying about 383 kcal and 25g protein. Patients’ nutritional intake and weight was intensively monitored by a dietitian and the regime adjusted accordingly. Using this approach less than 10% of patients lost more than 5% of their body weight during their hospital admission. This makes an interesting comparison to a study by McWhirter and Pennington (1994) where the majority of patients receiving standard treatment lost weight with an average weight loss of 6.4%. Kondrup’s study demonstrates that this is preventable with the use of appropriately designed hospital menus using fortified food. The patient groups examined did not include surgical patients with malignant disease but instead included patients with malignant disease who were still undergoing treatment.

A study examining geriatric patients under long-term hospital care over two consecutive six week periods found mean energy intake to increase by >450kcals/day with the provision of energy dense food, an increase of 35% (Olin et al 1996). This was sufficient to produce a 3.4% increase in body weight after three weeks. A more recent study by the same group (Olin et al 2003) found a 36% increase in voluntary energy intake (504 kcal/day) with the provision of energy dense meals to nursing home residents over a 15-week period. Despite differences in energy intake body weights were stable in both control and intervention groups.

Gall et al (1998) found the provision of fortified foods and between meal snacks to medical, elderly and orthopaedic patients was sufficient to remove the majority of patients from energy but not protein deficit. Mean energy intake was increased by 17.5% (p=0.007), protein intake increased by 8.2% but did not reach statistical significance. The diet was fortified to a level of 966 kcal/d. This may have been excessive as the majority of patients were removed from energy deficit with much lower intakes of fortified foods. The
fortified diet was not sufficiently high in protein to facilitate a significant increase in protein intake. The non-protein: nitrogen ratio of most standard supplements is 145:1 to 160:1 while the ratio of the fortified food and snacks in this study was 247:1. The study suggests however that smaller portion sizes offered more frequently might be more effective in improving nutrient intakes than the current system of food provision in hospital.

Barton et al (2000b) in a follow up study of a previous one that showed high rates of food wastage and inadequate protein and energy intakes, examined the impact of more energy dense reduced portion size meal provision in elderly rehabilitation patients. The fortified menu provided an additional 200kcal and 5g protein/day. Portion sizes were reduced by approximately 20%. Mean daily energy and protein intake was found to be 1711kcal and 48.7g protein on the fortified menu compared with 1425 kcal and 47.4g protein on the normal menu. Energy intake was closer to requirements on the fortified menu but protein intakes were not improved.

A recent systematic review examining the evidence for the relative benefits of dietary advice and oral supplements found no evidence to support the use of dietary counselling in the management of illness-related malnutrition (Baldwin and Parsons 2004). However the studies examined included patients from varied clinical backgrounds. A broad definition of dietary advice was used with advice ranging from individual dietary counselling with support to the routine provision of additional snack foods with details often not reported. It therefore cannot be established whether the intensity of advice had an impact on study findings. The review highlights the small number of studies that exist in this area and the poor quality of existing data and makes a recommendation for well-designed randomised controlled trials to address the issue.
1.7.2 Nutritional intake and nutritional status following oesophagogastrectomy

Few studies have examined food intake and nutritional status following oesophagogastrectomy for carcinoma. Yet one of the most important goals of oesophagogastrectomy must be to re-establish a socially acceptable and nutritionally adequate eating pattern with minimal side effects and without supplemental nutrition support. Studies outlined below have examined postoperative quality of life issues have reported ongoing problems of dysphagia and decreased quantity of food intake.

Baba et al (1997) questioned 44 ten-year survivors of oesophageal resection for carcinoma of the oesophagus and found the daily quantity of food intake was ‘satisfactory’ for 28 patients (65.1%) and ‘unsatisfactory’ in the remaining 15 (34.8%). No definition of what is considered to be a satisfactory food intake is given. Reflux and heartburn were frequent complaints in patients with unsatisfactory food intake compared to those with satisfactory food intake and patients in the former group failed to regain weight. Neither group achieved their previous preoperative weight ten years postoperatively.

McLarty et al (1997) examined 107 patients who survived five years or more following oesophageal resection. Patients with stage 1 or 11 disease only were included. The number of entirely asymptomatic patients was 17 (16%). Most patients reported one or more of the following symptoms: dysphagia to solids, (25%), pain on swallowing, (9%), dysphagia to pureed food, (9%), dysphagia to liquids (3%) and heartburn (60%). 37% of patients reported eating smaller more frequent meals. The number of patients who never regained lost weight after the operation was 52 (49%), 27 (25%) regained their initial preoperative weight and 6 (6%) gained weight compared with their preoperative weight.

Johansson and Walther (2000) examined 139 patients following oesophagectomy at three, six and twelve months postoperative for the presence of symptoms and reported dysphagia
in 71%, 73% and 77% respectively. Mean postoperative weight decreased significantly during the first postoperative year (p<0.001). All patients had approximately the same pattern of weight change over this time. Weight loss ceased after three months and further changes were not statistically significant. These findings contrast those of De Leyn et al (1992) who examined 80 patients following oesophagectomy for oesophageal malignancy. At three months, diarrhoea, dysphagia and fullness were present in 28%, 27% and 26% of the patients respectively. As in the previous study, at three months postoperative, 90% of patients lost some weight compared with preoperative status. However when weight at three months and one year postoperatively was compared, 90% of patients had re-established their preoperative weight or achieved weight gain one year postoperatively.

In a more recent study of 71 patients following curative oesophagectomy, half of the patients suffered from swallowing problems, regurgitation and fullness during or after a meal (Tabira et al 2002). The amount of food that 55 patients (77.5%) could take was less than half that taken in the preoperative state. In this study the duration of the postoperative period ranged from 8 to 253 months. Food related problems were the main problems affecting quality of life, which was found to deteriorate on discharge from hospital but improved within six months of the operation in disease free patients.

Ludwig et al (2001) evaluated 48 patients following near-total oesophagectomy. Preoperative weight loss occurred in 46% of patients with an average loss of 6.6±4.2kg. Weight loss was found to continue for the first six months. At six months and one year postoperative 41 patients were examined. 63% were able to gain weight, 15% maintained their weight and 22% lost weight. A three-day dietary record was completed at 36 months by 32 patients. It was found that mean energy intake for this group was 2179±502 kcal/day, 98% of the recommended energy intake as estimated based on IBW. Overall 78% were able to meet or exceed daily energy intake recommendations based on IBW.
Approximately one half to two thirds of the patients reported the need to eat smaller portions than had been eaten preoperatively. Nonetheless the diet and variety of foods eaten were considered normal or only minimally restricted in 85% by 6.2 months postoperative. By following up the patients at two weeks, six months and one year, the authors found that the mean time required to achieve what the patients considered to be a socially acceptable diet was six months and that there was a significant amount of adjustment and experimentation with diet necessary in the first three months. In this series, the majority of patients presented over IBW and postoperatively established and maintained a body weight closer to IBW.

Other studies which have monitored the nutritional status of a range of GI surgery patients following discharge home have demonstrated progressive weight loss up to eight weeks post-surgery (Beattie et al 2000) and four months post surgery patients remained below their preoperative weight (Keele et al 1997).

Edington et al (1997) using BMI indices in combination with anthropometry demonstrated that 8.1% of patients were mildly malnourished and 2.4% were severely malnourished within six weeks of major surgery. The longer-term effects of surgery were also examined by Corish et al (1998) who reported that in 3 months following discharge 70% lost weight.

Actual results differ between the studies reported. It is clear that food related problems and weight loss are issues for this patient group and affects quality of life after operation. The differing results between studies can, in part, be explained by different disease stages being examined, patients being examined at different times postoperatively and also different degrees of resection with some surgeons performing oesophagogastrrectomy and others using the stomach in the reconstruction.
1.7.3 Nutritional status and nutritional intake following gastrectomy

Weight loss is the most frequent complication of total gastrectomy (Brain and Stammers 1951, Adams 1967). A substantial weight loss amounting to about 10% of the preoperative weight has been reported to occur during the early postoperative period (Liedman 1999). This has been attributed in the past to malabsorption due to bacterial overgrowth, relative pancreatic enzyme deficiency and shortened small intestinal transit time (Wirts and Goldstein 1963, Drasar et al 1969). In 1975, it was first suggested that malnutrition after total gastrectomy might however be due to an inadequate energy intake (Bradley et al 1975). Loss of the reservoir function, lack of appetite, and altered intestinal motility are all suggested factors behind the low food intake (Liedman 1999). In the cured patient, body weight has been found to stabilise and a slow process of recovery is started (Braga et al 1988).

In a nutritional follow up of 23 patients following total gastrectomy for cancer of the stomach, average daily intake was insufficient (1458 kcal) in the first postoperative month. Only patients without evidence of distant metastases at the time of surgery were included, as persistence of neoplastic disease will alter dietary intake and nutritional status postoperatively. At discharge patients were instructed on a high protein high-energy dietary intake with small frequent meals. By the sixth postoperative month average daily intake had increased to 2118 kcal (Braga et al 1988). Only nine patients had not achieved the Recommended Daily Allowance (RDA) by this time, seven of whom were over 70 years old, which may explain the difference as the elderly may have more difficulty in getting an adequate food intake after surgery. There was no difference in stage of disease between those that achieved the RDA and those that did not. In all patients a decrease in body weight > 10% was observed with respect to usual body weight at discharge. However those patients who reached the RDA by the sixth month achieved a statistically significant 2kg average rise in bodyweight in the six-month postoperative period.
confirming the ability to regain weight after total gastrectomy if an adequate dietary intake is maintained. Regarding visceral protein status, average values were lower than normal in the first postoperative month but above normal in the sixth month in all but three of the 14 patients who achieved the RDA.

Sategna-Guidettti and Bianco (1989) reported on 27 patients who had undergone total gastrectomy with no evidence at surgery of secondary malignancies and found weight loss > 10% in 66% of patients within the first year. Patients were evaluated after a median of nine months after surgery and were not receiving nutritional support. 70% of subjects had a daily energy intake < 30kcal/kg body weight, 21% had a protein intake < 1g/kg body weight and most patients acknowledged a reduced food intake after surgery. The reduced food intake was reported to be due to early satiety and ‘fear’ of eating. Mean fat malabsorption was 37.4 ±4.6%. No statistical correlation was found between percentage of fat malabsorption and percentage of weight loss or kcal/kg intakes.

In another nutritional follow up study patients were as before recommended a high protein, high-energy diet with small frequent meals (Braga et al 1990). One month after total gastrectomy 16 of 28 (57%) patients did not reach 1500 kcal/day. However a monthly check of energy intake revealed a progressive increase in food intake in most patients. This is attributed to a spontaneous adaptation by the patient to the altered anatomy and also to the nutritional follow up programme. Those patients who exceeded 2000 kcal/day one year after operation achieved a significant increase in the average values of body weight, serum albumin and total iron binding capacity. This confirms the ability of these patients to gain weight if an adequate food intake is taken.

Curran and Hill (1990) examined six patients who underwent total gastrectomy for adenocarcinoma. They were followed up for a median of 45 months after surgery.
Patients achieved a mean daily energy intake of 2224 kcal similar to their required intake of 2284 kcal. Protein intake was not significantly different from the required. Unlike the previous study no significant weight change was observed however and mean body weight remained significantly lower than the recalled ‘well’ weight. The authors explain this as energy lost as steatorrhoea.

In another study of the nutritional status of 24 Korean patients two years post total gastrectomy and subsequent immunochemotherapy, average daily energy intake was found to be lower than the average daily energy intake of Korean adults. Weight was an average of 15% less than the preoperative bodyweight at the time of the study. Weight loss was found to increase until 4.2 years after the operation and then tended to decrease. This is attributed to fat malabsorption. The faecal fat excretion was found to be high 28.6 g/d, as well as inadequate energy intake (Bae et al 1998).

Thus while there may be energy losses caused by steatorrhoea, inadequate energy intake appears to be the main cause of malnutrition after total gastrectomy.

1.7.4 Total versus subtotal gastrectomy

An adequate dietary intake has been shown to be possible after total gastrectomy (Bradley et al 1975). However numerous studies have demonstrated the failure of patients to achieve nutrient goals (Braga et al 1988, Sategna-Guidetti. and Bianco 1989, Braga et al 1990). The inadequate nutrient intake demonstrated following total or subtotal gastrectomy might be related to early postprandial satiety, absence of hunger and alteration of intestinal motility (Braga et al 1990). Malabsorption has not been demonstrated to be a major clinical problem if an adequate dietary intake is maintained (Bradley et al 1975, Pellegrini et al 1986). As transit of food through the small intestine is slower in
gastrectomised patients than in control patients and because the proximal jejunum empties rapidly during the meal, a normal meal size can be consumed (Pellegrini et al 1986).

One study examining patients who had undergone total gastrectomy (TG) or partial gastrectomy (PG) found no substantial difference in nutrient intake between the TG and PG groups and their intakes were similar to that previously measured in healthy elderly subjects (Von Holstein et al 1992). This contrasts the findings of Bozzetti et al (1990) when they compared the nutritional status of patients following total (TG) and subtotal gastrectomy (SG). While both groups were in similar nutritional states preoperatively, body weight deteriorated more severely in the total gastrectomy group. After TG, patients had a lower energy intake distributed in a higher number of light meals over the day than those having SG. The size of the residual stomach may be an important indicator of nutritional status as the volume of food eaten has been found to return to close to preoperative levels within a shorter period after a limited gastrectomy than after standard gastrectomy (Takahashi et al 1998).

For patients undergoing either TG or SG, in order to obtain an adequate nutritional intake postoperatively dietary education is essential with strict nutritional follow up to avoid weight loss in the early postoperative course where the main dietary problems occur (Braga et al 1998).

Food provision and food intake in hospital has been shown to persistently fail to meet the energy and protein requirements of postoperative patients. Patients following major upper GI surgery are particularly vulnerable to inadequate dietary intake with a prolonged period of ‘nil-by-mouth’ in the immediate postoperative period followed by problems of early satiety and lack of appetite, which may be prolonged due to the altered intestinal anatomy. Fortified food provision has been examined most extensively in elderly, medical and
geriatric patients under long term care and has been found to have beneficial effects in improving energy intake. Studies are lacking on the use of fortified foods following upper GI surgery. It seems logical to suggest that provision of nutrient dense foods to this group during hospitalisation may be a particularly useful means of improving nutrient intake given their limited capacity for food storage with the absence of the stomach reservoir function.

While early postoperative enteral nutrition is frequently provided to this patient group it is not used extensively following discharge home (Murphy et al 2005). Given the large body of evidence for continued weight loss and food related problems following discharge home it also seems logical that continued jejunostomy feeding at home may be an appropriate means of maintaining an adequate nutritional intake and maintaining nutritional status until an adequate oral intake can be sustained. In order to examine these hypotheses further the current study is proposed.
1.8 Current practice for the management of patients following upper GI surgery in England

There is a lack of defined clinical guidelines as to what constitutes best practice for the nutritional management of these patients. An attempt was made to determine the nutritional management of these patients in designated major cancer centres in England. A questionnaire was designed (Appendix 1) and sent to the dietetic departments of those hospitals in England that have been allocated by Cancer Network Boards throughout England to perform upper gastrointestinal surgery in patients with upper gastrointestinal carcinoma (Murphy et al 2005).

Questions were divided into three main sections relating to (1) nutritional assessment, (2) preoperative nutritional support and (3) postoperative nutritional support in patients with oesophageal carcinoma. The postal questionnaires were returned anonymously and the data aggregated.

Statistical Analysis

All data were entered into a database (Excel for Windows 2000). Comparisons between hospitals with and without dedicated dietetic support were made using the Chi-square test or Fishers exact test as appropriate using the Statistical Package for Social Sciences (SPSS) version 11 (SPSS Corporation, Chicago, Illinois, USA).

A ‘p’ value <0.05 was considered significant.

Results

Eighty-two centres were identified and a total of 66 (80%) responses were received. One centre had two consultants with differing practices regarding postoperative nutritional support so 67 responses were considered. Thirty-one centres (47%) have a dietitian dedicated to the management of these patients.
Preoperative nutritional assessment

This is performed in 22 (33%) centres, with body weight, height, BMI and percentage weight loss the most frequently measured parameters, measured in 95%, 86%, 91% and 82% of cases. Units with a dedicated dietitian are more likely to perform a routine nutritional assessment than those without (55% versus 14%) (p=0.001, $\chi^2$=12.17).

Preoperative nutritional support

In 11 (17%) centres, preoperative nutritional support is provided routinely. In the majority, (n=50, 75%), it is given only when patients are considered ‘malnourished’.

Postoperative nutritional support

Early postoperative nutritional support is routine practice in 47 (70%) centres. Six (9%) centres initiate nutritional support only if patients are considered malnourished and three (4%) centres, only if postoperative complications occur. When questioned on the mode of nutritional support chosen, 43 of 56 (77%) use the jejunal route with only two (3%) centres providing solely parenteral nutrition and 11 (20%) offering both enteral and parenteral nutrition. Those units with a dedicated dietitian are more likely to provide postoperative nutritional support within 24-48 hours routinely compared to those without (87% versus 57%), (p=0.013, $\chi^2$=7.195). The modes of preoperative and postoperative nutritional support used are outlined in Table 1.1.
Table 1.1 Modes of preoperative and postoperative nutritional support

<table>
<thead>
<tr>
<th></th>
<th>Preoperative (%)</th>
<th>Postoperative (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TPN</td>
<td>17(26)</td>
<td>2(3)</td>
</tr>
<tr>
<td>Nasogastric tube feeding</td>
<td>38(58)</td>
<td>0(0)</td>
</tr>
<tr>
<td>Jejunal feeding</td>
<td>0(0)</td>
<td>43(65)</td>
</tr>
<tr>
<td>Sip feed</td>
<td>23(35)</td>
<td>56(85)</td>
</tr>
<tr>
<td>Food snacks</td>
<td>15(23)</td>
<td>54(82)</td>
</tr>
<tr>
<td>Sip feed and food snacks</td>
<td>48(73)</td>
<td>45(68)</td>
</tr>
</tbody>
</table>

Results are numbers of centres (%).

A protocol is in place for postoperative feeding in 29 (51%) centres. Feeding protocols were not more commonly used in centres with a dedicated dietitian compared to those without (62% versus 39%) (p=0.066, \(\chi^2=3.378\)). Whole protein low residue feeds are the most frequently used enteral feeds (61%). Whole protein fibre containing feeds are used in 21% of cases and high energy feeds in 13%.

Dietetic input into the decision to continue / discontinue enteral feeding is reported in 42 (74%), cases. Timing of discontinuing feeding and tube removal varies considerably between centres (Figures 1 and 2).

Oral nutritional support

Oral nutritional supplements are frequently used in this patient group to improve nutritional intake in the postoperative period. They are offered routinely on the introduction of oral fluids in 26 (39%) cases and later in the postoperative course in 30 (45%). In the majority of centres, (n=44, 71%), supplements are continued for an undetermined length of time following discharge. Food snacks (e.g. yoghurt, biscuits,
milk) are available and offered in addition to oral nutritional supplements in 54 (81%) of centres.

Follow up

Patients receive a dietetic review following discharge from hospital in 42 (64%) centres. Patients are more likely to be reviewed following discharge from hospitals with a dietitian dedicated for upper GI carcinoma patients (81% versus 49%) (p=0.007, χ²=7.31).
Figure 1.1 Timing of discontinuing postoperative nutritional support

- On diet
- 7-10 days postop
- On improving diet
- Achieving 50-75% requirements
- Discharge

Figure 1.2 Timing of jejunostomy tube removal

- Achieving adequate diet
- On / prior to discharge
- OPD 1- 6 weeks
- No set time
Discussion

This study shows that 66% of specialist centres for the management of patients with upper gastrointestinal carcinoma do not perform a nutritional assessment preoperatively. The situation is somewhat better in those centres with a dedicated dietitian.

This study also shows that jejunal feeding is the most frequently used mode of delivery of postoperative nutrition support with 77% of centres choosing this route and only 3.5% choosing to use parenteral nutrition. However, 16% of centres provide no postoperative nutritional support and 9% provide nutritional support only if complications occur.

Several studies have found evidence of clinical benefits of supplementation of ward diet with oral supplements following surgery irrespective of their preoperative nutritional status (Beier-Holgersen and Boesby 1996, Keele et al 1997). Yet this study shows that only 46% (26 of 56) of centres routinely provide oral nutritional supplements on commencing oral fluids.

A high proportion of centres (53%) lack formal dietetic input into the management of their upper GI carcinoma patients. This questionnaire shows that centres with dedicated support are more likely to perform preoperative nutritional assessments of patients, more likely to have protocol guided early postoperative enteral nutrition and more likely to be formally reviewed following discharge home where continued nutritional problems are frequently encountered. Even in those centres with a dedicated dietitian the nutritional management of these patients is not uniform.

With the establishment of fewer centres doing a greater volume of cases (part of the action plan for improving outcomes guidance for upper gastrointestinal carcinoma) (Department of Health 2000), it would seem appropriate that dedicated dietitians be employed in these centres and strict protocols established.
1.9 Summary

Although many operable cancer patients either present with malnutrition or become malnourished after surgery, the perioperative nutritional management of these patients remains an area of controversy.

The postoperative period is associated with deterioration in nutritional status due to hypermetabolism post injury. While traditionally parenteral nutrition support may have been the chosen route for the perioperative nutrition support of upper GI surgical patients, it is now accepted that enteral nutrition support is better unless the patient cannot tolerate it (Lewis et al 2001a, Maxfield et al 2001). There has been an increased awareness of the dangers associated with parenteral nutrition and also an increased availability of enteral support options. In choosing the route to administer nutrients, factors such as availability and access of a functioning gut, compliance and comfort of the patient, the need for hospitalisation to start a PN regimen and costs should be taken into consideration (Bozzetti 1989). Evidence is conflicting as to the usefulness of postoperative enteral nutrition support in all patients undergoing gastrointestinal surgery, with some studies showing evidence of clinical benefit: Beier-Holgersen and Boesby (1996), Braga et al (2002b), but others no benefit: Heslin et al (1997) and Watters et al (1997).

It is well documented that intakes of energy and protein during the postoperative phase in surgical patients fall well below estimated requirements (Hackett et al 1979, Todd et al 1984, Rana et al 1992, and Keele et al 1997). The benefits of postoperative enteral feeding found in normally nourished surgical patients suggest that reduced nutritional intake may be a factor that predisposes patients to developing complications. While results are conflicting in terms of the usefulness of early postoperative enteral nutrition support in normally nourished, mildly or moderately malnourished patients, there is sufficient evidence that the clinical outcome of less severely malnourished surgical
patients, including those that are normally nourished, can be improved by the administration of oral dietary supplements postoperatively once patients are allowed free fluids (Rana et al 1992, Keele et al 1997). However poor compliance with supplements is a frequently encountered problem (Ovensen et al 1991).

The inadequacy of current catering and feeding practices which are modelled on institutional catering for the healthy rather than being targeted to the needs of the sick have been highlighted in a number of recent reports (Allison 1999). High food wastage rates have been reported (Barton et al 2000a) providing evidence that patients are not gaining the necessary nutrient and energy intake. Appropriately designed hospital menus using fortified foods have been found to be effective in reducing weight loss during hospitalisation and improving nutritional intake (Gall et al 1998, Kondrup et al 1998). Numerous studies have demonstrated the failure of patients post upper GI surgery to achieve nutrient goals (Braga et al 1988, Sategna-Guidetti and Bianco 1989, Johansson and Walther 2000, Tabira et al 2000). This is associated with problems of early satiety, absence of hunger and altered intestinal motility (Braga et al 1988, Braga et al 1990, Tabira et al 2000). It is therefore proposed that the provision of individualised food prescriptions to this patient group may be of benefit in improving nutritional intake and nutritional status postoperatively.

Nutritional problems are not resolved on discharge home with numerous studies demonstrating continued weight loss for six months to one year postoperative (Johansson and Walther 2000, Ludwig et al 2001). As a follow on to this study it is therefore proposed that continued supplementary enteral feeding at home may be of benefit in improving nutritional intake and nutritional status postoperatively.
Chapter Two

Methodology

Study 1
2.1 Hypothesis

This research is based on the hypotheses that the provision of normal foods enriched with energy and protein to patients following gastrectomy or oesophagogastric for carcinoma may improve energy and protein intake and nutritional status postoperatively.

2.2 Aims

To examine the perioperative nutritional status and energy and the protein intake of patients undergoing surgery for gastric and oesophageal carcinoma, to introduce a system of fortified food provision with intensive dietary advice and supervision and to examine its impact on nutritional status and energy and protein intake.

2.3 Objectives

1. To examine the perioperative nutritional status of patients admitted for gastrectomy or oesophagogastric.

2. To determine the energy and protein intake of these patients following resection for gastric and oesophageal carcinoma and to examine the contribution of all feeding sources to total energy and protein intake.

3. To examine the effect of total gastrectomy compared with subtotal gastrectomy on oral intake in gastric carcinoma patients.

4. To instigate a system of food provision where selected foods are enriched with energy and protein while remaining palatable and acceptable to patients and to examine the impact of fortified food provision on energy and protein intake.

5. To compare the energy and protein intake contribution of food to those receiving standard hospital treatment with those receiving fortified foods.

6. To examine morbidity and mortality in this patient group and associated factors.
2.4 Study Design

The investigation was a two-phase study conducted on an upper gastrointestinal surgical ward in a District General Hospital.

Phase 1: Control phase

This phase of the study was observational. From the point of introduction of oral intake postoperatively, nutritional intake of consecutive patients who successfully underwent surgical resection for carcinoma of the oesophagus and stomach respectively was assessed daily. The contribution of artificial nutrition support (PN or jejunostomy feeding), oral nutritional supplements and hospital food to daily energy and protein intake was determined. The former was obtained by monitoring fluid charts. The latter was determined by a combination of direct food weighing, observation and the 24-hour recall method. Examination of micronutrient intake was considered to be beyond the scope of this study as it would require more specialised investigations not routinely performed at the hospital site.

All patients underwent a nutritional assessment preoperatively and weekly thereafter until discharge. An attempt was made to review patients within a month of discharge when body weight was measured.

All patients were given high-energy high protein dietary advice on discharge from hospital and encouraged to continue to take oral nutritional supplements if they were found to be acceptable while in hospital.

Phase 2: Intervention phase

In this phase of the study, consecutive patients who successfully underwent surgical resection for carcinoma of the oesophagus and stomach were offered a selection of energy
and protein enriched foods from the time of introduction of oral intake until discharge (Appendix 2). Enriched food items were offered either at mealtimes in addition to a standard hospital main course or in between meals, depending on individual preference and capacity. Nutrient intake was determined as before, by food weighing, observation and 24-hour recall method.

All patients underwent a nutritional assessment preoperatively and weekly thereafter until discharge. Patients were advised on continuing food fortification and/or oral nutritional supplements at the time of discharge. An attempt was made to review patients within a month of discharge when body weight was measured and energy and protein intake established where possible by the 3-day dietary recall method.

Comparison was made between the nutritional status of the control and intervention groups preoperatively, on the seventh postoperative day and on discharge. Comparison of the energy and protein intake of the two groups was made on the seventh, eighth, ninth, tenth postoperative day and on the day of discharge.

2.5 Subjects
Patients were considered eligible for inclusion in the study if they were admitted with gastric or oesophageal carcinoma and after appropriate investigations were considered suitable candidates for surgery. There were no exclusion criteria.

2.6 Assessments
2.6.1 Determination of food and fluid intake
Nutrient intake was assessed from the first postoperative day until discharge. A food record chart was the chosen means of recording food and fluid intake. Nursing and
auxiliary staff were instructed to observe food eaten and to document the amount consumed in household measures i.e. one cup of milk, a half bowl of Cornflakes. Duplicate food items were weighed by the dietitian prior to commencing the study so as to obtain a more accurate estimate of food intake. At the midday meal the weighed food intake method was used by the investigating dietitian to determine food intake. Patients were allowed to choose their own food at mealtimes from the ward trolley and were given considerable encouragement to eat. Subsequently plates were weighed and then each item of a composite meal. Actual food eaten was then determined by weighing the plate again on completion of the meal. All patients were questioned on their food and fluid intake over the previous 24-hour period to verify the food record charts. This was not possible on weekend days but did not pose a great problem as most patients were competent in documenting food intake in conjunction with nursing staff.

Nutrient intake was determined by direct food weighing at the midday meal only as this was considered to be the most substantial meal of the day and also the only meal served within dietetic working hours. No funding was available for a dietetic assistant or other member of staff to perform the task at breakfast or teatime. Oral intake was monitored and recorded and macronutrient content was determined from the seventh to the tenth postoperative day and on the day of discharge. These particular days were chosen as the median number of days before commencement of oral intake was five to seven. Consequently the days chosen would represent macronutrient intake in the early postoperative stage, midway through hospitalisation and at the end of hospital stay.

2.6.2 Assessment of nutritional status

Five indices of nutritional status were chosen: height and weight (to establish BMI), serum albumin and C reactive protein (CRP), serum haemoglobin and lymphocyte count. These parameters were measured preoperatively, seven days postoperatively and on the day of
discharge from hospital. These indices of nutritional status were chosen on the basis that they are objective, minimally invasive, easy to obtain and have been widely used in previous studies (Bozzetti 1990, Thoresen 2002). Upper arm anthropometry has been used in carcinoma patients and was performed in the early part of the study but was considered invasive by patients and therefore not continued. BMI has been found to correlate closely with mid upper arm circumference (MUAC) (Powell-Tuck and Hennessy 2003) and was easy to obtain in this patient group. Unintentional weight loss over three to six months was also established.

2.6.3 Diagnosis of malnutrition

In this study a combination of BMI and weight loss was used to identify malnutrition. BMI cut-off values of <20 kg/m² and >25 kg/m² have been agreed to classify underweight and overweight respectively (Office of Population Censuses and Surveys 1993, 1994). Although there are limitations to using a single cut-off value for detecting clinically relevant weight loss, there is general agreement that unintentional weight loss of >10% over 3-6 months is significant. Weight loss in excess of the normal intra-individual variation (suggested to be 5% over 3-6 months) may be used as a warning signal for the development of malnutrition (Stratton et al 2003).

While biochemical parameters are considered in this study, a combination of BMI <20kg/m² and weight loss >10% over 3-6 months was used to identify malnutrition as used in a number of recent studies (Bruun et al 1999, Tessier et al 2000, Edington et al 2000).
2.6.4 Nutritional Measurements

Anthropometry

(a) Body weight

Patients were weighed by their bedside in their bedclothes on a stand on Seca ward scales. The same set of scales was used throughout the study. Body weight was recorded at the same time of day and at the same postoperative stage (preoperative, day 7 postoperative and the day prior to discharge for all patients).

(b) Height

Height was measured on a wall-mounted stadiometer on the ward or in the outpatient department if they were seen prior to hospital admission. The stadiometer remained static for the duration of the study.

The following calculations were made:

(a) Body Mass Index (BMI)

This was determined using the formula:

\[ \text{BMI} = \frac{\text{weight (kg)}}{\text{height}^2 \text{ (m)}}. \]

(b) Percentage weight loss

Patients were asked to recall their usual or ‘well’ weight. Medical notes were examined for any record of weight in those unable to recall usual weight. Percentage weight loss was then calculated using the formula:

\[ \% \text{ Weight loss} = \frac{\text{Usual weight (kg)} - \text{Current weight (kg)}}{\text{Usual weight (kg)}} \times 100 \]
Biochemistry

(a) Serum albumin

Serum albumin was measured by the hospital biochemistry department. Venous blood samples were obtained by a phlebotomist or junior doctor and serum albumin levels measured using a bromocresolgreen (BCG) dye binding method on an Olympus AU600 analyser (Olympic Optic Company, Great Western Industrial Park, Deanway, Southall, Middlesex, UB 2 4SB) (Doumas et al 1971).

(b) Haemoglobin level and lymphocyte count

Haemoglobin levels and lymphocyte count were measured by the hospital haematology department by spectrophotometry and laser light diffraction respectively on an abbotcell-dyn 4000 (Olympic Optic Company) (Lewis et al 2001b).

(c) C Reactive Protein (CRP)

CRP levels were measured by the hospital biochemistry department. Venous blood samples were obtained by a phlebotomist or junior doctor and serum CRP levels measured using an immunoturbidometric method on an Olympus AU600 analyser (Olympic Optic Company) (Price et al 1987). Reference ranges used for biochemical parameters measured are documented in Appendix 3.

Nutritional Requirements

(a) Energy

Approximate basal metabolic rate was determined using the Schofield Equation (Schofield 1985). This is considered to be the most appropriate equation that is available for BMR calculation at present (Todorovic and Micklewright 2004). Adjustments were then made for stress and activity level.
A stress factor of 20% (post surgery) and a 15% combined factor for activity and diet-induced thermogenesis (DIT) was then applied (Todorovic and Micklewright 2004). At the point of discharge energy requirements were recalculated and a 25% activity factor only was applied, as the patients were no longer in the catabolic phase.

(b) Protein

Protein requirements were estimated using the Elia table for Nitrogen requirements (Elia 1990). As this patient group were considered to be hypermetabolic postoperatively, Nitrogen requirements were calculated using 0.2g Nitrogen /kg (Todorovic and Micklewright 2004). At the point of discharge protein requirements were recalculated using 0.17g Nitrogen /kg as the patients were no longer in the catabolic phase.

Energy and protein intake were assessed in this study as more detailed assessment of micronutrient intake was considered beyond the scope of the study. Furthermore the food enricher chosen provided macronutrients only.

2.7 Procedure

2.7.1 Phase 1: Control phase

All patients with oesophageal carcinoma and most with gastric carcinoma received a feeding jejunostomy tube at the time of laparotomy and feeding was commenced on the second postoperative day as per ward protocol (Appendix 4). When certain postoperative complications occurred or where lower GI surgery was also carried out, parenteral nutrition (PN) was the feeding method of choice for the immediate postoperative period. This was at the discretion of the operating surgeon.

Patients were visited on a daily basis by the investigating dietitian and surgical team until discharge. Patients with a jejunostomy tube were commenced on a standard enteral feed.
Osmolite (Abbott Laboratories) or Nutrison Standard (Nutricia) was the chosen feed in the presence of normal serum biochemistry (see Appendix 5 for nutritional composition). In cases where parenteral nutrition was instigated, its nutritional contribution was recorded. This was achieved by daily monitoring of fluid charts completed routinely by nursing staff. On the introduction of free oral fluids, whole milk and oral nutritional supplements (Appendix 5) were encouraged by the dietitian. Intake was monitored and recorded on fluid charts.

Patients then progressed onto a ‘light diet’ (soup and pudding) and ultimately to normal/soft ward diet. Nursing staff documented food and fluid intake at breakfast, teatime and in between meals on food record charts. They were instructed to complete the charts with as much attention to detail as possible. Food intake was weighed by the dietitian and recorded at the main midday meal but this procedure was limited to weekdays only. On weekend days nursing staff were responsible for recording all food intake. Information documented by nursing staff was confirmed by the dietitian directly questioning patients.

2.7.2 Phase 2: Intervention phase

Normal food can be enriched with energy and protein in a number of ways. For example, using household food items such as cream, butter, skimmed milk powder, using energy providing nutritional products such as glucose polymers eg. Maxijul, Polycose, using nutritional products providing protein eg. Vitapro, Maxipro or both energy and protein eg. ProCal.

As the aim of the study was to investigate if energy and protein intake could be improved by means of food fortification, attention was focused on the use of products providing both energy and protein. In the initial pilot testing a combination of ProCal and Vitapro was
chosen in preference to other products as together these could be added at a greater level and to a wider variety of foods with a less detrimental effect on taste and texture. The composition of these products is documented in Appendix 6.

A range of food items considered appropriate for fortification were selected (Appendix 2) and patients were allowed to choose their preferred option. They were encouraged to choose either the soft textured option or standard hospital main course at mealtimes and a fortified item was offered as a pudding or as a snack in between meals. These comprised largely of soft milky puddings due to the ease with which the nutritional products could be incorporated into such foods. The level of fortification was adjusted depending on palatability and stability tests carried out by a group of dietitians. A target level of fortification was set as 25-30g protein/day and 350-400kcals/day. This could be achieved by fortifying foods with 30g Vitapro and 45g (3 sachets) ProCal. All food enrichment was carried out by the principle investigator or a trained assistant to ensure consistency.

2.7.3 Monitoring of complications

All patients were monitored for the occurrence of complications from the first postoperative day until discharge. This involved daily observation of the patient and liaison with the surgical team.

2.8 Ethical Considerations

Ethical approval was granted by Gwent Research Ethics Committee (Appendix 7(a)). Control patients were given standard treatment, consequently consent was only needed from patients in the intervention groups. These patients were informed of the nature of the study preoperatively and were assured that participation was voluntary. Written informed consent was attained before entering into the study (Appendix 7(a)). All patients agreed to participate.
2.9 Data Analysis

Nutrient intakes were determined using the computer software package Comp Eat version 5. The nutritional composition of the products used to fortify the food was added to the database prior to the study commencement. All foods eaten by patients were on the database.

Statistical analysis was performed using SPSS for Windows (Version 9.0; SPSS Inc; 1998). Non-parametric tests were used as body weight and nutritional intake data did not show a normal distribution when plotted graphically. For paired or matched samples the Wilcoxon test for non-parametric data was used and the Mann-Whitney U test was used when comparing two independent samples as both tests do not require the assumption that the population is normally distributed. Non-Parametric tests may be more powerful in detecting population differences when certain assumptions are not satisfied (Greenhalgh 1997). Data on nutritional intake and nutritional status was recorded at time points determined a priori: preoperative, day 7 postoperative, discharge and four weeks postoperative. Comparison was made between preoperative results and the other chosen time points. There is an increased probability of detecting intervention effects where none exist with multiple analyses ("false positives" owing to multiple comparisons — type I errors), however this is of more concern when these are conducted post-hoc as a "fishing expedition", and undue emphasis is given to positive findings (Lord et al 2004). Analyses were decided upon a priori in this case and not post hoc which reduces the likelihood of false positive results. A ‘p’ value <0.05 was considered significant.
Chapter Three

Results

Study 1
3.1 Patient details

(a) Gastric carcinoma

(i) Control group

This comprised initially of 24 consecutive patients who underwent total or subtotal gastrectomy (18 male, 6 female), age range 27-83 years, from May 1999 to September 2001. Potentially curative surgery was performed in 19 cases; five patients had a palliative resection. There were three operative deaths during the course of the study (12.5% mortality), two underwent a palliative resection. Operative deaths did not progress to food intake and consequently are excluded from the analysis. Cause of death in these two cases was anastomotic leak with chest sepsis for one patient and dyspnœa and renal failure for the other. Volvulus at the jejunostomy site requiring relaparotomy with subsequent acute pancreatitis and multisystem failure was the cause of death in the third case.

(ii) Intervention group

The intervention group initially comprised of 21 consecutive patients who successfully underwent total or subtotal gastrectomy (14 male, 7 female), age range 47-81 years from October 2001 to September 2003. Potentially curative surgery was performed in 17 cases, four patients had a palliative resection. There were two operative deaths during the course of the study (9% mortality), both underwent palliative resections. In one case a palliative resection was performed despite the patient being a high-risk candidate due to almost total dysphagia and an extremely poor quality of life. The patient suffered a probable myocardial infarction (MI) postoperatively. The second death occurred in a patient with advanced stage of disease who suffered chest sepsis and a peri-anastomotic abscess postoperatively. The cause of death was overwhelming sepsis following relaparotomy.

Details of the final control and intervention groups are presented in Table 3.1.

Details of all patients including operative deaths are outlined in Appendix 8.

The two groups were well matched regarding age, sex, operation type and stage of disease.
Table 3.1 Details of the patients: Gastric carcinoma

<table>
<thead>
<tr>
<th></th>
<th>Control group (n=21)</th>
<th>Intervention group (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male: Female</td>
<td>15:6</td>
<td>14:5</td>
</tr>
<tr>
<td>Age (years)</td>
<td>69 (27-83)</td>
<td>67 (47-81)</td>
</tr>
<tr>
<td>Operation type:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total gastrectomy</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Subtotal gastrectomy</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Potentially curative resection</td>
<td>18</td>
<td>17</td>
</tr>
<tr>
<td>Stage of disease (Guillou and Monson 2001)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>II</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>III</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>IV</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Postoperative nutrition support</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parenteral nutrition only (PN)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>PN and jejunostomy feeding</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Jejunostomy feeding</td>
<td>12</td>
<td>8</td>
</tr>
</tbody>
</table>

Results are numbers of patients. Age is expressed as median (range)

A greater proportion of the control group (n=21, 100%) received early nutrition support compared with the intervention group (n=11, 58%) ($\chi^2 = 11.053$, p=0.001).
(b) Oesophageal carcinoma

(i) Control group

This comprised of 26 consecutive patients (17 male, 9 female), age range 46-77 years who underwent oesophagogastrectomy from May 1999 to September 2001. Potentially curative surgery was performed in 24 cases and two patients had a palliative resection. There were three operative deaths, (11.5%) mortality, all had a potentially curative resection. Cause of death was cardiac arrest due to pulmonary embolus in one case, respiratory infection in another and iatrogenic tracheal perforation in the third case.

(ii) Intervention group

The intervention group comprised of 20 consecutive patients (15 male, 5 female), age range 38-78 years who successfully underwent oesophagogastrectomy from October 2001 to September 2003. Potentially curative surgery was performed in 19 cases, one patient had a palliative resection. There was one operative death (5% mortality) following curative surgery. This patient developed a chylothorax and chylous leak requiring relaparotomy. Cause of death was a postoperative cardiac arrest.

Details of all patients including operative deaths are outlined in Appendix 8. Details of the final control and intervention groups are presented in Table 3.2. The two groups were well matched with no difference in age, sex, operation type and stage of disease.
Table 3.2 Details of the patients: Oesophageal carcinoma

<table>
<thead>
<tr>
<th></th>
<th>Control group (n=23)</th>
<th>Intervention group (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male: Female</td>
<td>16:7</td>
<td>15:4</td>
</tr>
<tr>
<td>Age (years)</td>
<td>60 (46-77)</td>
<td>62 (38-78)</td>
</tr>
<tr>
<td>Operation type: Transhiatal oesophagogastricomy</td>
<td>21</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Potentially Curative Resection</td>
<td>21</td>
<td>18</td>
</tr>
<tr>
<td>Stage of Disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Guillou and Monson 2001)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>I</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>II</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>III</td>
<td>13</td>
<td>14</td>
</tr>
<tr>
<td>IV</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Jejunostomy tube feeding alone</td>
<td>18</td>
<td>17</td>
</tr>
<tr>
<td>Jejunostomy feeding and PN</td>
<td>5</td>
<td>2</td>
</tr>
</tbody>
</table>

Results are numbers of patients. Age is expressed as median (range)
Objective 1. To examine the perioperative nutritional status of patients admitted for gastrectomy or oesophagogastrectomy and to compare the nutritional status of control and intervention groups.

3.2 Preoperative nutritional status.

(a) Gastric carcinoma

Details of the preoperative nutritional status of gastric carcinoma patients are presented in Table 3.3. Details including the operative deaths are documented in Appendix 8.

Table 3.3 Preoperative nutritional status in gastric carcinoma patients: serum biochemistry and anthropometry

<table>
<thead>
<tr>
<th></th>
<th>Control group (n=21)</th>
<th>Intervention group (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (kgs)</td>
<td>65* (38-90)</td>
<td>77* (49-121)</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>23.6** (17.5-31)</td>
<td>26.2** (19.6-33.5)</td>
</tr>
<tr>
<td>Preop weight loss (%)</td>
<td>5.5# (0-16.4)</td>
<td>0# (0-21.8)</td>
</tr>
<tr>
<td>Albumin (g/l)</td>
<td>39.5 (29-47)</td>
<td>39 (20-44)</td>
</tr>
<tr>
<td>CRP (mg/l)</td>
<td>&lt;10 (&lt;10-35.3)</td>
<td>&lt;10 (&lt;10-132)</td>
</tr>
<tr>
<td>Lymphocyte count (x10⁹/l)</td>
<td>1.7 (0.9-2.5)</td>
<td>1.6 (1.1-2.9)</td>
</tr>
<tr>
<td>Haemoglobin (g/dl)</td>
<td>12.5 (10.3-16.9)</td>
<td>13.3 (9.2-15.7)</td>
</tr>
</tbody>
</table>

* p=0.078, ** p=0.054, p=# 0.235 (Mann Whitney U test)
Results are median (range).

BMI < 20kg/ m² and unintentional weight loss >10% in three to six months were the criteria chosen to identify malnutrition.
(i) Control group

In the control group, using these criteria, only two patients (9.5%) can be considered malnourished. Median levels of all the other parameters chosen as indicators of nutritional status were within the normal range preoperatively with the exception of haemoglobin where the median level was slightly below the normal range at 12.5g/dl.

(ii) Intervention group

In the intervention group, no patient can be considered malnourished. Median levels of all the parameters chosen as indicators of nutritional status were within the normal range preoperatively. In fact median BMI was 26.2kg/m² indicating overweight.

The control and intervention groups were well matched with no difference observed in the anthropometric or biochemical parameters measured preoperatively. There was a tendency towards overweight in the intervention group (p=0.054) and a tendency for preoperative weight loss to be less in the intervention group (0 versus 5.5%) however the difference between the two groups was not found to be significant (p=0.235). There was no difference between the two groups in the incidence of malnutrition or in the numbers at nutritional risk (p=0.488 $\chi^2=1.905$ and p=0.36, $\chi^2=0.973$ respectively).
(b) Oesophageal carcinoma

Details of the preoperative nutritional status of oesophageal carcinoma patients are presented in Table 3.4. Details including the operative deaths are documented in Appendix 8.

Table 3.4 Preoperative nutritional status in oesophageal carcinoma patients: serum biochemistry and anthropometry

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control group (n=23)</th>
<th>Intervention group (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (kgs)</td>
<td>76.5* (51.6-104.5)</td>
<td>75* (44-103)</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>25** (19-32)</td>
<td>24.5** (18-30.5)</td>
</tr>
<tr>
<td>Preoperative weight loss (%)</td>
<td>5.4# (0-17.6)</td>
<td>3.2# (0-20)</td>
</tr>
<tr>
<td>Albumin (g/l)</td>
<td>42 (23-48)</td>
<td>41 (36-46)</td>
</tr>
<tr>
<td>CRP (mg/l)</td>
<td>N/A</td>
<td>&lt;10 (&lt;10-33.4)</td>
</tr>
<tr>
<td>Lymphocyte count (x10⁹/l)</td>
<td>1.5 (0.7-3.6)</td>
<td>1.5 (0.7-3.8)</td>
</tr>
<tr>
<td>Haemoglobin (g/dl)</td>
<td>14.1 (10.7-16.1)</td>
<td>14.1 (12.7-16.3)</td>
</tr>
</tbody>
</table>

* p=0.860, **p=0.139, #p=0.790 (Mann Whitney U test)

Results are median (range)

(i) Control and intervention groups

Using the chosen criteria to identify malnutrition, no patient in the oesophageal carcinoma control or intervention groups could be considered malnourished preoperatively. Median levels of the biochemical parameters measured as indicators of nutritional status (serum albumin, lymphocyte count and serum haemoglobin) were within the normal range preoperatively.
The two groups were well matched with no difference observed in the biochemical or in the anthropometric parameters measured preoperatively.

These data show that gastric and oesophageal carcinoma patients entered into this study were not severely malnourished overall preoperatively with a median weight loss <10% and median BMI and serum albumin within the normal (or overweight) range. A considerable proportion of patients were at nutritional risk.

Fifty two percent of the gastric carcinoma control group experienced weight loss >5% in three to six months. In this group, 36%, (n=4) of those with >5% weight loss also had a low BMI. Thirty seven percent of the gastric carcinoma intervention patients experienced weight loss >5% in three to six months. In this group, 29% (n=2) of those with >5% weight loss also had a low BMI.

Fifty two percent of the oesophageal carcinoma control group experienced weight loss >5% in three to six months. Of these 14% (n=2) also had a low BMI. Forty seven percent of the oesophageal carcinoma intervention patients experienced weight loss >5% in three to six months. Of these 11% (n=1) also had a low BMI.

The nutritional status of the intervention groups was comparable with the controls. In the case of the gastric carcinoma groups the trend towards a higher body weight and BMI in the intervention group must be considered when interpreting the results.
3.3 Nutritional status during hospitalisation

(a) Gastric carcinoma

Tables 3.5 (a) and 3.5 (b) show the nutritional parameters measured in the gastric carcinoma control and intervention groups during hospitalisation.

Table 3.5 (a) Nutritional status in gastric carcinoma control patients: serum biochemistry and anthropometry during hospitalisation

<table>
<thead>
<tr>
<th></th>
<th>Preoperative (n=21)</th>
<th>Study day 7 (n=21)</th>
<th>Discharge (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (kgs)</td>
<td>65* (38-90)</td>
<td>62.5 (45-87.5)</td>
<td>62.5* (41-87.5)</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>23.6* (17.5-31)</td>
<td>23.5 (16.6-31)</td>
<td>22* (16.5-31)</td>
</tr>
<tr>
<td>Albumin (g/l)</td>
<td>39.5** (29-47)</td>
<td>27** (20-36)</td>
<td>31** (24-46)</td>
</tr>
<tr>
<td>CRP (mg/l)</td>
<td>&lt;10 (&lt;10-35.3)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Lymphocyte count (x10⁹/l)</td>
<td>1.7**# (0.9-2.5)</td>
<td>0.95** (0.3-1.9)</td>
<td>1.2# (0.7-2.4)</td>
</tr>
<tr>
<td>Haemoglobin (g/dl)</td>
<td>12.5#* (10.3-16.9)</td>
<td>11.9# (9.5-14)</td>
<td>11.4* (9.8-13.3)</td>
</tr>
</tbody>
</table>

Results are median (range)
*p <0.006,**p <0.0001 vs preoperative values, #p = 0.043,
■p = 0.026 (Wilcoxon signed ranks test)

Using the Wilcoxon signed ranks test, results obtained on day seven postoperative and on the day of discharge were compared with preoperative results.

- Body weight and BMI were lower at discharge (p<0.006).
- Serum albumin was lower on the seventh postoperative day and remained lower at discharge (p<0.0001).
- Serum lymphocyte count was lower on the seventh postoperative day (p<0.0001) and remained lower on discharge (p=0.043)
- Serum haemoglobin levels were also lower on the seventh postoperative day (p=0.026) and remained lower on discharge (p<0.006).
Table 3.5 (b) Nutritional status in gastric carcinoma intervention patients: serum biochemistry and anthropometry during hospitalisation

<table>
<thead>
<tr>
<th></th>
<th>Preoperative (n=19)</th>
<th>Study day 7 (n=19)</th>
<th>Discharge (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body weight (kgs)</strong></td>
<td>77 (49-121)</td>
<td>79 (52-126)</td>
<td>71 (47-127)</td>
</tr>
<tr>
<td><strong>Body Mass Index (kg/m²)</strong></td>
<td>26.2 (19.6-33.5)</td>
<td>27.7 (20.6-35)</td>
<td>26.2 (18.6-35)</td>
</tr>
<tr>
<td><strong>Albumin (g/l)</strong></td>
<td>39*# (20-44)</td>
<td>28* (17-36)</td>
<td>33# (24-39)</td>
</tr>
<tr>
<td><strong>CRP (mg/l)</strong></td>
<td>&lt;10**# (&lt;10-132)</td>
<td>96** (25.5-158)</td>
<td>37# (&lt;10-321)</td>
</tr>
<tr>
<td><strong>Lymphocyte count (x10⁹/l)</strong></td>
<td>1.6** (1.1-2.9)</td>
<td>1.3** (0.5-1.9)</td>
<td>1.4 (0.7-3.2)</td>
</tr>
<tr>
<td><strong>Haemoglobin (g/dl)</strong></td>
<td>13.3**# (9.2-15.7)</td>
<td>12.3# (9.9-13.1)</td>
<td>11.9** (10.4-26.6)</td>
</tr>
</tbody>
</table>

Results are median (range)
*p=0.001, # p<0.013, **p=0.002, ■ p=0.041
(Wilcoxon signed ranks test)

Using the Wilcoxon signed ranks test, results obtained on day seven postoperative and on the day of discharge were compared with preoperative results.

- Serum albumin was lower on the seventh postoperative day (p=0.001) and remained lower at discharge (p<0.013).
- Serum CRP was higher on the seventh postoperative day (p=0.002) and remained higher at discharge (p=0.041).
- Serum lymphocyte count was lower on the seventh postoperative day (p=0.002).
- Serum haemoglobin was also lower on the seventh postoperative day (p<0.013) and remained lower on discharge (p=0.002).

There was a trend towards a higher BMI in the intervention group preoperatively compared to the control group (p=0.054). BMI was higher on the seventh postoperative day and remained higher on discharge (p=0.032 and p=0.023 respectively). Percentage preoperative weight loss and weight loss in hospital was not different between the two groups. No difference was observed between the control and intervention groups in the other nutritional parameters monitored during hospitalisation with the exception of serum
lymphocyte count which was higher in the intervention group on the seventh postoperative day (p=0.024).

(b) Oesophageal carcinoma

Tables 3.6 (a) and 3.6 (b), show the nutritional parameters measured in the oesophageal carcinoma groups during hospitalisation.

Table 3.6 (a) Nutritional status in oesophageal carcinoma control patients: serum biochemistry and anthropometry during hospitalisation

<table>
<thead>
<tr>
<th></th>
<th>Preoperative (n=23)</th>
<th>Study day 7 (n=23)</th>
<th>Discharge (n=23)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body weight (kgs)</strong></td>
<td>76.5* (52-105)</td>
<td>74 (52.5-101)</td>
<td>72* (50.5-93)</td>
</tr>
<tr>
<td><strong>Body Mass Index (kg/m²)</strong></td>
<td>25* (19-32)</td>
<td>27 (18.9-31.4)</td>
<td>23.5* (17.4-33.2)</td>
</tr>
<tr>
<td><strong>Albumin (g/l)</strong></td>
<td>42#** (23-48)</td>
<td>26** (16-34)</td>
<td>34# (27-43)</td>
</tr>
<tr>
<td><strong>CRP (mg/l)</strong></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Lymphocyte count (x10^9/l)</strong></td>
<td>1.5** (0.7-3.6)</td>
<td>0.9** (0.2-2.1)</td>
<td>1.3 (0.4-3.1)</td>
</tr>
<tr>
<td><strong>Haemoglobin (g/dl)</strong></td>
<td>14.1# (10.7-16.1)</td>
<td>11.8# (10.5-15.1)</td>
<td>12.4# (9.1-14.6)</td>
</tr>
</tbody>
</table>

Results are median (range)

*p=0.004, **p<0.0001, #p=0.001 (Wilcoxon signed ranks test)

Using the Wilcoxon signed ranks test, results obtained on day seven postoperative and on the day of discharge were compared with preoperative results.

- Body weight and BMI were lower on discharge (p=0.004).
- Serum albumin was lower on the seventh postoperative day (p<0.0001) and remained lower on discharge (p=0.001).
- Serum lymphocyte count was lower on the seventh postoperative day (p<0.0001).
- Serum haemoglobin was lower on the seventh postoperative day and remained lower on discharge (p=0.001).
Table 3.6 (b) Nutritional status in oesophageal carcinoma intervention patients: serum biochemistry and anthropometry during hospitalisation

<table>
<thead>
<tr>
<th></th>
<th>Preoperative (n=19)</th>
<th>Study day 7 (n=19)</th>
<th>Discharge (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body weight (kgs)</strong></td>
<td>75* (44-103)</td>
<td>69 (42-92)</td>
<td>66.5* (39.5-96)</td>
</tr>
<tr>
<td><strong>Body Mass Index (kg/m²)</strong></td>
<td>24.5** (18-30.5)</td>
<td>21.7 (17.9-27)</td>
<td>23** (16.8-28.4)</td>
</tr>
<tr>
<td><strong>Albumin (g/l)</strong></td>
<td>41* (36-46)</td>
<td>24* (18-32)</td>
<td>32* (27-37)</td>
</tr>
<tr>
<td><strong>CRP (mg/l)</strong></td>
<td>&lt;10 # (&lt;10-33.4)</td>
<td>55 # (10-216)</td>
<td>24.5 # (&lt;10-159)</td>
</tr>
<tr>
<td><strong>Lymphocyte count (x10^9/l)</strong></td>
<td>1.5* (0.7-3.8)</td>
<td>1.1* (0.4-2.2)</td>
<td>1.5 # (0.5-2.2)</td>
</tr>
<tr>
<td><strong>Haemoglobin (g/dl)</strong></td>
<td>14.1* (12.7-16.3)</td>
<td>12* (10-14.1)</td>
<td>11* (1.4-14.2)</td>
</tr>
</tbody>
</table>

Results are median (range)
*p<0.0001 vs preoperative values, ** p=0.001, # p=0.001, ■ p=0.005
(Wilcoxon signed ranks test)

Using the Wilcoxon signed ranks test, results obtained on day seven postoperative and on the day of discharge were compared with preoperative results.

- Body weight and BMI were lower on discharge (p<0.0001 and p=0.001 respectively)
- Serum albumin was lower on the seventh postoperative day and remained lower on discharge (p<0.0001).
- Serum CRP was higher on the seventh postoperative day (p=0.001) and remained higher on discharge (p=0.005).
- Serum lymphocyte count was lower on the seventh postoperative day (p<0.0001).
- Serum haemoglobin was also lower on the seventh postoperative day and remained lower on discharge (p<0.0001).

No difference was found between control and intervention groups in the nutritional parameters monitored.
3.4 Nutritional status post discharge

(a) Gastric carcinoma

Perioperative weight and weight loss for gastric carcinoma patients is compared in the control and intervention groups in Table 3.7.

Table 3.7 Body weights and percentage perioperative weight loss in gastric carcinoma patients

<table>
<thead>
<tr>
<th></th>
<th>Control group (n=21)</th>
<th>Intervention group (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative weight (kg)</td>
<td>65* (38-90)</td>
<td>77* (49-121)</td>
</tr>
<tr>
<td>Preoperative weight loss (%)</td>
<td>5.5# (0-16.4)</td>
<td>0# (0-21.8)</td>
</tr>
<tr>
<td>In hospital weight loss (%)</td>
<td>4.5μ (-8-17.4)</td>
<td>3.1μ (-7.7-13.7)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Control group (n=9)</th>
<th>Intervention group (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight: 4 weeks post discharge (kg)</td>
<td>56.9 ** (36.7-75.2)</td>
<td>68** (47.2-115)</td>
</tr>
<tr>
<td>Weight loss: preop to 4 weeks post discharge (%)</td>
<td>6.7*** (3.4-11.5)</td>
<td>5.9*** (2.2-15.9)</td>
</tr>
<tr>
<td>Weight loss: discharge to 4 weeks post discharge (%)</td>
<td>3+ (-14.7-10.5)</td>
<td>4+ (-9.55-11.76)</td>
</tr>
</tbody>
</table>

Results are median (range)
*p=0.054, # p=0.235, μ p=0.688, **p=0.028 , *** p= 0.512 , + p= 0.431
(Mann Whitney U test)

At four weeks post discharge, a significant difference is observed in body weight between the gastric carcinoma control and intervention groups (p=0.028) although no difference in the percentage weight loss from discharge to four weeks post discharge (p= 0.431) or from preoperative to four weeks post discharge (p= 0.512) is observed.

A high proportion of both groups continued to lose weight following discharge from hospital. Six of nine (67%) of the gastric carcinoma control patients continued to lose weight following discharge. Median weight loss was 3%. Ten of fourteen patients (71%) in the intervention group continued to lose weight with a median weight loss of 4%. Data is not available on all patients as they were not all reviewed four weeks postoperatively. In
some cases they were missed in clinic due to annual leave or other commitments, in other cases they were reviewed within a week of discharge and were not then followed up in clinic for another three months.

(b) Oesophageal carcinoma

Perioperative weight and weight loss for oesophageal carcinoma patients is compared in the control and intervention groups in Table 3.8.

Table 3.8 Body weights and perioperative weight loss in oesophageal carcinoma patients

<table>
<thead>
<tr>
<th></th>
<th>Control group (n=23)</th>
<th>Intervention group (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative weight (kg)</td>
<td>76.5* (52-105)</td>
<td>75* (44-103)</td>
</tr>
<tr>
<td>Preoperative weight loss (%)</td>
<td>5.4** (0-17.6)</td>
<td>3.2** (0-20)</td>
</tr>
<tr>
<td>In hospital weight loss (%)</td>
<td>5.1# (-7.7-14.7)</td>
<td>5.7# (-2.5-10.2)</td>
</tr>
<tr>
<td>Weight: 4 weeks post discharge (kg)</td>
<td>71*** (50.3-93.1)</td>
<td>67*** (40-95)</td>
</tr>
<tr>
<td>Weight loss: preop to 4 weeks post discharge (%)</td>
<td>5.3μ (-0.8-14.7)</td>
<td>6.8μ (-1.3-12.6)</td>
</tr>
<tr>
<td>Weight loss: discharge to 4 weeks post discharge (%)</td>
<td>0.4+ (-4.6-14.3)</td>
<td>1.0+ (-1.6-7.4)</td>
</tr>
</tbody>
</table>

Results are median (range)
*p= 0.860, **p=0.790 # p= 0.237, ***p= 0.654, μ p= 0.331, + p=0.478
(Mann Whitney U test)

No difference in perioperative weights or in the extent of weight loss is observed between control and intervention groups. A high proportion of both groups continued to lose weight following discharge from hospital. In the oesophageal carcinoma control group, 11 of 20 (55%) patients continued to lose weight following discharge. Median weight loss was 0.4%. In the intervention group, 10 of 18, (55%) experienced continued weight loss following discharge with a median weight loss of 1.0% (p=0.478).
Objective 1: Summary of results

- The gastric and oesophageal carcinoma patients entered into this study were not severely malnourished preoperatively with a median weight loss <10% and median BMI and serum albumin within the normal range. A considerable proportion of patients were found to be at nutritional risk.

- In all groups a significant reduction occurred in serum albumin, serum haemoglobin and lymphocyte count during hospitalisation. Serum albumin levels failed to recover to normal preoperative levels by the time of discharge. No difference was found between control and intervention groups in the nutritional parameters monitored.

- A high proportion of patients in all groups continued to lose weight following discharge.
Objective 2. To determine the energy and protein intake of these patients following resection for gastric or oesophageal carcinoma and to examine the contribution of all feeding sources to total energy and protein intake.

3.5 Postoperative nutritional intake

All energy and protein intake data is expressed in tables as a percentage of estimated requirements achieved. The contribution of enteral and/or parenteral nutrition, oral nutritional supplements and food to estimated requirements is outlined in Figures 3.1, 3.2, 3.3, 3.4, and documented in Appendix 9, Tables A10 and A11.

(a) Gastric carcinoma

Maximum energy and protein intake was achieved on the seventh postoperative day when 77% and 147% of energy and 67% and 101% of protein requirements were achieved in the control and intervention groups respectively. Total energy and protein intake subsequently declined with the reduction in supplementary enteral /parenteral nutrition support. By the time of discharge when both groups were dependent on oral intake alone to meet energy and protein requirements, intake fell to 57% and 59% of energy and 60% and 55% of protein requirements for control and intervention groups respectively, far short of requirements.

(b) Oesophageal carcinoma

Maximum energy and protein intake was achieved on the eighth postoperative day in the control group when 99% of energy and 86% of protein requirements were achieved. In the intervention group this was achieved on the seventh postoperative day when 103% of energy and 94% of protein requirements were achieved. Total energy and protein intake subsequently declined with the reduction in supplementary enteral /parenteral nutrition support. By the time of discharge when both groups were dependent on oral intake alone
to meet energy and protein requirements, intake fell to 55% and 50% of energy and 48% and 49% of protein requirements, for control and intervention groups respectively, far short of estimated requirements.

3.5.1 Early postoperative nutrition support

(a) *Gastric carcinoma*

In the control group, nineteen of 21 patients (90%) received a jejunostomy feeding tube at laparotomy. Eighteen patients (86%) received enteral feeding at some point during hospitalisation. Parenteral Nutrition (PN) was initiated for postoperative nutrition support in nine cases (43%). In two cases PN alone was used to provide postoperative nutrition support. These patients underwent more extensive surgery due to colonic involvement of the tumour. In a further three cases PN was used initially to provide early postoperative nutrition support and enteral feeding was delayed due to colonic resection. In another case, early enteral feeding was not initiated due to a leak in the jejunostomy tube. In another case the jejunostomy tube split. In the remaining cases PN was commenced due to persistent vomiting on jejunostomy tube removal and the occurrence of an anastomotic leak postoperatively.

In the intervention group, significantly fewer patients (9 of 19, 47%) received a jejunostomy feed postoperatively ($\chi^2=8.827$, p=0.003). PN was used for postoperative nutrition support in three cases (16%). Extensive colonic resection resulted in PN being chosen over enteral feeding in two cases and a jejunostomy tube leak in the third case resulted in discontinuation of enteral feeding and initiation of PN. In one case jejunal feeding though initiated was discontinued on the third day due to a possible leak that was not confirmed. This patient remained nil-by-mouth until oral intake was permitted and thus received no further artificial nutrition support. Consequently, enteral feeding was continued beyond the second postoperative day in only seven cases (37%). A total of
eleven patients (58%) received some form of early postoperative artificial nutrition support in the intervention group compared with 100% in the control group. This decision was at the discretion of the operating surgeon.

(b) Oesophageal carcinoma

All patients with oesophageal carcinoma received a feeding jejunostomy tube at laparotomy and early enteral feeding commenced. Five patients (22%) in the control group received PN during their hospital stay. In four patients PN was commenced and enteral feeding discontinued due to postoperative complications: an anastomotic leak, a chylous leak, volvulus around the jejunostomy tube site and jejunostomy tube blockage. One patient received PN for a short period before commencing enteral feeding on the request of the operating surgeon. Two patients in the intervention group received PN postoperatively (11%), initiated due to jejunal volvulus in one case and the splitting of the jejunostomy tube in the other case.

3.5.2 Contribution of early postoperative nutritional support to energy and protein intake

(a) Gastric carcinoma

Although nine patients in the control group received PN at some stage in their inpatient course, only two patients received PN over the time period monitored (from the seventh to the tenth postoperative day and on the day of discharge). Consequently, it is not surprising that the median contribution of PN to energy and protein intake was found to be zero over this time period.

In the intervention group three patients received PN but only two received it over the time period studied as the third patient had progressed to oral intake by the seventh postoperative day. PN met their full energy and protein requirements until the ninth
postoperative day when in one case it was reduced with the introduction of food intake. The second case continued to receive parenteral nutrition, as this patient was slow to progress to oral intake.

Eighteen of the control group received a jejunostomy feed at some point during their hospital stay. By day 7 this contributed 47% of their energy and protein requirements. By day 9 the median contribution of jejunostomy feeding to energy and protein intake was zero (Figures 3.1(a) and (b)). This is not surprising, as the median duration of jejunostomy feeding was seven days in this group (range 0-23). The jejunostomy feeding was reduced on successful introduction of oral intake and discontinued prior to discharge. Jejunostomy feeding was continued beyond the second postoperative day in only seven patients in the intervention group (37%). In these cases jejunal feeding met full energy and 80% of protein requirements on the seventh postoperative day. As in the control group it was reduced as oral intake increased. By day ten postoperative the median contribution of jejunostomy feeding to energy and protein intake was 51% and 39% respectively. The duration of feeding was longer than in the control group (median, nine days) but the difference was not significant. It was discontinued in all patients prior to discharge. Details of the contribution of jejunostomy feeding to energy and protein intake in control and intervention groups is illustrated in Figures 3.1 (a) and (b) and Figures 3.2 (a) and (b) and documented in Appendix 9.
Figure 3.1 (a) Median percentage contribution of nutrient sources to energy requirements in gastric carcinoma control patients.

Figure 3.1(b) Median percentage contribution of nutrient sources to protein requirements in gastric carcinoma control patients.
Figure 3.2(a) Median percentage contribution of nutrient sources to energy requirements in gastric carcinoma intervention patients.

Figure 3.2(b) Median percentage contribution of nutrient sources to protein requirements in gastric carcinoma intervention patients.
(b) *Oesophageal carcinoma*

Although five patients in the control group received PN postoperatively only one patient received PN over the time period studied. Consequently, the median contribution of PN to nutrient intake over the time period studied was zero.

In the intervention group only one patient received PN over the time period studied.

Jejunostomy feeding was the major contributor to energy and protein intakes in both control and intervention groups from day seven to day ten postoperative. In the control group nutrient contribution of jejunostomy feeding peaked on day eight providing 87% and 77% of energy and protein requirements respectively. Jejunostomy feeding was then reduced but still contributed to 33.6% and 31% of energy and protein requirements on day ten. In the intervention group this peak occurred on day seven. By day ten, jejunostomy feeding contributed to 51% and 52% of energy and protein requirements.

Details of the contribution of jejunostomy feeding to energy and protein intake in control and intervention groups is illustrated in Figures 3.3 (a) and (b) and Figures 3.4 (a) and (b) and documented in Appendix 9.
Figure 3.3(a) Median percentage contribution of nutrient sources to energy requirements in oesophageal carcinoma control patients.

Figure 3.3(b) Median percentage contribution of nutrient sources to protein requirements in oesophageal carcinoma control patients.
Figure 3.4 (a) Median percentage contribution of nutrient sources to energy requirements in oesophageal carcinoma intervention patients.

Figure 3.4(b) Median percentage contribution of nutrient sources to protein requirements in oesophageal carcinoma intervention patients.
3.5.3 Contribution of oral nutritional supplements to energy and protein intake

Oral nutritional supplements were offered on introduction of free oral fluids to all control group patients and those patients in the intervention groups that failed to tolerate milk. They were encouraged throughout hospitalisation in the control groups but offered to intervention group patients only when diet was poorly tolerated or compliance with fortified foods was poor.

(a) Gastric carcinoma

On day seven postoperative, 35% of control group patients (7 of 20) offered supplements accepted at least one. On the day of discharge, 38% of patients (8 of 21) were taking at least one supplement. In the intervention group, 21% of patients (4 of 19) offered supplements were taking at least one on day seven. On the day of discharge, 26% of patients (5 of 19) were accepting at least one supplement.

The highest median contribution to energy and protein requirements was achieved on day ten in the control group, 7.4% and 4% for energy and protein respectively. At this time compliance with supplements was 50%, with 7 of the 14 remaining inpatients accepting supplements. By the time of discharge, although 38% of patients (8 of 21) were taking at least one supplement, the median contribution to energy and protein intake was zero.

In the intervention group the median contribution of supplements to energy and protein intake was zero over the time period monitored. Median contribution of supplements to energy and protein intake in the control and intervention groups is illustrated in Figures 3.1 (a) and (b) and Figures 3.2 (a) and (b) respectively and recorded in Appendix 9.

(b) Oesophageal carcinoma

On day seven postoperative, 13% of control patients (3 of 23) were taking at least one supplement. This increased to 48% on day eight, with 11 patients accepting a supplement.
By the time of discharge, 30% of patients (7 of 23) were accepting a supplement but the median contribution to energy and protein intake was zero.

In the intervention group 26% of patients (5 of 19) accepted a supplement on the seventh postoperative day. This was maintained on day eight and day nine and by the time of discharge 42% (8 of 19) of patients accepted a supplement drink. The highest median contribution of oral nutritional supplements to energy and protein intake was achieved on day eight in the control group, 8% and 6% of energy and protein requirements respectively. In the intervention group this occurred on the day of discharge where nutritional supplements contributed 9% and 6% of energy and protein requirements respectively.

Median contribution of supplements to energy and protein intake in control and intervention groups is illustrated in Figures 3.3 (a) and (b) and Figures 3.4 (a) and (b) respectively and recorded in Appendix 9.

3.5.4 Contribution of food to energy and protein intake

(a) Gastric carcinoma

The contribution of food to postoperative energy and protein intake in control and intervention groups is illustrated in Figures 3.1 (a) and (b) and Figures 3.2 (a) and (b) respectively and recorded in Appendix 9. Food intake tended to increase from day seven to day ten in both groups. Energy and protein derived from food was higher on day seven, eight and nine postoperative and on the day of discharge in the intervention group compared with the controls but the difference was not significant. By the time of discharge, only 57% of energy and 60% of protein requirements were met in the control group and 59% of energy and 55% of protein requirements were met in the intervention group.
(b) *Oesophageal carcinoma*

The contribution of food to postoperative nutrient intake in control and intervention groups is illustrated in Figures 3.3 (a) and (b) and 3.4 (a) and (b) respectively and recorded in Appendix 9. As in the gastric carcinoma group, food intake tended to increase from day seven to day ten postoperative in the oesophageal groups but no difference in the energy and protein contribution from food is observed between control and intervention groups. On discharge, 55% of energy and 48% of protein requirements were achieved in the control group and 50% of energy and 49% of protein requirements were achieved in the intervention groups.

3.5.5 **Food intake four weeks post discharge**

Details of food intake on follow up four weeks post discharge are detailed in Table 3.9 below. Data is only available for intervention group patients and is incomplete as some patients were missed at their out patient follow up appointment.

**Table 3.9 Energy and protein intake four weeks post discharge: percentage requirements achieved.**

<table>
<thead>
<tr>
<th></th>
<th>Gastric carcinoma intervention group (n=10)</th>
<th>Oesophageal carcinoma intervention group (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Energy Requirements</td>
<td>57 (43-87)</td>
<td>62 (44-105)</td>
</tr>
<tr>
<td>% Protein Requirements</td>
<td>61 (43-73)</td>
<td>58 (26-149)</td>
</tr>
</tbody>
</table>

Results are median (range)
Objective 2: Summary of Results

- Although food intake increased during hospitalisation in all groups, the maximum contribution of food to energy and protein requirements did not exceed 59% of energy and 55% of protein requirements.

- No difference in the energy and protein contribution from food was found between control and intervention groups.

- Early enteral feeding was extensively used in the patient groups studied and made an important contribution to energy and protein intake in the early postoperative period.

- Oral nutritional supplements were routinely offered to control group patients and only to those patients in the intervention groups who failed to tolerate diet or who complied poorly with fortified foods. Intake of supplements was poor with a median contribution to energy and protein requirements of zero on the day of discharge in all gastric carcinoma patients and control group patients with oesophageal carcinoma.

- Although data is not available for all patients four weeks postoperative, results from those patients examined suggest a continued failure to achieve >65% of energy and protein requirements.
**Objective 3. To examine the effect of total gastrectomy compared with subtotal gastrectomy on oral intake in gastric carcinoma patients.**

3.6 Total versus subtotal gastrectomy

Details of the patients are described in Table 3.10 below. It includes both control and intervention patients. The two groups were similar with respect to age, stage of disease, preoperative nutritional status and the number of days to introduction of oral intake.

**Table 3.10 Patient details: Total and subtotal gastrectomy**

<table>
<thead>
<tr>
<th></th>
<th>Total gastrectomy (n=19)</th>
<th>Subtotal gastrectomy (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male:Female</td>
<td>12:7</td>
<td>17:4</td>
</tr>
<tr>
<td>Age (years)</td>
<td>67 (49-83)</td>
<td>67 (27-81)</td>
</tr>
<tr>
<td>Potentially curative resection</td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>Stage of disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>II</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>III</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>IV</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Preoperative BMI (kg/m²)</td>
<td>26.2 (18.5-33.5)</td>
<td>23.6 (17.5-33.5)</td>
</tr>
<tr>
<td>Preoperative weight loss (%)</td>
<td>2.2 (0-22)</td>
<td>3.7 (0-12)</td>
</tr>
</tbody>
</table>

Details are numbers of patients. Anthropometric results are median (range)

3.6.1 Energy and protein intake following total and subtotal gastrectomy

The energy and protein contribution from food intake following total and subtotal gastrectomy is compared in Table 3.11. Energy and protein contribution from all sources is documented in Appendix 10.
Table 3.11 Energy and protein requirements and percentage contribution of food to requirements following total and subtotal gastrectomy

<table>
<thead>
<tr>
<th></th>
<th>Total gastrectomy (n=19)</th>
<th>Subtotal gastrectomy (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Energy</td>
<td>Protein</td>
</tr>
<tr>
<td>Energy and protein</td>
<td>1691 (1348-2134)</td>
<td>75 (49-108)</td>
</tr>
<tr>
<td>requirements (kcal/d</td>
<td></td>
<td></td>
</tr>
<tr>
<td>and g/d)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Food day 7 (%)</td>
<td>23 (0-90)</td>
<td>14 (0-92)</td>
</tr>
<tr>
<td>Food day 8 (%)</td>
<td>40 (0-93)</td>
<td>35 (0-104)</td>
</tr>
<tr>
<td>Food day 9 (%)</td>
<td>46 (0-118)</td>
<td>31 (0-130)</td>
</tr>
<tr>
<td>Food day 10 (%)</td>
<td>35 (0-78)</td>
<td>40 (0-96)</td>
</tr>
<tr>
<td>Food discharge (%)</td>
<td>59 (3-116)</td>
<td>53 (3-119)</td>
</tr>
</tbody>
</table>

Food intake results are median percentage requirements achieved (range).

No difference was found in nutrient intake between the two groups over the time period examined. The oral intake of both groups fell far short of requirements. On the day of discharge 59% of energy requirements were met by both groups. Protein intake was 53% and 61% of requirements for total and subtotal gastrectomy patients respectively.

**Objective 3: Summary of results**

The performance of subtotal gastrectomy did not result in a greater energy and protein intake compared with a total gastrectomy. Intake was found to be far short of requirements by the time of discharge in both patient groups.
Objective 4. To instigate a system of food provision where selected foods are enriched with energy and protein while remaining palatable and acceptable to patients and to examine the impact of fortified food provision on energy and protein intake.

3.7 Impact of fortified food provision on energy and protein intake.

The provision of fortified foods to both the gastric and oesophageal carcinoma intervention groups resulted in significantly higher individual energy and protein intakes over the time period examined (Table 3.12 and Table 3.13). Intake however was not sufficient to meet the full energy and protein requirements of patients.

Table 3.12 Percentage contribution of food to energy and protein requirements postoperatively in gastric carcinoma intervention patients

<table>
<thead>
<tr>
<th></th>
<th>Excluding fortified foods (n=19)</th>
<th>Including fortified foods (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% Energy Requirements</td>
<td>% Protein Requirements</td>
</tr>
<tr>
<td>Day 7</td>
<td>23* (0-59)</td>
<td>20 (0-71)</td>
</tr>
<tr>
<td>Day 8</td>
<td>27* (0-64)</td>
<td>21* (0-67)</td>
</tr>
<tr>
<td>Day 9</td>
<td>36* (0-82)</td>
<td>33* (0-99)</td>
</tr>
<tr>
<td>Day 10</td>
<td>33* (0-64)</td>
<td>35* (0-76)</td>
</tr>
<tr>
<td>Discharge</td>
<td>44* (27-103)</td>
<td>41* (30-88)</td>
</tr>
</tbody>
</table>

Results are median percentage requirements achieved (range). *p<0.003, •p<0.003 (Wilcoxon signed ranks test)
Table 3.13 Percentage contribution of food to energy and protein requirements postoperatively in oesophageal carcinoma intervention patients

<table>
<thead>
<tr>
<th></th>
<th>Intervention group (Excluding fortified foods) (n=19)</th>
<th>Intervention group (Including fortified foods) (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% Energy Requirements</td>
<td>% Protein Requirements</td>
</tr>
<tr>
<td>Day 7</td>
<td>0 (0-38)</td>
<td>0 (0-58)</td>
</tr>
<tr>
<td>Day 8</td>
<td>2* (0-53)</td>
<td>1# (0-48)</td>
</tr>
<tr>
<td>Day 9</td>
<td>11* (0-50)</td>
<td>16μ (0-109)</td>
</tr>
<tr>
<td>Day 10</td>
<td>23* (0-51)</td>
<td>15# (0-61)</td>
</tr>
<tr>
<td>Discharge</td>
<td>36* (7-68)</td>
<td>36 μ (9-94)</td>
</tr>
</tbody>
</table>

Results are median percentage requirements achieved (range).
* p<0.018, # p<0.018, μ p<0.005, • p< 0.005
(Wilcoxon signed ranks test)

**Objective 4: Summary of results**

The provision of fortified food to patients in the intervention groups resulted in the achievement of a higher percentage of their energy and protein requirements than if the food provided had not been fortified. The maximum contribution of food to energy and protein requirements still fell far short of requirements. It was achieved in both the gastric and oesophageal carcinoma groups on the day of discharge when 59% and 50% of energy and 55% and 49% of protein requirements were met.
Objective 5. To compare the energy and protein contribution of food to those receiving standard hospital treatment with those receiving fortified foods.

3.8 Energy and protein intake in control versus intervention group patients

Details of energy and protein intakes of gastric and oesophageal carcinoma control and intervention groups are documented in Table 3.14 and Table 3.15 below. No difference was found in the percentage contribution of food to energy or protein requirements between control and intervention groups on the days examined (Mann Whitney U test).

Table 3.14 Percentage contribution of food to energy and protein requirements postoperatively in gastric carcinoma patients

<table>
<thead>
<tr>
<th></th>
<th>Control group (n=21)</th>
<th>Intervention group (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%Energy Requirements</td>
<td>% Protein Requirements</td>
</tr>
<tr>
<td>Day 7</td>
<td>22 (0-90)</td>
<td>17 (0-92)</td>
</tr>
<tr>
<td>Day 8</td>
<td>34 (0-88)</td>
<td>40 (0-92)</td>
</tr>
<tr>
<td>Day 9</td>
<td>43 (0-87)</td>
<td>36 (0-93)</td>
</tr>
<tr>
<td>Day 10</td>
<td>40 (0-75)</td>
<td>46 (0-95)</td>
</tr>
<tr>
<td>Discharge</td>
<td>57 (4-110)</td>
<td>60 (3-105)</td>
</tr>
</tbody>
</table>

Results are median percentage (range)
Table 3.15 Percentage contribution of food to energy and protein requirements postoperatively in oesophageal carcinoma patients

<table>
<thead>
<tr>
<th></th>
<th>Control group (n=23)</th>
<th>Intervention group (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%Energy Requirements</td>
<td>% Protein Requirements</td>
</tr>
<tr>
<td>Day 7</td>
<td>0 (0-88)</td>
<td>0 (0-73)</td>
</tr>
<tr>
<td>Day 8</td>
<td>4 (0-103)</td>
<td>3 (0-150)</td>
</tr>
<tr>
<td>Day 9</td>
<td>33 (0-110)</td>
<td>32 (0-100)</td>
</tr>
<tr>
<td>Day 10</td>
<td>31 (0-101)</td>
<td>35 (0-109)</td>
</tr>
<tr>
<td>Discharge</td>
<td>55 (20-103)</td>
<td>48 (21-109)</td>
</tr>
</tbody>
</table>

Results are median percentage (range)

No difference was found in the percentage contribution of food to energy or protein requirements between control and intervention groups on the days examined (Mann Whitney U test).

**Objective 5: Summary of results**

The provision of fortified food to the intervention group of patients did not result in a higher contribution of food to energy and protein intake compared with control group patients.
Objective 6. To examine morbidity and mortality in this patient group and associated factors.

3.9 Morbidity and mortality

(a) Gastric carcinoma

Details of morbidity and mortality are presented in Table 3.16 below.

Excluding operative deaths there was no difference in the incidence of postoperative complications between the control and intervention groups (19% versus 10%) ($\chi^2=0.588$, $p=0.451$). There was no correlation between stage of disease and morbidity in the control group ($r=0.073$, $p=0.755$) or in the intervention group ($r=0.387$, $p=0.102$). Those patients with morbidity in the control group but not the intervention group had a longer postoperative stay than those without morbidity ($p=0.006$).

Table 3.16 Clinical outcome in gastric carcinoma

<table>
<thead>
<tr>
<th>Morbidity</th>
<th>Control group (n=24)</th>
<th>Intervention group (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastomotic leak</td>
<td>2(1)</td>
<td>1</td>
</tr>
<tr>
<td>Respiratory sepsis</td>
<td>3</td>
<td>1(1)</td>
</tr>
<tr>
<td>Wound infection</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Renal failure</td>
<td>1(1)</td>
<td></td>
</tr>
<tr>
<td>Acute pancreatitis</td>
<td>1(1)</td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td></td>
<td>1(1)</td>
</tr>
<tr>
<td><strong>Total morbidity</strong></td>
<td><strong>7</strong></td>
<td><strong>4</strong></td>
</tr>
<tr>
<td><strong>Total mortality</strong></td>
<td><strong>3</strong></td>
<td><strong>2</strong></td>
</tr>
</tbody>
</table>

Figures are numbers of patients. Operative deaths in parentheses.
(b) *Oesophageal carcinoma*

Details of morbidity and mortality are presented in Table 3.17 below.

Excluding operative deaths there was no difference in morbidity rates between control and intervention groups (43% vs 37%) ($\chi^2=0.190$, $p=0.663$). There was no correlation between stage of disease and morbidity rates in control ($r=-0.213$, $p=0.330$) or in intervention groups ($r=-0.246$, $p=0.310$).

Control group patients with morbidity had a longer hospital stay ($p=0.001$) and tended to be younger ($p=0.057$) than those with no morbidity. In the intervention group there was no difference in length of hospital stay or in age between those with morbidity and those with no morbidity.

<table>
<thead>
<tr>
<th>Morbidity</th>
<th>Control (n=26)</th>
<th>Intervention (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastomotic leak</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Wound infection</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Respiratory Infection</td>
<td>5(1)</td>
<td>3</td>
</tr>
<tr>
<td>Jejunal volvulus</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Other complications</td>
<td>5(2)</td>
<td>3(1)</td>
</tr>
<tr>
<td><strong>Total morbidity</strong></td>
<td>13</td>
<td>8</td>
</tr>
<tr>
<td><strong>Total mortality</strong></td>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>

Figures are numbers of patients. Operative deaths in parentheses.

3.9.1 Morbidity and nutritional status

(a) *Gastric carcinoma*

Excluding operative deaths, patients who developed complications in the control group were well nourished preoperatively with measured biochemical parameters within the normal range. One patient suffered >5% weight loss but maintained a normal BMI and serum albumin. In the intervention group both patients who developed complications had a BMI<20kg/m² and suffered >5% weight loss preoperatively.
No correlation was found between preoperative serum albumin and morbidity
\( (r=-0.174, \ p=0.464 \text{ and } r=-0.126, \ p=0.608) \) or between preoperative BMI and morbidity
\( (r=0.02, \ p=0.931 \text{ and } r=0.094, \ p=0.701) \) in the control and intervention groups respectively.

(b) Oesophageal carcinoma

Excluding operative deaths, the patients who developed complications in both the control and intervention groups had a good nutritional status with median levels of all biochemical and anthropometric parameters within the normal range preoperatively. No correlation was found between preoperative serum albumin and morbidity
\( (r=0.397, \ p=0.068 \text{ and } r=-0.01, \ p=0.967) \) or between preoperative BMI and morbidity
\( (r=0.0, \ p=1.0 \text{ and } r=0.159, \ p=0.515) \) in the control and intervention groups respectively.

3.9.2 Morbidity and nutrient intake

(a) Gastric carcinoma

All patients in the control group were given some form of early nutrition support. Seventy five percent of control group patients with morbidity (3 of 4) were commenced on PN postoperatively. In one case early enteral feeding was commenced but discontinued and PN initiated due to a postoperative anastomotic leak, in another case PN was chosen over enteral feeding due to colonic resection and in the other case a ‘difficult dissection’ was described by the operating surgeon and PN was used in the early postoperative period and enteral feeding was delayed. A difference was found in the achievement of energy and protein requirements between those with morbidity and those without on day 10 only (\( p=0.02 \)). At this time 50% (2 of 4) of the patients with morbidity were achieving >95% of nutritional requirements compared with 18% (\( n=3 \)) without morbidity. This can be explained by the continuation of artificial nutrition support in this group.
In the intervention group 58% of patients received postoperative nutrition support. PN was commenced postoperatively in the two patients with morbidity. In one case early enteral feeding was discontinued due to an anastomotic leak and in the other case PN was chosen over enteral feeding due to colonic resection. The complication in this case was a minor wound infection. No difference was found in the achievement of energy and protein requirements between those with and without morbidity.

(b) Oesophageal carcinoma

In both the control and intervention groups all patients received early enteral feeding. However, 30% of controls with morbidity (n=3) and 14% of intervention patients with morbidity (n=1) were later commenced on PN. In the former group this was due to the occurrence of jejunal volvulus, an anastomotic leak and a chylous leak. In the latter, jejunal volvulus necessitated tube removal. In both the control and intervention groups there was no difference in the achievement of energy and protein requirements between those that had morbidity and those without.

3.9.3 Morbidity associated with early postoperative feeding

There were no complications associated with PN usage in either the gastric or oesophageal carcinoma groups.

All patients who received enteral feeding tolerated it well. Feeding was commenced on the first or second postoperative day and the feeding rate progressively increased until the target feeding rate was achieved. It was then continued until oral intake was established. The incidence of complications associated with jejunostomy feeding overall was 9% (7 of 82). There were two minor complications in the gastric carcinoma control group where the feeding tube split at an early stage and one major complication where volvulus at the jejunostomy site required relaparotomy. This patient subsequently died due to acute
pancreatitis and multi organ failure. There were two complications in the oesophageal carcinoma control group: one incidence of volvulus around the jejunostomy site and one incidence of jejunal tube blockage. In the intervention group there was a further two complications associated with jejunostomy feeding: one incidence of volvulus around the jejunostomy site and one incidence where the tube split (Table 3.18).

Table 3.18 Complications associated with jejunostomy feeding

<table>
<thead>
<tr>
<th></th>
<th>Gastric carcinoma</th>
<th>Oesophageal carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jejunal tube volvulus</td>
<td>1(1)</td>
<td>2</td>
</tr>
<tr>
<td>Split tube</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Tube blockage</td>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>

Results are numbers, operative deaths in parentheses

3.10 Postoperative course

(a) Gastric carcinoma

There was no difference between the control and intervention groups in the number of days jejunostomy feeding was received, in the number of days before commencing oral diet or in the length of hospital stay.

Table 3.19 Postoperative course in gastric carcinoma

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Intervention group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postoperative days</td>
<td>12(6-33)</td>
<td>12(7-35)</td>
</tr>
<tr>
<td>Jejunostomy days</td>
<td>7(0-23)</td>
<td>9(2-16)</td>
</tr>
<tr>
<td>Food days</td>
<td>6(1-28)</td>
<td>8(3-22)</td>
</tr>
<tr>
<td>Days to food intake</td>
<td>5(2-39)</td>
<td>6(4-12)</td>
</tr>
</tbody>
</table>

Results are median number of days (range)

(b) Oesophageal carcinoma

As found in the gastric carcinoma groups, there was no difference in the number of days jejunostomy feeding was received, in the number of days before commencing oral diet or
in the length of hospital stay between the control and intervention groups with oesophageal carcinoma.

Table 3.20 Postoperative course in oesophageal carcinoma

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Intervention group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postoperative days</td>
<td>18(10-52)</td>
<td>15(9-32)</td>
</tr>
<tr>
<td>Jejunostomy days</td>
<td>10(3-34)</td>
<td>12(3-30)</td>
</tr>
<tr>
<td>Food days</td>
<td>10(2-39)</td>
<td>8(3-22)</td>
</tr>
<tr>
<td>Days to food intake</td>
<td>7(4-29)</td>
<td>7(5-27)</td>
</tr>
</tbody>
</table>

Results are median (range)

**Objective 6: Summary of results**

- No difference in morbidity or mortality was found between control and intervention groups. The occurrence of postoperative complications was not found to be correlated with preoperative nutritional status. No difference was found in the achievement of energy and protein requirements in those with morbidity compared with no morbidity.

- The use of postoperative nutrition support was widespread. No complications were found to be associated with parenteral nutrition usage. The incidence of complications associated with jejunal feeding was 9% overall of which 4% were major complications.
3.11 Summary of results (Study 1)

The hypothesis of this study was that the provision of fortified foods postoperatively to patients following gastrectomy or oesophagogastrrectomy might improve energy and protein intakes and nutritional status compared to standard postoperative care. The study aimed to examine the nutritional status and the energy and protein intake of patients undergoing surgery for carcinoma and to examine the impact of fortified food provision on nutritional status and energy and protein intake postoperatively.

The patients entered into the study were well nourished preoperatively but experienced deterioration in nutritional status during hospitalisation and following discharge. Nutritional intake results demonstrate the difficulties these patients experience in achieving nutrient requirements postoperatively. Feeding difficulties were universal. The provision of fortified foods postoperatively failed to significantly increase energy and protein intakes compared to the control groups who received standard postoperative care. Morbidity and mortality were not found to be associated with preoperative nutritional status.
Chapter Four

Methodology

Study 2
4.1 Hypothesis

The follow on to the previous study is based on the hypothesis that continuing jejunostomy feeding beyond the early postoperative stage in patients following surgical resection of oesophageal carcinoma may improve energy and protein intake and maintain nutritional status postoperatively.

4.2 Aims

To provide early postoperative enteral nutrition via a feeding jejunostomy tube and to continue supplementary feeding for up to four to six weeks following discharge home. To examine the impact of supplementary feeding on nutritional status and energy and protein intake during hospitalisation and following discharge.

4.3 Objectives

1. To examine the perioperative nutritional status of consecutive patients who following surgery for oesophageal carcinoma, continue jejunostomy feeding at home (enteral feeding group) and to compare their nutritional status with a control group previously discharged home following surgery with dietary advice alone (fortified food/intervention group with oesophageal carcinoma study 1).

2. To determine the energy and protein intake of patients following resection for oesophageal carcinoma and to examine the contribution of all feeding sources to total energy and protein intake (enteral feeding group). To compare the contribution of nutrient sources in the enteral feeding and fortified food groups during hospitalisation and to examine the postoperative course in both groups.
3. To compare the nutritional status and the energy and protein intake of those patients with oesophageal carcinoma discharged home with dietary advice alone (fortified food group, study 1) with the enteral feeding group, four weeks following discharge home.

4. To examine morbidity associated with postoperative jejunostomy feeding in the enteral feeding group.

4.4 Study Design

This investigation represents the third phase of a three-phase study conducted on patients undergoing surgery for oesophagogastric carcinoma.

Phase 3: Home Enteral Feeding (HEF) phase

This phase of the study involves consecutive patients who successfully underwent surgical resection for oesophageal carcinoma, received a jejunostomy feeding tube at laparotomy and continued supplementary jejunostomy feeding at home. All patients underwent a nutritional assessment preoperatively and weekly thereafter until discharge. Nutrient intake was determined during hospitalisation as previously described (section 2.6.1).

Four to six weeks following discharge, patients were requested to complete a food diary for a 3-day period documenting all food and fluid consumed. Energy and protein intake was established using the computer software package Comp Eat 5. At this time, body weight, BMI, serum albumin, lymphocyte count and serum CRP were measured. Comparison was made between the nutritional status of this group and the (fortified food group (study 1), preoperatively, on discharge and four weeks following discharge. Comparison of the energy and protein intake of the two groups was made on the seventh, eighth, ninth, tenth postoperative day, on the day of discharge and four weeks following discharge.
4.5 Subjects

Patients were considered eligible for inclusion in the study if they were admitted with oesophageal carcinoma and after appropriate investigations were considered suitable candidates for surgery. Patients who failed to tolerate jejunostomy feeding or who had problems with the jejunostomy tube prior to discharge home were excluded.

4.6 Assessments

Determination of food and fluid intake, assessment of nutritional status and determination of nutritional requirements were performed and calculated as previously described (section 2.6).

4.7 Procedure

4.7.1 Phase 3: Home Enteral Feeding (HEF) phase

Jejunostomy feeding was commenced on the second postoperative day in all patients with oesophageal carcinoma who received a feeding jejunostomy tube at the time of laparotomy and progressed as per ward protocol (Appendix 4).

Patients were visited daily by the investigating dietitian and surgical team until discharge. Nutritional intake was monitored and recorded in hospital for four days from the seventh postoperative day and again on the day of discharge. Patients were commenced on a standard enteral feed, Osmolite, (Abbott Laboratories), (see Appendix 5 for nutritional composition) in the presence of normal serum biochemistry. The nutritional contribution of the enteral feed was recorded. This was achieved by daily monitoring of fluid charts completed routinely by nursing staff. On the introduction of 'free' oral fluids, whole milk was encouraged by the dietitian. Intake was monitored and recorded on fluid charts. Patients then progressed onto a 'light diet' (soup and pudding) and if tolerated normal/soft
ward diet was introduced. Nursing staff documented food and fluid intake at breakfast, teatime and in between meals on food record charts. They were instructed to complete the charts with as much attention to detail as possible. Food intake was weighed by the dietitian and recorded at the main midday meal but this procedure was limited to weekdays only. On weekend days nursing staff were responsible for recording all food intake. Information documented by nursing staff was confirmed by the dietitian by directly questioning patients using the 24-hour recall method. All patients were trained on the use of the enteral feeding pump and equipment prior to discharge and were advised to continue supplementary feeding (Osmolite 500ml overnight) for a period of 4-6 weeks.

4.7.2 Monitoring of complications
All patients were monitored for the occurrence of complications from the first postoperative day until discharge. This involved daily observation of the patient and liaison with the surgical team.

4.8 Ethical Considerations
Ethical approval was granted by South West Devon Research Ethics Committee (Appendix 7 (b)). Patients were informed of the nature of the study preoperatively and were assured that participation was voluntary. Written informed consent was attained before entering into the study (Appendix 7 (b)). All patients agreed to participate.

4.9 Data Analysis
Nutrient intakes were determined using the computer software package Comp Eat version 5. All foods eaten by patients were on the database. Statistical analysis was performed using SPSS for Windows (Version 9.0; SPSS Inc; 1998). As before the Mann-Whitney U test was used for inter group analysis for non-parametric data. For paired samples the Wilcoxon test for non-parametric data was used (see section 2.9).
Chapter Five

Results

Study 2
5.1 Patient Details: Enteral Feeding Group (Study 2)

This group comprised 32 consecutive patients who successfully underwent surgery for oesophageal carcinoma from January 2004 to December 2004. Potentially curative surgery was performed in 14 cases. There were six postoperative deaths (19% mortality). A further five patients were withdrawn as they were not discharged home with jejunal feeding. In one case the enteral feed was found to be associated with profound diarrhoea and was discontinued prior to discharge, in another case an anastomotic leak required the institution of PN and jejunostomy feeding was not subsequently recommenced, in another case the jejunostomy tube blocked, could not be unblocked and was subsequently removed, in the remaining two cases the tube was inadvertently pulled out by the patients or ‘fell out’. Details of all patients are documented in Appendix 11, Table A13.

This ‘enteral feeding group’ was compared with the oesophageal carcinoma patients from the previous study who received fortified foods in hospital. Details of the enteral feeding group and fortified food group from the previous study are presented in Table 5.1. The two groups were well matched with no difference in age, male: female, or stage of disease. Transhiatal oesophagogastrectomy was the most commonly performed operation in the fortified food group. Ivor Lewis oesophagogastrectomy was more commonly performed in the enteral feeding group. This occurred as the two groups had a different operating surgeon.
Table 5.1 Details of the patients: enteral feeding and fortified food groups

<table>
<thead>
<tr>
<th></th>
<th>Fortified food group (study 1) (n=19)</th>
<th>Enteral feeding group (study 2) (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male:Female</td>
<td>15:4</td>
<td>14:7</td>
</tr>
<tr>
<td>Age (years)</td>
<td>62(38-78)</td>
<td>65(40-83)</td>
</tr>
<tr>
<td>Preoperative chemotherapy</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>Operation type:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ivor Lewis oesophagogastrectomy</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>Mc Keowns oesophagogastrectomy</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Transhiatal oesophagogastrectomy</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>Stage of disease (Guillou and Monson 2001)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>I</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>II</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>III</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>IV</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Postoperative jejunostomy tube feeding days (in hospital)</td>
<td>12 (3-30)</td>
<td>13(8-49)</td>
</tr>
<tr>
<td>Home jejunostomy tube feeding days</td>
<td>0</td>
<td>23(10-56)</td>
</tr>
</tbody>
</table>

Results are numbers of patients. Age and number of jejunostomy days are expressed as median (range)
Objective 1. To examine the perioperative nutritional status of consecutive patients who following surgery for oesophageal carcinoma continue jejunostomy feeding at home (enteral feeding group) and to compare their nutritional status with a control group previously discharged home following surgery with dietary advice alone (fortified food group, study 1).

5.2 Preoperative nutritional status
Details of the preoperative nutritional status of the enteral feeding and fortified food groups are presented in Table 5.2.

Table 5.2 Preoperative nutritional status in oesophageal carcinoma patients: serum biochemistry and anthropometry

<table>
<thead>
<tr>
<th></th>
<th>Fortified food group (study 1) (n=19)</th>
<th>Enteral feeding group (study 2) (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (kgs)</td>
<td>75* (44-103)</td>
<td>73.5* (50-122)</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>24.5** (18-30.5)</td>
<td>26.3** (21.1-52.7)</td>
</tr>
<tr>
<td>Preoperative weight loss (%)</td>
<td>3.2*** (0-20)</td>
<td>4.7*** (0-20)</td>
</tr>
<tr>
<td>Albumin (g/l)</td>
<td>41µ (36-46)</td>
<td>43µ (37-50)</td>
</tr>
<tr>
<td>CRP (mg/l)</td>
<td>&lt;10# (&lt;10-33.4)</td>
<td>&lt;10# (&lt;10-10)</td>
</tr>
<tr>
<td>Lymphocyte count (x10⁹/l)</td>
<td>1.5+ (0.7-3.8)</td>
<td>1.7+ (0.8-3.0)</td>
</tr>
</tbody>
</table>

Results are median (range)
* p= 0.688, ** p=0.065, *** p= 0.915, µ p=0.258, # p=0.752 + p= 0.639 (Mann Whitney U test)
The two groups were well matched with no difference observed in the biochemical or in the anthropometric parameters measured preoperatively. Details including the operative deaths are documented in Table A14 Appendix 11.

As before, BMI < 20kg/ m² and unintentional weight loss >10% in three to six months were the criteria chosen to identify malnutrition. Using these criteria to identify malnutrition, no patient in the enteral feeding group could be considered malnourished preoperatively. Median levels of the biochemical parameters measured as further indicators of nutritional status (serum albumin, CRP and lymphocyte count) were within the normal range preoperatively (Table 5.2). A considerable proportion of both groups were at nutritional risk. Forty seven percent of the fortified food group (n=9) and 48% (n=10) of the enteral feeding group experienced weight loss >5% in the previous three to six months.
5.3 Nutritional status during hospitalisation

Results of the fortified food group and the enteral feeding group are documented in Table 5.3 and Table 5.4 respectively.

Table 5.3 Nutritional status in oesophageal carcinoma patients receiving fortified foods (study 1): serum biochemistry and anthropometry during hospitalisation

<table>
<thead>
<tr>
<th></th>
<th>Preoperative (n=19)</th>
<th>Study day 7 (n=19)</th>
<th>Discharge (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body weight (kgs)</strong></td>
<td>75* (44-103)</td>
<td>69 (42-92)</td>
<td>66.5* (39.5-96)</td>
</tr>
<tr>
<td><strong>Body Mass Index (kg/m²)</strong></td>
<td>24.5* (18-30.5)</td>
<td>21.7 (17.9-27)</td>
<td>23* (16.8-28.4)</td>
</tr>
<tr>
<td><strong>Albumin (g/l)</strong></td>
<td>41* (36-46)</td>
<td>24* (18-32)</td>
<td>32* (27-37)</td>
</tr>
<tr>
<td><strong>CRP (mg/l)</strong></td>
<td>&lt;10* (&lt;10-33.4)</td>
<td>55* (10-216)</td>
<td>24.5* (&lt;10-159)</td>
</tr>
<tr>
<td><strong>Lymphocyte count (x10⁹/l)</strong></td>
<td>1.5* (0.7-3.8)</td>
<td>1.1* (0.4-2.2)</td>
<td>1.5 (0.5-2.2)</td>
</tr>
</tbody>
</table>

Results are median (range)
*p<0.005 vs preoperative values (Wilcoxon signed ranks test)

Table 5.4 Nutritional status in the enteral feeding group: serum biochemistry and anthropometry during hospitalisation

<table>
<thead>
<tr>
<th></th>
<th>Preoperative (n=21)</th>
<th>Study day 7 (n=21)</th>
<th>Discharge (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body weight (kgs)</strong></td>
<td>73.5* (50-122)</td>
<td>81* (54-124)</td>
<td>76.5 (54-117)</td>
</tr>
<tr>
<td><strong>Body Mass Index (kg/m²)</strong></td>
<td>26.3* (21.1-52.7)</td>
<td>28.7* (22.8-54.7)</td>
<td>27.5 (22.2-51.1)</td>
</tr>
<tr>
<td><strong>Albumin (g/l)</strong></td>
<td>43* (37-50)</td>
<td>28* (15-37)</td>
<td>31* (26-39)</td>
</tr>
<tr>
<td><strong>CRP (mg/l)</strong></td>
<td>&lt;10* (&lt;10-10)</td>
<td>31* (&lt;10-224)</td>
<td>15* (&lt;10-133)</td>
</tr>
<tr>
<td><strong>Lymphocyte count (x10⁹/l)</strong></td>
<td>1.7* (0.8-3.0)</td>
<td>1.0* (0.6-11.4)</td>
<td>1.2** (0.6-2.1)</td>
</tr>
</tbody>
</table>

Results are median (range)
*p<0.0001, **p=0.002 vs preoperative values (Wilcoxon signed ranks test)
The fortified food group experienced a significant fall in body weight and consequently BMI during hospitalisation, though BMI remained within the normal range on discharge (23 kg/m²). The enteral feeding group experienced a significant rise in body weight from preoperative to the seventh postoperative day (*p<0.0001) but no significant overall change in body weight from preoperative to discharge (p=0.1). By the time of discharge no difference in body weight was found between the two groups though BMI was higher in the enteral feeding group (p=0.001).

A significant fall in serum albumin and lymphocyte count and rise in serum CRP occurred through the hospital course in both groups. Serum albumin was significantly higher on the seventh postoperative day (p=0.001) in the enteral feeding group but was not different at the time of discharge. No difference was found between the two groups in the other biochemical parameters monitored during hospitalisation or on discharge. Serum levels of albumin and CRP remained abnormal in both groups on discharge.
**Objective 1: Summary of results**

- No difference was observed in the preoperative nutritional status of the enteral feeding group compared with the fortified food group. No patient in either group could be considered malnourished though a considerable proportion was at nutritional risk.

- Biochemical parameters measured during hospitalisation followed a similar course in both groups with no difference in serum levels observed by the time of discharge.

- In contrast to the enteral feeding group where no overall change occurred in body weight from preoperative to the time of discharge, the body weight and BMI of the fortified food group was lower on discharge compared with preoperative (P<0.005)
Objective 2. To determine the energy and protein intake of patients following resection for oesophageal carcinoma and to examine the contribution of all feeding sources to total energy and protein intake (enteral feeding group). To compare the contribution of nutrient sources in the enteral feeding and fortified food groups during hospitalisation and to examine the postoperative course in both groups.

5.4 Postoperative nutritional intake

All energy and protein intake data is expressed in tables as before as a percentage of estimated requirements achieved. The contribution of enteral and/or parenteral nutrition, oral nutritional supplements and food to estimated energy and protein requirements is outlined in Figures 5.1 (a) and 5.1 (b) and is documented in Appendix 12, Table A15.

In the enteral feeding group maximum energy and protein intake was achieved on the seventh postoperative day when 99% of energy and 79% of protein requirements were achieved. At the time of discharge 93% of energy and 95% of protein requirements were achieved in the enteral feed group, significantly higher than the fortified food group (p<0.0001).

5.4.1 Early postoperative nutritional support and the contribution of early postoperative nutritional support to energy and protein intake (enteral feeding group)

All patients received a feeding jejunostomy tube at laparotomy and early enteral feeding commenced and progressed according to the standard ward protocol (Appendix 4). Details of the contribution of jejunostomy feeding to energy and protein intake in the enteral feeding group is illustrated in Figures 5.1 (a) and 5.1 (b) and documented in Appendix 12.
Jejunostomy feeding was the major contributor to energy and protein intake in the early postoperative phase. The contribution of jejunostomy feeding peaked on day seven postoperative. Jejunostomy feeding was then reduced and by day 10 postoperative it contributed to 33% of energy and 34% of protein requirements.

5.4.2 Contribution of oral nutritional supplements to energy and protein intake (enteral feeding group)

The median contribution of oral nutritional supplements to energy and protein intake was zero from day seven to day 9 postoperative. They contributed a median of 3% of energy and 6% of protein requirements on day 10 postoperative.

Median contribution of oral nutritional supplements to energy and protein intake is illustrated in Figures 5.1 (a) and 5.1 (b) and documented in Appendix 12.

5.4.3 Contribution of food to energy and protein intake (enteral feeding group)

The contribution of food to postoperative energy and protein intake is illustrated in Figures 5.1 (a) and 5.1 (b) respectively and recorded in Appendix 12. Food intake increased progressively from postoperative day seven to day 10. On discharge, a median of 51% of energy and 57% of protein requirements was achieved from oral food intake.
Figure 5.1 (a) Median percentage contribution of nutrient sources to energy requirements in the enteral feeding group
Figure 5.1(b) Median percentage contribution of nutrient sources to protein requirements in the enteral feeding group
5.4.4 Energy and protein intake during hospitalisation (enteral feeding and fortified food groups compared)

No difference was found between the two groups' calculated energy and protein requirements and no difference was found in total energy and protein intake from day seven to day 10 postoperative. The enteral feeding group achieved a higher proportion of energy and protein requirements on the day of discharge (p<0.0001 and p=0.002 respectively). The contribution of jejunostomy feeding to energy and protein intake was significantly higher in the fortified food group on the seventh postoperative day compared with the enteral feeding group (103% and 71% of energy and 94% and 56% of protein requirements respectively) (p=0.012 and p=0.004). All patients in the enteral feeding group continued to receive supplementary jejunal feeding throughout hospitalisation. It was discontinued prior to discharge in the fortified food group and consequently the contribution of jejunostomy feed to energy and protein intake was significantly less at this time point (p<0.0001).

No difference was found in the contribution of oral nutritional supplements to energy and protein intakes in the two patient groups over the time period studied.

Food intake increased from day seven to day 10 in both groups though the enteral feeding group achieved a greater percentage of energy and protein requirements from food on day 7, day 8 and day 10 postoperative (p<0.03).
5.5 Postoperative course (enteral feeding group)

Details of morbidity during hospitalisation are presented in Table 5.5 below.

Table 5.5 Postoperative morbidity

<table>
<thead>
<tr>
<th>Morbidity</th>
<th>Study 1 Fortified food group (n=19)</th>
<th>Study 2 Enteral feeding group (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jejunal volvulus</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Respiratory sepsis</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Wound infection</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Total morbidity</td>
<td>7</td>
<td>5</td>
</tr>
</tbody>
</table>

Figures are numbers of patients.

There was no difference in the incidence of postoperative complications between the fortified food and enteral feeding groups (37% versus 24%) ($\chi^2=0.807$, $p=0.494$). Morbidity was not found to affect length of hospital stay.

5.5.1 Morbidity and nutritional status

Using the criteria chosen to diagnose malnutrition, no patient in the enteral feeding group who developed complications could be considered malnourished preoperatively. One patient experienced >10% weight loss preoperatively but maintained a normal BMI. No correlation was found between preoperative serum albumin and morbidity ($r=-0.228$ and $p=0.321$) or between preoperative BMI and morbidity ($r=-0.058$ $p=0.803$).

5.5.2 Morbidity and nutrient intake

All patients received early enteral feeding. No difference in the achievement of nutrient requirements was found between those that had morbidity and those without.
Objective 2: Summary of results

- Jejunostomy feeding was the main contributor to energy and protein intake in the early postoperative phase.
- The intake of oral nutritional supplements was low.
- Food intake progressively increased during hospitalisation in both groups. The maximum contribution of food to energy and protein intake was achieved on the day of discharge when a median of 51% of energy and 57% of protein requirements were achieved from food intake. No difference was found in total energy and protein intake from day seven to day 10 postoperative between the enteral feeding and the fortified food groups. The enteral feeding group achieved a higher proportion of energy and protein requirements on the day of discharge (p<0.0001).
- No difference was found between the two groups in the incidence of postoperative complications.
- Morbidity was not found to be associated with preoperative nutritional status.
Objective 3. To compare the nutritional status and the energy and protein intake of those patients with oesophageal carcinoma discharged home with dietary advice alone (fortified food group, study 1) with the enteral feeding group, four weeks following discharge home.

5.6 Nutritional status and nutritional intake post discharge (enteral feeding group)

5.6.1 Nutritional status post discharge

Perioperative weight and weight loss is compared in the fortified food and enteral feeding groups in Table 5.6.

Table 5.6 Perioperative body weight and percentage weight loss

<table>
<thead>
<tr>
<th></th>
<th>Fortified food group (study 1) (n=19)</th>
<th>Enteral feeding group (study 2) (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative weight (kg)</td>
<td>75+ (44-103)</td>
<td>73.5+ (50-122)</td>
</tr>
<tr>
<td>Discharge weight (kg)</td>
<td>67µ (40-96)</td>
<td>76.5µ (54-117)</td>
</tr>
<tr>
<td>Weight 4 weeks post discharge (kg)</td>
<td>67# (40-95)</td>
<td>71.5# (46-113)</td>
</tr>
<tr>
<td>Weight loss preoperative to four weeks post discharge (%)</td>
<td>7* (-1.3-12.6)</td>
<td>4.9* (-2.3-12.9)</td>
</tr>
<tr>
<td>Weight loss discharge to four weeks post discharge (%)</td>
<td>1.3** (-2.5-7.5)</td>
<td>6.3** (-2.3-18.0)</td>
</tr>
</tbody>
</table>

+ p=0.688, µ p= 0.14, # p= 0.321, *p=0.04, **p=0.001 (Mann Whitney U test)
Results are median (range)
Serum biochemistry four weeks post discharge is documented in Table 5.7.

**Table 5.7 Serum biochemistry four weeks post discharge.**

<table>
<thead>
<tr>
<th></th>
<th>Fortified food group (n=19)</th>
<th>Enteral feeding group (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Albumin</strong></td>
<td>36.5 (34-44)*</td>
<td>41 (30-46) *</td>
</tr>
<tr>
<td><strong>CRP</strong></td>
<td>&lt;10 (&lt;10-19)</td>
<td></td>
</tr>
<tr>
<td><strong>Lymphocyte count</strong></td>
<td>1.6 (0.8-2.4)</td>
<td>1.3 (0.5-2.2)</td>
</tr>
</tbody>
</table>

Results are median (range) *p=0.021 (Mann Whitney U test)

5.6.2 Nutritional intake four weeks post discharge

Details of nutrient intake on discharge and on follow up four weeks post discharge are detailed in Table 5.8 below.

**Table 5.8 Contribution of nutrient sources to energy and protein requirements on discharge and four weeks post discharge: percentage requirements achieved.**

<table>
<thead>
<tr>
<th></th>
<th>Study 1</th>
<th>Study 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% Energy Requirements (n=17)</td>
<td>% Protein Requirements (n=17)</td>
</tr>
<tr>
<td><strong>Food on discharge</strong></td>
<td>50 (27-82)</td>
<td>49 (21-110)</td>
</tr>
<tr>
<td><strong>Jejunostomy feed on discharge</strong></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total intake discharge</strong></td>
<td>62* (30-122)</td>
<td>67* (26-127)</td>
</tr>
<tr>
<td><strong>Oral intake 4 weeks post discharge</strong></td>
<td>62 (44-105)</td>
<td>68 (26-149)</td>
</tr>
<tr>
<td><strong>Jejunostomy feed 4 weeks post discharge</strong></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total intake 4 weeks post discharge</strong></td>
<td>62* (44-105)</td>
<td>68** (26-149)</td>
</tr>
</tbody>
</table>

Results are median (range) *p<0.0001, **p<0.011 (Mann Whitney U test)
Objective 3: Summary of results

- Total energy and protein intake was significantly higher on discharge (p<0.0001) and at four weeks post discharge (p<0.0001 and p<0.011 for energy and protein respectively) in the enteral feeding group compared with the fortified food group.

- Percentage weight loss from preoperative to four weeks following discharge home was less in the enteral feeding group compared with the fortified food group (p=0.04).

- Serum albumin was higher at four weeks post discharge in the enteral feeding group compared with the fortified food group (p=0.021).
Objective 4. To examine morbidity associated with postoperative jejunostomy feeding in the enteral feeding group

5.7 Morbidity associated with postoperative jejunostomy feeding

All patients received a jejunostomy feeding tube at laparotomy. Feeding was commenced on the first postoperative day and the feeding rate progressively increased according to the ward protocol until the desired target feeding rate was achieved. Enteral feeding to meet calculated energy and protein requirements was continued until oral intake was established at which time it was reduced to overnight to facilitate daytime oral intake. All patients were trained in hospital to set up the enteral feed and discharged home when competent with the procedures involved and medically fit for discharge. No major complications associated with jejunostomy feeding occurred in this group. Minor complications are outlined in Table 5.9 below.

Table 5.9 Complications associated with jejunostomy feeding

<table>
<thead>
<tr>
<th>Complication</th>
<th>Enteral feeding group (Intent to treat) (n=32)</th>
<th>Enteral feeding group (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tube fell out/pulled out</td>
<td>7(1)</td>
<td>4</td>
</tr>
<tr>
<td>Feed not tolerated (diarrhoea)</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Tube blocked</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total morbidity</td>
<td>9</td>
<td>4</td>
</tr>
</tbody>
</table>

Results are numbers. Operative deaths in parentheses

The overall incidence of complications was 28% (9 of 32) (intent to treat). In five cases (16%), problems with the jejunostomy tube/ feed occurred during hospitalisation resulting in these patients being withdrawn from the study. In three of these the feeding tube was inadvertently pulled out or ‘fell out’ during hospital stay, in another case the tube became
blocked and could not be unblocked. In another case severe diarrhoea necessitated feed cessation and the tube was removed prior to discharge on the request of the consultant.

All patients who were discharged home with jejunostomy feeding were included in the study. In this group the only reported complication was early tube displacement. This occurred in 19% (4 of 21) of cases resulting in the feed being stopped prematurely.

<table>
<thead>
<tr>
<th>Objective 4: Summary of results</th>
</tr>
</thead>
<tbody>
<tr>
<td>• The incidence of complications associated with jejunostomy feeding was 28% (intent to treat).</td>
</tr>
<tr>
<td>• Complications were minor relating to tube blockage, diarrhoea and early displacement.</td>
</tr>
</tbody>
</table>
5.8 Summary of results (Study 2)

The hypothesis of this study was that continuing postoperative supplementary enteral feeding through hospitalisation and following discharge home following surgery for oesophageal carcinoma may improve total energy and protein intakes and maintain or improve nutritional status compared with the provision of dietary advice alone. The study aimed to examine the nutritional status and energy and protein intake of patients undergoing surgery for carcinoma, and to examine the impact of continuing supplementary enteral feeding through hospitalisation and for four to six weeks at home, on nutritional status and energy and protein intake.

The patient population was well nourished preoperatively. Nutritional intake results were in agreement with the previous study (study 1) demonstrating the difficulties these patients experience in achieving nutrient requirements by the oral route postoperatively.

The continuation of supplementary enteral feeding throughout hospitalisation and following discharge was associated with an improved total energy and protein intake at the time of discharge and four weeks following discharge home. The supplementary enteral feeding did not compromise oral intake. Weight loss was attenuated over the perioperative period and serum albumin levels improved compared with the group discharged home with dietary advice alone. Supplementary enteral feeding was found to be safe and associated with a low level of minor complications.
Chapter Six

Discussion
The population of study 1 comprised 40 consecutive patients who underwent gastrectomy for gastric carcinoma (21 control, 19 intervention patients), and 42 consecutive patients who underwent oesophagogastrectomy for oesophageal carcinoma (23 control, 19 intervention patients) and progressed to food intake.

The population of study 2 comprised 21 consecutive patients who underwent oesophagogastrectomy for oesophageal carcinoma and were discharged home with supplementary enteral feeding. This group was compared with 19 patients with oesophageal carcinoma (intervention group, study 1) who underwent oesophagogastrectomy and were discharged home with dietary advice alone.

6.1 Perioperative nutritional status of gastric and oesophageal carcinoma patients

6.1.1 Preoperative nutritional status of gastric and oesophageal carcinoma patients

(a) Study 1

(i) Gastric carcinoma: control group

Median levels of four of the five indices of nutritional status chosen; height, weight, (to establish BMI), serum albumin, C reactive protein and lymphocyte count were within the normal range preoperatively. Median serum haemoglobin was slightly lower than the reference range at 12.5g/dl. Median weight loss was 5.5% (0-16.4%) suggesting nutritional risk.

Using the chosen criteria to diagnose malnutrition, (BMI<20kg/m² and weight loss >10% over three to six months), incidence of malnutrition in this group was 9.5% (n=2). This is considerably lower than documented elsewhere for gastric carcinoma (DeWys et al 1980, Rey-Ferro et al 1997). These studies use different criteria to define malnutrition, consequently differing results are inevitable. In the study by Ray-Ferro et al (1997), the incidence of mild, moderate and severe malnutrition was 5%, 42.5% and 15% respectively.
The Nutrition Risk Index (an index derived from serum albumin and the ratio of actual to usual body weight according to an equation) was the criteria used by the group (NRI>97.5, NRI 83.5-97.5, NRI <83.5 for mild, moderate and severe malnutrition). In the DeWys study, the incidence of malnutrition in gastric carcinoma patients was 65%, but the criteria used to diagnose malnutrition was weight loss >5% in six months. Applying this criterion to the current study the incidence of malnutrition would be more comparable at 52.3% (11 of 21). It has been suggested that weight loss of >5% alone may be more an indicator of nutritional risk than diagnostic of malnutrition (Stratton et al 2003). It is for this reason that a combination of BMI and weight loss was chosen to identify malnutrition in the current study. By combining BMI <20kg/m² and weight loss >5% the incidence of malnutrition in the current group would be 19% (4 of 21) and 17% (4 of 24, intent to treat).

(ii) Gastric carcinoma: intervention group

The intervention group was well nourished on presentation. Median level of albumin, CRP, haemoglobin and lymphocyte count was within the normal range preoperatively. Median BMI was 26.2 kg/m² indicating overweight. Using the chosen criteria to diagnose malnutrition no patient could be considered malnourished. Median percentage weight loss was zero (range: 0-21.8%). Using the criterion of DeWys et al (1980) described above to diagnose malnutrition, the incidence was 37% (7 of 19).

The intervention group was overweight preoperatively (BMI 26.2kg/m² ). The control group was within the normal weight category (BMI 23.6kg/m² ). Although BMI was higher in the intervention group and percentage preoperative weight loss less at the outset (5.5% versus 0%) compared to the control group the difference was not found to be statistically significant. There was no difference in the incidence of malnutrition or risk of malnutrition between the groups.
(i) Oesophageal carcinoma: control group

None of the patients in the oesophageal carcinoma control group were considered malnourished. Median levels of all indices of nutritional status measured were within the normal range preoperatively. Median preoperative weight loss was 5.4% (0-17.6 %) suggesting nutritional risk (Stratton et al 2003).

(ii) Oesophageal carcinoma: intervention group

Median levels of the chosen indices of nutritional status were within the normal range preoperatively and no patients were considered malnourished using the chosen criteria. Median preoperative weight loss was 3.2% (0-20%).

No difference was found in the preoperative nutritional status of the intervention group compared to the controls.

Previous studies have reported a high incidence of malnutrition in oesophageal carcinoma patients (Martin et al 1999, Daly et al 2000). In both of these studies, preoperative weight loss was the only criterion used to identify malnutrition and the reported incidence was 58% and 57% respectively. If these criteria were used in the control patient group then the incidence of malnutrition would be 74% (17 of 23) (77%, 20 of 26 intent to treat). It is weight loss >5-10% that is generally considered to be clinically significant (Allison 1995, Detsky et al 1987, American Society for Parenteral and Enteral Nutrition 1989, Elia 2000).

Riccardi and Allen (1999) reported marasmus, defined as weight loss >10%, in 70% of oesophageal carcinoma patients. In the current study, if weight loss >10% alone is considered to identify malnutrition, then the number in the control group is reduced to 17% (4 of 23) (19%, 5 of 26, intent to treat) and in the intervention group is 26% (5 of 19), (30%, 6 of 20 intent to treat).
(b) Study 2
In the enteral feeding group median levels of the chosen indices of nutritional status were within the normal range and no patient was considered malnourished preoperatively. Median BMI was above the normal reference range (26.3 kg/m²) suggesting overweight. Median weight loss was 4.7% (0-20%). Using the criterion of Riccardi and Allen (1999), the incidence of malnutrition was 9.5% (2 of 21)(22%, 7 of 32 intent to treat).
No difference was found in the preoperative nutritional status of patients in the enteral feeding group compared with the oesophageal carcinoma patients receiving fortified food (study 1).

Results from the current study suggest that this group of patients may be better nourished than previously reported in the literature. The use of different criteria to define malnutrition in studies as well as the inclusion of patients with advanced disease beyond the scope of surgery make the comparison of results between studies difficult. In the DeWys study (1980), patients were examined at a stage when the disease was beyond the scope of surgery. This is important as stage of disease has been reported to be one of the factors contributing to protein calorie malnutrition (Saito et al 1991, Bozzetti et al 1981). A standard method to define malnutrition is needed to enable comparison of results between studies.

6.1.2 Nutritional status during hospitalisation
(a) Study 1

Biochemistry: Gastric carcinoma
In both the gastric control and intervention groups a significant reduction occurred in all of the biochemical parameters measured during hospitalisation.
Body weight: Gastric carcinoma

A significant reduction in body weight and BMI occurred during hospitalisation in the control group, this was not reflected in the intervention group where no significant change in body weight occurred during hospitalisation. Interestingly when percentage weight change during hospitalisation is examined, no significant difference was found between control and intervention groups (4.5% (-8%-17.4%) and 3.1% (7.7%-13.7%) respectively). The two groups were managed by the same surgical team. Fluid status which impacts on body weight was not formally assessed and documented. Fluid overload / the presence of oedema (not reported) may have been a contributory factor to the weight gain observed in the intervention group from preoperative to day seven postoperative. Fewer patients, 53%, ($\chi^2 =12.835$ p=0.0001) received early postoperative nutritional support in the intervention group compared with the control group where all patients received early postoperative nutritional support. Those patients in the intervention group who did not receive early nutrition support were maintained on intravenous fluids until oral intake was permitted.

Salt and water retention has been found to be exacerbated by starvation (Keys et al 1950) and by the response to injury (Allison 2004), consequently these patients may have been more vulnerable to fluid overload postoperatively

The intervention group had a tendency towards overweight at the outset. It has been reported that starvation, (water only), for 5 days even when uncomplicated by disease produces less weight loss (5%) in individuals with a BMI of 35kg/m$^2$ than in individuals with a BMI of 18kg/m$^2$ where weight loss may be 10% (Stratton et al 2003). It is possible therefore that the higher body weight at the outset may be another factor contributing to the attenuation in weight loss that occurred in the intervention group during hospitalisation compared to the controls rather than the effect of any intervention.

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Biochemistry: Oesophageal carcinoma

The postoperative course of these patients was similar to those with gastric carcinoma. Both control and intervention groups experienced a significant reduction in serum albumin and lymphocyte count and rise in serum CRP during hospitalisation.

Body weight: Oesophageal carcinoma

Weight loss of 5.1% (-7.7-14.7%) and 5.7% (-2.5-10%) occurred during hospitalisation in the control and intervention groups respectively.

(b) Study 2

Biochemistry: Oesophageal carcinoma patients, enteral feeding group

A significant reduction in serum albumin and lymphocyte count and rise in serum CRP from preoperative to the seventh postoperative day occurred in this patient group. Levels improved by the time of discharge but failed to return to normal levels by the time of discharge.

Body weight: Oesophageal carcinoma patients, enteral feeding group

A significant rise in body weight occurred from preoperative to the seventh postoperative day. By the time of discharge no difference was found in body weight from preoperative.

Deterioration in nutritional status during hospital stay has been reported in a number of studies. In particular, a substantial proportion report weight loss including those who are undernourished or well nourished on admission to hospital (McWhirter and Pennington 1994, Corish et al 2000a, Arnold et al 2001). In surgical patients this can be attributed in part to the catabolic effects of the injury (Maxfield et al 2001) and partly to the effects of partial or total starvation (Bruun et al 1999). Traditional perioperative management of GI surgical patients involves: fluids only on the day prior to surgery, nil by mouth for a period
of four to five days until the introduction of sips of water and subsequently the introduction of free fluids with a gradual building up to diet (Catchpole 1989). Starvation, (water only), for 5 days even when uncomplicated by disease produces a weight loss of 5% of body weight which typically occurs in individuals with a BMI of 35kg/m², and 10% of body weight which occurs in individuals with a BMI of 18kg/m² (Stratton et al 2003). In the presence of severe disease weight loss can be even faster (Stratton et al 2003). Christensen and Kehlet (1984) reported an average weight loss of 5% 10 days postoperatively in a group of GI surgical patients. Keele et al (1997) reported postoperative weight loss of 5.3% in GI surgical patients managed in the traditional way. These results are comparable with the results of the current study (study 1). Studies specifically examining patients following total gastrectomy have reported even greater weight loss. Liedman (1999) reported 10% weight loss in the early postoperative period. Braga et al (1998) reported a decrease in body weight >10% with respect to usual body weight at discharge. Percentage weight loss during hospitalisation in both studies is greater than the current one. This may be related to the provision of early postoperative nutrition support to the majority of patients and the good nutritional status of the patients preoperatively. In the absence of a control group that did not receive nutrition support it is not possible to establish if nutrition support provision resulted in an attenuation of weight loss. In the gastric carcinoma intervention group, 47% of patients received standard postoperative care but no difference in weight loss was found between those that received postoperative nutrition support.

The enteral feeding group of study 2 experienced no overall change in body weight during hospitalisation with significant weight gain from preoperative to day 7 postoperative. Median weight change during hospitalisation was -1.1% (-19.7-3.9%). The enteral feeding group were overweight at the outset (BMI 26.3 kg/m²) but no difference was found in body weight or BMI between this group and the fortified food group preoperatively. It is recognised that body weight is affected by changes in fluid status such as oedema,
ascites or dehydration (Carney and Meguid 2002). Fluid prescriptions in the perioperative period are variable between centres with patients sometimes receiving in excess of 5litres of water and 500ml sodium/day as maintenance requirements (Allison and Lobo 2004). Elderly patients are particularly susceptible to fluid and electrolyte imbalance due to a reduced cardiac and renal reserve (Allison and Lobo 2004). Patients are vulnerable to fluid overload postoperatively as salt and water retention is exacerbated by starvation and weight loss (Keys et al 1950) and by the response to injury (Allison 2004). The observed rapid weight gain is most likely to be a reflection of fluid status and not true body weight.

The two groups were managed at different centres. Differences in postoperative fluid management between centres is the most likely explanation for the difference in body weight between the fortified food and enteral feeding groups on the seventh postoperative day and the difference in weight loss experienced from discharge to four weeks postoperative. Postoperative fluid infusions were not monitored in the patients included as it was considered beyond the scope of the study.

The rise in serum CRP and fall in serum albumin that occurred across all the study groups is not surprising and is associated with the acute phase response to injury, with the liver increasing production of acute phase proteins while decreasing production of constitutive proteins such as albumin (Elia 2001). Levels should return to baseline unless the postoperative course is complicated by sepsis, which prolongs the acute phase response (Elia 2001). In the current study, levels improved by the time of discharge but did not reach normal preoperative levels (Appendix 3). CRP levels are not available for the control patients (study 1) during hospitalisation as its measurement was included in the methodology later in the intervention part of the study. There is a lack of information in the literature on the time taken for recovery of biochemical parameters to normal and the length of postoperative stay in uncomplicated patients is an important factor. No difference was found between the groups examined in length of postoperative stay.
Early enteral feeding has been associated with a blunting of the acute phase response (Kudsk et al 1994). In the gastric carcinoma intervention group no difference was found in the biochemical parameters measured between those that received postoperative nutrition support and those that received standard postoperative care. In the absence of an adequately sized control group not receiving postoperative nutrition support it is not possible to establish if enteral feeding was associated with a blunting of the acute phase response.

6.1.3 Nutritional status four weeks following discharge home

(a) Study 1

In the case of gastric carcinoma patients, a high proportion of both the control and intervention groups continued to lose weight on discharge, 67% (6 of 9) and 71% (10 of 14) respectively. Median weight loss four weeks following discharge was 3% and 4% for control and intervention groups respectively. Similarly, in the oesophageal carcinoma groups weight loss continued four weeks post discharge in 55% (11 of 20) of control patients and 55% (10 of 18) of intervention patients. Median weight loss was 0.4% and 1.0% respectively. The difference in weight loss between the control and intervention groups for both gastric and oesophageal carcinoma was not significant. All patients were given high-energy high-protein dietary advice on discharge. Patients who complied with oral dietary supplements during hospitalisation were offered them on discharge and encouraged to continue with them until reviewed by the dietitian four weeks later. Continued weight loss is not surprising given that both intervention groups were achieving less than 65% of calculated energy and protein requirements when reviewed in clinic four weeks later.
(b) Study 2

In the enteral feeding group, 95% of patients lost weight on discharge (20 of 21). Median percentage weight loss four weeks from discharge home was greater in this group than in the group of patients receiving fortified foods in hospital, (study 1), 6.3% (-2.3-18%) versus 1.3 % (-2.5-7.5%). Median percentage weight loss from preoperative to four weeks post discharge was less in the enteral feeding group at 4.9% (-5.2-12.9%) versus 7% (-1.3-12.6%) in the group of patients receiving fortified foods in hospital. The latter result may be a better reflection of the true change that occurred in body weight in the perioperative period and is suggestive that the enteral feeding group may have experienced less body weight loss overall. The weight gain in the enteral feeding group from preoperative to the seventh postoperative day can be attributed to a gain in fluid and not true body weight. The two groups were managed by different surgical teams. Unfortunately fluid management was not examined in the two groups postoperatively. Median BMI four weeks following discharge was significantly higher in the enteral feeding group. At this time fewer patients in the enteral feeding group had a BMI<20kg/m² compared with the fortified food group, (4.7% compared with 28%). Furthermore serum albumin was higher in the enteral feeding group compared to the group receiving fortified foods.

The longer-term effects of surgery on nutritional status were examined by Corish et al (1998), who reported that in 3 months following discharge 70% of patients lost weight. Another study examining nutritional status within six weeks after major surgery using BMI indices in combination with anthropometry, demonstrated that 8.1% were mildly malnourished and 2.4% were severely malnourished (Edington et al 1997). Nutritional status prior to surgery was not reported. Keele et al (1997) examining postoperative patients found that all patients remained below their admission weight one month postoperative irrespective of the continued provision of oral dietary supplements.
There is evidence that the practice of continued home jejunostomy feeding in patients failing to meet nutritional requirements at the time of discharge is not widespread (Murphy et al 2005). Consequently there is no research evidence with which to compare the results of study 2. Gerndt and Orringer (1994) in a series of 378 patients with malignant disease reported jejunostomy feeding to be continued for more than three weeks in 12% of patients and more than two months in 7.7% but no details of the impact on nutritional status or nutritional intake is recorded.

The continuation of supplementary enteral feeding at home does appear to have had some effect in attenuating weight loss in the enteral feeding group as weight loss was less from preoperative to four weeks following discharge than in the oesophageal carcinoma group discharged with dietary advice alone. Continued weight loss in the latter group is not surprising as these patients were achieving less than 65% of calculated energy and protein requirements when reviewed in clinic four weeks post discharge. Patients in the home enteral feeding group were achieving 99% of energy and 95% of protein requirements at the same time point.

The study set out to continue supplementary jejunostomy feeding for a period of 4-6 weeks at home following discharge. Only 71% of patients (n=15) continued to receive supplementary feeding when reviewed in clinic. Jejunostomy feeding was actually continued for a median of 25 (10-56) days. It cannot therefore be expected for supplementary feeding to have a dramatic effect on body weight in all patients however the results are suggestive of attenuation in weight loss.
6.2 Postoperative nutritional intake

6.2.1 Contribution of early postoperative nutrition support to energy and protein intake and impact on nutritional status

(a) Study 1

The majority of patients (89%) received either enteral or parenteral nutrition support in the early postoperative period as they were considered to be at nutritional risk due to a delay in the introduction of oral intake postoperatively. The decision to initiate early postoperative nutrition support following surgery is at the discretion of the operating surgeon. At the time of commencement of the study all patients undergoing gastrectomy and oesophagogastrectomy were considered at nutritional risk and were given postoperative nutrition support irrespective of their preoperative nutritional status. Consequently, in the control groups, early postoperative enteral or parenteral nutrition was commenced in all patients and reduced on the introduction of oral intake. Maximum nutritional intake was achieved by day seven and eight. Jejunostomy feeding was well established by this time and contributed 83% and 77% of energy and protein requirements in the oesophageal carcinoma control group and 47% of energy and protein requirements in the gastric carcinoma control group. This difference is not surprising as the oesophageal carcinoma control group was slower to progress to oral diet and consequently continued to receive jejunostomy feeding until oral intake was established. Total energy and protein intake fell in both groups from the eighth postoperative day as jejunostomy feeding was reduced to facilitate oral intake. Jejunostomy feeding was reduced despite findings that enteral tube feeding might improve appetite and food intake in patients with cancer (Van Bokhorst-de van der Schueren et al 2001). As a result, in the case of the control group, patients became reliant on oral dietary supplements and standard hospital diet to meet nutritional requirements.
All patients with oesophageal carcinoma in the intervention group received enteral or parenteral nutrition support postoperatively, however 53%, (10 of 19), of the gastric carcinoma intervention group did not. This was the decision of the operating surgeon as these patients had a good preoperative nutritional status with a tendency to be overweight (median BMI preoperative: 26.2 kg/m²). The oesophageal carcinoma intervention group followed a similar course to the controls with the maximum contribution of jejunostomy feeding to energy and protein intake achieved on the seventh postoperative day (103% of energy and 94% of protein requirements). In the case of those patients in the gastric carcinoma intervention group that received jejunostomy feeding, maximum contribution to nutrient intake was achieved on the seventh postoperative day where it contributed 101% of energy and 80% of protein requirements respectively. In both groups jejunostomy feeding was subsequently reduced and discontinued prior to discharge.

(b) Study 2

All patients included in this study received enteral nutrition support postoperatively. The energy and protein contribution of jejunostomy feeding was lower in the enteral feeding group on the seventh postoperative day (71% of energy and 56% of protein requirements) than in the group receiving fortified foods. This may be attributed to the earlier reduction in jejunostomy feeding and earlier introduction of oral intake in the enteral feeding group.

Both control and intervention group patients with oesophageal carcinoma (study 1) experienced weight loss during hospitalisation despite the extensive use of early postoperative nutrition support. The enteral feeding group of study 2 however demonstrated weight gain during hospitalisation. The rapid gain in weight combined with the extensive weight loss experienced from discharge to four weeks following discharge suggests that this may reflect a gain in fluid rather than true body weight.
Enteral tube feeding has been found to improve body weight or reduce weight loss in a range of hospital patients (Bastow et al 1983, Carr et al 1996, McWhirter and Pennington 1996). In the current study it is not possible to establish if the provision of early postoperative nutrition support had an impact on body weight due to the absence of an adequately sized control group not receiving nutritional support. The provision of early postoperative nutrition support is a routine part of the care of this patient group given their high risk of malnutrition (Saito et al 1991). The postoperative weight loss that occurred in the population of study 1 was less than reported elsewhere for these patient groups but comparable with studies of other surgical patients where no nutritional support was given postoperatively. It is possible that early nutrition support may have contributed to an attenuation of weight loss. However it was only given for a short period of time during hospitalisation.

6.2.2 Contribution of oral nutritional supplements to energy and protein intake and impact on nutritional status

(a) Study 1

All patients in the control groups were offered oral nutritional supplements on the introduction of oral fluids postoperatively. They were offered to intervention group patients at this stage only when milk was not tolerated or refused. They continued to be encouraged in the control groups until discharge. In the intervention group they were subsequently only offered when tolerance of solid food was poor or when fortified foods were refused as it was considered unethical to withhold them. In the oesophageal and gastric carcinoma control groups, the maximum contribution to nutrient intake was achieved on day 8 and day 10 postoperative when a median of 8% and 7.4% of energy requirements and 6% and 4% of protein requirements were met by oral nutritional supplements respectively. In the gastric carcinoma intervention group, the median contribution of oral nutritional supplements to energy and protein intake was zero over the
time period examined. In the oesophageal carcinoma intervention group, a maximum contribution to energy and protein intake of 9% and 6% was achieved on the day of discharge. No difference in the contribution of oral nutritional supplements to energy and protein intake between the control and intervention groups was found. This demonstrates that compliance with supplements was poor despite considerable encouragement especially in the case of control groups where they were the only option available to supplement standard food provision.

(b) Study 2

Patients included in the enteral feeding group were offered oral nutritional supplements when real food snacks, (eg yoghurt, cake bar, cream crackers with cheese) which were offered mid-morning and mid-afternoon were refused or not tolerated. The contribution of supplements to energy and protein intake was not different to the group receiving fortified foods with a maximum contribution of 3% and 4% to energy and protein intake respectively on day 10 postoperative. This low level of compliance overall is not surprising and has been reported elsewhere (Ovensen et al 1991, Lawson et al 2003). In this patient group taste fatigue is a problem as for many with severe dysphagia preoperatively oral nutritional supplements may have been the principle source of nutrition for some time.

The provision of oral nutritional supplements postoperatively has been shown in a number of studies to improve the nutritional intake and nutritional status of patients (assessed by body weight and/or anthropometry). This has been shown in both undernourished patients (BMI<20kg/m²), (McWhirter and Pennington 1996, Beattie et al 2000, Potter et al 1998, Baldwin and Pearson 2004), and well nourished patients, BMI>20kg/m², (Rana et al 1992, Keele et al 1997). In the latter study a significant improvement in nutritional intake
occurred over the first four days of the study period. Thereafter the difference was not significant. In the former study an improvement occurred over the first seven days.

A study by MacFie et al (2000) examining elective gastrointestinal surgical patients found weight loss was reduced in those given supplements but the reduction was not significant. This is not surprising as the increase in total energy intake in those receiving supplements was modest in comparison to those not receiving supplements and insufficient to achieve a significant weight gain.

There is considerable variation between studies examining the effects of oral dietary supplements in terms of sample size, the magnitude of supplements provided and the degree of pre-existing malnutrition. The duration of feeding is equally varied with some showing benefit with less than seven days of supplementation, (Rana et al 1992), whereas others have involved more prolonged supplementation (Beattie et al 2000). Oral nutritional supplements were offered to all control group patients and some patients in the intervention groups in study I on introduction of free oral fluids. The fact that supplements were the only option available to supplement oral intake in between meals in the control group resulted in them being continuously encouraged in this group until discharge. In the intervention groups the main emphasis was on the use of fortified foods to supplement dietary intake. Supplements were offered and encouraged where compliance with fortified foods was poor. No difference in the contribution of supplements to nutrient intake between the control and intervention groups was demonstrated. Compliance was poor and the median contribution to energy and protein intake unlikely to be sufficient to achieve weight gain. In the oesophageal and gastric carcinoma control groups the maximum contribution of oral nutritional supplements to energy intake was achieved on day 8 and day 10 at 8% and 7.4% respectively. Given the median energy requirements for these groups were 1840 kcals and 1783 kcals respectively,
these figures correspond to 147 kcals and 132 kcals. Given that this is the maximum contribution over the time period monitored, the potential of oral nutritional supplements to contribute towards weight gain is limited. The corresponding result for the intervention group was 9%, (representing 174 kcals) and achieved on discharge in the oesophageal carcinoma patients. In the gastric carcinoma group the median contribution of oral nutritional supplements was zero for the time period monitored.

In study 2, patients in the enteral feeding group were encouraged to take real food snacks in between meals. Oral nutritional supplements were offered as an alternative to food snacks when compliance was poor. Maximum contribution to energy and protein intake was achieved on day 10 postoperative at 3% and 6% respectively. Median intake on the remaining days monitored was zero.

It must be considered that oral nutritional supplements were routinely offered to patients in the control groups only (study 1) and the impact of supplements on nutritional status and nutritional intake was not an objective of the current study. However it seems reasonable to suggest from the results that their contribution to weight gain or even attenuation of weight loss in this group is limited.

6.2.3 Contribution of food to energy and protein intake

(a) Study 1

In the oesophageal and gastric carcinoma control and intervention groups it was a median of 6-8 days before oral food intake was introduced. Food intake subsequently increased in all groups. In the control groups, maximum food intake was achieved on the day of discharge when only 55% of energy and 48% of protein requirements were met in the oesophageal carcinoma group and 57% of energy and 60% of protein requirements were met in the gastric carcinoma group. In the intervention groups, maximum food intake was achieved on the day of discharge for both gastric and oesophageal carcinoma groups when
59% and 50% of energy and 55% and 49% of protein requirements were achieved respectively. No difference was found in the energy and protein contribution from food between control and intervention groups despite the provision of fortified to the intervention groups.

(b) Study 2

In the enteral feeding group, food intake progressively increased from the time of introduction until the day of discharge when 57% and 51% of energy and protein requirements was achieved respectively. Both groups were given intensive dietary counselling. The patients in the fortified food group had a slower progression to food intake illustrated by a greater number of days before food was introduced. This may explain the higher contribution of food to energy and protein intake on day 7, day 8 and day 10 postoperative and the lower contribution of jejunostomy feed on day seven postoperative to the enteral feed group compared to the fortified food group of study 1 The use of different catering systems and different staff in study 1 and study 2 may also be a contributing factor.

It appears that only a certain level of food intake is possible in this patient group in the early postoperative period. Following major upper GI surgery with the absence of the stomach reservoir, appetite may be slow to recover. In addition problems of nausea and early satiety are frequent (Braga et al 1988). These results are consistent with reports in the literature of inadequate food intakes in surgical patients (Keele et al 1997, Mughal and Meguid 1987). In the former study intakes of energy and protein were below estimated requirements for the entire hospital stay. In the latter study failure to take at least 60% of estimated requirements was found to continue for a mean of 30 days in malnourished patients and 12 days in well-nourished patients.
Many other reports of inadequate food intake exist in the literature (Todd et al 1984, Rana et al 1992, Barton et al 2000a). It is difficult to make a direct comparison with their results and those of the current study as they report mean daily energy and protein intake and compare with estimated average requirements of energy (Department of Health 1991) and recommended reference nutrient intakes (RNI) for protein. In the current study energy and protein intakes are expressed as a percentage of calculated requirements to overcome individual differences in requirements and to take into account the fact that nutrient requirements of patients with disease are increased compared with the normal healthy individual (Elia 1996).

6.2.4 The impact of fortified food on energy and protein intake (study 1)

Studies examining the effect of changes in the energy or protein density of the diet have predominantly been undertaken in elderly subjects in institutions (Olin et al 1996, Gall et al 1998, Barton et al 2000b). In the former study increasing the energy content of a hospital diet from 1670kcal to 2520kcal daily resulted in significantly increased energy intakes and body weight after 3 weeks. Barton et al (2000b) found that by increasing energy provision by 14%, (200kcal), while reducing portion sizes by 20%, energy intake was increased from 1425kcal to 1711kcal. No improvement was found in protein intakes with this type of fortification. Study 1 aimed to increase energy intakes by 350-400kcal /day and protein intakes by 25-30g /day through the provision of foods enriched with energy and protein. This level of fortification was chosen as it was found to be the maximum amount of the supplements ProCal and Vitapro that could be added to foods without adversely affecting palatability. Furthermore, three fortified food items daily was found to be the maximum number accepted by patients as postoperative problems of nausea and early satiety severely restrict oral intake. It was sufficient to achieve a significant increase in individual energy and protein intakes over the time period studied. However by the time of discharge, energy and protein intake remained inadequate
providing 59% of energy and 55% of protein requirements in gastric carcinoma patients and 50% of energy and 49% of protein requirements in oesophageal carcinoma patients. No difference in energy and protein intake or in percentage weight loss was observed between control and intervention groups. Weight loss was less in all groups during hospitalisation than has been reported elsewhere for this patient group (Liedman 1999, Braga et al 1998). This cannot be attributed to fortified food provision alone but may be due to the combined effects of early postoperative nutritional support, oral dietary supplements and encouragement with hospital food in the control groups and fortified food provision in the intervention groups. The good preoperative nutritional status of patients may also be a factor as weight loss in hospital has been found to be greater in malnourished patients (Stratton et al 2003).

6.2.5 Food intake in patients following total and subtotal gastrectomy (study 1)

Nutrient contribution from food was found to increase from day 7 postoperative to the day of discharge following both total and subtotal gastrectomy. By the time of discharge a maximum of 59% of energy requirements was achieved in both groups. No difference in energy and protein intake was found over the time periods examined.

Reports of energy intake in these patients in the literature are conflicting with some studies reporting no substantial difference in intake between total and subtotal gastrectomy groups (Von Holstein et al 1992) and others reporting a lower energy intake following total gastrectomy (Braga et al 1998). In the current study nutrient intake was examined in the early postoperative period when all patients have been found to have inadequate intakes. It may be that differences in intake become evident later following discharge home when the residual stomach in subtotal gastrectomy groups may allow a greater volume of food intake. A comparison of the two groups following discharge home warrants further study.
6.2.6 Contribution of home enteral feeding to energy and protein intake and impact on nutritional status

Energy and protein intake four weeks following discharge

At the time of discharge no difference was found in oral energy and protein intake between the two groups. When the contribution of the supplementary enteral feed in the enteral feeding group is taken into account, energy and protein intake was significantly greater. The patients of the fortified food group were reliant on oral intake to meet their nutritional requirements at the time of discharge. The enteral feeding group patients continued supplementary enteral feeding through hospitalisation and following discharge home (500ml Osmolite). At four weeks post discharge, energy and protein intakes remained significantly higher in the enteral feeding group. No difference in oral intake was found between the two groups at this time point. Consequently the difference in nutrient intake can be attributed to the supplementary enteral feed. It seems reasonable to infer from these results that the overnight feeding did not compromise oral food intake and may be a useful means of augmenting energy and protein intake.

Biochemistry

At four weeks following discharge serum albumin was normal in both groups but was significantly higher in the enteral feeding group compared to the fortified food group. This higher level was in association with a normal serum CRP. Serum albumin was not measured at four weeks post discharge for the patient group of study 1 and consequently this data is unavailable. It is recognised that serum albumin may be more a prognostic indicator of complications or mortality than a marker of nutritional status in acute illness (Carney and Meguid 2002). Its long half-life of 21 days make serum levels a better reflection of long-term nutritional intake. The higher level in the enteral feeding group at four weeks post discharge in the presence of a normal serum CRP is suggestive that the supplementary feeding may have been of benefit in improving serum levels.
Body weight

While the enteral feeding group lost significantly more weight from discharge to four weeks following discharge (6.3% versus 1.3%), weight loss from preoperative to four weeks post discharge was less compared with the fortified food group. The rapid postoperative gain in body weight in the enteral feeding group during hospitalisation is not likely to represent true body weight but a gain in fluid. The most likely explanation for this is different fluid management strategies in the two centres. If this were the case it would explain the higher weight loss from the time of discharge to four weeks following discharge in the enteral feeding group. Weight loss experienced over the more prolonged period from preoperative to four weeks post discharge may be a better reflection of true perioperative weight change. Energy and protein intake was higher at the time of discharge and at four weeks post discharge in the enteral feeding group suggesting that the enteral feed may have been an important factor in attenuating weight loss in this patient group.
6.3 Limitations of the study

As in all research methods this study has limitations, which must be considered when interpreting the results.

6.3.1 Sample size

Sample size calculations estimate the number of people required to show statistically significant differences (Vivanti and Ash 2003). Sizes employed in other studies may indicate required numbers or it may be necessary to do power calculations (Vivanti and Ash 2003). Predicting the numbers needed to show benefit from feeding is clearly difficult if there is no previous data to base assumptions on. There is no data in the literature on the effect of food fortification or continued home enteral feeding on body weight or nutritional intake in upper GI surgical patients. There have only been four studies examining the benefit of feeding surgical patients after discharge from hospital, all these studies were using patients who had undergone colonic surgery. In these studies between 0 and 5% changes were seen in body weight with oral nutritional supplements. Assuming a 3% change in weight with fortified food or jejunostomy feed, 40 patients in each group would be needed to have a power of 0.8, based on a significance level of 0.05.

Although there is a high incidence of gastric and oesophageal carcinoma in South Wales and England only a small proportion present with a stage of disease that is curative by surgery. In the case of study 1 with no exclusion criteria and all patients agreeing to participate it was only possible to recruit a total of 40 patients with gastric carcinoma and 40 patients with oesophageal carcinoma over the four-year period. In the case of study 2 with no exclusion criteria and all patients agreeing to participate it was possible to recruit a total of 21 patients with oesophageal carcinoma over the final year of the study. When analysed by control and intervention groups the sample size was relatively small. This
study could therefore be considered a ‘trial run’ to create data to use for power calculations to perform a future randomised controlled trial.

6.3.2 Study design

It is recognised that the best means to show evidence of benefit of an intervention is by a randomised controlled trial. With low patient numbers and time constraints this was not feasible in this case. Randomised controlled trials are expensive to administer and time consuming. In the setting of a District General Hospital with no supplementary research funding to support such a trial it was not considered to be a feasible option. Instead the study was conducted in two phases, an initial control phase followed by an intervention phase. Control and intervention groups were comparable at the outset with no significant differences in patient characteristics or nutritional status preoperatively.

Study 1 was carried out over a four-year period, September 1999 to October 2003. Study 2 took place from January to December 2004. While the same surgeon and dietitian presided for the duration of study 1 some changes in practice cannot be out ruled. For example, there was a tendency for the gastric carcinoma intervention group patients to be overweight preoperatively resulting in a surgical decision not to provide early postoperative nutrition support. With greater liaison between the surgical team and dietitian there was a tendency to continue enteral feeding for longer during hospitalisation in those patients in whom enteral feeding was commenced. More prolonged use of jejunal feeding during hospitalisation may have compromised oral intake.

Study 2 took place at a different hospital site and consequently while dietetic input remained the same the surgical team differed. The surgical procedures were the same however the results suggest different postoperative fluid management strategies. Fluid status was not monitored which must be considered when interpreting the results.
6.3.3 Food fortification

A number of studies conducted in different patient groups examining the impact of food fortification on energy and protein intakes have been successful in removing patients from energy but not protein deficit (Olin et al 1996, Gall et al 1998, Barton et al 2000b). This reflects the relative ease with which the energy density of foods can be increased. Enhancing food protein content presents more problems. A range of high protein powdered supplements is currently available and can theoretically be incorporated into foods. The hospital catering service operates a bulk catering system where hot food for lunch is prepared in the morning and kept warm in bulk trolleys until delivered to the ward. At ward level patients are given the choice of two main course options and can choose their desired portion size thus allowing for varying appetites. Cold choices only are available in the evening. Trolley temperatures were found to vary considerably and protein-enriched foods were found to have a low level of stability in these conditions, which restricted the high protein choices for patients. Consequently, the standard main course was not fortified due to stability and palatability problems and also to give patients the opportunity to choose their desired option at ward level at mealtimes. The hospital catering system offers traditional meal choices to patients i.e. roast meats, fried fish, which offer limited opportunity for manipulation. In pilot tests the fortification of mashed potato with high protein products was attempted but found to be unacceptable by patients. Food handling regulations forbade the addition of products to food at ward level. Consequently the choice of suitable foods for fortification was limited (Appendix 2).

Early satiety was a frequently encountered problem. When patients rejected a fortified item after the hospital main course it was kept at ward level and consumption within two to three hours was encouraged by the dietitian. Frequently nursing staff failed to offer fortified items especially on weekend days in the absence of dietetic input. Fortified ice cream was one of the most popular choices but the absence of a freezer in the ward kitchen
and poor compliance from catering staff resulted in this option not being available outside dietetic working time. Consequently the provision of fortified foods was not always optimal.

6.3.4 Nutritional Measurements

Body weight was chosen as one of the indices of nutritional status. It was anticipated when chosen, that the provision of fortified foods (study 1) and the continuation of supplementary jejunal feeding at home (study 2) would have a positive impact on body weight. While steps were taken to ensure the measurement was accurate (by ensuring the same scales was used throughout the study, that the scales were regularly calibrated and that patients were measured at the same time and in the same conditions) other factors exist that may have an impact on body weight, for example fluid status. The rapid gain in weight observed in the enteral feeding group during hospitalisation (study 2) cannot be attributed to an accretion of tissue mass but is much more likely to be related to the accumulation of fluid. The presence of oedema was not recorded and this must be considered when interpreting the results.

6.3.5 Home Enteral Feeding

The objective of the study was for enteral feeding to be continued for a period of four to six weeks. The final study group comprised 21 patients who were discharged home with supplementary enteral feeding. In practice, only 15 patients continued to receive the supplementary feed when reviewed in clinic. In four cases the tube fell out prematurely, in two cases the patients chose to discontinue the feed prematurely. Some of this early discontinuation could have been avoided by more rigorous patient monitoring at home. Better education of community staff regarding care of the tube may also have reduced the number of tubes prematurely falling out.
6.4 Recommendations for further study

1. Randomised controlled trials assessing the impact of dietary fortification on clinical outcome compared with routine clinical care in this patient group, are lacking. There is currently little evidence with which to assess the relative efficacy of oral nutritional supplements and dietary manipulation. Not only are there a small number of studies in this area but also the quality of existing data is poor (Baldwin and Parsons 2004). In this study no difference was found in nutrient intake between control groups where supplements were continuously encouraged in addition to standard hospital diet and intervention groups where fortified food was encouraged. However supplements were not withheld from intervention group patients where the tolerance of solid food was poor as this was considered to be unethical making comparison of the effects of supplements and fortified food difficult.

2. It appears that only a certain level of food intake is tolerated in this particular patient group in the early postoperative period despite dietary fortification in the intervention groups of study 1 and intensive dietetic input in all groups. Jejunostomy feeding was found to be well tolerated with a low incidence of complications overall, 9% (10 of 103). Given the failure of the patients in study 1 to exceed 60% of energy and protein requirements from oral intake it was proposed that continuation of jejunostomy feeding through hospitalisation and following discharge may be a useful means of enabling these patients to meet nutritional requirements and from this proposal Study 2 was progressed. It is recognised that a randomised controlled trial is the best means of obtaining evidence of benefit for an intervention. However it was not feasible in this case due to time constraints and the need for large patient numbers. This study was therefore seen as a means of establishing the feasibility of a larger trial. In view of the promising results from the current study in terms of the improvement in nutritional intake and the attenuation in weight loss
achieved by the supplementary feeding, a randomised controlled trial of supplementary enteral feeding is recommended. The impact of supplementary feeding on quality of life is also an important factor that was not addressed in the current study and warrants further investigation.
6.5 Conclusions

The nutritional status of this patient population preoperatively was better than previously reported in the literature, however inadequacy of oral intake postoperatively renders them vulnerable to deterioration in nutritional status.

Study 1

The provision of food fortified with energy and protein resulted in a significant improvement in individual energy and protein intakes in the intervention groups. However the food fortification failed to significantly improve energy and protein intakes compared with those receiving standard treatment. It is evident that this patient group has a limited capacity for food postoperatively. Oral energy and protein intake did not exceed 60% of requirements during hospitalisation in all groups. Weight loss occurred in all groups and no difference was found in the extent of weight loss during hospitalisation between control and intervention groups. No improvement in oral intake was found when patients were reassessed at four weeks post discharge with further weight loss demonstrated, suggesting that dietary advice alone at the time of discharge is insufficient to prevent further deterioration in nutritional status.

Study 2

The use of continued supplementary enteral feeding through hospitalisation and following discharge home resulted in a significant improvement in total energy and protein intakes. Four weeks following discharge, 99% of energy and 95% of protein requirements were met. Weight loss from preoperative to four weeks post discharge was less compared with the group receiving fortified foods during hospitalisation. Complications associated with enteral feeding were few and minor. The improved nutritional intakes and attenuation of weight loss suggests that this may be a useful treatment modality to prevent further deterioration in the nutritional status of this vulnerable patient group. A larger randomised controlled trial is recommended to determine its potential to improve clinical outcome measures and improve quality of life for this patient group.
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Appendices
Appendix 1

The nutritional management of upper gastrointestinal surgery patients: an examination of current dietetic practice

A Nutritional Assessment

1. Does your hospital have a dietitian dedicated to the nutritional management of patients undergoing upper gastrointestinal surgery i.e. oesophagectomy, gastrectomy?

   Yes ☐
   No ☐

2. Is a nutritional assessment performed on all patients preoperatively?

   Yes ☐
   No ☐

   If no, go to question 5, if yes, go to question 3.

3. Is this performed by a dietitian?

   Yes ☐
   No ☐

4. What parameters are measured?

   Weight ☐
   Height ☐
   BMI ☐
   % Weight loss over past 3-6 months ☐
   Arm anthropometry ☐
   Other ☐
B. Preoperative nutrition support

5. Are patients given preoperative nutrition support?
   Yes ☐
   No ☐
   Only if considered malnourished ☐

If yes, which of the following are offered?

(a) Nutritional supplement drinks ☐
(b) Extra food snacks ☐
(c) Both (a) and (b) ☐
(d) Nasogastric tube feeding ☐
(e) TPN ☐

C. Postoperative nutrition support

6. Do oesophagectomy patients *routinely* receive artificial nutrition support in the early postoperative period?
   Yes ☐
   No ☐
   Only if malnourished preoperatively ☐
   Only if complications occur postoperatively ☐

If no, go to question 14.

7. If yes, do they receive:

(a) Jejunostomy tube feeding ☐
(b) Nasojejunal feeding ☐
(c) TPN ☐
(d) Both PN and jejunostomy feeding ☐

8. How soon postoperative is artificial feeding initiated?

9. Is there a protocol in place for initiating feeding?
   Yes ☐
   No ☐

10. If patients are fed enterally, what is the standard feed that is used?
11. At what stage is jejunal feeding discontinued?

12. At what stage is the feeding tube removed?

13. Does the dietitian have an input into the decision to continue or discontinue feeding?

14. Are oral nutritional supplements offered:
   (a) Routinely on introduction of oral fluids
   (b) Later in the postoperative period if oral intake is inadequate
   (c) Only if a medical or nursing referral is received

15. If oral nutritional supplements are offered, for how long are they continued?

16. Are real food snacks readily available?
   Yes ☐
   No ☐

If yes, are these offered:
   (a) In addition to oral nutritional supplements
   (b) As an alternative to oral nutritional supplements

17. Are the patients reviewed by a dietitian following discharge?
   Yes ☐
   No ☐
   Only if referred by medical or nursing staff ☐

18. If yes, is this
    (a) Telephone contact ☐
    (b) Outpatient appointment ☐
Appendix 2(a) High protein menu

Breakfast
Orange Juice
Cornflakes / Weetabix / Shredded wheat / Porridge with milk
Scrambled egg and toast

Lunch
Fortified soup
Ward main course (Roast meat or fish with mashed potato and vegetables)
Fortified tinned milk pudding / ward sponge or crumble with fortified custard / fortified jelly and ice cream

Tea
Soup or sandwich or hot soft option
Fortified ice cream and jelly / fortified angel delight / cold tinned milk pudding.
Appendix 2 (b) Food fortification instructions and nutritional composition of fortified foods

Food items were fortified with one large scoop (11g) Vitapro and one sachet (15g) of ProCal. Each patient was encouraged to take three fortified items daily to achieve the target level of fortification.

Fortification instructions are detailed below.

A. Soup Fortification Instructions:

1. Take 11g of Vitapro
2. Add 1 sachet of ProCal powder (15g)
3. Mix to a paste with a little warm water
4. Gradually add the mixture to ½ tin of warm soup and mix until smooth
5. Label the soup with patient’s name and ward
6. Place in the appropriate food trolley just before it is transferred to the ward.

B. Fortification Instructions for tinned milk puddings and custard:

1. Take 11g Vitapro
2. Add 1 sachet of ProCal powder (15g)
3. Mix to a paste with a little warm water
4. Gradually add the mixture to 1/3 tin (150g) of milk pudding or 100ml custard and mix until smooth
5. Label with patient’s details and place in the appropriate trolley just before it is transferred to the ward.
C. Fortification Instructions for mousse or Angel Delight:

1. Make up the 1 sachet of Angel delight with 300ml whole milk as directed on the packet
2. Take 33g Vitapro
3. Add 3 sachets of ProCal (3x15g)
4. Blend into the mousse until smooth
5. Pour into individual dishes to obtain 3-4 portions

D. Fortification Instructions for Fortified Ice Cream

1. Whip 150 ml whipping cream
2. Add 150 ml full cream milk
3. Add 30g Vitapro and one sachet Vanilla Calshake (Fresenius Kabi)
4. Whisk together until well blended
5. Pour into 4-5 individual dishes
6. Place in the deep freeze and use within three days.

E. Fortification Instructions for fortified Jelly

1. Dissolve one Rowntree’s Jelly in the microwave in a small amount of water
2. Allow to cool slightly
3. Add 1 whole carton of Enlive or Fortijuice sip feed
4. Mix together
5. Pour into individual dessert dishes to obtain 3 portions and use within three days.
Table A1. Nutritional composition of fortified foods (per portion)

<table>
<thead>
<tr>
<th>Nutritional composition/Portion</th>
<th>FortiJuice jelly (133g)</th>
<th>Enliven Jelly (133g)</th>
<th>Fortified ice-cream (80g)</th>
<th>Fortified Angel delight (142g)</th>
<th>Fortified Semolina (168g)</th>
<th>Fortified Rice pudding (168g)</th>
<th>Fortified custard (142g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (kcals)</td>
<td>235</td>
<td>235.0</td>
<td>218.6</td>
<td>285.4</td>
<td>257.5</td>
<td>270.2</td>
<td>246.7</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>5.2</td>
<td>5.7</td>
<td>6.8</td>
<td>14.13</td>
<td>14.9</td>
<td>14.6</td>
<td>13.0</td>
</tr>
<tr>
<td>Carbohydrate (g)</td>
<td>41.5</td>
<td>52.1</td>
<td>14.2</td>
<td>18.99</td>
<td>23.5</td>
<td>26.5</td>
<td>21.7</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>0.16</td>
<td>0.2</td>
<td>15.0</td>
<td>17.06</td>
<td>11.5</td>
<td>11.8</td>
<td>12.0</td>
</tr>
</tbody>
</table>
### Appendix 3 Reference ranges for biochemical parameters

**Table A2. Reference ranges for biochemical parameters**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin (g/l)</td>
<td>35-50</td>
</tr>
<tr>
<td>C reactive protein (mg/l)</td>
<td>0-10</td>
</tr>
<tr>
<td>Haemoglobin (g/dl)</td>
<td>13-18</td>
</tr>
<tr>
<td>Total lymphocyte count (x10⁶)</td>
<td>1-4</td>
</tr>
</tbody>
</table>
Appendix 4 Ward Jejunostomy Feeding Protocol

**Adult Jejunostomy Feeding Regimen**

**Patient Details**
- **Name:**
- **DOB:**
- **Hospital Number:**

- To prevent dehydration IV fluids should be given until adequate fluids are tolerated via the jejunostomy tube.
- Keep the patient **NIL BY TUBE** for 12 hours overnight after insertion of a jejunostomy tube except for flushing.
- Flush tube with 30mls sterile water using a 50ml syringe every 6 hours.

1. **Administer sterile water @ 30mls / hour x 6 hours. (180mls)**

After this time use freshly drawn drinking tap water except in immunocompromised patients (e.g., cancer patients on chemotherapy, transplant patients on immunosuppressive medications) where sterile water should be used. Once the water has run through→

2. **Feed Osmolite @ 30mls / hour x 8 hours. (240mls). Flush 30mls drinking tap water after 8 hours.**

If tolerating feed e.g. No abdominal discomfort, distension, pain, diarrhoea or vomiting→

3. **Feed Osmolite @ 45mls / hour x 8 hours. (360mls). Flush 30mls drinking tap water after 8 hours. Continue feed.**

If tolerating feed e.g. No abdominal discomfort, distension, pain, diarrhoea or vomiting→

4. **Feed Osmolite @ 60 mls / hour x 8 hours. (480mls). Flush 30mls drinking tap water after 8 hours. Continue feed.**

Continue to increase the feeding rate by 15 ml/hour every 8 hours until the target rate is established. Once target rate of __________ is established feed should be given for 24 hours, NO REST PERIOD.

- **Flushes:** Flush the jejunostomy tube with 30mls drinking tap water after each bottle feed. Minimum of 3 flushes /day while feeding is continuous. If feeding is discontinued flush the tube once daily.
- Giving sets must be changed daily.
- Document fluid balance hourly for the first 5 days then at each bottle change.
- Check with your ward pharmacist that all medications are suitable to be given into the jejunum. Change all medications to soluble or linctus forms if possible to prevent tube blockage.
- **N.B.** If diarrhoea a problem refer to the tube feeding guidelines on management of diarrhoea.

**Dietitian (contact) ________________________________**
Appendix 5 Nutritional composition of enteral feeds and oral nutritional supplements

Table A3. Nutritional composition of enteral feeds for postoperative nutritional support

<table>
<thead>
<tr>
<th>Nutritional composition/100ml</th>
<th>Nutrison Standard</th>
<th>Osmolite</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (kcal)</td>
<td>100</td>
<td>101</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Carbohydrate (g)</td>
<td>12.3</td>
<td>13.6</td>
</tr>
<tr>
<td>of which sugars</td>
<td>1.0</td>
<td>0.69</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>3.9</td>
<td>3.4</td>
</tr>
<tr>
<td>Fibre (g)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sodium (mmol)</td>
<td>4.3</td>
<td>3.83</td>
</tr>
<tr>
<td>Potassium (mmol)</td>
<td>3.8</td>
<td>3.79</td>
</tr>
<tr>
<td>Osmolality (mosm/kg H2O)</td>
<td>310</td>
<td>288</td>
</tr>
</tbody>
</table>

Table A4. Nutritional composition of oral nutritional supplements

<table>
<thead>
<tr>
<th>Nutritional composition/100ml</th>
<th>Nutricia Clinical Care</th>
<th>Abbott Laboratories</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fortisip</td>
<td>Fortijuce</td>
</tr>
<tr>
<td>Energy (kcal)</td>
<td>150</td>
<td>150</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Carbohydrate (g)</td>
<td>18.4</td>
<td>33.5</td>
</tr>
<tr>
<td>of which sugars</td>
<td>4.7</td>
<td>6</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>5.8</td>
<td>0</td>
</tr>
<tr>
<td>Fibre (g)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sodium (mmol)</td>
<td>4.6</td>
<td>0.7</td>
</tr>
<tr>
<td>Potassium (mmol)</td>
<td>5.1</td>
<td>0.5</td>
</tr>
<tr>
<td>Osmolarity (mosm/L)</td>
<td>455</td>
<td>700</td>
</tr>
</tbody>
</table>
Appendix 6 Products used for food fortification

**ProCal:** A bland tasting white powder consisting of vegetable oils, skimmed milk powder, lactose and sodium caseinate. It can be added to a wide variety of food and drink with minimum effect on taste, volume or texture.

**Vitapro:** A high biological value protein supplement. It is an instantised water soluble, cream coloured amorphous powder consisting of a specially selected blend of unsupplemented whole milk proteins, containing all the essential amino acids and low in electrolytes (Vitaflo data sheet May 2001). Being virtually tasteless and in an instantised form it can be easily incorporated into a dietary regime.

<table>
<thead>
<tr>
<th>Nutritional information</th>
<th>Vitapro /100g</th>
<th>ProCal /100g</th>
<th>Skimmed milk powder/100g</th>
<th>Maxijul /100g</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (kcals)</td>
<td>388</td>
<td>667</td>
<td>348</td>
<td>380</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>75</td>
<td>13.5</td>
<td>36.1</td>
<td>0</td>
</tr>
<tr>
<td>Carbohydrate (g)</td>
<td>9</td>
<td>26.8</td>
<td>52.9</td>
<td>95</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>6</td>
<td>56.2</td>
<td>0.6</td>
<td>0</td>
</tr>
</tbody>
</table>
Appendix 7 (a) Patient Information Sheet, Consent form and Ethical approval (Study 1).

PATIENT INFORMATION SHEET

Thank you for thinking about taking part in this study. If you are willing to take part you will be asked to sign this consent form and will be given a copy to keep.

INTRODUCTION

After your operation you may not feel like eating your usual amount for some time and this may result in weight loss. This study involves providing you with food that has been fortified with extra energy (calories) and protein to help to maintain your weight and an adequate nutrient intake after your operation.

WHY IS THIS STUDY BEING DONE?

This study is being done to determine if providing you with foods that are fortified with energy and protein can help you meet your nutritional requirements and prevent you losing weight whilst in hospital.

WHY HAVE I BEEN SELECTED?

All patients having your type of operation will be selected.

WHAT ARE WE ASKING YOU TO DO?

We are asking you to cooperate with the dietitian who will offer you a choice of fortified foods. She will also be recording all the food and drink that you manage to take each day until you go home.
DO I NEED TO TAKE PART?

Your participation is voluntary, however the information that you contribute is valuable and will be collated with the information received from other patients who have a similar operation. If the study is successful it will benefit patients in the future having this type of operation. You do not have to take part in this study and if you prefer not to, it will not affect your present or future care in any way.

WHAT HAPPENS IF I SUFFER AS A RESULT OF THE STUDY?

You should not suffer any problems as a result of participating in the study.

WHO WILL SEE ALL THE INFORMATION ABOUT ME?

All recorded information will be confidential.
PATIENT CONSENT FORM

Hospital: ........................................................................................................

Name of patient: ................................................................................................

Name of dietitian: ..............................................................................................

Title of study: An investigation into the perioperative nutritional status and nutritional intake of patients with gastric and oesophageal carcinoma undergoing surgical resection and an examination of the effect of food fortification on nutritional intake and nutritional intake postoperatively.

Statement by patient
I confirm that I consent to take part in a study for the treatment of
..........................................................................................................................

Details of the study have been explained to me by the above-named dietitian including the benefits, major risks and discomfort it may entail.
I understand what the study involves and that I can stop participating in the study at any time.
I am willing to take part in this study.

Signed ................................................................. Date
Statement by dietitian

I have explained the nature and the purpose of the study to the above-named patient and believe that the patient understands what the study involves.

Signed........................................................................Date

Statement by witness

Signed........................................................................Date
Mrs Paula Murphy
Dietitian
Nutrition and Dietetics Department
Royal Gwent Hospital
NEWPORT
NP20 2UB

Dear Mrs Murphy

Re: An investigation into the effect of food fortification on nutrition status and nutrient intake in patients undergoing potentially curative resections for gastric and oesophageal carcinoma

Thank you for your letter dated 9 October 2001 enclosing an amended patient information sheet, consent form and protocol as requested by the Gwent Research Ethics Committee at the meeting on 3 September 2001.

These amendments were noted and approval for the study has been granted under Chairman’s Action at the meeting on 29 October 2001.

Yours sincerely

Jeremy Winston
Jeremy H Winston
Chairman

Please note: it is the responsibility of the researcher to inform the Gwent Healthcare NHS Trust R & D office of the study to be undertaken

The Gwent Research Ethics Committee aims to be fully compliant with the ICH Harmonised Tripartite Guidelines for Good Clinical Practice
Appendix 7 (b) Patient Information Sheet, Consent form and Ethical approval (Study 2)

PATIENT INFORMATION SHEET
Thank you for thinking about taking part in this study. If you are willing to take part you will be asked to sign this consent form and will be given a copy to keep.

INTRODUCTION
It will be a number of days after your operation before you will be allowed to take anything by mouth. As a result, during your operation you will have a feeding tube placed so that you can obtain the nutrition you need. After your operation you may not feel like eating your usual amount for some time and weight loss is a frequently encountered problem. This study involves continuing tube feeding for 4-6 weeks at home to determine if this may help improve your nutritional state.

WHY IS THIS STUDY BEING DONE?
This study is being done to determine if continuing tube feeding at home can help you meet your nutritional requirements and prevent you losing weight following discharge from hospital.

WHY HAVE I BEEN SELECTED?
All patients having your type of operation will be invited to take part.

WHAT ARE WE ASKING YOU TO DO?
We are asking you to cooperate with the dietitian who will monitor your weight and will record all the food and drink that you manage to take for 5 days while you are in hospital. If you agree to take part you will continue to receive tube feeding at home. You will be
given a supply of feed and equipment so that you can continue the supplementary feeding at home. The feeding can take place at night so should not interfere with your normal eating or with your daily activities.

**DO I NEED TO TAKE PART?**

You do not have to take part and if you prefer not to, it will not affect your present or future care in any way. However if you do decide to take part the information that you contribute will be valuable and will be collated with the information received from other patients who have a similar operation. If the study is successful it will benefit patients in the future having this type of operation. You do not have to take part in this study.

**WHAT HAPPENS IF I DEVELOP PROBLEMS AS A RESULT OF THE STUDY?**

You should not develop any problems as a result of participating in the study. You will not have any extra procedures done to you as a result of the study.

**ARE THERE ANY ADVANTAGES TO TAKING PART IN THE STUDY?**

If continuing tube feeding at home is advantageous you will feel better and recover faster after your operation.

**WHO WILL SEE ALL THE INFORMATION ABOUT ME?**

All recorded information will be confidential. You will not be identified by name at any time.
FURTHER INFORMATION

If you have any questions about taking part in this study please contact your dietitian

Dietitian name:  Paula Murphy

Contact Tel. No.:  01752 763045
Patient Consent Form

Study No.

Study Title An investigation into the effect of continued jejunostomy feeding following discharge home for a period of 4-6 weeks on the nutritional intake and nutritional status of patients following surgical resection for oesophageal carcinoma.

Name of investigator: Paula Murphy

Tel. No.: 01752 763045

Please tick the boxes

☐ 1. I confirm that I have read and understand the information sheet for the above study and have had the opportunity to ask questions

☐ 2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving reason, without my medical care or legal rights being affected.

☐ 3. I agree to take part in the above study.

Patient ______________ Date __________ Signature ________

Researcher ___________ Date ___________ Signature ________ -
Dear Ms Murphy

Re: Plymouth Trial No 2165
An investigation into the effect of continued enteral feeding following discharge home on nutritional intake and nutritional status
Lead Investigator: Ms Paula Murphy

Thank you for your letter of 1 April 2004, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chairman.

CONFIRMATION OF ETHICAL OPINION

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation.

The favourable opinion applies to the following research site:

Site: Plymouth Hospitals NHS Trust
Derriford Hospital
Derriford Road
Plymouth PL6 8DH

CONDITIONS OF APPROVAL

The favourable opinion is given provided that you comply with the conditions set out in the attached document. You are advised to study the conditions carefully.
APPROVED DOCUMENTS

The final list of documents reviewed and approved by the Committee is as follows:

Application form
Patient Consent Form
Patient Information Sheet
Study Protocol
GP Letter

Dated 1 April 2004
Dated 1 April 2004 Version 2
Dated 1 April 2004 Version 2
Dated 1 April 2004 Version 2
Undated

MANAGEMENT APPROVAL

The study may not commence until final management approval has been confirmed by the organisation hosting the research.

NOTIFICATION OF OTHER BODIES

We shall notify Dr Lisa Vickers, R&D Manager that the study has a favourable ethical opinion.

Statement of compliance (from 1 May 2004)

This Committee is recognised by the United Kingdom Ethics Committee Authority under the Medicines for Human Use (Clinical Trials) Regulations 2004, and is authorised to carry out the ethical review of clinical trials of medicinal products.

The Committee is fully compliant with the Regulations as they relate to ethics committees and the conditions and principles of good clinical practice.

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

I hope you will be successful with your funding. The trial is undoubtedly worthwhile and I would have thought a drug company would have been willing supply support.

REC reference number: 2165  Please quote this number on all correspondence

Yours sincerely

MR A. J. R BEAUCHAMP
Dip. Healthcare Ethics
Chairman

Enclosure: Standard approval conditions SL-AC2
cc: Dr Lisa Vickers – R & D Manager
Appendix 8 Details of all gastric and oesophageal carcinoma patients including operative deaths (study 1)

Table A6 Details of all gastric carcinoma patients including operative deaths

<table>
<thead>
<tr>
<th></th>
<th>Control group (n=24)</th>
<th>Intervention group (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male:Female</td>
<td>18:6</td>
<td>14:7</td>
</tr>
<tr>
<td>Age (years)</td>
<td>70(27-83)</td>
<td>67(47-81)</td>
</tr>
<tr>
<td>Operation type:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total gastrectomy</td>
<td>12</td>
<td>11</td>
</tr>
<tr>
<td>Subtotal gastrectomy</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>Potentially curative resection</td>
<td>19</td>
<td>17</td>
</tr>
<tr>
<td>Stage of disease (Guillou and Monson 2001)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>II</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>III</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>IV</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Postoperative nutrition support</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total parenteral nutrition (TPN)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>PN and jejunostomy feeding</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Jejunostomy feeding</td>
<td>14</td>
<td>9</td>
</tr>
</tbody>
</table>

Details are numbers of patients. Age is expressed as median (range).
Table A7 Details of all oesophageal carcinoma patients including operative deaths

<table>
<thead>
<tr>
<th></th>
<th>Control group (n=26)</th>
<th>Intervention group (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male:Female</td>
<td>17:9</td>
<td>15:5</td>
</tr>
<tr>
<td>Age (years)</td>
<td>60(46-77)</td>
<td>62(38-78)</td>
</tr>
<tr>
<td>Operation type:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transhiatal oesophagogastricectomy</td>
<td>24</td>
<td>16</td>
</tr>
<tr>
<td>Ivor Lewis oesophagogastricectomy</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Mc Ewans oesophagogastricectomy</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Potentially Curative Resection</td>
<td>24</td>
<td>19</td>
</tr>
<tr>
<td>Stage of Disease (Guillou and Monson 2001)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>I</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>II</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>III</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>IV</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Operative mortality</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Jejunostomy tube feeding alone</td>
<td>21</td>
<td>17</td>
</tr>
<tr>
<td>Jejunostomy feeding and PN</td>
<td>5</td>
<td>3</td>
</tr>
</tbody>
</table>

Details are numbers of patients. Age is expressed as median (range).

Preoperative nutritional status of all patients (including operative deaths)

Details of the preoperative nutritional status of all gastric and oesophageal carcinoma patients (including operative deaths) are presented in Tables A8 and A9 respectively.

(a) Gastric carcinoma

BMI < 20kg/ m² and unintentional weight loss >10% in three to six months were the criteria chosen to identify malnutrition.

In the control group, using these criteria, none of the operative deaths could be considered malnourished at presentation. In the intervention group, anthropometric data is available for one of the two operative deaths only as the operation proceeded without the knowledge of the principal investigator. In this case preoperative serum albumin was low at 27g/l.
The other operative death occurred in a patient with a normal BMI and serum albumin preoperatively, but an 8.8% preoperative weight loss was reported, suggesting nutritional risk.

*(b) Oesophageal carcinoma*

The same criteria were used to identify malnutrition, (BMI < 20kg/ m² and unintentional weight loss >10% in three to six months) in oesophageal carcinoma patients.

None of the patients could be considered malnourished using the chosen criteria however one of the operative deaths in the control group experienced >10% weight loss but maintained a normal BMI and one experienced >5% weight loss but also maintained a normal BMI, indicating nutritional risk. All three operative deaths in the control group had a low serum albumin preoperatively. In the intervention group the one operative death had a normal preoperative BMI and serum albumin level but suffered significant preoperative weight loss (17%) again indicating nutritional risk.
Table A8 Preoperative nutritional status in gastric carcinoma patients including operative deaths: serum biochemistry and anthropometry

<table>
<thead>
<tr>
<th></th>
<th>Control group (n=24)</th>
<th>Intervention group (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body weight (kgs)</strong></td>
<td>66 (38-90)</td>
<td>74 (49-121)</td>
</tr>
<tr>
<td><strong>Body Mass Index (kg/m²)</strong></td>
<td>23.8 (17.5-31)</td>
<td>26.2 (19.6-33.5)</td>
</tr>
<tr>
<td><strong>Preop weight loss (%)</strong></td>
<td>5.3 (0-16.4)</td>
<td>0 (0-21.8)</td>
</tr>
<tr>
<td><strong>Albumin (g/l)</strong></td>
<td>39 (29-47)</td>
<td>39 (20-44)</td>
</tr>
<tr>
<td><strong>CRP (mg/l)</strong></td>
<td>&lt;10 (&lt;10-35.3)</td>
<td>&lt;10 (&lt;10-132)</td>
</tr>
<tr>
<td><strong>Lymphocyte count (x10⁹/l)</strong></td>
<td>1.7 (0.9-2.5)</td>
<td>1.6 (1.1-2.9)</td>
</tr>
<tr>
<td><strong>Haemoglobin (g/dl)</strong></td>
<td>12.5 (10.3-16.9)</td>
<td>13.3 (9.2-15.7)</td>
</tr>
</tbody>
</table>

Results are median (range)

Table A9
Preoperative nutritional status in oesophageal carcinoma patients including operative deaths: serum biochemistry and anthropometry

<table>
<thead>
<tr>
<th></th>
<th>Control group (n=26)</th>
<th>Intervention group (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body weight (kgs)</strong></td>
<td>69 (48-104.5)</td>
<td>73 (44-103)</td>
</tr>
<tr>
<td><strong>Body Mass Index (kg/m²)</strong></td>
<td>25 (19-32)</td>
<td>24.3 (18-30.5)</td>
</tr>
<tr>
<td><strong>Preoperative weight loss (%)</strong></td>
<td>5.6 (0-17.6)</td>
<td>4.2 (0-20)</td>
</tr>
<tr>
<td><strong>Albumin (g/l)</strong></td>
<td>41 (19-48)</td>
<td>41.5 (36-46)</td>
</tr>
<tr>
<td><strong>CRP (mg/l)</strong></td>
<td>N/A</td>
<td>&lt;10 (&lt;10-33.4)</td>
</tr>
<tr>
<td><strong>Lymphocyte count (x10⁹/l)</strong></td>
<td>1.4 (0.4-3.6)</td>
<td>1.5 (0.7-3.8)</td>
</tr>
<tr>
<td><strong>Haemoglobin (g/dl)</strong></td>
<td>13.9 (10.7-16.1)</td>
<td>14.1 (12.7-16.3)</td>
</tr>
</tbody>
</table>

Results are median (range)
Appendix 9 Median percentage energy and protein contribution from feeding sources in gastric and oesophageal carcinoma patients

(study 1)

Table A10. Median percentage energy and protein contribution from feeding sources in gastric carcinoma

<table>
<thead>
<tr>
<th></th>
<th>Control group (n=21)</th>
<th>Intervention group (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Energy (kcal/d)</td>
<td>Protein (g/d)</td>
</tr>
<tr>
<td>Energy and protein requirement</td>
<td>1783 (1209-2138)</td>
<td>70 (41-94)</td>
</tr>
<tr>
<td>PN day 2</td>
<td>98 (0-121)</td>
<td>87 (0-106)</td>
</tr>
<tr>
<td>(n=9 control, 3 intervention)</td>
<td>0 (0-126)</td>
<td>0 (0-112)</td>
</tr>
<tr>
<td>PN day 8</td>
<td>0 (0-126)</td>
<td>0 (0-86)</td>
</tr>
<tr>
<td>(n=9 control, 3 intervention)</td>
<td>0 (0-126)</td>
<td>0 (0-85)</td>
</tr>
<tr>
<td>PN day 9</td>
<td>0 (0-126)</td>
<td>0 (0-85)</td>
</tr>
<tr>
<td>(n=9 control, 3 intervention)</td>
<td>0 (0-126)</td>
<td>0 (0-85)</td>
</tr>
<tr>
<td>Jejunostomy feed day 2</td>
<td>32 (0-110)</td>
<td>29 (0-82)</td>
</tr>
<tr>
<td>(n=18 control, 9 intervention)</td>
<td>47 (0-104)</td>
<td>47 (0-128)</td>
</tr>
<tr>
<td>Jejunostomy feed day 7</td>
<td>27 (0-101)</td>
<td>25 (0-117)</td>
</tr>
<tr>
<td>(n=17 control, 9 intervention)</td>
<td>0 (0-126)</td>
<td>0 (0-86)</td>
</tr>
<tr>
<td>Jejunostomy feed day 9</td>
<td>0 (0-126)</td>
<td>0 (0-86)</td>
</tr>
<tr>
<td>(n=15 control, 8 intervention)</td>
<td>0 (0-126)</td>
<td>0 (0-86)</td>
</tr>
<tr>
<td>Jejunostomy feed day 10</td>
<td>32 (0-110)</td>
<td>29 (0-82)</td>
</tr>
<tr>
<td>(n=11 control, 7 intervention)</td>
<td>47 (0-104)</td>
<td>47 (0-128)</td>
</tr>
<tr>
<td>Jejunostomy feed on discharge</td>
<td>0 (0-50)</td>
<td>0 (0-30)</td>
</tr>
<tr>
<td>(n=18 control, 9 intervention)</td>
<td>0 (0-50)</td>
<td>0 (0-30)</td>
</tr>
<tr>
<td>Sip feed day 7</td>
<td>5 (0-44)</td>
<td>3 (0-50)</td>
</tr>
<tr>
<td>(n=20 control, 19 intervention)</td>
<td>0 (0-55)</td>
<td>0 (0-50)</td>
</tr>
<tr>
<td>Sip feed day 8</td>
<td>0 (0-50)</td>
<td>0 (0-46)</td>
</tr>
<tr>
<td>(n=20 control, 18 intervention)</td>
<td>0 (0-50)</td>
<td>0 (0-46)</td>
</tr>
<tr>
<td>Sip feed day 9</td>
<td>7.4 (0-50)</td>
<td>4 (0-46)</td>
</tr>
<tr>
<td>(n=14 control, 15 intervention)</td>
<td>0 (0-38)</td>
<td>0 (0-46)</td>
</tr>
<tr>
<td>Sip feed on discharge</td>
<td>0 (0-38)</td>
<td>0 (0-46)</td>
</tr>
<tr>
<td>(n=21 control, 19 intervention)</td>
<td>22 (0-90)</td>
<td>17 (0-92)</td>
</tr>
<tr>
<td>Food day 7</td>
<td>34 (0-88)</td>
<td>40 (0-92)</td>
</tr>
<tr>
<td>(n=20 control, 19 intervention)</td>
<td>43 (0-87)</td>
<td>36 (0-93)</td>
</tr>
<tr>
<td>Food day 8</td>
<td>40 (0-75)</td>
<td>46 (0-95)</td>
</tr>
<tr>
<td>(n=14 control, 15 intervention)</td>
<td>57 (0-110)</td>
<td>60 (3-105)</td>
</tr>
</tbody>
</table>

Results are median (range)
Table A11. Median percentage energy and protein contribution from feeding sources in oesophageal carcinoma

<table>
<thead>
<tr>
<th></th>
<th>Control group (n=23)</th>
<th>Intervention group(n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Energy and protein requirements (Kcal/d and g/d)</strong></td>
<td><strong>Energy</strong></td>
<td><strong>Protein</strong></td>
</tr>
<tr>
<td>PN day 2 (n=5 control, 2 intervention)</td>
<td>1840 (1205-2480)</td>
<td>77 (56-105)</td>
</tr>
<tr>
<td>PN day 7 (n=5 control, 2 intervention)</td>
<td>0 (0-60)</td>
<td>0 (0-46)</td>
</tr>
<tr>
<td>PN day 8 (n=5 control, 2 intervention)</td>
<td>0 (0-106)</td>
<td>0 (0-105)</td>
</tr>
<tr>
<td>PN day 9 (n=5 control, 2 intervention)</td>
<td>0 (0-106)</td>
<td>0 (0-105)</td>
</tr>
<tr>
<td>PN day 10 (n=5 control, 2 intervention)</td>
<td>0 (0-106)</td>
<td>0 (0-105)</td>
</tr>
<tr>
<td>Jejunostomy feed day 2 (n=23 control, 19 intervention)</td>
<td>24 (0-71)</td>
<td>20 (0-53)</td>
</tr>
<tr>
<td>Jejunostomy feed day 7 (n=23 control, 19 intervention)</td>
<td>83 (0-115)</td>
<td>77 (0-115)</td>
</tr>
<tr>
<td>Jejunostomy feed day 8 (n=23 control, 19 intervention)</td>
<td>87 (0-114)</td>
<td>77 (0-115)</td>
</tr>
<tr>
<td>Jejunostomy feed day 9 (n=23 control, 19 intervention)</td>
<td>51 (0-107)</td>
<td>52 (0-98)</td>
</tr>
<tr>
<td>Jejunostomy feed day 10 (n=23 control, 19 intervention)</td>
<td>33.6 (0-107)</td>
<td>31 (0-110)</td>
</tr>
<tr>
<td>Sip feed day 7 (n=23 control, 19 intervention)</td>
<td>0 (0-22)</td>
<td>0 (0-20)</td>
</tr>
<tr>
<td>Sip feed day 8 (n=23 control, 19 intervention)</td>
<td>8 (0-31)</td>
<td>6 (0-31)</td>
</tr>
<tr>
<td>Sip feed day 9 (n=23 control, 19 intervention)</td>
<td>0 (0-44)</td>
<td>0 (0-39)</td>
</tr>
<tr>
<td>Sip feed day 10 (n=23 control, 18 intervention)</td>
<td>0 (0-33)</td>
<td>0 (0-31)</td>
</tr>
<tr>
<td>Sip feed on discharge (n=23 control, 19 intervention)</td>
<td>0 (0-32)</td>
<td>0 (0-34)</td>
</tr>
<tr>
<td>Food day 7 (n=23 control, 19 intervention)</td>
<td>0 (0-88)</td>
<td>0 (0-73)</td>
</tr>
<tr>
<td>Food day 8 (n=23 control, 19 intervention)</td>
<td>4 (0-103)</td>
<td>3 (0-150)</td>
</tr>
<tr>
<td>Food day 9 (n=23 control, 19 intervention)</td>
<td>33 (0-110)</td>
<td>32 (0-100)</td>
</tr>
<tr>
<td>Food day 10 (n=23 control, 18 intervention)</td>
<td>31 (0-101)</td>
<td>35 (0-109)</td>
</tr>
<tr>
<td>Food on discharge (n=23 control, 19 intervention)</td>
<td>55 (20-103)</td>
<td>48 (21-109)</td>
</tr>
</tbody>
</table>

Results are median (range)
Appendix 10 Energy and protein intake following total and subtotal gastrectomy

Table A12 Energy and protein intake following total and subtotal gastrectomy

<table>
<thead>
<tr>
<th>Total gastrectomy (n=19)</th>
<th>Subtotal gastrectomy (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PN day 2 (n=6)</td>
<td></td>
</tr>
<tr>
<td>Protein</td>
<td>Energy</td>
</tr>
<tr>
<td>94 (0-113)</td>
<td>50 (0-102)</td>
</tr>
<tr>
<td>PN day 7 (n=6)</td>
<td></td>
</tr>
<tr>
<td>0 (0-126)</td>
<td>0 (0-86)</td>
</tr>
<tr>
<td>PN day 8 (n=6)</td>
<td></td>
</tr>
<tr>
<td>0 (0-126)</td>
<td>0 (0-86)</td>
</tr>
<tr>
<td>PN day 9 (n=6)</td>
<td></td>
</tr>
<tr>
<td>11 (0-126)</td>
<td>0 (-86)</td>
</tr>
<tr>
<td>PN day 10 (n=5)</td>
<td></td>
</tr>
<tr>
<td>106 (0-126)</td>
<td>79 (0-86)</td>
</tr>
<tr>
<td>Jejunostomy feed day 2</td>
<td></td>
</tr>
<tr>
<td>35 (0-71)</td>
<td>35 (0-820)</td>
</tr>
<tr>
<td>Jejunostomy feed day 7</td>
<td></td>
</tr>
<tr>
<td>75 (0-115)</td>
<td>67 (0-120)</td>
</tr>
<tr>
<td>Jejunostomy feed day 8</td>
<td></td>
</tr>
<tr>
<td>51 (0-112)</td>
<td>45 (0-117)</td>
</tr>
<tr>
<td>Jejunostomy feed day 9</td>
<td></td>
</tr>
<tr>
<td>37 (0-102)</td>
<td>31 (0-92)</td>
</tr>
<tr>
<td>Jejunostomy feed day 10</td>
<td></td>
</tr>
<tr>
<td>26 (0-99)</td>
<td>20 (0-88)</td>
</tr>
<tr>
<td>Jejunostomy feed discharge</td>
<td></td>
</tr>
<tr>
<td>0 (0-59)</td>
<td>0 (0-53)</td>
</tr>
<tr>
<td>Sip feed day 7</td>
<td></td>
</tr>
<tr>
<td>0 (0-44)</td>
<td>0 (0-46)</td>
</tr>
<tr>
<td>Sip feed day 8</td>
<td></td>
</tr>
<tr>
<td>0 (0-55)</td>
<td>0 (0-35)</td>
</tr>
<tr>
<td>Sip feed day 9</td>
<td></td>
</tr>
<tr>
<td>0 (0-41)</td>
<td>0 (0-43)</td>
</tr>
<tr>
<td>Sip feed day 10</td>
<td></td>
</tr>
<tr>
<td>0 (0-30)</td>
<td>0 (0-20)</td>
</tr>
<tr>
<td>Sip feed discharge</td>
<td></td>
</tr>
<tr>
<td>0 (0-38)</td>
<td>0 (0-46)</td>
</tr>
<tr>
<td>Food day 7</td>
<td></td>
</tr>
<tr>
<td>23 (0-90)</td>
<td>14 (0-92)</td>
</tr>
<tr>
<td>Food day 8</td>
<td></td>
</tr>
<tr>
<td>40 (0-93)</td>
<td>35 (0-104)</td>
</tr>
<tr>
<td>Food day 9</td>
<td></td>
</tr>
<tr>
<td>46 (0-118)</td>
<td>31 (0-130)</td>
</tr>
<tr>
<td>Food day 10</td>
<td></td>
</tr>
<tr>
<td>35 (0-78)</td>
<td>40 (0-96)</td>
</tr>
<tr>
<td>Food discharge</td>
<td></td>
</tr>
<tr>
<td>59 (3-116)</td>
<td>53 (3-119)</td>
</tr>
</tbody>
</table>

Results are median percentage requirements achieved (range)
Appendix 11 Details of all oesophageal carcinoma patients including operative deaths (study 2)

Table A13 Details of all oesophageal carcinoma patients including operative deaths (study 2)

<table>
<thead>
<tr>
<th>Enteral feeding group (n=32)</th>
<th>Male:Female</th>
<th>Age (years)</th>
<th>Operation type:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>22:10</td>
<td>70(40-84)</td>
<td>Transhiatal oesophagogastrectomy: 0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IvorLewis oesophagogastrectomy: 0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mc Ewans oesophagogastrectomy: 0</td>
</tr>
<tr>
<td>Potentially Curative Resection</td>
<td>14</td>
<td></td>
<td>I: 4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>III: 22</td>
</tr>
<tr>
<td>Operative mortality</td>
<td>6</td>
<td>Respiratory failure: 3</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oesophagobronchial fistula: 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Septicaemia: 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Multiple organ failure: 1</td>
<td></td>
</tr>
</tbody>
</table>

Details are numbers of patients. Age is expressed as median (range).
Table A14 Preoperative nutritional status in oesophageal carcinoma patients including operative deaths: serum biochemistry and anthropometry (study 2)

<table>
<thead>
<tr>
<th></th>
<th>Fortified food group (n=20)</th>
<th>Enteral feeding group (n=32)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body weight (kgs)</strong></td>
<td>73</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td>(44-103)</td>
<td>(43-122)</td>
</tr>
<tr>
<td><strong>Body Mass Index (kg/m²)</strong></td>
<td>24.3</td>
<td>24.0</td>
</tr>
<tr>
<td></td>
<td>(18-30.5)</td>
<td>(15.5-52.7)</td>
</tr>
<tr>
<td><strong>Preoperative weight loss (%)</strong></td>
<td>4.2</td>
<td>5.0</td>
</tr>
<tr>
<td></td>
<td>(0-20)</td>
<td>(0-20)</td>
</tr>
<tr>
<td><strong>Albumin (g/l)</strong></td>
<td>41.5</td>
<td>41</td>
</tr>
<tr>
<td></td>
<td>(36-46)</td>
<td>(32-50)</td>
</tr>
<tr>
<td><strong>CRP (mg/l)</strong></td>
<td>&lt;10</td>
<td>&lt;10</td>
</tr>
<tr>
<td></td>
<td>(&lt;10-33.4)</td>
<td>(&lt;10-66)</td>
</tr>
<tr>
<td><strong>Lymphocyte count (x10⁹/l)</strong></td>
<td>1.5</td>
<td>1.7</td>
</tr>
<tr>
<td></td>
<td>(0.7-3.8)</td>
<td>(0.8-4.1)</td>
</tr>
</tbody>
</table>

Results are median (range)
Appendix 12 Median percentage energy and protein contribution from feeding sources in oesophageal carcinoma patients (study 2)

Table A15. Median percentage energy and protein contribution from feeding sources in oesophageal carcinoma (study 2)

<table>
<thead>
<tr>
<th></th>
<th>Fortified food group (n=19)</th>
<th>Enteral feeding group (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Energy</td>
<td>Protein</td>
</tr>
<tr>
<td>Energy and protein requirements (kcal/d and g/d)</td>
<td>1938 (1381-2344)</td>
<td>80 (47-109)</td>
</tr>
<tr>
<td>PN day 7</td>
<td>62 (0-123)</td>
<td>47 (0-94)</td>
</tr>
<tr>
<td>(n=2 fortified food)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PN day 8</td>
<td>52 (0-103)</td>
<td>45 (0-89)</td>
</tr>
<tr>
<td>(n= 2 fortified food)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PN day 9</td>
<td>24 (0-47)</td>
<td>26 (11-40)</td>
</tr>
<tr>
<td>(n= 2 fortified food)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PN day 10</td>
<td>44 (0-88)</td>
<td>33 (0-66)</td>
</tr>
<tr>
<td>(n= 2 fortified food)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jejunostomy feed day 7</td>
<td>103 (0-109)</td>
<td>94 (0-153)</td>
</tr>
<tr>
<td>Jejunostomy feed day 8</td>
<td>79 (0-108)</td>
<td>78 (0-147)</td>
</tr>
<tr>
<td>Jejunostomy feed day 9</td>
<td>47 (0-107)</td>
<td>48 (0-109)</td>
</tr>
<tr>
<td>Jejunostomy feed day 10</td>
<td>51 (0-109)</td>
<td>52 (0-153)</td>
</tr>
<tr>
<td>Jejunostomy feed discharge</td>
<td>0* (0-33)</td>
<td>0* (0-37)</td>
</tr>
<tr>
<td>Sip feed day 7</td>
<td>0 (0-31)</td>
<td>0 (0-34)</td>
</tr>
<tr>
<td>Sip feed day 8</td>
<td>0 (0-28)</td>
<td>0 (0-28)</td>
</tr>
<tr>
<td>Sip feed day 9</td>
<td>0 (0-28)</td>
<td>0 (0-28)</td>
</tr>
<tr>
<td>Sip feed day 10</td>
<td>4 (0-38)</td>
<td>3.6 (0-28)</td>
</tr>
<tr>
<td>Sip feed on discharge</td>
<td>9 (0-28)</td>
<td>9 (0-28)</td>
</tr>
<tr>
<td>Food day 7</td>
<td>0** (0-49)</td>
<td>0** (0-66)</td>
</tr>
<tr>
<td>Food day 8</td>
<td>12** (0-90)</td>
<td>8** (0-76)</td>
</tr>
<tr>
<td>Food day 9</td>
<td>28 (0-88)</td>
<td>28 (0-73)</td>
</tr>
<tr>
<td>Food day 10</td>
<td>26** (0-90)</td>
<td>20** (0-89)</td>
</tr>
<tr>
<td>Food on discharge</td>
<td>50 (27-82)</td>
<td>49 (21-110)</td>
</tr>
</tbody>
</table>

Results are median (range)

*p=0.0001 **p<0.03 (Mann Whitney U test)