Health care resources consumed to treat postoperative infections: cost saving by perioperative immunonutrition
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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The use of peri-operative enteral immunonutrition in patients with gastrointestinal cancer, who were candidates for elective major surgery.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with gastrointestinal cancer who were candidates for elective major surgery. No selection criteria were given. The authors stated that the details were reported in another paper.

Setting
The setting was secondary care. The study was carried out in Milan, Italy.

Dates to which data relate
The dates for effectiveness evidence, resources used and prices used were not reported.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample as that used in the effectiveness study.

Study sample
No power calculations were reported. Consecutive patients with cancer undergoing major surgery were randomised before the operation and instructed to consume either peri-operative immunonutrition (n=102) or standard nutritional support (n=104). The authors did not report any evidence to suggest that the initial study sample was appropriate for the clinical study question. There were no details provided on the persons whom were invited, but refused to participate. Not all patients completed the pre-operative protocol of 1 L per day for 7 days, and the post-operative infusion of at least 7 L in the first week. These patients (12 and 8 in the intervention and control groups, respectively) were excluded from the 'core analysis' but were included in the intention to treat analysis.
Study design
This study was a single-centre, prospective, double-blind RCT. Patients were followed-up for the duration of the in-hospital stay, which was unclear. A blinded, independently-trained abstractor extracted the information on resource use associated with post-operative complications. The authors did not report the method of randomisation used or how the treatment allocation was concealed.

Analysis of effectiveness
This study reported two methods of analysis: core analysis, which was for treatment completers only, and intention to treat analysis. The groups were reported to be comparable in terms of the baseline patient characteristics of age, gender, Karnofsky index, weight loss, cancer site and duration of surgery. No adjustments were made for confounding factors. The primary health outcomes were the number of each type of complication, and the percentage of complication-free patients.

Effectiveness results
The intention to treat analysis showed a total of 52 complications in 21.8% (45 out of 206) of the total number of patients; there were 18 and 34 complications in the intervention and control groups, respectively. These comprised:

- anastomic leak, 5 intervention and 10 control;
- pneumonia, 4 intervention and 10 control;
- wound infection, 4 intervention and 6 control;
- urinary tract infection, 2 intervention and 3 control;
- sepsis, 1 intervention and 2 control;
- abscess, 1 intervention and 2 control;
- peritonitis, 1 in each of the intervention and control groups.

The core analysis showed a total of 46 complications; there were 14 and 32 complications in the intervention and control groups, respectively. These comprised:

- anastomic leak, 5 intervention and 10 control;
- pneumonia, 4 intervention and 9 control;
- wound infection, 3 intervention and 6 control;
- urinary tract infection, 2 intervention and 3 control;
- sepsis, 0 intervention and 2 control;
- abscess, 0 intervention and 2 control.

Both the intention to treat and the core analyses suggested that the treatment group was more effective than the control group, in terms of the number of complication-free patients: 83.3 versus 68.3% (p=0.009) and 84.4 versus 67.7% (p=0.006) for intention to treat analysis and core analysis, respectively.

Clinical conclusions
The authors concluded that peri-operative immunonutrition was more effective than the standard enteral diet in terms of reducing the number of patients with complications following major surgery for cancer.
Measure of benefits used in the economic analysis
The outcome measure used in the economic analysis was the number of complication-free patients.

Direct costs
The analysis included in-hospital-related costs and the costs of complications. The in-hospital-related costs covered board and lodgings, routine nurse and physician care, pre- and post-operative pharmacological treatment, materials used during surgery, the operating room, pre- and post-laboratory tests, diagnostic radiological procedures, and ambulatory follow-up. The costs of complications covered the medical costs associated with treating post-operative complications during the hospital stay and ambulatory visits. The cost of clinical nutrition was calculated separately for the pre- and post-operative phase. The mean intake per patient was multiplied by the price per litre, which was taken from the price of diets based on the Italian market.

The costs were not discounting due to the short timeframe of the study, i.e. less than one year. The unit prices for diagnostic and therapeutic services, drugs and devices were taken from the National List of Sanitary Costs produced by the Italian Ministry of Health. The number and average cost of each type of complication was recorded prospectively and reported separately. The dates relating to when the resources were measured, and the price year, were not reported.

Statistical analysis of costs
The costs were classed as stochastic data; since the data were skewed, 30,000 resamples were analysed using a non-parametric bootstrapping method. The clinical data were not tested statistically since they were classed as non-stochastic data.

Indirect Costs
No indirect costs were included in this analysis as they were not appropriate for the chosen study perspective.

Currency
All costs were reported in euros. The exchange rate at the time (unspecified date) was $1=0.95 euros.

Sensitivity analysis
The authors did not report explicitly that they conducted a sensitivity analysis, although they did report the effect on the cost-effectiveness analysis of removing one type of complication, i.e. anastomotic leak.

Estimated benefits used in the economic analysis
See the effectiveness results reported previously.

Cost results
The costs reported for the intention to treat analysis were:

- nutrition costs per patient, 347 euros for the treatment group and 103 euros for the control group;
- complication costs per patient, 768 euros for the treatment group and 2,345 euros for the control group;
- total costs per patient, 1,115 euros for the treatment group and 2,447 euros for the control group (p=0.038);
- total cost, 113,778 euros for the treatment group and 254,450 euros for the control group.

The costs reported for the core analysis were:
nutrition costs per patient, 391 euros for the treatment group and 115 euros for the control group;

complication costs per patient, 465 euros for the treatment group and 2,408 euros for the control group;

total costs per patient, 856 euros for the treatment group and 2,523 euros for the control group (p=0.027);

total cost, 76,988 euros for the treatment group and 242,248 euros for the control group.

### Synthesis of costs and benefits

The treatment group was less expensive and more effective than the control group: the total costs (nutrition and complications) were 113,778 and 254,450 euros for the treatment and control groups, respectively, and the proportions of complication-free patients were 83.3 and 68.3%. No incremental analysis was therefore considered necessary. The authors reported average cost-effectiveness ratios, but these were not informative about the outcomes of interest in an economic evaluation, namely the additional (incremental) costs and additional (incremental) benefits.

### Authors' conclusions

The authors concluded that the peri-operative use of immunonutrition appears to be cost-effective due to a substantial saving in the resources used to treat post-operative complications.

### CRD COMMENTARY - Selection of comparators

This study detailed clearly the cost implications of using peri-operative immunonutrition, rather than standard enteral nutrition, from the perspective of an Italian hospital. However, due to the lack of published supporting evidence, it was unclear if the comparator selected was relevant for this economic analysis.

Validity of estimate of effectiveness:

There was insufficient information to assess whether the study sample was representative of the study population. The statistical analysis was of differences in the number of complications between groups, rather than differences in the number of patients with no complications, i.e. the stated measure of effectiveness. This would not be adequate if the average number of complications per patient experiencing complications was one. The authors did not provide any information to support the equal weight given to each of the complications observed in the trial. This indicated an implicit assumption that the complications were of equal severity and had an equivalent impact on patients’ health status or health-related quality of life. This assumption was not supported by the authors' statement that, of the 52 reported complications reported, 40% were defined as major.

Validity of estimate of costs

The generalisability would have been enhanced had the authors given the price year and reported a breakdown of the costs of each complication, in terms of the products of the resource quantities and unit costs. The study perspective was stated clearly but the authors did not report the timeframe of the study. No sensitivity analysis was conducted, which would have indicated how robust the study's findings were to changes in cost and outcome parameters. Although the results indicated that the immunonutrition strategy was dominant, the study reported average cost-effectiveness ratios, which are not meaningful in this context. It would have been more accurate to report that the immunonutrition strategy was more effective and less costly than standard enteral nutrition, rather than saying it was more cost-effective.

Other issues

The results were compared with those of other studies in terms of, for example, the large variability of cost by complication and the effectiveness of enteral immunonutrition. The results do not seem to have been presented selectively.

The authors noted a number of factors that may limit the generalisability of the results to alternative settings or populations. These factors included:
differences in patients' characteristics and severity of illness between trials and routine practice, and between settings in routine practice;

differences in adherence to nutrition therapy by patients and physicians in trials and routine practice, and between alternative settings in routine practice;

differences in practice patterns between settings, which would affect the availability and use of services, the relative unit costs of services, and the total costs and effectiveness of interventions.

You, as a user of this database, should decide if one or more of these factors limit the generalisability of the study's findings to your setting.

Implications of the study
The authors suggested that immunonutrition is more effective and less costly than standard enteral nutrition. However, they caution that in view of the limited clinical data currently available, and the fact their study was among the first economic analyses of peri-operative immunonutrition, the results do not allow any firm conclusions to be drawn. They do, however, report that the significant difference in costs between the two regimens suggest that the positive results for peri-operative immunonutrition may be partially generalised to other hospitals, communities, countries and health care systems.

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