

# Costs, quality of life and cost-effectiveness of nutrition in gastrointestinal surgery

Citation for published version (APA):

Pattamatta, M. (2021). *Costs, quality of life and cost-effectiveness of nutrition in gastrointestinal surgery*. [Doctoral Thesis, Maastricht University]. Gildeprint Drukkerijen. <https://doi.org/10.26481/dis.20210125mp>

## Document status and date:

Published: 01/01/2021

## DOI:

[10.26481/dis.20210125mp](https://doi.org/10.26481/dis.20210125mp)

## Document Version:

Publisher's PDF, also known as Version of record

## Please check the document version of this publication:

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**SUMMARY**

Colorectal (CRC) and esophageal (EC) cancers are the most prominent and deadly cancers with high morbidity, mortality rates and increased healthcare expenditure. Postoperative complications such as postoperative ileus (POI) and anastomotic leakage (AL) are inevitable and they further reduce the functional capacity and quality of life in these patients.

The escalating clinical and economic burden of CRC and EC coupled with high costs of its management on one hand and limited health resources on the other hand, provide the rationale for fostering the search for cost-effective interventions for managing CRC and EC. Three randomized controlled trials were recently conducted with nutritional interventions such as gum chewing and perioperative enteral nutrition in CRC and early oral feeding in EC. In this dissertation, we provided an overview of cost-effectiveness of these interventions. In addition, the financial burden of CRC and EC, its complications and the quality of life was investigated.

Part I of this dissertation presented two studies conducted to assess the costs and quality of life of CRC and burden of its complications. In **chapter 2**, we explored the societal cost of illness of CRC and its drivers in the Netherlands. Our estimates revealed a 3-month societal cost of €3,211 with 45.5% of this cost attributable to productivity costs highlighting the high financial burden of CRC on Netherlands society and healthcare system. In **chapter 3**, we explored the clinical and economic burden of postoperative ileus using the data from SANICS II trial. It was observed that patients with POI had increased inflammatory parameters, higher costs, lowered functioning, reduced quality of life and utility. When we compared utilities between patients who had only POI with patients without any complications, the effect was much more remarkable. Consequently, it was demonstrated that there is an association between inflammatory markers in blood and postoperative complications and that inflammation is elevated after manipulation of intestine.

Part II of this thesis informed specifically the cost-effectiveness of interventions tested in the new trials (SANICS I, SANICS II and NUTRIENT II). In **chapter 4**, we performed an economic evaluation alongside SANICS I trial and explored whether gum chewing could be a cost-effective intervention and determined its effect on hospital costs and health-related quality of life. Patients in the intervention group were asked to chew gum at least three hours prior to surgery and again three hours after the end of surgery. Patients in control group received placebo dermal patch three hours prior to surgery. Mean costs for ward stay were significantly lower in the gum chewing group however no significant differences were seen in the overall in-hospital costs or utilities. Cost-effectiveness analysis for two postoperative complications POI and AL was determined. Gum chewing was seen to be dominant with lesser costs and more effects in more than 50% of the simulations for both POI and AL.

An economic evaluation was then performed alongside SANICS II trial from a societal perspective as seen in **chapter 5** of this thesis. SANICS II was a multicentre randomized controlled trial conducted in three Dutch and two Danish hospitals. Lipid enriched nutrition was administered just before, during and after the colorectal resection to patients in intervention group and compared to patients in standard care or no nutrition group. Societal costs, quality of life scores and utilities between the two groups did not differ significantly. Cost-effectiveness analysis for global quality of life was determined and it was observed that intervention resulted in an additional cost of €2,699 and a lower quality of life. We also observed that the intervention resulted in an additional cost of €2,941 for a marginal increase in QALY (0.003) suggesting that the intervention was not cost-effective compared to usual care. In **chapter 6**, we assessed the effect of direct oral feeding following minimally invasive esophagectomy on treatment costs and health-related quality of life. This study was performed for the NUTRIENT II trial population. NUTRIENT II was a multicenter prospective randomized controlled trial performed at two hospital units in the Netherlands and one hospital in Sweden. The trial studied effect of early oral feeding in comparison with standard of care (tube feeding) on functional recovery following esophagectomy. We observed that direct oral feeding resulted in similar costs (€26,014 versus €26,989,  $p=0.825$ ) but significantly reduced the need for home care assistance (48.9%) in comparison with the standard of care group (77.1%),  $p=0.004$ . We also observed that patients in the direct oral feeding progressed more quickly/steadily to recovery.

In conclusion, the findings of this dissertation present high quality evidence on economic implications of nutritional interventions in CRC and EC and further provide insights for public health policy makers about the debilitating financial burden of CRC and EC in the Netherlands.