Supplementary Document

Supplementary Table 1: Search Strategy

- "Preoperative Period",
- "Preoperative Care"
- "Preoperative"
- "preop"
- "perioperative"

Combined with

- "immunonutrition"
- "pharmacononutrition"
- "immune nutrients"
- "immune modulating nutrients"
- "dietary supplements"
- "oral supplement"
- "enteral nutrition"
- "nutritional support"
- "arginine"
- "omega-3 fatty acid"
- "glutamine"
- "enteric feeding"
- "diet therapy"
- "Nutrition(al) feed(s)"
- "Nutrition Disorders",
- "Nutrition Surveys",
- "Home/ or nutrition",
- "Total/Nutrition Therapy"

combined with

- "gastrointestinal surgery",
- "surgeries"
- "post-operative outcomes".

Detailed search strategy available on request

Supplementary Table 2: Excluded studies

| Study & Year | Cancer | IMN | Control | Reason for exclusion | Notes |
|---|---|---|---|--|--|
| Wachtler <i>et al.</i> 1995 ¹ | Upper GI surgery for cancer | Impact, Sandoz- Nutrition, Bern, Switzerland | Isocaloric isonitrogenous supplements | Pre-2000 so not recent enough. | |
| McCarter <i>et al.</i> 1998 ² | Upper Gastrointestinal cancer | Arginine alone Arginine combined with ω-3 fatty acids | Isocaloric isonitrogenous supplements | Pre-2000 so not recent enough. | |
| Hubner <i>et al.</i> 2012 ³ | Major abdominal surgery – benign and cancer | Impact, Novartis/ Nestlé Nutrition, Vevey, Switzerland | Isocaloric isonitrogenous supplements | Mixed population of cancer and benign patients. No availability to data on cancer patients alone. | Contact to obtain data on cancer patients alone failed. |
| Barker <i>et al.</i> 2013 ⁴ | Mixed upper and lower GI surgery (not only cancer) | Impact Advanced recovery (Nestle Medical Nutrition, MN, USA) | No supplements | Mixed population of cancer and benign patients. No availability to data on cancer patients alone. | Contact to obtain data on cancer patients alone failed. |
| Martin <i>et al.</i> 2017 ⁵ | Pancreatic cancer (electroporation of unresectable tumours) | Impact | No supplements | Pseudo-randomization, based on affordability and availability of supplement. | |
| Ashida <i>et al.</i> 2018 ⁶ | Pancreatic cancer - pancreaticoduodenectomy | Oral supplement containing eicosapentaenoic acid | Isocaloric isonitrogenous supplements | IMN product only contained a single component of immunonutrient and not a combination. So not comparable with the other studies. | |

References

- 1. Wachtler P, Axel Hilger R, Konig W, Bauer KH, Kemen M, Koller M. Influence of a pre-operative enteral supplement on functional activities of peripheral leukocytes from patients with major surgery. *Clin Nutr.* 1995; 14: 275-282.
- McCarter MD, Gentilini OD, Gomez ME, Daly JM. Preoperative oral supplement with immunonutrients in cancer patients. *JPEN J Parenter Enteral Nutr.* 1998; 22: 206-211.
- Hubner M, Cerantola Y, Grass F, Bertrand PC, Schafer M, Demartines N.
 Preoperative immunonutrition in patients at nutritional risk: results of a doubleblinded randomized clinical trial. *Eur J Clin Nutr.* 2012; 66: 850-855.
- Barker LA, Gray C, Wilson L, Thomson BN, Shedda S, Crowe TC. Preoperative immunonutrition and its effect on postoperative outcomes in well-nourished and malnourished gastrointestinal surgery patients: a randomised controlled trial. *Eur J Clin Nutr.* 2013; 67: 802-807.
- Martin RC, 2nd, Agle S, Schlegel M, et al. Efficacy of preoperative immunonutrition in locally advanced pancreatic cancer undergoing irreversible electroporation (IRE). *Eur J Surg Oncol.* 2017; 43: 772-779.
- 6. Ashida R, Okamura Y, Wakabayashi-Nakao K, Mizuno T, Aoki S, Uesaka K. The impact of preoperative enteral nutrition enriched with eicosapentaenoic acid on postoperative hypercytokinemia after pancreatoduodenectomy: the results of a double-blinded randomized controlled trial. *Dig Surg.* 2018 [Epub ahead of print].

Supplementary Table 3: The composition of IMPACT (Nestlé Health Science)

Oral Impact[®] is powder nutrients for oral feeding that provides 1.0 kcal/ml when reconstituted with water. And contains the following additional nutrients - ω -3 fatty acids, arginine, nucleotides and soluble fibre. For use under medical supervision. (Downloaded

from https://www.nestlehealthscience.co.uk/brands/impact/impact).

| Typical values | Per 100g | Per 74g (Tropical flavour*) | | | | |
|--------------------------------|----------|-----------------------------------|--|--|--|--|
| General | | | | | | |
| Energy kJ/kcal | 1763/418 | 1304/309 | | | | |
| Fat (22% kcal) g | 10 | 7 | | | | |
| of which saturates g | 5.1 | 4 | | | | |
| of which monounsaturates g | 2.1 | 1.5 | | | | |
| of which polyunsaturates g | 3.2 | 2.37 | | | | |
| Carbohydrate (54% kcal) g | 56 | 41.4 | | | | |
| of which sugars g | 30 | 22 | | | | |
| of which lactose g | 1.2 | 0.89 | | | | |
| Fibre (2% kcal) g | 4.1 | 3 | | | | |
| Protein (23% kcal) g | 24 | 18 | | | | |
| Salt (= Na(g) x 2.5) g | 1.1 | 0.8 | | | | |
| Vitamins | | | | | | |
| А µg | 520 | 385 | | | | |
| Dµg | 4.2 | 3.1 | | | | |
| Кµд | 27 | 20 | | | | |
| Cmg | 105 | 78 | | | | |
| B1 (Thiamin) mg | 0.49 | 0.36 | | | | |
| B2 (Riboflavin) mg | 0.8 | 0.59 | | | | |
| B6 mg | 0.7 | 0.52 | | | | |
| Niacin mg/mg NE | 1.7/6.5 | 1.3/4.8 | | | | |
| Folic acid µg | 140 | 104 | | | | |
| B12 µg | 2.5 | 1.8 | | | | |
| Pantothenic acid mg | 4 | 3 | | | | |
| Biotin µg | 20 | 15 | | | | |
| Emg a-TE | 12 | 8.9 | | | | |
| Minerals | | | | | | |
| Sodium mg/mmol | 434/19 | 321/14 | | | | |
| Chloride mg/mmol | 608/17 | 450/13 | | | | |
| Potassium mg/mmol | 543/14 | 402/10 | | | | |
| Calcium mg/mmol | 324/8.1 | 240/6.0 | | | | |
| Phosphorus mg/mmol | 292/9.4 | 216/7.0 | | | | |
| Magnesium mg/mmol | 70/2.9 | 52/2.2 | | | | |
| Iron mg | 4.9 | 3.6 | | | | |
| Zinc mg | 5 | 3.7 | | | | |
| Copper mg | 0.69 | 0.51 | | | | |
| lodine µg | 61 | 45 | | | | |
| Selenium µg | 25 | 18 | | | | |
| Manganese µg | 810 | 599 | | | | |
| Chromium µg | 41 | 30 | | | | |
| Molybdenum µg | 50 | 37 | | | | |
| Fluoride µg | 540 | 400 | | | | |
| Other nutrients | | | | | | |
| Choline mg | 165 | 122 | | | | |
| L-arginine g | 5.1 | 3.8 | | | | |
| Omega-3 g | 1.3 | 0.96 | | | | |
| MCT g | 3 | 2.2 | | | | |
| Nucleotides g | 0.6 | 0.4 | | | | |
| Osmolarity mOsm/l | 520 | | | | | |
| Osmolality mOsm/kg H2O | 620 | | | | | |
| Water content per 100ml: 2.4g | | | | | | |
| * See individual packs for oth | | | | | | |

* See individual packs for other flavours

Supplementary Figure 1: Funnel plot for infectious complications. The points correspond to the treatment effects (log weighted OR) from 14 individual studies, and the diagonal lines show the expected 95% confidence intervals around the pooled fixed effect log OR estimate.

