APPENDIX 1 – TARGETED LITERATURE REVIEW DATA SOURCES AND DATA COLLECTION PROCESS

Data sources

The databases searched were MEDLINE Daily, In-Process & Other Non-indexed citations, and e-pub ahead-of-print. Searches were conducted on 30\(^{th}\) October 2018 (TLR1) and 19\(^{th}\) February 2019 (TLR2) and spanned the period from the inception of the database to the day prior to the day of search. For TLR1 a date restriction was added to identify only studies published from 1990 onwards, as the premixed multichamber bag PN (introduced in the mid-1990s) is associated with safety improvements (e.g., reduction in rate of bloodstream infections and medication errors).

Search strategies are provided in the appendix.

Data collection process

Citations identified by the searches were assessed by a single reviewer based on title and abstract using the PICOs criteria, followed by second reviewer consultation for resolution of any queries/uncertainties around abstract screening. Full publications of potentially relevant citations were obtained and examined by a single reviewer. Final inclusion and exclusion of citations were verified by a second reviewer. Disputes regarding eligibility were resolved via discussions with third parties. All studies excluded based on the review of the full text were documented by an exclusion category, along with the reason for exclusion.

Data from the relevant publications were extracted by one reviewer and the information was checked and validated by a second reviewer.
# APPENDIX 2 – TARGETED LITERATURE REVIEW ELIGIBILITY CRITERIA

## Table 1: Eligibility criteria

| Criteria          | TLR 1 inclusion criteria                                                                 | TLR 2 inclusion criteria                                                                 |
|-------------------|------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|
| **Population**    | Oncology patients (with no restriction on cancer type) who are malnourished or at-risk of being malnourished. [patients receiving surgical treatment or where PN is strictly indicated are excluded] | Oncology patients (with no restriction on cancer type) who are malnourished or at-risk of malnutrition. [patients receiving surgical treatment or where PN is strictly indicated are excluded] |
| **Intervention and comparators** | SPN (not strictly indicated)                                                              | Impact of SPN on malnutrition marker studies:  
  - PN (not strictly indicated) either alone or as SPN  
  Association between malnutrition markers and clinical outcome studies:  
    - No restriction |
| **Outcomes**      | Clinical:  
  - OS  
  - PFS  
  - TTP  
  - Duration of chemotherapy  
  - Number of chemotherapy cycles  
  - Chemotherapy dose-limiting toxicity adjustments  
  Economic evaluation:  
    - Incremental cost effectiveness ratios  
    - Summary health outcomes (e.g. QALYs, LYG)  
    - Model summary (including perspective, time horizon and discounting) and structure  
    - Assumptions underpinning model structures  
    - Sources of clinical, cost and quality of life inputs  
  Cost/resource use:  
    - Direct medical costs  
    - Direct non-medical costs  
      - Transportation  
      - Childcare costs  
      - Additional caregiver costs  
    - Indirect/societal costs  
      - Productivity losses  
      - Absenteeism  
      - Presenteeism  
    - Withdrawal from labour force  
    - Caregiver burden  
    - Estimates of resource use  
    - Cost drivers including hospitalisation and length of stay  
    - Assumptions underpinning resource use  
    - Methods of valuation  
  HRQoL:  
  Outcomes including, but not limited to:  
  Malnutrition markers  
    - PhA assessed using BIA  
    - CRP, PAB, albumin, serum albumin, ghrelin, leptin, transferrin, insulin like growth factor, retinol-binding protein  
    - Muscle mass, muscle waste, BMI, body composition, handgrip strength, body cell mass, energy deficit, metabolic stress, PG-SGA, SGA, MNI  
  Clinical outcomes  
    - Mortality  
    - Overall survival  
    - HRQoL  
    - Progression free survival  
    - Time to progression  
    - Duration or completion of chemotherapy  
    - Number of chemotherapy cycles  
    - Chemotherapy dose-limiting toxicity adjustments  
    - Catabolic alterations in cancer patients  
    - Inadequate nutritional intake (caloric deficits)  
    - Muscle protein depletion (muscle mass, absolute muscularity and other body parts)  
    - Systemic inflammation  
    - Impairment of immune function  
    - Complications (e.g. infectious [pneumonia] and non-infectious)  
    - Depression, fatigue and malaise |
| Criteria        | TLR 1 inclusion criteria                                                                                                                                                                                                 | TLR 2 inclusion criteria |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|
|                 | • Utilities derived using generic preference-based instruments for relevant health states<br>• Direct utility estimates (e.g. standard gamble, time trade off, rating scales)<br>• Mapping studies, from disease-specific to generic preference-based measures or between different generic preference-based measures<br>• Disease-specific or generic non-preference based QoL questionnaires<br>• Descriptive summary of health states, and/or change in health status/QoL results |                                                                       |
| Study design/setting | Clinical:<br>• RCTs, with no restriction on phase or study design<br>• Observational studies, to include prospective cohort studies, case-control studies |                                                                       |
| Economic evaluations | N/A<br>• Cost-effectiveness analysis<br>• Cost-utility analysis<br>• Cost-minimisation analysis<br>• Cost-consequence analysis<br>• Cost-benefit analysis<br>• Cost offset analysis |                                                                       |
| Cost/resource use: | N/A<br>• Any studies reporting original cost and/or resource use data |                                                                       |
| HRQoL: | N/A<br>• Any studies reporting original HRQoL/HSUV data |                                                                       |
| Language of publication | English language publications (English language abstracts of foreign language publications are considered for inclusion) | N/A<br>• Any studies reporting original HRQoL/HSUV data |
APPENDIX 3 – TARGETED LITERATURE REVIEW 1 SEARCH STRATEGY

Platform: Ovid

Database: MEDLINE Daily, In-Process & Other Non-indexed citations, and e-pub ahead-of-print

Date searched: 30/10/2018

Hits: 3,463

Table 2: Medline search string – 1946 to October 29, 2018 (accessed 30th October 2018)

| # | Searches                                                                 | Results   |
|---|--------------------------------------------------------------------------|-----------|
| 1 | exp Neoplasms/                                                           | 3096999   |
| 2 | (oncolog* or neoplas* or cancer* or tumo?r* or carcino* or malignan*).mp. | 3852454   |
| 3 | exp cachexia/                                                            | 4999      |
| 4 | (cachexia or cachetic).ti,ab.                                           | 7517      |
| 5 | or/1-4                                                                  | 4175667   |
| 6 | exp Parenteral Nutrition/                                                | 23121     |
| 7 | ((parenteral or artificial or intravenous) adj2 (nutrition or feeding)).mp. | 32729     |
| 8 | (PN or TPN or SPN or HPN).ti,ab.                                        | 21976     |
| 9 | 6 and 8                                                                 | 5104      |
| 10| exp Enteral Nutrition/                                                  | 18433     |
| 11| ((enteral or enteric) adj2 (nutrition or feeding)).mp.                  | 23870     |
| 12| (feeding tube or percutaneous endoscopic gastrostomy line).ti,ab.       | 2592      |
| 13| EN.ti,ab.                                                               | 59955     |
| 14| 10 and 13                                                               | 877       |
| 15| 5 or 7 or 9 or 10 or 11 or 12 or 14                                     | 51005     |
| 16| 5 and 15                                                                | 7160      |
| 17| exp "costs and cost analysis/")                                         | 219358    |
| 18| costs.tw.                                                               | 186429    |
| 19| cost effective;.tw.                                                     | 117062    |
| 20| cost;.mp.                                                               | 622411    |
| 21| cost benefit analys;.mp.                                               | 76504     |
| 22| health care costs.mp.                                                   | 44397     |
| 23| or/17-22                                                               | 632805    |
| 24| 16 and 23                                                               | 363       |
| 25| randomized controlled trial.mp.                                         | 492497    |
| 26| randomized.mp.                                                          | 761228    |
| 27| placebo.mp.                                                            | 199370    |
| 28| or/25-27                                                               | 820763    |
| 29| 16 and 28                                                               | 963       |
| 30| exp "Quality of Life"/                                                  | 168084    |
| 31| exp "Surveys and Questionnaires"/                                       | 923078    |
| 32| exp Health Status/                                                      | 296032    |
| 33| exp Health Status Indicators/                                           | 277515    |
| 34| exp "Activities of Daily Living"/                                       | 64386     |
| 35| exp Health Surveys/                                                     | 513575    |
| 36| exp Quality-Adjusted Life Years/                                        | 10497     |
| 37| exp Treatment Outcome/                                                  | 897742    |
| 38| exp PSYCHOMETRICS/                                                      | 68847     |
| 39| (Quality of life or QOL or QoL or HRQL or HRQOL or HRQoL).ti,ab.        | 237988    |
| 40| (Quality adjusted life year or QALY).mp.                               | 9078      |
| 41| Health stat*.mp.                                                       | 146926    |
|   |   |
|---|---|
| 42 | Life quality.ti,ab. |
| 43 | (utilit* or "health utility index" or "utilities index").mp. |
| 44 | ("quality of wellbeing" or QWB or "quality of well-being" or "quality of well being").mp. |
| 45 | 16 and 45 |
| 46 | 1918 |
| 47 | Comparative studies/ |
| 48 | Follow-up studies/ |
| 49 | Time factors/ |
| 50 | chang$.tw. |
| 51 | evaluated.tw. |
| 52 | prospective$.tw. |
| 53 | retrospective$.tw. |
| 54 | baseline.tw. |
| 55 | cohort.tw. |
| 56 | case series.tw. |
| 57 | 16 and 58 |
| 58 | 3624 |
| 59 | 24 or 29 or 46 or 59 |
| 60 | 4521 |
| 61 | limit 60 to english language |
| 62 | Animal/ not Human/ |
| 63 | 3463 |
APPENDIX 4 – TARGETED LITERATURE REVIEW 2 SEARCH STRATEGY

Platform: Ovid

Database: MEDLINE Daily, In-Process & Other Non-indexed citations, and e-pub ahead-of-print

Date searched: 20/02/2019

Hits: 5,552

Table 3: Medline search string – 1946 to February 19, 2019 (accessed 20th February 2019)

| #  | Searches                                                                                          | Results   |
|----|---------------------------------------------------------------------------------------------------|-----------|
| 1  | exp Neoplasms/                                                                                    | 3134867   |
| 2  | (oncolog* or neoplas* or cancer* or tumo?r* or carcino* or malignan*).mp.                         | 3908100   |
| 3  | or/1-2                                                                                           | 4230645   |
| 4  | exp cachexia/                                                                                    | 4864      |
| 5  | (cachexia or cachectic).ti,ab.                                                                    | 7657      |
| 6  | exp Malnutrition/                                                                               | 116376    |
| 7  | exp nutritional status/                                                                          | 40366     |
| 8  | (malnutrition or maln* or undernutrition or nutrition* assessment or nutrition* status or sarcopenia).ti,ab. | 73999     |
| 9  | exp Sarcopenia/                                                                                 | 2987      |
| 10 | (Patient-Generated Subjective Global Assessment or subjective global assessment or PG SGA or PG-SGA or SGA or minimal nutrition assessment or MNI).ti,ab. | 8432      |
| 11 | or/4-10                                                                                         | 209186    |
| 12 | exp Biomarkers/                                                                                 | 681064    |
| 13 | biomarker*.ti,ab.                                                                               | 209533    |
| 14 | (h?emoglobin or albumin or C-reactive protein or CRP or ghrelin or adiponectin or leptin or insulin like growth factor or IGF-1 or transferrin or prognostic nutritional index or PNI or total protein or nitrogen balance or retinol binding protein).ti,ab. | 476049    |
| 15 | (weight loss or muscle waste or metabolic stress or body mass index or BMI or ((muscle or fat) adj2 mass)).ti,ab. | 307476    |
| 16 | inflammatory markers.ti,ab.                                                                      | 16415     |
| 17 | (energy adj2 (deficit or expenditure)).ti,ab.                                                     | 24400     |
| 18 | (bioimpedance or bioelectric* impedance).ti,ab.                                                   | 8246      |
| 19 | (reactance or resistance or phase angle).ti,ab.                                                   | 643837    |
| 20 | ((extracellular or body cell) adj2 mass).ti,ab.                                                    | 909       |
| 21 | (handgrip strength or body composition or anthropomet* markers or muscle thickness).ti,ab.        | 35529     |
| 22 | or/12-21                                                                                        | 2083055   |
| 23 | 3 and 11 and 22                                                                                 | 7611      |
| 24 | animals/ not humans/                                                                            | 4516275   |
| 25 | exp animals, laboratory/                                                                         | 832626    |
| 26 | exp animal experimentation/                                                                     | 8959      |
| 27 | exp models, animal/                                                                             | 528550    |
| 28 | exp rodentia/                                                                                    | 3089746   |
| 29 | (rat or rats or mouse or mice).ti.                                                                | 1283600   |
| 30 | or/24-29                                                                                       | 5384690   |
| 31 | 23 not 30                                                                                       | 6369      |
| 32 | limit 31 to english language                                                                    | 5787      |
| 33 | limit 32 to (address or autobiography or bibliography or biography or case reports or comment or dictionary or editorial or government document or guideline or interactive tutorial or legal case or letter or news or newspaper article) | 235       |
| 34 | 32 not 33                                                                                       | 5552      |
APPENDIX 5 – TARGETED LITERATURE REVIEW 1 FLOW OF STUDIES

In TLR1 the electronic database search identified 3,463 citations, of which one was identified as a duplicate and excluded. The remaining 3,462 citations were screened based on title and abstract, and 3,091 were then excluded, leaving 371 to be screened based on the full publications. During full text screening all these studies were subsequently excluded. Hand searching identified no additional citations that met the eligibility criteria. Therefore, no studies were identified for final inclusion. The overall flow of the studies for TLR1 is illustrated in Figure 1.

Figure 1: Flow of studies through TLR1