THE DO’S AND DON’TS OF PERFORMING A SCOPING REVIEW

ISPOR Nutrition Economics
Special Interest Group
Medical Nutrition – Terms, Definitions, Regulations & Emerging Good Practices For Economic Evaluation Working Group

Outline

- SIG Nutrition Economics – history & scope
- Medical Nutrition – first focus
- Scoping Review Methodological Overview
- Working Group Medical Nutrition Scoping Review
  - methodology
  - challenges
- Future steps
Moderator & Speaker

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Zoetermeer, The Netherlands

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What is Nutrition Economics?

- Merging of nutrition and health economics discipline
- Focus on interdependency between nutritional habits, health and public expenses
- To illustrate health and economic aspects of specific changes in the daily nutrition and nutrition recommendations through the lens of cost-effectiveness

Nutrition economics is defined as "a discipline dedicated to researching and characterizing health and economic outcomes in nutrition for the benefit of society" [1].
Many challenges in nutrition assessment
- from difficulty in establishing a correlation between a product’s consumption and future health status,
- to confounding factors
- and special methodological considerations, such as those encountered when assessing medical devices for reimbursement.

Many challenges in economic evaluations for nutrition

Goal: develop preliminary scientific guidelines for nutrition economic assessments and outcomes research.

ISPOR initiated the Nutrition Economics Special Interest Group (SIG) supported by experts in the fields of nutrition, medicine, pharmacology, epidemiology, and health economics.
Building the Foundation for Emerging Good Practices in Economic Evaluation

- Because this is a new discipline, our objective is to provide a foundation for emerging good practices in economic evaluation for nutrition

- First focus is on Medical Nutrition

Medical Nutrition

<table>
<thead>
<tr>
<th>Overall population</th>
<th>Diseased population (patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General nutrition</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Conventional food</td>
<td>Survival, energy, health, pleasure</td>
</tr>
<tr>
<td>Functional food</td>
<td>Targets specific body functions/risk factors</td>
</tr>
<tr>
<td>Infant formula/food</td>
<td>Age – specific needs</td>
</tr>
</tbody>
</table>

Enteral nutrition

Special enteral medical nutrition for all ages

Parenteral nutrition

Special parenteral (intravenously) medical nutrition for all ages

What is Medical Nutrition?

Medical nutrition comprises **parenteral nutrition** (regulated in pharmaceutical legislation), as well as all forms of **enteral nutrition** support that are regulated as "**foods for special medical purposes**" (FSMP), as defined by the European Commission Directive 1999/21/EC, independent of the route of application.

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(Medical) Nutrition/food

**Energy** (CHO, Fat), **Construction** (Protein), vit, min

(Medical) Nutrition

Novel synergistic **combinations** of nutrients

Nutrients focus on **multiple**

Physiological systems, safety has been proven

Pharma

(New) Chemical Entity

(one compound)

Focus on **single** intervention, adverse events
**EU Legislative Landscape**

- **Medicinal Products**
  - Patients
  - Under medical supervision
  - Treat, cure, prevent disease

- **Medical Devices**

- **Food Products**
  - Fortified Foods
  - Food Supplement
  - Specialized Nutritional Products
    - FSMP
    - IF
    - VLCD
      - Healthy infants

- **DRUGS**
  - Parenteral Solutions

- **Parenteral Medical nutrition**
- **Enteral Medical nutrition**

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**US Legislative Landscape**

- **FOODS**
  - Conventional Foods
  - Foods for Special Dietary Uses
  - Dietary Supplements
    - Hypoallergenic Foods
    - Diet Foods
    - Infant Formulas
    - Medical Foods
      - Exempt Infant Formulas
      - Orphan Medical Foods

- **DRUGS**
  - Parenteral Solutions

- **Parenteral Medical nutrition**
- **Enteral Medical nutrition**
Food for special medical purposes
Main 6 characteristics

1. Specially manufactured or formulated for the intended purpose.
2. Intended for the dietary management of patients.
3. To be used under medical supervision.
4. Full or partial nutrition.
5. Patients with a limited, impaired or disturbed capacity to take, digest, absorb, metabolize or excrete ordinary foodstuffs or certain nutrients contained therein or metabolites, or with other medically-determined nutrient requirements.
6. Patients whose dietary management cannot be achieved only by modification of the normal diet, by other foods for particular nutritional uses, or by a combination of the two.

Cost of illness analyses for malnutrition

<table>
<thead>
<tr>
<th>Part of world</th>
<th>Costs of malnutrition per year</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe(^1)</td>
<td>$432 billion</td>
<td>Total health and financial burden (10 diseases)</td>
</tr>
<tr>
<td>Europe(^2)</td>
<td>$170 billion</td>
<td>Total health and financial burden (overall-extrapolation of UK data)</td>
</tr>
<tr>
<td>USA(^3)</td>
<td>$157 billion</td>
<td>Public expenditure on malnutrition (6 diseases)</td>
</tr>
</tbody>
</table>

1. Inotai et al. e-SREN J2012;7:e196-e204  
2. Ljungqvist O, de Man F. Nutr Hosp 2009;24:368-70  
The DO’S and DON’TS of Performing A Scoping Review: Examples from the literature

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Syreon Research Institute
Budapest, Hungary

How do you call it?

- Most frequent terminologies in 494 scoping reviews:
  - Scoping review (73.5%)
  - Scoping study (10.5%)
  - ...
Key references of scoping reviews on methodology

- Highest cited methods papers in 494 scoping reviews:
  - Arksey et al, 2005 (55%)
  - Levac et al, 2010 (11.7%)
  - Centre for Reviews & Dissemination (3.4%)
  - Grant et al, 2009 (3.2%)

DOs and DON’Ts:
Where do the rules come from?

- First published framework in 2005 (Arksey et al.)
- Guidelines
  - Joanna Briggs Institute methodology guidance for scoping reviews
  - PRISMA extension for scoping reviews, under development
- Real-world patterns
  - “A scoping review of scoping reviews: advancing the approach and enhancing the consistency” (Pham et al, 2014)
  - patterns in 344 scoping reviews (up to 2012)
  - “A scoping review on the conduct and reporting of scoping reviews” (Tricco et al, 2016):
    - patterns in 494 scoping reviews (1999-2014)

Scoping Review Process

- Research question
- Protocol
- Search strategy
- Inclusion / exclusion criteria
- Title / abstract screening
- Quality assessment
- Data extraction
- Collating, summarizing and reporting

Identify the Research Topic: The Research Question

- JBI guidance (2015)
  - a clearly stated, broad question
  - consistent with review title
  - clearly detailed principal focus, to guide the review’s scope and breadth
  - context should be clearly defined (e.g. geographical and cultural factors, specific racial or sex-based interests, specific healthcare setting, etc).

- Real-world patterns (1999-2014)
  - Post-hoc compliance with JBI guidance in 97% of 494 scoping reviews (Tricco, 2016)

DO follow the established best practice
Protocol development

- **JBI guidance (2015)**
  - prospectively defined protocol
  - protocol amendments encouraged (iterative process), but must be documented in the ‘Methods’ section of the scoping review report.

  - Post-hoc compliance with JBI guidance only in **13%** (Tricco, 2016)
    - most papers did not mention the study protocol

  → **DO develop an *a priori* protocol**
  → **NO need for registering the protocol (yet)**
  → **DO mention the *a priori* protocol in the report**
  → **DO describe any protocol amendments in the report**

Identify the Evidence

  - Search strategy pre-specified in the protocol
  - iterative approach
    - initial limited search for relevant keywords and index terms
    - comprehensive search with all keywords and terms in >1 databases (**93%**)
    - search in grey literature (Yes **52%**; No 25%; Unclear 23%)
    - search in the reference list of all hits (Yes **56%**; No 4%; Unclear 39%)
  - report as a flowchart (Yes **47%**; No 53%)

  → **DO plan a comprehensive search strategy in the protocol**
  → **DON’T hesitate to amend the search strategy if needed**
  → **DO document any changes in your search**
  → **DO include grey literature and reference scanning**
  → **DO report the search process on a flowchart**
Sources of gray literature in scoping reviews

<table>
<thead>
<tr>
<th>Types of Grey Literature Searched (n = 494)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grey literature repository and library catalogue</td>
<td>57%</td>
</tr>
<tr>
<td>Government websites and agency databases</td>
<td>26%</td>
</tr>
<tr>
<td>Web search engines (i.e., Google, Google Scholar, Yahoo, Bing)</td>
<td>19%</td>
</tr>
<tr>
<td>Conference proceedings and abstracts</td>
<td>18%</td>
</tr>
<tr>
<td>Professional associations and organizations</td>
<td>10%</td>
</tr>
<tr>
<td>Key non-profit organizations</td>
<td>9%</td>
</tr>
<tr>
<td>Theses/dissertations</td>
<td>6%</td>
</tr>
<tr>
<td>Not reported</td>
<td>4%</td>
</tr>
</tbody>
</table>

→ DO select from the above, depending on review topic
→ DON’T ambition to cover all possible sources

Tricco et al. BMC Medical Research Methodology (2016), 16:15

Literature Selection: Inclusion and exclusion criteria

- JBI guidance (2015)
  - consistent with review title and research question(s)
  - pre-specified in the protocol
- Real-world patterns
    - "criteria were devised post hoc, based on increasing familiarity with the literature"; "a deadline was set, after which it was agreed that we would not include any more studies in the analysis"
  - Pham et al (up to 2012): I/E criteria not defined in 20.3% even in the report
  - Tricco et al (1999-2014): I/E criteria clearly reported in 67%

→ DO pre-specify I/E criteria
→ DON’T hesitate to amend I/E criteria if justified, and document the changes with their rationale
Literature Selection:
Title / abstract screening

- JBI guidance (2015) and real-world patterns (1999-2014)
  - Double title/abstract screening (Yes 36%; No 11%; Unclear 54%)
  - Double full-text screening (Yes 29%; No 9%; Unclear 62%)

→ DO double title/abstract and full-text screening
→ DO mention double screening in your paper

Quality assessment
of the overviewed evidence

- JBI guidance (2015)
  - provide an overview of the existing evidence base regardless of quality
  - a formal assessment of methodological quality of the included studies is generally not performed.
- Real-world patterns (1999-2014)
  - quality appraisal conducted only in 14%

→ DON’T assess the quality of included papers
→ DON’T worry about including lower quality evidence
Data extraction

- JBI guidance (2015): “data charting”
  - a draft charting table or form should be developed as part of the protocol
  - refinement of the charting forms may be required during the conduct of the full review, and reviewers may need to trial the extraction form

- Real-world patterns (1999-2014)
  - Pre-defined charting form: Yes 43%, No 6%, Unclear 51%

→ DO pre-specify the data extraction sheet
→ DON’T hesitate to amend it if justified, and document the changes with their rationale

Collating, Summarizing and Reporting

- An overview of all materials reviewed, without aggregation (Arksey, 2005)
- JBI guidance (2015):
  - an overview of the existing evidence base, regardless of quality.
  - no aggregation, present the range of located evidence as classified under main conceptual categories
    - as a ‘map’ of the data in a logical, diagrammatic, or tabular format
    - and/or in a descriptive format
  - pre-specified plan + refined when the reviewers have the greatest awareness of the contents of their included studies.

→ DO describe the range of located evidence
→ DO look for graphical presentation formats
→ DON’T aggregate the findings
Word clouds of specific definitions (preliminary example)

Malnutrition (35 definitions)
Enteral nutrition (8 definitions)

Network diagram of specific definitions (preliminary example)
Implications of findings

- JBI guidance (2015)
  - Implications are optional
    - future research based on gaps in knowledge?
    - future conduct of systematic reviews?

- Real-world patterns (1999-2014)
  - Evidence gaps identified in 85%
  - Future research opportunity in 84%
  - Recommended a systematic review in 12%
  - Specific policy or practice implications in 54%

Tricco et al. BMC Medical Research Methodology (2016), 16:15

Resource requirements

- Arksey, 2005:
  - 3 full time equivalent staff members for 6 months
    + an information officer to conduct literature searches

- JBI guidance (2015):
  - requires at least two reviewers

→ DON’T underestimate the resource requirements
Medical Nutrition Working Group Scoping Review: Methodology

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Nestlé Nutrition R&D
King of Prussia, PA, USA

Rationale for Medical Nutrition Scoping Review?

The Hierarchy of Evidence

- Systematic Reviews
- Randomized Controlled Trials
- Cohort Studies
- Case-Control Studies
- Case Series, Case Reports
- Editorials, Expert Opinion
### Why NOT a Systematic Review?

<table>
<thead>
<tr>
<th>Systematic Review¹</th>
<th>Scoping Review²</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AIM</strong></td>
<td>Collects empirical evidence to answer a well-defined research question</td>
</tr>
<tr>
<td><strong>Search Strategy</strong></td>
<td>Comprehensive - peer-reviewed publications</td>
</tr>
<tr>
<td><strong>Effort</strong></td>
<td>Time consuming</td>
</tr>
<tr>
<td><strong>Appraisal</strong></td>
<td>Assessment of the validity - risk of bias</td>
</tr>
<tr>
<td><strong>Synthesis</strong></td>
<td>Evidenced-based characteristics of the individual studies &amp; totality of evidence</td>
</tr>
</tbody>
</table>

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### Scoping Review Process*

**MN-Terms, Definitions & Regulations**

<table>
<thead>
<tr>
<th>Identify the Research Topic</th>
<th>Identify the Evidence</th>
<th>Literature Selection</th>
<th>Data Extraction</th>
<th>Collating, Summarizing and Reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refine Topic</td>
<td>Identify relevant sources of data</td>
<td>I &amp; E Criteria</td>
<td>Standardized data extracting process and forms</td>
<td>Overview of the literature reviewed</td>
</tr>
<tr>
<td>Formulate an answerable question</td>
<td>Standardize search strategy</td>
<td>Reviewer working in pairs- title &amp; abstract screening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Develop scoping review protocol</td>
<td></td>
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</tbody>
</table>

Step 1. Identify the Research Topic

**Goal:** To define the terms used and provide a foundation for development of emerging good practices for the economic evaluation of medical nutrition products.

**Topic refined**
To identify, examine and map existing literature to:
- Provide definitions of key **medical nutrition terminology**
- Identify **regulations** for medical nutrition
- Definition of **target populations**

**Identify Challenges**
- PN - Regulated in pharmaceutical legislation
- EN - Regulated as FSMP

Scoping Review Protocol Developed

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Step 2. Identify the Evidence

- A pre-specified search strategy - multiple sources:
  - Electronic databases
    - Proquest (EMBASE, Medline, CABA), CRD, CINAHL, Cochrane
  - Websites from Key professional, regulatory and government agencies
    - NICE, European Commission, EFSA, WHO EU, HHS, ASPEN, ANDA
  - Conference proceedings
  - Hand-searching of references
  - Recommendations from member stakeholders
Step 2. Identify the Evidence

- **Initial Search strategy**
  
  **CINAHL**: 300,000 records with first set of search terms

  - **Alternative Search Syntax** – with restriction to titles 651 records
    
    (TI ("oral nutrition* supplement*" OR ONS OR nutrition* N3 (intervention* OR support OR therap*) OR (oral OR enteral OR parenteral) N3 (nutrition OR feed* OR supplement*) OR sip N3 (feeds OR feeding) OR food W2 "special medical purposes" OR FSMP OR "medical nutrition" OR "medical food" OR (enteral OR tube) N3 (feed* OR nutrition) OR TPN OR ETF) AND TI (nutritional N3 (status OR risk) OR malnutrition OR undernutrition OR "under nutrition" OR malnourished OR undernourished OR underweight OR frail OR frailty OR sarcopenia OR sarcopenic OR cachexia OR cachectic OR nutrition* N3 (deplet* OR depriv*) OR disease OR illness OR trauma OR surgery OR "metabolic stress" OR fasting)) NOT TI (animal OR animals OR rat OR rats OR mice OR mouse OR rodent OR dogs OR (mineral OR vitamin) N3 supplement* OR "fortified food" OR pregnant OR pregnancy)

  - **Alternative Search Syntax** – Restricting to Abstract Available and Peer Reviewed: 296 records.

Do: Requested the assistance of a professional librarian!!! Important!

Step 2. Identify the Evidence

**DBs & Grey Literature/Organization**

Leadership team identified relevant government and organizational websites – conducted a search of “grey literature”


- The European Society for Clinical Nutrition and Metabolism (ESPEN), [http://www.espen.org/](http://www.espen.org/)

- European Society For Paediatric Gastroenterology, Hepatology And Nutrition (ESPGHAN), [www.espghan.org](http://www.espghan.org)

- FDA, [http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/MedicalFoods/default.htm](http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/MedicalFoods/default.htm)


- Academy of Nutrition and Dietetics, [http://www.eatright.org/](http://www.eatright.org/)

**Website’s search engine** put limits on the our search strategy

- Enter inclusion or exclusion criteria in “key combinations”
Step 3. Literature Selection
Inclusion Criteria

- **Target Population**
  - All ages
  - Disease related malnutrition
  - Diseases/illness like (non-exhaustive list), cancer, cardiac diseases, gastric and bowel diseases, neurological disorders, respiratory failure (e.g. COPD), dementia, inflammatory conditions like arthritis, kidney diseases etc.
  - Surgical patients
  - Trauma patients
  - Patients with other conditions preventing oral intake, e.g., coma, mechanical obstruction, dysphagia (inability to swallow), and metabolic or neurological disorders not caused by a disease like
    - Inherited biochemical disorders (including inborn errors of metabolism such as PKU; maple syrup urine disease; diagnosed lactase deficiency in infancy resulting in galactosemia without dietary management)
    - Diagnosed food allergy in infants (CMP)
    - Prematurity (infants born premature)

Step 3. Literature Selection
Inclusion Criteria (2)

- **All health care settings**
- **Enteral nutrition** = enteral feeding formulas, food for special medical purposes (FSMP), oral nutritional supplements (ONS), (enteral) tube nutrition/food ((E)TN), sip feed, oral medical nutrition/food
- **Parenteral nutrition** = parenteral feeding formulas, intravenous feeding/nutrition, (total) parenteral nutrition/food ((T)PV), medical nutrition
Step 3. Literature Selection

Exclusion Criteria

- “Life stages” such as pregnancy
- Classical nutrient deficiency disease such as scurvy or pellagra
- *Intended* weight loss
- Diabetes
- Term infant formula and follow-on formula
- Processed cereal-based food and baby food
- Total diet replacement for weight control
- Meal replacement for weight control
- “Lactose-free” or lactose intolerance in Adults
- “gluten-free” or ‘very low gluten’
- Food supplement, e.g. vitamin/mineral supplement
- Fortified food
- Ordinary foodstuff
- Non-English

Step 3. Literature Selection

Regulations

- **Included: European Union and USA**
  – The EU Food for Special Medical Purposes (FSMP) regulations are under discussion.
- **Excluded: All other countries**
  – Legislation and situation in Africa, Asia-Pacific and South America differs extensively from that of Europe and the USA
    – Exception: systematic reviews and general narrative reviews
Step 4. Data Extraction

- Standardize data collection process / extract forms
- Excel file with instructions, recording sheet, I & E criteria and term list

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Step 4. Data Extraction

- **Data extraction teams**
- **Titles & abstracts reviewed** by 2 team members according to the I & E criteria
  - Team reached agreement on whether to include or exclude record
  - Results reviewed by SIG co-chairs

**Do:** Provide additional instructions

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<table>
<thead>
<tr>
<th>Reference</th>
<th>Source Information</th>
<th>Include/Exclude</th>
<th>Study Objective</th>
<th>Population</th>
<th>Country</th>
<th>Health Care Setting</th>
</tr>
</thead>
</table>
Step 4.
Data Extraction

- Full article/resource reviewed for inclusion in full text review

- Instructions e-mailed to teams; encouraged to email or call with questions
- Pull-down options when practical
- Results reviewed by SIG co-chairs
- Do: Provide additional instructions
Step 5.
Collating, Summarizing & Reporting

Overview of the findings will be collated, summarized and reported in a manuscript.
- Locate additional references.
- Clean the data (cancer, pediatric vs pediatric, cancer).

- Analysis
  - Summary Statistics: Terms, Definitions, Regulations; record source, publication year, study populations, country, if a HE analysis was included)
  - Word clouds and network diagrams

- Tentative title: Medical Nutrition – Terms, Definitions, and Regulations in the EU and US

- Limit to a 4,000 words

- 18-24 month development period

Timeline

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIG Forum presentation ISPOR DC</td>
<td>May 23-25, 2016</td>
</tr>
<tr>
<td>SIG meeting at ISPOR Washington, DC</td>
<td>May 23-25, 2016</td>
</tr>
<tr>
<td>Analyze data</td>
<td>June 2016</td>
</tr>
<tr>
<td>Develop section outlines</td>
<td>July 2016</td>
</tr>
<tr>
<td>SIG members review outline</td>
<td>End of July 2016</td>
</tr>
<tr>
<td>Revisions made &amp; sentence outline developed</td>
<td>August 2016</td>
</tr>
<tr>
<td>Sentence outlines reviewed by leadership group</td>
<td>September 2016</td>
</tr>
<tr>
<td>Authors develop sections</td>
<td>October – December 2016</td>
</tr>
<tr>
<td>Comments from leadership group</td>
<td>January 2017</td>
</tr>
<tr>
<td>Revisions</td>
<td>Due end of 2017</td>
</tr>
<tr>
<td>Revised draft sent to ISPOR NE SIG Review Group</td>
<td>February 2017</td>
</tr>
</tbody>
</table>
Future steps

For more information...
Medical Nutrition WG webpage

Review Group: Please Join!

OR...

1. Go to the ISPOR homepage: [www.ispor.org](http://www.ispor.org).
2. Click on the GREEN Special Interest Group menu at the TOP of the homepage.
3. Select JOIN on the pull-down menu.
FORUM SLIDES are AVAILABLE!
http://www.ispor.org/Event/ReleasedPresentations/2016Washington

OR next week, slides will be added to the Medical Nutrition Working Group webpage, scroll down to ACTIVITIES