

New Types of Evidence and Product Innovation: From Patient Needs to Product Design and Development

MEDICAL FOODS WORKSHOP:
**Science, Regulation
and Practical Aspects**

AUGUST 13-14, 2019 WASHINGTON, DC

New Types Of Evidence And Product Innovation: From Patient Needs To Product Design And Development

- Moderator: Sarah Ohlhorst, American Society of Nutrition
- Panelists:
 - Dr. Peggy Guenter, ASPEN – A Brief Overview of ASPEN’s Research Value Proposition Project
 - **Dr. Satya Jonnalagadda, Abbott Nutrition – Product Design Considerations**
 - Dr. Krys Araujo, Nestle Health Science – Research and Evidence Development
- Q&A with Panelists

Product Design Considerations

Topics:

- Medical Nutrition Therapy
 - Nutrition Care Process
 - Patient Nutrition Considerations
- Product Design Considerations

Ignorance of Nutrition Is No Longer Defensible

Neal D. Barnard, MD, Physicians Committee for Responsible Medicine

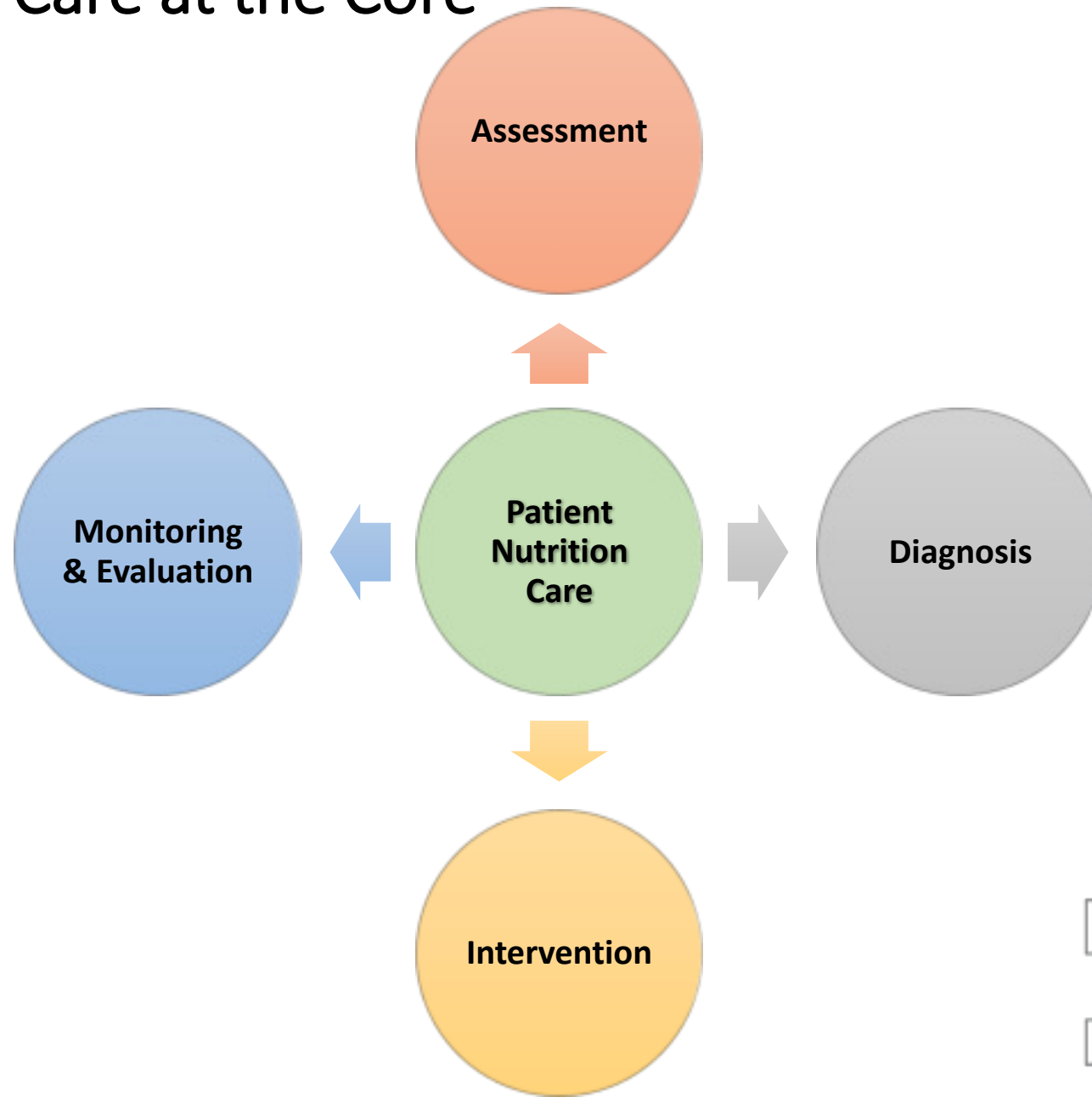
- Nutrition should be a required part of CME for physicians everywhere
- Physicians should work with RDNs. Physiciansmust recognize the role nutrition plays in disease, communicate it clearly to the patient, and refer the patient appropriately
- Electronic medical record services should include customizable nutrition questions and handouts, facilitating both education and research on the effect of nutrition interventions
- Physicians are role models and should embrace that fact. As physicians learn to talk with patients about nutrition, they must also practice what they preach
- **Rather than allowing nutritional ignorance to fester like a gangrenous sore, the medical community can take advantage of current knowledge for patient benefit, as well as their own**

https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2737323?guestAccessKey=800f6f0e-b771-43a0-886d-e1e9cc7b7d00&utm_content=weekly_highlights&utm_term=071319&utm_source=silverchair&utm_campaign=jama_network&cmp=1&utm_medium=email

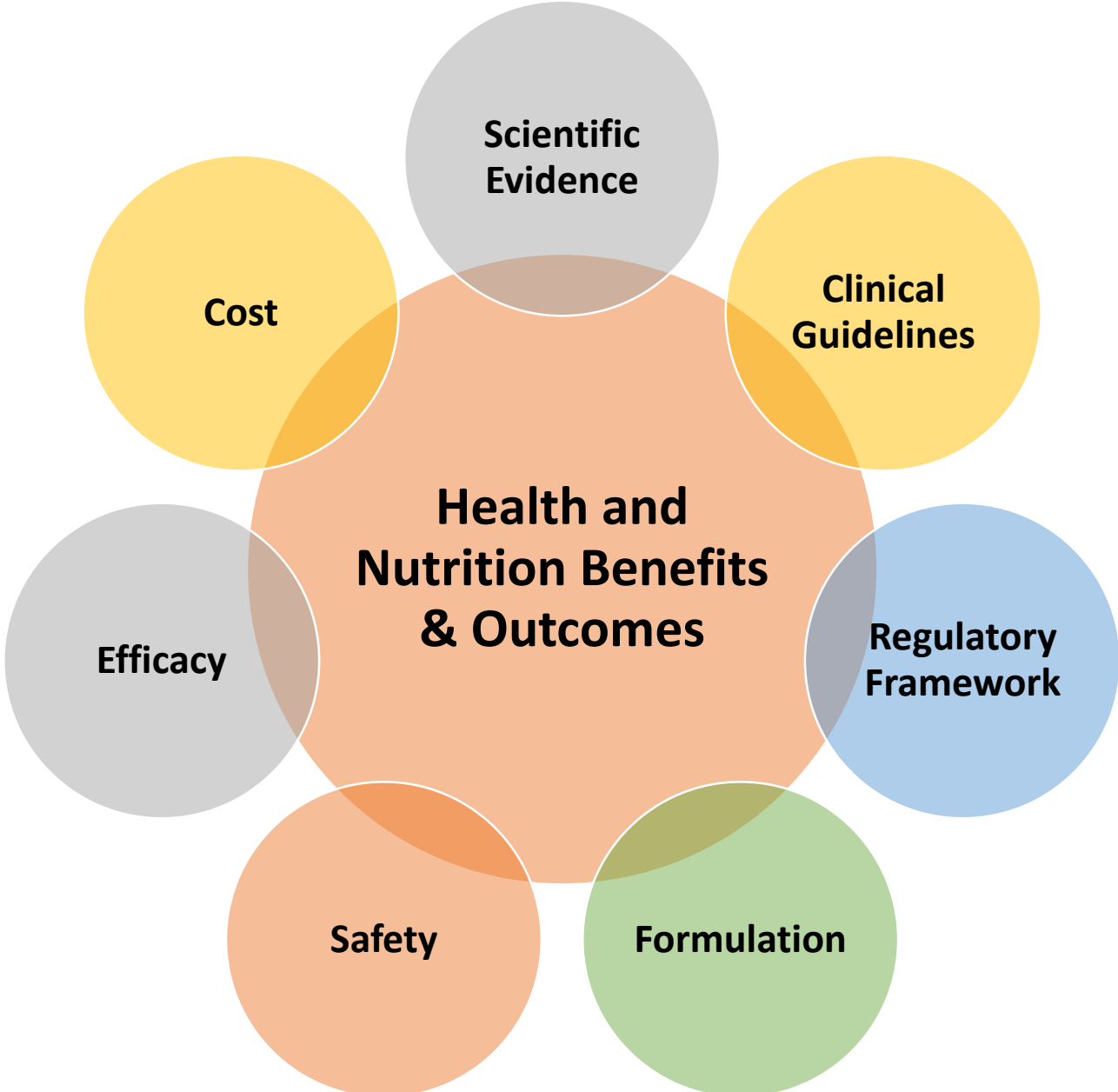
Medical Nutrition Therapy

- MNT is a specific application of the Nutrition Care Process in clinical settings that is focused on the management of diseases/clinical condition
- "Nutritional diagnostic, therapy, and counseling services for the purpose of disease management which are furnished by a registered dietitian or nutrition professional..." (Medicare MNT legislation, 2000)
- MNT involves in-depth individualized nutrition assessment, duration and frequency of care using the Nutrition Care Process to manage disease
- Nutrition Professional determines the nutrition diagnosis after analyzing assessment data and interaction with the patient(s) and initiate the nutrition intervention
- Nutrition Professional provides nutrition intervention/information for [xxx] health condition to the patient

Patient Nutrition Care at the Core



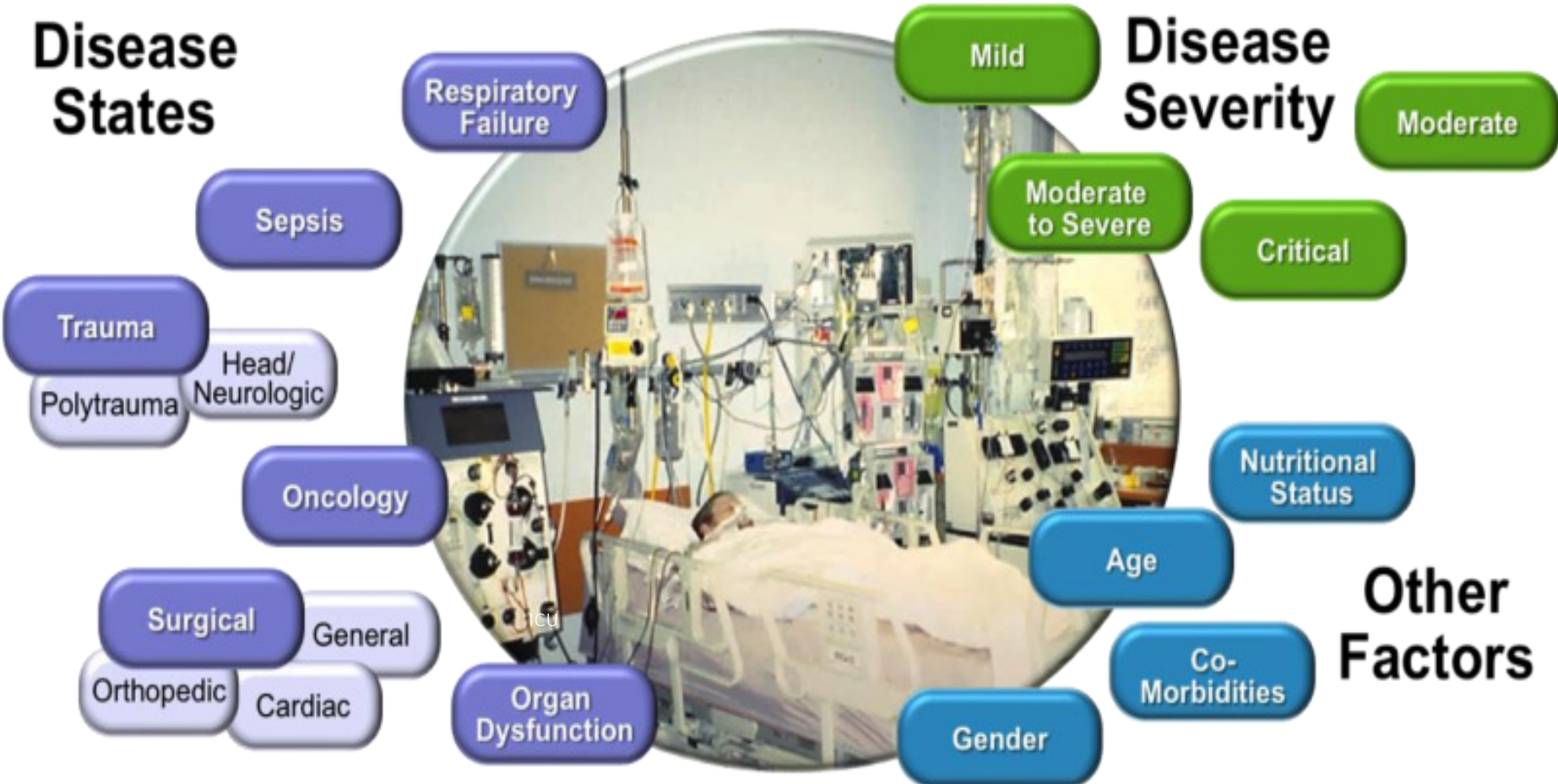
Patient Nutritional Needs Determines Products Design



Where Do We Start?

- Goal is to support the patient's nutritional needs based on ***health condition and specific nutritional requirements***
- Impairment in normal nutrient intake/digestion/absorption/tolerance
- Clinical Guidelines
- Existing/Emerging Body of Evidence

Patients Represent a Heterogeneous Population



**Variable Patient Populations Makes Predicting Nutritional Needs Challenging
Need to Take Into Account Many Factors to Determine Nutritional Needs**

Providing Adequate Nutrition in the ICU is Often Challenging

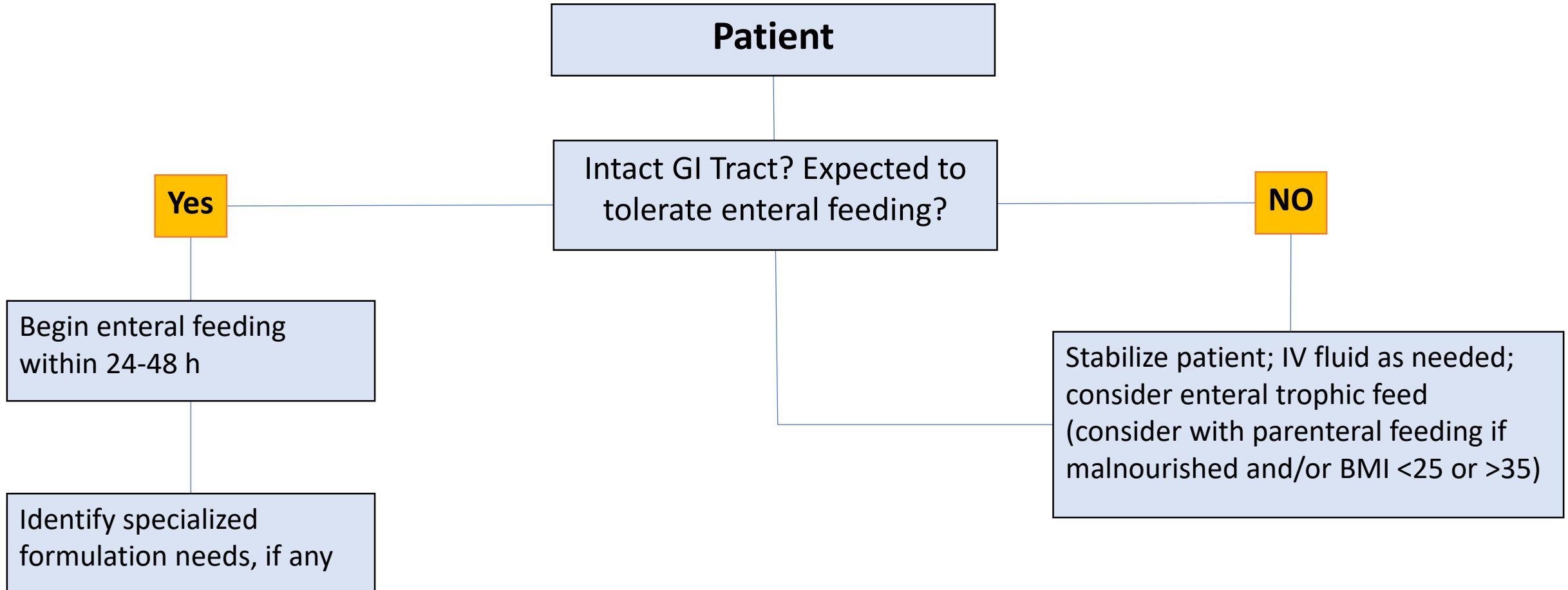
59% of Prescribed Calories

- Frequent, inappropriate cessation of feeding is often due to:
 - Gastrointestinal complications
 - Routine nursing care activities
 - Procedures or diagnostic tests
 - Technical issues with feeding access

60% of Prescribed Protein

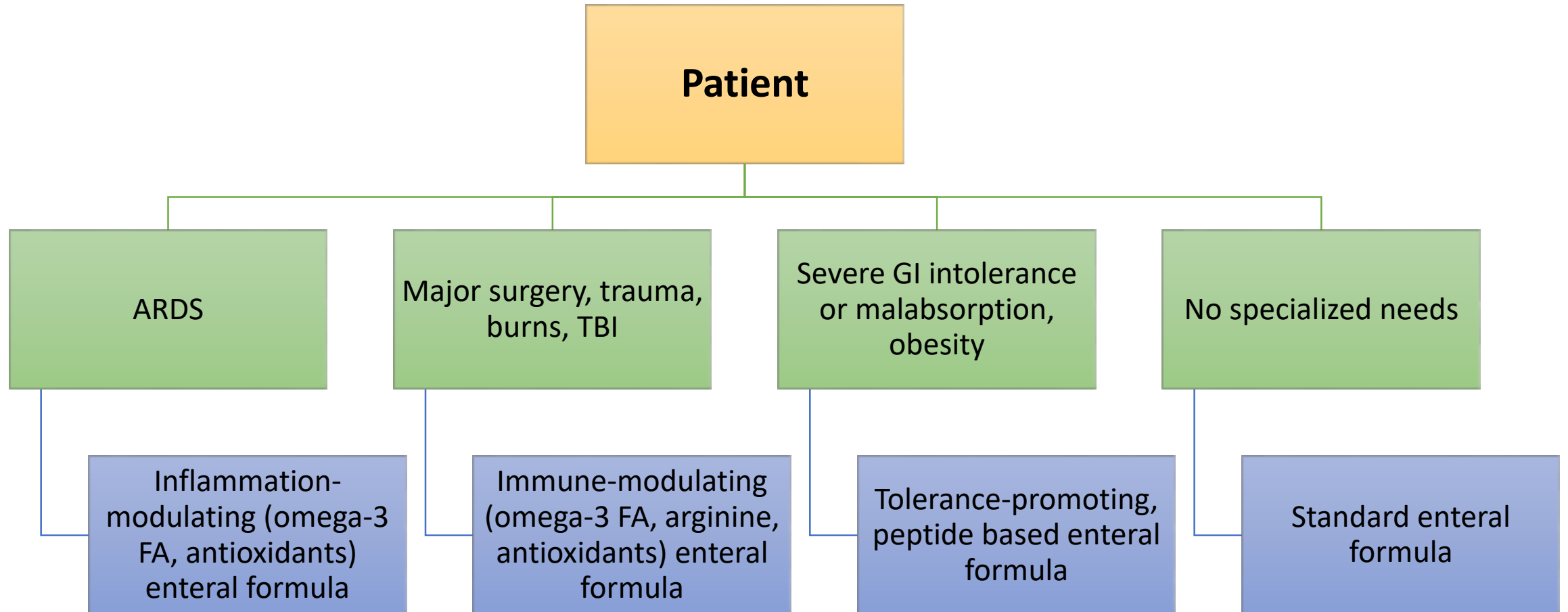
- Inadequate calorie and protein intake is associated with increased:
 - Risk for infectious complications
 - Length of hospital stay
 - Mechanical ventilation
 - Risk of complications
 - Mortality

Selecting the Right Medical Nutrition Therapy for the Patient Is Critical To Ensure Appropriate Recovery



Clave SA, et al. *JPEN J Parenter Enteral Nutr.* 2016;40(2):159-211.
Taylor BE, et al. *Crit Care Med.* 2016 Feb;44(2):390-438.
Choban P, et al. *JPEN J Parenter Enteral Nutr.* 2013;37(6):714-744.
Hegazi R, et al. *Crit Care.* 2011;15:234.

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Example: There Are Many Impacts Of Surgery On The Human Body and Proper Medical Nutrition Therapy Is Essential For Recovery

Physiological Response¹

- Rise in counter regulatory hormones
- Hyperglycemia and catabolism
- Proteolysis and lipolysis

Immunological Response²

- Shift to Th2 phenotype results in IL-4,10,13 production
- Breakdown of Arginine
- Increased risk of complications due to infections



Arginine Deficiency^{3,4,5,6}

- Associated with T-lymphocyte dysfunction
- Deficiency can impair
 - Cell growth & proliferation
 - Immune function
 - Wound healing

Insulin Sensitivity⁷

- More complex the surgery, the more insulin resistant the patient can become
- Surgical techniques – open vs. laparoscopic results in 50% fall in sensitivity

1. Gillis CG, Carli, F. *Anesthesiology* 2015;123(6):1455-72, 2. Adapted from Marik, PE. *J Trauma Acute Care Surg.* 2012 Oct;73(4):801-8, 3. Morris SM Jr. *Curr Opin Nutr Metab Care.* 2004;7:45-51, 4. Zhou M, et al. *J Nutr.* 2007;137(6 Suppl 2):1687S-1692S, 5. Mizock BA. *Nutrition.* 2010;26:701-707, 6. Santora R, et al. *J Surg Res.* 2010;161:288-294, 7. Ljungqvist O. *JPEN* Jul 2012;36(4):389-98

Condition Specific Therapeutic Areas and Specific Nutrition Requirements

Disease/Condition Specific Therapeutic Areas	Specific Nutrient Recommendations (Examples)	Reference
<i>In patients with burns > 20% body surface area</i>	<ul style="list-style-type: none"> Additional enteral doses of GLN (0.3-0.5 g/kg/d) should be administered for 10-15 days as soon as EN is commenced 	https://www.espen.org/files/ESPEN-Guidelines/ESPEN_guideline-on-clinical-nutrition-in-the-intensive-care-unit.pdf
<i>In polymorbid medical inpatients with pressure ulcers</i>	<ul style="list-style-type: none"> Specific amino-acids (arginine and glutamine) and b-hydroxy b-methylbutyrate (βHMB) can be added to oral/enteral feeds to accelerate the healing of pressure ulcer 	https://www.espen.org/files/ESPEN-Guidelines/PIIS0261561417302364.pdf
<i>In polymorbid medical older inpatients requiring enteral nutrition</i>	<ul style="list-style-type: none"> Formulas enriched in a mixture of soluble and insoluble fibers can be used to improve bowel function 	https://www.espen.org/files/ESPEN-Guidelines/PIIS0261561417302364.pdf
<i>Perioperative immunonutrition in malnourished patients is beneficial in colorectal cancer surgery</i>	<ul style="list-style-type: none"> Supplementation of enteral feeds with immunomodulators such as L-arginine, L-glutamine, n-3 fatty acids and nucleotides (immunonutrition) is thought to modify immune and inflammatory responses favourably and result in reduced postoperative infective complications and shorter LOS 	https://www.ncbi.nlm.nih.gov/pubmed/30426190
<i>Guidelines for Perioperative Care in Cardiac Surgery Enhanced Recovery After Surgery Society Recommendations</i>	<ul style="list-style-type: none"> A carbohydrate drink (a 12-ounce clear beverage or a 24-g complex carbohydrate beverage) 2 hours preoperatively reduces insulin resistance and tissue glycosylation, improves postoperative glucose control, and enhances return of gut function Preoperative oral carbohydrate loading may be considered before surgery 	https://jamanetwork.com/journals/jamasurgery/fullarticle/2732511?guestAccessKey=04f7090d-122c-4e94-a46f-22e49dab7c51

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<p><i>Dietary Supplements Containing Fish Oil for the Adult Oncology Patient</i></p>	<ul style="list-style-type: none"> • If sub-optimal symptom control or inadequate dietary intake has been addressed and the adult oncology patient is still experiencing loss of weight and lean body mass (LBM), the registered dietitian nutritionist (RDN) may consider use of dietary supplements containing eicosapentaenoic acid (EPA) as a component of nutrition intervention • Research indicates that dietary supplements containing fish oil (actual consumption, 0.77g to 6.0g of EPA per day), resulted in weight gain or weight stabilization and improvement or preservation of LBM in adult oncology patients with weight loss 	<p>https://www.andeal.org/template.cfm?template=guide_summary&key=4162</p>
<p><i>Diabetes-specific enteral nutrition formula in hyperglycemic, mechanically ventilated, critically ill patients</i></p>	<ul style="list-style-type: none"> • In high-risk ICU patients, both diabetes-specific formulas lowered insulin requirements, improved glycemic control and reduced the risk of acquired infections relative to the standard formula. Compared with the control-specific formula, the new-generation formula also improved capillary glycemia 	<p>https://www.ncbi.nlm.nih.gov/pubmed/26549276</p>

Product Development Requires Effective Multi-Disciplinary Teams

- It takes >35 different functions to bring products to market
- We are interdependent on each other and all have a critical role to play!
- Keeping functional teams aligned is vital to the success



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Product Formulation Design Initial Key Considerations

Target Consumer

- Nutritional Requirements
- Nutritional Recommendations

Desired Patient Benefits

- Clinical Benefit
- Nutritional Benefit

Regulations

- Global, Regional, Local Policies & Regulations
- Product Category
- Product Formulation Requirements
- Product Labeling Requirements

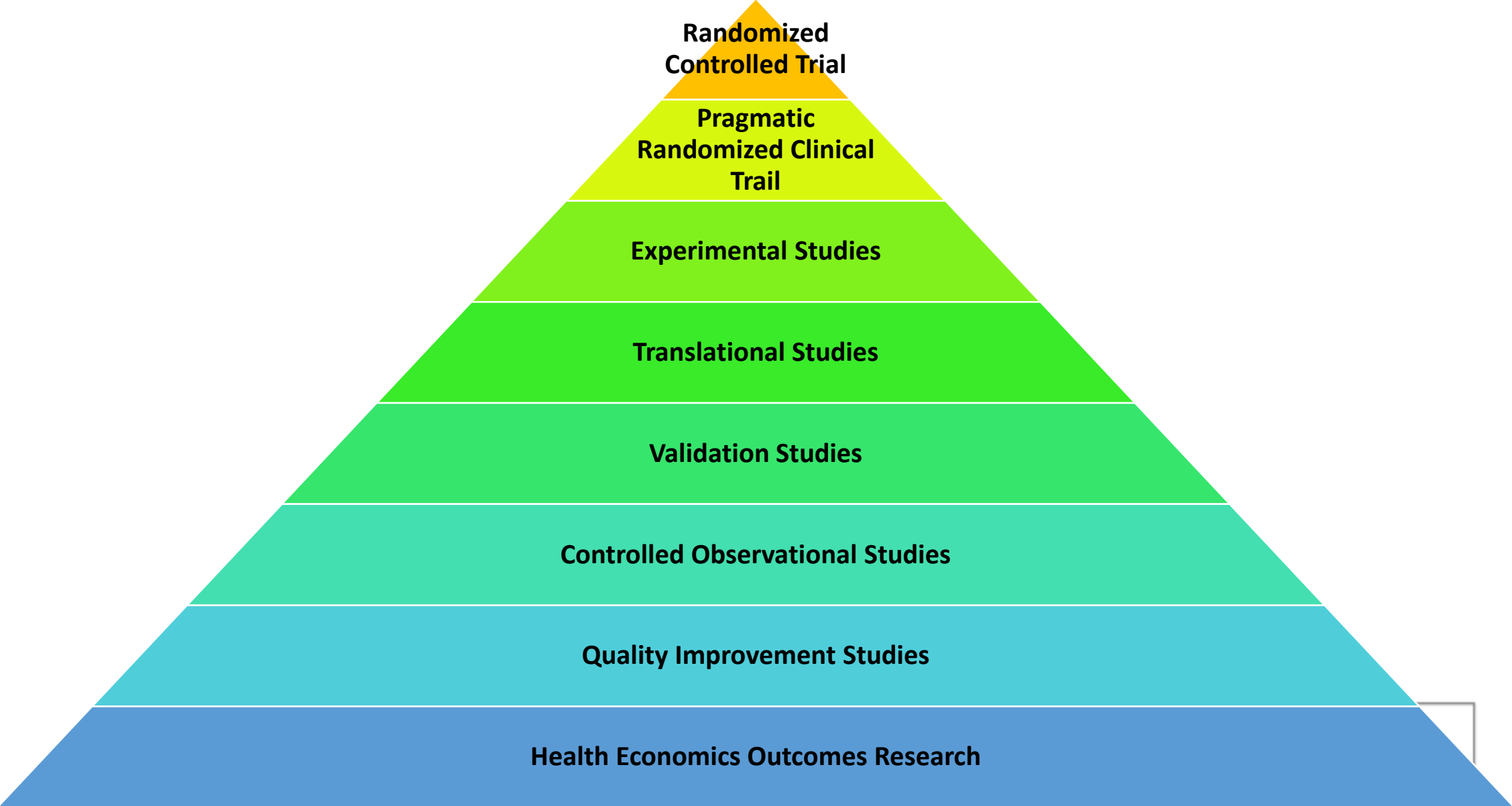
Level of Key Nutrients-Ingredients

- Per Serving, Per Day, etc.
- Regulatory Status
- Totality of Evidence

Totality of Evidence

- Product Benefits (clinical & nutrition)
- Clinical Guidelines
- Existing/Emerging Evidence
- Additional Evidence Requirements

Product Formulation Nutritional Benefit Substantiation Research Options



Adapted: Compher et al. Research Agenda 2018: The American Society for Parenteral and Enteral Nutrition. JPEN. 2018

Primary Goals of the Product Development Process

Meet nutritional, performance needs of the targeted population

Ingredient selection

Robust, stable, high quality formulation

Manufacturing process

Clinical substantiation

Meet needs of consumer

Packaging

Process of Bringing Products To Market

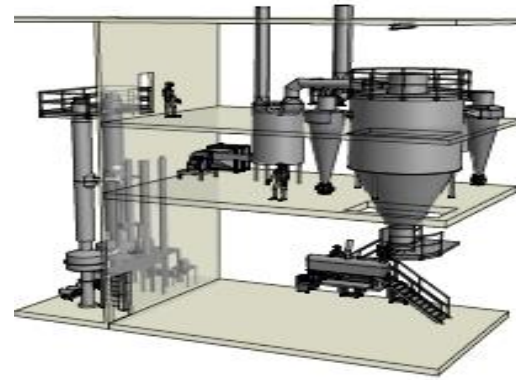
Rapid Prototyping
Lab Concept”



Process Research
Lab “Optimization”



Pilot Plant
“Reproducibility”



Commercial
Plant



Proof of Principle

- Fundamental R&D
- Deliver POP of product, process, & package
- Not scalable

Optimization

- Fast Formulation, Package, and Process Optimization
- Design of Experiments
- Potentially scalable

GMP Product , Scale up

- Clinical and Consumer Research Studies
- Scale up : “Right First Time”

Manufacturing, Launch

- Quality Testing
- Monitoring

USER EXPERIENCE CONSIDERS ALL ASPECTS OF HOW PEOPLE USE AND INTERACT WITH THE PRODUCT

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