

NUTRITIONAL DISCOVERIES IN MEDICAL NUTRITION





INTRODUCING NUTRICIA RESEARCH

To pioneer nutritional
discoveries to help
people live longer,
healthier lives.

.....

PART OF DANONE SINCE 2007



**NUTRICIA
RESEARCH**



**FRESH
DIARY**



WATERS

**MEDICAL
NUTRITION**

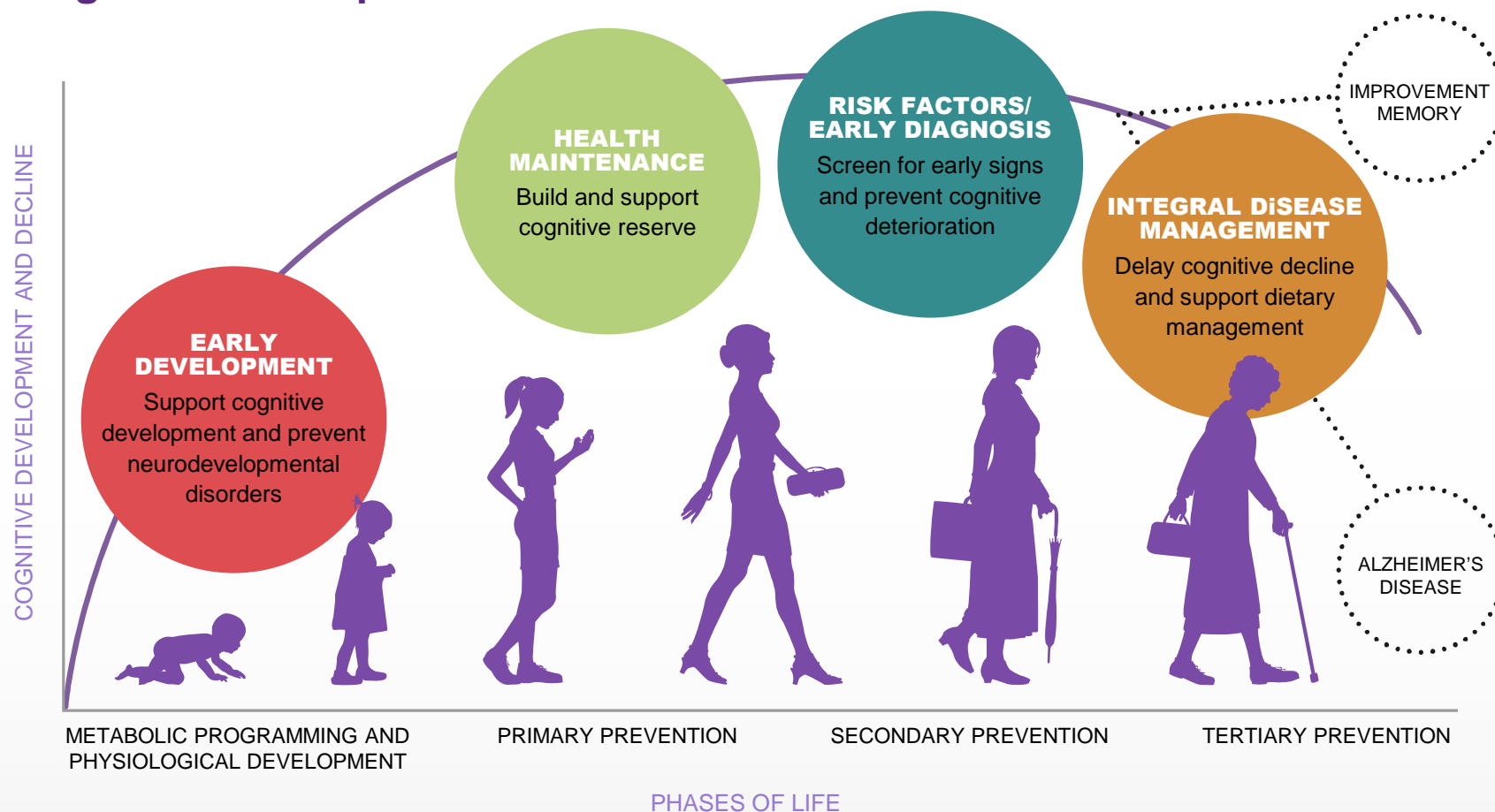


**EARLY LIFE
NUTRITION**

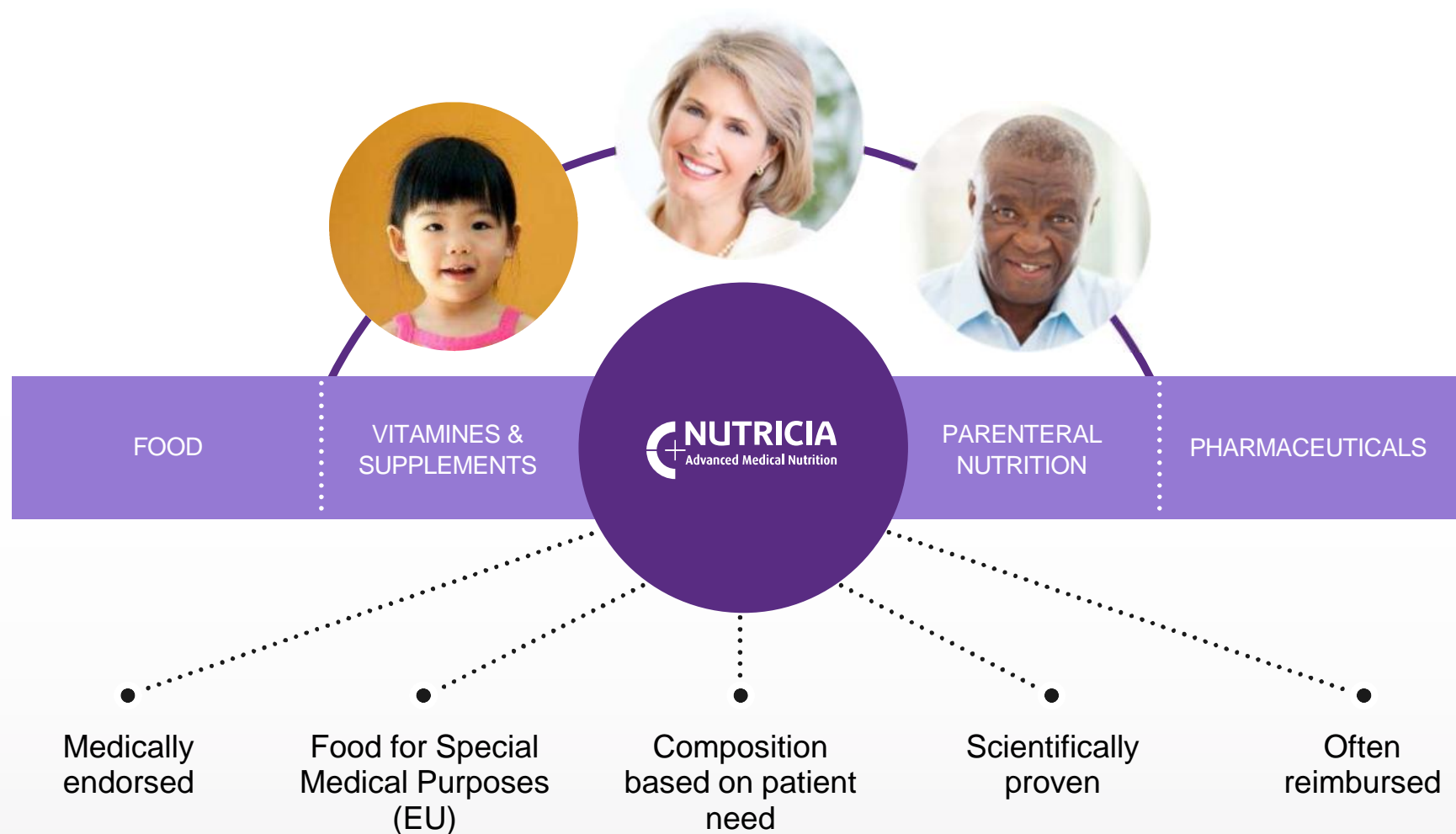


NOURISHING HEALTH THROUGHOUT OUR LIFESPAN

Cognitive development and decline



MEDICAL NUTRITION: A UNIQUE POSITION

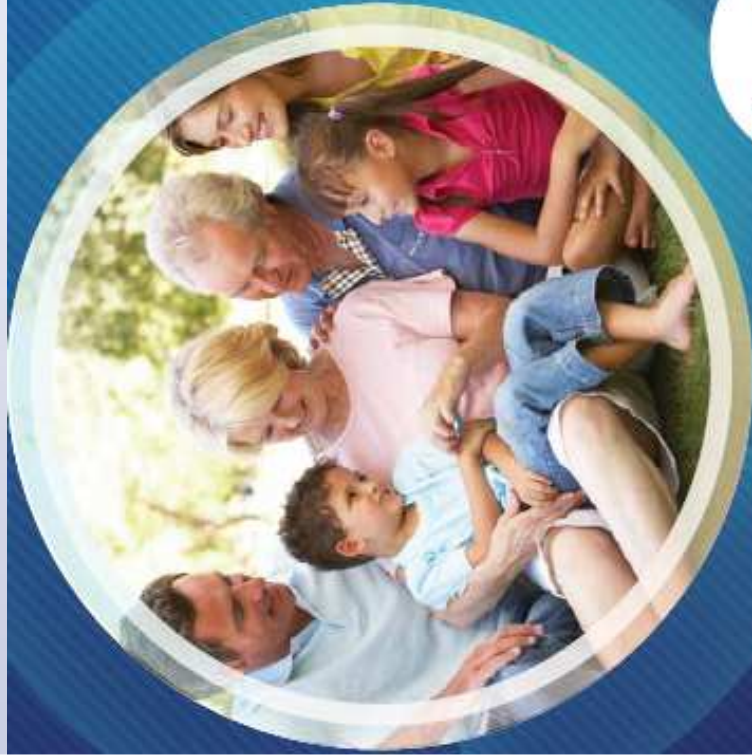


A COMPLETE SPECIALISED NUTRITION PORTFOLIO



For Paediatric and Adult Care in selected Therapeutic Areas





DANONE NUTRIÇÃO ESPECIALIZADA

Líder em Nutrição Especializada com mais de 100 anos de pesquisa e nutrição.

Portfólio completo e consolidado para

Hospitais e Alta Hospitalar



Soluções nutricionais em

Oncologia



Portfólio crescente nas farmácias para

Alergia e Desenvolvimento Infantil
& Nutrição no Envelhecimento





Hospitals and
for discharge
(Nutrison
range and
Nutridrink)

Nutritional solutions for
Oncology
(Compact protein,
FortiCare and Calogen)

Pharmacies and other
channels for CMA,
Faltering Growth and
Nutrition in Elderly



Portfólio completo e consolidado para
Hospitais e Alta Hospitalar



Soluções nutricionais em

Oncologia



Portfólio crescente nas farmácias para

**Alergia e Desenvolvimento Infantil
& Nutrição no Envelhecimento**



OUR INNOVATION PROCESS

CREATE AND DEVELOP A CONTINUOUS FLOW OF INNOVATIONS



OUR EXPERTS & STRATEGIC PARTNERSHIPS IN OUR CHOSEN LIFE SCIENCE AREAS

NUTRITION, METABOLISM & MUSCLE



**Assoc. Prof.
Ardy van Helvoort**

Medical Nutrition & Metabolism in
Disease Management



**Assistant Prof.
Yvette Luiking**

Translational Research in Aging &
In Disease Management

BRAIN & NEUROSCIENCES



**Professor
Adina Michael-Titus**

Neuroscience

MICROBIOLOGY & IMMUNOLOGY



**Professor
Johan Garssen**

Immunopharmacology
of Nutrition



**Professor
Jan Knol**

Gut Microbiology
of Early Life



**Assoc. Prof.
Leon Knippels**

Immunopharmacology
of Nutrition



Universiteit Utrecht



**NUTRICIA
RESEARCH**



OUR EXTENSIVE EXTERNAL NETWORK

STANDING STRONG TOGETHER

100

Academic centre
preclinical network

150

Hospitals
clinical network

Scientific
Advisory Boards

Strategic Partners
Harvard, MIT, Oxford,
Heidelberg, Karolinska
Tufts, VU and many others

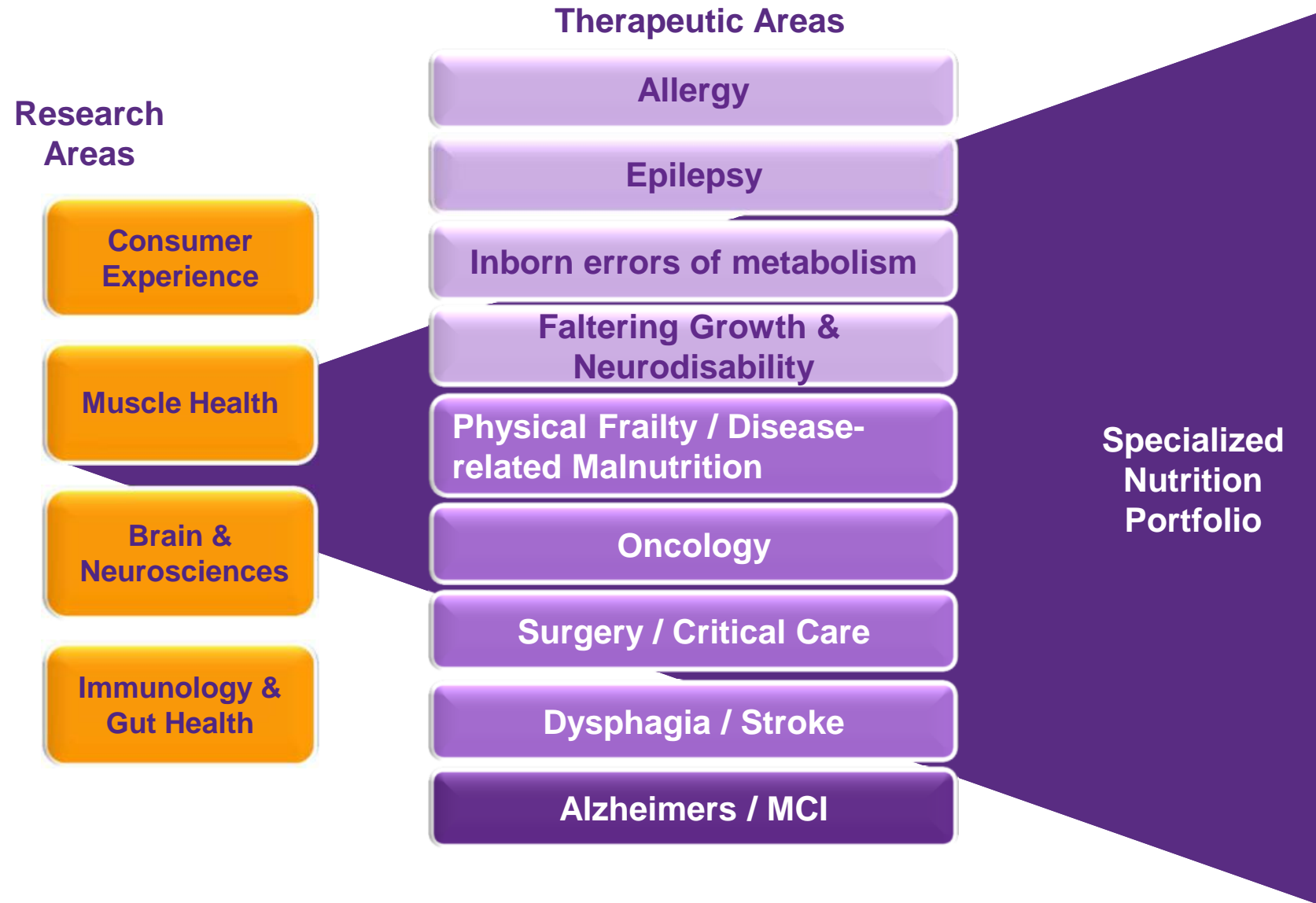
Consortia
EU LipiDiDiet, Top Institute
Food & Nutrition and
many others



NUTRICIA
RESEARCH



RESEARCH FEEDS INTO NUTRITION FOR THERAPEUTIC AREAS



SELECTED THERAPEUTIC AREAS

Paediatric Care



Allergy



Inborn Errors of Metabolism



Faltering Growth & Neurodisability



Epilepsy

Surgery & Intensive Care

Dysphagia & Stroke

Physical Frailty

Memory

Oncology



Adult Care

SCIENCE-DRIVEN, PATIENT LED

REIMBURSEMENT
SCREENING



PATIENT CARE



EVIDENCE
CLINICAL TRIALS



Patients

Payers

**Patient
Association**

**HCP
Support**

**KOL
Support**

**Strong
Science**



MEDICAL CREDIBILITY



RELATIONSHIP BUILDING
AWARENESS



TREATMENT GUIDELINES
SCIENTIFIC PUBLICATIONS

DUAL BENEFITS OF MEDICAL NUTRITION

Better quality of life

- children catch up in growth
- patients gain in strength and energy
- faster recovery for the sick
- elderly stay independent longer
- bed patients are more comfortable

Low cost of care

- fewer interventions
- shorter drug and therapy treatment times
- fewer hospital admission days
- fewer doctor return visits



IMPACT OF MALNUTRITION IN BRAZILIAN HOSPITAL COSTS

Retrospective cohort study review of 709 patients randomly selected from 25 Brazilian hospitals



Malnourished Patients



Well nourished Patients

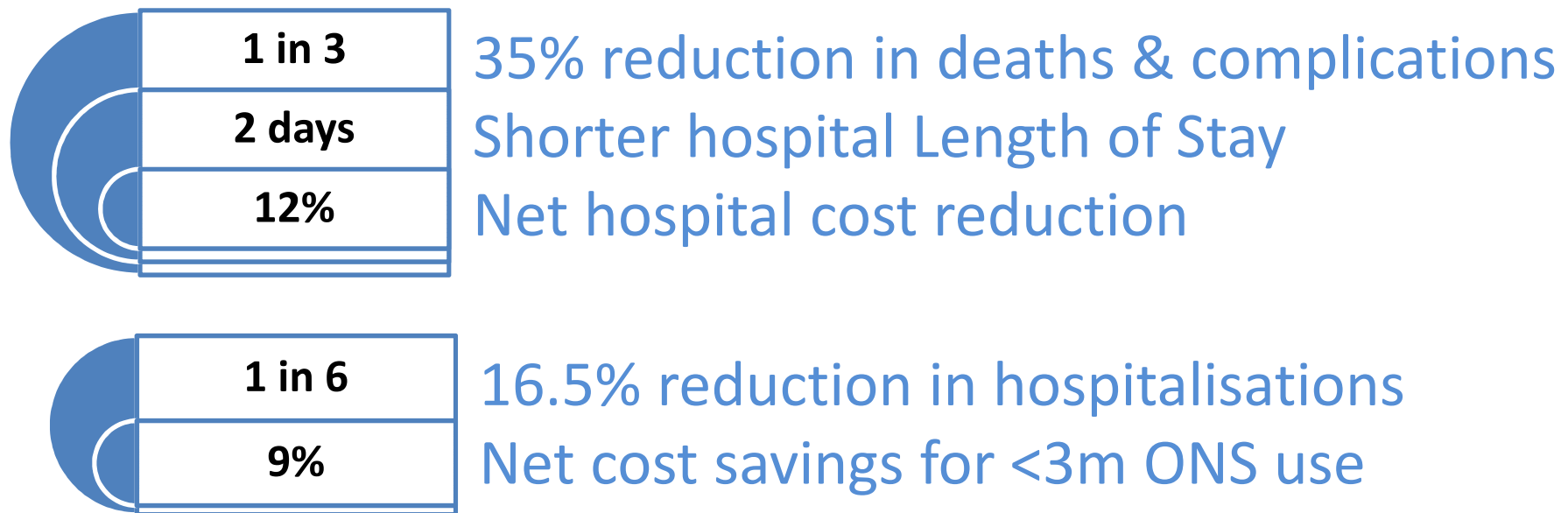
**Hospital length of stay
Complications
Mortality**

**16.6 days
27%
12,4%**

**10.1 days
16,8%
4,7%**

**Hospital costs in malnourished patients
increased up to **308.9%****

Key findings from review of Health Economics: tackling malnutrition with Oral Nutritional Supplements



Managing malnutrition with ONS can produce an **average cost saving of around 10%** compared to standard care across a broad range of patient groups

SURVEYS IN BRAZILIAN HOSPITALS SHOWED HIGH PREVALENCE OF MALNUTRITION AND COMPLICATIONS

Brazilian Survey – IBRANUTRI, 2001

Enrolled 4000 patients from public hospitals (SUS) all over the country

48.1% of malnutrition
12.1% of severe malnutrition

Complications:
Cancer patients had an almost **three-fold higher malnutrition rate** than non-oncologic patients (66.3% VS 42.9%).

New Survey, 2013

Included 473 patients from public, university and private hospitals in Brazil

52.4% of malnutrition
22.4% severe malnutrition

Complications:
17% prevalence of pressure ulcers and **98% of those patients with pressure ulcers were malnourished**

Waitzberg DL et al. Hospital malnutrition: the Brazilian national survey (IBRANUTRI): a study of 4000 patients. *Nutrition*. 2001 Jul-Aug;17(7-8):573-80. Brito PA et al. Prevalence of pressure ulcers in hospitals in Brazil and association with nutritional status--a multicenter, cross-sectional study. *Nutrition*. 2013 Apr;29(4):646-9.

A close-up portrait of an elderly woman with short, wavy, light-colored hair. She is smiling and looking slightly to the right. She is wearing a dark red or maroon jacket over a dark top, and large, ornate earrings. The background is a soft, out-of-focus indoor setting.

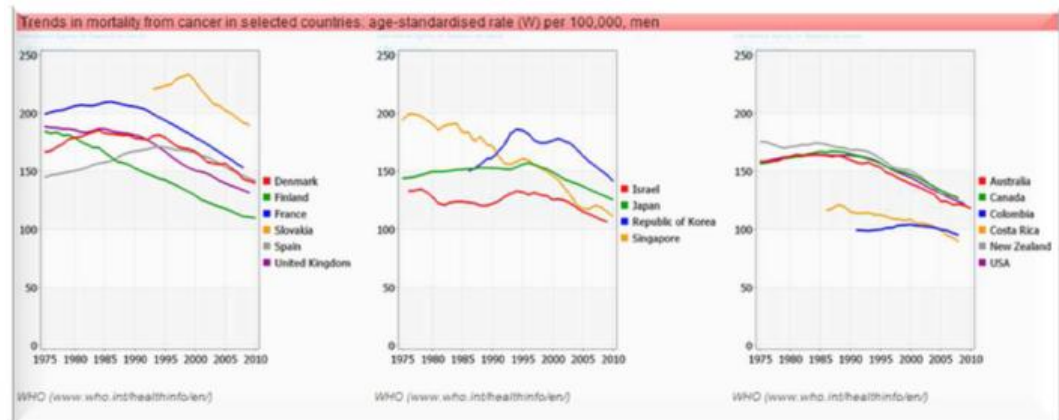
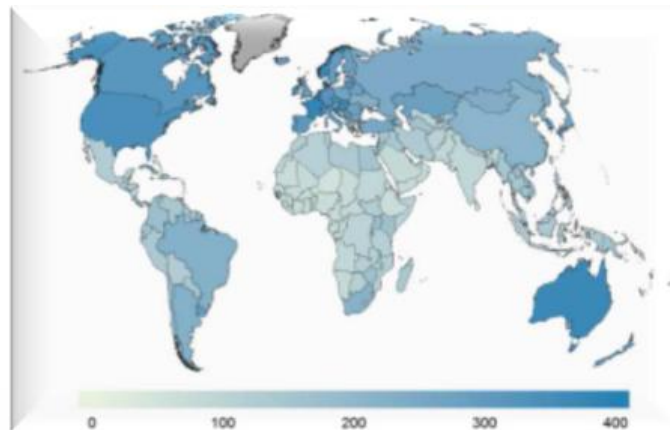
**NUTRICIA'S
AMBITION**

**TO ESTABLISH
ADVANCED
NUTRITION AS
AN INTEGRAL
PART OF
HEALTHCARE**

ADULT CARE ONCOLOGY



32.6 MIO PEOPLE LIVING WITH CANCER ...



As mortality rates decrease, cancer becomes a chronic disease

As a consequence, there will be an increasing need for nutritional support

HIGH PREVALENCE OF CANCER-RELATED MALNUTRITION WITH A SIGNIFICANT IMPACT ON CLINICAL STATUS

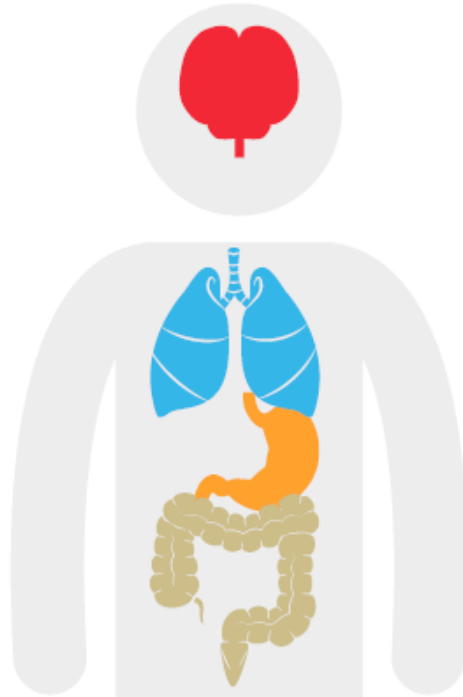
4 of the leading types of cancer go often together with **weight loss**

70% Head & neck

62% Lung

80% Stomach

58% Colorectal



Cancer-related malnutrition significantly impacts **clinical outcomes**

An extensive body of evidence of >50 references reports an impact on:

CLINICAL STATUS AND TREATMENT-RELATED OUTCOMES

- Reduced response to chemotherapy
- Increased chemotherapy induced toxicities
- Higher risk of post-operative complications
- Impaired immune function

COST OF CARE

- Longer hospital stay and higher readmission rate
- High prescription and consultation rates
- Increased post-operative complications

QUALITY OF LIFE

- Lower QOL and performance status
- Reduced muscle function
- Shorter survival

CANCER PATIENTS SPECIFICALLY LOSE MUSCLE MASS WHICH IS ASSOCIATED TO POOR CLINICAL OUTCOMES

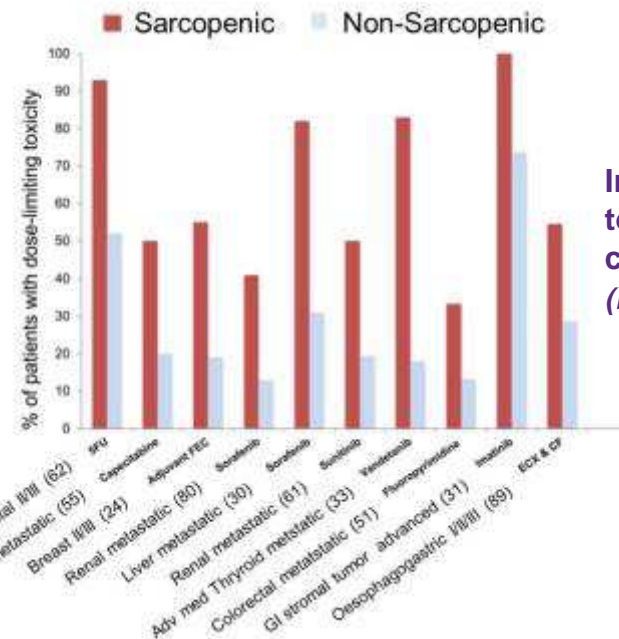
BMI does not reflect **muscle mass loss**

Same BMI

Different skeletal muscle index



Loss of muscle mass is a prognostic factor for **poor clinical outcomes**

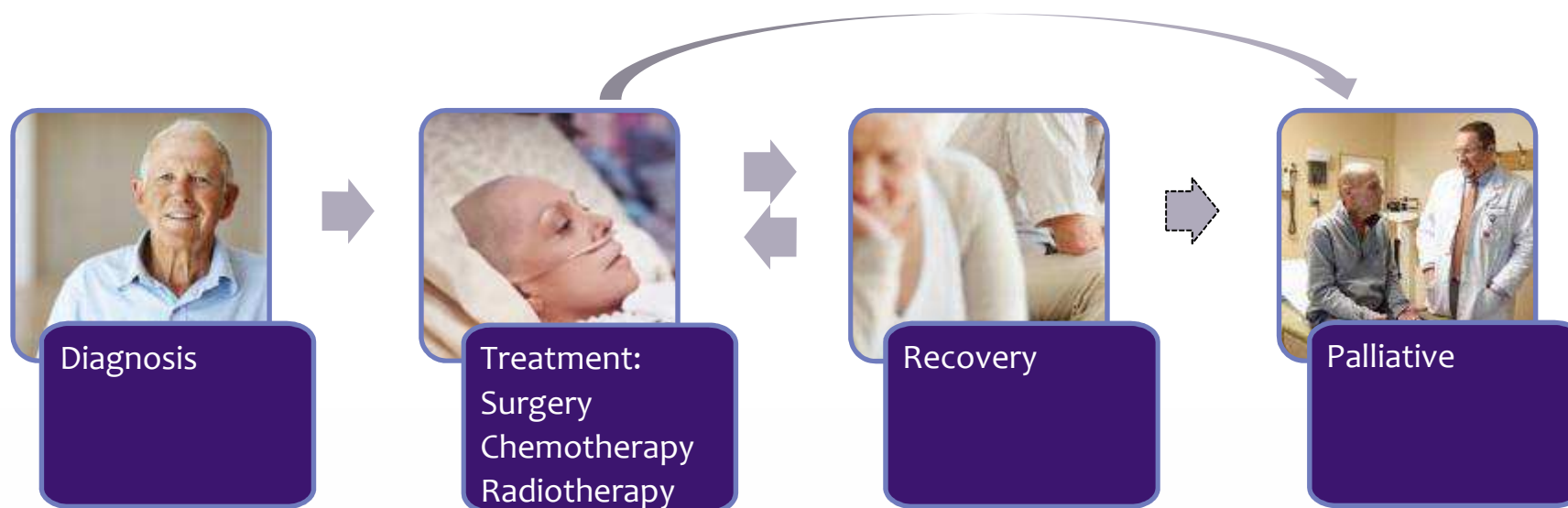


Increased dose-limiting toxicities during chemotherapy
(Prado, 2016)

“The most **clinically relevant** phenotypic feature of cancer cachexia is **muscle loss**, as this relates to **asthenia, fatigue, impaired physical function, reduced tolerance to treatment, impaired QOL and reduced survival.**” (Ryan, Prado, 2016)

BEST CARE IN ONCOLOGY

Recognizing that patients have different needs at the different stages of their journey



A PORTFOLIO OF PRODUCTS ADDRESSING THE NEEDS OF THE PATIENT AT THE DIFFERENT PHASE OF THEIR JOURNEY



NUTRICIA PRODUCTS ARE SUPPORTED BY CLINICAL EVIDENCE IN CANCER PATIENTS

Two phase randomised controlled clinical trial of postoperative oral dietary supplements in surgical patients

Gut 1997; 40: 393-399

A M Keele, M J Bray, P W Emery, H D Duncan, D B A Silk

Short term benefits of post-operative oral dietary supplements in surgical patients

Clinical Nutrition (1992) 11: 337-344
© Longman Group UK Ltd 1992

S. K. RANA, J. BRAY, N. MENZIES-GOW, J. JAMESON, J. J PAYNE JAMES, P. FROST and D. B. A. SILK



High energy



High energy
High protein



n-3 PUFA-enriched
Cancer-specific

Journal of Human Nutrition and Dietetics
An unblinded randomised controlled trial of preoperative oral supplements in colorectal cancer patients

S. T. Burden,*† J. Hill,‡ J. L. Shaffer,§ M. Campbell† & C. Todd† 2011 *J Hum Nutr Diet*

ORIGINAL ARTICLE

Support Care Cancer 2014

Preoperative nutritional support in cancer patients with no clinical signs of malnutrition—prospective randomized controlled trial

Pawel Kabata • Tomasz Jastrzębski • Michal Kąkol • Karolina Król • Maciej Bobowicz • Anna Kosowska • Janusz Jaskiewicz



Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: <http://www.elsevier.com/locate/cinu>

Original article

Muscle protein synthesis in cancer patients can be stimulated with a specially formulated medical food[☆]

Nicolaas E.P. Deutz^a, Ahmed Safar^b, Scott Schutzler^a, Robert Memelink^c, Arnv Ferrando^a, Horace Spencer^d, Ardy van Helvoort^c, Robert R. Wolfe^{a,*}

Clinical Nutrition 30 (2011) 759–768

Randomized control trials

Rapid EPA and DHA incorporation and reduced PGE₂ levels after one week intervention with a medical food in cancer patients receiving radiotherapy, a randomized trial

J. Faber^{a,b,*}, M. Berkhout^a, U. Fiedler^c, M. Avlar^d, B.J. Witteman^e, A.P. Vos^{a,b}, M. Henke^f, J. Garssen^{a,b}, A. van Helvoort^a, M.H. Otten^g, J. Arends^d

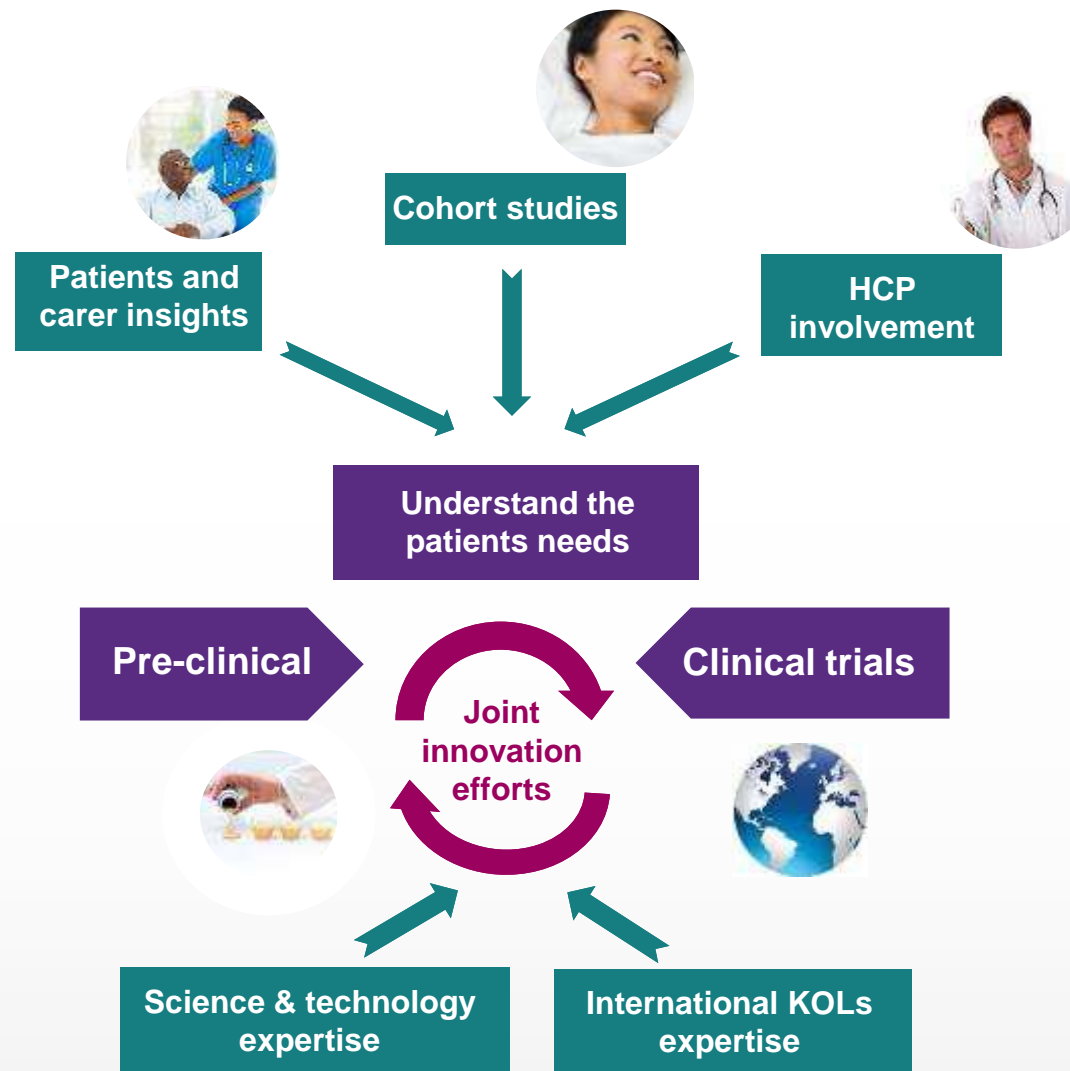
Clinical Nutrition 32 (2013) 338–345

Journal of Cachexia, Sarcopenia and Muscle (2015)
Published online in Wiley Online Library (wileyonlinelibrary.com) DOI: 10.1002/jcsm.12009

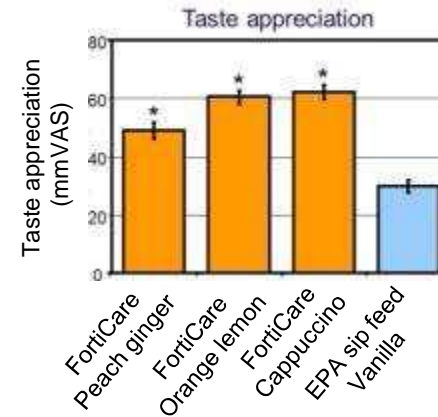
ORIGINAL ARTICLE

Improved body weight and performance status and reduced serum PGE₂ levels after nutritional intervention with a specific medical food in newly diagnosed patients with esophageal cancer or adenocarcinoma of the gastro-esophageal junction

OUR INTEGRATED INNOVATION PROCESS



INNOVATION TO IMPROVE PRODUCT EXPERIENCE AND BUILD PATIENT CONVENIENCE



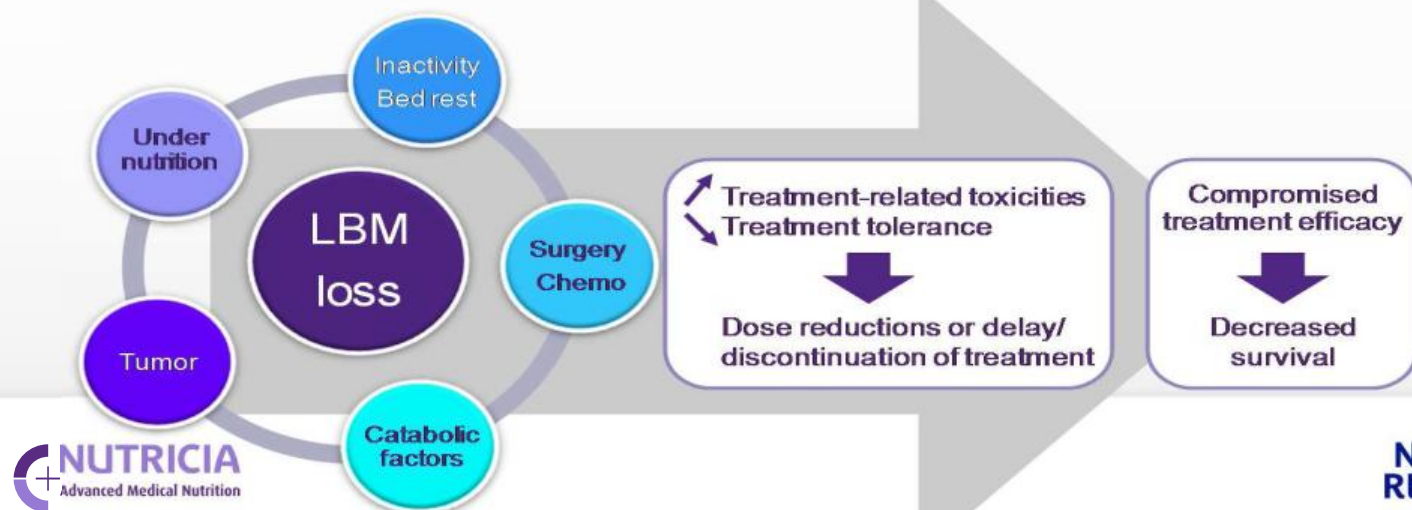
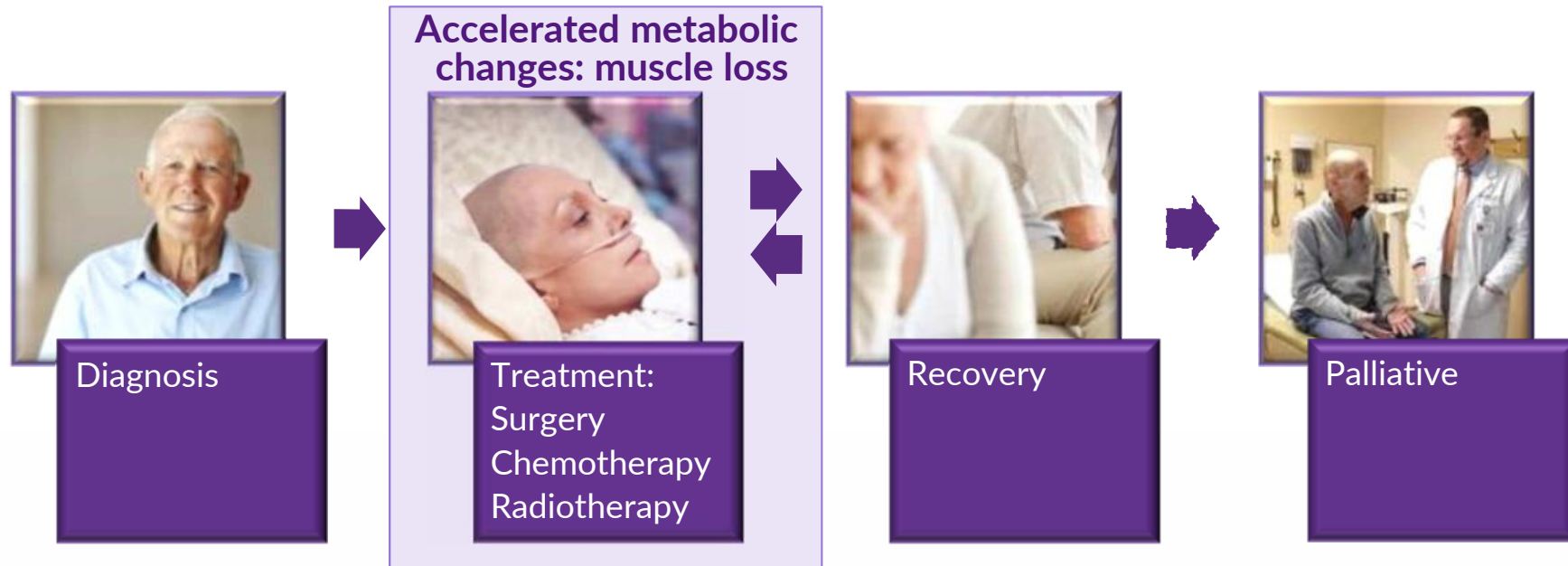
Appreciation
Specific flavours

Compacting
Smaller volume



Variety
Several flavours

MUSCLE MASS IS A PROGNOSTIC FACTOR FOR ENHANCE TREATMENT TOXICITIES AND REDUCED SURVIVAL



Nutricia Research ©



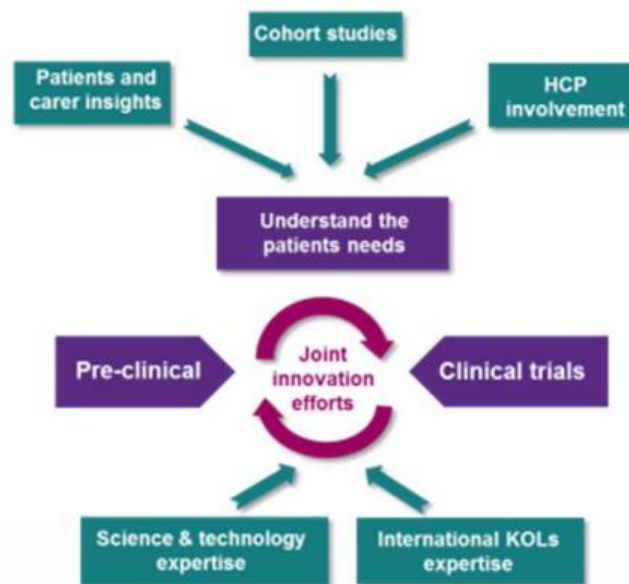
**DANONE
NUTRICIA
RESEARCH**

Rapid EPA and DHA incorporation and reduced PGE₂ levels after one week intervention with a medical food in cancer patients receiving radiotherapy, a randomized trial

J. Faber^{a,b,*}, M. Berkhout^a, U. Fiedler^c, M. Avlar^d, B.J. Witteman^e, A.P. Vos^{a,b}, M. Henke^f, J. Garssen^{a,b}, A. van Helvoort^a, M.H. Otten^g, J. Arends^d

Clinical Nutrition 32 (2013) 338–345

EVIDENCE GENERATION THROUGHOUT THE INNOVATION PROCESS



British Journal of Cancer (2014) 111, 1027–1034
© 2014 Cancer Research UK. All rights reserved 0959-9556/14 \$12.00
www.bjcr.com

Beneficial immune modulatory effects of a specific nutritional combination in a murine model for cancer cachexia

J Faber^{1,2*}, P Yui³, D Kogler⁴, K van Nieuwen⁵, JH Anglin⁶, A Lomax⁷, J Garces^{1,2} and A van Helvoort¹
¹Tumour Research – Center for Specialized Nutrition (Streeklabor voor Tumoren) Streeklabor, The Netherlands; ²Tumour Research Group
Research in Biogerontology, Department of Biogerontology, Biogerontology Research Center, University of Valencia, Spain; ³Department of Clinical Nutrition, University of
Groningen, Groningen, The Netherlands; ⁴Department of Pharmacology and Toxicology, University of Groningen, Groningen, The Netherlands; ⁵Department of Clinical Nutrition, University of
Groningen, Groningen, The Netherlands

Bacterial Translocation Is Reduced by a Specific Nutritional Combination in Mice with Chemotherapy-Induced Neutropenia^{1,2}

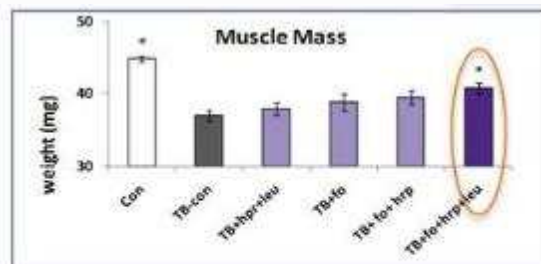
The Journal of Nutrition
Nutrition and Disease

Jesse Faber^{1,2*}, Kees van Lier³, Doreen Kogler⁴, Yvette Lohuis⁵, Johan Garces^{1,2},
Ade van Helvoort¹, Agnes Paul Van^{1,4} and Jan Kool¹

British Journal of Cancer (2015) 113, 717–722
© 2015 Cancer Research UK. All rights reserved 0959-9556/15 \$12.00
www.bjcr.com

Dietary supplementation with a specific combination of high protein, leucine, and fish oil improves muscle function and daily activity in tumour-bearing cachectic mice

K van Nieuwen^{1,2,3*}, D Kogler⁴, JH Anglin⁵, Y Lohuis⁶, M Gerschlager⁷, A Lomax⁸, K Arts⁹, J Faber¹, H Jansen¹,
BPI van der BEEK¹ and A van Helvoort¹



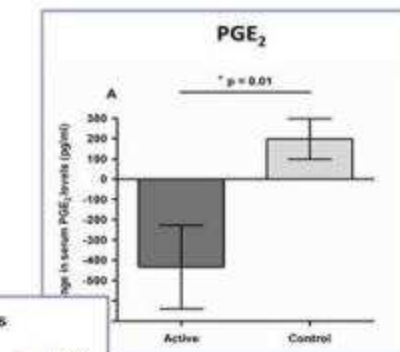
Leucine + EPA +DHA for gain in muscle mass

Journal of Cachexia, Sarcopenia and Muscle
In Association with the Society on Sarcopenia, Cachexia and Wasting Disorders

2015, 6: 32–44

Improved body weight and performance status and reduced serum PGE₂ levels after nutritional intervention with a specific medical food in newly diagnosed patients with esophageal cancer or adenocarcinoma of the gastro-esophageal junction

Jesse Faber^{1,2*}, Madelon J. Lohuis³, Madelon Spierdijk⁴, Sabine van den Broek⁵, Paul Van⁶,
Markus Berkhof⁷, Cor Lamers⁸, Hans Koster⁹, Hugo Thijssen¹⁰, Peter Smeets¹¹, Ade van Helvoort¹
& Ans van der Gaag¹

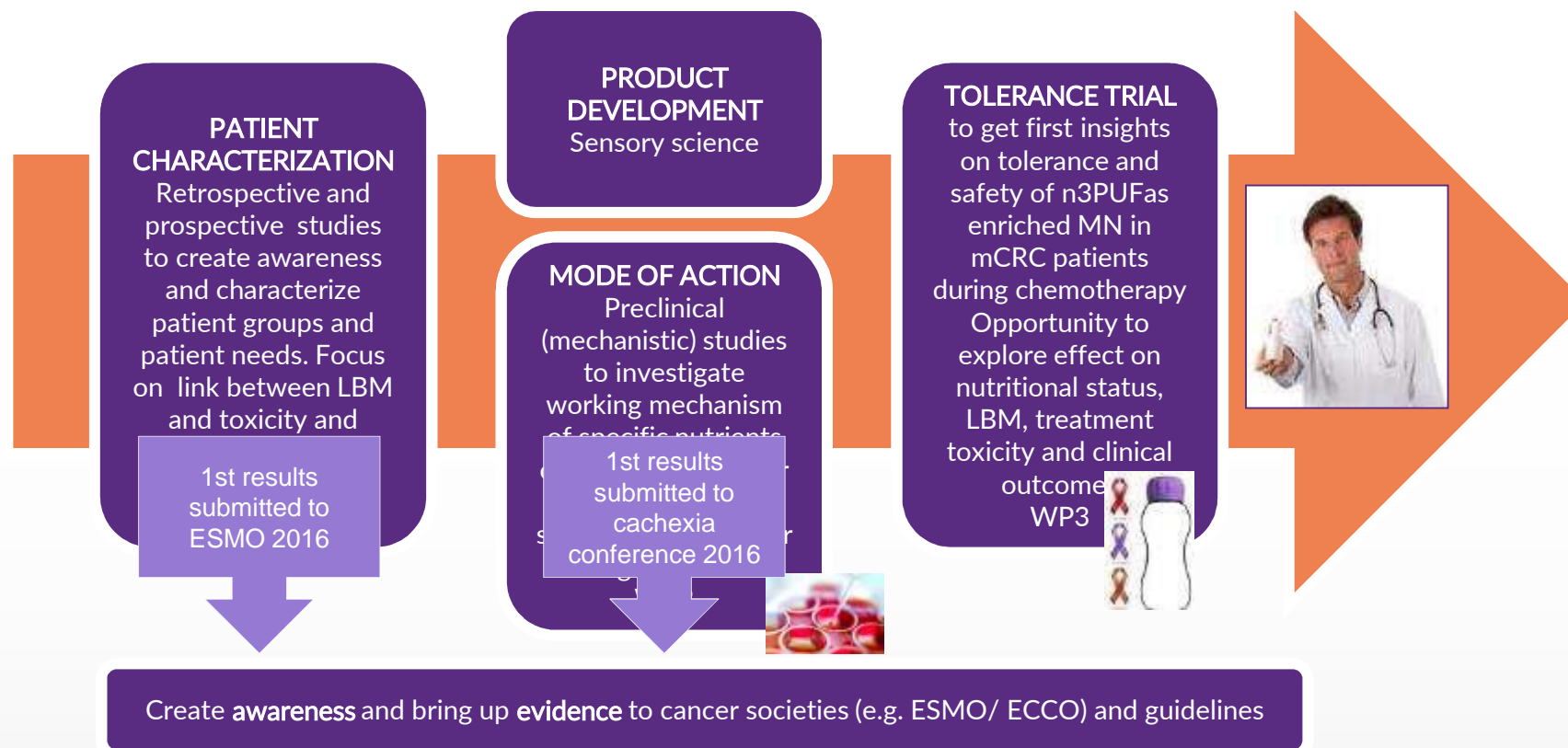


Reduced inflammation and improved bodyweight and performance status in cancer patients

NUTRICIA
Advanced Medical Nutrition

SUBSIDIZED STRATEGIC UTRECHT LIFE SCIENCE COLL. PATIENT CHARACTERIZATION AND EVIDENCE GENERATION DURING CHEMOTHERAPY

Key steps on the road to the oncologist...build on evidence



INTERNATIONAL NETWORK OF EXPERTS



PAEDIATRIC CARE ALLERGY



ALLERGY PREVALENCE: COW'S MILK ALLERGY IS THE MOST COMMON FOOD ALLERGY IN INFANTS

Epidemiology

- Prevalence of Cow's Milk Allergy is ~2-5%
- Onset virtually almost all in the 1st year of life
- Late onset reactions in CMA are often under diagnosed

Fiocchi et al 2010; Gupta et al 2012; Prescott et al 2013; Schoemaker et al 2015

CLINICAL PICTURE OF COW'S MILK ALLERGY IS COMPLEX AND MIGHT BE EVOLVING OVER TIME

Diverse clinical manifestations & related conditions

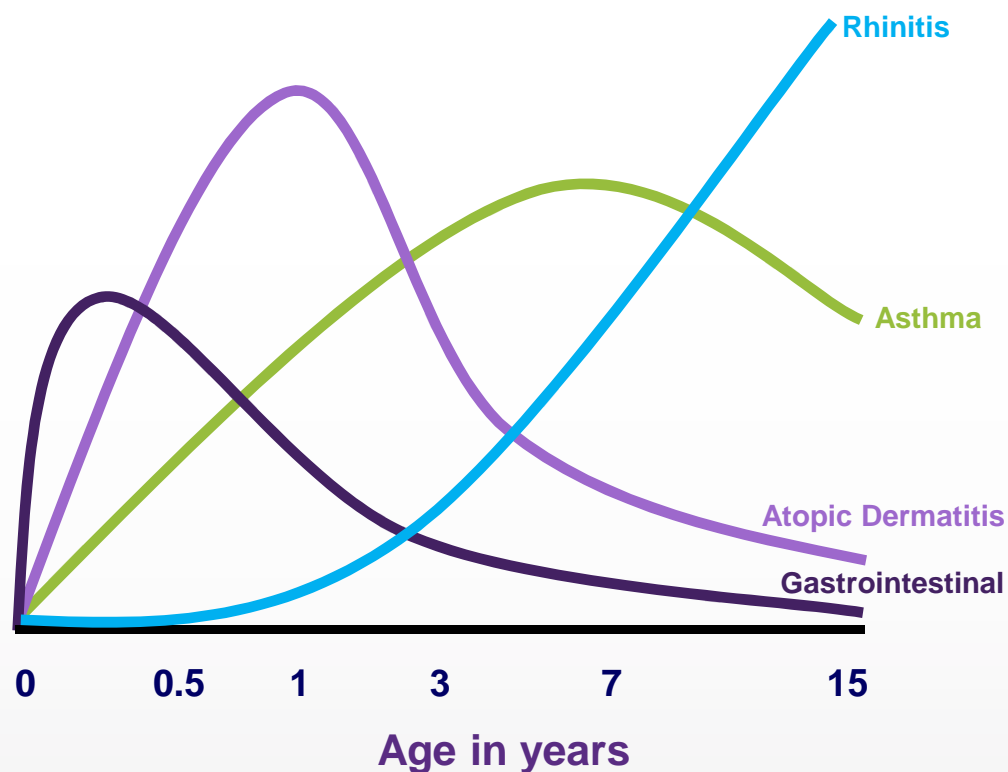


Prognosis

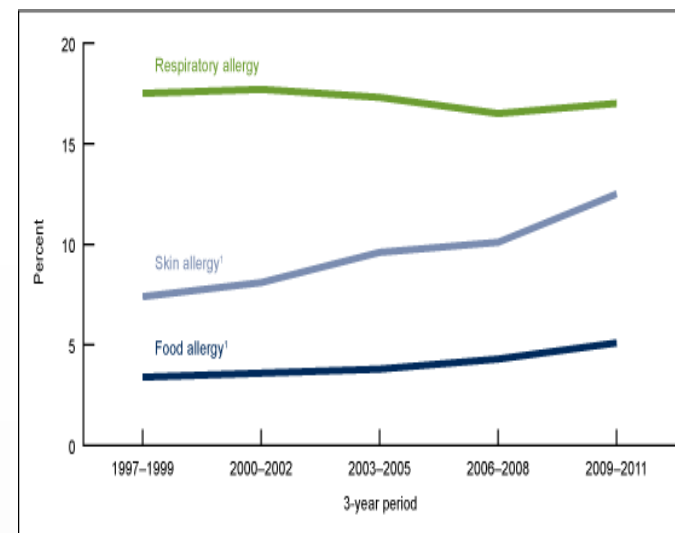
- 1 year – 50% acquire tolerance
- 3 years – 85% acquire tolerance

FOOD ALLERGY PREDISPOSES AN INDIVIDUAL TO OTHER ALLERGIES LATER IN LIFE

‘Allergic March’



‘March of Allergies’



The prevalence of food and skin allergies increased in children aged 0–17 years from 1997–2011.

CDC / NCHS 2013

DIETARY MANAGEMENT OF CMA IS BASED ON COW'S MILK ELIMINATION



NEOCATE RANGE IS ADAPTED TO DIFFERENT NEEDS



Infants



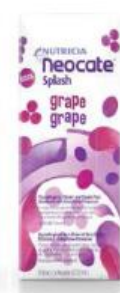
Children



Teenagers



Dietary management of CMA & multiple food protein allergies




> 70 STUDIES DEMONSTRATE NEOCATE ASSURES FAST SYMPTOM RESOLUTION & SUPPORTS GROWTH

Neocate








SUPPORTED BY
MORE THAN
30 YEARS OF
SCIENTIFIC
RESEARCH

30
YEARS
OF EXPERTISE

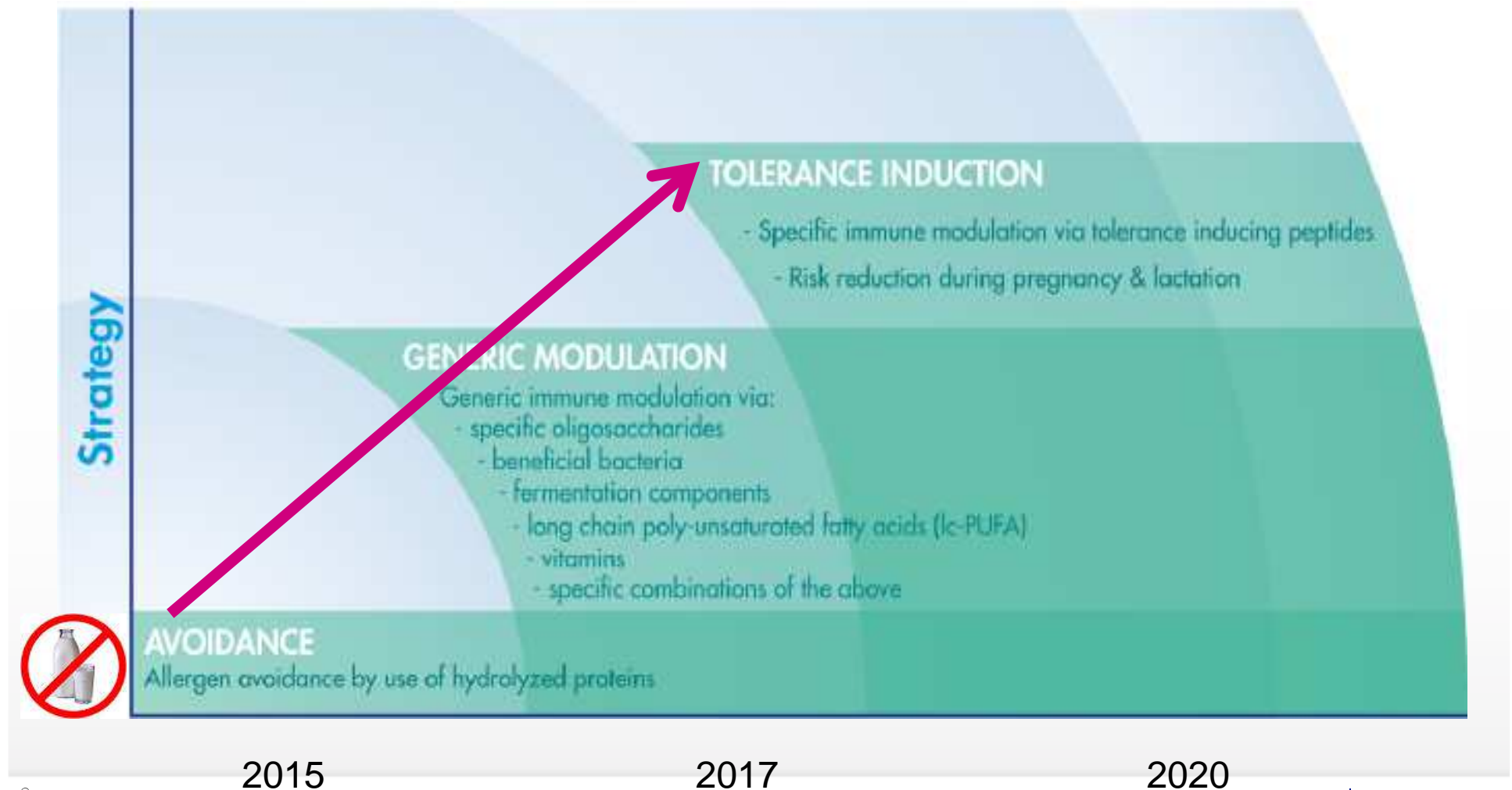


NUTRICIA
neocate

ExpertCare

-  Cow's Milk Allergy (CMA)
-  Multiple Food Allergy (MFA)
-  Atopic Dermatitis (AD)
-  Gastro-Oesophageal Reflux/Disease (GOR/D)
-  Eosinophilic Esophagitis (EoE)
-  Short Bowel Syndrome (SBS)
-  Other Gastrointestinal (GI) conditions

GROWING PREVALENCE OF ALLERGIES CALLS FOR INTERVENTIONS SUPPORTING TOLERANCE DEVELOPMENT



GUT MICROBIOTA PLAY AN IMPORTANT ROLE IN TOLERANCE DEVELOPMENT AND ALLERGY

Gut microbiota in allergic infants is altered vs. healthy infants:
↓ *Bifidobacteria*, ↑ “adult” species

Husby 2000; Kalliomaki, 2001, 2003; Ouwehand, 2001, Smehilova 2008, Thompson-Chagoyan, 2010, Bisgaard 2011, Abrahamsson 2012; Nyland 2013

Pre- and / or probiotics reduce the development of allergic manifestations

Isolauri 2000; Boehm, 2004; Kukkonen 2007, 2008; Arslanoglu 2008; Van Hoffen 2009; Van der Aa, 2010, 2011

Exposure to micro-organisms and their metabolites shapes immune function

Majamaa & Isolauri 1997; Kirjavainen & Gibson, 1999; Isolauri 2001; Gorbach 2002; Marteu & Shanahan 2003; Mercenier 2003; Boehm 2004; Viljanen 2005, Weston 2005; Sitek 2006, EAT study 2106



NEOCATE WITH SYNBIOTIC AIMS AT ALLERGEN ELIMINATION AND ACTIVE CMA MANAGEMENT

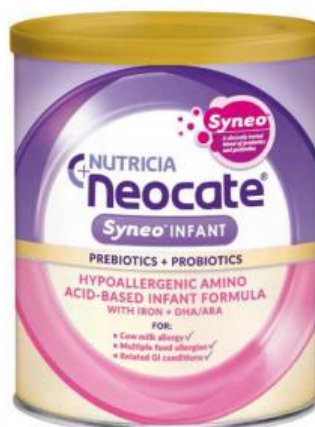
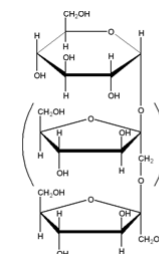
maximal allergen elimination



support tolerance development

- Hypoallergenic formula
- 100% amino acids
- 0-12 months
- with LCP

- sc-FOS / lc-FOS (9:1 ratio)
- 0.63g / 100 ml
- no GOS, to avoid CMP contamination

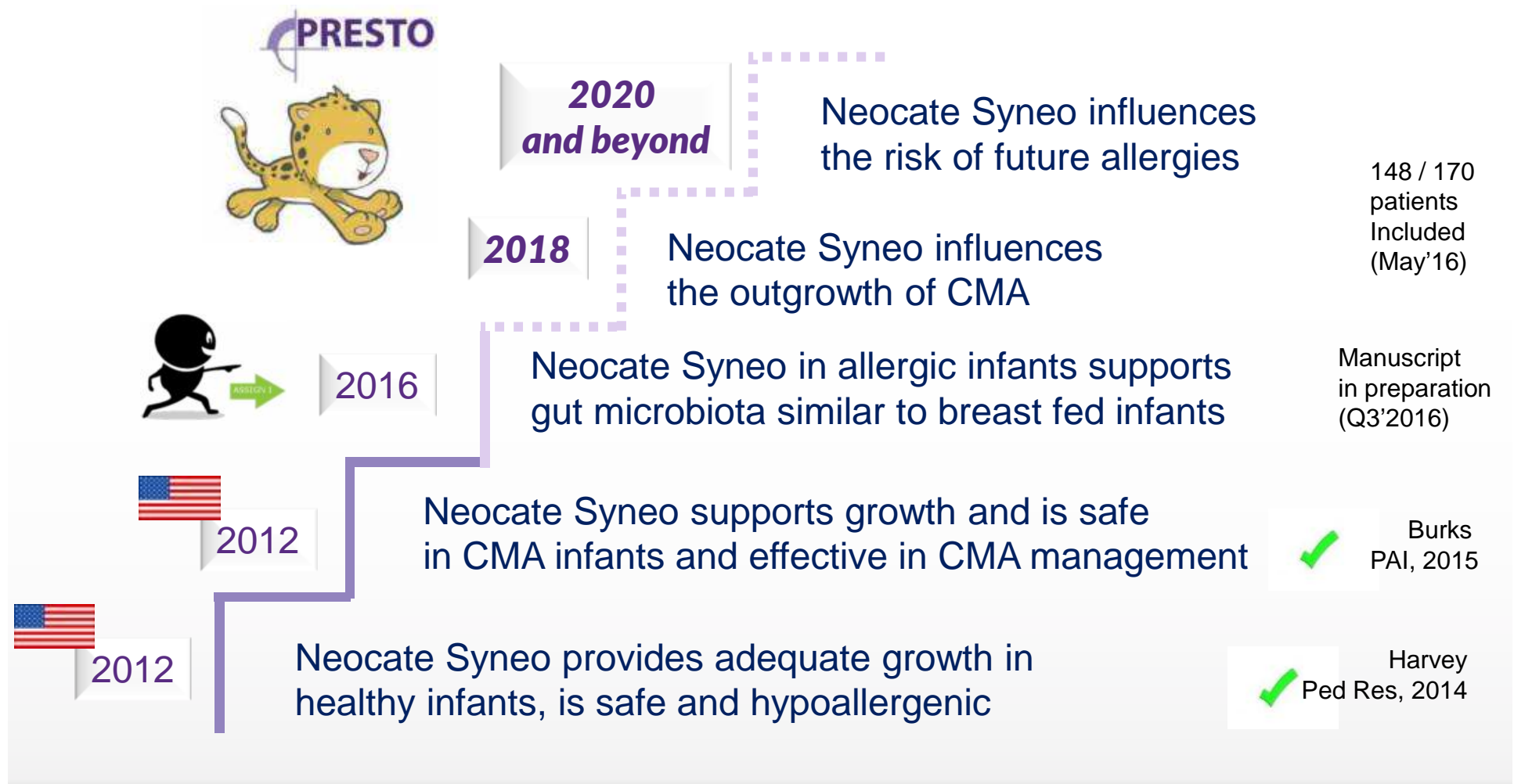


Bifidobacterium breve
M-16V 10⁸ CFU/g
powder

processed in a milk-free environment



NEOCATE WITH SYNBIOTIC: EVIDENCE PROGRAM





NEOCATE WITH SYNBIOTICS: MORE TO COME..

PRESTO TRIAL IN IGE MEDIATED CMA

Primary outcomes:

Tolerance to cow's milk (DBPCFC) 12 months

Other outcomes:

Tolerance to cow's milk (DBPCFC) 24 & 36 months

Incidence other allergies

...

**.. TO IMPROVE LONG TERM HEALTH OUTCOMES
IN INFANTS WITH CMP & MFP ALLERGY**





Thank you
Any questions?

.....