# Medical Nutrition Therapy in Cancer Patients Basic to Frontier in Onconutrition

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## Outlines

- Cancer Cachexia and Metabolic Alteration
- Medical Nutrition Therapy (MNT) in Cancer Patients
  - Energy and Protein Requirement
- Immunonutrients
  - Omega-3 fatty acids, Arginine, Glutamine
- Cancer Prevention

Data from World Cancer Research Fund (WCRF)

• Frontier Onconutrition

# Weight Loss and Malnutrition among Cancer Treatment

**Diagnose** Loss of weight and muscle

**50%** 

of cancer patients have some Nutrition deficit prior to diagnosis Treatment

Continued loss of weight and muscle

**85%** 

of patients experience malnutrition and weight loss at some point during cancer treatment Cachexia Distinct Metabolic Change

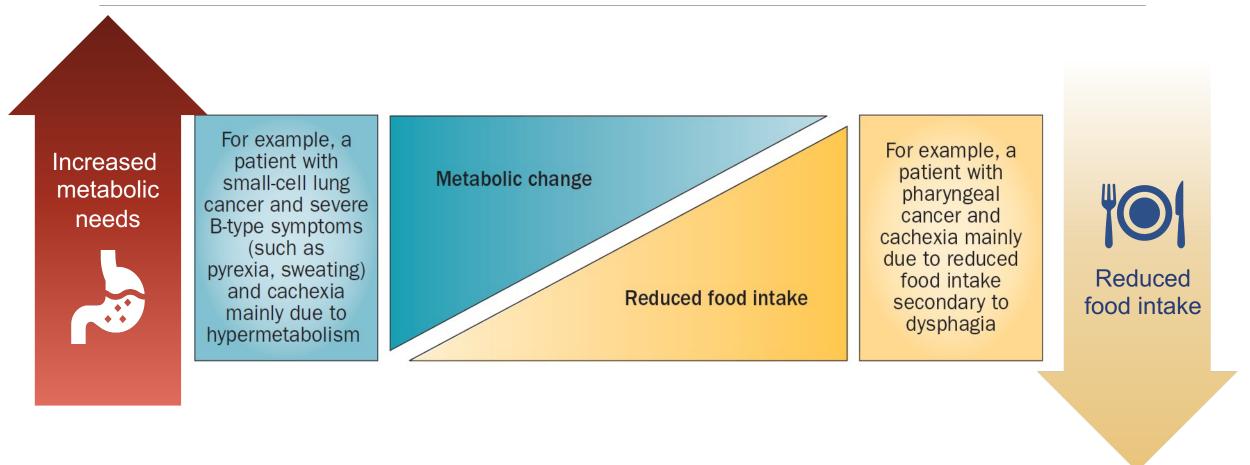
### **50%**

of all patients with cancer eventually develop a syndrome of cachexia

Halpern-Silveria D, et al. Support Care Cancer. 2010;18:617-625 2. Dewys WD, et al. AM J Med. 1980;(4):491-497
 3. Laviano A, et al. Nutrition. 1996;12;358-371 4. Aoyagi T, et al. World journal of gastrointestinal oncology. 2015 Apr 15;7(4):17.

# Metabolic Alteration during Cancer Cachexia

### Metabolic Change during Cancer Cachexia

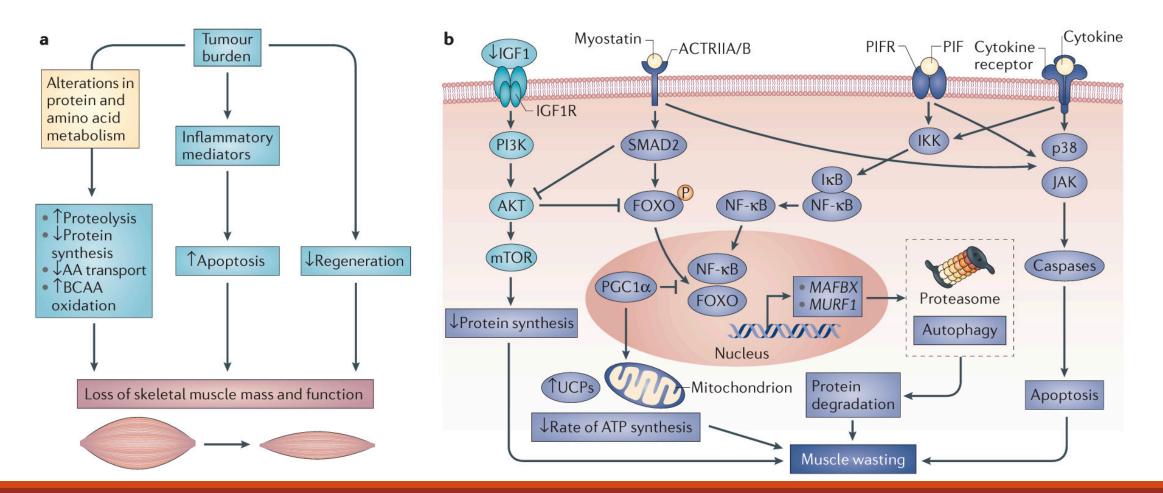


Fearon, K. et al .Understanding the mechanisms and treatment options in cancer cachexia. Nat. Rev. Clin. Oncol. 10, 90–99 (2013)

### **Metabolic change during Starvation and Cancer Cachexia**

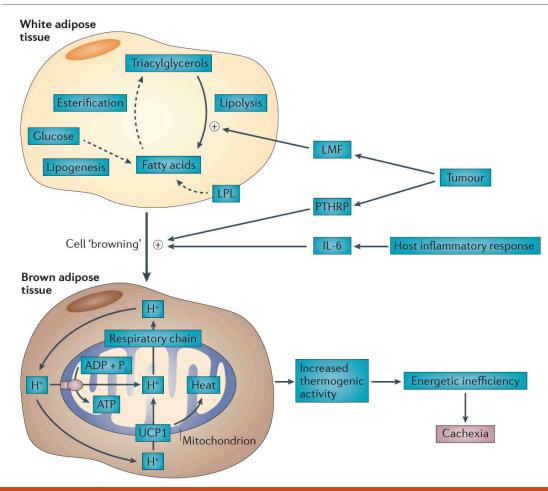
Physiologic characteristic	none	vation-rela inflamma pometabo	ation,	on, with inflammation		ation,
Metabolic rate		$\checkmark$			$\uparrow$	
Cytokines, Catecholamine, Glucagon, Cortisol		$\checkmark$			1	
Gluconeogenesis		$\checkmark$		7	$\uparrow$	
Proteolysis		$\checkmark$			$\uparrow\uparrow$	
Protein turn over		$\checkmark$			$\uparrow$	J
Fat catabolism		$\uparrow$			$\uparrow\uparrow$	
Albumin		Normal		Decre	ase, Eden	natous
Adaptation to starvation		Normal		Abnormal		

### Alterations in Metabolic Pathways and Intracellular Signals of Muscle Wasting

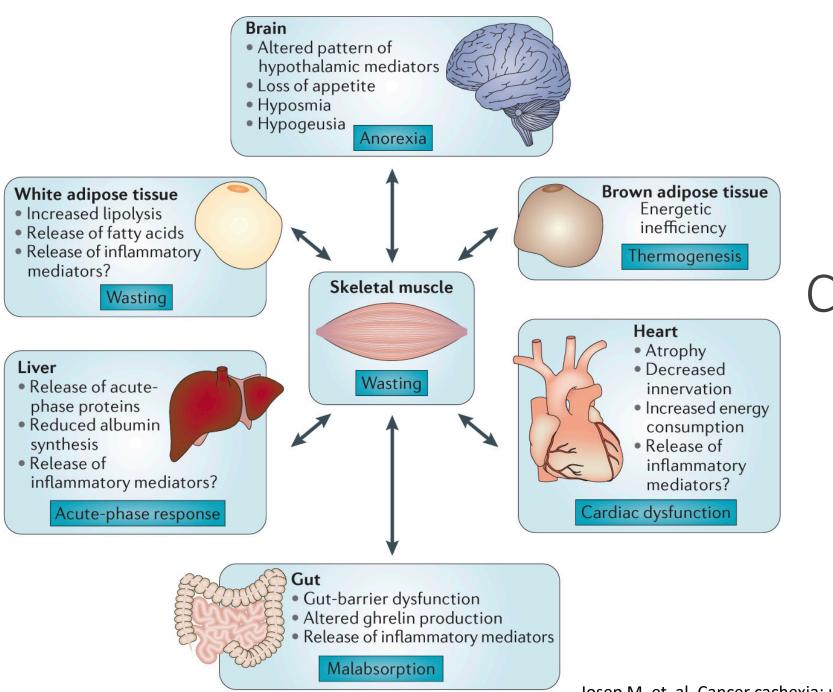


Josep M. et al. Cancer cachexia: understanding the molecular basis. Nat Rev Cancer. 2014

## Alterations in Metabolic Pathways in Adipocyte and Browning Adipose Effect



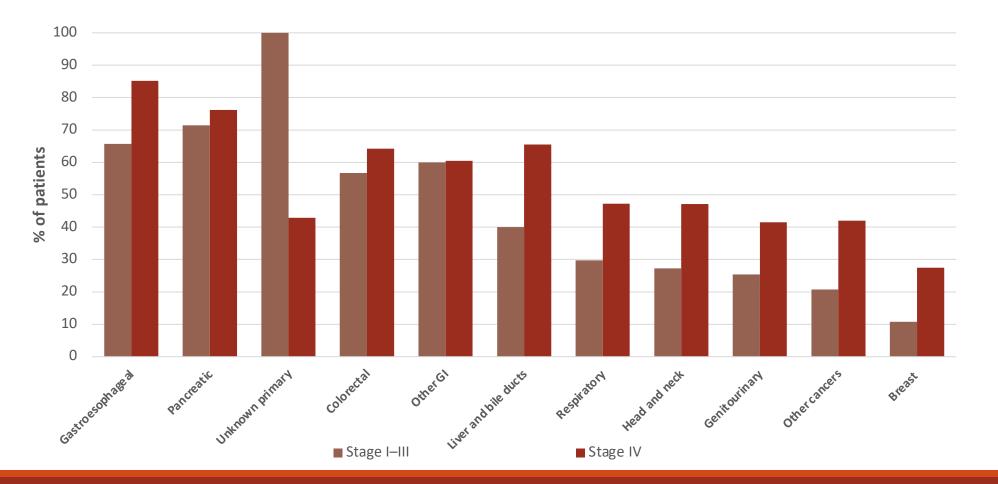
- Lipid Mobilizing Factor (LMF)
  - Adipose tissue wasting
  - Increase lipolysis
  - Decrease LPL activity
- Inflammatory Response
  - Browning adipose tissue
  - Promote UCP1
  - Heat production
  - Energetic inefficiency



### Cachexia Syndrome

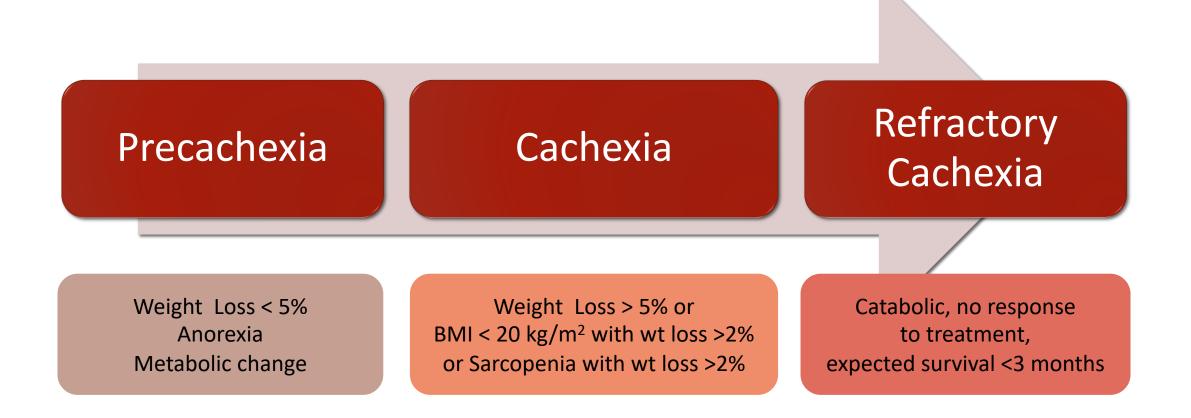
Josep M. et al. Cancer cachexia: understanding the molecular basis. Nat Rev Cancer. 2014

### Prevalence of Cachexia by Cancer Site and Stage



Maurizio Muscaritoli. et al. Prevalence of malnutrition in patients at first medical oncology visit: the PreMiO study. Oncotarget. 2017

### Cancer Cachexia Staging



J.Arend. et al. ESPEN expert group recommendations for against cancer-related malnutrition. Clin Nutr.2017

# Consequences of Malnutrition and Cancer Cachexia

Impaired Quality of Life, Decreased Muscle Function and Reduced Performance Status

Reduces Response to Chemotherapy, Increase CMT Toxicity

Impaired Immune Competence

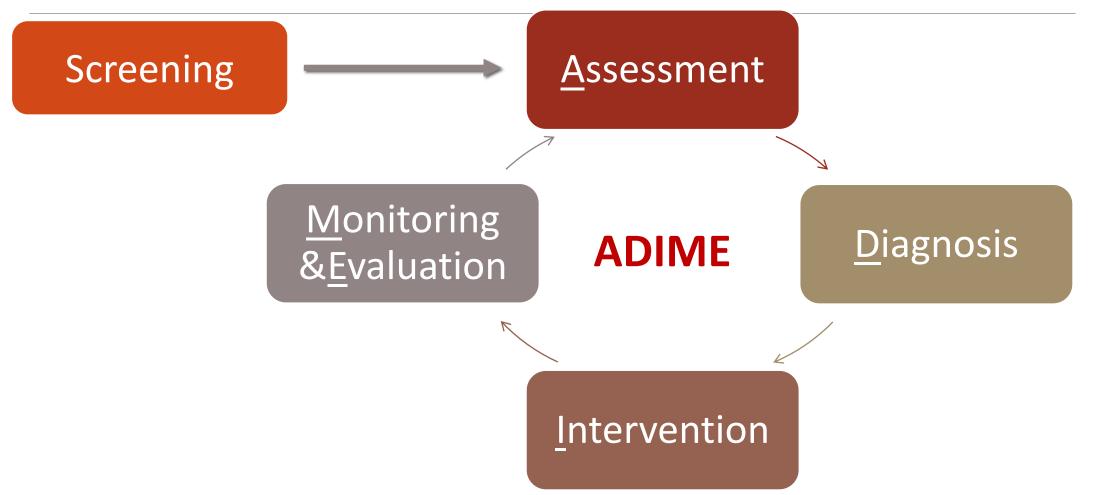
Increase Risks of Post-operative Complication

Longer Hospital Stay, and Increased Health Care Costs

**Decrease Free Survival** 

## Medical Nutrition Therapy for Cancer Patients

## Nutrition Care Process



Nutrition Care Process and Model Update: Toward Realizing People-Centered Care and Outcomes Management. J Acad Nutr Diet. Oct 2017

### Nutrition Screening

### แบบคัดกรองภาวะโภชนาการ

### สมาคมผู้ให้อาหารทางหลอดเลือดดำและทางเดินอาหารแห่งประเทศไทย

#### (SPENT Nutrition Screening Tool)

หัวข้อการคัดกรอง		ครั้งที่ 1 วันที่		ครั้งที่ 2 วันที่		ครั้งที่ 3 วันที่	
	ใช่	ไม่ใช่	ใช่	ไม่ใช่	ใช่	ไม่ใช่	
1. ผู้ป่วยมีน้ำหนักตัวลดลง โดยไม่ได้ตั้งใจในช่วง 6 เดือนที่ผ่านมาหรือไม่							
2. ผู้ป่วยได้รับอาหารน้อยกว่าที่เคยได้ (> 7 วัน)							
3. BMI < 18.5 หรือ ≥ 25.0 กก./ตร.ม. หรือไม่							
4. ผู้ป่วยมีภาวะโรควิกฤต หรือกึ่งวิกฤตร่วมด้วยหรือไม่							
ผู้คัดกรอง							

#### ผลการคัดกรอง

🔲 ถ้าตอบ ใช่ ≥ 2 ข้อ ทำการประเมินภาวะโภชนาการต่อ หรือปรึกษานักกำหนดอาหาร/ทีมโภชนบำบัด

🖵 ถ้าตอบ ใช่ < 1 ข้อ ให้คัดกรอง <u>ซ้ำสัปดาห์ละ 1 ครั้ง</u> ในช่วงที่อยู่โรงพยาบาล

### Nutrition Assessment

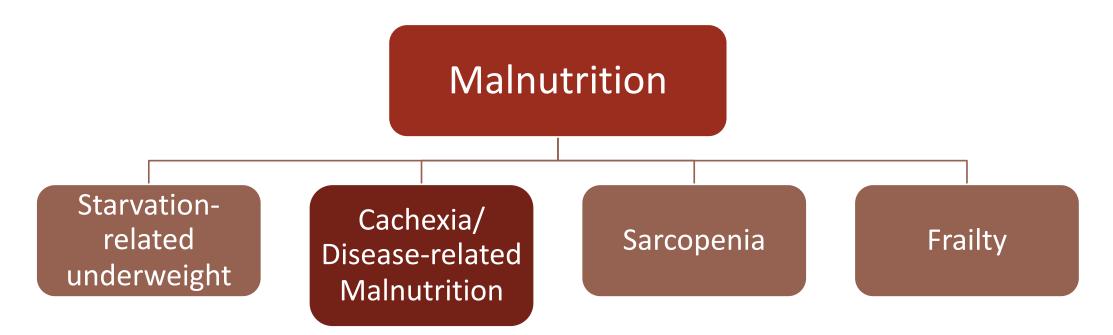
- A: Anthropometry
  - B: Biochemistry
  - C: Clinical Signs
  - D: Dietary Assessment
- Nutrition Assessment Tools
  - Nutrition Triage (NT)
  - Nutrition Alert Form (NAF)
  - Patient-generated Subjective Global Assessment (PG-SGA)

# Patient-generated Subjective Global Assessment (PG-SGA)

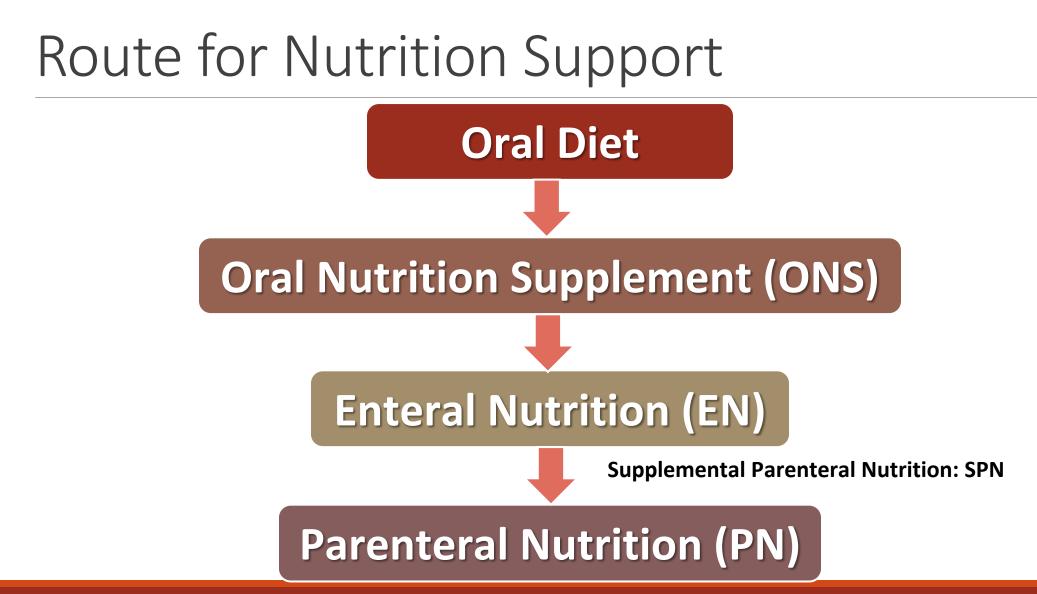
Scored Patient-Generated Subjective Global As กรอบที่ 1-4 สำหรับผู้ป่วยเป็นผู้กรอกข้อมูล [กรอบที่ 1-4 เป็น PG-SGA ฉบับย่อ]	sessment (PG-SGA)  ອ້ອມູລຜູ້ປ່ວຍ
<ol> <li>น้ำหนักตัว (ดูแผ่นงาบที่ 1) สรุปน้ำหนักด้วปัจจุบัน และน้ำหนักด้วล่าสุดของฉัน: ปัจจุบันฉันมีน้ำหนักด้วประมาณ กิโลกรัม ฉันสูงประมาณ เขนติเมตร</li> <li>เดือนก่อนฉันมีน้ำหนักประมาณ กิโลกรัม</li> <li>เดือนก่อนฉันมีน้ำหนักประมาณ กิโลกรัม</li> <li>เดือนก่อนฉันมีน้ำหนักประมาณ กิโลกรัม</li> <li>เดือนก่อนฉันมีน้ำหนักประมาณ กิโลกรัม</li> <li>ระหว่าง 2 สัปดาห์ที่ผ่านมา น้ำหนักของฉัน : <ul> <li>ฉิลดลง (1)</li> <li>ไม่เปลี่ยนแปลง (0)</li> <li>เพิ่มซื้น (0)</li> </ul> </li> <li>คะแนนรวมของกรอบที่ 1</li> <li>3. อาการ: ระหว่าง 2 สัปดาห์ที่ผ่านมา ฉันรับประทานอาหารได้ไม่เพียงพอ เนื่องจากฉันมีปัญหาดังต่อไปนี้ (เลือกได้มากกว่า 1 ข้อ)</li> </ol>	<ul> <li>2. การรับประทานอาหาร: เมื่อเปรียบเทียบกับการรับประทานอาหารตามปกติของฉัน ฉันคิดว่าในช่วง 1 เดือนที่ผ่านมา การรับประทานอาหารของฉัน         <ul> <li>ไม่เปลี่ยนแปลง (0)</li> <li>เพิ่มขึ้นกว่าปกติ (0)</li> <li>น้อยกว่าปกติ (1)</li> <li>ปัจจุบันฉันรับประทาน</li> <li>อาหารตามปกติ แต่บริมาณน้อยกว่าเดิม (1)</li> <li>อาหารตามปกติ แต่บริมาณน้อยกว่าเดิม (1)</li> <li>อาหารตามปกติ แต่บริมาณน้อยกว่าเดิมมาก (2)</li> <li>เฉพาะอาหารเหลวเท่านั้น (3)</li> <li>เฉพาะอาหารเสริมทางการแพทย์เท่านั้น (3)</li> <li>แทบไม่รับประทานอะไรเลย (4)</li> <li>ได้รับอาหารทางสายให้อาหาร หรือได้รับอาหารทางหลอดเลือดดำ (0)</li> </ul> </li> </ul>
<ul> <li>ไม่มีปัญหาในการรับประทานอาหาร (0)</li> <li>อาเจียน (3)</li> <li>เบื่ออาหาร,ไม่อยากรับประทานอาหาร (3)</li> <li>ท้องเสีย (3)</li> <li>คลื่นใส้ (1)</li> <li>ปากแห้ง (1)</li> <li>ท้องมูก (1)</li> <li>เห็บและบินซ่องปาก (2)</li> <li>อิ่มเร็ว (1)</li> <li>การรับรสเปลี่ยนหรือไม่รู้รส (1)</li> <li>อ่อนเพลีย (1)</li> <li>มีปัญหาการกลืน (2)</li> <li>ปวด; บริเวณ ? (3)</li> <li>อื่นๆ(1)**</li> <li>**ตัวอย่างเช่น ซึมเศร้า, ปัญหาทางการเงิน, หรือปัญหาสุขภาพฟัน</li> <li>คะแนนรวมของกรอบที่ 3</li> </ul>	<ul> <li>4. กิจกรรมต่างๆ และการทำงานของร่างกาย:</li> <li>ในช่วง 1 เดือนที่ผ่านมา ฉันทำกิจกรรมต่างๆได้ในระดับ</li> <li>ปกติ ไม่มีข้อจำกัด (0)</li> <li>ไม่เป็นปกติ แต่ยังสามารถทำกิจกรรมได้ใกล้เคียงกับปกติ (1)</li> <li>ไม่รู้สึกอยากทำอะไร อยู่บนเตียงหรือนั่งเก้ายี้ในช่วงเวลาน้อยกว่าครึ่งวัน (2)</li> <li>ทำกิจกรรมได้เพียงเล็กน้อย และใช้เวลาส่วนใหญ่ของวันอยู่บนเตียงหรือเก้าอี้ (3)</li> <li>ส่วนใหญ่จะนอนติดเดียง อยู่บนเตียงเกือบทั้งวัน (3)</li> </ul>

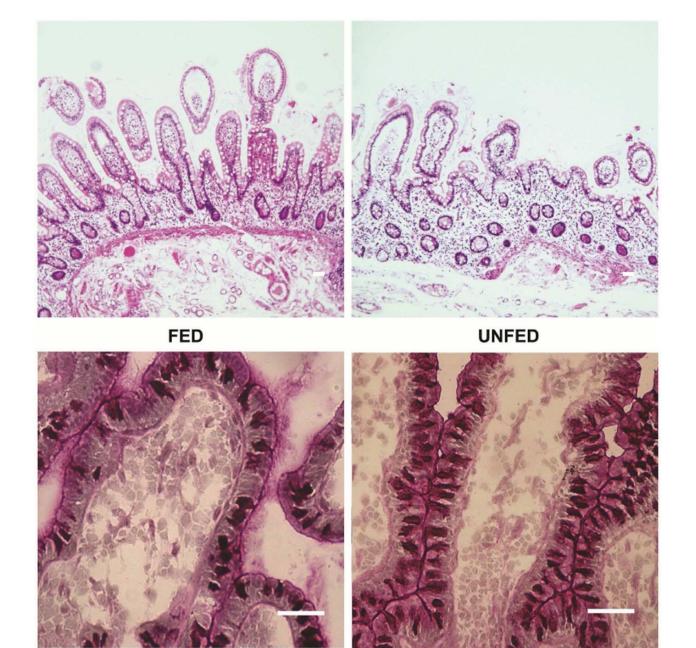
ร่านที่เหลือของแบบประเมินนี้กระกโดแนหหล่ พยาบาล นักกำหนดอาหาร หรือบุคลากรหางแพพย์อื่น ขอขอบคุณ ©FD Ottery 2005, 2006, 2015 v 3.22.15 Thailand 16-010 v07.09.17 email. faithetteryundpuldeal.com or info@nt.slobal.org

### Nutrition Diagnosis



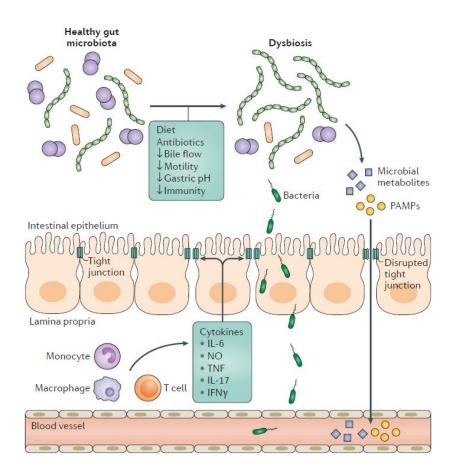
T. Cederholm. et al. ESPEN endorsed recommendation: Diagnostic criteria for malnutrition. Clin Nutr.2015





Matthew Ralls.et al. Enteral nutrition deprivation in patients leads to a loss of intestinal epithelial barrier function. Surgery. 2015

### Benefits of Enteral Nutrition



### Non-calorie protein Benefits of EN

- Increase GALT & MALT
   Increase Immunity response
- Increase Incretin Hormones help better glycemic control
- Increase Villi Proliferation
- Decrease Gut Permeability
- Decrease Bacterial Translocation

GALT : gut-associated lymphoid tissue MALT: mucosa-associated lymphoid tissue

## Indications and Contraindications of Enteral Nutrition

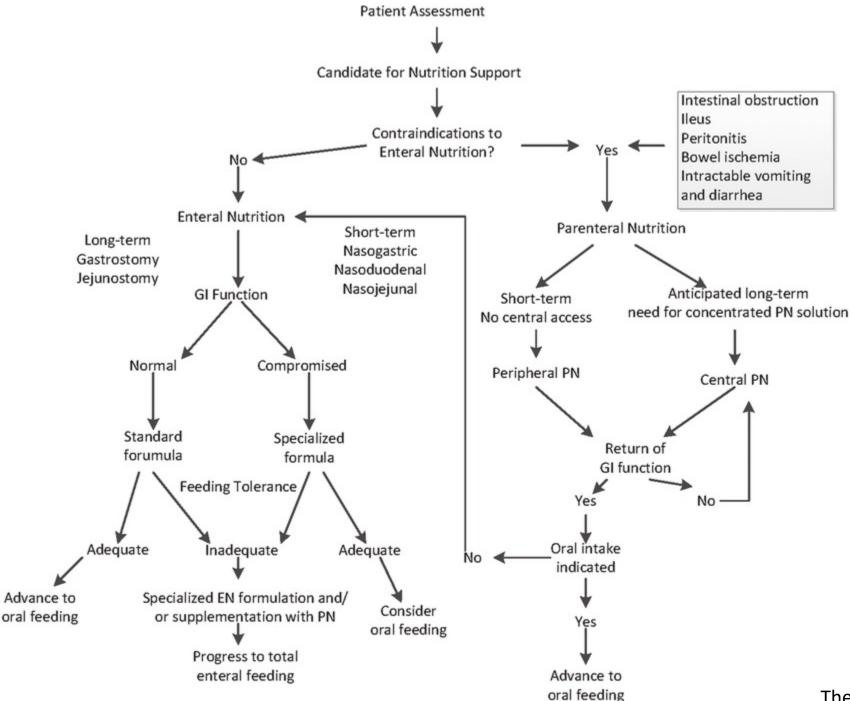
### Indications

Indications of EN should meet all these criteria

- Malnutrition patients or risks of malnourished in moderate to severe stage
- Inadequate oral intake or suspected inadequate < 60% of requirement >7 days
- Stable of hemodynamic and vital sign status
- Not in the end of life care
- Enteral Nutrition can be initiate after 24 -48 hours after hemodynamic was stable and without contraindications

### Contraindications

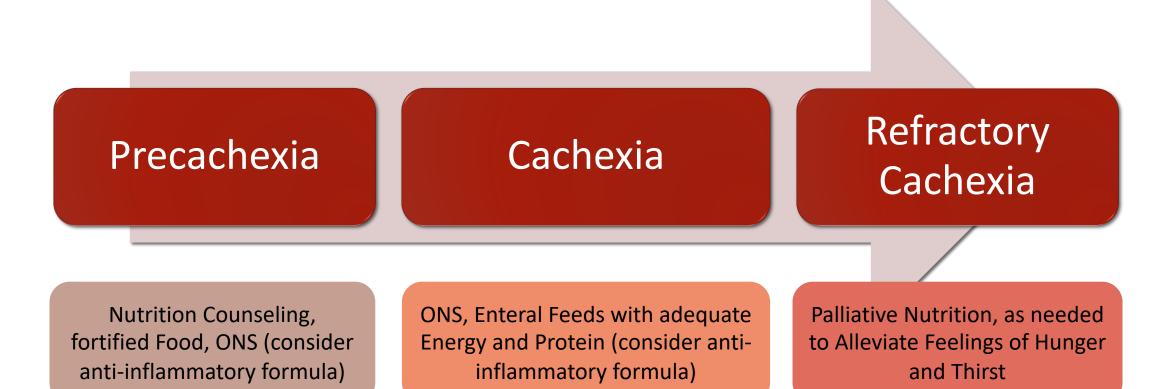
- Severe short-bowel syndrome (remaining small bowel <100-150 cm without colon or remaining small bowel <50-70 cm with presence of colon )</li>
- Other severe malabsorption conditions
- Severe GI bleed
- Distal high-output fistulas
- Paralytic ileus
- Intractable vomiting/diarrhea refractory to medical management
- Inoperative mechanical GI obstruction
- Inability to gain access to GI tract



Algorithm of Nutrition Support

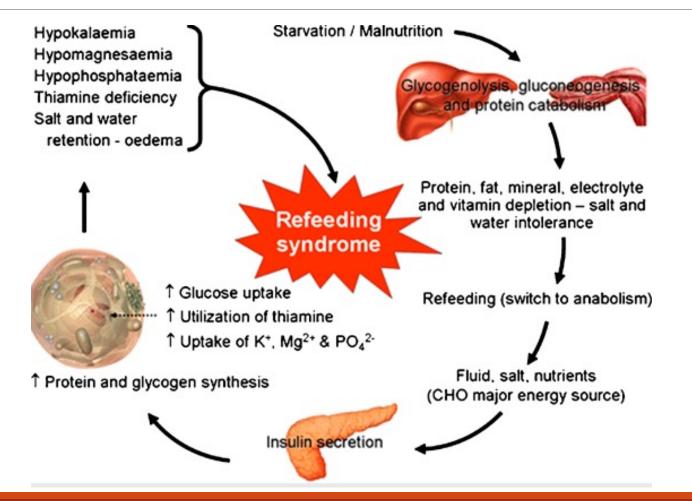
#### The ASPEN Adult Nutrition Support Core Curriculum

### Nutrition Intervention during Cancer Stage



J.Arend. et al. ESPEN expert group recommendations for against cancer-related malnutrition. Clin Nutr.2017

### **Refeeding Syndrome**



Z Stanga. et al. Nutrition in clinical practice-the refeeding syndrome illustrative cases and guidelines for prevention and treatment. Eur J Clin Nutr. 2007

### **Criteria for determining risks of Refeeding Syndrome (RFS)**

Minor risk factors	Major risk factors	Specific patient populations at high risk		
BMI < 18.5 kg/m <sup>2</sup>	BMI < 16 kg/m <sup>2</sup>	Hunger strike Chronic severe dieting		
Unintentional weight loss > 10% in past 3-6 mo	Unintentional weight loss > 15% in past 3-6 mo	History of bariatric surgery Short bowel syndrome		
Little or no nutritional intake for >5 d	Little or no nutritional intake for >10 d	Ture on wetiente		
History of alcohol abuse or drugs including insulin, chemotherapy, antacids, or diuretics	Low baseline level of potassium (K), Phosphate (P), or magnesium (Mg) before feeding	Tumor patients Frail elderly patients with chronic debilitating disease		
Low Risk of RFS :1 minor risk factor				

High Risk of RFS : 1 major or 2 minor risk factors Very High Risk : BMI < 14 kg/m<sup>2</sup>, Weight Loss > 20%, or Starvation > 15d

Natile Friedli. et al. Management and prevention of refeeding syndrome in medical inpatients. Nutrition. 2018

### Energy Requirement

Strength of recommendation STRONG	We recommend, that total energy expenditure of cancer patients, if not measured individually, be assumed to be similar to healthy subjects and generally between <u>25 – 30 kcal/kg/day</u>
Level of Evidence	Low

Maurizio Muscaritoli. et al. ESPEN Practical Guidelines: Clinical Nutrition in Cancer Patients. Clin Nutr. 2021

### Nutritional Management during Side Effects of Cancer Treatment

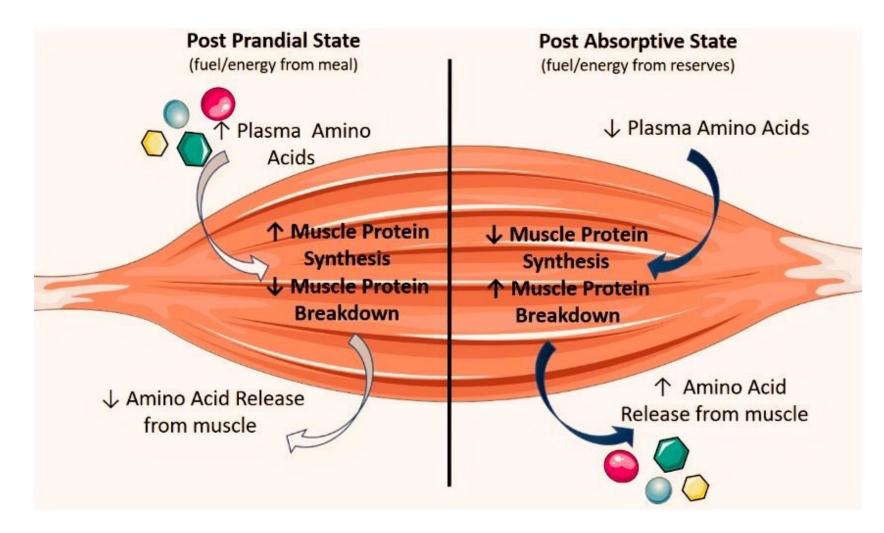
Symptoms	Nutritional Management
Dysphagia	Initiate texture-modified diet, obtain a swallow evaluation
Nausea/ Vomiting	Initiate small, frequent low-fat meals, initiate antiemetic drugs
Loos of appetite/ Early satiety	Initiate small, frequent meals, modify menu to preference, initiate appetite stimulant drugs
Taste changes	Modify menu to preference and tolerance, initiate mouth rinse
Mouth sores	Initiate texture modification, modify menu to tolerance, initiate mouth rinse containing anesthetic, pain management
Diarrhea	Initiate a low-fiber and residue diet, antidiarrheal drugs, increase fluids or Oral Rehydration Solution (ORS), considered Zn supplement
Constipation	Initiate fiber-containing diet or fiber containing enteral nutrition formula, laxative, soluble fiber supplement, increase fluids
Fatigue	Provide suffient energy and protein, increased fluids, sleep mangement

### Protein Requirement

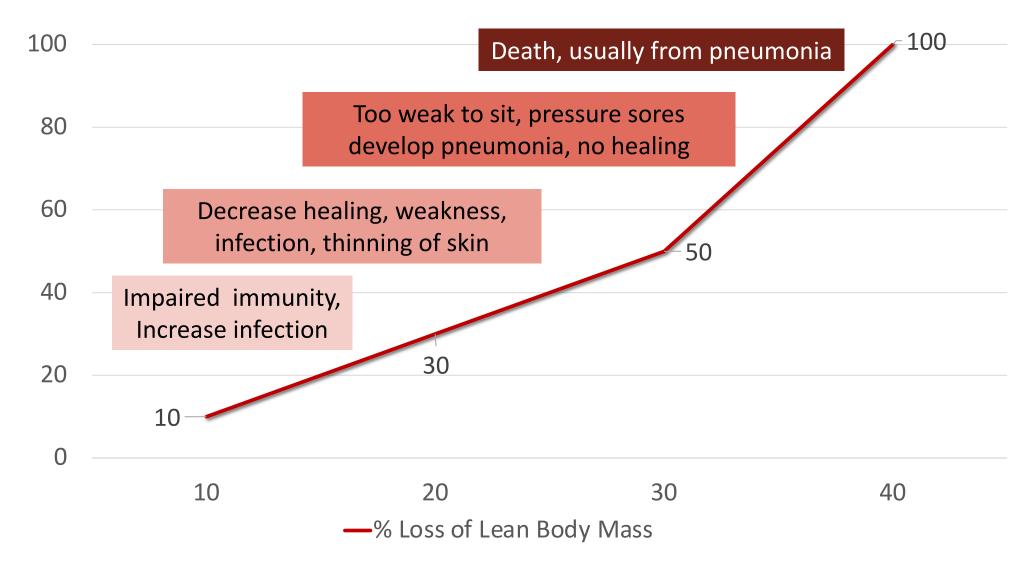
Strength of	We recommend that protein intake should
recommendation	be <u>above 1 g/kg/d</u> , if possible up to
STRONG	<u>1.5 g/kg/day</u>
Level of Evidence	Moderate

Maurizio Muscaritoli. et al. ESPEN Practical Guidelines: Clinical Nutrition in Cancer Patients. Clin Nutr. 2021

### Muscle Protein Synthesis (MPS)



### Loss of Lean Body Mass and Mortality



Demling RH. Nutrition, Anabolism, and the Wound Healing Process: An Overview. Eplasty. 2009

### Nutrition Plan for Adequate Protein Intake

- Eggs
  - Add to fried rice, salads, soups, sandwich
  - Make omelet instead of boiled egg
- Meat, Poultry, Fish and Seafoods
  - Add to main dish
  - Deep fried meat
  - Dried meat
- Milk
  - Add in soup, smoothie
  - Make ice cream, dessert, chocolate drink
  - Hard cheese

### Immuno-modulating Formula

- High Protein Distribution
- High Concentration, High Caloric Dense
- Immuno-nutrients
  - Omega-3 Fish Oil; EPA
  - Glutamine
  - Arginine
  - Ribonucleotide



	NEO-MUNE	Prosure	Oral Impact	Nutricia Forticare
Name				HUTTER FOR THE STATE OF THE STA
Company	Thai Otsuka	Abbott	Nestle	BJC HEALTHCARE
Caloric distribution C:P:F (%)	50:25:25	61:21:18	53:22:25	49:22:29
Kcal/ 1 scoop (g)	35 (8.5 g)	280 kcal/ 220 mL	303 kcal/ sachet (74 g)	204 kcal/ 125 mL
Protein(g)/ 1 serving	15.4 (250 kcal)	14.6 (280 kcal, bottle)	17 (303 kcal, Sachet)	11.0 (204 kcal, bottle)
Protein(g)/ 1,000 kcal	61.5 Casein, Glutamine 6.16 g , Arginine 12.3 g	52 Whey, Casein	56 Whey, L-arginine 12.5g, R-Nucleotide 1.5g	54 Milk protein isolate
Fat source	Fish oil 5.5 g /1,000 kcal, MCT oil (12% total calorie),	Fish oil (EPA 1.0 g, DHA 0.43 g) /bottle, MCT oil	Fish oil 3.4 g /sachet, MCT oil (6% total calorie)	Fish oil (EPA 0.751 g, DHA 0.373 g) /bottle
Osmolality mOsm/kg.H2O	400	753	620	730

## Omega-3 Fatty acids to Improve Appetite and Body Weight

Strength of recommendation WEAK	In patients with advanced cancer undergoing CMT and at risk of weight loss or malnourished, we suggest to use supplementation with long-chain N-3 fatty acids or fish oil to stabilize or improve appetite, food intake, lean body mass and body weight
Level of Evidence	Low

Effective Dose of Fish Oil was 4 – 6 g/d, or Long-chain Omega-3 Fatty Acids (EPA) was 1 – 2 g/d for Decrease Inflammatory Response

Maurizio Muscaritoli. et al. ESPEN Practical Guidelines: Clinical Nutrition in Cancer Patients. Clin Nutr. 2021

#### Immunonutrients

Strength of recommendation STRONG	In upper GI cancer patients undergoing surgical resection in the context of traditional perioperative care We recommended oral/enteral immunonutrition (arginine, n-3 fatty acids, nucleotides)								
Level of Evidence	High								
Pre- or Perioperative Intake of ONS (3x250 ml) enriched with immune modulating substrates for 5 – 7 days reduces postoperative morbidity and length of stay after major abdominal cancer surgery									

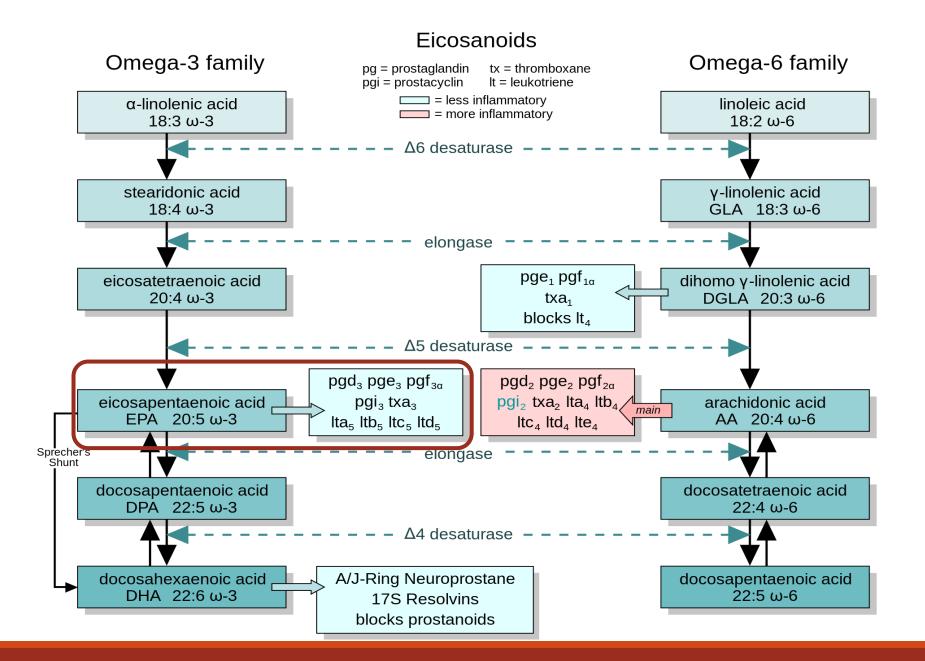
Maurizio Muscaritoli. et al. ESPEN Practical Guidelines: Clinical Nutrition in Cancer Patients. Clin Nutr. 2021

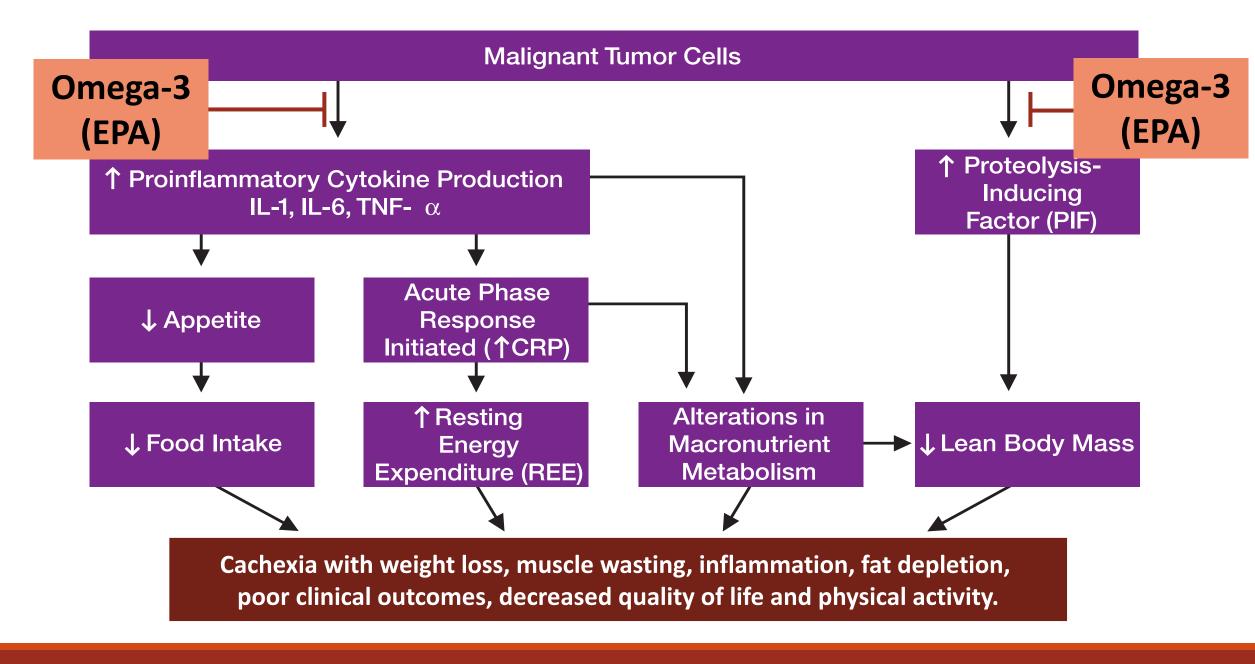
### <u>Eicosapentaenoic</u> <u>Acid</u> (EPA) an Anti-inflammatory Nutrition

- Long-chain omega-3 fatty acid (20:5n-3) found naturally in deep-sea oily fish
- Component of cell membranes
- Decreases proinflammatory cytokine production
- Down-regulates the inflammatory response
- Down-regulates level/activity of proteolysis-inducing factor (PIF)

Eicosapentaenoic acid (EPA)

1. Wigmore SJ, et al. *Nutrition*. Jan 1996;12(1 Suppl):S27-30. 2. Wigmore SJ, et al. *Clin Sci (Lond)*. Feb 1997;92(2):215-221. 3. Barber MD, et al. *Nutr Cancer*. 2001;40:118-124. 4. Endres S, et al. *N Engl J Med*. Feb 2 1989;320(5):265-271. 5. Jho D, et al. *Am Surg*. Jan 2003;69(1):32-36. 6. Lorite MJ, et al. *Br J Cancer*. 1997;76(8):1035-1040.





Cabal-Manzano, et al. Br J Cancer. 2001;84:1599-1601. Argiles JM, et al. Curr Opin Clin Nutr Metab Care. 2003;6(4):401-406. Tisdale MJ. Physiology (Bethesda). 2005;20:340-348. Tisdale MJ. Physiol Rev. 2009;89(2):381-410.

# Clinical Evidence The Benefits of Immune-Modulating Formula

### Effect of a Protein and Energy Dense n-3 fatty acid enriched oral supplement on loss of weight and lean tissue in cancer

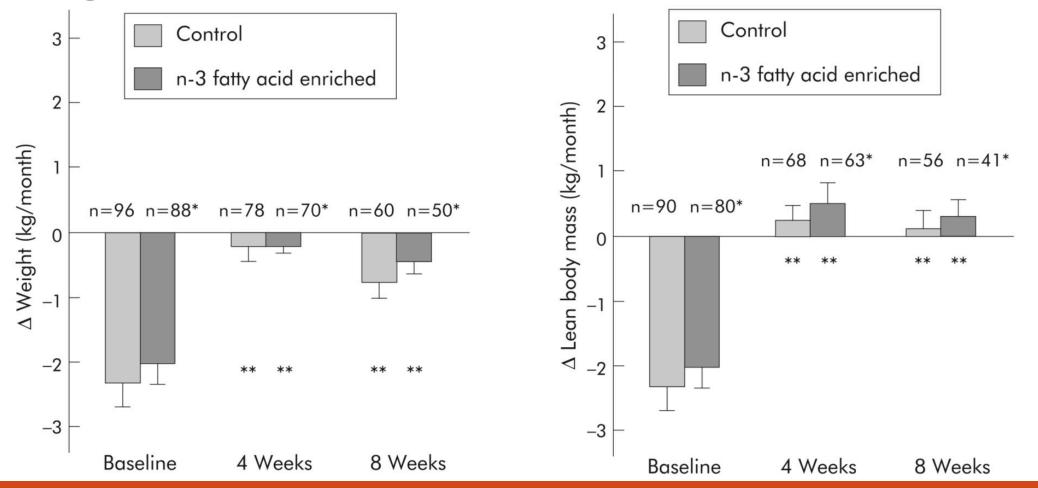
#### Study design

- Prospective, randomized, controlled, double-blind multicenter trial in 200 patients with advanced unresectable malnourished pancreatic cancer mean weight loss at baseline 3.3kg/month
- 2 servings ProSure<sup>®</sup> vs control ONS per day for 8 weeks (isocaloric isonitrogenous control)
- After 8 weeks of intervention mean weight loss in ProSure<sup>®</sup> vs. Control change in LBM in ProSure<sup>®</sup> vs. Control

= -0.25 kg/mo vs. -0.37 kg/mo

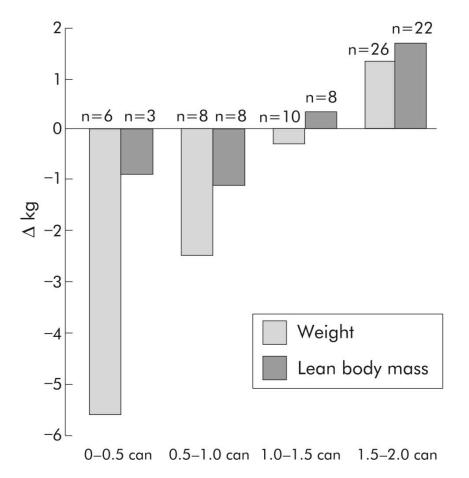
= +0.27 kg/mo vs. +0.12 kg/mo

#### Effect of a Protein and Energy Dense n-3 fatty acid enriched oral supplement on loss of weight and lean tissue in cancer



Fearon. Et al. Effect of a Protein and Energy Dense n-3 fatty acid enriched oral supplement on loss of weight and lean tissue in cancer. Gut. 2003

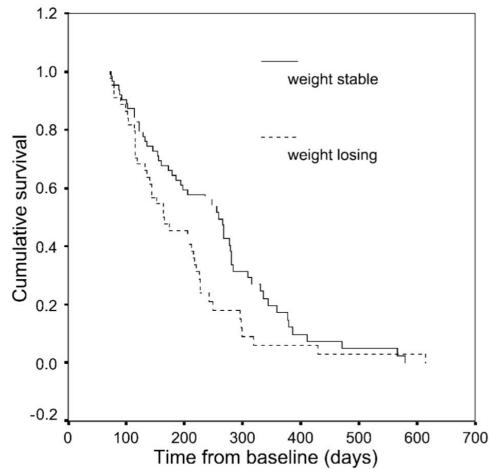
#### Effect of a Protein and Energy Dense n-3 fatty acid enriched oral supplement on loss of weight and lean tissue in cancer



Adherence to dietary intervention show more effective on weight gain, lean body mass and clinical outcome

Fearon. Et al. Effect of a Protein and Energy Dense n-3 fatty acid enriched oral supplement on loss of weight and lean tissue in cancer. Gut. 2003

Weight Stabilization is associated with Improved Survival Duration and Quality of Life in Unresectable Pancreatic Cancer

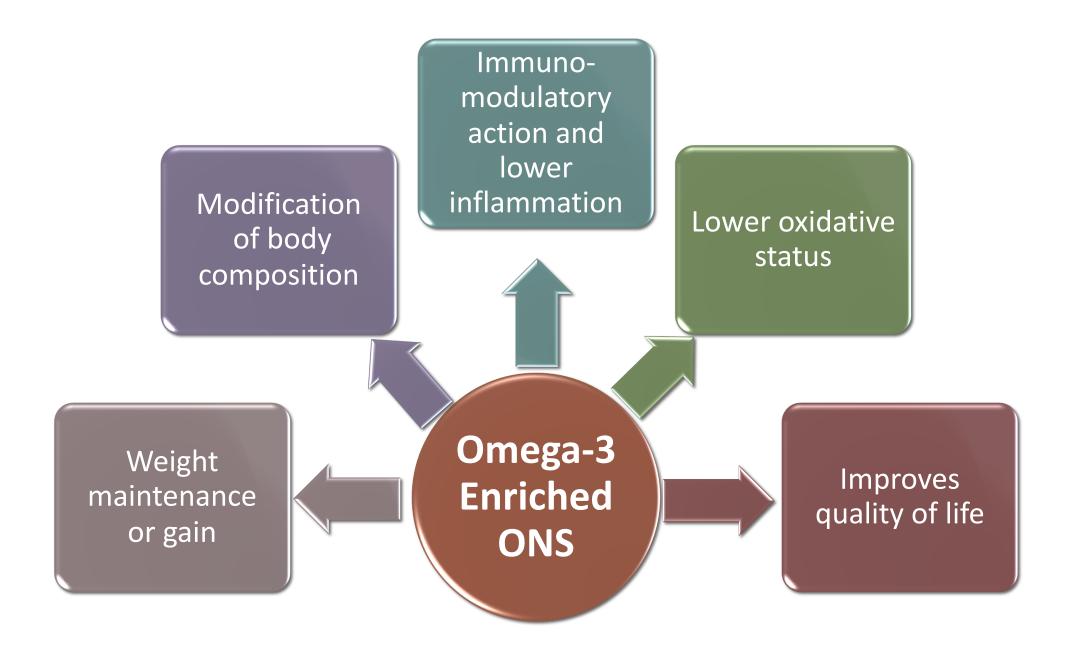


Weight stable patients have longer survival than patients with weight loss among unresectable pancreatic cancer patients

Wendy Davidson. et al. Weight Stabilisation is associated with Improved Survival Duration and Quality of Life in Unresectable Pancreatic Cancer. Clin Nutr. 20004 Omega-3 Supplements for Patients in CMT/RT: A Systematic Review

#### **Study design**

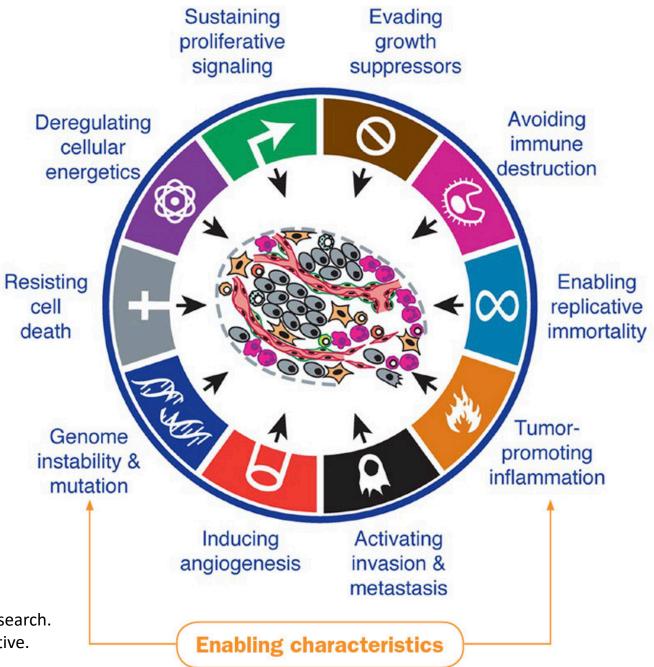
- 10 RCT studies, (N = 11 92 / study), duration 5 12 weeks
- Oncologic patients undergoing chemotherapy and/or radiotherapy
- Intervention
  - Oral Nutrition Supplement with N-3 fish oil or Fish oil supplement
- Comparator
  - Did not received supplement
  - Or Isocaloric, isonitrogenous supplement



Juliana Silva. Omega-3 supplements for patients in chemotherapy and/or radiotherapy: A systematic review. Clin Nutr. 2014

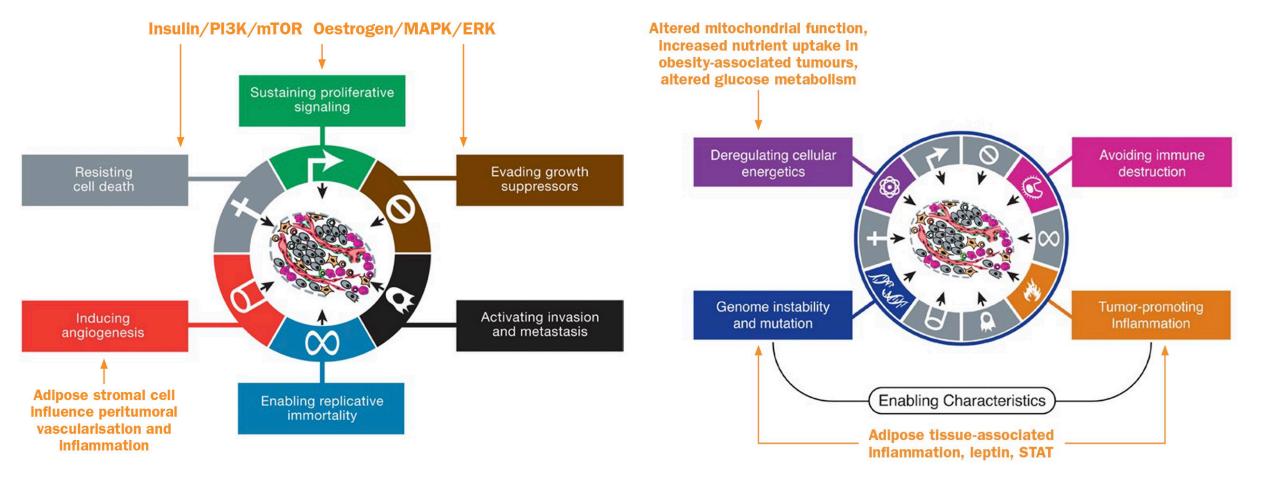
# Cancer Prevention

## Hallmarks of Cancer



World Cancer Research Fund/American Institute of Cancer Research. Diet, Nutrition, Physical Activity and Cancer: a Global Perspective. Continuous Update Project Expert Report 2018

### Obesity and The Hallmarks of Cancer



World Cancer Research Fund/American Institute of Cancer Research.

Exposure	Systemic impact	Cell function	Hallmarks possibly affected
	Hyperinsulinemia	mTOR/PI3K/AKT, MAPK	Reduced apoptosis; increased proliferation, genome instability
	Increased oestradiol	MAPK/ERK/PI3K	Increased proliferation in ER+ tissues; genome instability
Greater body fatness	Inflammation	STAT3/NF-ĸB	Reduced apoptosis, increased cell division, altered macrophage function, etc.; genome instability
		E.g. WNT, P53	E.g. cellular energetics, etc.
	Folate deficiency	DNA uracil misincorporation	Genome instability
Lower fruit and vegetable intake	Low dietary fibre intake	Low butyrate	Reduced apoptosis; increased proliferation
vegetable littake	Low levels of carotenoids, vitamin A, C, E	Oxidative stress, inflammation	Increased inflammation, genomic instability, reduced apoptosis; increased proliferation
Greater intake of red and processed meat	Elevated exposure to nitrites; endogenous N-nitroso compound	DNA adduct formation -> mutations in p53, KRAS, etc.	Reduced apoptosis; increased proliferation; genomic instability
	formation	Oxidative stress, inflammation	Increased inflammation, genomic instability World Cancer Research Fund/American Institute of Cancer

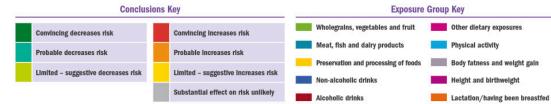
Exposure	Systemic impact	Cell function	Hallmarks possibly affected
Greater intake of dairy foods	Higher IGF-I	mTOR/PI3K/AKT, MAPK	Reduced apoptosis; increased proliferation
	Elevated acetaldehyde	Oxidative stress, lipid peroxidation	Increased inflammation, genomic instability
	Increased oestradiol	MAPK/ERK/PI3K	Increased proliferation in ER+ tissues
Greater alcohol intake	Inflammation	STAT3/NF-ĸB	Reduced apoptosis, increased cell division, altered macrophage function, etc.
	Folate deficiency; interference with 1-carbon metabolism	DNA uracil misincorporation	Genome instability
	Reduction in insulin	mTOR/PI3K/AKT, MAPK	Increased apoptosis; reduced proliferation, less genome instability
Greater physical	Reduction in oestradiol and testosterone	MAPK/ERK/PI3K	Reduced proliferation in ER+ tissues; reduced genome instability
activity	Reduced inflammation (long term); improved	STAT3/NF-ĸB	Increased apoptosis, increased cell division, altered macrophage function etc; reduced genome instability
	immune function	E.g. WNT, P53	E.g. cellular energetics, etc.
Greater height	Higher IGF-I	mTOR/PI3K/AKT, MAPK	Reduced apoptosis; increased proliferation World Cancer Research Fund/American Institute of Cancer



#### **Summary of conclusions**



2018	Wholegrains Refined grains Foods containing distary fibre	Arrandmas Non-starchy vegetables (geader intake) Non-starchy vegetables (low intake) Preserved non-starchy vegetables	Fruit (greater Intake) Fruit (low intake) Citrus fruit	Non starchy vegotables & fruit Foods containing carotenoids Foods containing beta-carotene Foods containing vitamin C	Foods containing isoffavones Non-starchy vegetables or fruit <sup>18</sup> (aggregated)	Red meat <sup>21</sup> Processed meat <sup>22</sup>	Foods containing haem iron Fish Cantonese style salted fish	Grilled (brothed) or barbecued (charbrolled) meat and fish Dairy products Dists hitch in calcium	Foods preserved by salting	Arsenic in drinking water <sup>20</sup>	Mate <sup>11</sup> Coffee Too	rea Sugar sweetened drinks	Alcoholic drinks 35	Healthy dietary patterns Mediterranean type' dietary pattern		Glycaemic load Glycaemic load Foods & drinks containing Fructose Foods containing saturated fatty	acids Foods containing retinol Vitamin D (food containine.	serum, supplements) Low plasma alpha-tocopherol concentrations Low plasma selenium	High-dose beta-carotene supplements	Beta-carotene Calcium supplements Multivitamin supplements	Physical activity <sup>54</sup>	Vigorous physical activity Walking	Sedentary behaviours Screen time	Adult body fatness Body fatness in young adulthood	Adult weight gain Adult attained height <sup>72,74</sup>	Greater birthweight <sup>14</sup>	Lactation <sup>13</sup> Having been breastfed
MOUTH, PHARYNX, LARYNX 2018														41										62			
NASOPHARYNX 2017 (SLR)							25																				
OESOPHAGUS (ADENOCARCINOMA) 2016																					55			62			
OESOPHAGUS (SQUAMOUS CELL CARCINOMA) 2016																					55						
LUNG 2017		4	4	11 13 15	17												47		49								
STOMACH 2016			7 9			23			29				36											63			
PANCREAS 2012													36			46								62			
GALLBLADDER 2015																								64			
LIVER 2015	1												36											65			
COLORECTUM 2017	2	6	8	16			24	26					37				-48	8		52 53	56			62			
BREAST PREMENOPAUSE 2017		5		12				27					38								57	57		66 71		76 79	
BREAST POSTMENOPAUSE 2017		5		12									38								57	57		66 71	72	79	
OVARY 2014																								67			
ENDOMETRIUM 2013											32					45							59	68			
CERVIX 2017 (SLR)																								69			
PROSTATE 2014				14				28											5	1				70			
KIDNEY 2015													39											62			
BLADDER 2015				10																							
SKIN 2017 (SLR)											33		40						50						75	77	
AERODIGESTIVE CANCERS <sup>20</sup> (AGGREGATED) 2016–2018					19																						
RISK OF WEIGHT GAIN, OVERWEIGHT OR OBESITY 2018 <sup>\$1, 52</sup>	1											-34		42	43 44						58		60 61				80



To reference this matrix please use the following citation: World Cancer Research Fund/American Institute for Cancer Research. Continuous Update Project. Diet, Nutrition, Physical Activity and the Prevention of Cancer. Summary of evidence. Available at: wcrf.org/matrix. Accessed on DD-MM-YYYY Abbreviation: SLR, systematic literature review.

#### dietandcancerreport.org

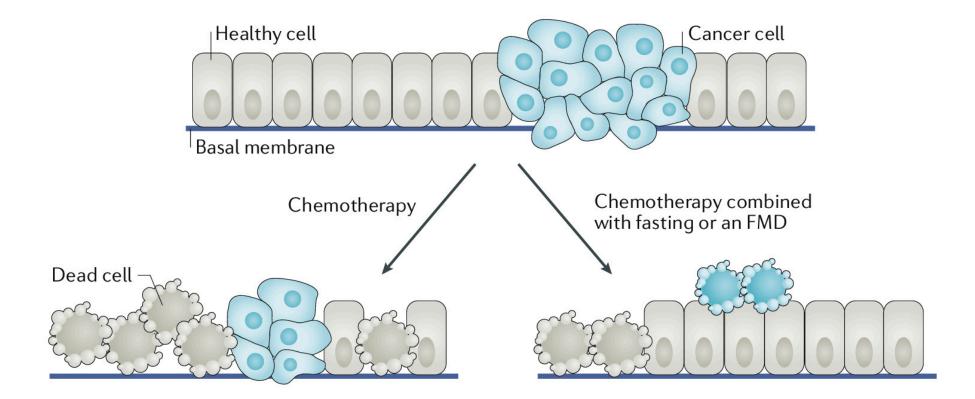
 $\ensuremath{\textcircled{O}}$  2018 World Cancer Research Fund International. All rights reserved

#### SUMMARY OF STRONG EVIDENCE ON DIET, NUTRITION, PHYSICAL ACTIVITY AND THE PREVENTION OF CANCER

To reference this matrix please use the following citation: World Cancer Research Fund International/American Institute for Cancer Research. Continuous Update Project: Diet, Nutrition, Physical Activity and the Prevention of Cancer. Summary of Strong Evidence. Available at: wcrf.org/cupmatrix accessed on DD-MM-YYYY Abbreviation: SLR, systematic literature review.	Wholegrains	Foods containing dietary fibre	Aflatoxins	Foods containing beta-carotene	Non-starchy vegetables or fruit (aggregated) <sup>2</sup>	Red meat	Processed meat	Cantonese-style salted fish	Dairy products	Foods preserved by salting	Arsenic in drinking water	Mate	Coffee	Sugar sweetened drinks	Alcoholic drinks	'Mediterranean type' dietary pattern	"Western type' diet	'Fast foods'	Glycaemic load	High-dose beta-carotene supplements	Beta-carotene	Calcium supplements	Physical activity (moderate and vigorous)	Vigorous physical activity	Walking	Screen time (children) <sup>15</sup>	Screen time (adults) <sup>15</sup>	Adult body fatness <sup>16</sup>	Body fatness in young adulthood <sup>19</sup>	Adult weight gain	Adult attained height $^{\rm 21}$	Greater birthweight	Lactation <sup>22</sup>	Having been breastfed
MOUTH, PHARYNX, LARYNX 2018																																		
NASOPHARYNX 2017 (SLR)																																		
OESOPHAGUS (ADENOCARCINOMA) 2016																																		
OESOPHAGUS (SQUAMOUS CELL CARCINOMA) 2016																																		
LUNG 2017																				10														
<b>STOMACH</b> 2016															5													17						
PANCREAS 2012																																		
GALLBLADDER 2015																																		
LIVER 2015													, , ,		5																			
COLORECTUM 2017									4						6							12	13											
BREAST PREMENOPAUSE 2017				a											7																			
BREAST POSTMENOPAUSE 2017															1																			
<b>OVARY</b> 2014																																		
ENDOMETRIUM 2013																																		
PROSTATE 2014																					11							18						
KIDNEY 2015															8																			
BLADDER 2015																																		
<b>SKIN</b> 2017 (SLR)																															20			
AERODIGESTIVE CANCERS (AGGREGATED) 2016-2018 1					3																													
RISK OF WEIGHT GAIN, OVERWEIGHT OR OBESITY 2018 <sup>23,24</sup>																	9						14											
Convincing decreases risk	[		Prob	able	decr	eases	s risk				Prob	able	incre	eases	risk				Com	vincir	ng ind	reas	es ris	k	[		Sub	stant	ial ef	fect	on ris	k unl	ikey	

# Frontier in Onconutrition

#### Fasting and Cancer Molecular Mechanisms and Clinical Application



Alessio Nencioni. et al. Fasting and cancer: molecular mechanisms and clinical application. Nature Reviews Cancer. 2018

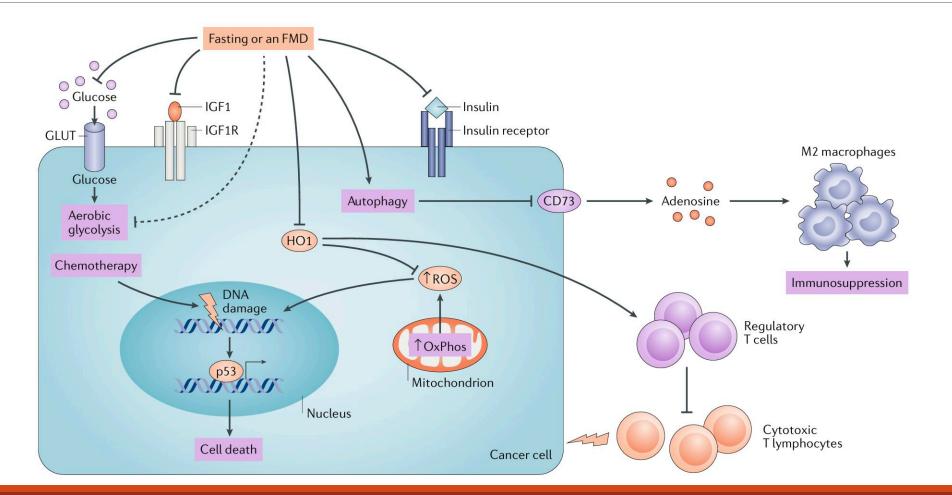
#### Fasting and Cancer Molecular Mechanisms and Clinical Application

Type of diet	Restriction in calories	Composition	Schedule	IGF1 reduction (humans)	Glucose reduction (humans)	Ketone bodies increase (humans)	Location of pro-regenerative effects	Protection from chemotherapy toxicity
Fasting or FMD	>50%	Vegan and low-protein and low-sugar, high-plant-based fat composition, with micronutrient supplementation	Typically 2–5 consecutive days per month	Yes	Yes	Yes	Haematopoietic system, central nervous system, skeletal muscle and pancreatic β-cells (mouse data) <sup>22,25,41,153</sup>	Yes (mouse data and DNA damage analyses in patient leukocytes) <sup>12,25,26,29,51–53</sup>
Calorie restriction	20–40%	Reduction in all diet constituents except for vitamins and minerals	Chronic	Only in the presence of protein restriction <sup>117</sup>	No	No	Intestinal niche stem cells (mouse data) <sup>118,119</sup>	Yes (effect lower than that with fasting or FMDs; mouse data) <sup>51</sup>
Ketogenic diet	None (isocaloric)	High-fat, low- carbohydrate composition, with adequate protein content	Chronic	Yes	No	Yes	Peripheral nerves (rat data) <sup>87</sup>	NA

FMD, fasting-mimicking diet; NA, not available.

Alessio Nencioni. et al. Fasting and cancer: molecular mechanisms and clinical application. Nature Reviews Cancer. 2018

#### Fasting and Cancer Molecular Mechanisms and Clinical Application



Alessio Nencioni. et al. Fasting and cancer: molecular mechanisms and clinical application. Nature Reviews Cancer. 2018



## Together We Can Help Improve Outcome of Cancer Patients



#### THANK YOU

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