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FOR CLINICAL
NUTRITION AND
METABOLISM



Ernæringsbehandling og strategier hos kreftpasienter

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Tilpasset etter original presentasjon utarbeidet til ESPEN LLL course

Module 26

Nutritional Treatment Strategies in Cancer Patients



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Learning objectives



- To understand the role of nutrition in relation to metabolism, nutritional status, functioning, treatment tolerance, and quality of life
- To discuss indications for starting and ending nutritional treatment
- To understand indications for dietary counselling, food modification, oral nutritional supplements, tube feeding, and parenteral nutrition

Vurderinger ved ernæringsbehandling

- Cancer prognosis
- Expected benefit on quality of life and potentially on survival
- Potential burden associated with nutritional care
 - expectations and wishes of patient and close relatives/partners



Arends et al., Clin Nutr 2017



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Mål for ernæringsbehandling

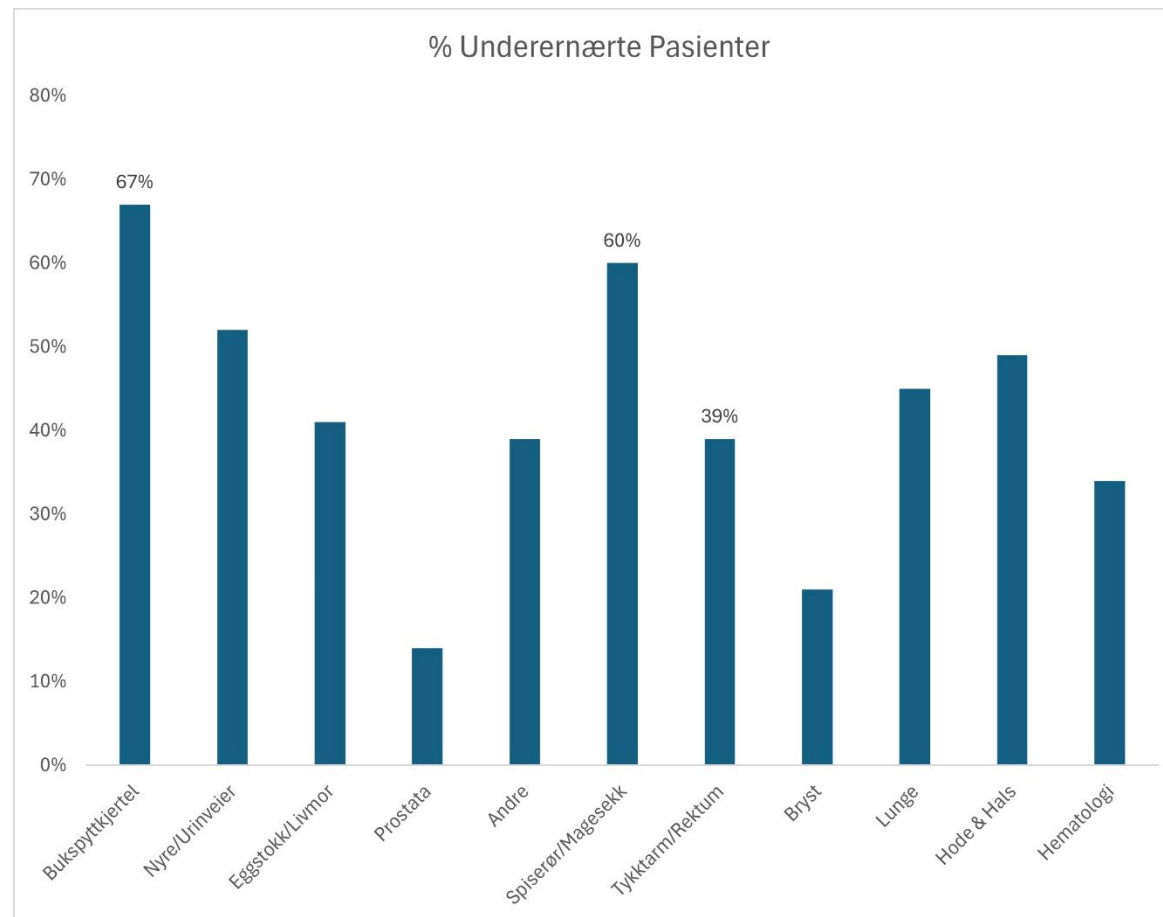


- **To secure adequate intake** of energy, protein, macro- and micronutrients
 - to diminish metabolic disturbances and nutrition impact symptoms
 - to optimize nutritional status
 - to enable undergoing planned anti-cancer treatment
 - to reduce risk of reductions / interruptions of scheduled anti-cancer treatments

Optimizing nutritional status requires **anabolic competence**

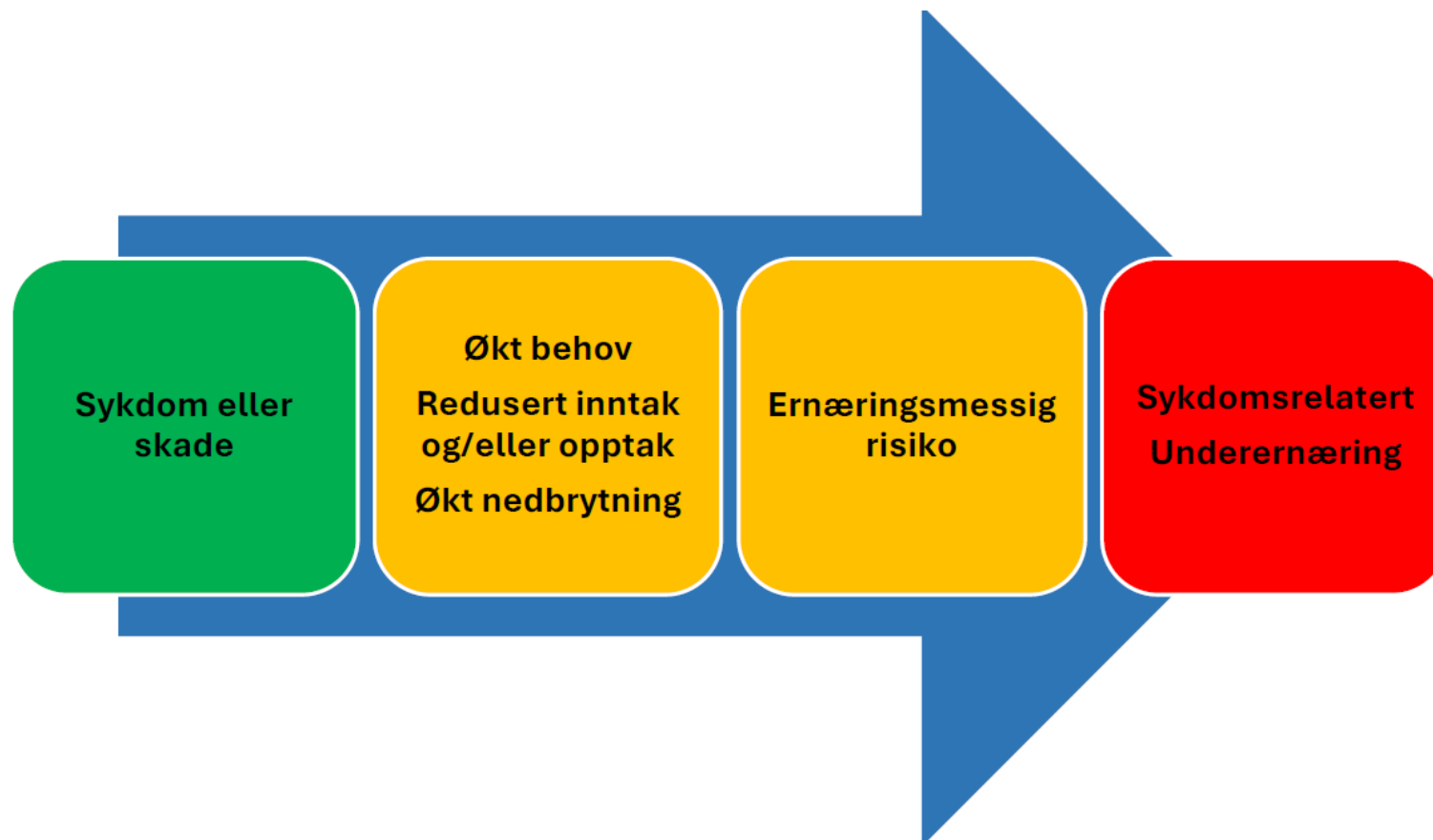
Arends et al., Clin Nutr 2017

Underernæring fordelt på ulike kreftformer



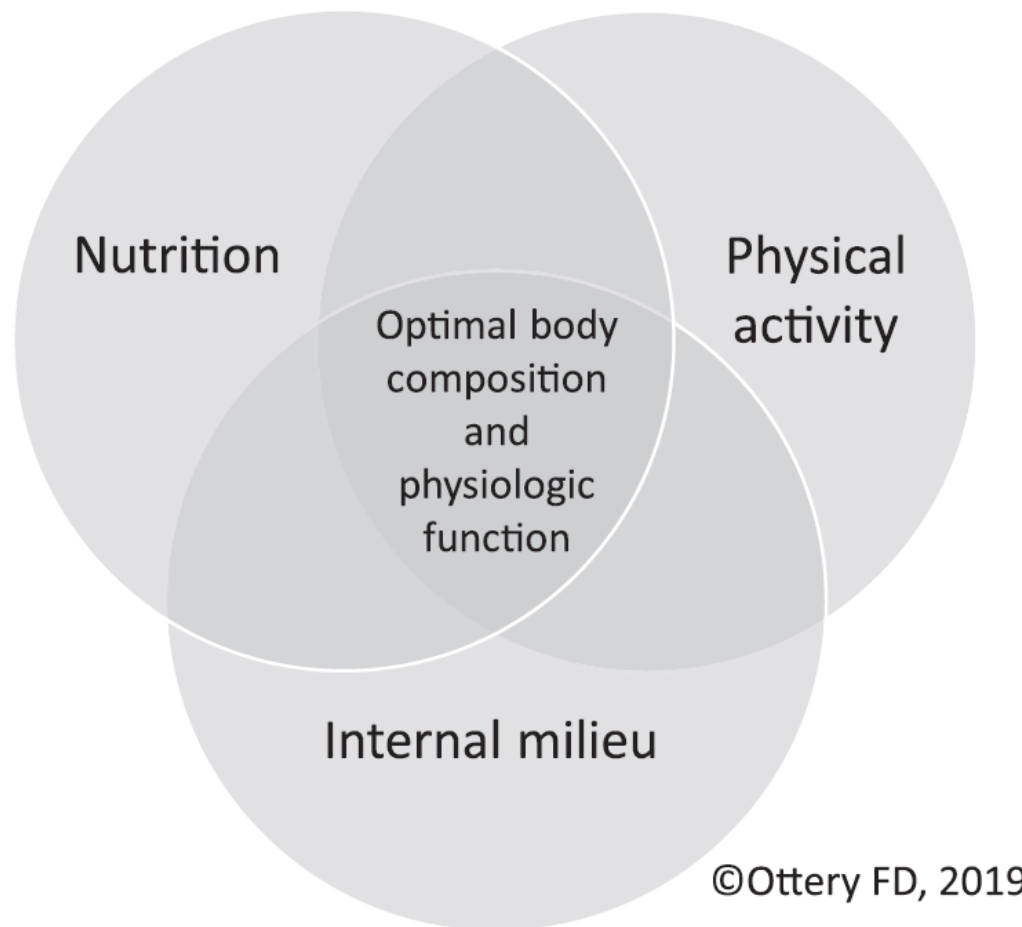
Torbergson, 2024
Etter Hebutterne, 2014

Sykdomsrelatert underernæring



Frigstad, 2024

Anabol kapasitet



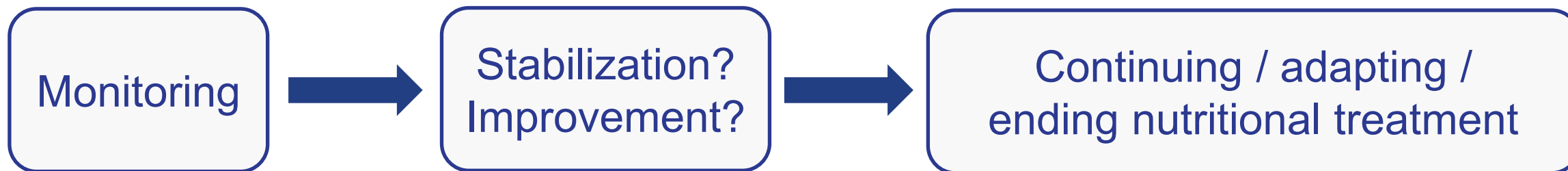
Anabolic Competence:

That state which optimally supports protein synthesis and lean body mass, as well as global aspects of muscle and organ function, immune competence, and quality of life

Langer et al., Nutrition 2001
Reckman et al, Nutrition 2019

Utfallsmål og oppfølging

- **Short- and medium-term outcomes** of nutritional treatment should be defined together with the patient, including:
 - Changes in dietary intake
 - Changes in nutritional status
 - Changes in physical function
 - Changes in perceived quality of life



Arends et al., Clin Nutr 2017



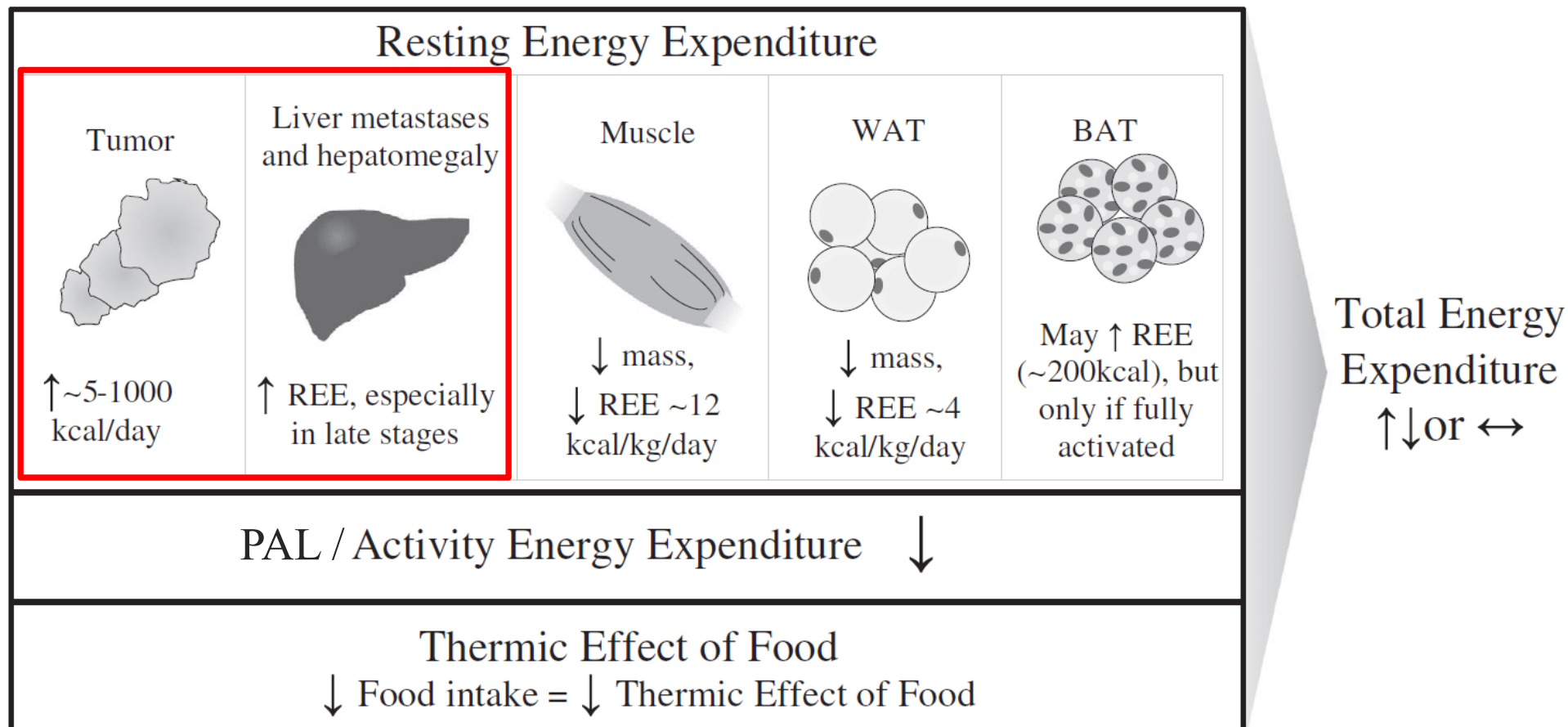
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Ernæringsbehandling



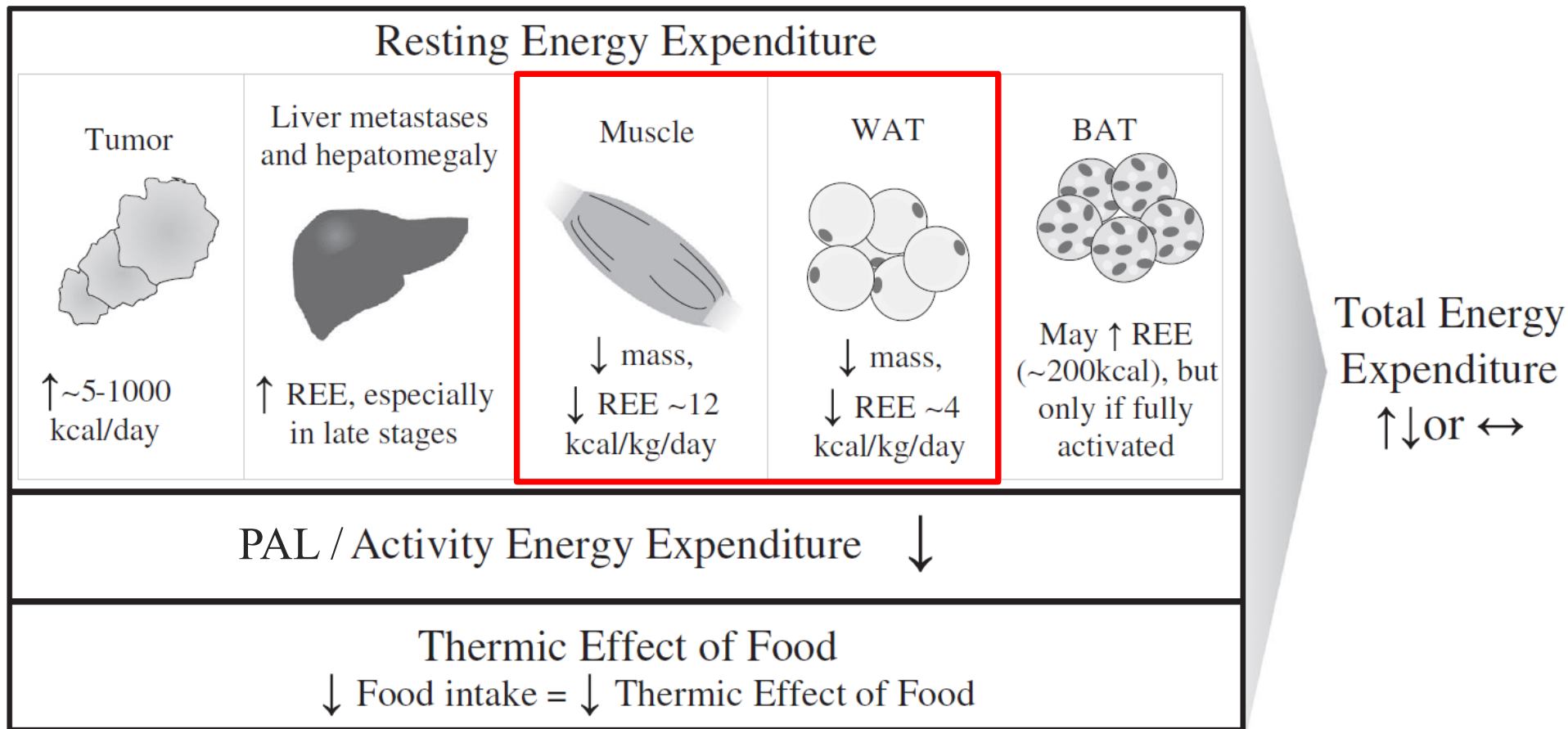
- Dietary counselling by a **trained nutrition professional** is 1st line of nutritional treatment
- Individualized dietary counselling by a trained professional (compared to conventional food without dietary education) improves nutritional intake, body weight, and quality of life, but not mortality
- Nutritional treatment preferably **initiated when patients are not yet severely malnourished** and when goals of care include maintaining or improving nutritional status
 - malnutrition is **associated with poorer clinical outcomes**
 - difficult to revert overt malnutrition in cancer patients with metabolic derangements

Kreftsykdom kan øke hvilemetabolisme



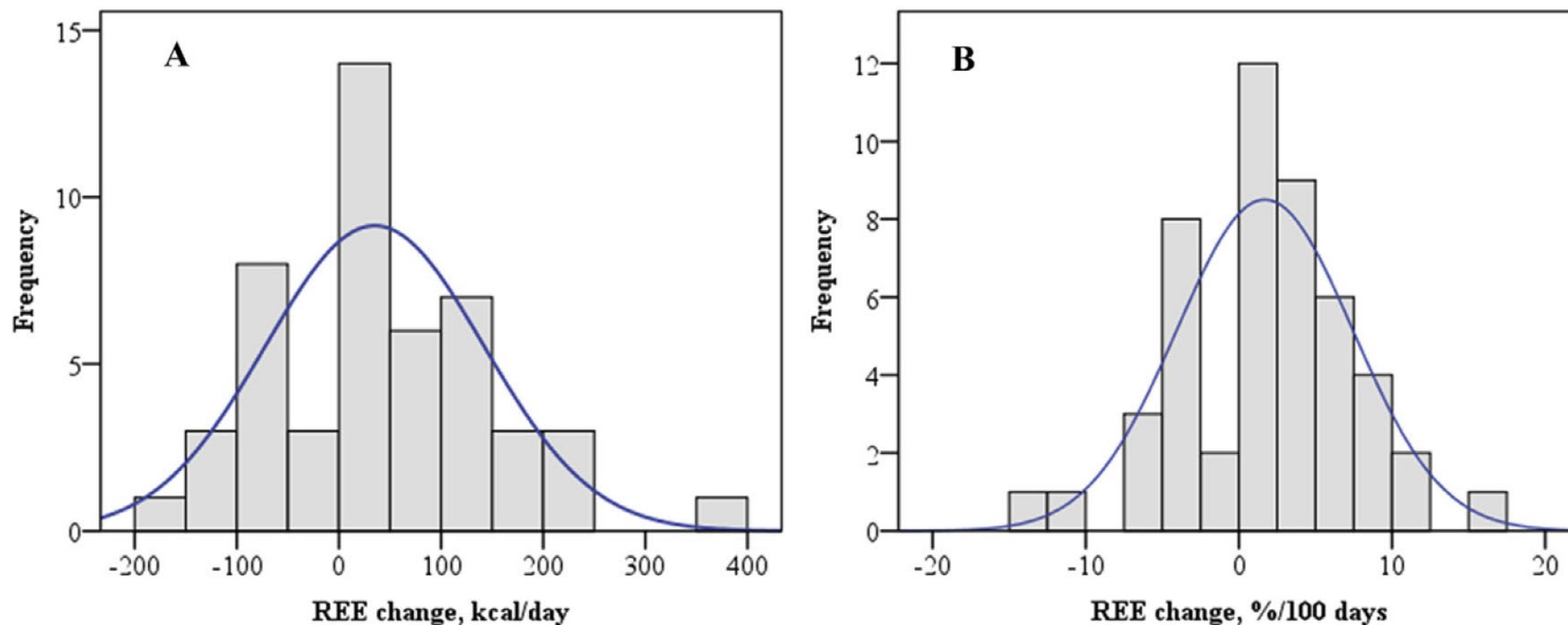
Purcell et al., Eur J Clin Nutr 2016

Tap av muskelmasse og redusert fysisk aktivitet



Purcell et al., Eur J Clin Nutr 2016

Hvilemetabolismen er ikke konstant over tid ved kreftsykdom



Purcell et al., Eur J Clin Nutr 2020

Betydning av inflammasjon

Linear regression analysis showing the determinants of resting energy expenditure change in patients with colorectal cancer (n = 46).

	Coefficient	95% CI	R ²	SEE	P
Model			0.433	88.0	0.001
Intercept	−369.7	−751.9, 12.6			0.058
FFM change, kg	1.5	−10.7, 13.8			0.975
CRP change, mg/L	1.7	0.8, 2.5			<0.001
Age, y	0.7	−1.7, 3.0			0.579
Stage ^a	81.3	3.1, 159.5			0.042
Days between visits	0.3	−0.4, 0.9			0.405

CI: confidence interval; CRP: C-reactive protein; FFM: fat-free mass; SEE: standard error of the estimate.

^a Compared to stage III.

Anbefalinger

Energi

B2 – 1	Energy requirements
Strength of recommendation STRONG	<i>We recommend, that total energy expenditure of cancer patients, if not measured individually, be assumed to be similar to healthy subjects and generally ranging between 25 and 30 kcal/kg/day.</i>
Level of evidence Questions for research	Low improve prediction of energy requirements in the individual patient

Consensus

Arends et al., Clin Nutr 2017

Anbefalinger

Protein

B2 – 2	Protein requirement
Strength of recommendation STRONG	<i>We recommend that protein intake should be above 1 g/kg/day and, if possible up to 1.5 g/kg/day</i>
Level of evidence Questions for research	Moderate effect on clinical outcome of increased supply (1–2 g/kg/day) and composition of protein/amino acids

Strong consensus

Arends et al., Clin Nutr 2017

Older adults: ↑ protein requirements

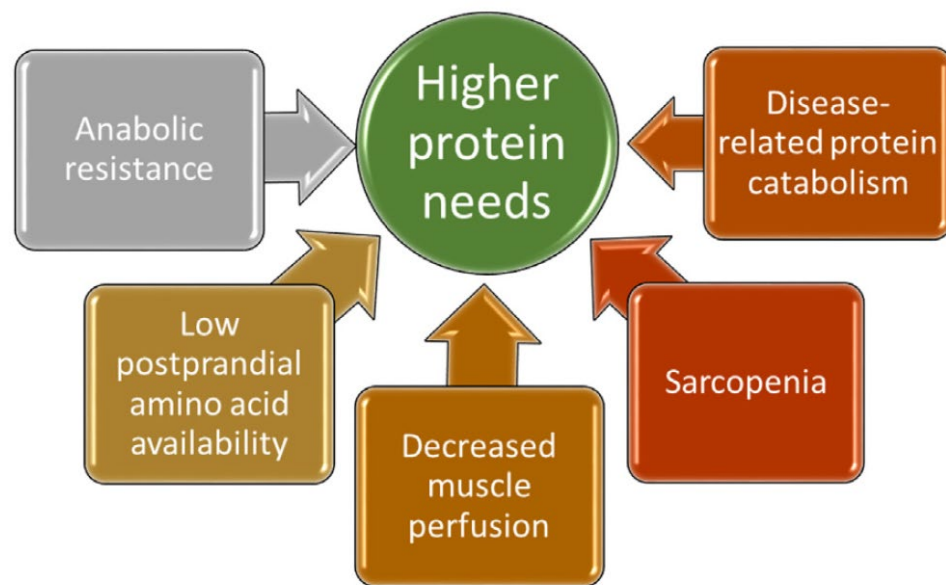


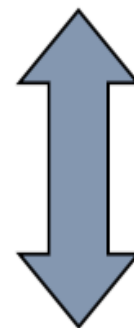
Fig. 2. Protein status: factors leading to higher protein needs in older persons.

Older adults with (risk of) acute/chronic disease-related malnutrition:
1.2 – 1.5 gram protein/kg body weight
and even higher amounts
if severe illness or injury

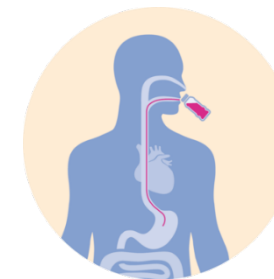
Målrettede ernæringstiltak

Intravenøs næring
Sondenæring
Næringsdrikker
Beriking og mellommåltider
Mattilbud
Måltidsmiljø
Symptomlindring og medisinsk behandling

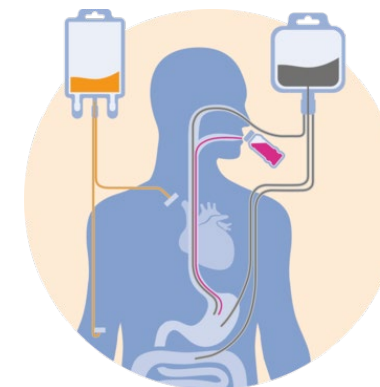
Medisinsk
ernæringsbehandling



Matomsorg



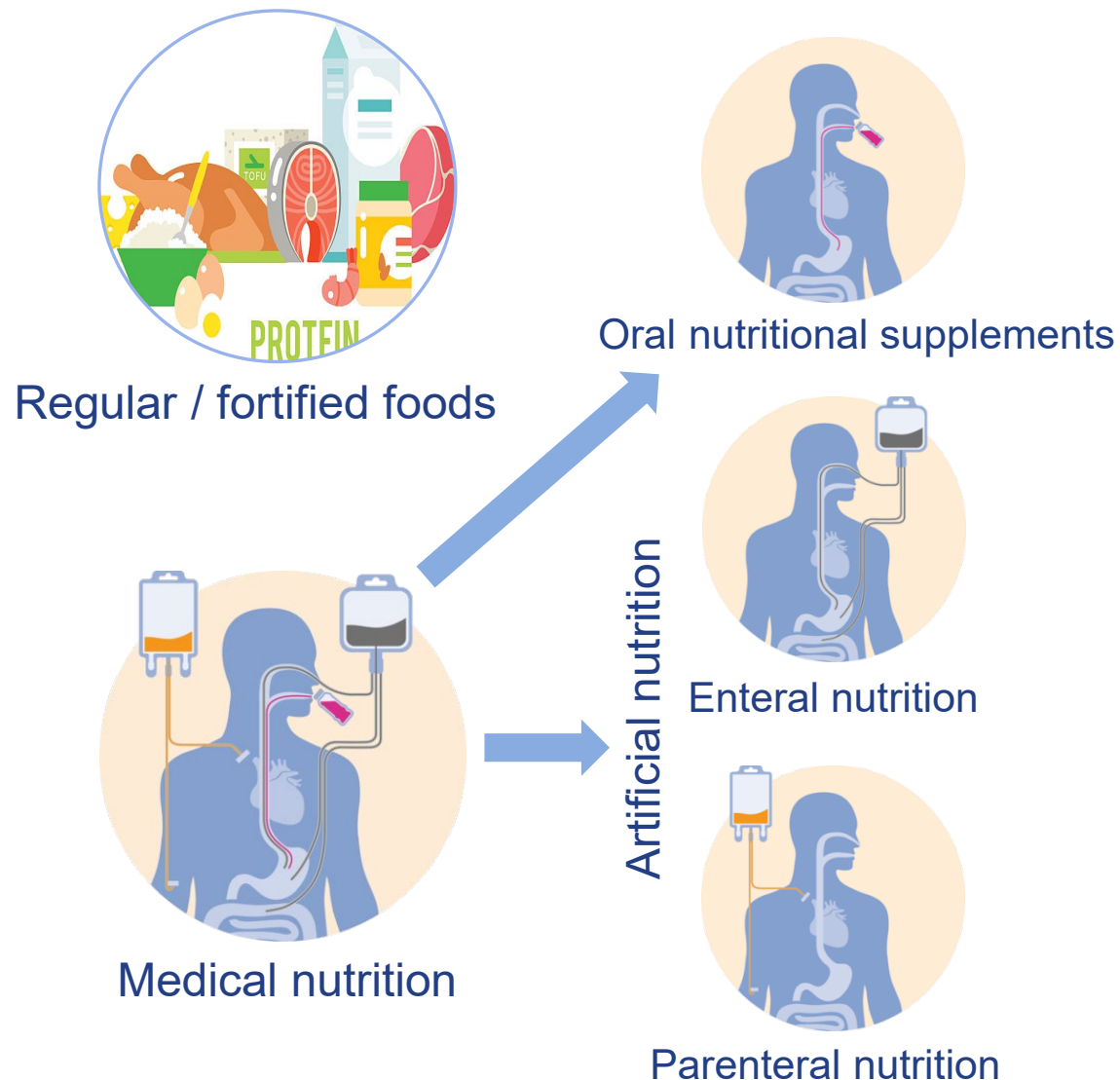
Oral nutritional supplements



Medical nutrition

Målrettede ernæringstiltak fra matomsorg til
medisinsk ernæringsbehandling (Helsedirektoratet)

Behandlungsstrategier



Start EN / PN if:

- No food for >1 week
- Unable to eat
(e.g. <60% of requirements
for >1-2 weeks)
- Unable to digest or
absorb food

Effekt av ernæringsbehandling



- ↑ nutritional status
- ↑ QoL
- ↑ dietary intake

Langius et al., Clin Nutr 2013

Zhang et al., Supp Care Cancer 2020
Kiss et al., Nutr Cancer 2014



- ↑ body weight
- ↑ dietary intake
- ↑ QoL

Reece et al., Supp Care Cancer 2020
de van der Schueren et al., Ann Oncol 2018

Baldwin et al., J Natl Cancer Inst 2012

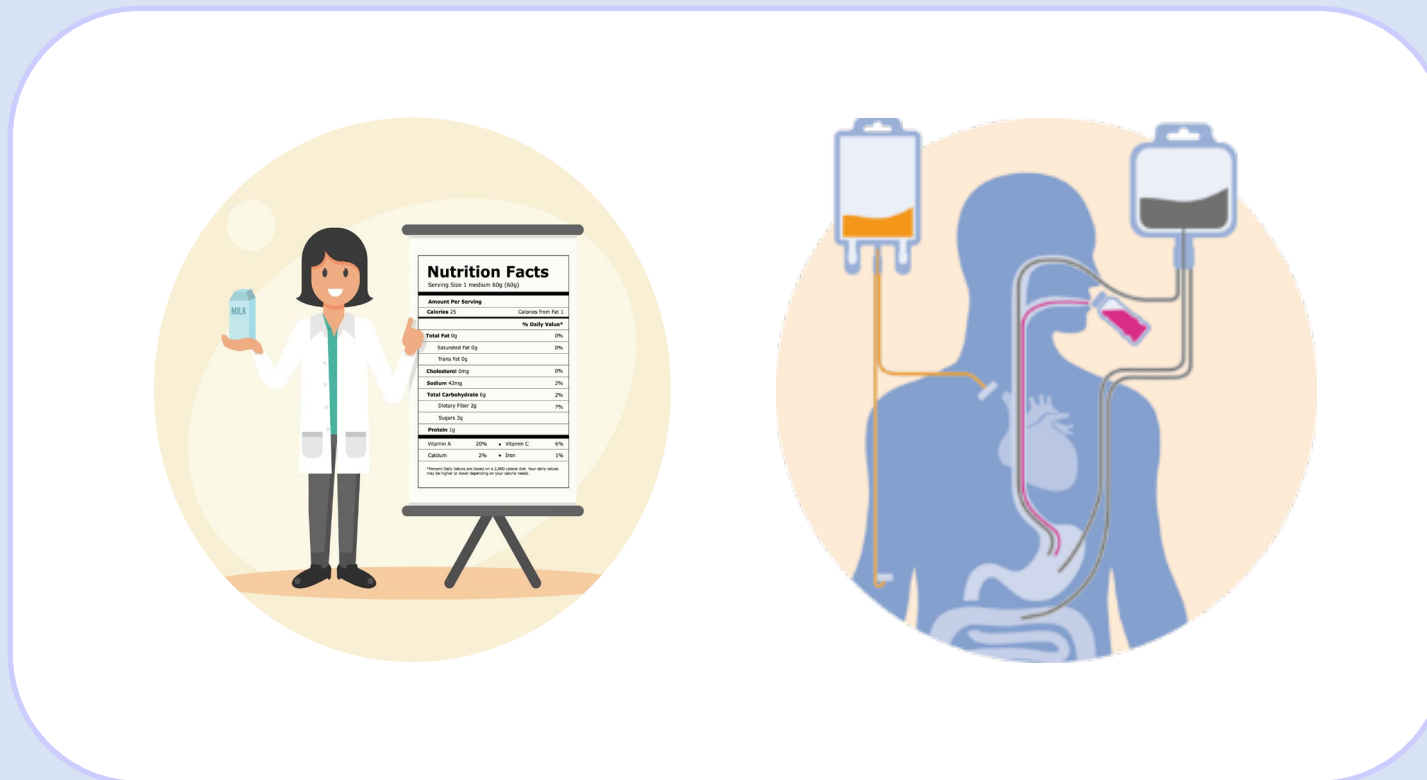


- ↓ weight loss
- ↓ frequency + duration of treatment interruptions/rehospitalizations
- ↓ post-op infectious complications
- ↓ length of stay

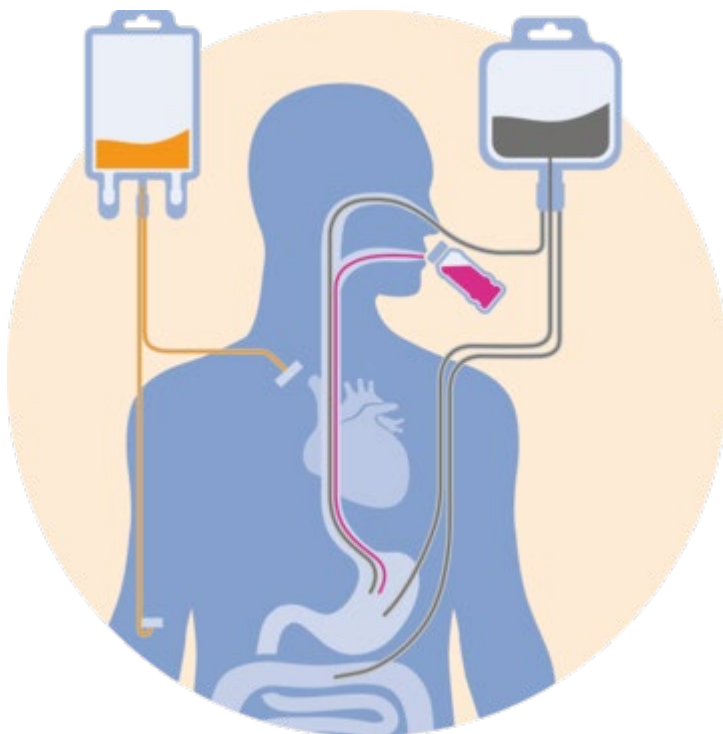
Paccagnella et al., Supp Care Cancer 2010
Lee et al., Arch Otolaryngol Head Neck Surg 1998

Cao et al., 2021

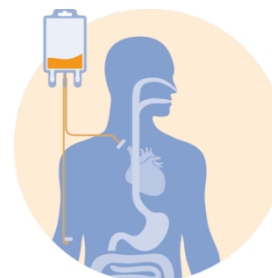
God veiledning er en forutsetning



Enteral eller parenteral ernæring?

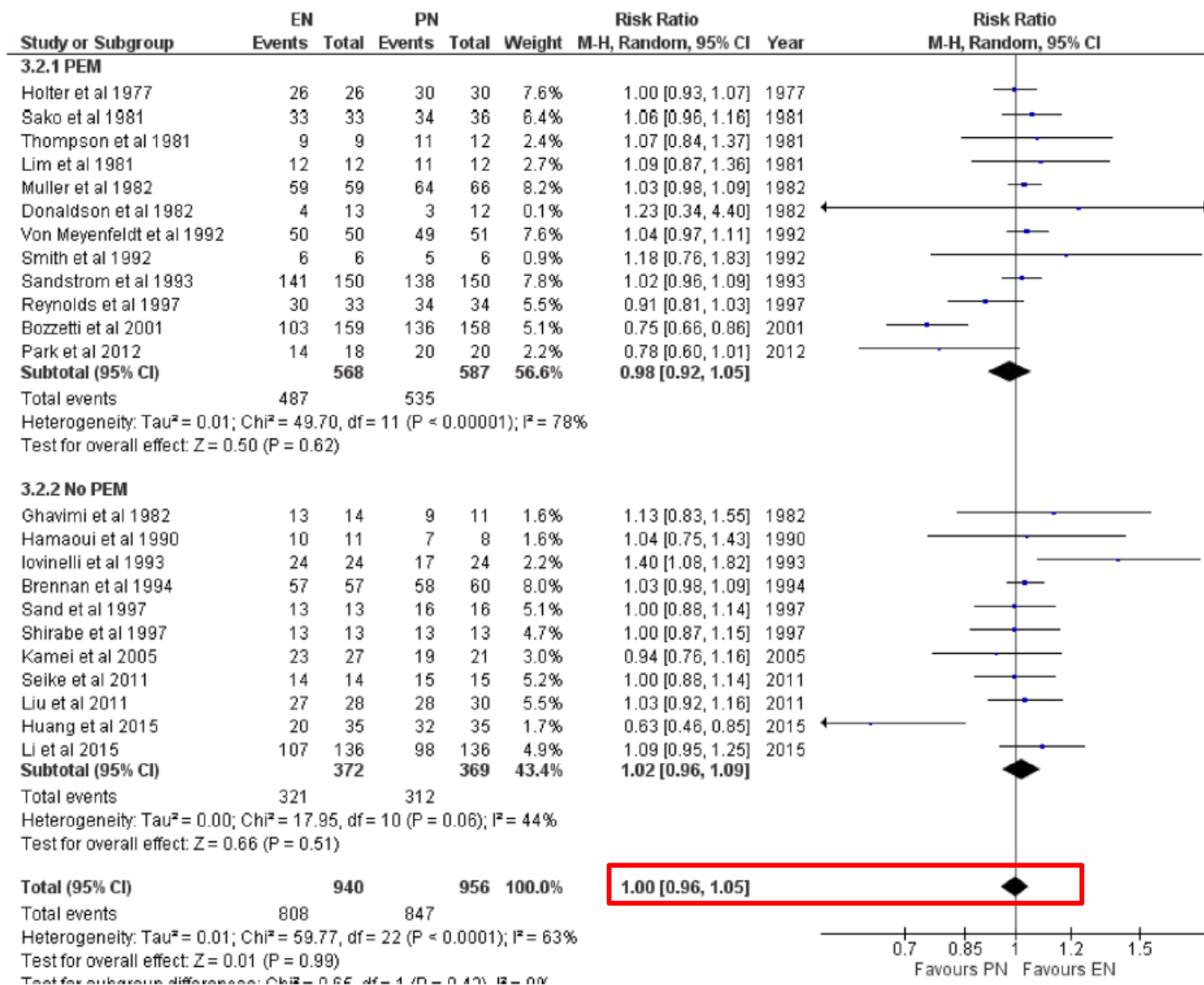


Enteral nutrition



Parenteral nutrition

Ingen forskjell i komplikasjoner



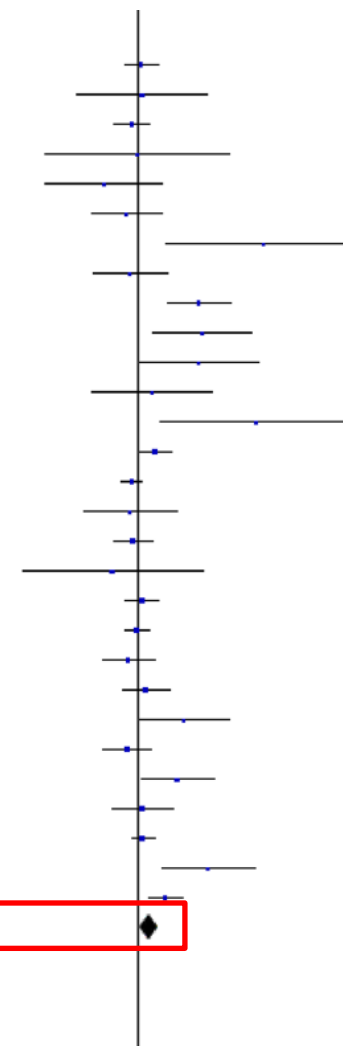
Chow et al., Supp Care Cancer 2020

Flere infeksjoner ved PN

1.3.2 Adults

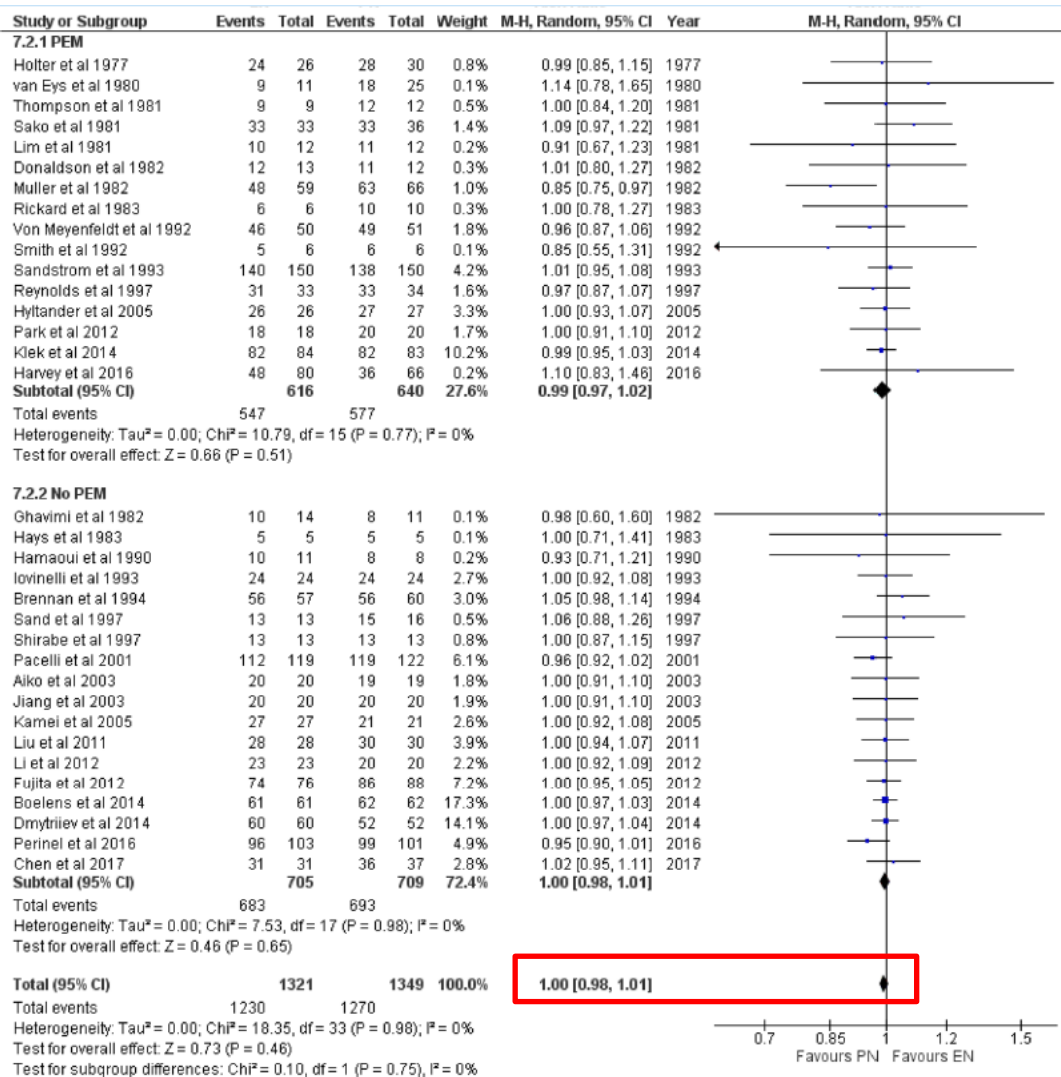
Holter et al 1977	25	26	28	30	5.0%	1.03 [0.91, 1.16]	1977
Thompson et al 1981	7	9	9	12	1.5%	1.04 [0.64, 1.67]	1981
Sako et al 1981	30	33	34	36	4.8%	0.96 [0.84, 1.10]	1981
Lim et al 1981	7	12	7	12	0.9%	1.00 [0.51, 1.97]	1981
Muller et al 1982	21	59	30	66	1.8%	0.78 [0.51, 1.21]	1982
Hamaoui et al 1990	10	11	8	8	3.1%	0.93 [0.71, 1.21]	1990
Von Meyenfeldt et al 1992	20	50	8	51	0.8%	2.55 [1.24, 5.25]	1992
Iovinelli et al 1993	19	24	20	24	3.1%	0.95 [0.72, 1.25]	1993
Sandstrom et al 1993	93	150	59	150	3.5%	1.58 [1.25, 1.99]	1993
Brennan et al 1994	37	57	24	60	2.2%	1.62 [1.13, 2.34]	1994
Reynolds et al 1997	23	33	15	34	1.7%	1.58 [1.02, 2.45]	1997
Sand et al 1997	10	13	11	16	1.7%	1.12 [0.72, 1.75]	1997
Shirabe et al 1997	12	13	5	13	0.8%	2.40 [1.19, 4.86]	1997
Bozzetti et al 2001	134	159	116	158	5.1%	1.15 [1.02, 1.29]	2001
Pacelli et al 2001	108	119	115	122	5.6%	0.96 [0.90, 1.03]	2001
Aiko et al 2003	15	20	15	19	2.4%	0.95 [0.67, 1.34]	2003
Kamei et al 2005	25	27	20	21	4.7%	0.97 [0.84, 1.12]	2005
Seike et al 2011	7	14	9	15	0.9%	0.83 [0.43, 1.62]	2011
Liu et al 2011	27	28	28	30	5.0%	1.03 [0.92, 1.16]	2011
Li et al 2012	23	23	20	20	5.4%	1.00 [0.92, 1.09]	2012
Park et al 2012	16	18	19	20	4.1%	0.94 [0.77, 1.13]	2012
Fujita et al 2012	60	76	65	88	4.3%	1.07 [0.90, 1.27]	2012
Boelens et al 2014	39	61	28	62	2.5%	1.42 [1.01, 1.97]	2014
Klek et al 2014	60	84	64	83	4.2%	0.93 [0.77, 1.11]	2014
Huang et al 2015	31	35	23	35	3.1%	1.35 [1.03, 1.76]	2015
Perinel et al 2016	62	102	59	101	3.6%	1.04 [0.83, 1.31]	2016
Luo et al 2017	34	34	42	44	5.5%	1.04 [0.96, 1.13]	2017
Chen et al 2017	27	31	19	37	2.4%	1.70 [1.21, 2.39]	2017
Wang et al 2018	66	66	51	63	5.0%	1.23 [1.00, 1.50]	2018
Subtotal (95% CI)	1387		1430	94.6%		1.09 [1.02, 1.17]	

Total events 1048 951
Heterogeneity: $\tau^2 = 0.02$; $\chi^2 = 98.88$, $df = 28$ ($P < 0.00001$); $I^2 = 72\%$
Test for overall effect: $Z = 2.59$ ($P = 0.010$)



Chow et al., Supp Care Cancer 2020

Ingen forskjell i mortalitet



Chow et al., Ann Pall Med 2016

Anbefalinger N3-fettsyrer



B5 – 7

N-3 fatty acids to improve
appetite and body weight

Strength of recommendation
WEAK

*In patients with advanced cancer
undergoing chemotherapy 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
Questions for research

Low
Effect of long chain N-3 fatty acids on
body composition and clinical outcome
in cancer patients undergoing
antineoplastic treatment
Effect of long chain N-3 fatty acids on
quality of life and clinical outcome in
patients with cancer cachexia

Strong consensus

Safe dose:
1.8 g/day EPA
5 g/day EPA + DHA

Arends et al., Clin Nutr 2017

Anbefalinger

Immunonutrition (næringsdrikker)

C1 – 4	Immunonutrition (arginine, N-3 fatty acids, nucleotides) in perioperative care
Strength of recommendation STRONG	<i>In upper GI cancer patients undergoing surgical resection in the context of traditional perioperative care we recommend oral/enteral immunonutrition.</i>
Level of evidence Questions for research	High Specifying the role of the individual constituents of immunonutrition regimens

Strong consensus

Arends et al., Clin Nutr 2017

Anbefalinger

Probiotika (ved diare)

C2 – 5	Radiation-induced diarrhea: probiotics
Strength of recommendation —	<i>There are insufficient consistent clinical data to recommend probiotics to reduce radiation-induced diarrhea.</i>
Level of evidence Questions for research	Low Effect of probiotics on radiation-induced diarrhea and treatment completion rate
<u><i>Strong consensus</i></u>	

Arends et al., Clin Nutr 2017

Probiotics Update

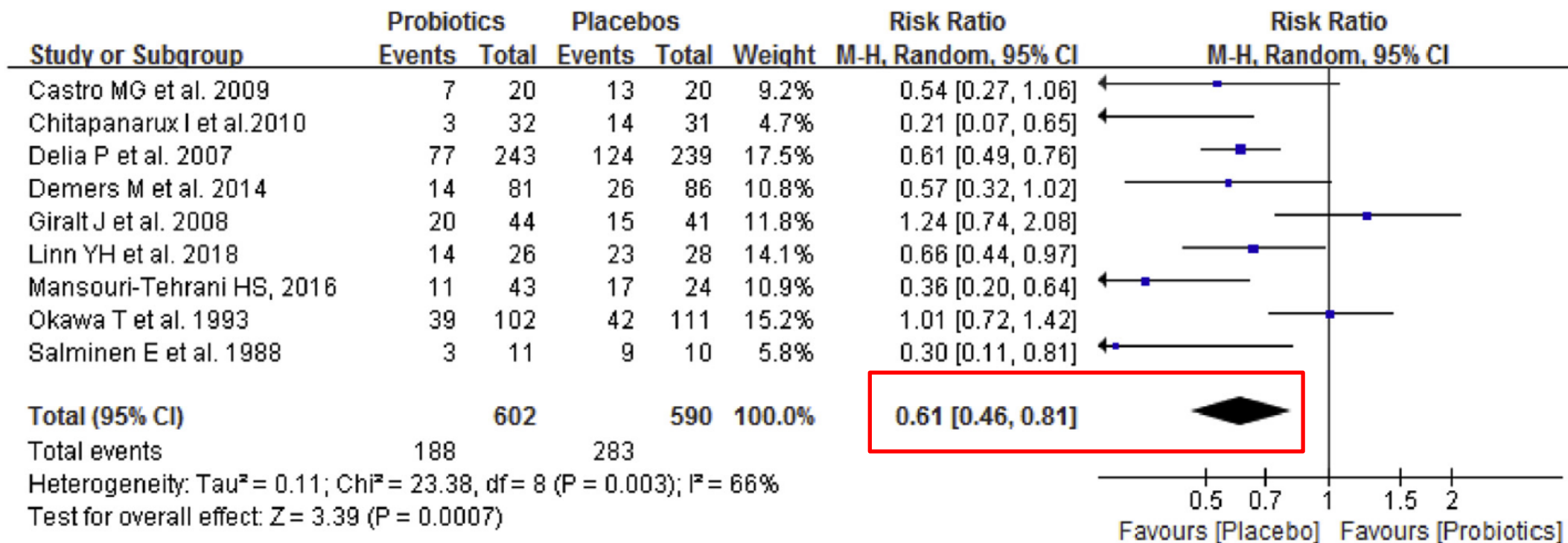


Fig. 4. Forest plot comparing probiotics with placebo with respect to incidence of radiotherapy-induced diarrhea in patients with cervical cancer.

Anbefalinger

Restriktiv kreftdiett

B3 – 2	Potentially harmful diets
Strength of recommendation STRONG	<i>We recommend to not use dietary provisions that restrict energy intake in patients with or at risk of malnutrition.</i>
Level of evidence Questions for research	Low Effects of fasting or fasting mimicking diets on wanted and unwanted effects of anticancer agents

Strong consensus

Arends et al., Clin Nutr 2017



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Restriktiv kreftdiett

PROSJEKT
KREFTFRI
n=1



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[Kreftfri.no](#) > [Livsstilsendringer](#) > [Kosthold ved kreft](#) > [En restriktiv kreftdiett](#)

En restriktiv kreftdiett

Ved en restriktiv kreftdiett søker man å hold plasma-aminosyrenivåene akkurat innenfor det området som kreves for å opprettholde generell helse, for normale celler vil raskt utnytte aminosyrer frigjort av nedbrytningen av maten, mens de overflødige aminosyrene typisk vil fremme vekstfaktorer og være tilgjengelig for bruk av kreftcellene.

Typer av energirestriktive dietter

Terminology	Dietary Intervention
Fasting	Consumption of only water, for a period varying from 12 h to 3 weeks
Short term fasting (STF)	Fasting for an average of 3–5 consecutive days
Periodic fasting	Fasting repeated every 2 or more weeks
Intermittent fasting	Alternate day fasting (≥ 16 h) or 48 h of fasting/week
Fasting mimicking diet (FMD)	A regimen providing low calories, low amounts of proteins, and high amounts of fats. FMD provides 4600 KJ (11% protein, 46% fat, and 43% carbohydrates) for day 1 and 300 KJ (9% protein, 44% fat, and 47% carbohydrates) for days 2–5
Calorie restriction (CR)	20–40% reduction in calorie intake with reduction of all ingredients without intercepting the intake of vitamins and minerals, usually used by experts as synonym to dietary restriction (DR)



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Restriktiv diett

Rasjonale



- Fasting causes a differential stress response in the setting of unfavorable conditions, empowering the survival of normal cells, while killing cancer cells
- Autophagy → natural process of cellular repair and cleaning
- Preclinical studies suggest that energy restrictions could hinder both cancer growth and progression, besides enhancing the efficacy of chemotherapy and radiation therapy
- However, insufficient clinical evidence for beneficial effects of energy restricting diets in patients with cancer

Deligiorgi et al., Int J Mol Sci 2020
Ibrahim et al., Supp Care Cancer 2021



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Restriktiv diett

Kontraindikasjoner



- Patients with cancer are at greater risk of weight loss due to the toxic effect of cancer therapies and cachexia
→ energy restriction may contribute to weight and muscle loss
- Anti-inflammatory effect of energy restricted diets could be detrimental to cancer patients who may be immunodeficient due to the disease or its therapy
- Fasting may cause mild side effects, including headaches, dizziness, nausea, dyspepsia, and fatigue

Ibrahim et al., Supp Care Cancer 2021

Ketogen diett

- High in fat, low in carbohydrates
- Mechanisms for the anti-tumour effects:
 - lowering blood glucose and insulin levels
 - increasing levels of fatty acids, ketone bodies, beta-hydroxybutyrate, and decanoic acid if MCT oil is part of the ketogenic diet→ targeting the Warburg effect
- Warburg effect (aerobic glycolysis)
= increased glucose uptake and fermentation of glucose to lactate, rather than using mitochondrial pathway of oxidative phosphorylation (as in normal cells), even if oxygen is available



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Ketogen diett

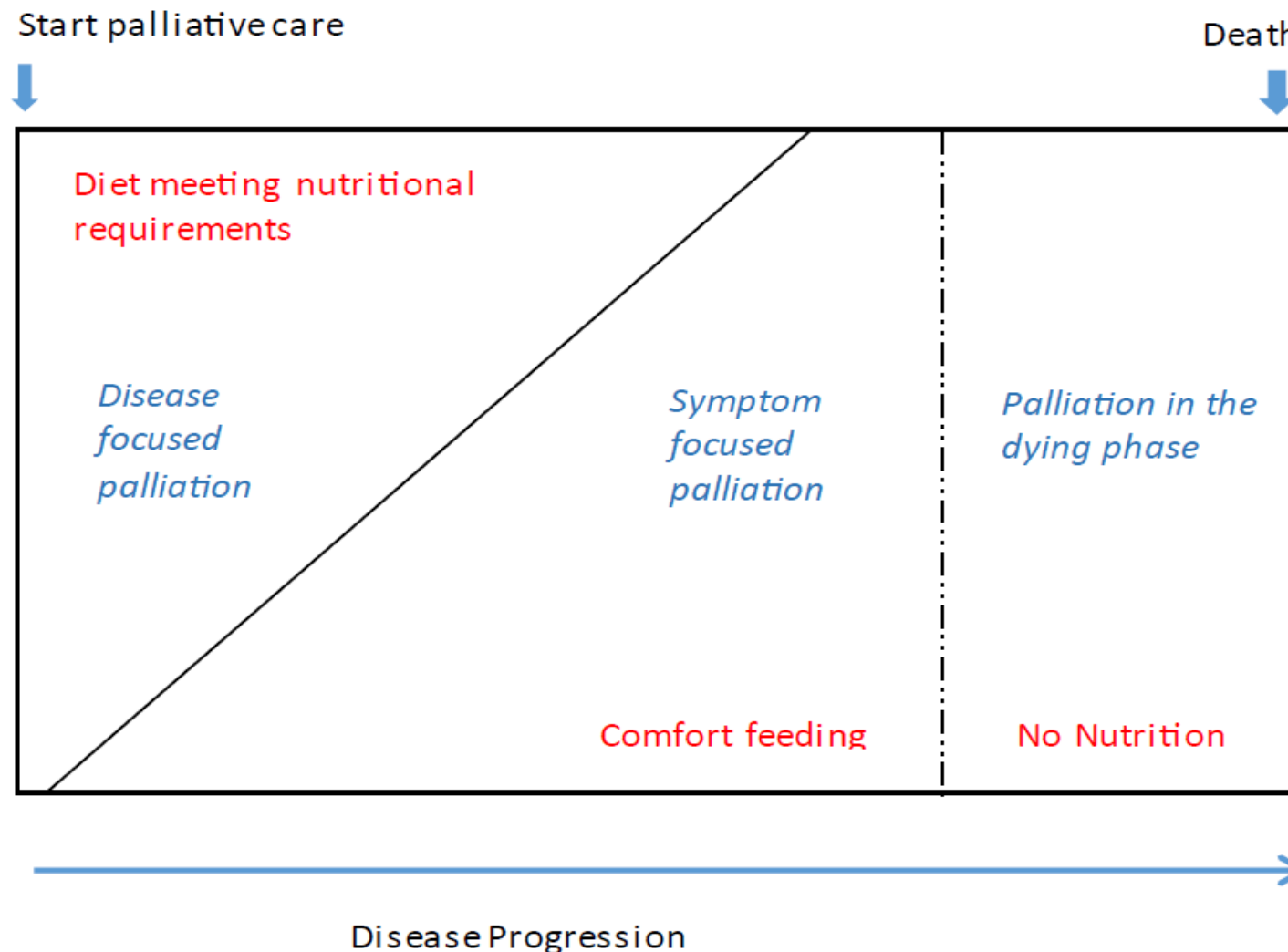
Kontraindikasjoner



- Animal studies not conclusive regarding anti-tumour effect
- Case and cohort studies: some positive results concerning anti-tumour effects, body composition, physical functioning and metabolic parameters
- Robust evidence from studies with clinical endpoints such as overall survival is lacking
- Ketogenic diet may be problematic to adhere to, due to:
 - problems with preparation and palatability of foods
 - poor equipment in the hospital setting
 - perceived burden from the blood sampling twice a day,
 - problems with socializing

Klement, Curr Opin Clin Nutr Metab Care 2019
Schwartz et al., Front Nutr 2018

Ernæring og palliasjon



DDOG/LWDO 2013: derived from De Graeff et al. 2010 Beijer et al., Clin Nutr 2017



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Key messages

- Dietary counselling by trained nutrition professional is 1st line nutritional treatment
- Start dietary counselling to early, to maintain/improve nutritional status
- Protein: 1.0-1.5 g/kg/day
- ≥ 2 g/day N-3 fatty acids/ fish oil in patients with advanced cancer undergoing chemotherapy and at risk of weight loss or malnourished
- immunonutrition in pts. with upper GI cancer undergoing surgical resection

- Probiotics are not recommended in pts. with radiation-induced diarrhea
- Energy restricting diets and ketogenic diets not recommended in patients with cancer

THANK
YOU