



Nutritional Challenges in Childhood Cancers

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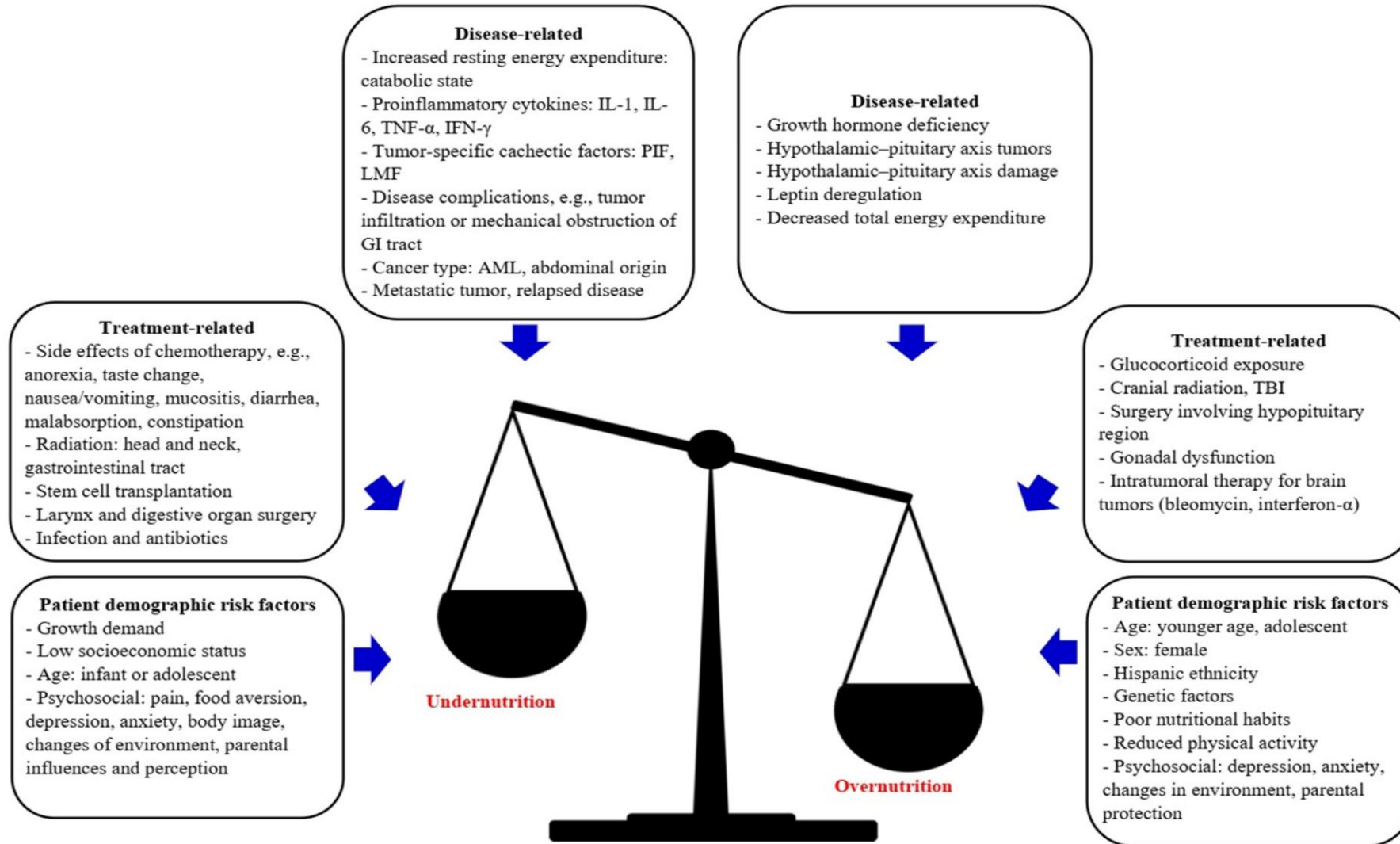
Outlines

- Prevalence of Malnutrition in Childhood Cancers
- Pathophysiology
- Nutritional assessment
- Treatment, intervention and Follow up

Nutritional Problems in Childhood Cancers

- **Malnutrition** defines as “deficiencies, excesses, or imbalances in a person’s intake of energy and/or nutrients”
- Referring to both **undernutrition** and **overnutrition**
- Malnutrition is common among pediatric cancer patients, especially in low- and middle-income countries.
- The incidence of undernutrition in **LMICs** ranges from **8.1% to 50.0%**, while the incidence of overnutrition ranges from **2.0% to 17.1%** among **children with cancer**.

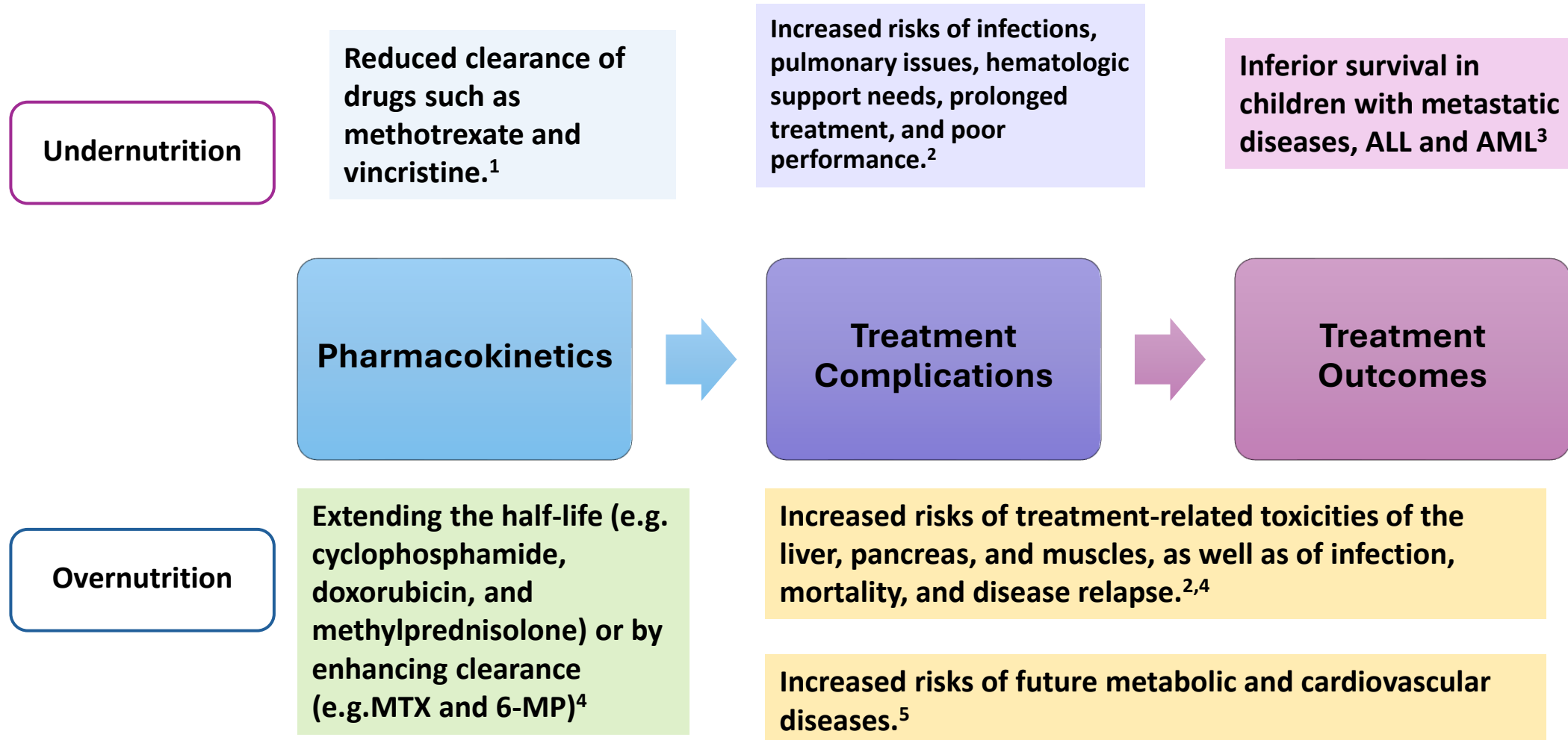
Pathophysiology



Disease and Treatment risk factors

High Risk Factors for Undernourishment	High Risk Factors for Overnourishment
Solid tumors with advanced stages at diagnosis	Total body or abdominal or cranial irradiation
Ewing sarcoma	Craniopharyngioma
Medulloblastoma and other high grade brain tumors	Administration of prolonged corticosteroid therapy or other drugs increasing body fat stores
Diencephalic tumors	
Head and neck tumors	
Age < 2 months	
Relapsed disease	
Administration of highly emetogenic regimens	
Administration of regimens associated with severe gastrointestinal complications, such as constipation, diarrhea, loss of appetite, mucositis, or enterocolitis	
Administration of radiation to the oropharynx, esophagus, or abdomen	
Post-surgical complications, such as prolonged ileus or short gut syndrome	
Stem cell transplantation with myeloablative conditioning regimens	

Impact of Nutrition on Cancer Treatment



¹Tripodi SI. Tumori, 2023

²Orgel E. J Clin Oncol, 2014

³Co-Reyes E. PBC 2012

⁴Rogers PC. PBC, 2005

⁵Neville KA. The Journal of Clinical Endocrinology & Metabolism, 2006

Nutritional Status at Diagnosis of Childhood Cancer

Overall nutritional status of subjects.

Types of cancer	Overall nutritional status			<i>p</i> -value
	Adequately nourished <i>n</i> (%)	Inadequately nourished <i>n</i> (%)	Severely undernourished <i>n</i> (%)	
Hematologic cancer	16 (43.2)	12 (32.4)	9 (24.3)	0.393
Solid cancer	23 (56.1)	12 (29.3)	6 (14.6)	
CNS cancer	2 (50)	0 (0)	2 (50)	
Total	41 (50)	24 (29.3)	17 (20.7)	

n, number; CNS, central nervous system.

p-value was used to compare overall nutritional status among types of cancer.

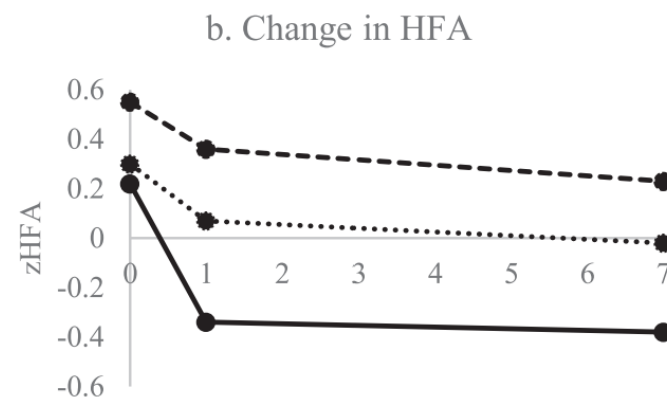
Nutritional Status at Diagnosis of Childhood Cancer

Prevalence of undernutrition by combined nutritional assessment and stages of cancer subgroups.

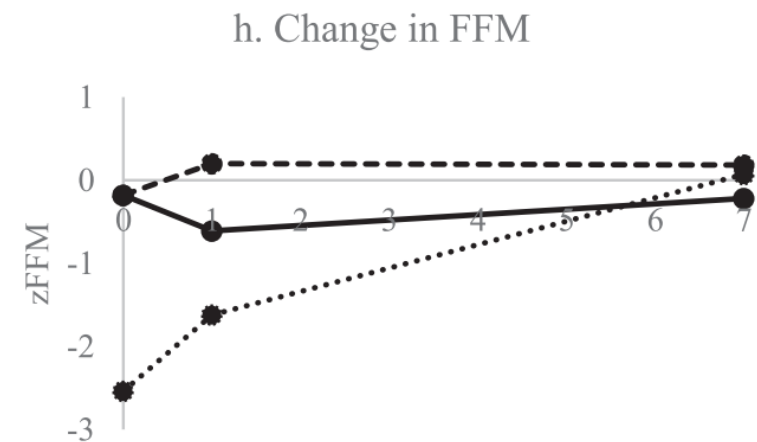
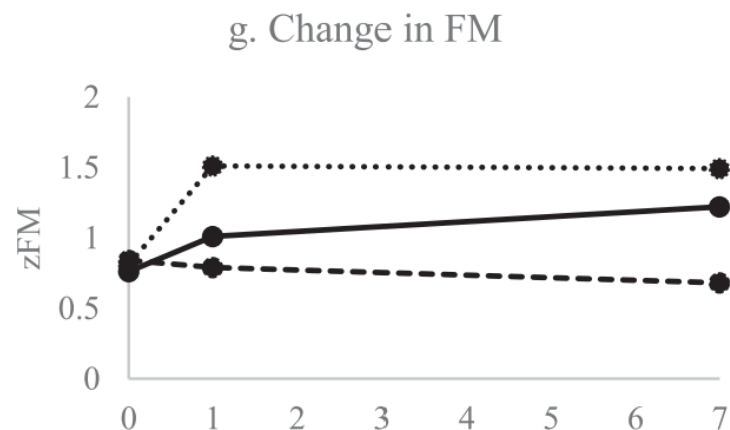
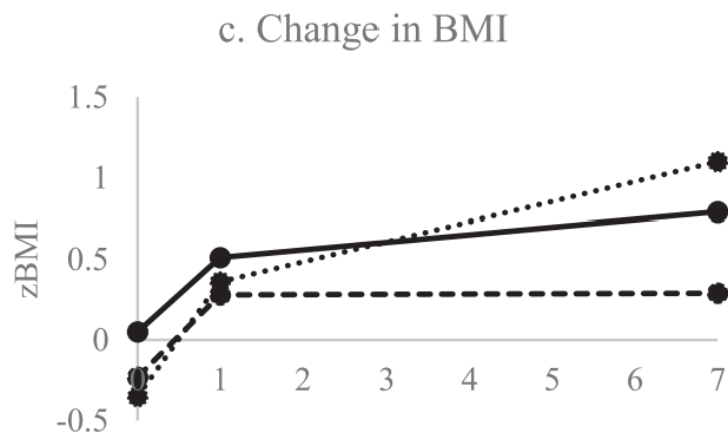
Stages of lymphoma and solid cancer	Combined nutritional assessment			Total <i>n</i> (%)	<i>p</i> -value
	Adequately nourished <i>n</i> (%)	Inadequately nourished <i>n</i> (%)	Severely undernourished <i>n</i> (%)		
1	8 (88.9)	0	1 (11.1)	9 (16.3)	0.033
2	11 (73.3)	3 (20.0)	1 (6.7)	15 (27.3)	
3	6 (37.5)	8 (50.0)	2 (12.5)	16 (29.1)	
4	5 (33.3)	6 (40.0)	4 (26.7)	15 (27.3)	
Total	30 (54.5)	17 (31.0)	8 (14.5)	55 (100)	

n, number; *p*-value was used to compare nutritional status among stages of cancer.

Nutritional Changes in Childhood Cancer



— Hematologic malignancies
- - - Solid tumors
..... Brain tumors



Nutritional Assessment

Basic assessment

- **Screening Tools**
- **A. Anthropometric measures**
- **B. Biochemistry exams**
- **C. Clinical**
- **D. Dietary History**

Advance technique

- **Bioelectrical impedance analysis (BIA)**
- **Dual-energy x-ray absorptiometry (DXA)**
- **Computed tomography (CT)**
- **Magnet resonance imaging (MRI)**

Screening Tools



Screening tools	SCAN	STAMP	STRONG _{kids}
Target population	Children with cancer	General hospitalized children	General hospitalized children
Validation studies available for specific pediatric cancers and timepoints?	Yes, cross-sectionally evaluated at diagnosis, active treatment, maintenance, post therapy	No	Yes, no specific time point
Components	6 questions	2 questions and anthropometric data	4 questions
Criteria used	• Risk of cancer • Treatment intensity • GI tract symptoms • History of poor intake • History of weight loss • Signs of undernutrition	• Diagnosis • Dietary intakes • Weight and height	• Underlying disease with risk of malnutrition • Signs of poor nutritional status • Diarrhea, poor intake or history of nutritional supplement • History of weight loss or stunt growth

Nutritional Status (WHO definition)

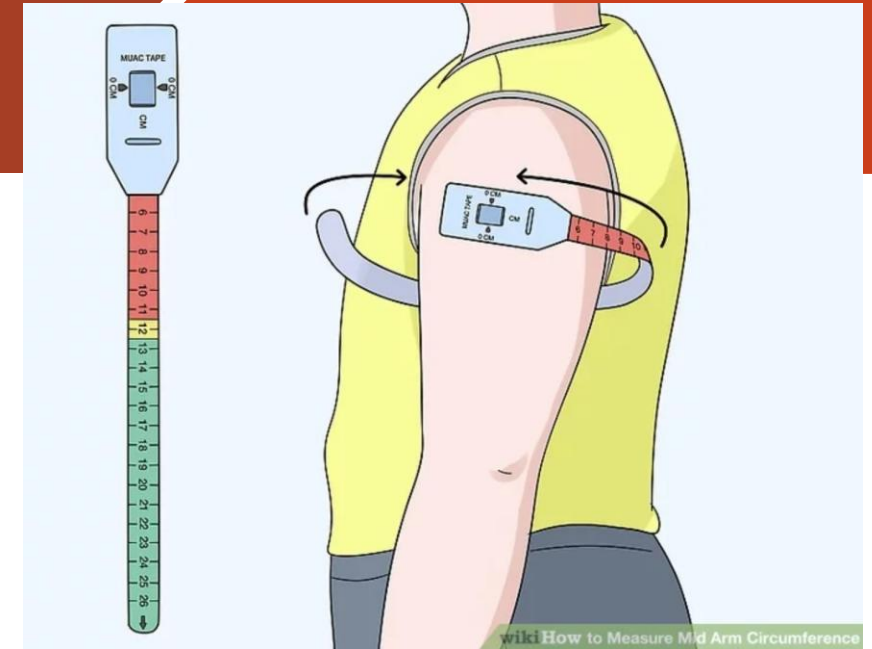


Undernutrition	Acute undernutrition or wasting: WFH < −2 SD
	Chronic undernutrition or stunting: HFA < −2 SD
Overweight	<5 years: WFH > +2 SD
	5–19 years: BMI-for-age > +1 SD
Obesity	<5 years: WFH > +3 SD
	5–19 years: BMI-for-age > +2 SD

Basic Assessment

Mid-upper arm circumference

- **Use in Undernutrition Screening:**
 - Less affected by abdominal mass, amputation, or edema.
 - Positively correlates with fat-free mass (FFM), as evaluated using BIA and DXA.^{1,2}
 - Useful for serial monitoring of nutritional status, especially in resource-limited settings.



	Acute malnutrition	Severe acute malnutrition
6 mo- 5 yr	MUAC < 12.5 cm.	MUAC < 11.5 cm..
> 5 yr- < 10 yr	MUAC < 15.5 cm.	MUAC < 13.0 cm.
10 yr - 14 yr	MUAC < 18.5 cm..	MUAC < 16.0 cm.

¹Barr R et al. J Pediatr Hematol Oncol 2011; 33(3): e101-4.

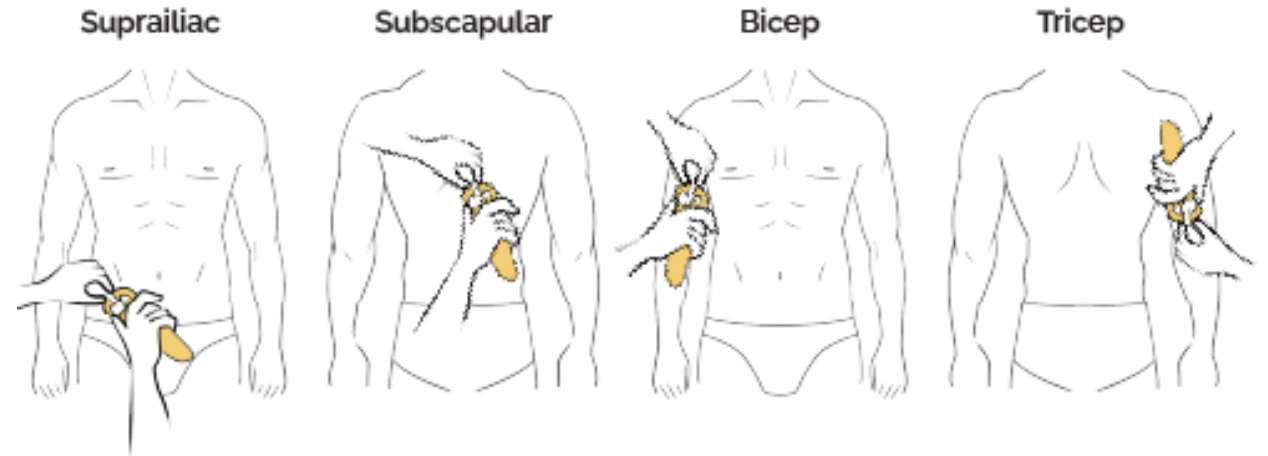
²Revuelta Iniesta R. Clin Nutr ESPEN 2019.

³World Health Organization, 2009.

Basic Assessment

Skin fold thickness

- Estimates total body fat as most fat is stored subcutaneously.
- Most common sites: Triceps, Subscapular
- Studies on childhood cancers during treatment and survivorship demonstrate that TSFT positively correlates with fat mass (FM), as confirmed by DXA and BIA.¹⁻³



¹Karlage RE et al. *Cancer* 2015.

²Barr R et al. *J Pediatr Hematol Oncol* 2011.

³Revuelta Iniesta R et al. *Clin Nutr ESPEN* 2019.

Basic Assessment

Anthropometric Measure

- Wt, Ht, BMI, HC
- MUAC, Skin fold thickness
- Waist measurement (WC, W/H, W/Ht)
- Grip Strength

Biochemistry

- CBC
- Blood sugar, BUN, Cr, electrolyte
- serum albumin, pre-albumin, and transferrin
- Lipid
- Liver function test

Clinical

- Signs of malnutrition e.g. subcutaneous loss. Muscle wasting, edema
- Signs of specific vitamin or mineral deficiencies

Dietary History

- 24-hour recall
- Food frequency questionnaires
- Food diary
- Remote food photography method

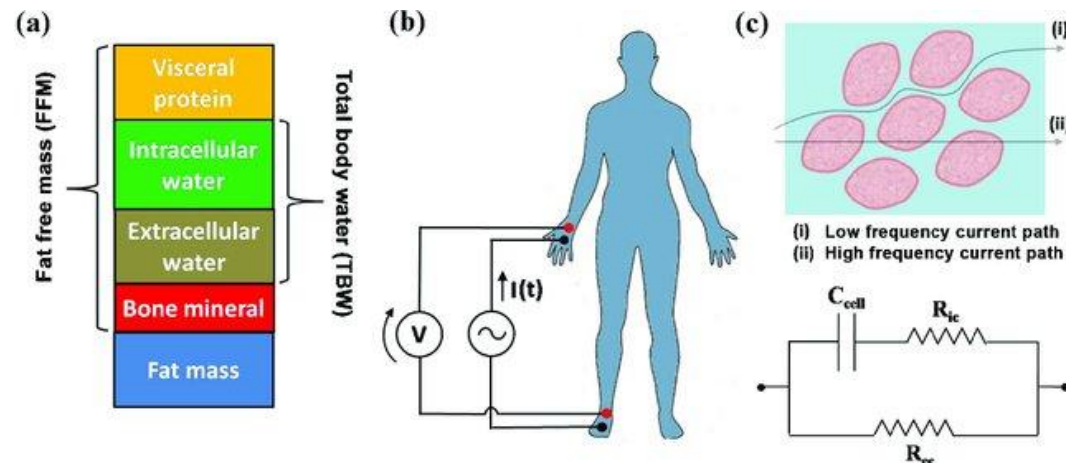
Advance Body Composition Assessment

Bioelectrical impedance analysis (BIA)

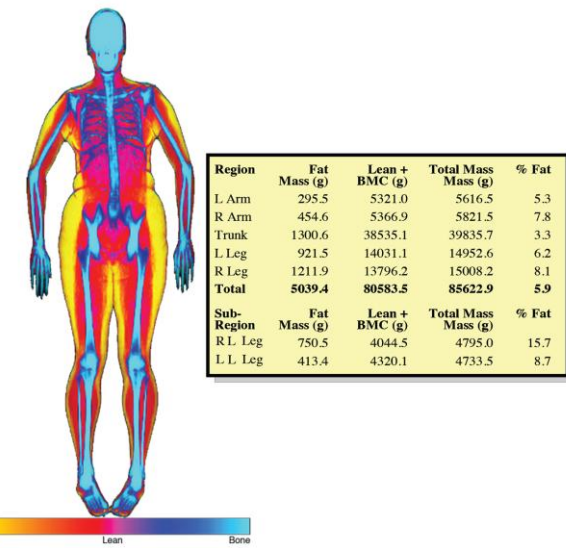


Mean changes in nutritional status established in 3, 9 and 18 months intervals.

Growth	0–3 Months			0–9 Months			0–18 Months		
	Change	95% CI	<i>p</i> Value	Change	95% CI	<i>p</i> Value	Change	95% CI	<i>p</i> Value
BMI C	1.5	1.31–3.47	<0.001	15.9	–0.1 to 0.2	0.6	19	1.31–3.47	<0.001
HFA C	–1.3	–5.9 to 0.04	0.05	–3.9	–0.4 to 0.02	0.07	–4.2	–0.005 to 0.24	0.06
Body composition									
FFM% AA	–0.9%	–1.6 to (–0.5)	<0.001	–4.1%	–0.09 to 0.06	0.7	–4.87%	–0.01 to 0.02	0.7
FFM% BIA	–1.71%	–0.78 to (–0.01)	<0.05	–2.83%	–0.13 to (–0.01)	<0.02	–3.88%	–0.01 to 0.01	0.8
FM% AA	1.92%	–0.01 to 0.02	0.8	5.22%	–0.06 to 0.08	0.7	5.98%	–0.01 to 0.02	0.8
FM% BIA	1.71%	0.006–0.077	<0.05	3.1%	0.01–0.1	<0.02	3.9%	–0.01 to 0.01	0.4

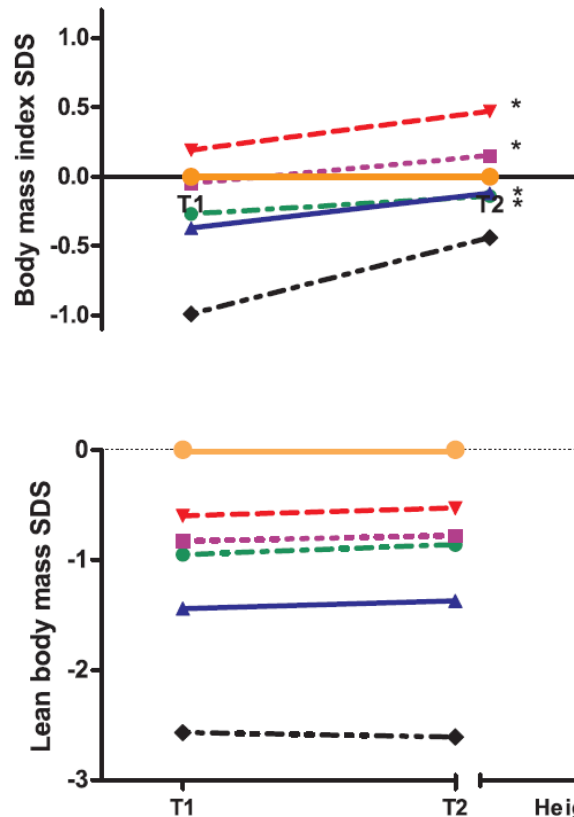


Advance Body Composition Assessment

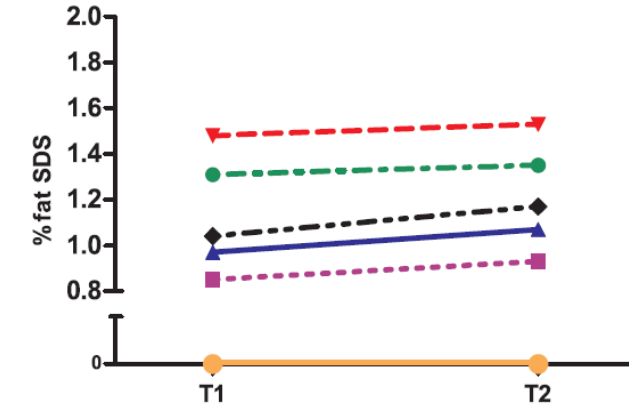
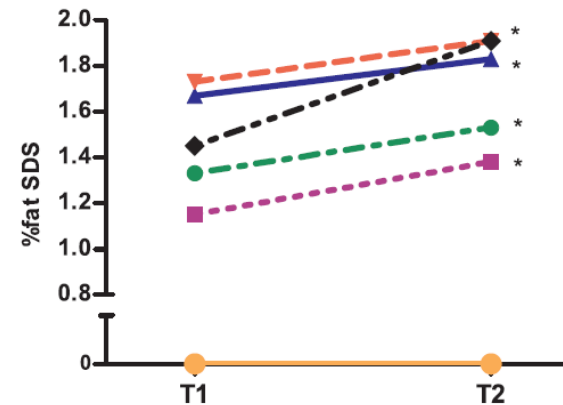
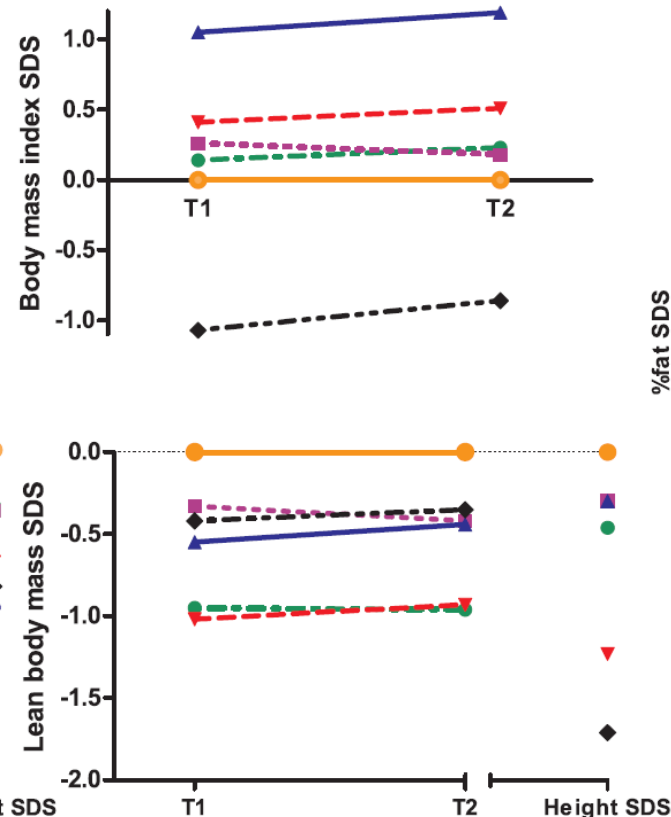


Dual-energy x-ray absorptiometry (DXA)

Male



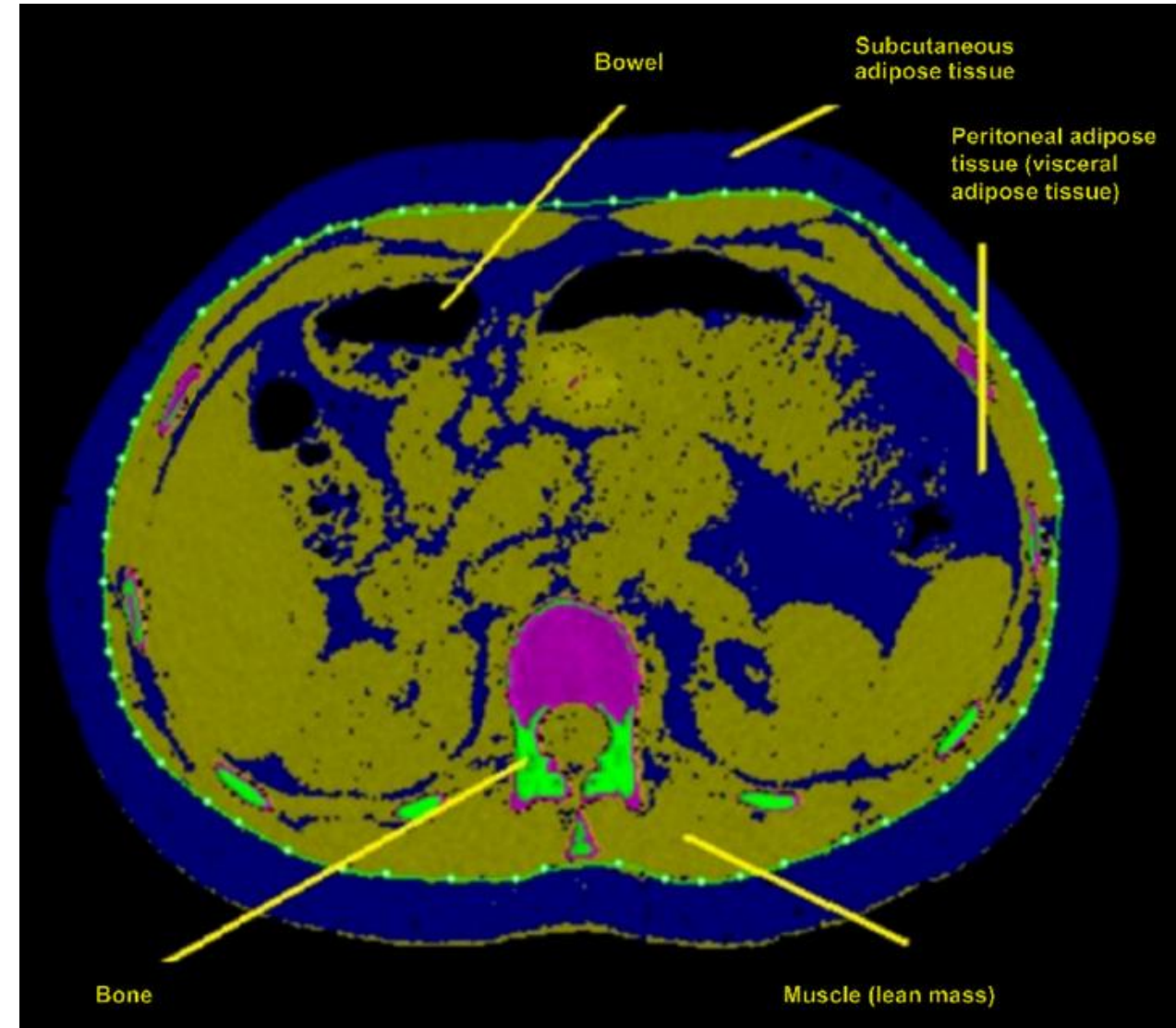
Female



- No CRT nor corticosteroids
- Corticosteroids
- ▲ Brain tumor irradiation (BRT)
- ▼ Cranial Radiotherapy (CRT)
- ◆ Total Body Irradiation (TBI)
- Dutch references

Quantitative CT (QCT) in Childhood ALL

BMI and QCT Assessment in
Childhood ALL at Diagnosis and
After Therapy (N = 189)



Quantitative CT (QCT) in Childhood ALL

Body composition	Location	At diagnosis				Off-therapy			
		Mean	SD	Pearson correlation coefficient	<i>p</i>	Mean	SD	Pearson correlation coefficient	<i>p</i>
LT ^a	L1	147.313	37.556	−0.062	0.399	116.348	120.904	0.129	0.078
	L2	121.486	35.971	−0.094	0.200	93.393	94.256	0.108	0.140
SAT ^a	L1	22.088	21.101	0.640	<0.001	40.947	51.015	0.566	<0.001
	L2	32.058	25.373	0.616	<0.001	52.239	62.388	0.551	<0.001
VAT ^a	L1	11.618	10.917	0.427	<0.001	19.215	18.482	0.539	<0.001
	L2	14.420	12.528	0.515	<0.001	20.104	16.882	0.551	<0.001
TAT ^a	L1	33.705	28.969	0.627	<0.001	60.162	66.654	0.583	<0.001
	L2	46.478	34.440	0.641	<0.001	72.343	75.788	0.576	<0.001
LT/TAT	L1	8.622	9.865	−0.291	<0.001	3.399	2.690	−0.461	<0.001
	L2	4.301	3.538	−0.346	<0.001	2.088	1.513	−0.485	<0.001
VAT/SAT	L1	0.936	1.175	−0.243	0.001	0.682	0.569	−0.385	<0.001
	L2	0.662	0.733	−0.140	0.055	0.492	0.310	−0.260	<0.001

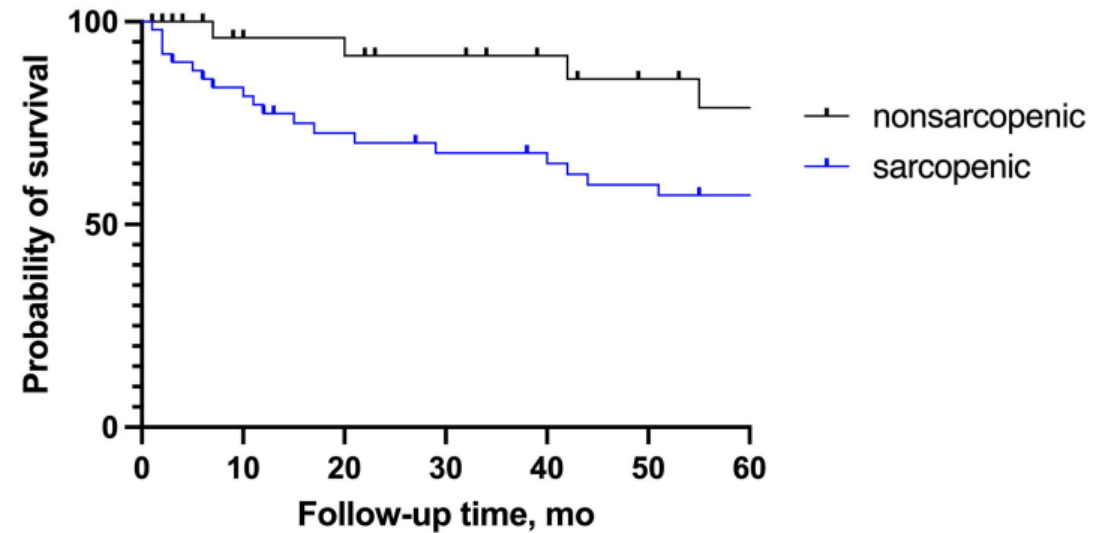
Quantitative CT in Childhood ALL

Variable ^a	L1		L2	
	Estimate ^b	<i>p</i>	Estimate ^b	<i>p</i>
LT ^c				
Time point (off-therapy)	-25.498	0.007	-23.330	0.002
Age (≥10 years)	-38.271	0.005	-33.342	0.002
Sex (female)	-19.755	0.035	-17.277	0.020
LT/TAT				
Time point (off-therapy)	-4.905	<0.001	-2.089	<0.001
Age (≥10 years)	-2.222	0.045	-0.865	0.040
Sex (female)	-1.863	0.023	-0.618	0.059
TAT ^c				
Time point (off-therapy)	24.093	<0.001	23.264	<0.001
Age (≥10 years)	16.543	0.036	18.210	0.044
Sex (female)	2.007	0.745	1.918	0.787

Variable ^a	L1		L2	
	Estimate ^b	<i>p</i>	Estimate ^b	<i>p</i>
SAT ^c				
Time point (off-therapy)	17.233	<0.001	18.083	<0.001
Age (≥10 years)	11.388	0.058	14.690	0.046
Sex (female)	2.216	0.633	2.905	0.606
VAT ^c				
Time point (off-therapy)	6.843	<0.001	5.165	<0.001
Age (≥10 years)	5.281	0.023	3.637	0.093
Sex (female)	-0.211	0.909	-0.989	0.599

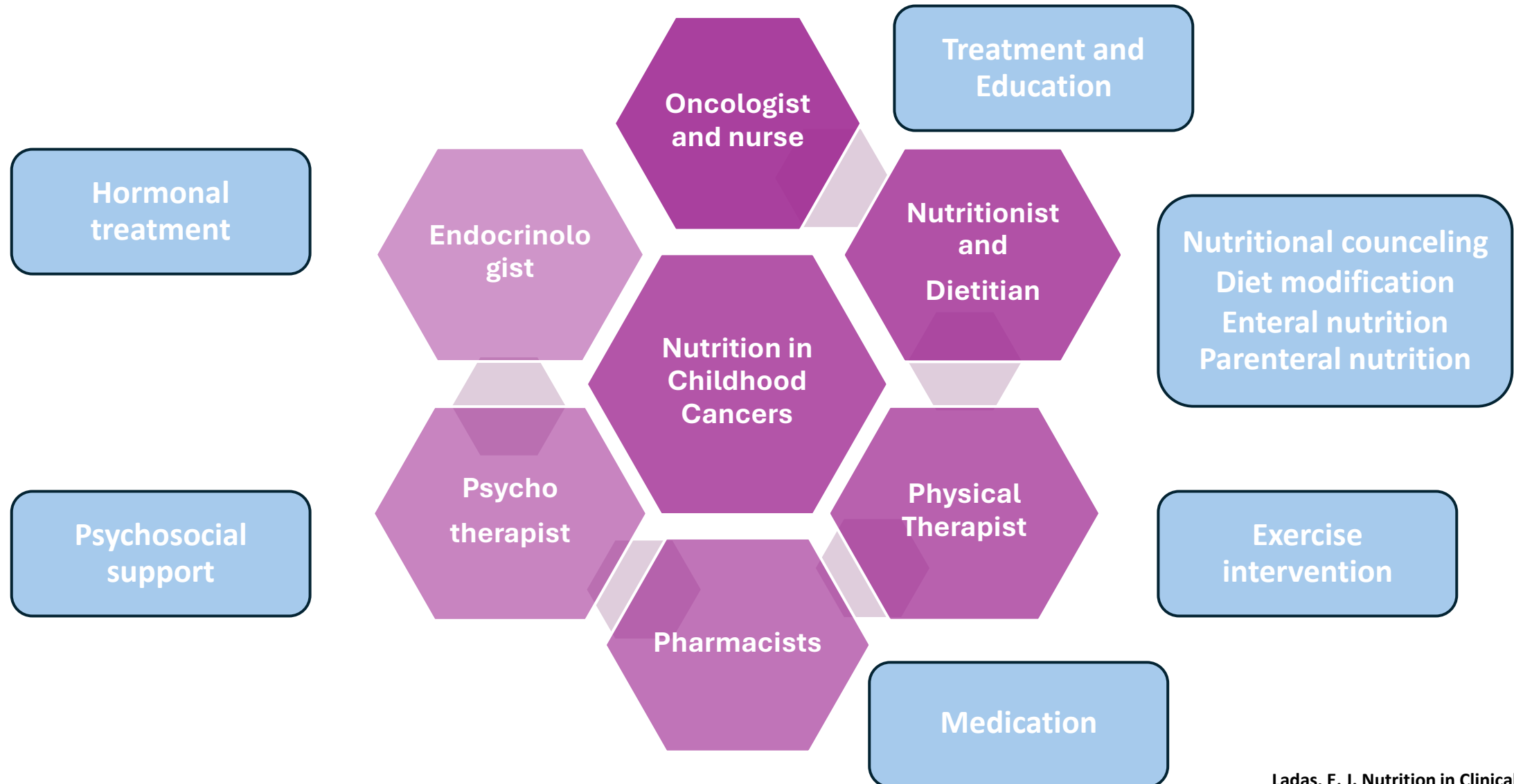
Nutritional Effect in Neuroblastoma

- Retrospective analysis of children with neuroblastoma ages 1–15 years, who were treated from 2008 to 2016.
- Psoas muscle area (PMA) was measured from cross-sectional images, using CT or MRI scans at lumbar disc levels L3-4 and L4-5.
- 101 children with neuroblastoma were enrolled.
- Preoperative sarcopenia was associated with 5-year survival after surgery, with a hazard ratio of 4.18 (95% CI: 1.01–17.26).

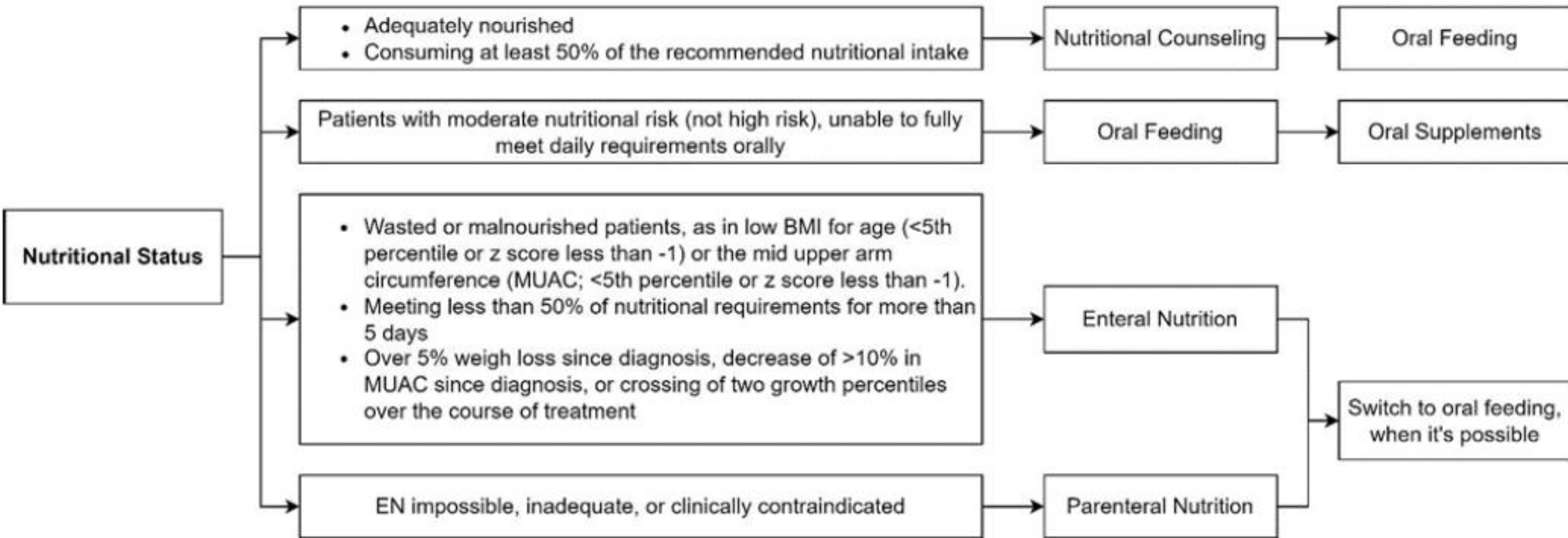


No. at risk							
nonsarcopenic	30	23	22	19	16	13	11
sarcopenic	50	39	30	27	26	23	21

Multidisciplinary Team on Nutritional Intervention



Nutritional Intervention



Nutritional Intervention

Oral nutritional supplements

- Two systematic reviews, including 4 studies, investigated the use of oral nutritional supplements, such as **Ready-to-Use Therapeutic Food (RUTF) and oral supplements (isocaloric and hypercaloric)**, to improve nutrition in various childhood cancers. The intervention duration ranged from 1 to 6 months.
- The findings demonstrated benefits in **improving weight status**, with some studies also reporting a **reduction in treatment-related complications**, such as infections and mucositis, in the intervention group.

Nutritional Intervention

Appetite Stimulants agents

- Two systematic reviews, including 4 studies, investigated the use of appetite stimulants agent—**megestrol acetate, cyproheptadine, or their combination**—to improve nutrition in children with various childhood cancers.
- The intervention duration ranged from 1 to 6 months.
- The findings demonstrated benefits in **improving weight status** in children with cancer-related or treatment-related weight loss, anorexia, or cachexia.

Nutritional Intervention

References	Dietary Compound	Outcomes
Klement et al. [72]	Mediterranean diet	It decreases inflammatory signaling, producing SCFA that positively influences cancer prevention and treatment
Gupta et al. [77] Maia et al. [78]	Neutropenic diet	It does not bring benefits and does not contain a bacterial load lower than a normal diet
Bai et al. [68] Masetti et al. [69]	Probiotics	They can influence the prophylaxis of infections in cancer patients, but more safety data are needed regarding probiotics, especially due to the lack of knowledge about the risk of infections in giving live microorganisms to immunocompromised children
Zheng et al. [87]	FOS	They stimulate the synthesis of IgA, increasing the production of mucins, modulating inflammatory cytokines, which leads to a decrease in the inflammatory state and a positive physical growth

FN; febrile neutropenia; FOS, fructo-oligosaccharides; GM, gut microbiome; NS, nutritional status; RUTFs, ready-to-use therapeutic foods.

Nutritional Intervention

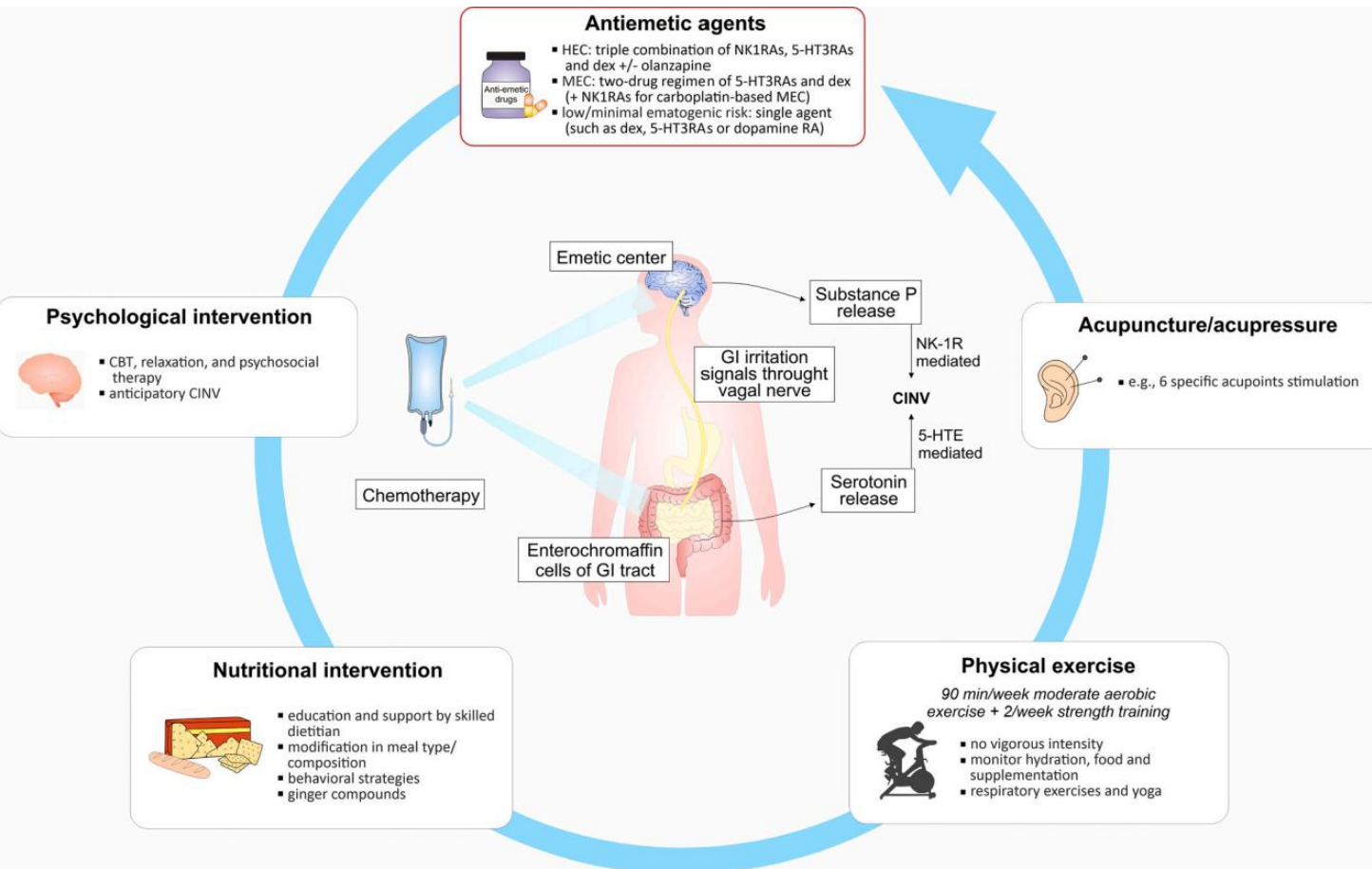
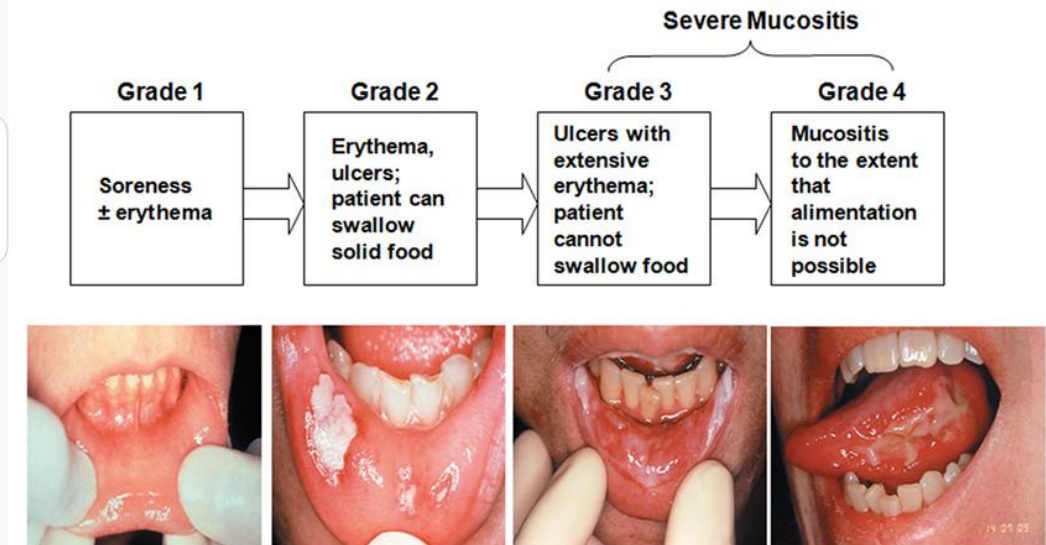


Fig. 1. Pathophysiology and current pharmacologic and non-pharmacologic intervention to manage CINV.

World Health Organization's Oral Toxicity Scale



Nutritional Intervention

Physical exercise training interventions for children and young adults during and after treatment for childhood cancer (Review)

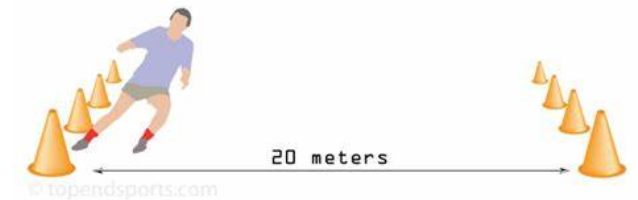
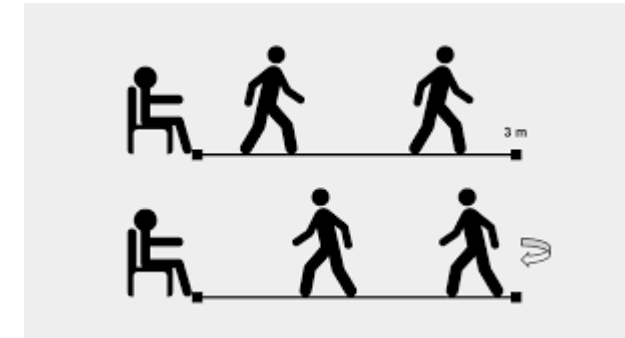
Braam KI, van der Torre P, Takken T, Veening MA, van Dulmen-den Broeder E, Kaspers GJL

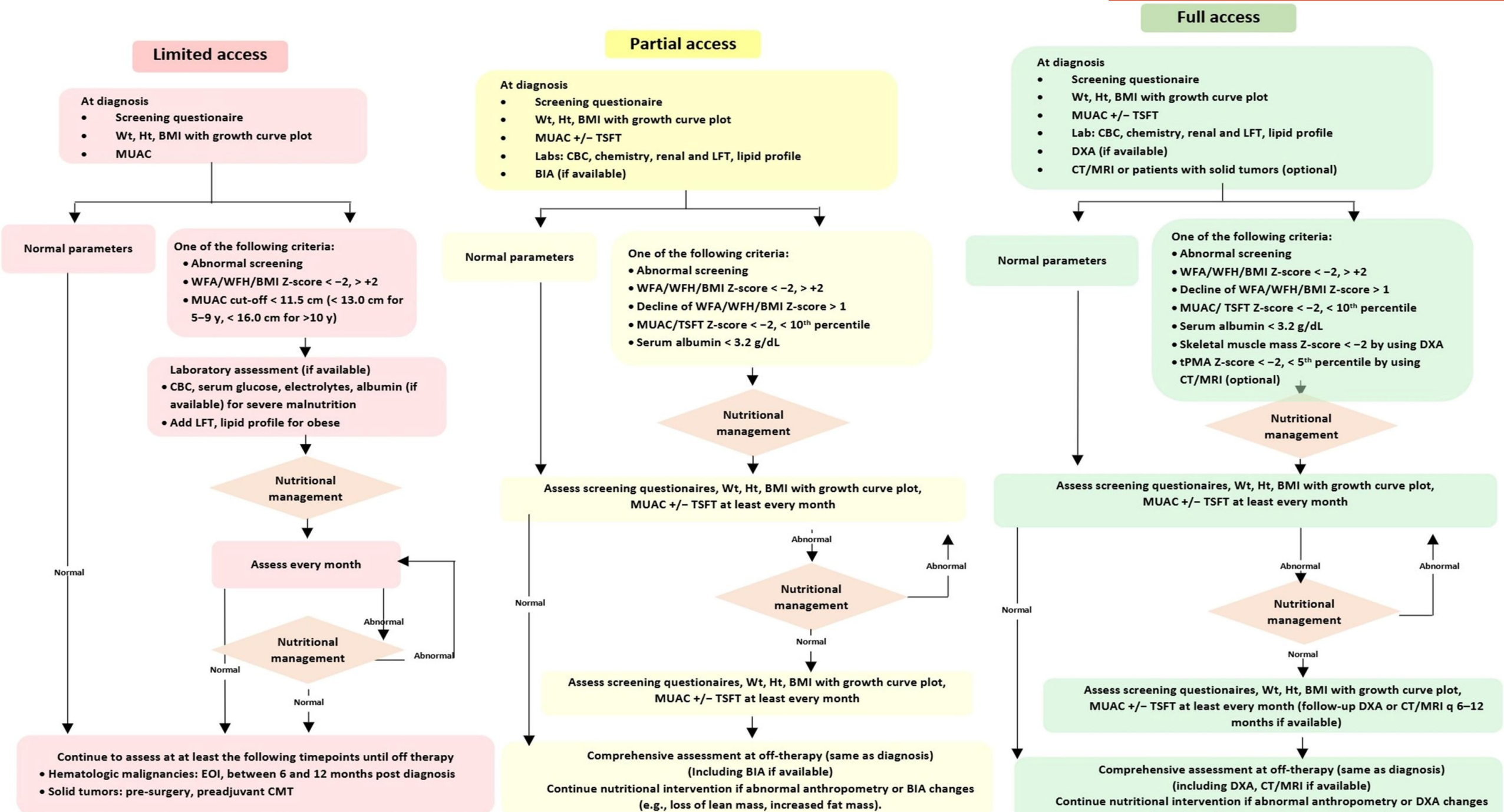
- Cardiorespiratory Fitness: Improved in intervention group (9-min run-walk test, 20-m shuttle run, timed up-and-go test).
- Bone Mineral Density: Increased significantly in intervention group.
- BMI & Flexibility: No significant difference, except for passive ankle dorsiflexion improvement.
- Muscle Strength: Back and leg strength improved significantly.
- Quality of Life & Fatigue: No major differences, except for cancer-related worries.

Conclusions: There were some benefits of physical exercise training on body composition (percentage of fat mass, muscles, and bones), flexibility, cardiorespiratory fitness, muscle strength and quality of life.

The analysis included 171 children with ALL undergoing treatment.

Training sessions varied from 15 to 60 minutes, with differing interventions and durations, while the control group received usual care.





Survivorship Follow-Up

Nutritional Risk	Proposal
No nutritional risks	First year: every 6 months After first year: annually
Presence of nutritional risk (i.e., inadequate eating habits, sedentary lifestyle, hypertriglyceridemia, high cholesterol levels) or well-nourished	First year: every 3 months Second to fifth year: every 6 months From fifth year onward: annually
Undernourished	Monthly assessment until normal nutrition status
Obese	Every 3 months

Conclusions

- **Nutrition** is a key factor influencing treatment outcomes in pediatric cancer.
- **Nutritional challenges** can arise from diagnosis through survivorship.
- **Comprehensive assessment and appropriate interventions** help reduce complications, enhance treatment efficacy, and improve quality of life.
- **A multidisciplinary team** is crucial in addressing nutritional challenges and optimizing patient care.
- **Standardized care tailored to different settings** ensures high-quality and effective nutritional support.

An aerial photograph of a city at dusk. In the foreground, a large, brightly lit roundabout with a green center is visible. Several roads radiate from the roundabout. In the background, a tall, modern building stands out against the darkening sky. Other city buildings and greenery are visible in the mid-ground.

Thank you for your attention

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