

La Nutrizione Artificiale dall'ospedale al domicilio

Federico Bozzetti

Cagliari 25-26 Marzo 2009

Nutrition of the cancer patient

- Prevalence of malnutrition
- Effect of malnutrition on the outcome:
 - survival
 - response to therapy
 - quality of life
- Nutritional support: success and failure
 - surgical patients
 - non surgical patients
- A practical approach
 - identification of pts at nutritional risk
 - starvation vs cachexia
 - examples of benefit from AN
- The regimen
- Enteral vs parenteral nutrition

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Impact of cancer, type, site, stage and treatment on the nutritional status of patients.

Bozzetti F, Migliavacca S, Scotti A, Bonalumi MG, Scarpa D, Baticci F, Ammatuna M, Pupa A, Terno G, Sequeira C, Masserini C, Emanuelli H.

This study analyzed the nutritional status of cancer patients in relation to type and site of origin of the tumor, stage of disease, and previous chemical or radiation therapy. The analysis was performed on 321 patients (280 with cancer and 41 controls). The nutritional parameters included per cent of weight loss, anthropometric indices (arm circumference, triceps skinfold, arm muscle circumference), creatinine-height index, serum protein, albumin, total iron binding capacity and cholinesterase, C3 and C4 components of complement, total peripheral lymphocytes, and skin tests. The statistical comparison between patients with different tumors and controls, between patients with different stages of the same tumor, and between patients treated with or without previous chemical or radiation therapy led to the following conclusions: 1) **malnutrition is mainly related to the type and site of origin of the tumor and, in the early stages of disease, is more pronounced in patients with cancer of the esophagus and stomach;** 2) except in patients with breast and cervix cancer, **malnutrition gets more severe as the disease becomes advanced;** 3) **chemical or radiation therapy has a variable impact on the nutritional status,** but in selected patients it causes a drop in body weight, arm circumference, arm muscle circumference, and peripheral lymphocytes; 4) body weight, cutaneous delayed hypersensitivity and serum albumin are the most commonly altered parameters.

Table 37.1 – Incidence of malnutrition in cancers of different sites.

Reference	Tumour type or site	Incidence of malnutrition
Issell <i>et al.</i> ¹⁷	Lung (squamous cell)	50%
	Breast	36%
	Sarcoma	39%
	Colon	54%
	Prostate	56%
	Lung (small cell)	60%
	Lung	61%
	Pancreas	83%
DeWys <i>et al.</i> ¹⁵	Gastric	83%
Samuels <i>et al.</i> ¹⁸	Testicular cancer	25%
Nixon <i>et al.</i> ¹⁹	Colorectal cancer	60%
Popp <i>et al.</i> ²⁰	Diffuse lymphoma	55%
Shamberger <i>et al.</i> ²¹	Sarcoma	66%
Goodwin & Torres ²²	Head and neck cancer	72%
Clamon <i>et al.</i> ²³	Lung (small cell)	about 50%
Rickard <i>et al.</i> ²⁴	Neuroblastoma	56%
Bashir <i>et al.</i> ²⁵	Bronchial carcinoma	66%
	Breast	9%
	Rectum	40%
Larrea <i>et al.</i> ²⁶	Oesophagus	79%
Tan <i>et al.</i> ²⁷	General cancer population	63%
	General cancer population	– 60%

The incidence of weight loss in cancer patients

Tumor type	Weight loss, %		
	None	1-10%	> 10%
Lymphoma	52	33	15
Leukemia	61	35	4
Sarcoma	60	33	7
Breast	64	30	6
Colon	46	40	14
Prostate	44	46	10
Lung	39	46	15
Pancreas	19	57	26
Stomach	17	49	38

**WEIGHT LOSS and NUTRITIONAL RISK by
PRIMARY TUMOR**
in 1000 OUTPATIENTS
(median values)

	WL%	NRS
Esophagus	16.0	3.0
		3.0
Pancreas	15.1	2.0
Stomach	13.3	2.0
Head&Neck	7.8	2.0
Lung	6.6	1.0
Colon&Rectum	5.4	1.0
Small bowel	3.2	

WEIGHT LOSS and NUTRITIONAL RISK by STAGE IN 1000 OUTPATIENTS (median values)

UICC	WL%	UICC	NRS
0	2.1	0	0
I	6.4	I	1.0
II	8.1	II	2.0
III	9.0	III	2.0
IV	6.9	IV	2.0

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The impact of weight loss in cancer patients

Median survival, weeks

Tumor type	No weight loss	Weight loss
Lymphoma	107	55
Leukemia	8	4
Sarcoma	46	25
Breast	70	45
Colon	43	21
Prostate	46	24
Lung	20	14
Pancreas	14	12
Stomach	18	16

Cancers with WL representing an adverse prognostic marker

- Breast (*Swenerton 1979, Coates 1980*)
- Esophagus/GE junction (*Pedersen 1982, Fein 1985*)
- GI (*Andreyev 1998*)
- Others (*Harvey 1981*)

Cachexia is the main cause for death in “terminal” cancer patients

1 out of 4-20 cancer patients
(*Warren 1932, Klastersky 1972, Inagaki 1974, Ambrus 1975*)

Weight Loss associated with a Poor Response to CT

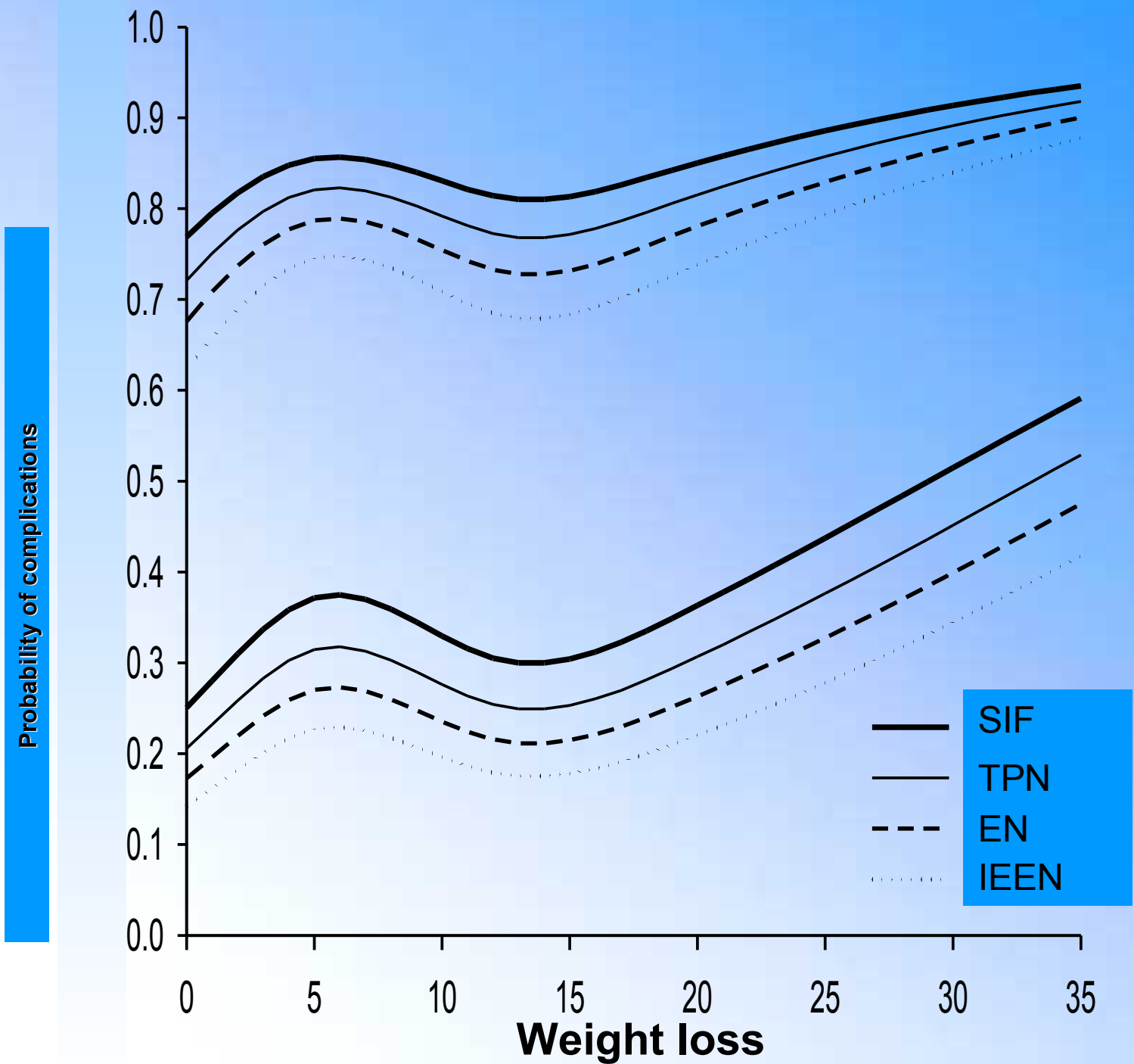
- Breast cancer (*DeWys 1980*)
- GI cancer (*Andreyev 1998*)

Weight Loss associated with Poor Quality of Life

- Acute leukemia (*Ollenschlager 1982*)
- Others (*DeWys 1980*)

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AMERICAN
GASTROENTEROLOGICAL
ASSOCIATION MEDICAL POSITION
STATEMENT: PARENTERAL NUTRITION
(*Gastroenterology* 121:966-969;2001)

AGA TECHNICAL REVIEW ON
PARENTERAL NUTRITION
(*Gastroenterology* 121:970-1001;2001)

Table 5. Meta-Analysis of Oncologic Trials

Outcome	Absolute risk difference ^a	Confidence intervals	Number of studies (patients) included
Mortality ^b	0%	-5%, +5%	19 (1050)
Total complication rate	+40%	+14%, +66%	8 (333)
Infectious complication rate	+16%	+8%, +23%	18 (823)
Tumor response	-7% ^c	-12%, -1%	15 ^d (910)
Bone marrow toxicity	+22%	-10%, +54%	3 (134)
Gastrointestinal toxicity	+1%	-9%, +11%	6 (310)

^aThis represents the difference between the outcome in the treated group and the control group; a negative number represents a benefit for the treated group.

^bAlthough 1 bone marrow transplantation trial reported an improved survival,⁹⁴ this was not demonstrated when all 4 trials⁹¹⁻⁹⁵ were combined; absolute risk difference equaled -5% (-14%, +5%). Only 3 of these trials provided parenteral nutrition during the time when the transplantation was performed⁹²⁻⁹⁵; when only these 3 trials were combined, absolute risk difference equaled -9% (-22%, +4%).

^cA negative absolute risk difference indicates that the response rate in the control group was higher than in the recipients of the parenteral nutrition.

^d13 of these 15 RCTs were chemotherapy trials.

Effects of TPN on pts receiving oncologic therapy

19 RCTs (1050 pts)

- No benefit on mortality
- Increase in total complications rate
- No constant effect on tumor response
- No protection against bone marrow or GI toxicity

Major criticism

- >90% of these RCTs published before 1990
- Nutritional regimens suboptimal as regards composition and duration
- Severe malnutrition was not a criteria for entering pts in the RCTs

ARTIFICIAL NUTRITION AS MEDICAL THERAPY OR AS A SUPPORTIVE CARE

... the studies on artificial nutrition in cancer patients were randomized only if patients were not malnourished, or if two different nutritional regimens were compared...

STATEMENT of the ASPEN BOARD of DIRECTORS (ASPEN Guidelines 2002)

...a major distinction between therapeutic trials of the efficacy of a drug and feeding of nutrients to be essential to maintenance of human health and survival must be made. Withholding a drug will not produce disease in otherwise healthy humans, whereas essential nutrients must be provided to both healthy and ill people. Patients with advanced malnutrition or who are at risk for becoming severely malnourished must be fed to prevent death by starvation...

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Clinical Nutrition (2003) 22(4): 415–421
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doi:10.1016/S0261-5614(03)00098-0

Available online at www.sciencedirect.com



SPECIAL ARTICLE

ESPEN Guidelines for Nutrition Screening 2002

J. KONDRUP,* S. P. ALLISON,[†] M. ELIA,[‡] B. VELLAS,[¶] M. PLAUTH[§]

**Rigshospitalet University Hospital Copenhagen, Denmark, [†]Queen's Medical Centre, Nottingham, UK, [‡]University of Southampton, Southampton, UK, [¶]University Hospital Centre, Toulouse, France, [§]Community Hospital Dessau, Germany (Correspondence to: JK, Nutrition Unit-5711, Rigshospitalet University, 9 Blegdamsvej, 2100 Copenhagen, Denmark)*

Abstract—Aim: To provide guidelines for nutrition risk screening applicable to different settings (community, hospital, elderly) based on published and validated evidence available until June 2002.

Note: These guidelines deliberately make reference to the year 2002 in their title to indicate that this version is based on the evidence available until 2002 and that they need to be updated and adapted to current state of knowledge in the future.

In order to reach this goal the Education and Clinical Practice Committee invites and welcomes all criticism and suggestions (button for mail to ECPC chairman).

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Nutritional Risk Screening (NRS 2002)

Table 1 Initial screening			
		Yes	No
1	Is BMI <20.5?		
2	Has the patient lost weight within the last 3 months?		
3	Has the patient had a reduced dietary intake in the last week?		
4	Is the patient severely ill ? (e.g. in intensive therapy)		

Yes: If the answer is 'Yes' to any question, the screening in Table 2 is performed.
No: If the answer is 'No' to all questions, the patient is re-screened at weekly intervals. If the patient e.g. is scheduled for a major operation, a preventive nutritional care plan is considered to avoid the associated risk status.

Table 2 Final screening			
Impaired nutritional status		Severity of disease (≈ increase in requirements)	
Absent Score 0	Normal nutritional status	Absent Score 0	Normal nutritional requirements
Mild Score 1	Wt loss >5% in 3 mths or Food intake below 50–75% of normal requirement in preceding week	Mild Score 1	Hip fracture* Chronic patients, in particular with acute complications: cirrhosis*, COPD*, <i>Chronic hemodialysis, diabetes, oncology</i>
Moderate Score 2	Wt loss >5% in 2 mths or BMI 18.5 – 20.5 + impaired general condition or Food intake 25–60% of normal requirement in preceding week	Moderate Score 2	Major abdominal surgery* Stroke* <i>Severe pneumonia, hematologic malignancy</i>
Severe Score 3	Wt loss >5% in 1 mth (>15% in 3 mths) or BMI <18.5 + impaired general condition or Food intake 0-25% of normal requirement in preceding week in preceding week.	Severe Score 3	Head injury* Bone marrow transplantation* <i>Intensive care patients (APACHE>10).</i>
Score:	+	Score:	= Total score

Starvation vs Cachexia

STARVATION (lack of nutrients)

- Hypophagia due to GI obstruction or iatrogenic (RT&CT)
- Diarrhoea (tumor- or therapy-dependent)
- GI fistula

CACHEXIA (due to cytokines or other mediators)

- Anorexia(± dysgeusia)
- Early satiety
- APR (low serum albumin, high PCR, ur.urea N>5g/d)
- Fever (increased RME)

Clinical conditions suggesting the need of a nutritional intervention

- non volitional weight loss (10%UBW)
- NRS 2002 > 3
- low body mass index
- clinical signs of nutritional deprivation
- hypophagia (anorexia, dysgeusia, early satiety, nausea, vomiting...), diarrhoea or pathological losses through fistulas
- an expected prolonged period of (semi)starvation (CT&RT&SURG)
- severity of basic disease

Clinical benefit from AN in wasted/hypophagic pts

- Cancer of the head and neck undergoing RT&CT (level I RCT, Grade A)
- GI tumors candidate to neoadjuvant CT&RT
- Severe GI toxicity from CT/RT
- Conditions in which wasting/hypophagia contraindicate an oncologic therapy

PARENTERAL NUTRITION at HOME

How long may survive an healthy subject or a cancer patient undergoing total energy deprivation?

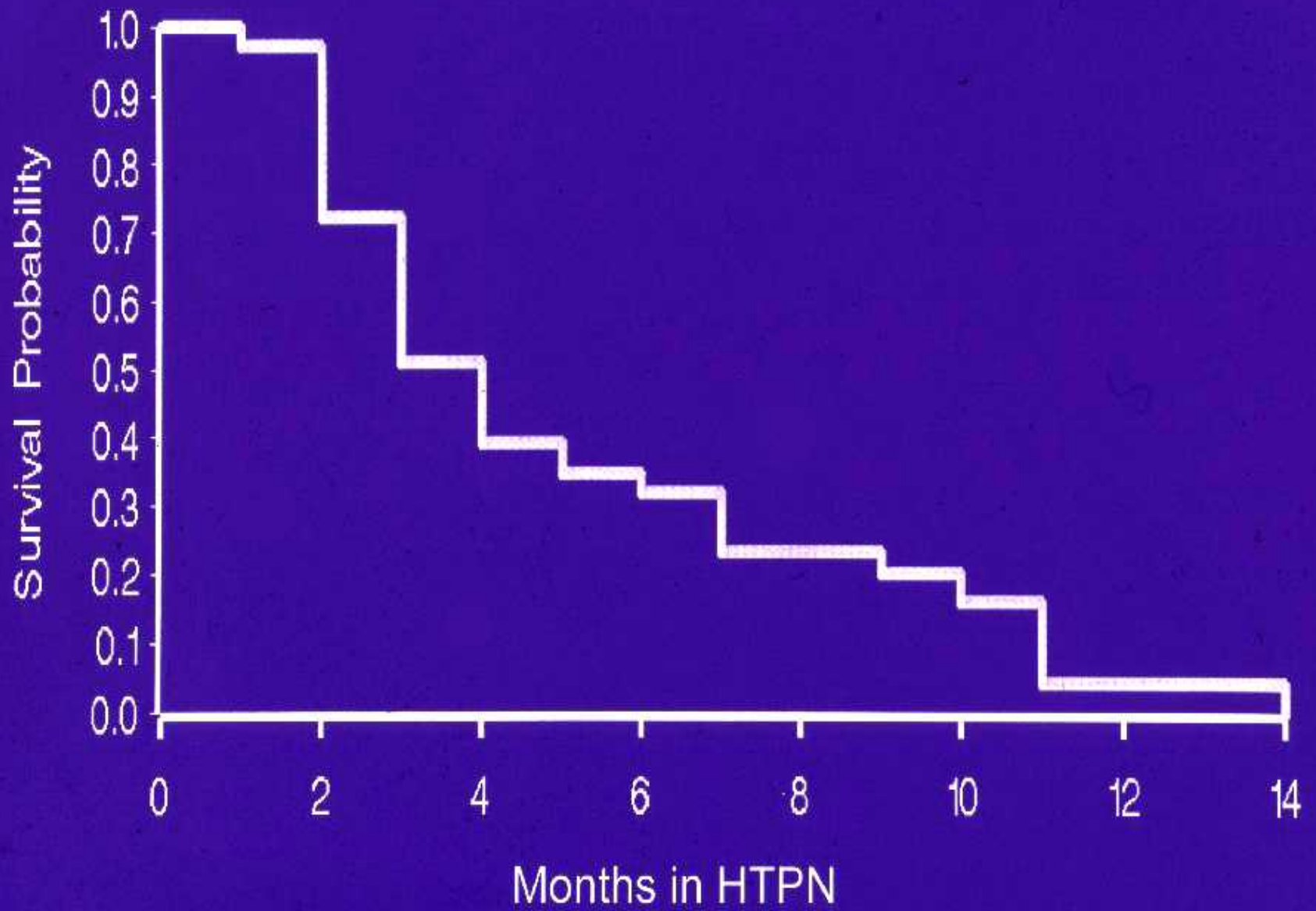
How long may survive.....?

Malnutrition incompatible with survival occurs when:

- weight loss is $>33-37\%$ of UBW
- protein depletion is $>30\%$
- fat depletion is $>70\%$
- BMI is 13 and 11 for men and females, respectively

How long may survive.....?

60 to 75 days according to the data of
Leningrad siege, the Warsaw Ghetto and the
Irish hunger strikers



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Oxidation rate in pts infused with lipid (kg/d)*

WL=0.90 g

WS=0.72 g

CTR=0.53 g

**Korber 1999*

LIPID CLEARANCE (g/kg/d)*

LCT: CTR 1.4 WS 2.3 WL 3.5

MCT/LCT: CTR 1.2 WS 1.6 WL 2.1

**Korber 1999*

ENERGY SUBSTRATES: CHO

PROS'

- Utilized by all tissues
- Exclusive fuel for CNS, BM, renal medulla etc.
- Anabolic effect through insulin

CONS'

- Better utilized by the tumor than by the host
- ↑ water retention
- ↑infectious risk due to hyperglycaemia

ENERGY SUBSTRATES: FAT

PROS'

- High caloric density
- Good utilization of exogenous fat and lipid oxidation
- May be enriched with N-3 PUFA
- Better utilized by the host than by the tumor

CONS'

- Long-term safety for LCTs at ≤ 1 g/kg/d

Specificity of nutritional regimen for terminal cancer patients

Water	$\leq 30\text{mL/kg}$
np Energy	$\sim 30 \text{ kcal/kg}$
glucose	$\leq 50\%$
fat	$\geq 50\%$
Amino acid	$1-1.5 \text{ g/kg}$
Sodium	$\leq 1\text{mEq/kg}$

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Nutritional support (enteral)

PROS

- **SIMPLE**
- **LOW COST**
- **SAFER**
- **METABOLICALLY BETTER**

CONS

- **IT REQUIRES A FUNCTIONING GUT**
- **NG TUBE IS OFTEN REQUIRED**
- **CRITICAL VOLUME TO MEET THE NUTRITIONAL REQUIREMENTS**
- **ADVERSE EFFECTS FORCE TO WITHDRAW NUTRITION**
- **COMPLIANCE MAY BE POOR**

Nutritional support (parenteral)

PROS

- **YOU CAN GIVE AS MUCH AS YOU WANT**
- **A WORKING GUT IS NOT REQUIRED**
- **REGIMEN MAY BE ADJUSTED WITHOUT WITHDRAWAL**
- **BETTER MODULATION OF SUBSTRATES**
- **COMPLIANCE MAY BE BETTER (PTS MAY HARBOUR A CVC FOR OTHER PURPOSES)**

CONS

- **MORE EXPENSIVE**
- **MORE DEMANDING**
- **POTENTIALLY MORE DANGEROUS**

***...knowledge is the enemy of
disease...***