28° CONGRESSO NAZIONALE ANDID
Oltre la dieta: update in nutrizione e dietetica
Napoli, 13-14 Maggio 2016

Il supporto nutrizionale in corso di chemioterapia: evidenze e nuove frontiere

SERVIZIO SANITARIO REGIONALE EMILIA-ROMAGNA
Azienda Ospedaliero-Universitaria Policlinico di Modena

Università degli Studi di Modena e Reggio Emilia
Ateneo fondato nel 1175

Filippo VALORIAN
Dietista
Unità di Malattie del Metabolismo e Nutrizione Clinica
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DIAGNOSIS | TREATMENT | FOLLOW-UP

Cancer Prevention

MALNUTRITION
Prevention / Treatment

Cancer Prevention

Caccialanza R. et al. Journal of Cancer. 201

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Prevalence of Malnutrition and Current Use of Nutrition Support in Patients With Cancer

Xavier Hébuterne, MD, PhD[1]; Etienne Lemarié, MD[2]; Mauricette Michallet, MD, PhD[3]; Claude Beauvillain de Montreuil, MD[4]; Stéphane Michel Schneider, MD, PhD[1]; and François Goldwasser, MD, PhD[5]

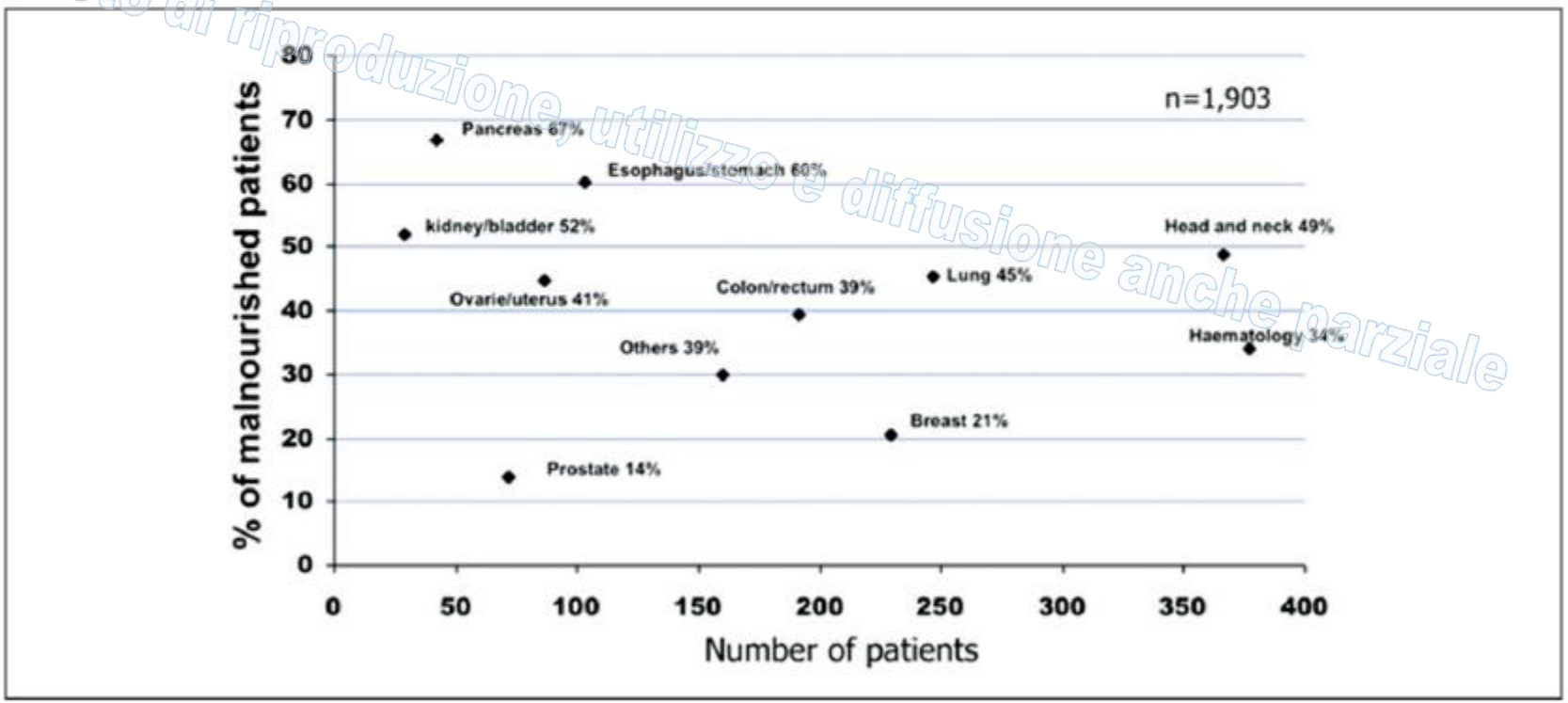
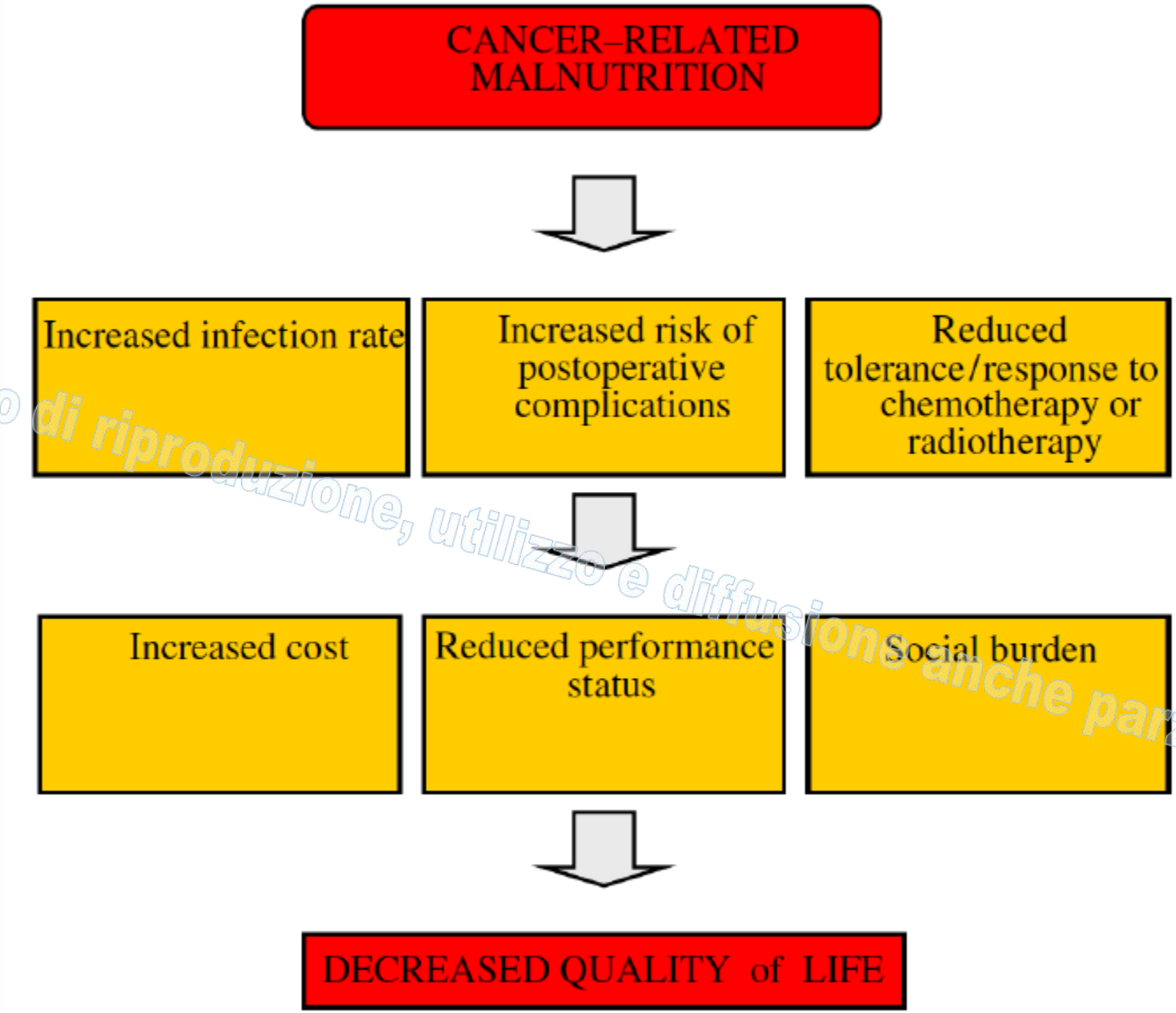


Figure 1. Prevalence of malnutrition in various types of cancer.



Caro MMM. et al. Clinical Nutrition. 200

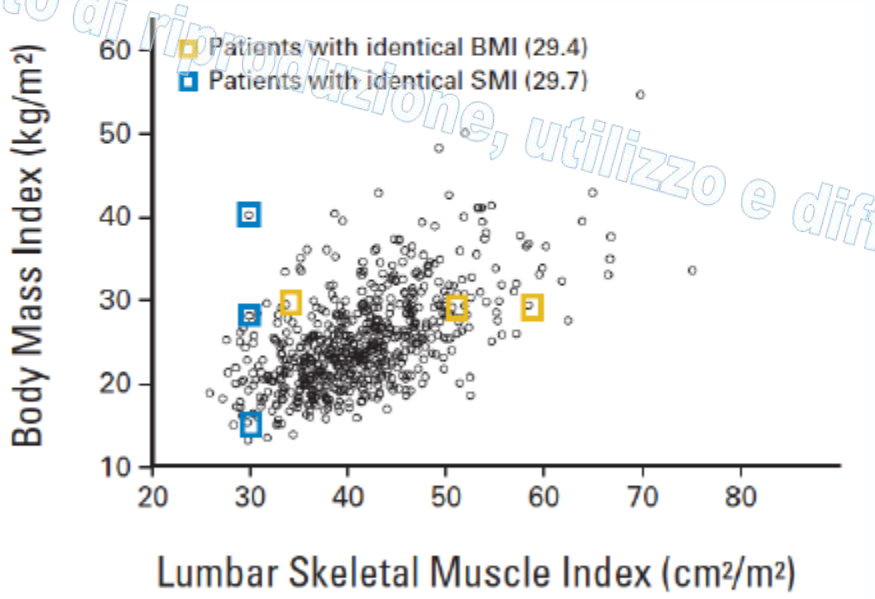
VOLUME 31 · NUMBER 12 · APRIL 20 2013

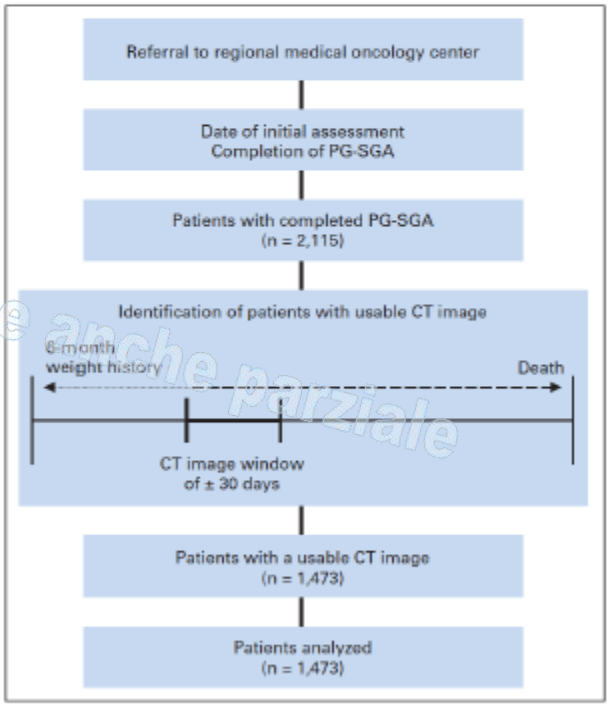
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Cancer Cachexia in the Age of Obesity: Skeletal Muscle Depletion Is a Powerful Prognostic Factor, Independent of Body Mass Index

Lisa Martin, Laura Birdsell, Neil MacDonald, Tony Reiman, M. Thomas Clandinin, Linda J. McCargar, Rachel Murphy, Sunita Ghosh, Michael B. Sawyer, and Vickie E. Baracos





Conclusion

CT images reveal otherwise occult muscle depletion. Patients with cancer who are cachexic by the conventional criterion (involuntary weight loss) and by two additional criteria (muscle depletion and low muscle attenuation) share a poor prognosis, regardless of overall body weight.

VOLUME 33 · NUMBER 1 · JANUARY 1 2015

JOURNAL OF CLINICAL ONCOLOGY

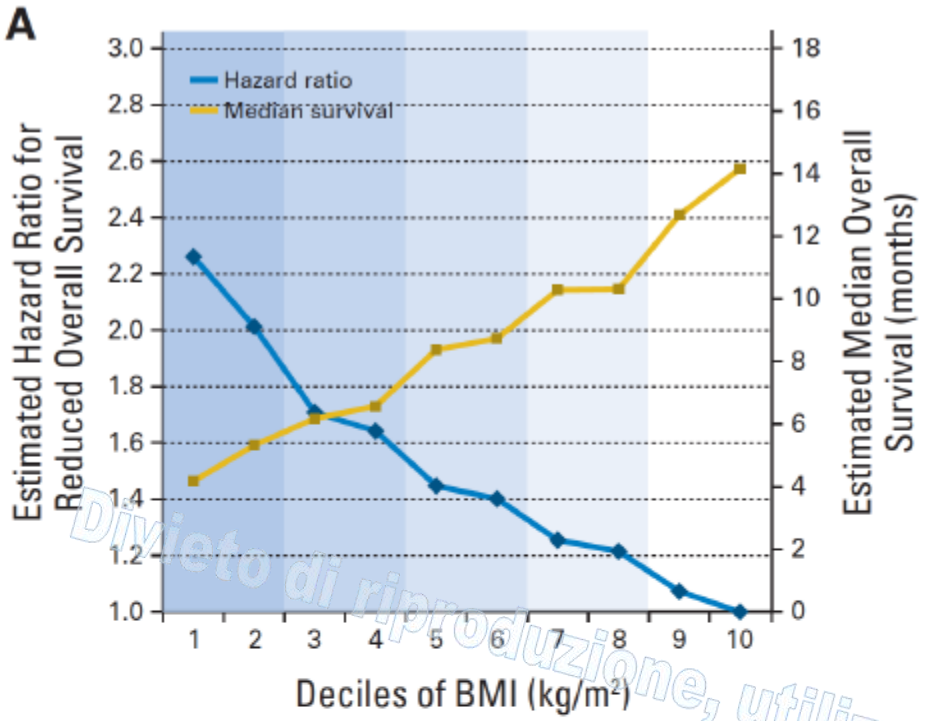
ORIGINAL REPORT

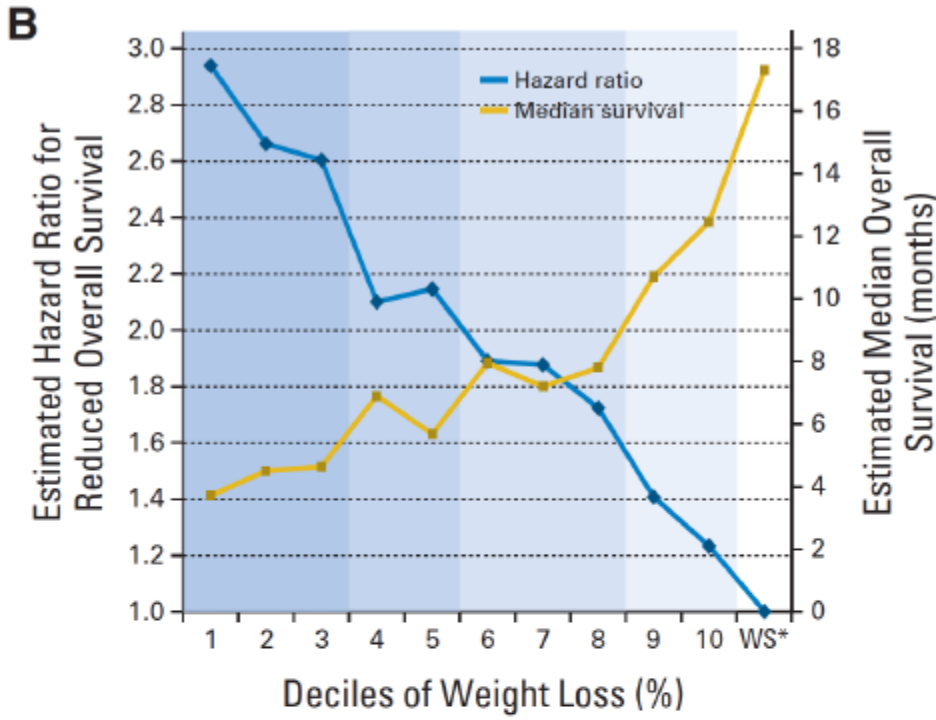
Diagnostic Criteria for the Classification of Cancer-Associated Weight Loss

Lisa Martin, Pierre Senesse, Ioannis Gioulbasanis, Sami Antoun, Federico Bozzetti, Chris Deans, Florian Strasser, Lene Thoresen, R. Thomas Jagoe, Martin Chasen, Kent Lundholm, Ingvar Bosaeus, Kenneth H. Fearon, and Vickie E. Baracos

Table 2. Demographics and Clinical Characteristics of the Training and Validation Samples

Demographic or Clinical Characteristic	Training Sample (n = 8,160) No. of Patients	%	Validation Sample (n = 2,693) No. of Patients	%
Age, years	8,160		2,693	
Mean	65.3		61.3	
SD	11.8		12.7	
Weight, kg	7,848		2,693	
Mean	69.6		65.9	
SD	16.9		14.6	
Height, m	7,532		2,690	
Mean	1.69		1.67	
SD	0.1		0.09	
BMI, kg/m^2	8,160		2,690	
Mean	24.4		23.4	
SD	5.1		4.6	
Weight loss, %*	8,138		2,693	
Mean	−9.7		−7.0	
SD	8.4		6.7	
Sex				
Male	4,949	60.6	1,367	50.7
Female	3,211	39.4	1,326	49.2
Cancer site				
Colorectal	1,395	17.1	300	11.1
Breast	227	2.8	453	16.8
Gastroesophageal	947	11.6	222	8.2
Genitourinary	300	3.7	544	20.2
Head and neck	997	12.2	308	11.4
Other cancers	285	3.5	339	12.6
Other GI	207	2.5	27	1.0
Pancreas	831	10.2	162	6.0
Respiratory	2,561	31.4	234	8.7
Unknown primary	121	1.5	1	0.0
Hematologic	148	1.8	54	2.0
Liver and intrahepatic bile ducts	141	1.7	49	1.8
Cancer stage				
I	279	3.4	77	3.0
II	555	6.8	127	4.9
III	1,274	15.7	221	8.5
IV	6,010	74.0	2,173	83.6
ECOG performance status				
0	1,234	17.6	571	21.2
1	2,560	36.5	899	33.4
2	1,551	22.1	767	28.5
3	1,494	21.3	434	16.1
4	176	2.5	18	0.7
WHO BMI categories, kg/m^2				
< 18.5	817	10.0	320	11.9
18.5-24.9	3,974	48.7	1,504	55.8
25.0-29.9	2,325	28.5	656	24.4
≥ 30.0	1,044	12.8	210	7.8
Weight change				
Weight stable (± 2.4%)	1,847	22.6	808	30.0
Weight loss (> −2.4%)	6,290	77.1	1,885	70.0





Legend for Deciles of BMI

Decile	n	Minimum	Maximum	Median	Mean	SD
1	816.0	11.0	18.4	17.1	16.8	1.3
2	816.0	18.5	20.1	19.3	19.3	0.5
3	815.0	20.2	21.5	20.9	20.8	0.4
4	807.0	21.6	22.7	22.1	22.1	0.3
5	834.0	22.8	23.8	23.2	23.3	0.3
6	792.0	23.9	25.1	24.4	24.5	0.4
7	827.0	25.2	26.5	25.7	25.7	0.4
8	816.0	26.6	28.2	27.3	27.3	0.5
9	821.0	28.3	30.9	29.4	29.4	0.8
10	816.0	31.0	60.2	33.3	34.7	4.1

Legend for Deciles of BMI

Decile	n	Minimum	Maximum	Median	Mean	SD
1	624	-55.6	-23.1	-26.9	-28.4	5.0
2	634	-23.1	-18.4	-20.4	-20.5	1.4
3	625	-18.3	-15.3	-16.7	-16.7	0.9
4	633	-15.3	-13.2	-14.2	-14.2	0.6
5	629	-13.1	-11.1	-12.1	-12.1	0.6
6	631	-11.1	-9.2	-10.0	-10.1	0.5
7	629	-9.2	-7.5	-8.3	-8.3	0.5
8	618	-7.5	-5.7	-6.6	-6.6	0.5
9	629	-5.7	-4.1	-5.0	-5.0	0.5
10	638	-4.1	-2.5	-3.2	-3.3	0.5
WS*	1,848	-2.4	2.4	0.0	-0.2	0.9

Both % of weight loss and BMI independently predict survival (*P < 0.01*)

J Clin Oncol 33:90-99. © 2014 by American Society of Clinical Oncolog

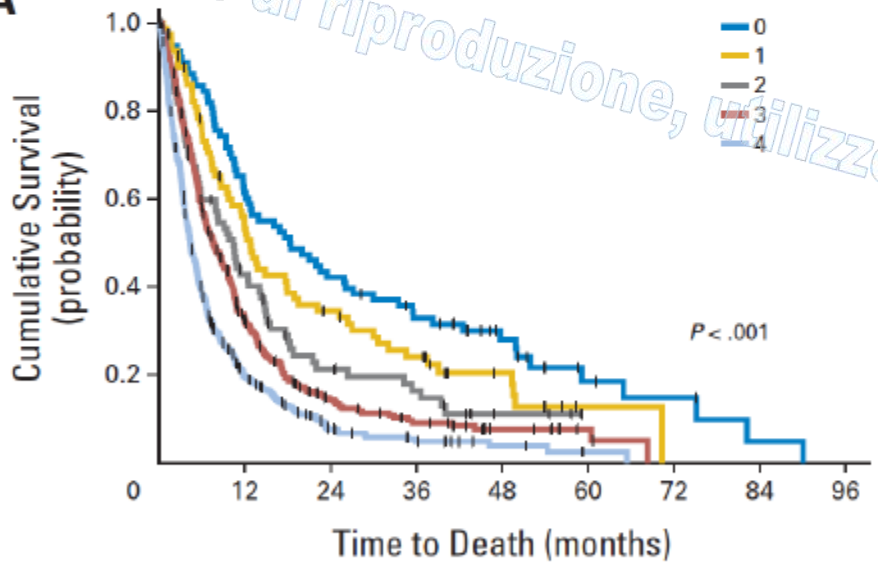
BMI (kg/m²)

Weight Loss (%)	28	25	22	20	
2.5	1.0*	0.9	1.2	1.3	1.8	1.0
6	1.3	1.4	1.6	1.5	1.8	1.3
11	1.6	1.9	2.1	2.2	3.1	1.8
15	1.9	1.9	2.1	3.1	3.1	2.1
	1.9	3.2	2.8	3.1	3.1	2.7
	1.0	1.2	1.4	1.6	2.1	Overall

BMI (kg/m²)

Weight Loss (%)	28	25	22	20
2.5	0	0	1	1	3
6	1	2	2	2	3
11	2	3	3	3	4
15	3	3	3	4	4
	3	4	4	4	4

A



Risk of reduced survival is a function of BMI and % weight loss.

BMI-adjusted WL grading system is a useful tool in efforts to predict survival because it is independent of cancer site, stage, and PS and strongly discriminates survival differences

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Special Diets for Cancer Patients

Are we looking for a Magic Formula ?

Counseling Patients on Cancer Diets: A Review of the Literature and Recommendations for Clinical Practice

JUTTA HUEBNER[1], SABINE MARIENFELD[2], CLARE ABBENHARDT[3], CORNELIA ULRICH[3], KARSTEN MUENSTEDT[4], OLIVER MICKE[5], RALPH MUECKE[6] and CHRISTIAN LOESER[7]

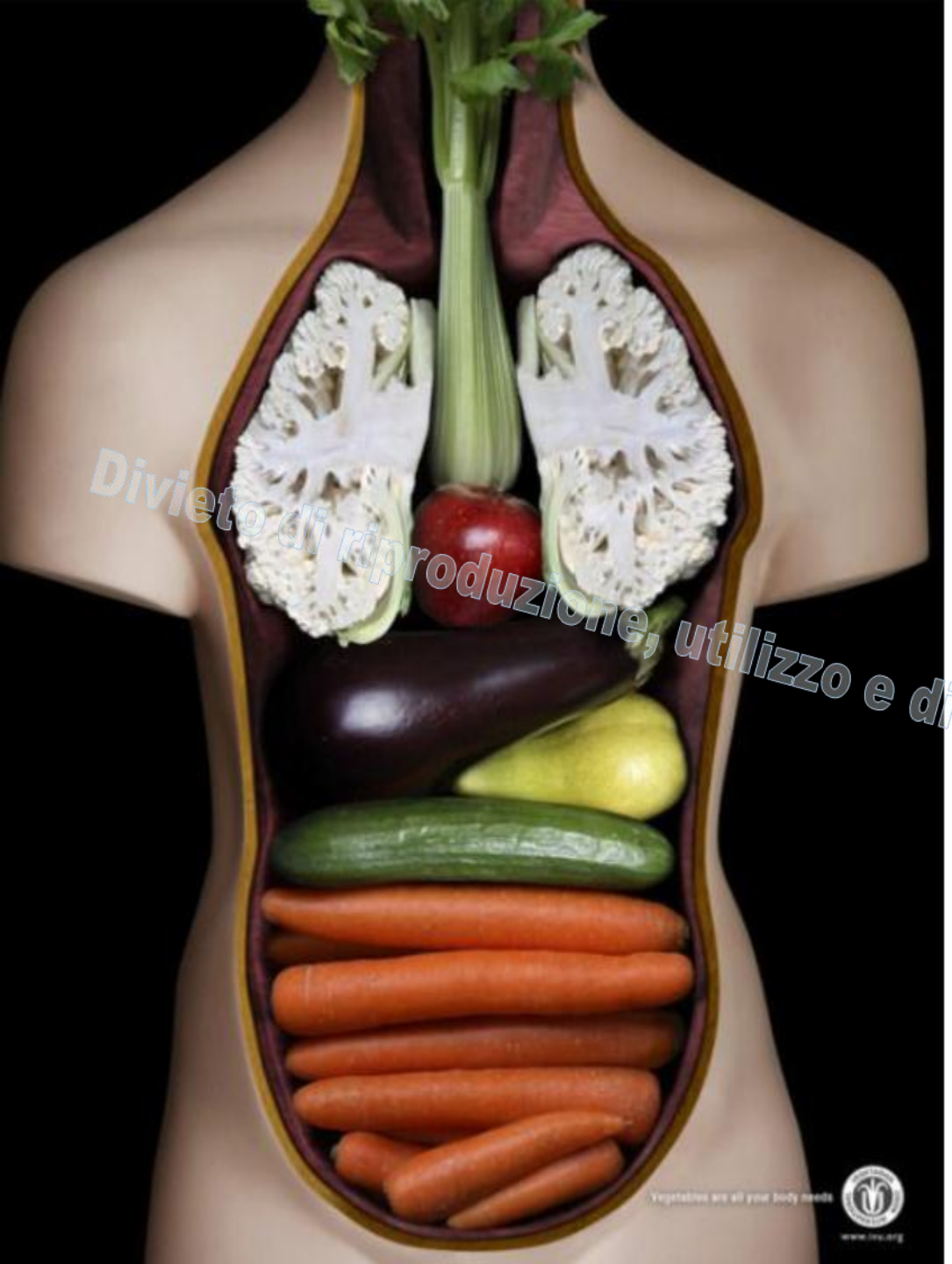
Table I. *Hits for "cancer diet" in online searches via Google.*

Cancer diet	Google Germany	Google UK	Google USA	Google Canada	Total number of hits
Breuß' cancer cure	4	0	0	0	4
Budwig's diet	12	6	3	6	27
Low carb diet	17	1	1	4	23
Macrobiotics	2	2	3	1	8
Gerson's regime	4	5	4	4	17
Alkaline diet	3	1	4	0	8
Raw cost	3	4	2	4	13
Fasting	2	0	0	0	2
Bircher-Benner diet	1	0	0	0	1
Livingston-Wheeler Regimen	0	0	1	0	1
Kelley/Gonzalez Regimen	0	0	1	1	2
Vegan diet	0	0	1	0	1
Moermann diet	1	1	1	1	4

One major concern with any cancer diet is that patients may rely only on these diets and delay or omit cancer treatments.

This may entail relapse or progress of disease and suffering from cancer-related symptoms.

Considering the lack of evidence of benefits from cancer diets and potential harm by malnutrition, oncologists should engage more in counseling cancer patients on such diets.



Vegetarian Diets

Dietary Patterns

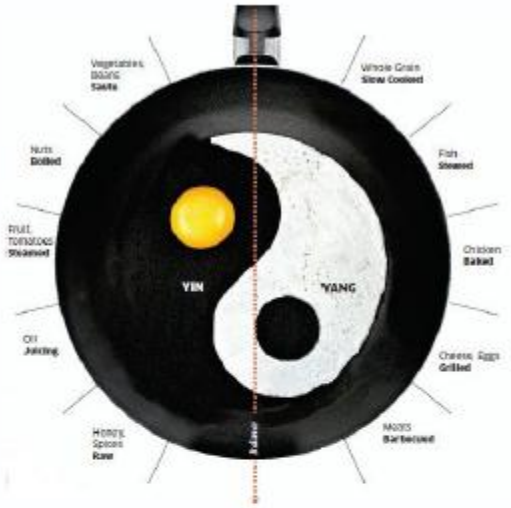
Table 1. Classification of dietary patterns *.

Dietary Pattern	Definition	Beef	Poultry/Fish	Dairy/Eggs
Non-vegetarian	Eat red meat, poultry, fish, milk, and eggs more than once a week			
Semi-vegetarian	Eat red meat, poultry, and fish less than once per week and more than once per month			
Vegetarian				
Pesco-	Eat fish, milk, and eggs but no red meat nor poultry			
Lacto-ovo-	Eat eggs, milk, or both but no red meat, fish, nor poultry			
Vegan	Eat no red meat, fish, poultry, dairy, and eggs			

Lap Tai Le, Joan Sabaté. Nutrients 2014, 6, 2131-2147

The Other Faces of Vegetarianism

Macrobiotic Diet



Based largely on grains, legumes, and vegetables. Fruits, nuts, and seeds are used to a lesser extent. Some peolple eat limited amounts of fish.

Raw Food Diet

Consisting mainly or exclusively of uncooked and unprocessed fruits, vegetables, nuts, seeds, sprouted grains and beans. In rare instances unpasteurized dairy products and even raw meat and fish.

Fruitarian Diet

Based on fruits, nuts, and seeds. Avocado and tomatoes are commonly included. Other vegetables, grains, beans, and animal products are excluded.

1. Position of the American Dietetic Association: Vegetarian Diets. *J Am Diet Assoc*. 2009

Cancer Mortality & Vegetarianism

Mortality in vegetarians and nonvegetarians: detailed findings from a collaborative analysis of 5 prospective studies[1–3]

Timothy J Key, Gary E Fraser, Margaret Thorogood, Paul N Appleby, Valerie Beral, Gillian Reeves, Michael L Burr, Jenny Chang-Claude, Rainer Frentzel-Beyme, Jan W Kuzma, Jim Mann, and Klim McPherson

Description of the studies selected for analysis

Study	Location	Median year of recruitment[1]	Number of subjects[2]	End of follow-up	Person-years at risk	Mean length of follow-up
		y	*n*		*y*	*y*
Adventist Mortality (1)	California	1960 (1959–1960)	24 538	December, 1965	138 304	5.6
Health Food Shoppers (2)	United Kingdom	1974 (1973–1979)	9878	December, 1995	182 156	18.4
Adventist Health (3)	California	1976 (1976–1980)	28 952	December, 1988	320 818	11.1
Heidelberg (4)	Germany	1978 (1978–1981)	1757	May, 1989	17 317	9.9
Oxford Vegetarian (5)	United Kingdom	1981 (1980–1984)	11 047	December, 1995	150 799	13.7

Death rate ratios and 95% CIs and the number of deaths for vegetarians compared with nonvegetarians by study, adjusted for age, sex, and smoking status, and for all studies combined

	Cancer					Ischemic heart disease	Cerebrovascular disease	Other causes	All causes
	Stomach	Colorectal	Lung	Breast	Prostate				
Study									
Adventist Mortality (1)									
Death rate ratio	0.64 (0.30, 1.36)	1.37 (0.73, 2.56)	0.59 (0.10, 3.28)	0.65 (0.28, 1.52)	1.41 (0.49, 4.04)	0.74 (0.63, 0.88)	0.65 (0.48, 0.87)	0.96 (0.83, 1.11)	0.83 (0.76, 0.92)
Number of deaths	30	41	6	26	15	598	182	737	1635
Health Food Shoppers (2)									
Death rate ratio	1.23 (0.62, 2.47)	0.90 (0.58, 1.39)	1.13 (0.67, 1.92)	1.74 (1.11, 2.72)	1.31 (0.65, 2.66)	0.97 (0.81, 1.16)	0.99 (0.78, 1.26)	1.20 (1.06, 1.37)	1.11 (1.02, 1.21)
Number of deaths	34	90	66	79	32	521	292	1013	2127
Adventist Health (3)									
Death rate ratio	1.58 (0.68, 3.70)	1.01 (0.66, 1.56)	0.69 (0.37, 1.27)	0.52 (0.27, 0.97)	0.79 (0.44, 1.41)	0.62 (0.53, 0.73)	0.93 (0.73, 1.19)	0.88 (0.79, 0.97)	0.80 (0.74, 0.87)
Number of deaths	26	104	96	64	66	921	317	1970	3564
Heidelberg (4)									
Death rate ratio	2.66 (0.32, 21.7)	0.35 (0.06, 2.11)	—[3]	1.09 (0.18, 6.67)	1.67 (0.14, 19.6)	0.45 (0.22, 0.95)	1.69 (0.69, 4.15)	1.45 (0.92, 2.30)	1.17 (0.85, 1.63)
Number of deaths	8	5	2	5	3	29	31	102	185
Oxford Vegetarian (5)									
Death rate ratio	0.46 (0.11, 1.85)	0.94 (0.49, 1.80)	0.66 (0.31, 1.37)	1.10 (0.57, 2.12)	0.42 (0.16, 1.09)	0.90 (0.68, 1.20)	1.17 (0.76, 1.80)	1.12 (0.91, 1.36)	1.00 (0.87, 1.15)
Number of deaths	9	38	33	36	21	195	87	400	819
χ^2_4 For heterogeneity between studies	4.83	2.56	2.52	10.89 ($P < 0.05$)	4.71	15.98 ($P < 0.01$)	8.73	18.35 ($P < 0.01$)	36.09 ($P < 0.0001$)
All studies									
Death rate ratio[2]	1.02 (0.64, 1.62)	0.99 (0.77, 1.27)	0.84 (0.59, 1.18)	0.95 (0.55, 1.63)	0.91 (0.60, 1.39)	0.76 (0.62, 0.94)	0.93 (0.74, 1.17)	1.06 (0.90, 1.24)	0.95 (0.82, 1.11)
Number of deaths	107	278	203	210	137	2264	909	4222	8330

For all the other causes of death examined (cancers / cerebrovascular diseases) NO overall association with vegetarianism was expected and NONE was observed.

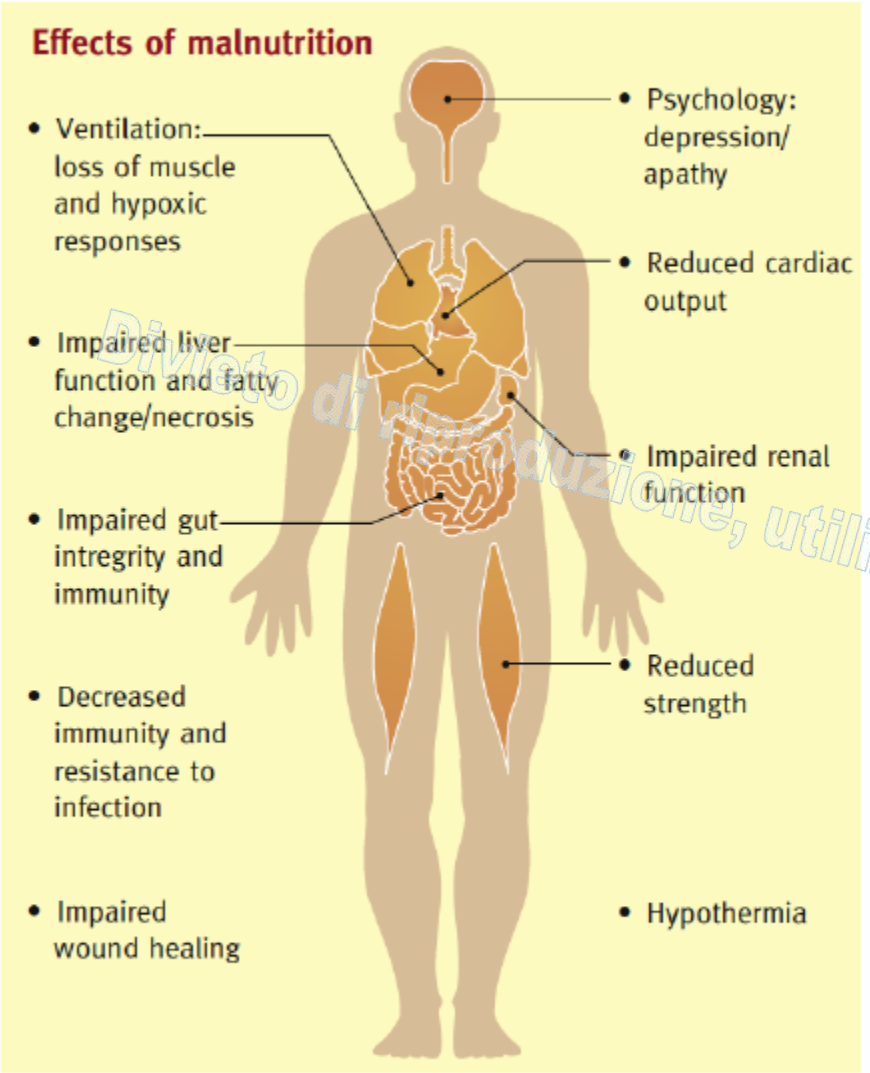
Vegetarian Dietary Patterns and Mortality in Adventist Health Study 2

JAMA Intern Med. 2013

Dr. Michael J. Orlich, MD, Dr. Pramil N Singh, DrPH, Dr. Joan Sabaté, MD, DrPH, Dr. Karen Jaceldo-Siegl, DrPH, Ms. Jing Fan, MS, Dr. Synnove Knutsen, MD, PhD, Dr. W. Lawrence Beeson, DrPH, and Dr. Gary E. Fraser, MBchB, PhD

Characteristic	Deaths, Hazard Ratio (95% CI)				
	All-Cause	Ischemic Heart Disease	Cardiovascular Disease	Cancer	Other
All (N = 73 308), No. of deaths[a,b]	2580	372	987	706	867
Vegetarian					
Vegan	0.85 (0.73–1.01)	0.90 (0.60–1.35)	0.91 (0.71–1.16)	0.92 (0.68–1.24)	0.74 (0.56–0.99)
Lacto-ovo	0.91 (0.82–1.00)	0.82 (0.62–1.06)	0.90 (0.76–1.06)	0.90 (0.75–1.09)	0.91 (0.77–1.07)
Pesco	0.81 (0.69–0.94)	0.65 (0.43–0.97)	0.80 (0.62–1.03)	0.94 (0.72–1.22)	0.71 (0.54–0.94)
Semi	0.92 (0.75–1.13)	0.92 (0.57–1.51)	0.85 (0.63–1.16)	0.94 (0.66–1.35)	0.99 (0.72–1.36)
Nonvegetarian	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Men (n = 25 105), No. of deaths[a]	1031	169	390	273	368
Vegetarian					
Vegan	0.72 (0.56–0.92)	0.45 (0.21–0.94)	0.58 (0.38–0.89)	0.81 (0.48–1.36)	0.81 (0.53–1.22)
Lacto-ovo	0.86 (0.74–1.01)	0.76 (0.52–1.12)	0.77 (0.59–0.99)	1.01 (0.75–1.37)	0.89 (0.69–1.15)
Pesco	0.73 (0.57–0.93)	0.77 (0.45–1.30)	0.66 (0.44–0.98)	1.10 (0.73–1.67)	0.60 (0.39–0.93)
Semi	0.93 (0.68–1.26)	0.73 (0.33–1.60)	0.75 (0.43–1.32)	1.15 (0.65–2.03)	1.03 (0.62–1.71)
Nonvegetarian	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Women (n = 48 203), No. of deaths[a,c]	1529	203	597	433	499
Vegetarian					
Vegan	0.97 (0.78–1.20)	1.39 (0.87–2.24)	1.18 (0.88–1.60)	0.99 (0.69–1.44)	0.70 (0.47–1.05)
Lacto-ovo	0.94 (0.83–1.07)	0.85 (0.59–1.22)	0.99 (0.81–1.22)	0.85 (0.67–1.09)	0.93 (0.75–1.17)
Pesco	0.88 (0.72–1.07)	0.51 (0.26–0.99)	0.90 (0.66–1.23)	0.86 (0.61–1.21)	0.81 (0.58–1.15)
Semi	0.92 (0.70–1.22)	1.09 (0.60–1.98)	0.93 (0.64–1.34)	0.85 (0.56–1.30)	0.97 (0.64–1.47)
Nonvegetarian	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]

No significant associations with reduced cancer mortality were detected.



Vengetarian Diets & Nutritional Risks

RESEARCH

Review

A Systematic Review and Meta-Analysis of Changes in Body Weight in Clinical Trials of Vegetarian Diets

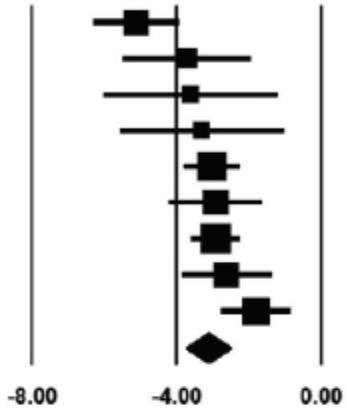
Neal D. Barnard, MD; Susan M. Levin, MS, RD, CSSD; Yoko Yokoyama, PhD, MPH

Consistent evidence from clinical trials shows that the prescription of plant-based diets is consistently associated with weight loss in study groups, despite the absence of specific guidance on energy intake or exercise.

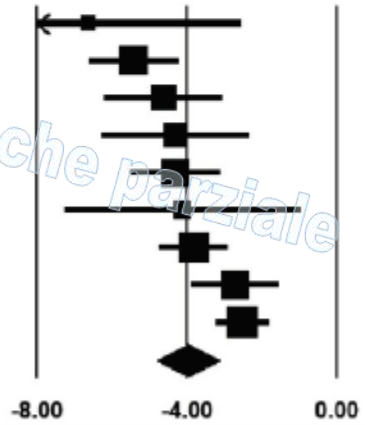
The prescription of vegetarian diets reduces mean body weight, suggesting that they may be helpful for prevention and management of weight-related conditions

J Acad Nutr Diet. 2015;115:954-969

Study name	Subgroup within study	Mean	Lower limit	Upper limit	*p*-value
Ferdowsian 2010[26]	Vegan	-5.1	-6.3	-3.9	<0.0001
Barnard 2009[24]	Vegan	-3.7	-5.5	-1.9	<0.0001
Turner-McGrievy 2007[22]	Vegan	-3.6	-6.0	-1.2	0.003
Dansinger 2005[21]	Vegetarian	-3.3	-5.6	-1.0	0.004
Mishra 2013b[27]	Vegan	-3.0	-3.8	-2.2	<0.0001
Kjeldsen-Kragh 1991[14]	Vegetarian	-2.9	-4.2	-1.6	<0.0001
Mishra 2013a[27]	Vegan	-2.9	-3.6	-2.2	<0.0001
Gardner 2007[23]	Vegetarian	-2.6	-3.8	-1.4	<0.0001
Nenonen 1998[17]	Vegan	-1.8	-2.8	-0.8	0.0002
Total		-3.1	-3.7	-2.5	<0.0001



Study name	Subgroup within study	Mean	Lower limit	Upper limit	*p*-value
Dansinger 2005[21]	Vegetarian	-6.6	-10.7	-2.5	0.002
Ferdowsian 2010[26]	Vegan	-5.4	-6.6	-4.2	<0.0001
Kjeldsen-Kragh 1991[14]	Vegetarian	-4.6	-6.2	-3.0	<0.0001
Barnard 2009[24]	Vegan	-4.3	-6.3	-2.3	<0.0001
Mishra 2013a[27]	Vegan	-4.3	-5.5	-3.1	<0.0001
Turner-McGrievy 2007[22]	Vegan	-4.1	-7.2	-1.0	0.01
Mishra 2013b[27]	Vegan	-3.8	-4.7	-2.9	<0.0001
Nenonen 1998[17]	Vegan	-2.7	-3.9	-1.5	<0.0001
Barnard 2000[19]	Vegan	-2.5	-3.2	-1.8	<0.0001
Total		-4.0	-4.8	-3.1	<0.0001



Prescription of vegetarian diets (ovo-lacto-vegetarian diets or vegan diets) was associated with a mean weight change of 3.4 kg (CI 4.4-2.4; *P<0.001*) in an intention-to-treat analysis and 4.6 kg (CI 5.4-3.8; *P<0.001*) in a completer analysis (omitting missing post-intervention values).

J Acad Nutr Diet. 2015;115:954-969

Guidelines	Protein Requirement
DAA 2005	1.4 g/kg/day
ESPEN 2006 (EN)	- Minimum: 1 g/kgBW/day - Target: 1.2-2 g/kgBW/day
ADA 2006	• Nitrogen balance = (Protein Intake/6.25) – (UUN+4) : Positive 4 – 6 g/day is desirable : Negative – consideration to increase protein intake • Grams of protein per kilogram of body weight formulas (consider of renal and/or hepatic dysfunction) • Protein needs for nutrition support: kilocalorie-to-nitrogen ratio of 125:1
European Oncological Disease 2007	In excess of 1.4g/kg/day
DAA 2008	1.2 g/kg/day
ESPEN 2009 (PN)	- Minimum: 1 g/kgBW/day - Target: 1.2-2 g/kgBW/day
COSA 2011 (HNC)	at least 1.2g/kg/day

Nutritional adequacy of plant-based diets for weight management: observations from the NHANES[1–3]

Bonnie Farmer

Am J Clin Nutr 2014:

Adjusted mean intakes of selected nutrients for vegetarians and nonvegetarians aged ≥19 y, NHANES 1999–2004[1]

Nutrient[2]	Vegetarians (n = 851)	Nonvegetarians (n = 12,441)
Energy (kcal)	1877 ± 42	2241 ± 11*
Protein (g)	63.4 ± 0.7	83.6 ± 0.4*
Fiber (g)	20.3 ± 0.6	15.4 ± 0.2*
Vitamin A (μg RAE)	718 ± 28	603 ± 10*
Vitamin C (mg)	112 ± 6.5	91 ± 1.6*
Vitamin E (mg AT)	8.3 ± 0.3	7.0 ± 0.1*
Vitamin B-12 (μg)	3.8 ± 0.2	5.3 ± 0.1*
Magnesium (mg)	322 ± 5	281 ± 2*
Iron (mg)	16.9 ± 0.4	15.5 ± 0.1*
Zinc (mg)	10.1 ± 0.2	12.1 ± 0.1*

[1] All values are means ± SEMs. Modified from reference 16. *$P < 0.01$ (ANOVA). AT, α-tocopherol; RAE, retinol activity equivalents.

[2] Energy intake adjusted for sex and ethnicity; all other nutrients adjusted for energy, sex, and ethnicity.

Dietary data show that caloric intake of vegetarians is typically lower than that of nonvegetarians, with a difference of as much as 424 kcalories/d

Diet and body mass index in 38 000 EPIC-Oxford meat-eaters, fish-eaters, vegetarians and vegans

EA Spencer[1]*, PN Appleby[1], GK Davey[1] and TJ Key[1]

[1]*Cancer Research UK Epidemiology Unit, University of Oxford, Oxford, UK*

Table 2 Mean BMI (kg/m^2) by sex and diet group, adjusted for age, adjusted for age+lifestyle factors[a] and adjusted for age+lifestyle factors[a]+dietary factors[b]

	Men	*Women*
Factors adjusted for	*Mean (95% CI)*	*Mean (95% CI)*
Age		
Meat-eaters	24.41 (24.31, 24.50)	23.52 (23.46, 23.58)
Fish-eaters	23.30 (23.12, 23.49)	22.66 (22.57, 22.76)
Vegetarians	23.37 (23.26, 23.49)	22.71 (22.64, 22.78)
Vegans	22.49 (22.23, 22.75)	21.98 (21.76, 22.19)
Range of mean values	1.92	1.54
Age+lifestyle factors[a]		
Meat-eaters	24.39 (24.29, 24.48)	23.49 (23.43, 23.55)
Fish-eaters	23.35 (23.17, 23.54)	22.70 (22.61, 22.80)
Vegetarians	23.38 (23.26, 23.49)	22.73 (22.65, 22.80)
Vegans	22.53 (22.27, 22.79)	22.01 (21.80, 22.23)
Range of mean values (% reduction)	1.86 (3%)	1.48 (4%)
Age+lifestyle factors +dietary factors[b]		
Meat-eaters	24.09 (23.97, 24.20)	23.24 (23.17, 23.31)
Fish-eaters	23.45 (23.27, 23.64)	22.83 (22.73, 22.92)
Vegetarians	23.67 (23.54, 23.80)	22.96 (22.88, 23.04)
Vegans	23.13 (22.83, 23.43)	22.56 (22.32, 22.79)
Range of mean values (% reduction)	0.95 (50%)	0.68 (56%)

[a]Lifestyle factors adjusted for: smoking, education level, physical activity, marital status, ethnicity and in women only, parity.
[b]Dietary factors adjusted for: energy intake, % protein, % fat, % saturated fat, % polyunsaturated fat, % carbohydrate, fibre intake, % sugars and alcohol intake.

Age-adjusted mean BMI was significantly different between the four diet groups, being highest in the meat-eaters (24.41 kg/m^2 in men, 23.52 kg/m^2 in women) and lowest in the vegans (22.49 kg/m^2 in men, 21.98 kg/m^2 in women).

International Journal of Obesity (2003) **27**, 728–73

Table 1 Characteristics by sex and diet group

Variable	Men				Women			
	Meat-eater (n = 4318)	*Fish-eater (n = 1095)*	*Vegetarian (n = 2888)*	*Vegan (n = 570)*	*Meat-eater (n = 13506)*	*Fish-eater (n = 5096)*	*Vegetarian (n = 9419)*	*Vegan (n = 983)*
Median age at recruitment (y)	48	41	38	35	45	38	34	32
Mean body mass index (kg/m^2)	24.49	23.29	23.28	22.34	23.69	22.60	22.51	21.75
Mean nutrient intake/day								
Energy (kJ)	9344	9011	8872	8232	8039	7782	7632	7034
Protein (% energy)	15.8	13.9	13.0	12.9	17.1	14.8	13.8	13.4
Fat (% energy)	32.4	31.4	31.2	28.5	31.6	30.8	30.4	27.9
Saturated fat[a] (% energy)	10.9	9.6	9.4	5.1	10.4	9.4	9.4	5.1
Polyunsaturated fat[a] (% energy)	5.2	5.7	5.7	7.7	5.1	5.4	5.3	7.2
Monounsaturated fat[a] (% energy)	10.0	9.0	8.7	8.2	9.5	8.7	8.4	7.8
Carbohydrate (% energy)	46.7	49.4	51.1	54.3	48.3	51.0	52.8	56.1
Total sugars (% energy)	23.1	23.3	23.7	23.3	24.5	25.2	25.8	25.0
Fibre (g)	18.7	22.2	22.7	28.1	19.0	21.4	21.8	26.5
Alcohol (g)	16.3	16.7	14.6	12.6	8.3	9.0	8.0	6.5

Differences in macronutrient intakes accounted for about half the difference in mean BMI between vegans and meat-eaters.

High protein and low fibre intakes were the factors most strongly associated with increasing BMI.

Fasting, Intermittent Fasting & Caloric Restriction

REVIEW

Fasting vs dietary restriction in cellular protection and cancer treatment: from model organisms to patients

C Lee and VD Longo

Oncogene (2011) 30, 3305–3316

Andrus Gerontology Center, Department of Biological Sciences and Norris Cancer Center, University of Southern California, Los Angeles, CA, USA

Drug Resistance Updates 15 (2012) 114–122

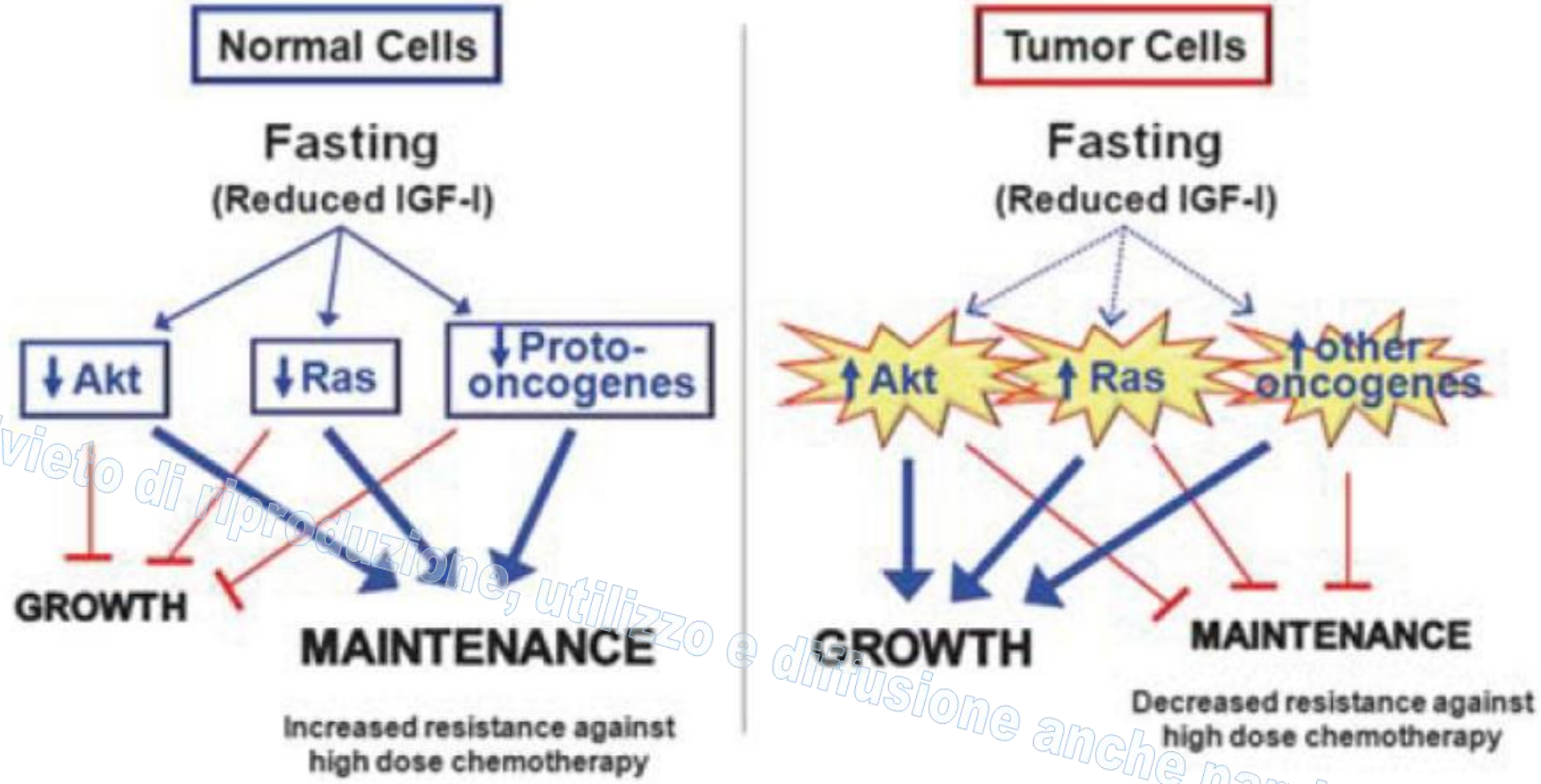
Contents lists available at SciVerse ScienceDirect

Drug Resistance Updates

journal homepage: www.elsevier.com/locate/drup

Starvation, detoxification, and multidrug resistance in cancer therapy

Changhan Lee[a,1], Lizzia Raffaghello[b,1], Valter D. Longo[a,*]



Changes in the levels of glucose, IGF-I, IGFBP-1 and in other proteins caused by fasting have the POTETIAL to improve the efficacy of chemotherapy against tumors by protecting normal cells and tissues and POSSIBLY by diminishing multidrug resistance in malignant cells.

Drug Resistance Updates 15 (2012) 114–122

Oncogene (2011) 30, 3305–3316

Fasting and cancer treatment in humans: A case series report

Fernando M. Safdie[1,6], Tanya Dorff [2,3,6], David Quinn[2,3], Luigi Fontana[4], Min Wei[1], Changhan Lee[1], Pinchas Cohen[5], and Valter D. Longo[1]

	Gender	Age	Primary Neoplasia	Stage at Diagnosis
Case 1	Female	51	Breast	IIA
Case 2	Male	68	Esophagus	IVB
Case 3	Male	74	Prostate	II
Case 4	Female	61	Lung (NSCLC)	IV
Case 5	Female	74	Uterus	IV
Case 6	Female	44	Ovary	IA
Case 7	Male	66	Prostate	IV/DI
Case 8	Female	51	Breast	IIA
Case 9	Female	48	Breast	IIA
Case 10	Female	78	Breast	IIA

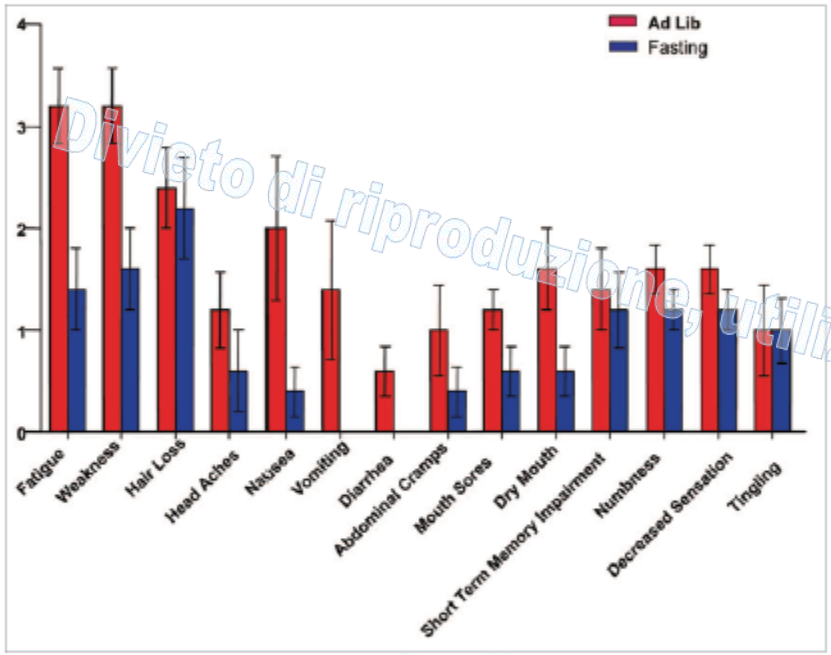
We describe 10 cases in which patients diagnosed with a variety of malignancies had voluntarily fasted prior to (48-140 hours) and/or following (5-56 hours) chemotherapy (different drugs).

None of patients, who received CT in combination with fasting, reported significant side effects caused by the fasting itself other than hunger and lightheadedness

AGING, December 2009, Vol.1 No.12

Fasting and cancer treatment in humans: A case series report

Fernando M. Safdie[1,6], Tanya Dorff [2,3,6], David Quinn[2,3], Luigi Fontana[4], Min Wei[1], Changhan Lee[1], Pinchas Cohen[5], and Valter D. Longo[1]



The six patients who underwent CT with or without fasting reported a reduction in fatigue, weakness, and gastrointestinal side effects while fasting.

Fasting did not prevent the CT-induced reduction of tumor volume or tumor markers.

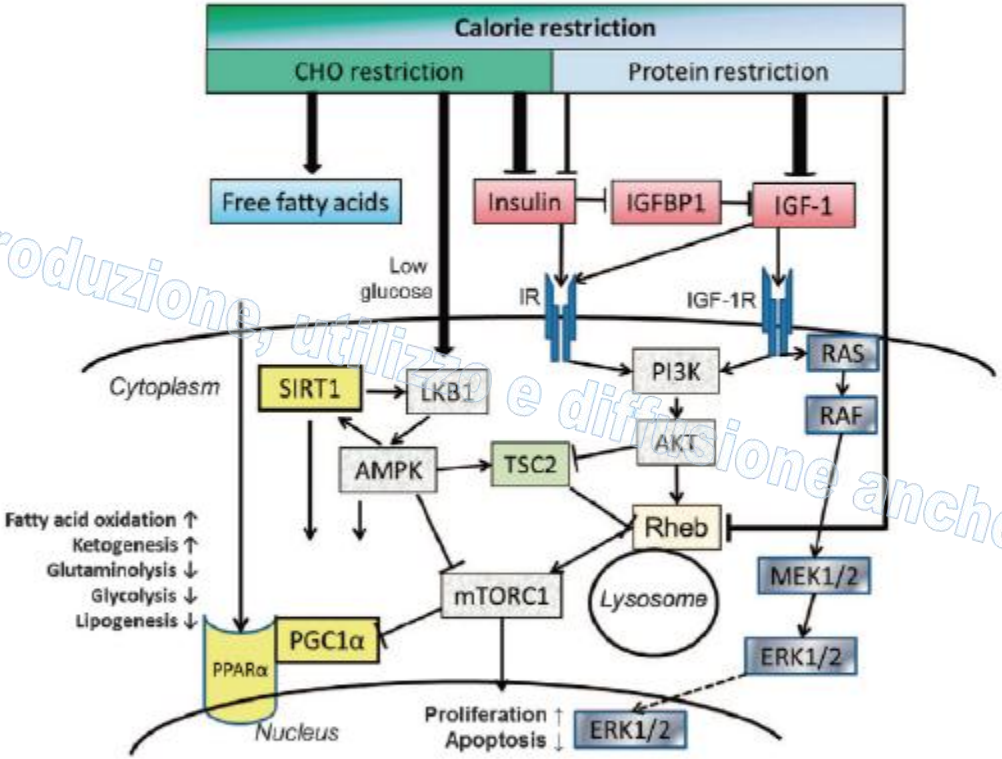
Although these cases suggest that fasting in combination with CT is feasible, safe, and has the potential to ameliorate side effects caused by CT, they are not meant to establish practice guidelines for patients undergoing CT. Only RCT will determine the effect of fasting on clinical outcomes.

AGING, December 2009, Vol.1 No.12

REVIEW

Dietary and pharmacological modification of the insulin/IGF-1 system: exploiting the full repertoire against cancer

RJ Klement[1] and MK Fink[2]



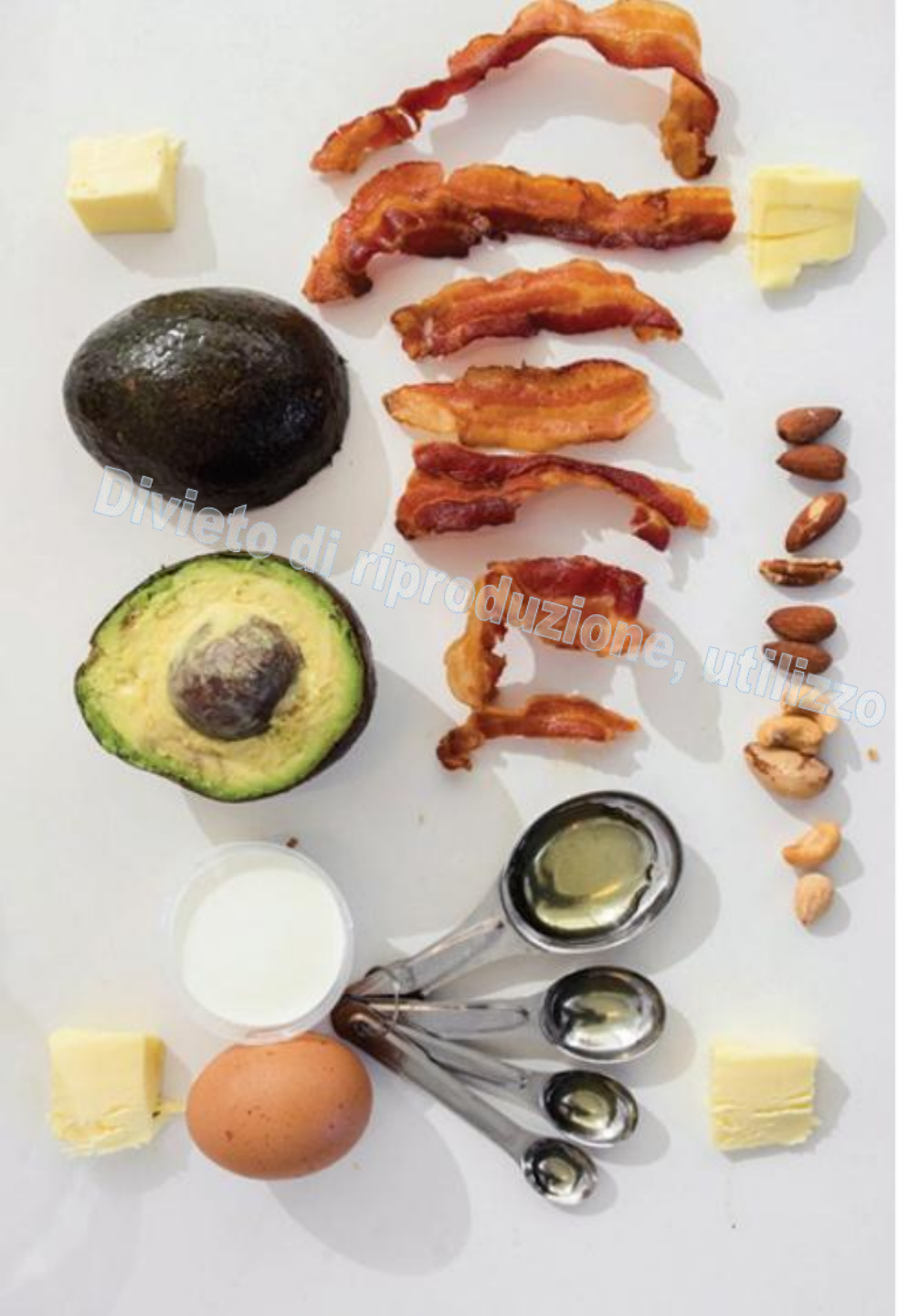
Although preclinical data are promising, we point out that insulin regulation and the metabolic response to a certain diet often differ between mice and humans. Thus, the need for collecting more human data has to be emphasized.

Oncogenesis (2016) **5,** e193; doi:10.1038/oncsis.2016.2; published online 15 February 2016

Health effects of intermittent fasting: hormesis or harm? A systematic review[1]

Benjamin D Horne,[2,3] Joseph B Muhlestein,[2,4] and Jeffrey L Anderson[2,4]*

Conclusions: Clinical research studies of fasting with robust designs and high levels of clinical evidence are sparse in the literature. Whereas the few randomized controlled trials and observational clinical outcomes studies support the existence of a health benefit from fasting, substantial further research in humans is needed before the use of fasting as a health intervention can be recommended. *Am J Clin Nutr* 2015;102:464–70.

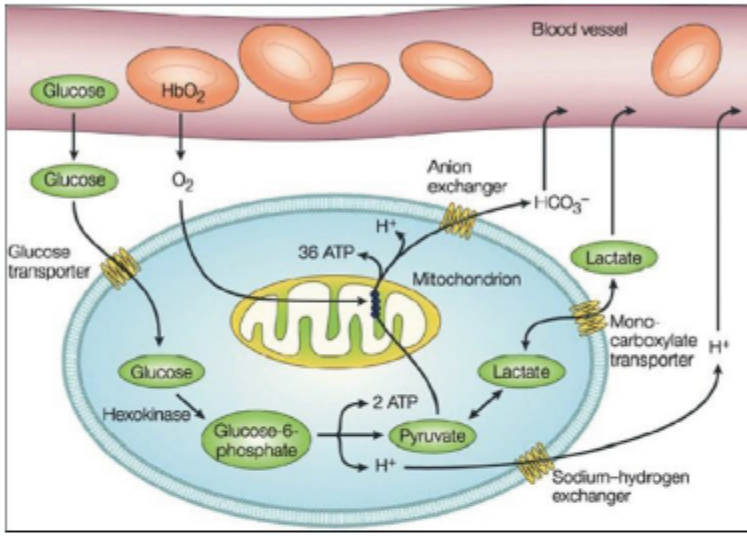


Ketogenic Diet

Warburg Effect

Cancer cells are able to produce ATP by a high rate of anaerobic respiration (glycolysis).

This process of producing energy mainly by the non-oxidative breakdown of glucose (Warburg Effect) requires a sufficient source of glucose since glucose and not oxygen is used to produce ATP. It occurs even under sufficient oxygen supply.

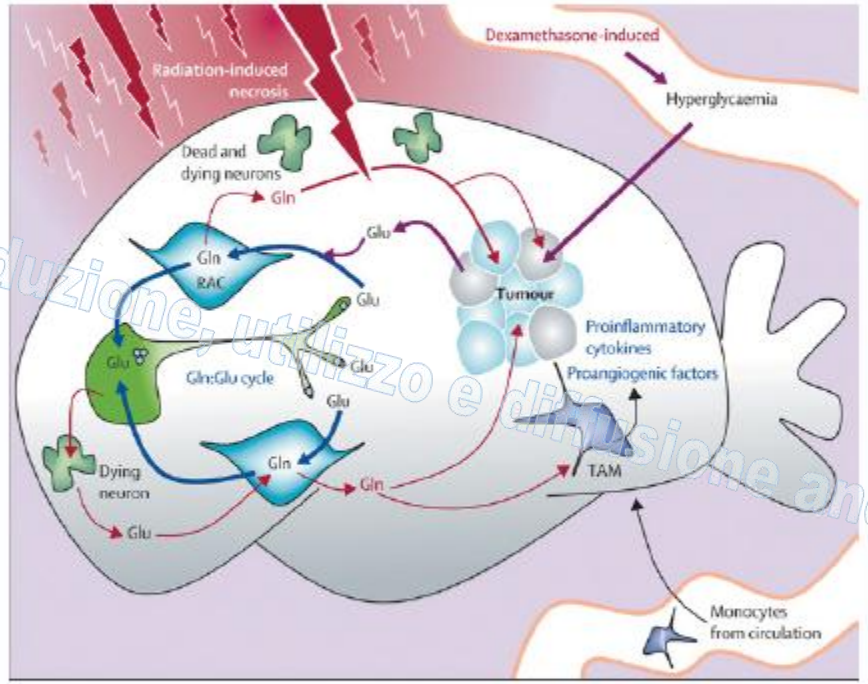


1. Ketone Bodies (KB) and fatty acids inhibit glycolysis and cancer cells are unable to metabolize them (mitochondrial dysfunction);
2. KB could be toxic for some cancer cells;
3. KB have the potential to promote the antioxidative defense mechanisms in normal tissues (↓ ROS);
4. KB could promote apoptosis and reduce angiogensis.

1-Seyfried, 2003
2-Mulrooney T.J et al,. 2011
3-Maurer G.D. et al. 2011
4- Skinner R., et al. 2009
5- Seyfried T.N. 2012

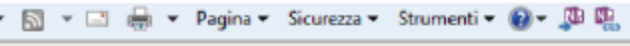
1- Nebeling LC et al. *Effects of a ketogenic diet on tumor metabolism and nutritional status in pediatric oncology patients: **two case reports.*** J. Am Coll Nutr , ***1995.***

2- Giulio Zuccoli et al. *Metabolic management of glioblastoma multiforme using standard therapy together with a restricted ketogenic diet: **Case Report.*** Nutr Metab, **2010**



3- Fine EJ et all. Targeting insulin inhibition as a metabolic therapy in advanced cancer: a pilot safety and feasibility dietary trial **in 10 patients**. Nutrition**, 2012**.

4- Champ CE et al. Targeting metabolism with a ketogenic diet during the treatment of glioblastoma multiforme. J Neurooncol, **2014**



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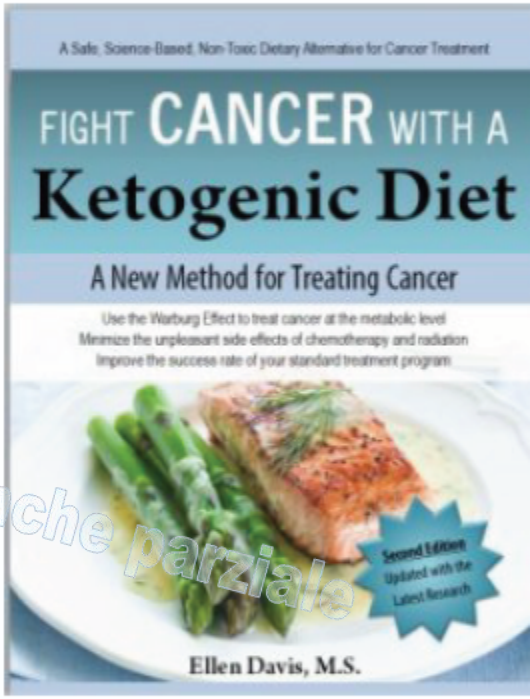
Rank	Status	Study
1	Recruiting	Ketogenic Diet Phase 1 for Head & Neck Cancer **Condition:** Head and Neck Neoplasms **Intervention:** Dietary Supplement: Ketogenic diet
2	Recruiting	Ketogenic Or LOGI Diet In a Breast Cancer Rehabilitation Intervention (KOLIBRI) **Condition:** Quality of Life **Interventions:** Other: Standard diet (SD); Other: Experimental 1: Ketogenic diet (KD).; Other: Experimental 2: "Low glycæmic and insulinemic" diet (LOGI)

Clinical Trials: KD and Cancer

- N° 16 lavori
- 9 ongoing, 3 completati, 2 sospesi (manca documentazione), 2 sconosciuti (non notizie da 2 anni)
- Media di pazienti arruolati: tra 10 e 20
- Studi pilota o fase 1
- Sedi di neoplasia: 6 glioblastoma , 2 polmone, 1 mammella, 1 pancreas, 3 non specificato, 1 su composizione corporea in corso di RT
- 2 su patologie non oncologiche: 1 su Sturge Weber Syndrome, 1 su Tourette Syndrome



Clinical Nutrition xxx (2015) 1–8

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Clinical Nutrition

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Opinion paper

Toward a cancer-specific diet

Federico Bozzetti [a,*], Beth Zupec-Kania [b]

Results: Despite the paucity of data it appears that modulation of tumour growth by the calorie restriction/nutritional support is unlikekly in humans for several reasons: the different tumour cells growth rate and different tumour/host carcass ratio and duration of treatment, between tumour-bearing animals and patients.

Conclusion: There is a large consensus in literature that maintaining a normal body weight and preserving the lean body mass through an adequate nutrition is beneficial in cancer patients. The nutritional approach through a ketogenic diet which may be toxic for the cancer cells while is well utilized and tolerated by the patient seems promising in a next future.

Take Home Messages

- Weight loss and impaired nutritional status affect morbidites, tollerance to antineoplastic therapies, QoL and survival.
- There is NO association between vegetarianism and cancer mortality.
- More animal products are excluded (vegan and macrobiotic diet), more risks increse (weigth loss, malnutrition, nutritional adequacy).

Take Home Messages

- Caloric restriction in vulnerable individuals, like cancer patients receiving active anti-cancer therapies, may favour weight loss, malnutrition and cachexia.

- Although preclinical data are promising, further research in humans is needed before the use of fasting or ketogenic diet as a useful and safe intervention could be recommended in cancer patients.

Il compito degli uomini di cultura è più che mai oggi quello di seminare dei dubbi, non già di raccogliere certezze.

Norberto Bobbio (1909-2004)

Grazie

valorianifilippo@gmail.com