G20 I22 SMO

XVIII CONGRESSO NAZIONALE

FRAGILITÀ MUSCOLO-SCHELETRICA
STILI DI VITA E APPROPRIATEZZA TERAPEUTICA
LE SFIDE PER IL FUTURO

ADMIRE
ALDOSTERONE-MINERALOCORTICOID RECEPTOR
NETWORK

Metabolismo muscolare e terapia chetogenica di precisione

Prof. Massimiliano Caprio
San Raffaele Roma University
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Reviews in Endocrine and Metabolic Disorders (2020) 21:1–3
https://doi.org/10.1007/s11154-020-09546-9

Confusion in the nomenclature of ketogenic diets blurs evidence

Pierpaolo Trimboli[1] · Marco Castellana[2] · Diego Bellido[3] · Felipe F. Casanueva[4]

Published online: 21 February 2020

Diet description	Abbreviation	Carbohydrates	Calories	Lipids
Very-low-calorie ketogenic diet	VLCKD	<30–50 g/day	<700–800 kcal/day	<30–40 g/day
Low-calorie ketogenic diet	LCKD	<30–50 g/day	>700–800 kcal/day and < TEE	>30–40 g/day
Isocaloric ketogenic diet	ICKD	<30–50 g/day	In line with TEE	70–80% of daily calorie intake

Legend: *TEE* total energy expenditure

What is VLCKD?

VLCKD represents a nutritional intervention that mimics fasting through a marked restriction of daily carbohydrate intake, usually **lower than 30 g/day** (≃13% of total energy intake), with a relative increase in the proportions of fat (≃44%) and protein (≃43%) and a total daily energy intake <800 Kcal.

VLCKD should not be considered as a high-protein diet, since its daily protein intake is approximately 1.2-1.5 g/Kg of ideal body weight

VLCKD is based on **protein preparations of high biological value derived from green peas, eggs, soy and whey**. Each protein preparation is composed by approximately 18 g protein, 4 g carbohydrate, 3 g fat (**mainly high-oleic vegetable oils**) and provides approximately 100–150 kcal.

Therefore, **VLCKD is characterized by a low lipid content**, mainly deriving from olive oil (≃ 20 g per day), **of which polyunsaturated fatty acids (PUFA) <10 %**

Caprio M et al. J Endocrinol Invest 2019

Journal of Endocrinological Investigation
https://doi.org/10.1007/s40618-019-01061-2

CONSENSUS STATEMENT

Very-low-calorie ketogenic diet (VLCKD) in the management of metabolic diseases: systematic review and consensus statement from the Italian Society of Endocrinology (SIE)

2019

M. Caprio[1,2] · M. Infante[3] · E. Moriconi[1,4] · A. Armani[1] · A. Fabbri[3] · G. Mantovani[5] · S. Mariani[4] · C. Lubrano[4] · E. Poggiogalle[4] · S. Migliaccio[6] · L. M. Donini[4] · S. Basciani[4] · A. Cignarelli[7] · E. Conte[7] · G. Ceccarini[8] · F. Bogazzi[9] · L. Cimino[10] · R. A. Condorelli[10] · S. La Vignera[10] · A. E. Calogero[10] · A. Gambineri[11] · L. Vignozzi[12] · F. Prodam[13] · G. Aimaretti[13] · G. Linsalata[14] · S. Buralli[14] · F. Monzani[14] · A. Aversa[15] · R. Vettor[16] · F. Santini[8] · P. Vitti[9] · L. Gnessi[4] · U. Pagotto[11] · F. Giorgino[7] · A. Colao[17] · A. Lenzi[4] on behalf of the Cardiovascular Endocrinology Club of the Italian Society of Endocrinology

Table 2 Indications for the use of VLCKD in metabolic diseases

Strong recommendations	Strength of recommendations and quality of evidence according to GRADE system
Severe obesity	(1 ØØØO)
Management of severe obesity before bariatric surgery	(1 ØØØO)
Sarcopenic obesity	(1 ØØØO)
Obesity associated with type 2 diabetes (preserved beta cell function)	(1 ØØØO)
Obesity associated with hypertriglyceridemia	(1 ØØØO)
Obesity associated with hypertension	(1 ØØØO)
Pediatric obesity associated with epilepsy and/or with a high level of insulin resistance and/or comorbidities, not responsive to standardized diet	(1 ØØØO)

Journal of Endocrinological Investigation
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Weak recommendations	
Obesity associated with dysbiosis of the gut microbiota	(2 ØØØO)
Obesity associated with high levels of LDL-cholesterol and/or low levels of HDL-cholesterol	(2 ØØØO)
Obesity associated with non-alcoholic fatty liver disease (NAFLD)	(2 ØØØO)
Obesity associated with heart failure (NYHA I–II)	(2 ØOOO)
Obesity associated with atherosclerosis	(2 ØOOO)
Male obesity secondary hypogonadism	(2 ØØØO)
Obesity associated with polycystic ovary syndrome (PCOS)	(2 ØOOO)
Menopausal transition-related obesity	(2 ØOOO)
Neurodegenerative disorders associated with sarcopenic obesity	(2 ØOOO)

KETOGENIC THERAPY: EFFECTS ON AGING AND LIFE-SPAN

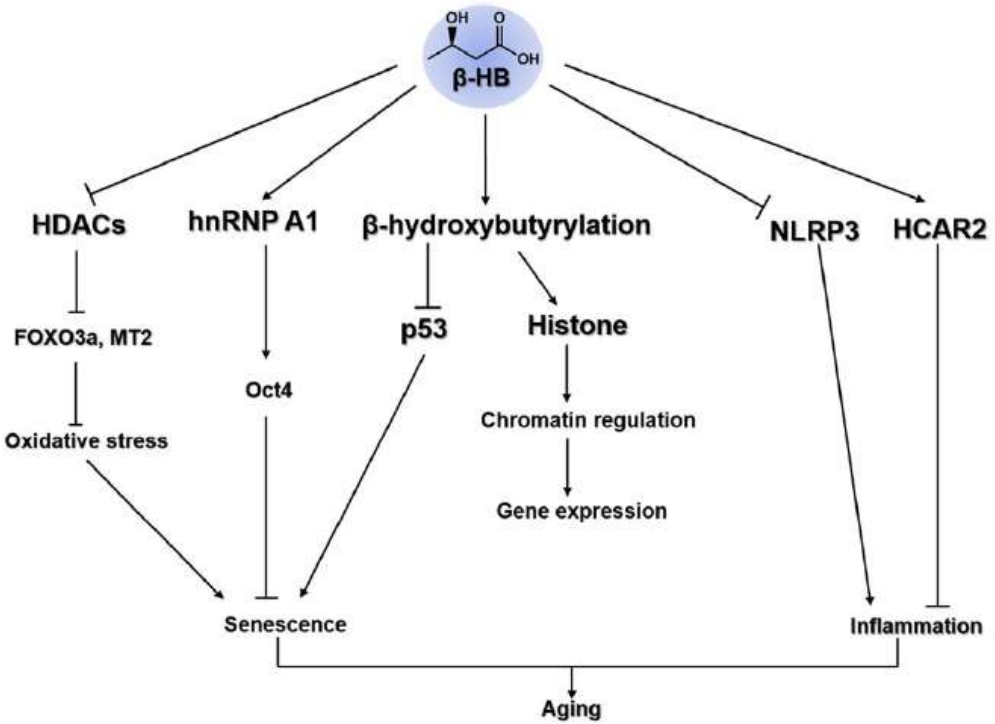
Han et al. *Experimental & Molecular Medicine* (2020) 52:548–555
https://doi.org/10.1038/s12276-020-0415-z

Experimental & Molecular Medicine

β-hydroxybutyrate and its metabolic effects on age-associated pathology

Young-Min Han[1], Tharmarajan Ramprasath[1] and Ming-Hui Zou[1]

Target molecules and cellular signaling of β-HB are associated with the aging process, which is accelerated by senescence and inflammation. β-HB delays senescence via HDAC inhibition, hnRNP A1-mediated Oct4 expression, and β-hydroxybutyrylation on p53. Furthermore, β-HB suppresses inflammation by NLRP3 inhibition or HCAR2 activation and reduces the contribution to aging-associated diseases.



Original Research Communications

Effects of 3-hydroxybutyrate and free fatty acids on muscle protein kinetics and signaling during LPS-induced inflammation in humans: anticatabolic impact of ketone bodies

Henrik H Thomsen,[1,2] Nikolaj Rittig,[2] Mogens Johannsen,[3] Andreas B Møller,[4] Jens Otto Jørgensen,[2] Niels Jessen,[4,5,6] and Niels Møller[2]

[1]Department of Medicine, Viborg Regional Hospital, Viborg, Denmark; [2]Department of Internal Medicine and Endocrinology MEA, and; [3]Department of Forensic Medicine, Bioanalytical Unit, and; [4]Research Laboratory for Biochemical Pathology, Department of Clinical Medicine, and; [5]Department of Biomedicine; and [6]Clinical Pharmacology, Aarhus University, Aarhus, Denmark

Spotlight

Anticatabolic Effects of Ketone Bodies in Skeletal Muscle

Andrew P. Koutnik,[1] Dominic P. D'Agostino,[1] and Brendan Egan,[2,*]

TEM 1377 No. of Pages 3 ARTICLE IN PRESS

Trends in Endocrinology & Metabolism

CellPress REVIEWS

J Physiol 595.9 (2017) pp 2857–2871

TOPICAL REVIEW

Metabolism of ketone bodies during exercise and training: physiological basis for exogenous supplementation

Mark Evans[1], Karl E. Cogan[1] and Brendan Egan[1,2]

Developmental Cell, Vol. 6, 673–684, May, 2004, Copyright ©2004 by Cell Press

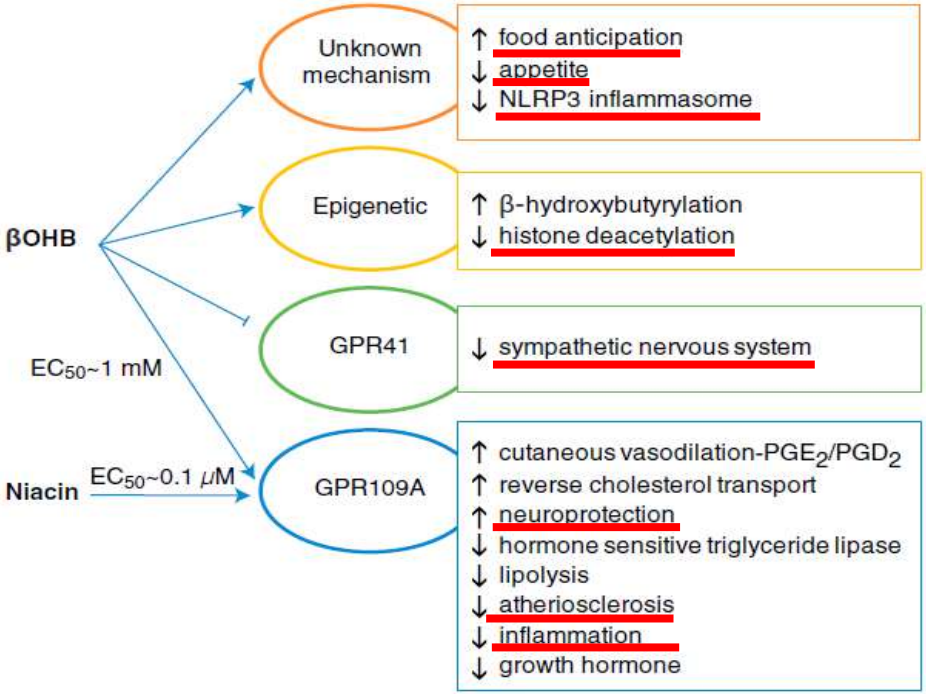
Deacetylase Inhibitors Increase Muscle Cell Size by Promoting Myoblast Recruitment and Fusion through Induction of Follistatin

β-Hydroxybutyrate Elicits Favorable Mitochondrial Changes in Skeletal Muscle

Int. J. Mol. Sci. 2018, *19*, 2247

β-hydroxybutyrate Inhibits Class I Histone Deacetylases

UN METODO PER TANTE INDICAZIONI DIVERSE



- Riduzione dell'infiammazione (GPR109A è abbondantemente espresso da monociti e macrofagi)
- Riduzione dell stress ossidativo
- Aumento delle proteine antiossidanti
- Riduzione dell'appetito/aumento della sazietà
- Miglioramento delle proteine mitocondriali

Applicazioni in diversi contesti clinici!

Puchalska P and Crawford PA, Cell Metabolism 2017

Open access Review

BMJ Nutrition, Prevention & Health

Genetic variants for personalised management of very low carbohydrate ketogenic diets

Lucia Aronica ,[1,2] Jeff Volek,[3] Angela Poff,[4] Dominic P D'agostino[4]

December 2020

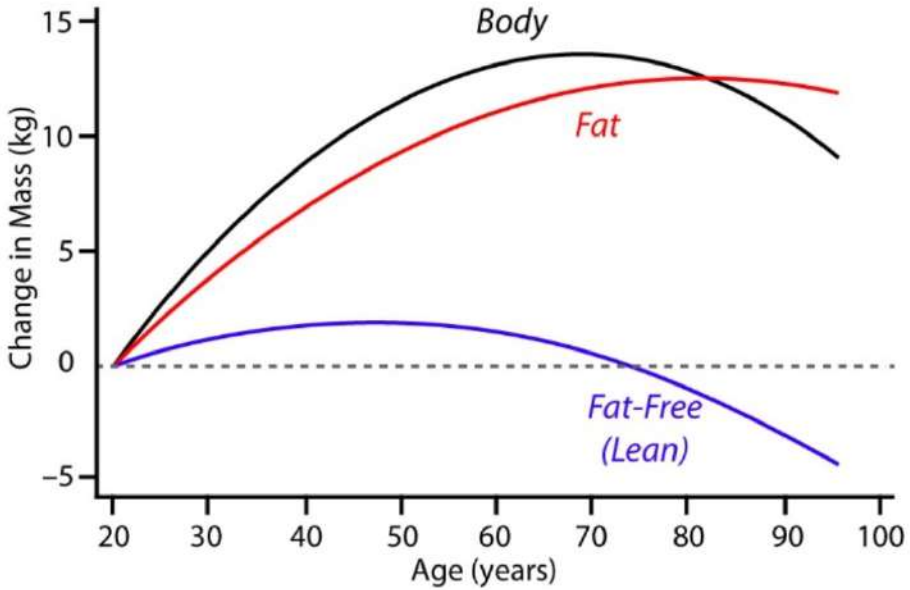
As the field of precision medicine is gaining traction, **nutrition research is experiencing a 'gold rush' for biomarkers that may enable the selection of personalised dietary interventions to maximise an individual's likelihood of successful response**.

These biomarkers include both genetic factors and dynamic biomarkers that respond to lifestyle factors such as physiological markers, epigenetics and transcriptomics, metabolomics and the microbiome.

The use of biomarkers of dietary response would be of particular clinical relevance for the selection and individualised risk–benefit analysis of **therapeutic diets, such as the ketogenic diet (KD), which provide alternative or complementary therapies to standard-of-care treatments**

A personalised lifestyle approach to ketogenic diets would enable to maximise both therapeutic effectiveness and long-term safety for patients

Modificazioni nella composizione corporea con l'età



IMC

Massa grassa

Massa muscolare

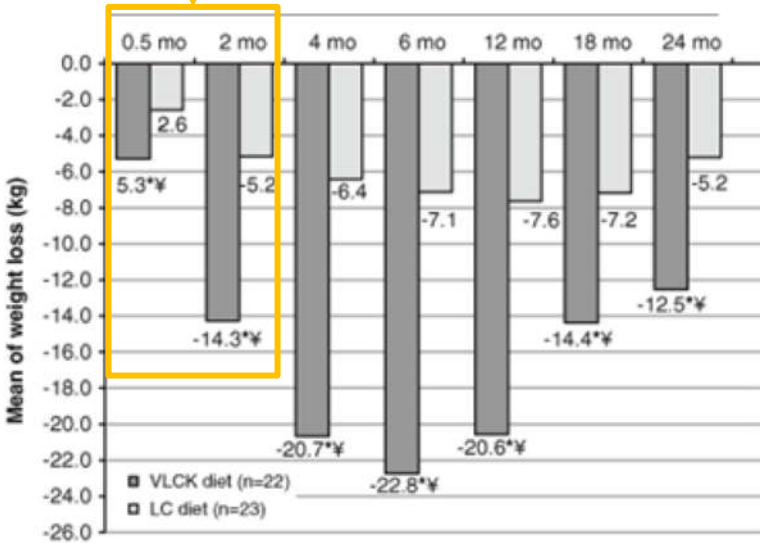
Con l'età si assiste ad un progressivo **aumento** della **massa grassa e** una **diminuzione** della **massa muscolare**.

Bhasin S, et al. *Endotext*. 2022.

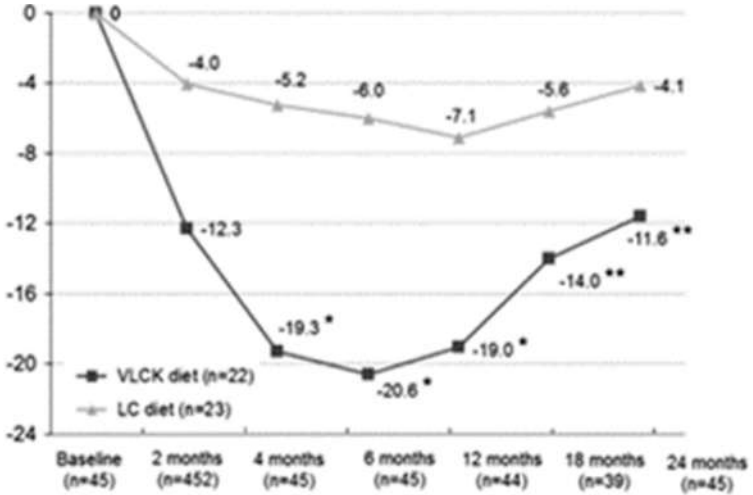
Obesity treatment by very low-calorie-ketogenic diet at two years

Ketosis

Weight loss



Change in waist



Moreno B et al. Endocrine 2016

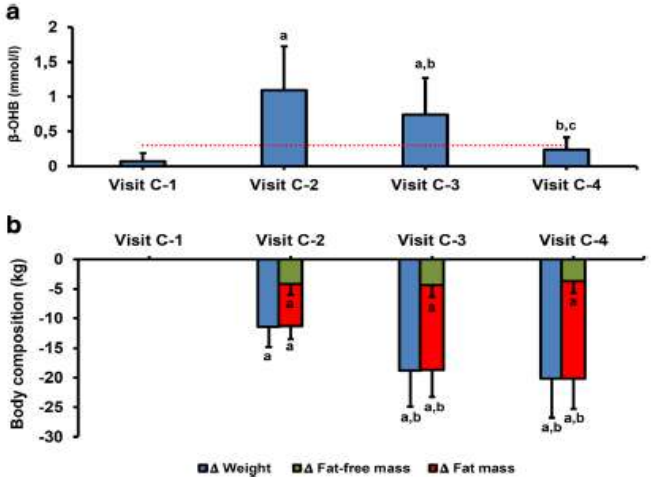
Gomez-Arbelaez et al. Nutrition & Metabolism (2018) 15:18
DOI 10.1186/s12986-018-0249-z

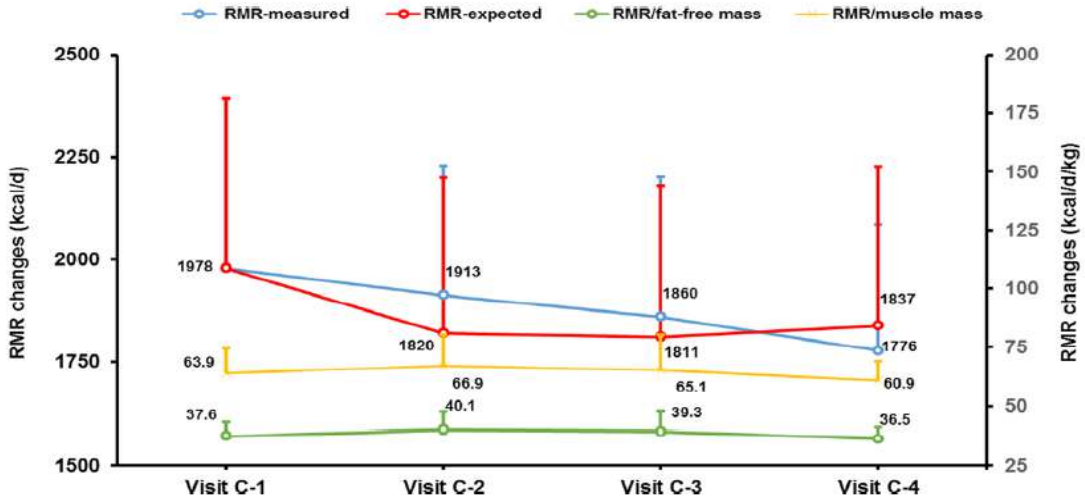
Nutrition & Metabolism

RESEARCH Open Access

Resting metabolic rate of obese patients under very low calorie ketogenic diet

Diego Gomez-Arbelaez[1†], Ana B. Crujeiras[1,5†], Ana I. Castro[1,5], Miguel A. Martinez-Olmos[1,5], Ana Canton[1,5], Lucia Ordoñez-Mayan[1], Ignacio Sajoux[2], Cristobal Galban[3], Diego Bellido[4] and Felipe F. Casanueva[1,5*]





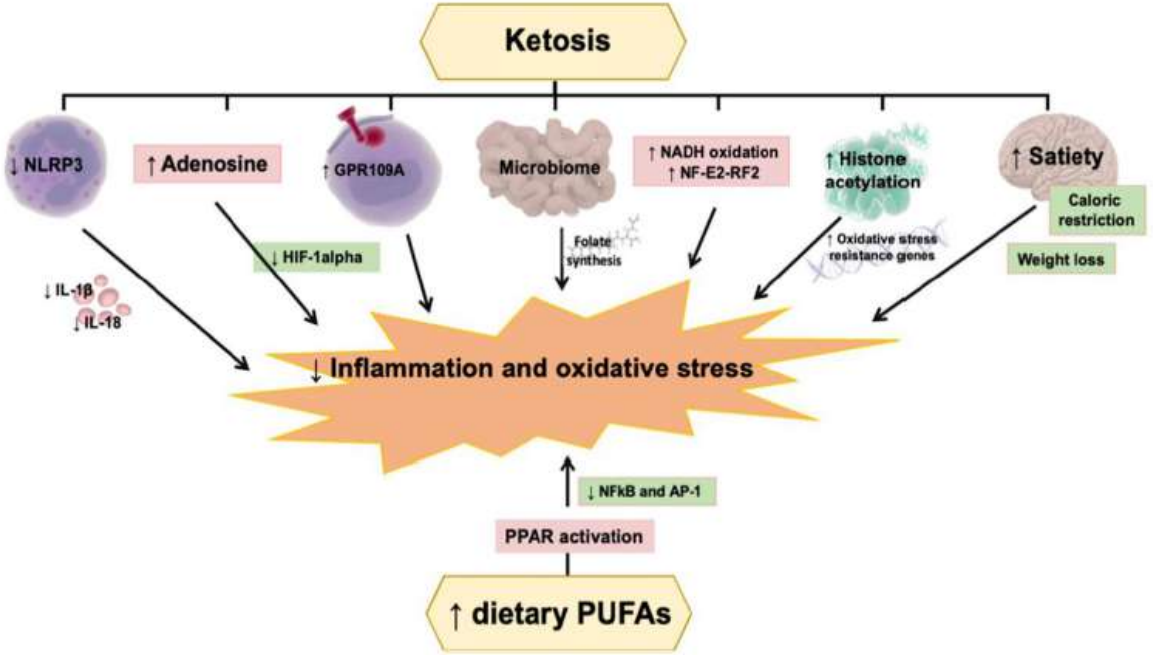
CRITICAL REVIEWS IN FOOD SCIENCE AND NUTRITION
hiips://doi.org/10.1080/10408398.2022.2054935

Taylor & Francis
Taylor & Francis Group

REVIEW

Could very low-calorie ketogenic diets turn off low grade inflammation in obesity? Emerging evidence

Luigi Barrea[a,b*], Massimiliano Caprio[c,d*], Mikiko Watanabe[e*], Giuseppe Cammarata[f*], Alessandra Feraco[c,d], Giovanna Muscogiuri[b,g,h], Ludovica Verde[b,g], Annamaria Colao[b,g,h] and Silvia Savastano[b,g]and on behalf of Obesity Programs of nutrition, Education, Research and Assessment (OPERA) Group



World Health Organization 2020 guidelines on physical activity and sedentary behaviour

Fiona C Bull ,[1,2] Salih S Al-Ansari,[3] Stuart Biddle,[4] Katja Borodulin,[5,6] Matthew P Buman ,[7] Greet Cardon,[8] Catherine Carty,[9,10] Jean-Philippe Chaput ,[11] Sebastien Chastin ,[12] Roger Chou,[13] Paddy C Dempsey,[14,15] Loretta DiPietro,[16] Ulf Ekelund ,[17,18] Joseph Firth,[19,20] Christine M Friedenreich,[21] Leandro Garcia,[22] Muthoni Gichu,[23] Russell Jago ,[24] Peter T Katzmarzyk,[25] Estelle Lambert ,[26] Michael Leitzmann,[27] Karen Milton ,[28] Francisco B Ortega,[29] Chathuranga Ranasinghe,[30] Emmanuel Stamatakis ,[31] Anne Tiedemann,[32] Richard P Troiano ,[33] Hidde P van der Ploeg,[34,35] Vicky Wari,[36] Juana F Willumsen[1]

Table 1 Glossary of terms

Term	Definition
Aerobic physical activity	Activity in which the body's large muscles move in a rhythmic manner for a sustained period of time. Aerobic activity—also called endurance activity—improves cardiorespiratory fitness. Examples include walking, running, swimming and bicycling.
Balance training	Static and dynamic exercises that are designed to improve an individual's ability to withstand challenges from postural sway or destabilising stimuli caused by self-motion, the environment or other objects.
Bone-strengthening activity	Physical activity primarily designed to increase the strength of specific sites in bones that make up the skeletal system. Bone-strengthening activities produce an impact or tension force on the bones that promotes bone growth and strength. Examples include any type of jumps, running and lifting weights.
Disability	From the International Classification of Functioning, Disability and Health, an umbrella term for impairments, activity limitations and participation restrictions, denoting the negative aspects of the interaction between an individual (with a health condition) and that individual's contextual factors (environmental and personal factors).
Domains of physical activity	Physical activities can be undertaken in various domains, including one of more of the following: leisure, occupation, education, home and/or transport.
Household domain physical activity	Physical activity undertaken in the home for domestic duties (such as cleaning, caring for children, gardening, etc).
Leisure-domain physical activity	Physical activity performed by an individual that is not required as an essential activity of daily living and is performed at the discretion of the individual. Examples include sports participation, exercise conditioning or training and recreational activities such as going for a walk, dancing and gardening.
Light-intensity physical activity (LPA)	On an absolute scale, light intensity refers to physical activity that is performed between 1.5 and 3 METs. On a scale relative to an individual's personal capacity, light-intensity physical activity is usually a 2–4 on a rating scale of perceived exertion scale of 0–10. Examples include slow walking, bathing or other incidental activities that do not result in a substantial increase in heart rate or breathing rate.
Metabolic equivalent of task (MET)	The metabolic equivalent of task, or simply metabolic equivalent, is a physiological measure expressing the intensity of physical activities. One MET is the energy equivalent expended by an individual while seated at rest, usually expressed as $mLO^2/kg/min$.
Moderate- intensity physical activity (MPA)	On an absolute scale, moderate-intensity refers to the physical activity that is performed between 3 and <6 times the intensity of rest (METs). On a scale relative to an individual's personal capacity, MPA is usually a 5 or 6 on a rating scale of perceived exertion scale of 0–10.
Moderate-to-vigorous intensity physical activity (MVPA)	On an absolute scale, MVPA refers to the physical activity that is performed at >3 METs (ie, >3 times the intensity of rest). On a scale relative to an individual's personal capacity, MPA is usually a 5 or above on a scale of 0–10.
Multicomponent physical activity	Multicomponent physical activity are activities that can be done at home or in a structured group or class setting and combine all types of exercise (aerobic, muscle strengthening and balance training) into a session, and this has been shown to be effective. An example of a multicomponent physical activity programme could include walking (aerobic activity), lifting weights (muscle strengthening) and could incorporate balance training. Examples of balance training can include walking backwards or sideways or standing on one foot while doing an upper body muscle-strengthening activity, such as bicep curls. Dancing also combines aerobic and balance components.
Occupation domain physical activity	See work domain physical activity.
Physical activity (PA)	Any bodily movement produced by skeletal muscles that requires energy expenditure.
Physical inactivity	An insufficient physical activity level to meet present physical activity recommendations.
Recreational screen time	Time spent watching screens (television (TV), computer, mobile devices) for purposes other than those related to school or work.
Sedentary screen time	Time spent watching screen-based entertainment while sedentary, either sitting, reclining or lying. Does not include active screen-based games where physical activity or movement is required.
Sedentary behaviour	Any waking behaviour characterised by an energy expenditure of 1.5 METs or lower while sitting, reclining or lying. Most desk-based office work, driving a car and watching television are examples of sedentary behaviours; these can also apply to those unable to stand, such as wheelchair users. The guidelines operationalise the definition of sedentary behaviour to include self-reported low movement sitting (leisure time, occupational and total), TV viewing or screen time and low levels of movement measured by devices that assess movement or posture.
Transport domain physical activity	Physical activity performed for the purpose of getting to and from places, and refers to walking, cycling and wheeling (ie, the use of non-motorised means of locomotion with wheels, such as scooters, roller-blades, manual wheelchair, etc). In some contexts, operation of a boat for transport could also be considered transport-related physical activity.
Vigorous-intensity physical activity (VPA)	On an absolute scale, vigorous intensity refers to physical activity that is performed at 6.0 or more METs. On a scale relative to an individual's personal capacity, VPA is usually a 7 or 8 on a rating scale of perceived exertion scale of 0–10.
Work domain physical activity	Physical activity undertaken during paid or voluntary work.

Obesity Facts

Consensus Statement

Obes Facts
DOI: 10.1159/000521241

Received: November 21, 2021
Accepted: November 26, 2021
Published online: February 23, 2022

Definition and Diagnostic Criteria for Sarcopenic Obesity: ESPEN and EASO Consensus Statement

Lorenzo M. Donini[a] Luca Busetto[b] Stephan C. Bischoff[c] Tommy Cederholm[d] Maria D. Ballesteros-Pomar[e] John A. Batsis[f] Juergen M. Bauer[g] Yves Boirie[h] Alfonso J. Cruz-Jentoft[i] Dror Dicker[j] Stefano Frara[k] Gema Frühbeck[l] Laurence Genton[m] Yftach Gepner[n] Andrea Giustina[k] Maria Cristina Gonzalez[o] Ho-Seong Han[p] Steven B. Heymsfield[q] Takashi Higashiguchi[r] Alessandro Laviano[a] Andrea Lenzi[a] Ibolya Nyulasi[s] Edda Parrinello[a] Eleonora Poggiogalle[a] Carla M. Prado[t] Javier Salvador[u] Yves Rolland[v] Ferruccio Santini[w] Mireille J. Serlie[x] Hanping Shi[y] Cornel C. Sieber[z] Mario Siervo[A] Roberto Vettor[b] Dennis T. Villareal[B] Dorothee Volkert[z] Jianchun Yu[C] Mauro Zamboni[D] Rocco Barazzoni[E]

DEFINIZIONE

- Sarcopenic obesity (SO) is a clinical and functional condition characterized by the coexistence of obesity, characterized by excess fat mass (FM), and sarcopenia. Sarcopenia, defined as low skeletal muscle mass and function, has been identified and described as a geriatric syndrome with a multifactorial aetiology whose prevalence increases with age.

- However, sarcopenia may arise in individuals with obesity at any age.

- Obesity can independently lead to loss of muscle mass and function, due to the negative impact of adipose tissue-dependent metabolic derangements, such as oxidative stress, inflammation and insulin resistance, all of which negatively affect muscle mass.

VLCKD E ATTIVITA' FISICA: SI PUO' FARE?

frontiers | Frontiers in Nutrition

TYPE Original Research
PUBLISHED 29 September 2022
DOI 10.3389/fnut.2022.955024

Very low calorie ketogenic diet combined with physical interval training for preserving muscle mass during weight loss in sarcopenic obesity: A pilot study

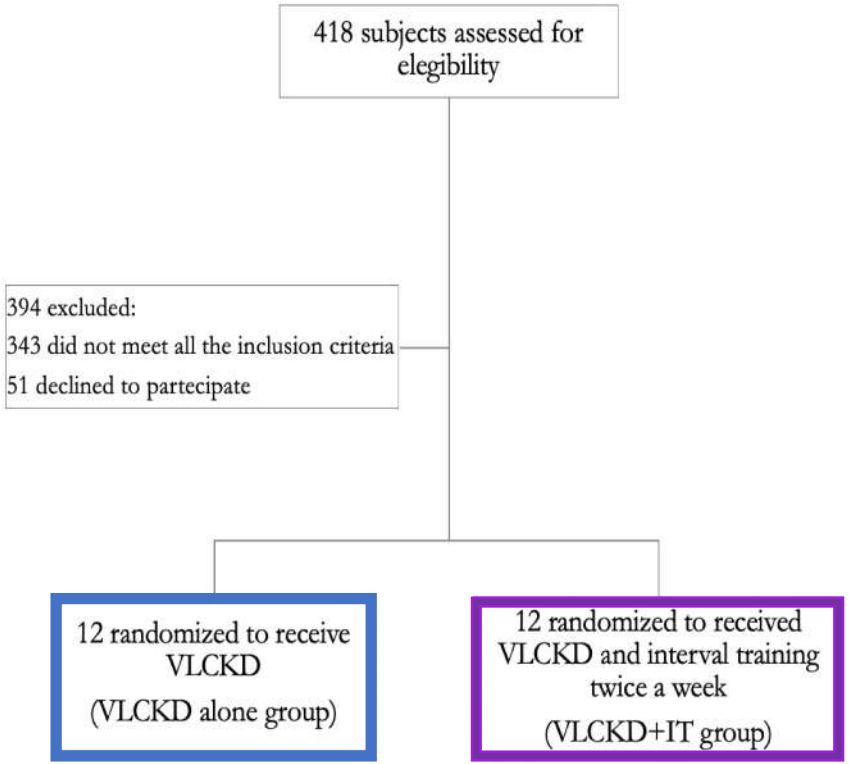
Elisabetta Camajani[1,2], Alessandra Feraco[2,3], Stefania Proietti[4], Sabrina Basciani[1], Luigi Barrea[5,6], Andrea Armani[2,3], Mauro Lombardo[2], Lucio Gnessi[1] and Massimiliano Caprio[2,3]*

Background: The prevalence of sarcopenic obesity (SO) is increasing worldwide, posing important challenges to public health and national health care system, especially during the COVID pandemic. In subjects with SO, it is essential to reduce body weight, and to preserve lean mass, to avoid worsening of muscle function. Adequate nutrition and correct physical activity is essential to counteract SO progression. Very Low Calorie Ketogenic Diet (VLCKD), a well-established nutritional intervention for obesity, has been also indicated for the treatment of SO. To date, the effects of physical training during VLCKD have not been investigated.

Aim: This pilot study aims to determine the efficacy of VLCKD combined with interval training, compared to a VLCKD alone, on weight-loss, body composition, and physical performance in participants with SO.

The inclusion criteria were as follows:
women and men,
age between 50 and 70 years old,
BMI between 30 and 40 kg/m^2
WC ≥102 cm for men and ≥88 cm for women,
sarcopenia, insulin resistance (Homeostasis Model Assessment-Insulin Resistance, HOMA-IR ≥ 2.5) or type 2 diabetes mellitus treated only with metformin.

The exclusion criteria were as follows:
lack of informed consent,
hypersensitivity to components of meals replacement,
type 1 diabetes,
cell failure in type 2 diabetes mellitus, insulin therapy or concomitant use of sodium/glucose cotransporter 2 (SGLT2) inhibitors,
gastrointestinal diseases,
hydroelectrolytic alterations,
psychiatric disturbances,
kidney failure [estimated glomerular filtration rate (eGFR) < 60 mL/min],
liver failure,
heart failure (NYHA III-IV),
respiratory failure,
unstable angina or cardiac arrhythmias; recent stroke or myocardial infarction (<12 months)



Camajani et al, in press. DOI 10.3389/fnut.2022.955024

Nutritional an Physical Intervention

Dietary intervention (VLCKD):

- All patients followed a VLCKD [780-800 kcal/day, with the following composition in macronutrients:
  - carbohydrates 26 g (13.5%),
  - fats 35 g (40.4%)
  - proteins 80-90 g (1.2 -1.4 g/Kg)]
- Patients were given four or five meals/day [timing was at main meals (8 a.m., 1.00 p.m. and 8.00 pm), mid-morning and mid-afternoon].
- Supplements of vitamins, minerals and omega-3 fatty acids, were provided in accordance to international recommendations (EFSA)
- It was also recommended to drink not less than 2.0-2.5 l of water per day.

Physical training intervention (IT):

- Seven days after the beginning of the nutritional protocol, the patients enrolled in the VLCKD+IT group started Interval Training (IT) twice a week.
- Due to pandemic, physical exercise sessions were carried out via Zoom platform with a personal trainer and each session lasted 30-35 minutes.
- Each session of physical exercise was structured as follows:
  - an initial warm up
  - breathing and stretching of the posterior chain,
  - Interval training: functional exercises for 20-30 seconds with a 10-15 second pause,
  - proprioception and balance
  - breathing

Camajani et al, in press. DOI 10.3389/fnut.2022.955024

TABLE 2 Participants characteristics at baseline (T0).

	All	VLCKD	VLCKD + IT	*P*-value
Patients, *N* (%)	24	12 (50%)	12 (50%)	
Sex, *N* (%)				
M	3 (12.5)	2 (16.7)	1 (8.3)	0.537
F	21 (87.5)	10 (83.3)	11 (91.7)	
Age (years)	56.3 ± 5.3	56.0 ± 6.7	56.5 ± 3.8	0.795
Weight (Kg)	91.1 ± 9.8	90.6 ± 7.2	91.6 ± 12.2	0.810
BMI (kg/m^2)	33.9 ± 3.4	33.9 ± 3.0	33.9 ± 3.8	0.973
HOMA-IR ≥ 2.5, *N* (%)	24 (100%)	12 (50%)	12 (50%)	1.000
FM, median (IQR)	36.36 (32.0–47.5)	35.90 (32.2–47.2)	40.02 (31.6–47.6)	0.887$^+$
FFM (Kg)	52.4 ± 5.1	52.6 ± 5.4	52.2 ± 5.0	0.830
Comorbidity				
Type 2 diabetes mellitus	2	1	1	1.000
Hypertension	24	12	12	1.000
Hypercholesterolemia	16	7	9	0.386

Variables with normal distribution are expressed as mean ± SD, those with non-normal distribution as median (interquartile range) with Mann Whitney. VLCKD, very low calorie ketogenic diet; IT, interval training; BMI, body mass index; HOMA-IR, homeostatic model assessment for insulin resistance; FM, fat mass; IQR, interquartile range; FFM, fat free mass. $^+$Mann Whitney.

Camajani et al, in press. DOI 10.3389/fnut.2022.955024

TABLE 3 Participants characteristics at baseline (T0) and at the end of the study (T6).

	VLCKD				VLCKD + IT				*P*-value
	T0	T6	Δ	*p*	T0	T6	Δ	*p*	
Weight (kg)	90.5 ± 7.1	81.0 ± 6.1	−9.6 ± 1.61	<0.001	91.6 ± 12.1	81.1 ± 11.5	−10.4 ± 3.2	<0.001	0.451
WC (cm)	101.2 ± 9.7	92.3 ± 8.6	−8.9 ± 3.5	**<0.001**	100.7 ± 8.3	91.7 ± 8.1	−9.1 ± 2.5	**<0.001**	0.895
HC (cm)	122.7 ± 9.2	115.2 ± 9.6	−7.5 ± 1.4	**<0.001**	123.0 ± 10.1	113.0 ± 10.5	−10.0 ± 3.0	**<0.001**	**0.025**
FM (kg)	40.53 ± 11.63	33.97 ± 10.94	−6.5 ± 1.9	**<0.001**	39.59 ± 8.62	28.69 ± 8.67	−11.0 ± 3.4	**<0.001**	**0.001**
FFM (kg)	52.62 ± 5.42	50.32 ± 5.46	−2.3 ± 1.3	**<0.001**	52.16 ± 5.04	52.46 ± 5.01	0.3 ± 1.0	0.329	**<0.001**
BMI (kg/m^2)	33.8 ± 3.0	30.2 ± 2.6	−3.6 ± 0.6	**<0.001**	33.9 ± 3.8	29.9 ± 3.5	−4.0 ± 1.3	**<0.001**	0.389
BMR (kcal)	1513.75 ± 100.92	1455.58 ± 93.16	−58.1 ± 35.0	**<0.001**	1491.16 ± 106.75	1499.41 ± 105.85	8.2 ± 22.1	0.224	**<0.001**
BCM (kg)	30.39 ± 4.84	26.56 ± 4.09	−3.8 ± 3.5	**0.003**	27.65 ± 3.11	29.34 ± 6.85	1.6 ± 4.5	0.226	**0.003**

Variables with normal distribution are expressed as mean ± SD, those with non-normal distribution as median (interquartile range). VLCKD, very low calorie ketogenic diet; IT, interval training; WC, waist circumference; HC, hip circumference; FM, fat mass; FFM, fat free mass; BMI, body mass index; BMR, basal metabolic rate; BCM, body cell mass. The bold represents statistically significant values.

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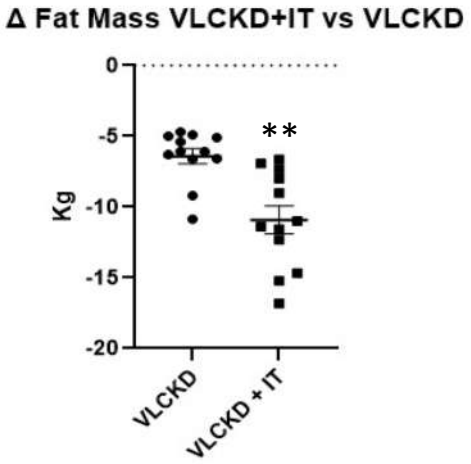
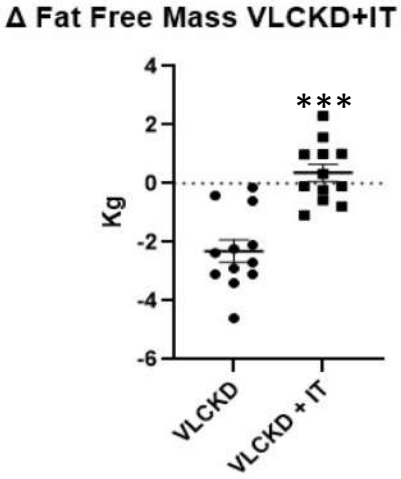
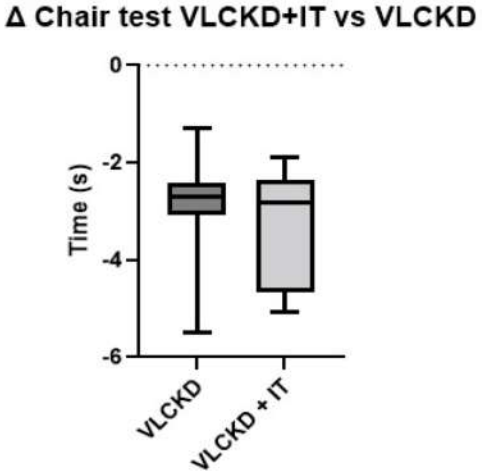




Grouped ranking charts of observed relative differences (% variation vs basal values) from T0 to T6 in fat mas and fat free mass in VLCKD and VLCKD+IT groups.

***: p=0.001*

****: p<0.001*



Box plot of pooled ranking of observed relative differences (% variation vs basal values) from T0 to T6 in Chair stand test in VLCKD and VLCKD+IT groups.

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TABLE 6 Participants characteristics at baseline (T0) and at the end of the study (T6).

	VLCKD				VLCKD + IT				*P*-value
	T0	T6	Δ	*p*	T0	T6	Δ	*p*	
Fasting glycemia (mg/dL)	105.9 ± 12.8	86.6 ± 12.5	−16.3 ± 9.5	**<0.001**	101.4 ± 11.7	87.0 ± 8.6	−14.4 ± 8.4	**<0.001**	0.606
Fasting insulin (μIU/ml)	11.8 (11.0–13.75)	8.1 (7.25–9.75)	–	**0.002***	12.7 (11.25–14.57)	9.0 (8.3–9.4)	–	**0.002***	0.630+
HOMA-IR	3.9 ± 2.9	1.8 ± 0.6	−2.1 ± 2.6	**0.018**	3.3 ± 0.8	1.8 ± 0.4	−1.5 ± 0.6	**<0.001**	0.474
BUN (mg/dl)	37.3 ± 7.8	32.3 ± 5.6	−5.0 ± 4.3	**0.002**	34.1 ± 9.1	30.4 ± 5.9	−3.7 ± 6.5	0.075	0.579
Creatinine (mg/dl)	0.82 ± 0.18	0.78 ± 0.16	−0.04 ± 0.06	**0.046**	0.80 ± 0.13	0.72 ± 0.08	−0.08 ± 0.09	**0.017**	0.276
eGFR (ml/min)	83.87 ± 15.51	88.84 ± 15.21	4.97 ± 9.74	0.105	82.50 ± 14.84	91.69 ± 11.05	9.18 ± 10.78	**0.013**	0.327
AST (U/L)	23.5 ± 5.7	19.8 ± 5.3	−3.6 ± 4.9	**0.026**	32.3 ± 12.9	24.6 ± 6.7	−7.7 ± 10.9	**0.032**	0.251
ALT (U/L)	26.0 ± 11.1	19.1 ± 6.7	−6.8 ± 8.2	**0.015**	37.8 ± 14.6	26.3 ± 12.1	−11.5 ± 11.5	**0.005**	0.267
Total cholesterol (mg/dl)	203.7 ± 38.6	161.8 ± 30.5	−41.9 ± 20.1	**<0.001**	212.8 ± 23.6	185.0 ± 17.3	−27.8 ± 23.9	**0.002**	0.133
HDL cholesterol (mg/dl)	49.5 (41.2–63.7)	51.5 (40.0–63.0)	−1.0 (−6.5; 2.0)	0.431*	47.5 (42.5–52.2)	53.0 (50.5–64.0)	6.0 (1.25; 9.75)	**0.003***	**0.002**+
LDL cholesterol (mg/dl)	127.5 ± 36.7	93.8 ± 23.8	−33.7 ± 24.5	**0.001**	139.9 ± 31.0	110.9 ± 18.5	−29.0 ± 29.9	**0.006**	0.678
Triglycerides (mg/dl)	132.8 ± 38.1	83.5 ± 16.9	−49.3 ± 30.0	**<0.001**	114.9 ± 25.2	80.4 ± 12.2	−34.5 ± 24.6	**0.001**	0.199
Vitamin D (ng/dl)	18.1 ± 8.3	21.1 ± 9.6	2.9 ± 2.5	**0.002**	24.8 ± 11.4	31.0 ± 9.7	6.1 ± 5.4	**0.003**	0.080

Variables with normal distribution are expressed as mean ± SD, those with non-normal distribution as median (interquartile range) with Wilcoxon test. VLCKD, very low calorie ketogenic diet; IT, interval training; HOMA-IR, homeostasis model assessment-insulin resistance; BUN, blood urea nitrogen; eGFR, glomerular filtration rate; AST, aspartate aminotransferase; ALT, alanine aminotransferase; HDL, high density lipoprotein; LDL, low density lipoprotein. *Wilcoxon test; +Mann Whitney. The bold represents statistically significant values.

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2022

NUOVA CHIAVE DI LETTURA DELLA TERAPIA CHETOGENICA

UN APPROCCIO INTEGRATO DI PRECISIONE, CHE PREVEDE L'AZIONE SINERGICA DI:

- Un percorso terapeutico validato scientificamente per la gestione del paziente, che segue i principi delle VLCKD.

- Un'integrazione specifica di micronutrienti e nutraceutici per favorire il ripristino degli equilibri cellulari e funzionali.

- La combinazione con adeguato esercizio fisico, opportune modifiche dello stile di vita, e terapia farmacologica

.

TERAPIA CHETOGENICA DI PRECISIONE

Il paziente viene accompagnato fino alla fase di **mantenimento**, la fase piu importante, ma anche la più delicata e la più complessa da controllare.

L'**obiettivo**: ristabilire un equilibrio alimentare e fisiologico che si protragga nel tempo, riducendo il rischio di ricadute e favorendo uno stato di "buona salute" a **lungo termine**.

Potenziale aumento della percentuale di successo e riduzione del rischio di ripresa ponderale

Vantaggi della terapia chetogenica sulle comorbidità associate all'obesità

- ✓ Miglior controllo glicometabolico
- ✓ Azione anti-infiammatoria
- ✓ Riduzione del rischio oncologico (colon, mammella, pancreas, fegato)
- ✓ Riduzione della terapia farmacologica
- ✓ Miglioramento della performance fisica e della produttività lavorativa
- ✓ **Mantenimento della massa magra**
- ✓ **Personalizzazione del trattamento (**combinazione con altre strategie nutrizionali/psicoterapiche/farmacologiche/chirurgiche)

GRAZIE DELL'ATTENZIONE!

ONE SIZE DOES NOT FIT ALL!!!!

Uno sguardo al futuro

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