Società Medico Chirurgica di Ferrara dal 1846

Con il Patrocinio

Ordine dei Medici Chirurghi e degli Odontoiatri della provincia di FERRARA





Obesità: oltre il peso
Stili di vita e terapie innovative

Sabato 31 ottobre 2026

Aula Magna Nuovo Arcispedale S. Anna
Cona, Ferrara

VLEKT e obesità: indicazioni e sicurezza

Massimiliano Caprio, MD, PhD
San Raffaele Roma University
IRCCS San Raffaele, Rome, Italy

Disclosures

Prof. Massimiliano Caprio has received funding from the following companies:

For providing educational sessions

- SDM, Therascience, Eli Lilly, Novo Nordisk, Boehringer Ingelheim, Bayer

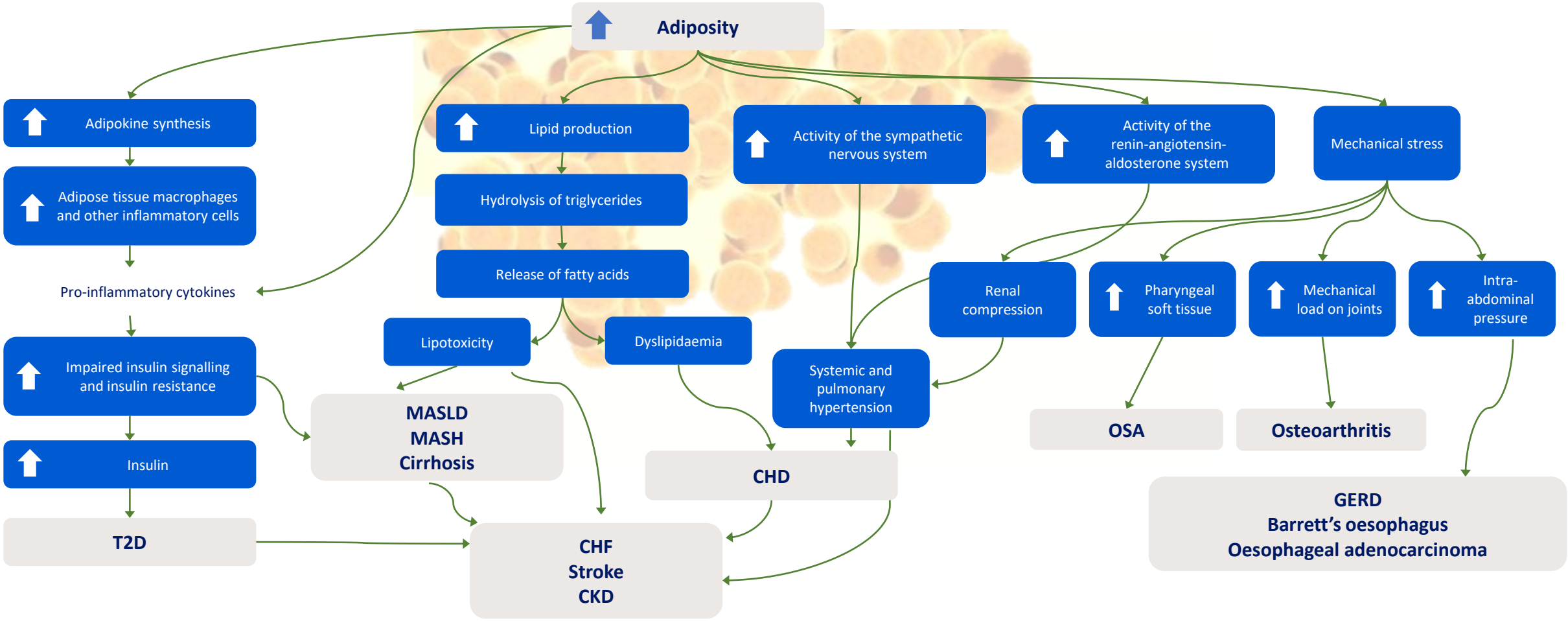
Institutional research grant support or funding for clinical trials

- Bayer, SDM, New Penta, Pharmanutra, Eli Lilly

Institutional Scientific Board and/or consulting

- Eli Lilly, Novo Nordisk, SDM

Excess adiposity impairs health





i'm gonna do this wack ass crash diet vogue printed in the 70s and die

WINE AND EGGS / 3 *days* / *loss*: 5 *lbs* (2.5 *k.*)

Breakfast:	1 egg, hard-boiled 1 glass white wine (dry, preferably Chablis) Black coffee
Lunch:	2 eggs, hard-boiled is best, but poached if necessary 2 glasses white wine Black coffee
Dinner:	5 oz. (150 g.) steak, grilled with black pepper, lemon juice Remainder of white wine (one bottle allowed per day) Black coffee

Available online at www.sciencedirect.com

Nutrition, Metabolism & Cardiovascular Diseases

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

VIEWPOINT

Ketogenic diet for epilepsy and obesity: Is it the same?

A. Tagliabue [a], M. Armeno [b], K.A. Berk [c], M. Guglielmetti [a,*], C. Ferraris [a], J. Olieman [c], E. van der Louw [c]

[a] Ketogenic Metabolic Therapy Laboratory, Department of Public Health Experimental and Forensic Medicine, University of Pavia, Italy
[b] Ketogenic Diet Team Unit, Clinical Nutrition Department, Hospital Pediatría Prof Dr JP Garrahan, Buenos Aires, Argentina
[c] Department of Internal Medicine, Division of Dietetics, Erasmus MC University Medical Centre Rotterdam, Rotterdam, the Netherlands

Received 1 September 2023; received in revised form 9 January 2024; accepted 10 January 2024

ADI E.T.S. Associazione Italiana di Dietetica e Nutrizione Clinica

SINut Società Italiana di Nutraceutica — KETONUT Keto diets and Nutraceuticals — President Prof. Luigi Barrea

VERY LOW ENERGY KETOGENIC THERAPY (VLEKT)

The term "ketogenic diet" (KD) is used for a wide variety of diets with diverse indications ranging from obesity to neurological diseases, as if it was the same diet.

This **terminology is confusing** for patients and the medical and scientific community.

The term "ketogenic" diet implies a dietary regimen characterized by increased levels of circulating ketone bodies that should be measured in blood (beta-hydroxybutyrate), urine (acetoacetate) or breath (acetone) to verify the "ketogenic metabolic condition"

Table 1 Different ketogenic dietary approaches in epilepsy/neurological diseases and obesity treatment.

Diet description (abbreviation)	Carbohydrates	Lipids	Protein	Energy	*Reported Blood Ketone Levels (β-hydroxybutyrate)*	Prevailing use according to literature (ref)
Classical Ketogenic Diet (CKD) [2,5,23]	3–15 % energy	70–90 % energy	According to Dietary Reference Values for age range	According to energy requirements	>1.5 and up to 5 mmol/L in children [28,45,46]	Seizure control, brain energy substrate i.e. epilepsy, GLUT1-DS and other neurological diseases [2,5,23]
Medium Chain Triglycerides Ketogenic Diet (MCT-KD) [5]	20 % energy	10–25 % (infants) 40–60 % (adults)	According to Dietary Reference Values for age range	According to energy requirements	>1.5 and up to 5 mmol/L in children [28,45,46]	Seizure control, brain energy substrate i.e. epilepsy and other neurological diseases [2,5,23,47]
Modified Atkins Diet (MAD) [5]	10 g in children 15 g/day in adolescents 20 g/day in adults	Not measured, fat sources are encouraged	Ad libitum	According to energy requirements; caloric intake needs to be verified during the treatment	Variable depending on food choices and caloric intake	Seizure control, brain energy substrate i.e.epilepsy and other neurological diseases [5,48]
Very Low-Carbohydrate Ketogenic Diet [9]	<20–50 g/day	Not specified	Not specified	Ad libitum	0.5–1.5 mmol/L Ketosis may not occur depending on individual variability [49,50]	Weight loss, glycemic control i.e.obesity diabetes and other endocrine-metabolic diseases [10,51]
Very Low-Calorie Ketogenic Diet *Semi-starvation* [18]	<30–50 g/day	<30–40 g/day	0.8–1.2 g/kg ideal body weight	<700–800 kcal/day	0.5–1.2 mmol/L in the active ketosis phase [24,25]	Weight loss, glycemic control i.e.obesity diabetes and other endocrine-metabolic diseases, migraine [18,52]

GLUT1-DS = GLUT1 Deficiency Syndrome.

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

VLCKD (or **VLEKT** – Very low Energy ketogenic therapy) 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.**

VLEKT 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

European Guidelines for Obesity Management in Adults with a Very Low-Calorie Ketogenic Diet: A Systematic Review and Meta-Analysis

2022

Giovanna Muscogiuri[a, b] Marwan El Ghoch[c] Annamaria Colao[a, b]
Maria Hassapidou[d] Volkan Yumuk[e] Luca Busetto[f] Obesity Management
Task Force (OMTF) of the European Association for the Study of Obesity (EASO)

VLCKD is associated with a significant reduction in body weight and BMI at 1, 2, 4, 6, 12, and 24 months, and appears to be associated with larger weight loss rates compared to other diets with a different energy content (i.e., LCD and VLCD) of the same duration

VLCKD is associated with a significant reduction of WC and FM, and this reduction is significantly larger than those achieved with other weight loss interventions of the same duration

VLCKD was associated with a reduction of the HOMAIR index and an improvement in insulin sensitivity, and this effect was superior to that of other weight loss programs

A significant reduction in TG from baseline was associated with a VLCKD and it was shown to be superior compared to other diets

Table 3 Supplementation with micronutrients (vitamins, mineral salts and omega-3) recommended in active steps

	RDA[a]
Magnesium	240 mg
Potassium	3.9 g
Calcium	1000 mg
Vitamin C	105 mg
Vitamin E	13 mg
Selenium	55 µg
Vitamin A	700 µg
Vitamin B5	30 µg
Vitamin B6	1.3 mg
Vitamin B1	1.2 mg
Vitamin B2	1.6 mg
Folic acid	400 µg
Vitamin B12	2.4 µg
Vitamin D	15 µg
Omega-3	250 mg of EPA-DHA

RDA recommended daily allowance; *PRI* recommended intake of the population; *LARN* reference intake levels of nutrients and energy for the Italian population; *EPA* eicosapentaenoic acid; *DHA* docosahexaenoic acid

[a]RDA according to PRI of LARN adult between 18 and 60 years old

CONSENSUS STATEMENT

Ketogenic nutritional therapy (KeNuT)—a multi-step dietary model with meal replacements for the management of obesity and its related metabolic disorders: a consensus statement from the working group of the Club of the Italian Society of Endocrinology (SIE)—diet therapies in endocrinology and metabolism

L. Barrea[1] · M. Caprio[2,3] · E. Camajani[2,3] · L. Verde[4] · S. Perrini[5] · A. Cignarelli[5] · F. Prodam[6,7] · A. Gambineri[8,9] · A. M. Isidori[10] · A. Colao[11,12,13] · F. Giorgino[5] · G. Aimaretti[6] · G. Muscogiuri[11,12,13]

Why focus on meal replacement in weight management?

- Self Efficacy: sense of confidence about the ability to complete a behaviour

- A large variety of stimuli in a given meal is associated with higher calorie intake!

- Stimulus narrowing: based on concept of sensory specific satiety

A meal replacement tipically «narrows» the stimulus by providing a limited range of flavours, textures and macronutrient within and between eating episodes; therefore, it decreases hedonic drive for food and increases satiety

Weight loss achieved with meal replacement is associated with disease remission and control (Optiwin, Droplet, Direct)

Wingo BC et al. J Nutr Educ Behav 2013; Raynor and Epstein. Psychol Bull 2001

Table 2 Indications and contraindications for VLCKD prescription

INDICAZIONI	CONTROINDICAZIONI
Obesity (BMI ≥ 30.0 kg/m^2)	Pregnancy and breastfeeding
Obesity with one or more comorbidities (T2DM[a], locomotors system disorder, NAFLD)	Childhood[b]
Overweight (BMI = 25.0–29.9 kg/m^2) with abdominal obesity (waist circumference > 102 cm in men and > 88 cm in women)	Rare metabolic disorders (porphyria, carnitine deficiency, carnitine palmitoyltransferase deficiency, carnitine-acylcarnitine translocase deficiency, mitochondrial fatty acid β-oxidation disorders, and pyruvate carboxylase deficiency)
Overweight/obesity, PCOS and hypogonadism	Type 1 diabetes, type 2 diabetes with beta cell failure or concomitant treatment with SGLT2 inhibitors
Weight loss before bariatric surgery or in case of weight regain after bariatric surgery	Organ failure (liver, kidney, or heart NYHA III e IV)
Overweight/obesity and neurological/neurodegenerative disorders (Parkinson, Alzheimer, amyotrophic lateral sclerosis, epilepsy)	Recent myocardial infarction or cerebrovascular stroke
Overweight/obesity and pulmonary dysfunctions (OSAS, COPD, OHS, asthma)	Severe psychiatric disorders
Overweight/obesity and psoriasis	Severe eating disorders
	Alcohol and substance abuse

T2DM type 2 diabetes mellitus; *NAFLD* non-alcoholic fatty liver disease; *OSAS* obstructive sleep apnoea syndrome; *PCOS* polycystic ovary syndrome; *OSAS* obstructive sleep apnoea syndrome; *COPD* chronic obstructive pulmonary diseases; *OHS* obesity hypoventilation syndrome

[a]Use of sodium/glucose cotransporter 2 (SGLT2) inhibitors or insulin therapy is forbidden

[b]During childhood VLCKD could be prescribed in particular condition (epilepsy, high insulin resistance)

Patikorn et al. BMC Medicine (2023) 21:196
https://doi.org/10.1186/s12916-023-02874-y

BMC Medicine

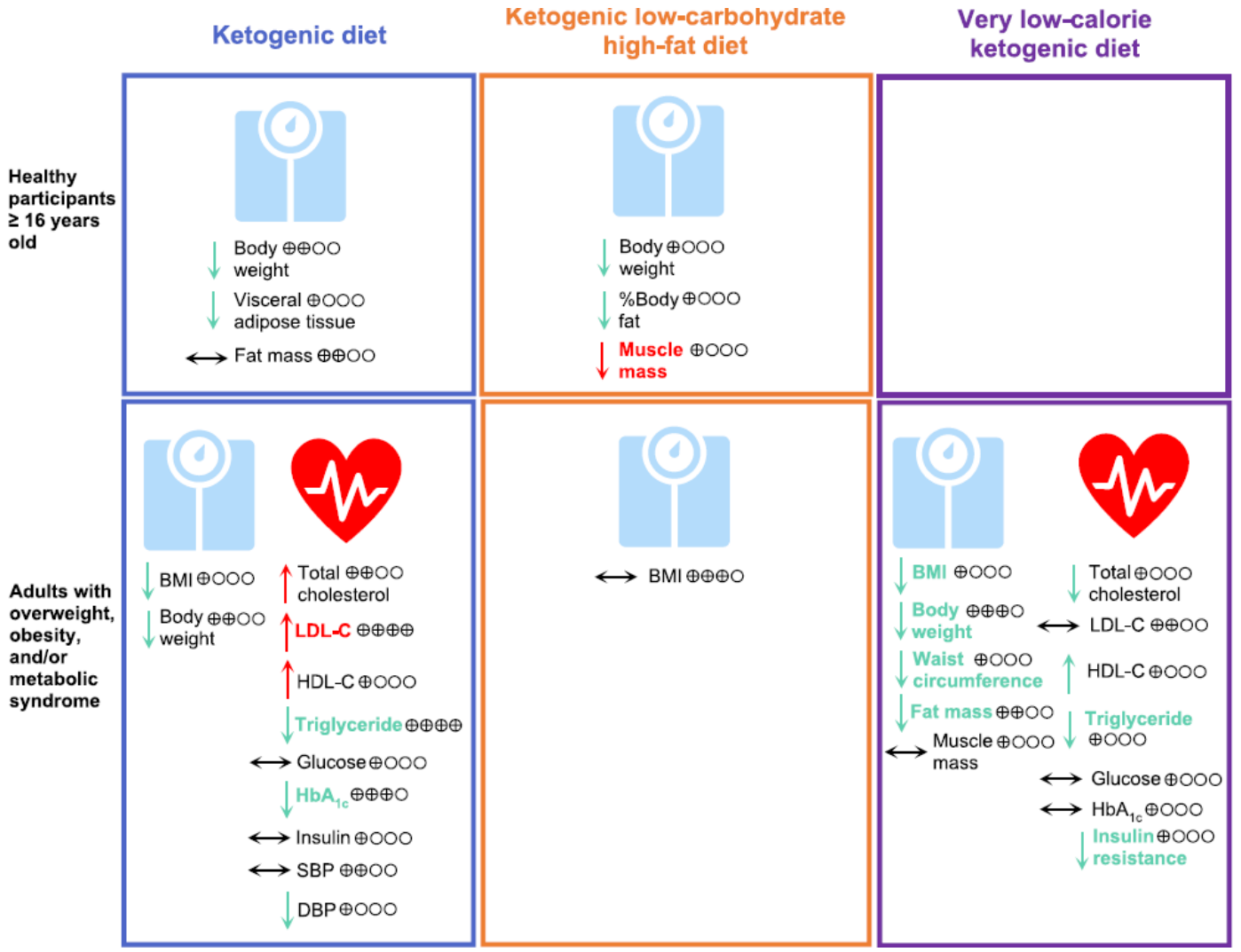
RESEARCH ARTICLE Open Access

Effects of ketogenic diet on health outcomes: an umbrella review of meta-analyses of randomized clinical trials

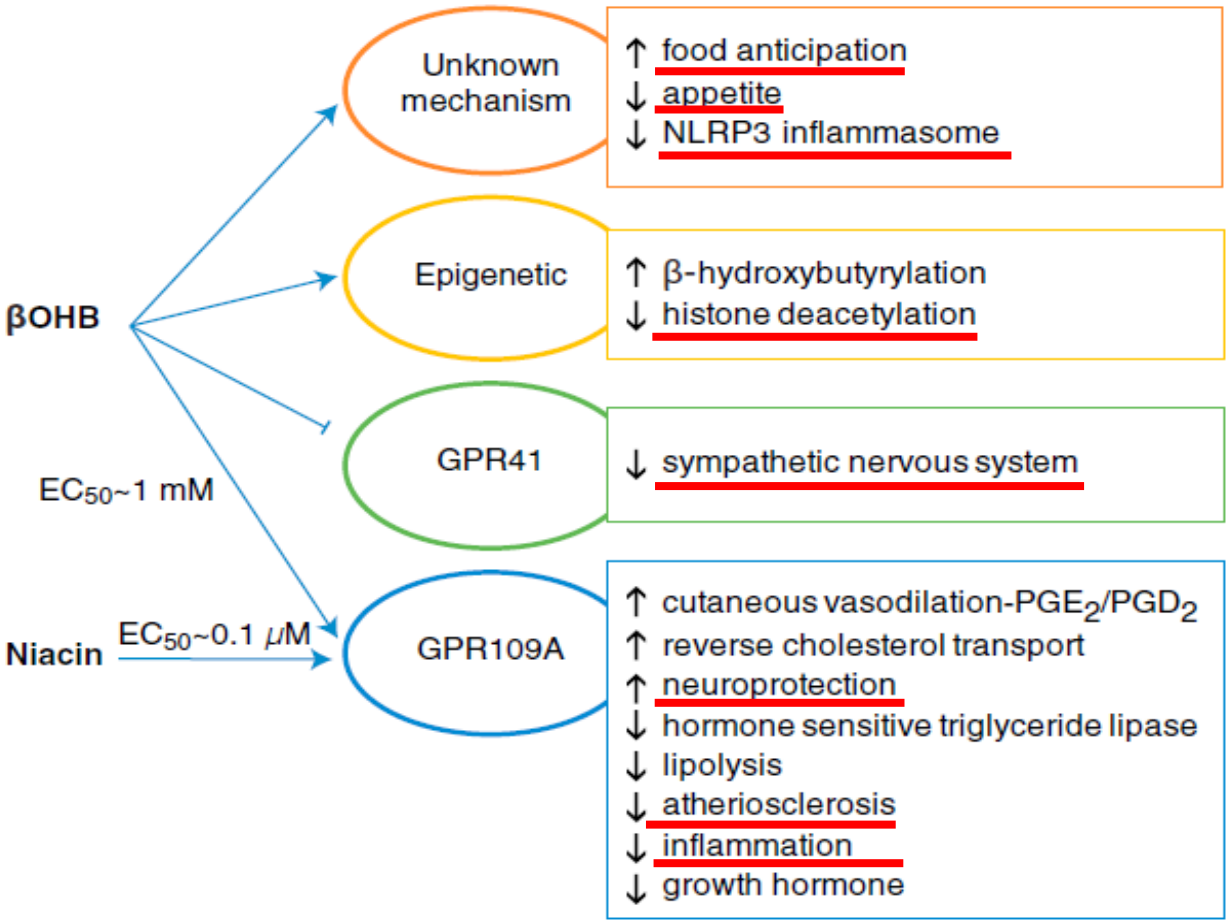
Chanthawat Patikorn[1,2], Pantakarn Saidoung[1], Tuan Pham[3], Pochamana Phisalprapa[4], Yeong Yeh Lee[5], Krista A. Varady[6], Sajesh K. Veettil[1*] and Nathorn Chaiyakunapruk[1,7*]

17 meta-analyses comprising 68 RCTs (median [interquartile range, IQR] sample size of 42 [20–104] participants and **follow-up period of 13 [8–36] weeks**) and 115 unique associations

Associations of Types of Ketogenic Diet with Health Outcomes



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

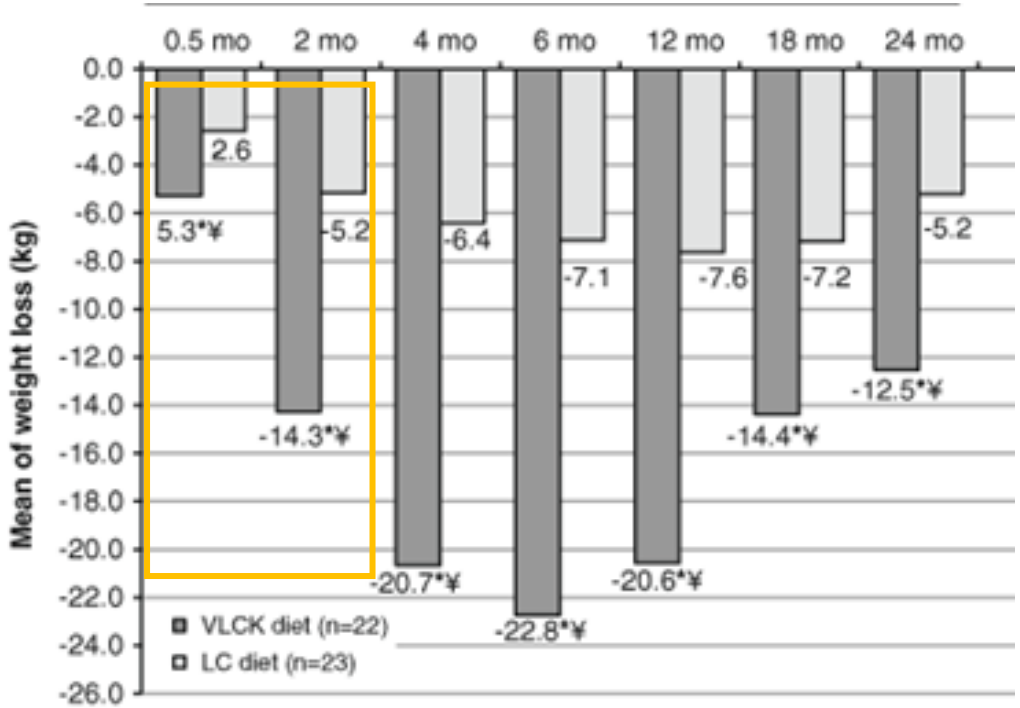
Applicazioni in diversi contesti clinici!

Puchalska P and Crawford PA, Cell Metabolism 2017

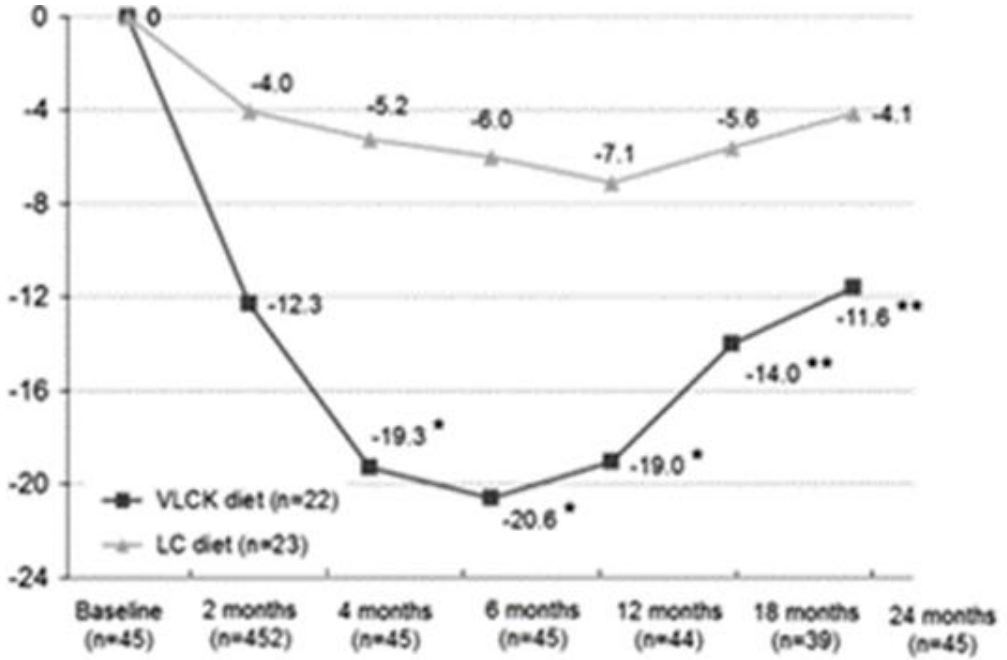
Obesity treatment by VLEKT at two years

Ketosis

Weight loss



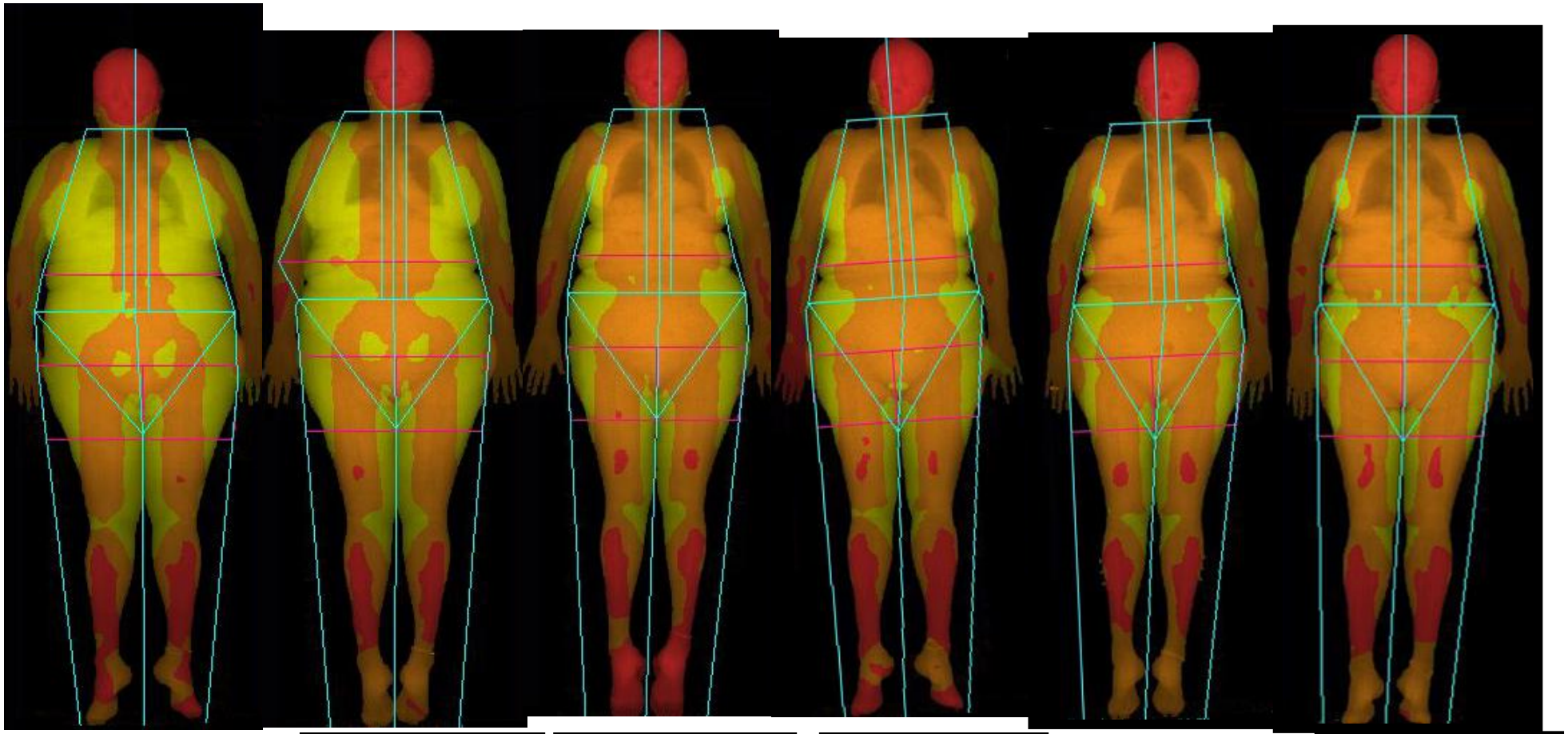
Change in waist



Moreno B et al. Endocrine 2016

DEXA *scan*

Courtesy of Felipe Casanueva



WEIGHT- 100 BMI - 35	WEIGHT- 87.1 BMI - 30.5	WEIGHT- 78.7 BMI - 27.5	WEIGHT- 75.3 BMI - 26.3	WEIGHT- 72.5 BMI - 25.3	WEIGHT- 71.7 BMI - 25

nutrients

MDPI

Article

Impact of a Very Low-Calorie Ketogenic Diet (VLCKD) on Changes in Handgrip Strength in Women with Obesity

Luigi Barrea [1,2,*,†], Giulia de Alteriis [2,3,†], Giovanna Muscogiuri [2,3,4,†], Claudia Vetrani [2,3], Ludovica Verde [3], Elisabetta Camajani [5,6], Sara Aprano [2,3], Annamaria Colao [2,3,4] and Silvia Savastano [2,3]

A total of 247 women with obesity, aged 35.4 ± 10.5 years, met the inclusion/exclusion criteria and were included in the analyses.

All subjects were evaluated at baseline and after 45 days of the active stage of the VLEKT

Diet composition:

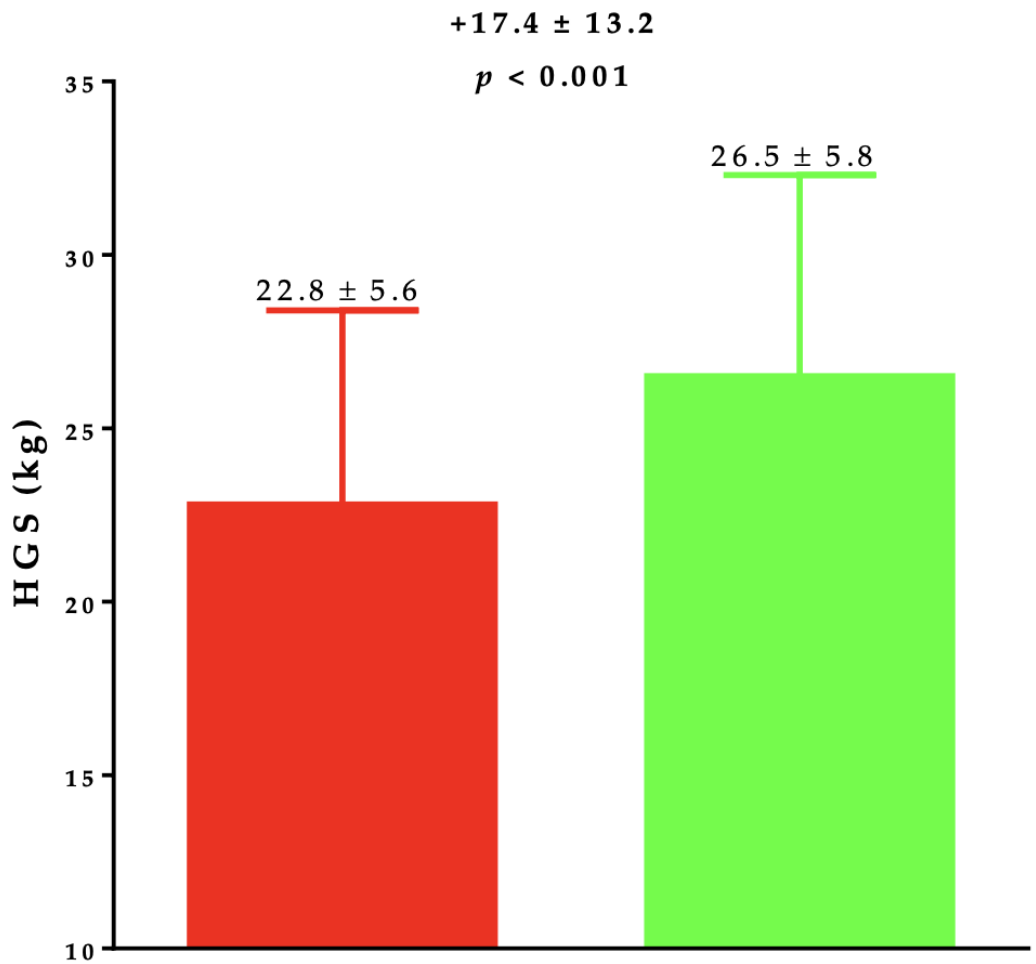
total energy intake was <800 kcal/day

and it was provided by 13% carbohydrates (<30 g/day), 43% protein (1.3 g/kg ideal body weight), and 44% fat.

During the VLEKT, replacement meals with high biological value were used, with protein coming from whey, soy, eggs, and peas.

According to international recommendations, supplementation of B-complex vitamins; vitamins C and E; minerals, including potassium, sodium, magnesium, and calcium; and omega-3 fatty acids at the same dosage was planned to maintain the physiological acid/base balance.

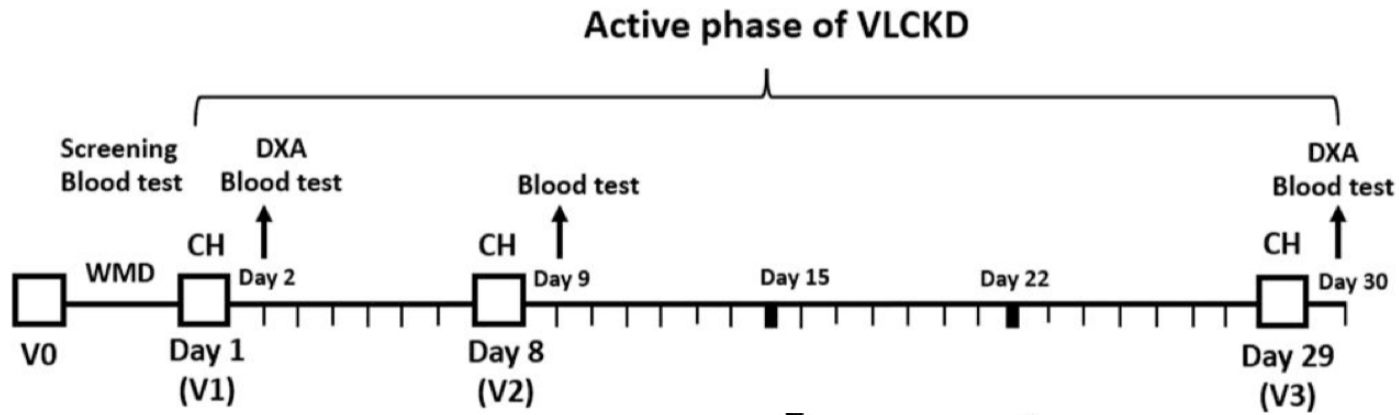
Parameters	Participant Baseline Mean ± SD or Number (%) $n = 247$	Participant 45th Day of VLCKD Mean ± SD or Number (%) $n = 247$	Δ%	* p-Value
Weight (kg)				**<0.001**
BMI (kg/m^2)				**<0.001**
Overweight (n, %)				^{2} = 48.54, p **< 0.001**
Grade I obesity (n, %)				^{2} = 0.22, p = 0.641
Grade II obesity (n, %)				^{2} = 2.29, p = 0.130
Grade III obesity (n, %)				^{2} = 15.07, p **< 0.001**
WC (cm)				**<0.001**
WC < 88 cm				χ^2 = 12.30, p **< 0.001**
WC ≥ 88 cm				
HGS (kg)				χ^2 = 16.53, p **< 0.001**
<16 kg				
>16 kg				
Physical Activity				χ^2 = 0.00, p = 0.922
Yes				
No				
BIA parameters				0.129
R (Ω)				**<0.001**
Xc (Ω)				**<0.001**
FM (kg)				**0.001**
FFM (kg)				**<0.001**
hs-CRP levels (mg/L)				

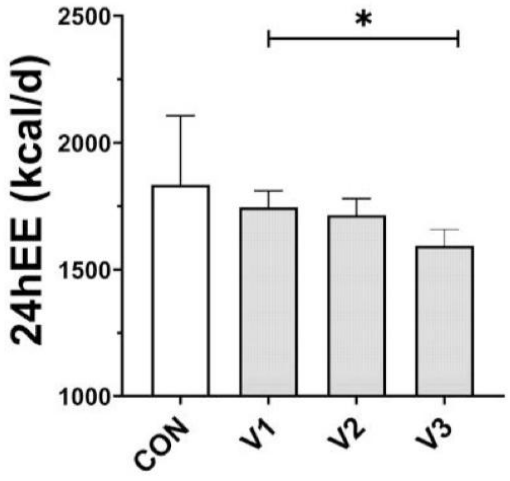


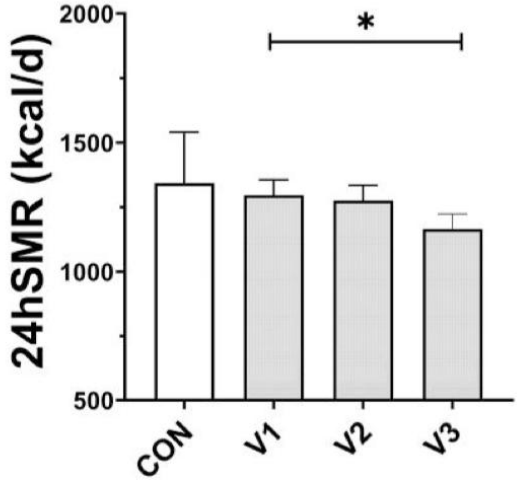
The Journal of Clinical Endocrinology & Metabolism, 2025, **110**, e4158–e4168
https://doi.org/10.1210/clinem/dgaf196
Advance access publication 2 April 2025
Clinical Research Article

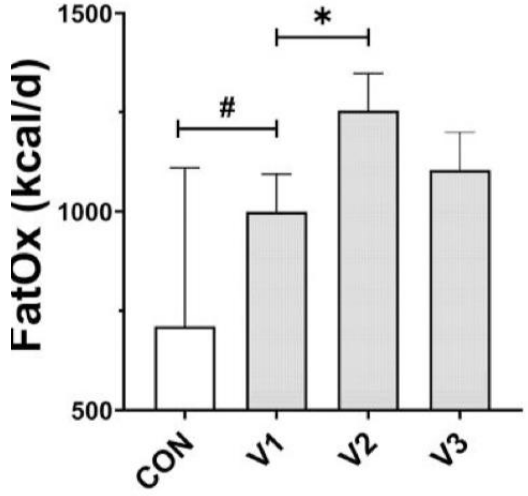
Effects of 1-Month Very-Low-Calorie Ketogenic Diet on 24-Hour Energy Metabolism and Body Composition in Women With Obesity

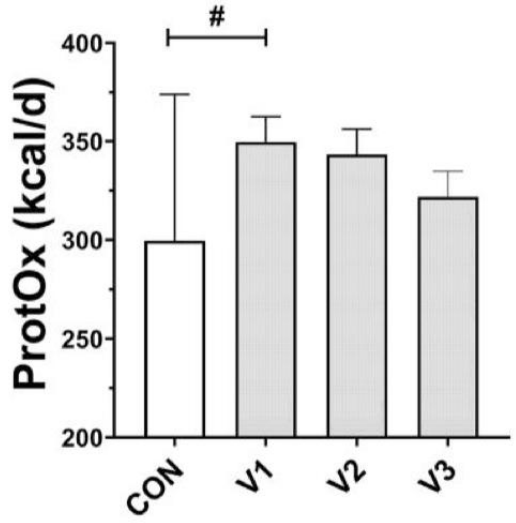
Alessio Basolo,[1] Paolo Piaggi,[2] Valentina Angeli,[1] Paola Fierabracci,[1] Chiara Bologna,[1] Edda Vignali,[3] Daniela Troiani,[1] Roberta Jaccheri,[1] Caterina Pelosini,[4] Melania Paoli,[4] Guido Salvetti,[1] Luca Chiovato,[5] Jonathan Krakoff,[6] Alberto Landi,[2] and Ferruccio Santini[1]







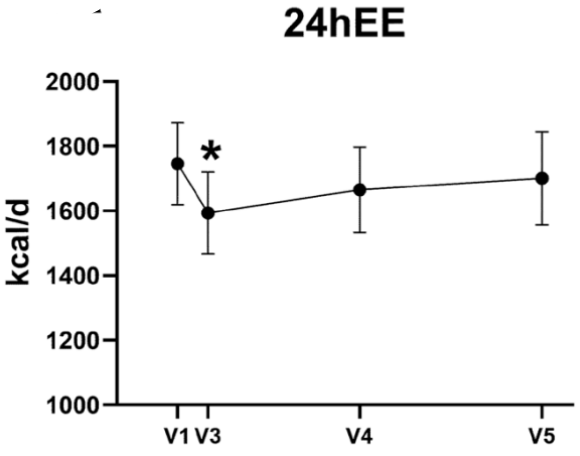


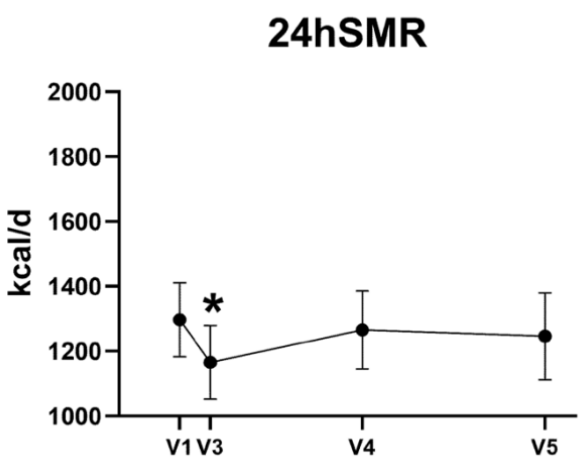


Six- and Twelve-Month Changes in Body Composition and 24-h Energy Expenditure After a Very Low-Calorie Ketogenic Diet

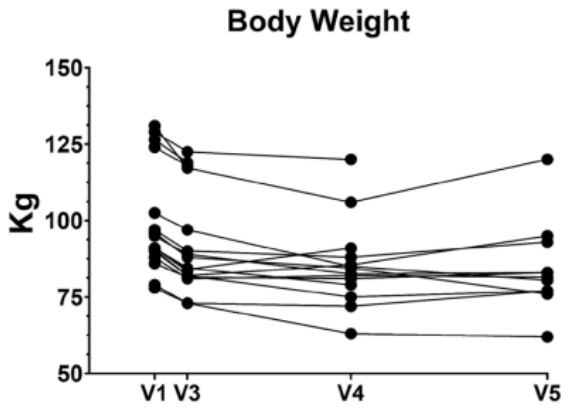
Alessio Basolo[1] | Paolo Piaggi[2] | Valentina Angeli[1] | Paola Fierabracci[1] | Chiara Bologna[1] | Giordano Paolucci[1] | Guido Salvetti[1] | Luca Chiovato[3] | Jonathan Krakoff[4] | Alberto Landi[2] | Ferruccio Santini[1]

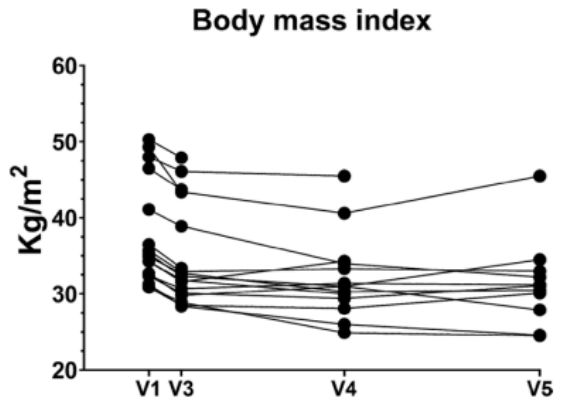
[1]Obesity and Lipodystrophy Center, Endocrinology Unit 1, University Hospital of Pisa, Pisa, Italy | [2]Department of Information Engineering, Uni of Pisa, Pisa, Italy | [3]Istituti Clinici Scientifici Maugeri IRCCS, Pavia, PV, Italy | [4]Obesity and Diabetes Clinical Research Section, National Instit Diabetes and Digestive and Kidney Diseases, NIH, Phoenix, Arizona, USA

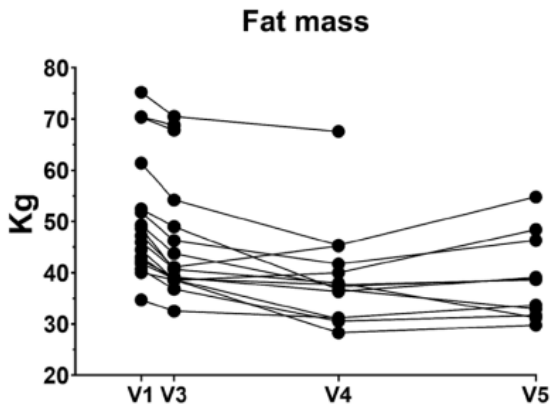


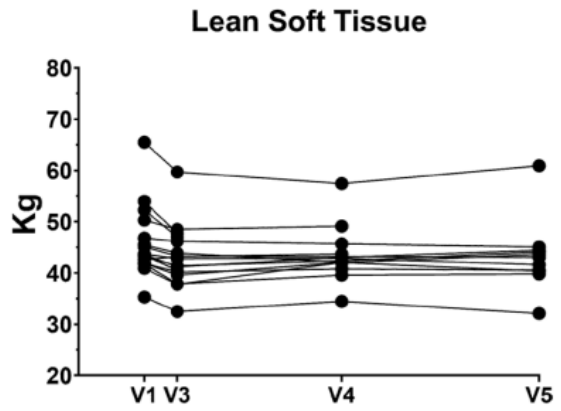


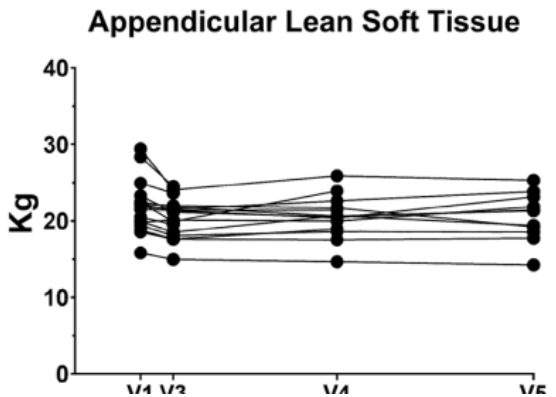
The metabolic adaptation observed during the active VLCKD phase, characterized by marked caloric restriction and negative energy balance, was no longer evident after the refeeding phase

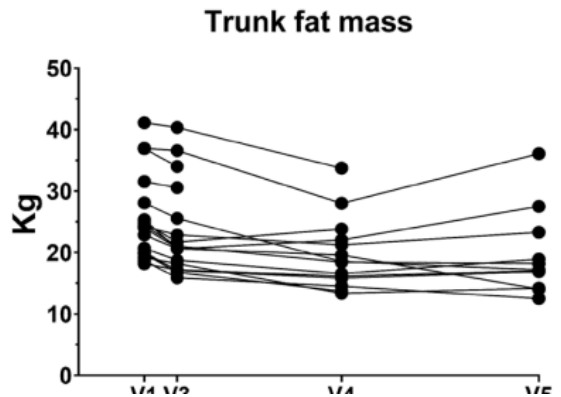












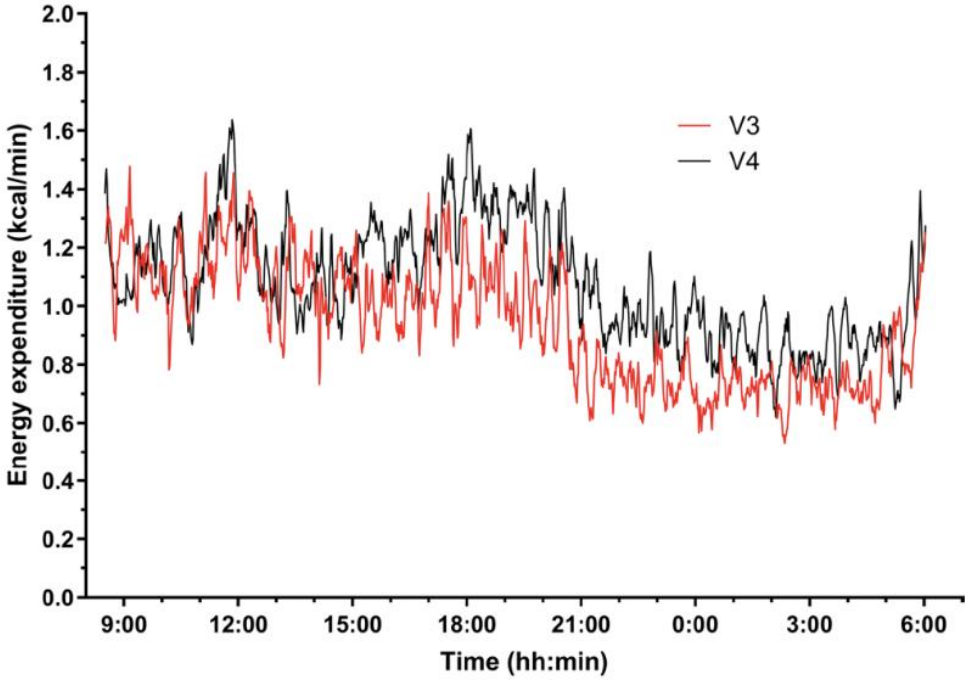
Six- and Twelve-Month Changes in Body Composition and 24-h Energy Expenditure After a Very Low-Calorie Ketogenic Diet

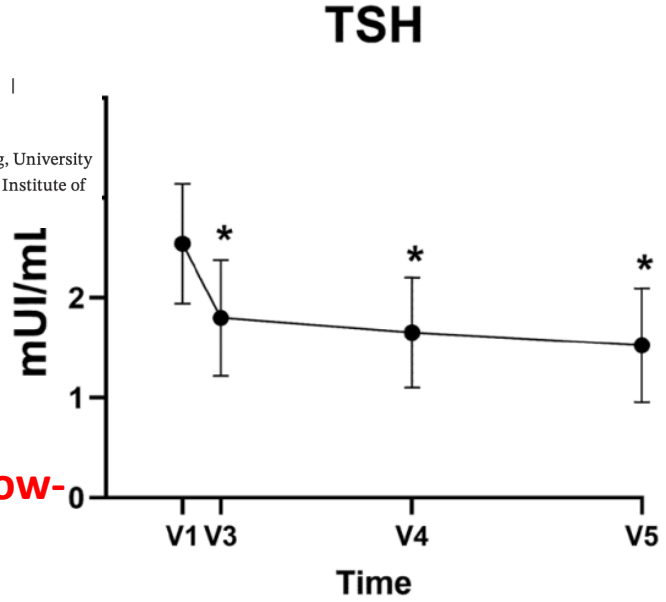
Alessio Basolo[1] | Paolo Piaggi[2] | Valentina Angeli[1] | Paola Fierabracci[1] | Chiara Bologna[1] | Giordano Paolucci[1] | Guido Salvetti[1] | Luca Chiovato[3] | Jonathan Krakoff[4] | Alberto Landi[2] | Ferruccio Santini[1]

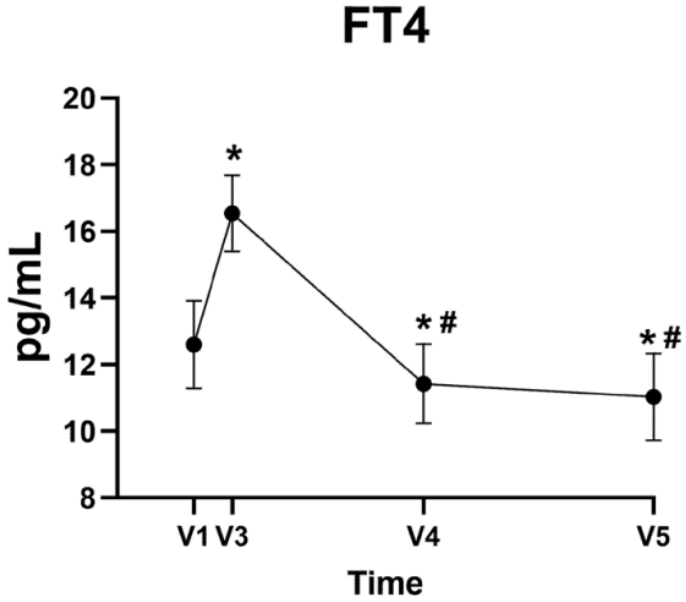
[1]Obesity and Lipodystrophy Center, Endocrinology Unit 1, University Hospital of Pisa, Pisa, Italy | [2]Department of Information Engineering, University of Pisa, Pisa, Italy | [3]Istituti Clinici Scientifici Maugeri IRCCS, Pavia, PV, Italy | [4]Obesity and Diabetes Clinical Research Section, National Institute of Diabetes and Digestive and Kidney Diseases, NIH, Phoenix, Arizona, USA

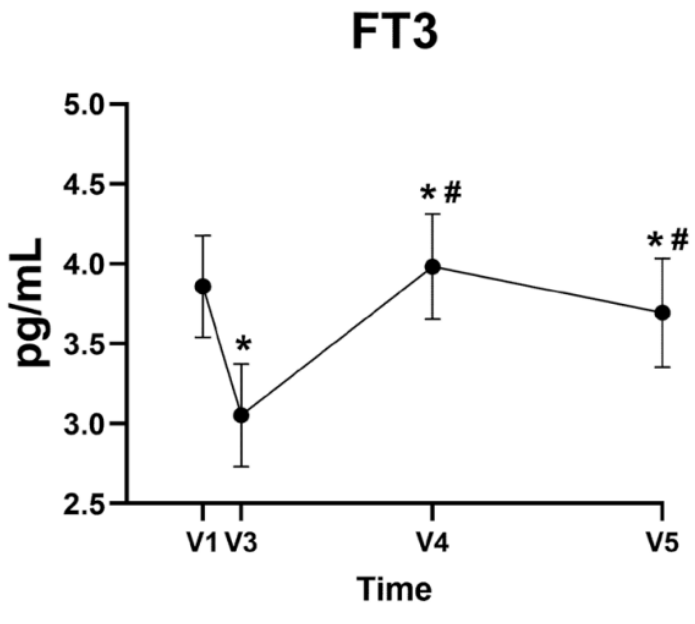
The early reduction in energy expenditure is not sustained after dietary reintroduction

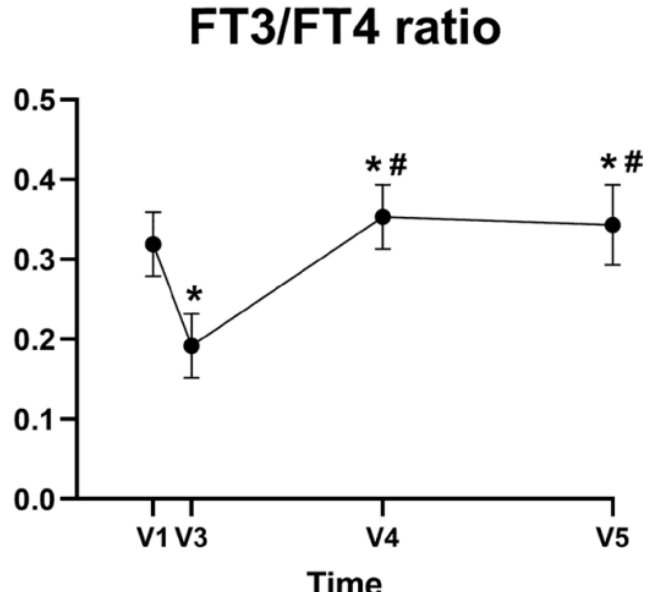
VLEKT has a beneficial role in the control of body weight, when implemented within a structured follow-up program









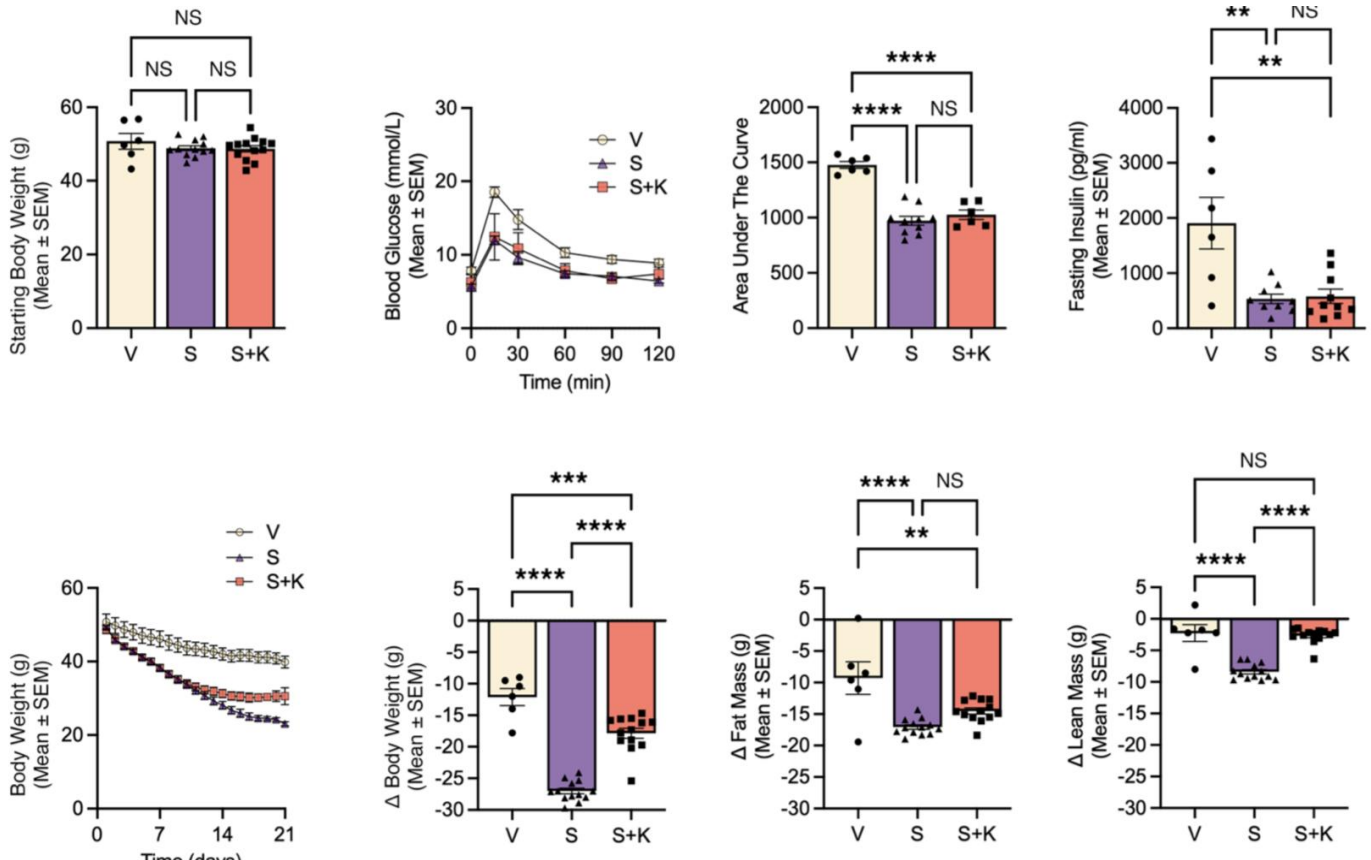


JCI insight

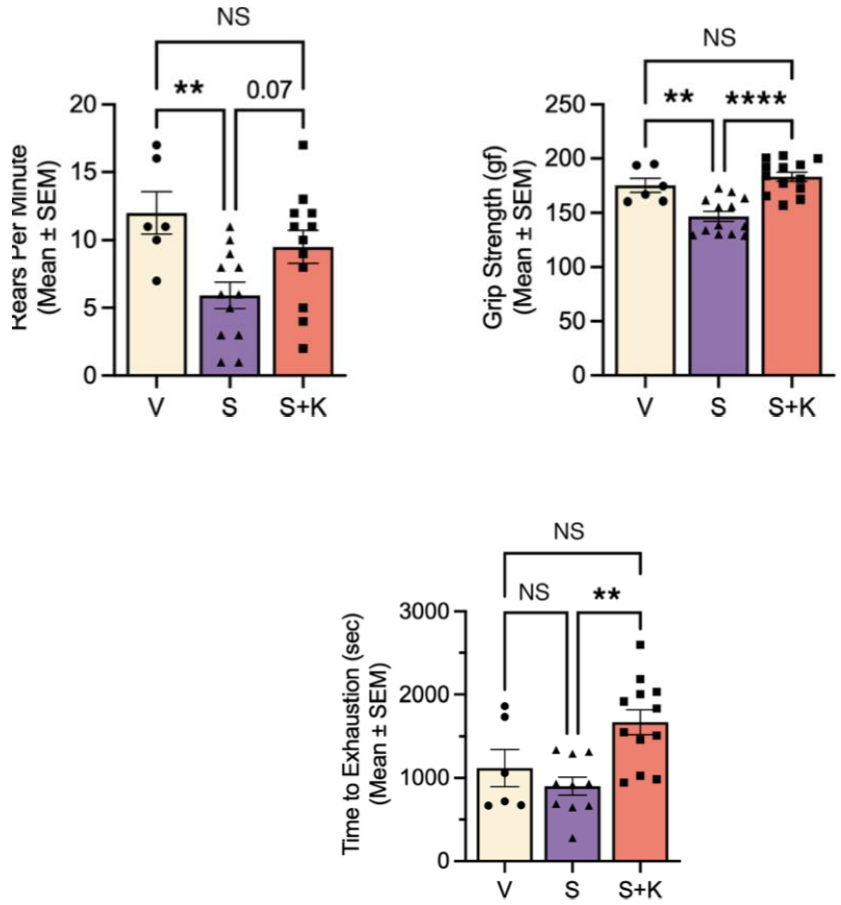
Semaglutide-induced loss of skeletal muscle mass is blunted by co-administration of ketone esters

Yasser Abuetabh, Mya A. Schmidt, Masaaki Naganuma, Ramana Vaka, Mahmoud A. El-Ghiaty, Shelly Braun, Ethan A. Kwan, Matthieu C.P. Zolondek, Darius Sahid, Laibah Khan, Rajat K. Shandal, Ashley L. Trudeau, Yaning Li, Sufyan O. Malik, Qiuyu Sun, Danica K. Roth, Daniela Y. Morales-Llamas, Jody L. Levasseur, Mourad Ferdaoussi, Richard P. Fahlman, Jason R.B. Dyck

Ketone ester co-administration prevents semaglutide-induced lean mass loss without impacting fat loss.



Ketone ester co-administration with semaglutide treatment prevents functional muscular decline and enhances physical performance.

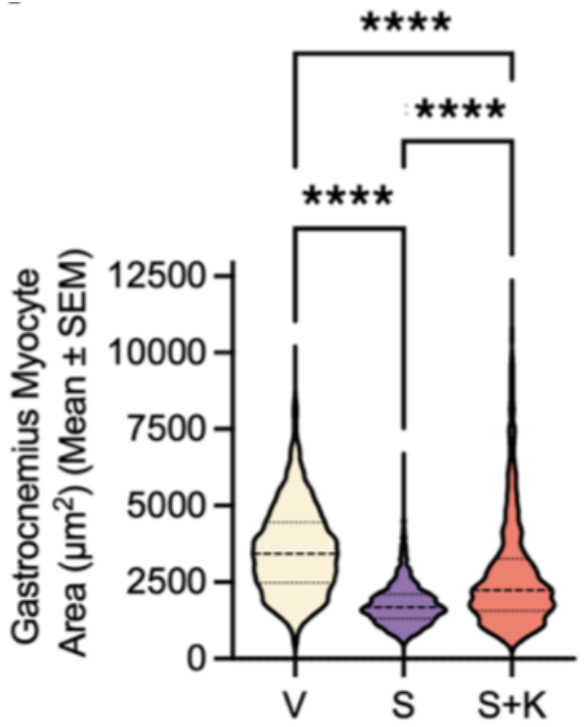


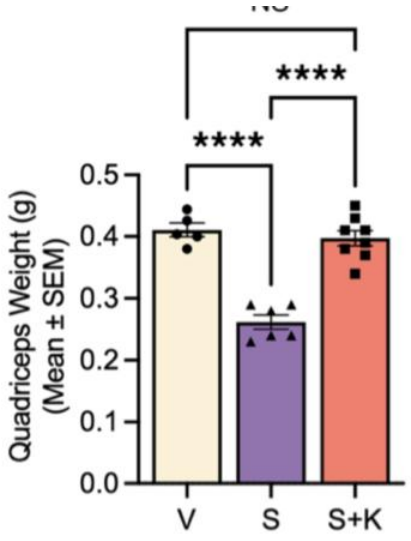
JCI insight

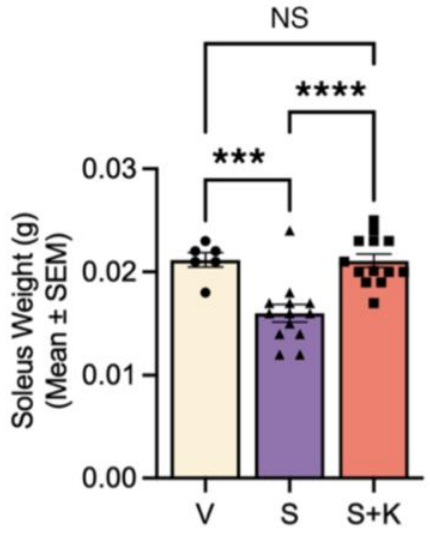
Semaglutide-induced loss of skeletal muscle mass is blunted by co-administration of ketone esters

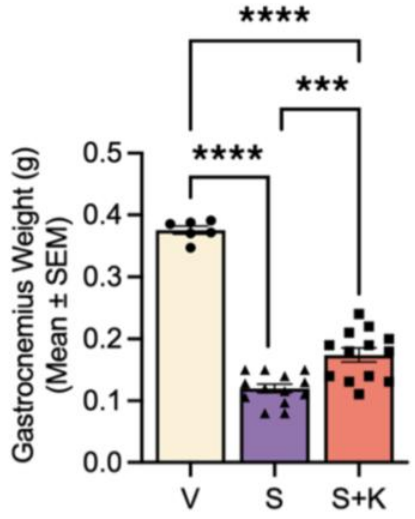
Yasser Abuetabh, Mya A. Schmidt, Masaaki Naganuma, Ramana Vaka, Mahmoud A. El-Ghiaty, Shelly Braun, Ethan A. Kwan, Matthieu C.P. Zolondek, Darius Sahid, Laibah Khan, Rajat K. Shandal, Ashley L. Trudeau, Yaning Li, Sufyan O. Malik, Qiuyu Sun, Danica K. Roth, Daniela Y. Morales-Llamas, Jody L. Levasseur, Mourad Ferdaoussi, Richard P. Fahlman, Jason R.B. Dyck

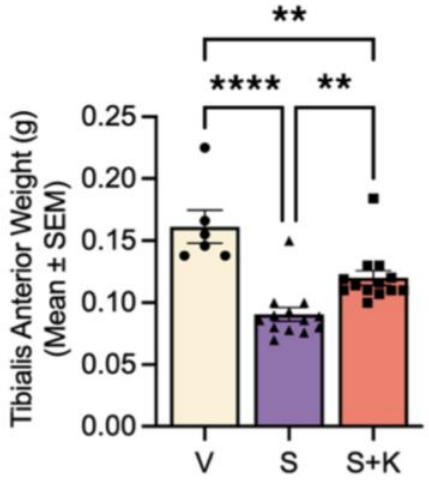
Reductions in skeletal muscle mass induced by semaglutide are blunted by ketone ester co-therapy







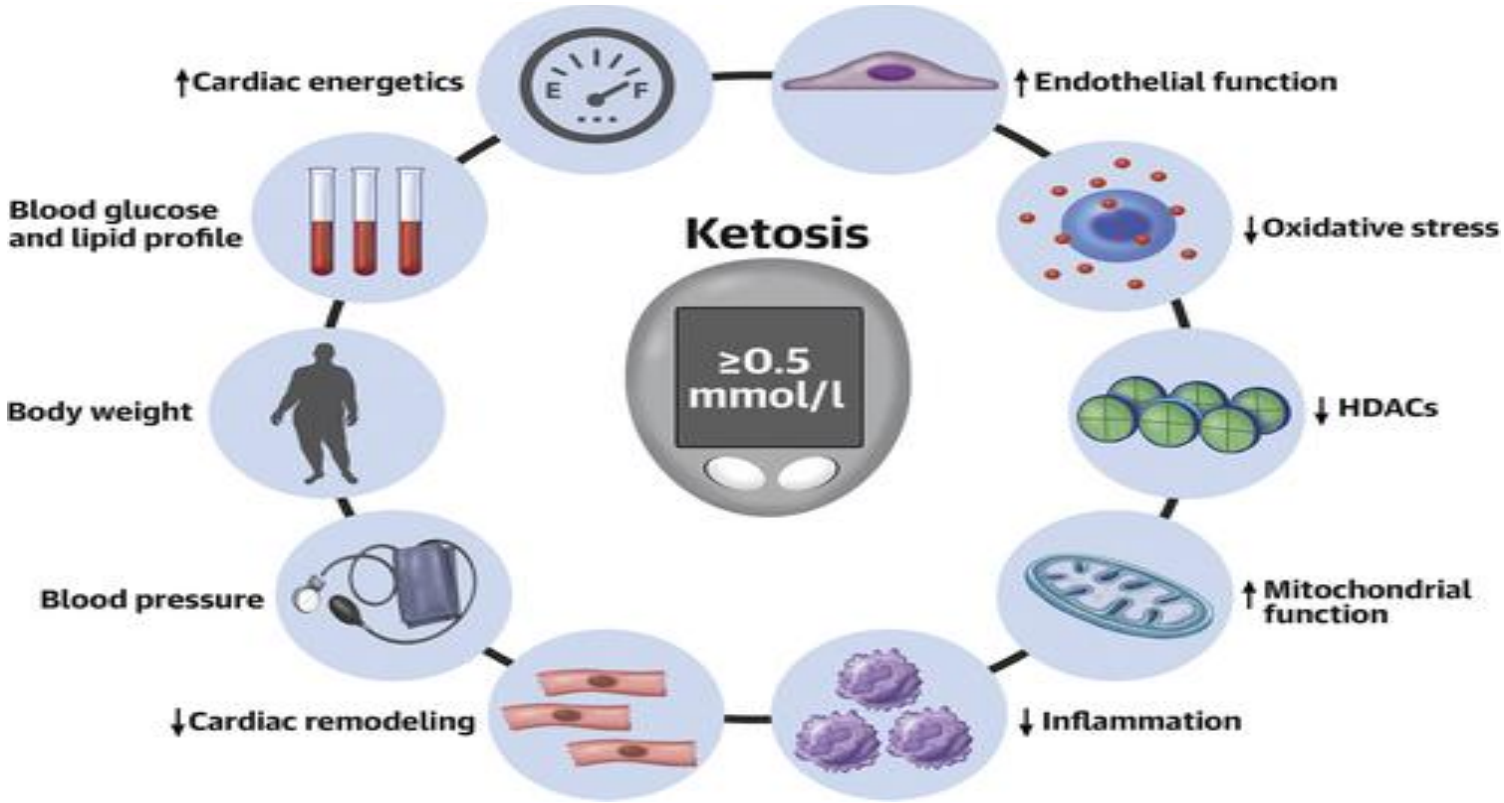




Therapeutic Potential of Ketone Bodies for Patients With Cardiovascular Disease

JACC Focus Seminar

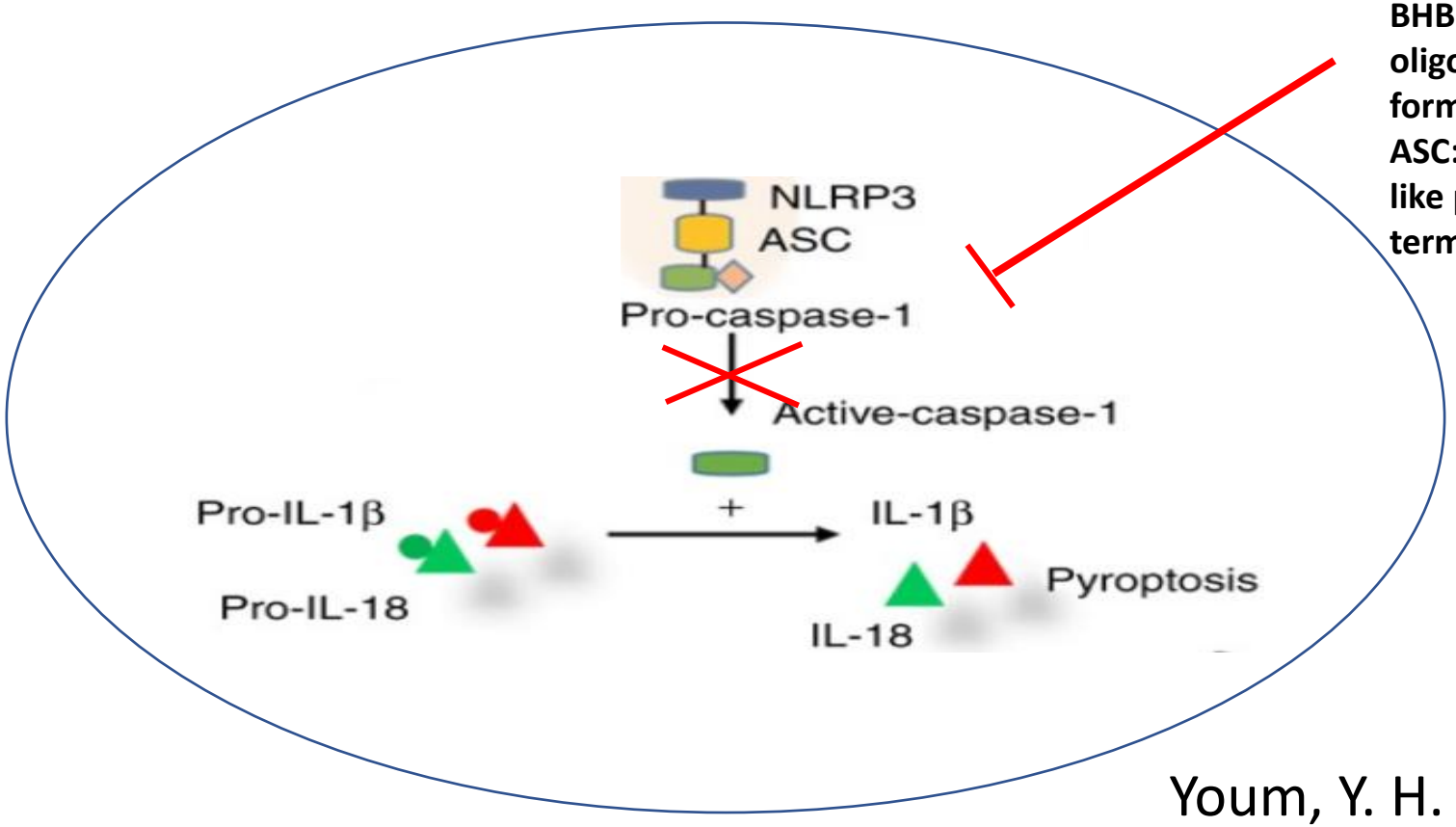
Salva R. Yurista, MD, PhD,[a] Cher-Rin Chong, PhD,[b,c] Juan J. Badimon, PhD,[d] Daniel P. Kelly, MD,[e] Rudolf A. de Boer, MD, PhD,[a] B. Daan Westenbrink, MD, PhD[a]



Salva R. Yurista et al. *J Am Coll Cardiol* 2021

NLRP3 inflammasome: a critical driver of adipose tissue inflammation during obesity

The ketone body β-hydroxybutyrate (BHB) inhibits NLRP3 inflammasome activation thereby linking innate immunity and metabolism



BHB prevents K efflux, reduces ASC oligomerization and speck formation
ASC: apoptosis-associated speck-like protein containing a carboxy-terminal CARD

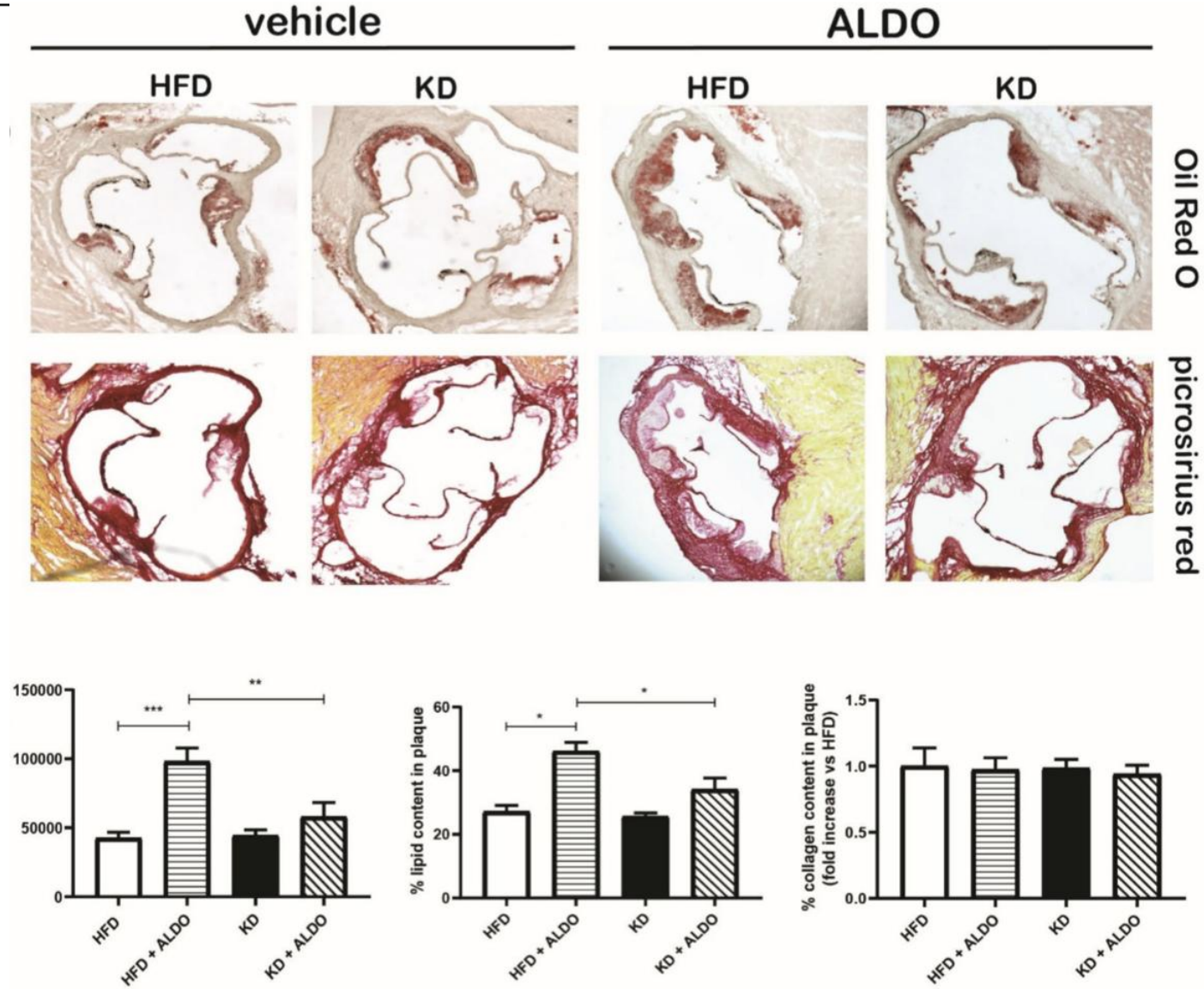
Youm, Y. H. et al. *Nat. Med.* **21**, 263–269 (2015)

Journal of Endocrinological Investigation
https://doi.org/10.1007/s40618-025-02740-z

RAPID COMMUNICATION

Protective effects of ketogenic diet on aldosterone-induced atherosclerosis in ApoE−/− mice

Andrea Armani[1,2] · Vincenzo Marzolla[2] · Caterina Mammi[2] · Laura Vitiello[1,3] · Eleonora Bellucci[1,2] · Alessandra Feraco[1,2] · Stefania Gorini[1,2] · Massimiliano Caprio[1,2]

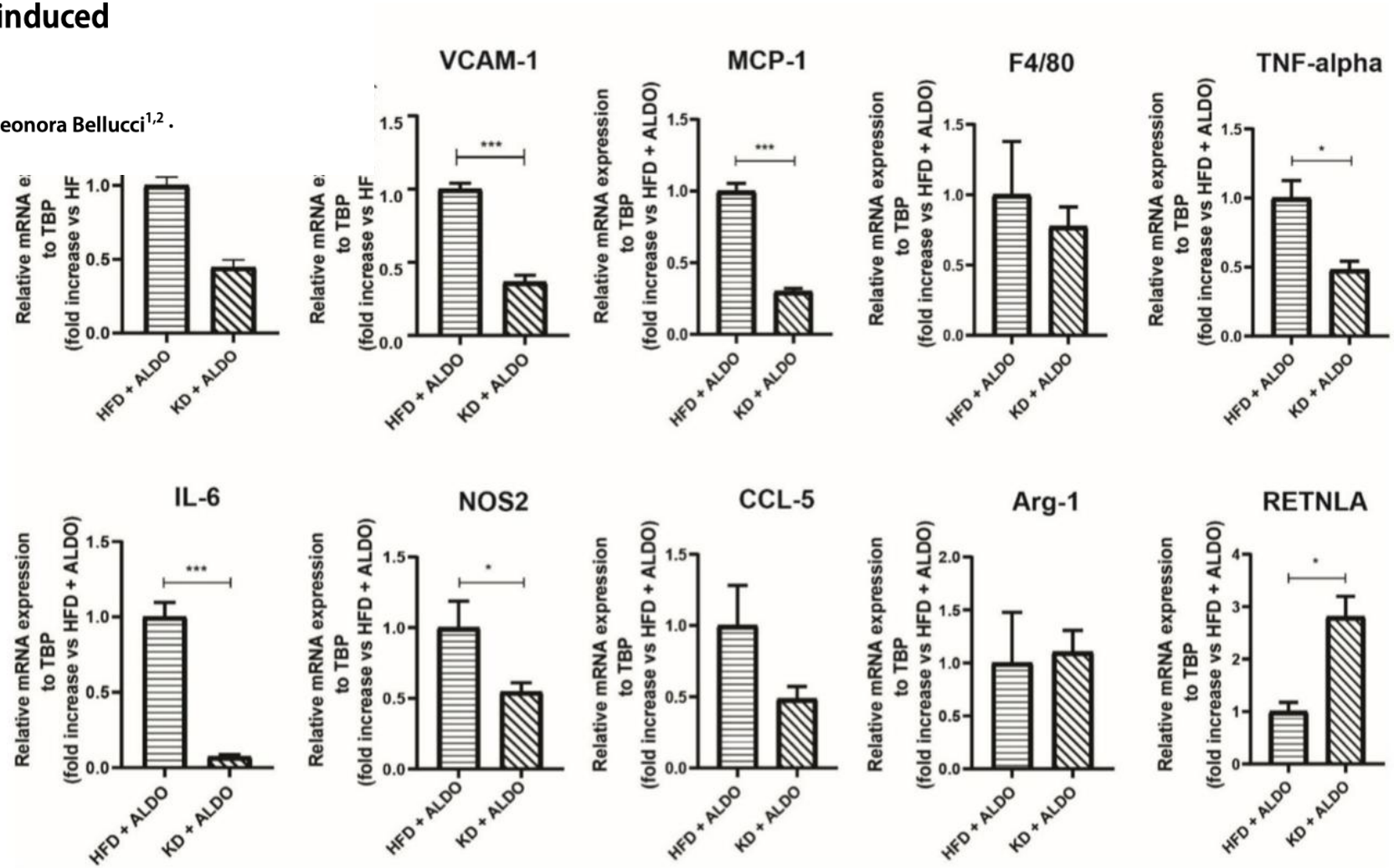


Journal of Endocrinological Investigation
https://doi.org/10.1007/s40618-025-02740-z

RAPID COMMUNICATION

Protective effects of ketogenic diet on aldosterone-induced atherosclerosis in ApoE−/− mice

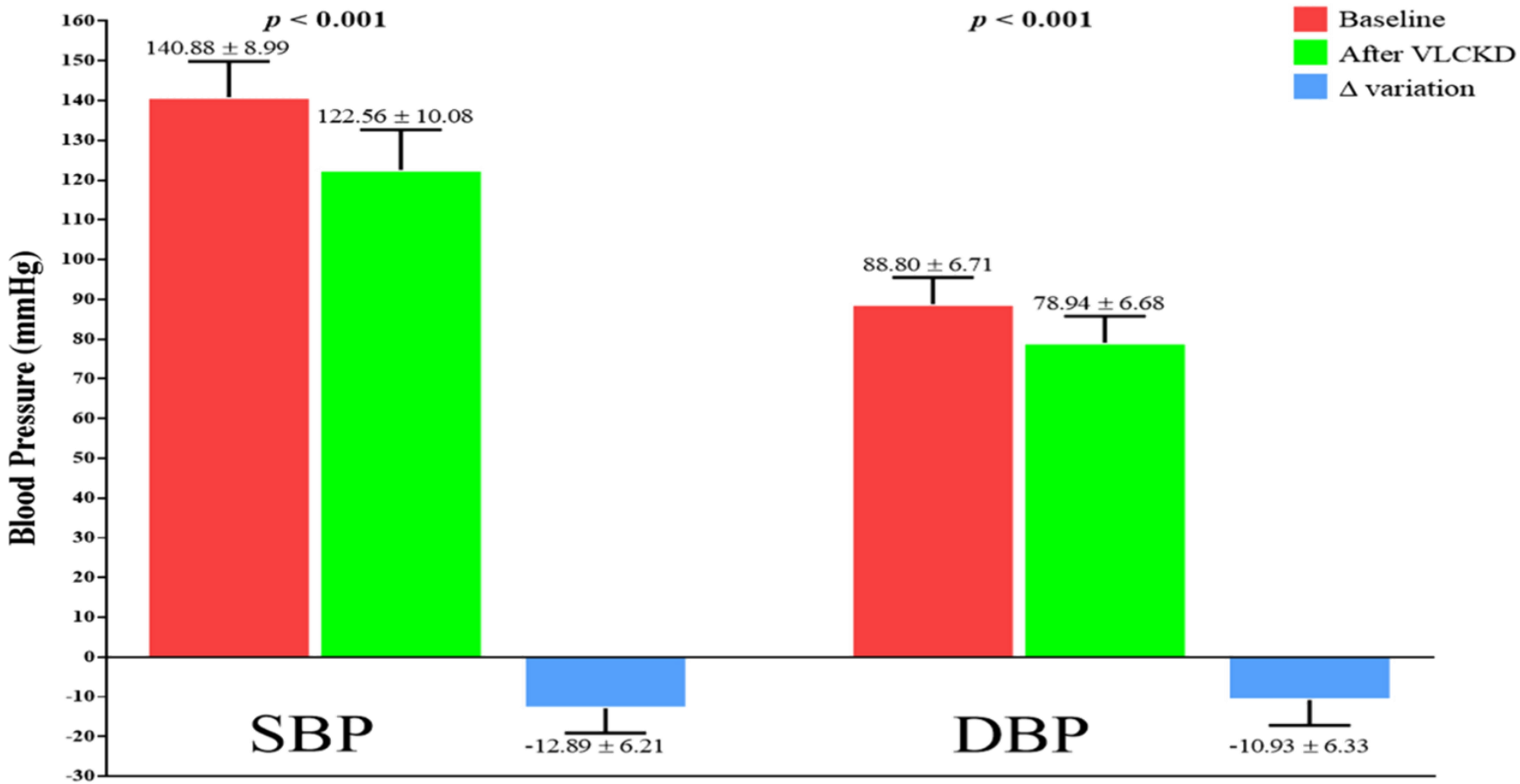
Andrea Armani[1,2] · Vincenzo Marzolla[2] · Caterina Mammi[2] · Laura Vitiello[1,3] · Eleonora Bellucci[1,2] · Alessandra Feraco[1,2] · Stefania Gorini[1,2] · Massimiliano Caprio[1,2]



Research | Open Access | Published: 17 February 2023

Very low-calorie ketogenic diet (VLCKD): an antihypertensive nutritional approach

Luigi Barrea, Ludovica Verde, Pasquale Santangeli, Stefania Lucà, Annamaria Docimo, Silvia Savastano, Annamaria Colao & Giovanna Muscogiuri



Meccanismi coinvolti nella regolazione glicometabolica in corso di VLEKT

- Perdita di grasso addominale
- Restrizione calorica
- Ridottissimo contenuto di carboidrati
- Composizione specifica della dieta
- Ruolo specifico dei corpi chetonici
- Inibizione endogena DPP4

VLCKD, insulin resistance and type 2 diabetes

Recommendations

- VLCKD should be considered to obtain an early efficacy on glycemic control, particularly in obese patients with short duration of the disease (1 ØØØO).
- VLCKD should be considered to reduce the use of glucose-lowering agents, including insulin (1 ØØØO).

In obese non-diabetic patients, the effect of VLCKD is powerful in reducing plasma insulin levels; consequently, HOMA-IR and HOMA-beta, which represent markers of insulin resistance and beta-cell function, respectively, display significant improvements after this type of dietetic intervention

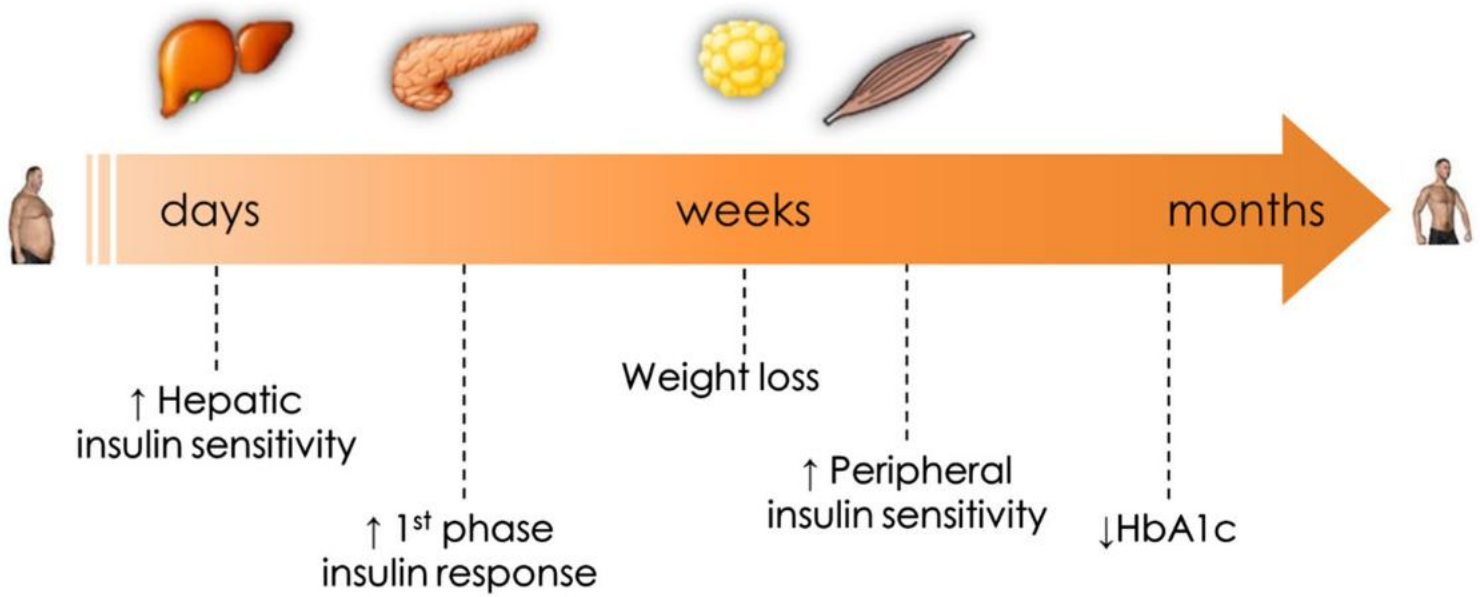


Fig. 2 Effects of VLCKD on glucose homeostasis and metabolic parameters in obese subjects with or without type 2 diabetes

Caprio M et al. J Endocrinol Invest 2019

ORIGINAL ARTICLE

Short-term safety, tolerability and efficacy of a very low-calorie-ketogenic diet interventional weight loss program versus hypocaloric diet in patients with type 2 diabetes mellitus

A Goday[1,2,3], D Bellido[4], I Sajoux[5], AB Crujeiras[6,7], B Burguera[8,9], PP García-Luna[10], A Oleaga[11], B Moreno[12] and FF Casanueva[6,7]

Table 3. Efficacy outcomes

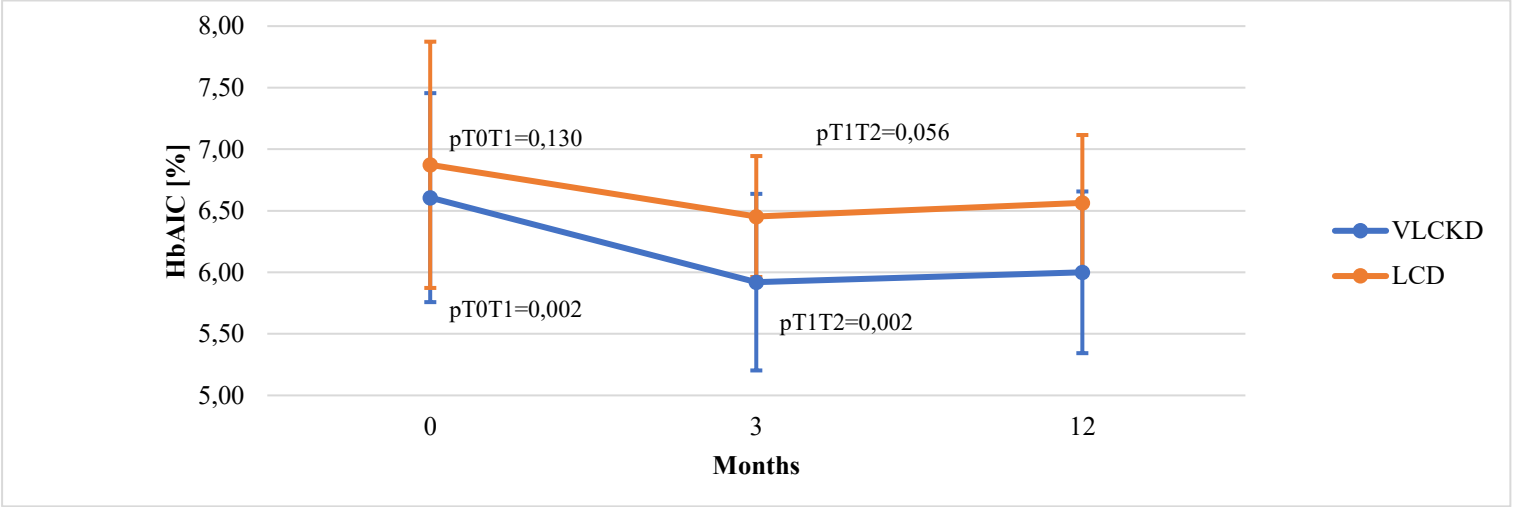
	VLCK diet group (n = 45)			*LC diet group (n = 40)*		
	Baseline	*4 months*	P-*value*[a]	*Baseline*	*4 months*	P-*value*[a]
Body weight						
Body weight (kg)	91.5 (11.4)	76.8 (9.1)	< **0.0001**	90.0 (11.3)	84.95 (13.6)	0.5960
Weight lost > 5% of weight	–	40 (97.6%)	–	–	18 (50.0%)[†]	–
Weight lost > 10% of weight	–	35 (85.4%)	–	–	6 (16.7%)[†]	–
BMI (kg m^{-2})	33.3 (1.5)	27.9 (1.8)	< **0.0001**	32.9 (1.6)	31.0 (2.2)	< **0.0001**
Waist (cm)	108.1 (8.6)	96.1 (7.6)	< **0.0001**	105.8 (8.5)	100.4 (9.2)	**0.0481**
Glycemic control						
Fasting glycemia (mg dl^{-1})	136.9 (34.4)	108.9 (20.4)	< **0.0001**	140.5 (43.1)	123.3 (24.3)	0.1821
HbA1c (%)	6.9 (1.1)	6.0 (0.7)	< **0.0001**	6.8 (1.0)	6.4 (0.8)	0.1453
Patients with HbA1c ⩾ 7%	21 (46.7%)	5 (12.8%)	**0.0008**	15 (34.9%)	9 (25.7%)	0.3828
HOMA Index	6.9 (4.4)	3.5 (1.9)	< **0.0001**	5.8 (2.9)	4.6 (2.5)[†]	**0.0010**
Patients treated with oral antidiabetic drugs	33 (73.3%)	20 (50.0%)	**0.0267**	38 (86.4%)	30 (83.3%)	0.7057
Lipid profile						
Total cholesterol (mg dl^{-1})	200.1 (36.0)	187.5 (46.3)	0.1615	199.4 (51.0)	191.7 (34.1)	0.4489
Triglycerides (mg dl^{-1})	150.5 (54.4)	114.6 (57.2)	**0.0040**	176.1 (92.0)	158.3 (61.0)	0.3308
LDL-c (mg dl^{-1})	112.7 (33.6)	110.6 (38.4)	0.7892	109.8 (45.5)	107.1 (29.9)	0.7629
HDL-c (mg dl^{-1})	55.9 (11.1)	54.5 (11.3)	0.5728	55.1 (11.7)	52.4 (10.0)	0.3017

Article

Very-Low-Calorie Ketogenic Diet as a Safe and Valuable Tool for Long-Term Glycemic Management in Patients with Obesity and Type 2 Diabetes

Eleonora Moriconi [1,2], Elisabetta Camajani [2,3], Andrea Fabbri [4], Andrea Lenzi [5] and Massimiliano Caprio [1,3,*]

Kinetics of HbA1c % in patients following a VLCKD vs a LCD



	ΔT0-T1 (mean ± DS)		P-value	ΔT2-T0 (mean ± DS)		P-value
	VLCKD	LCD		VLCKD	LCD	
HbA1c%	0,69 ± 0,65	0,42 ± 1,01	0,533	0,61 ± 0,54	0,13 ± 0,76	0,070

Moriconi E et al. Nutrients 2021

Variation of pharmacological therapy at baseline and after 12 months

	VLCKD group		LCD group	
	Baseline	After 12 months	Baseline	After 12 Months
Subjects	15			
Men	8			
Women	7			
Diabetes Duration (years)				
Diet				
Metformin			15	8
Sulphonylurea			0	0
Metformin + GLP-1 agonist			0	6
Metformin + SGLT2 inhibitor	3	0	0	1
DD4-inhibitor	2	0	0	0

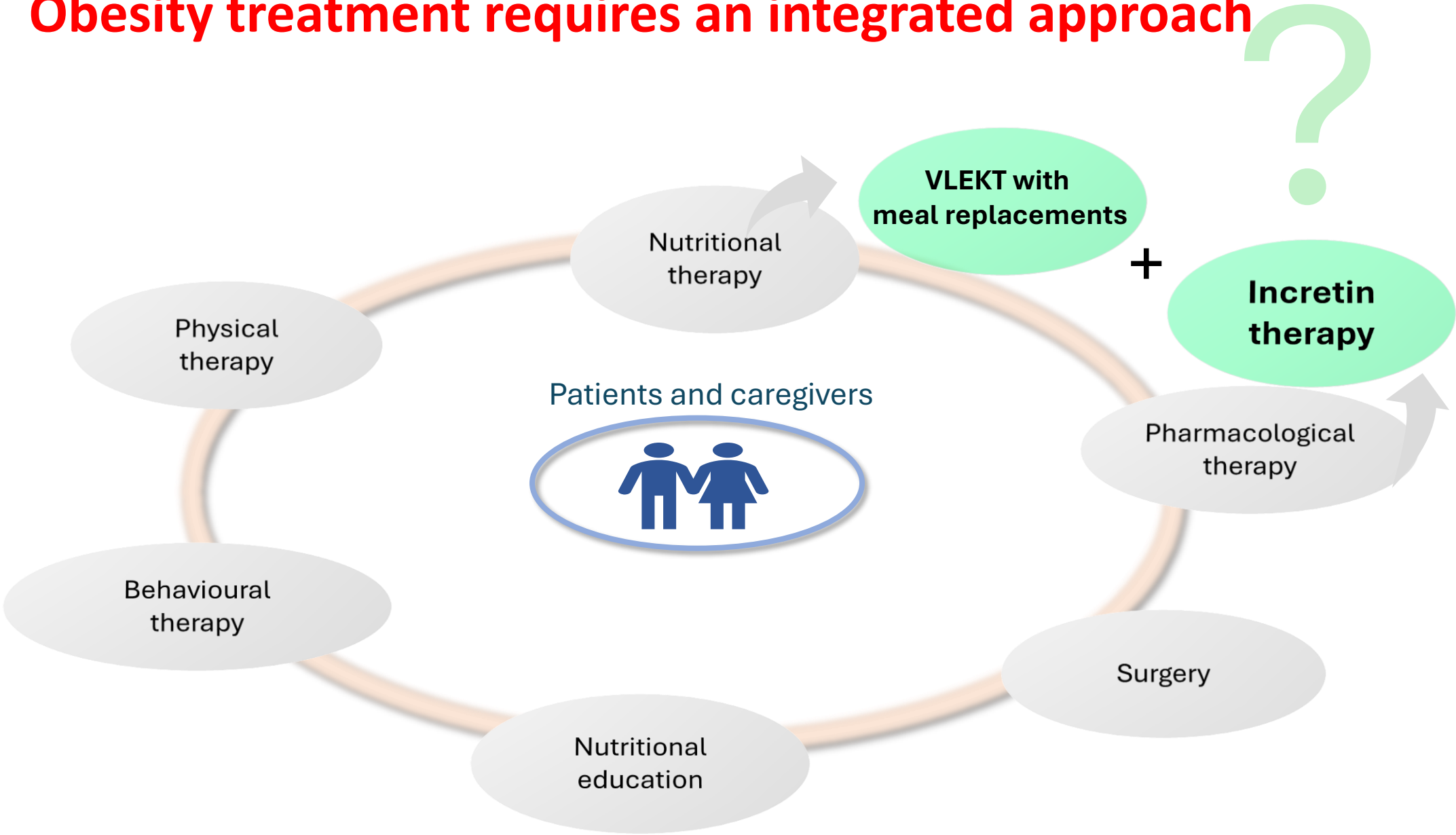
26.6% stopped antidiabetic drugs

73.3% were taking Metformin at the end of the study

46.6% increased antidiabetic medications

Moriconi E et al. Nutrients 2021

Obesity treatment requires an integrated approach



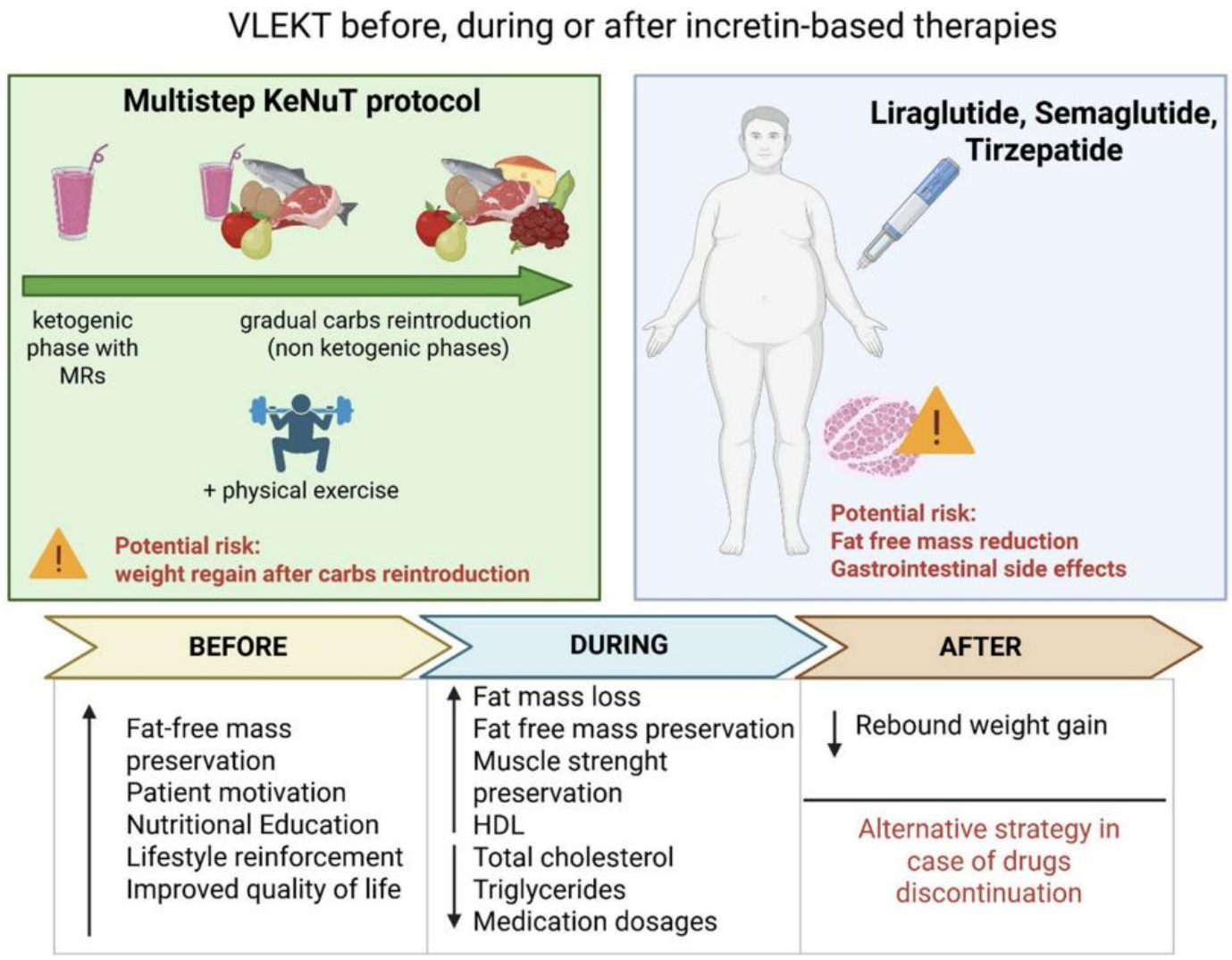
Current Obesity Reports (2026) 15:13
https://doi.org/10.1007/s13679-026-00695-7

REVIEW

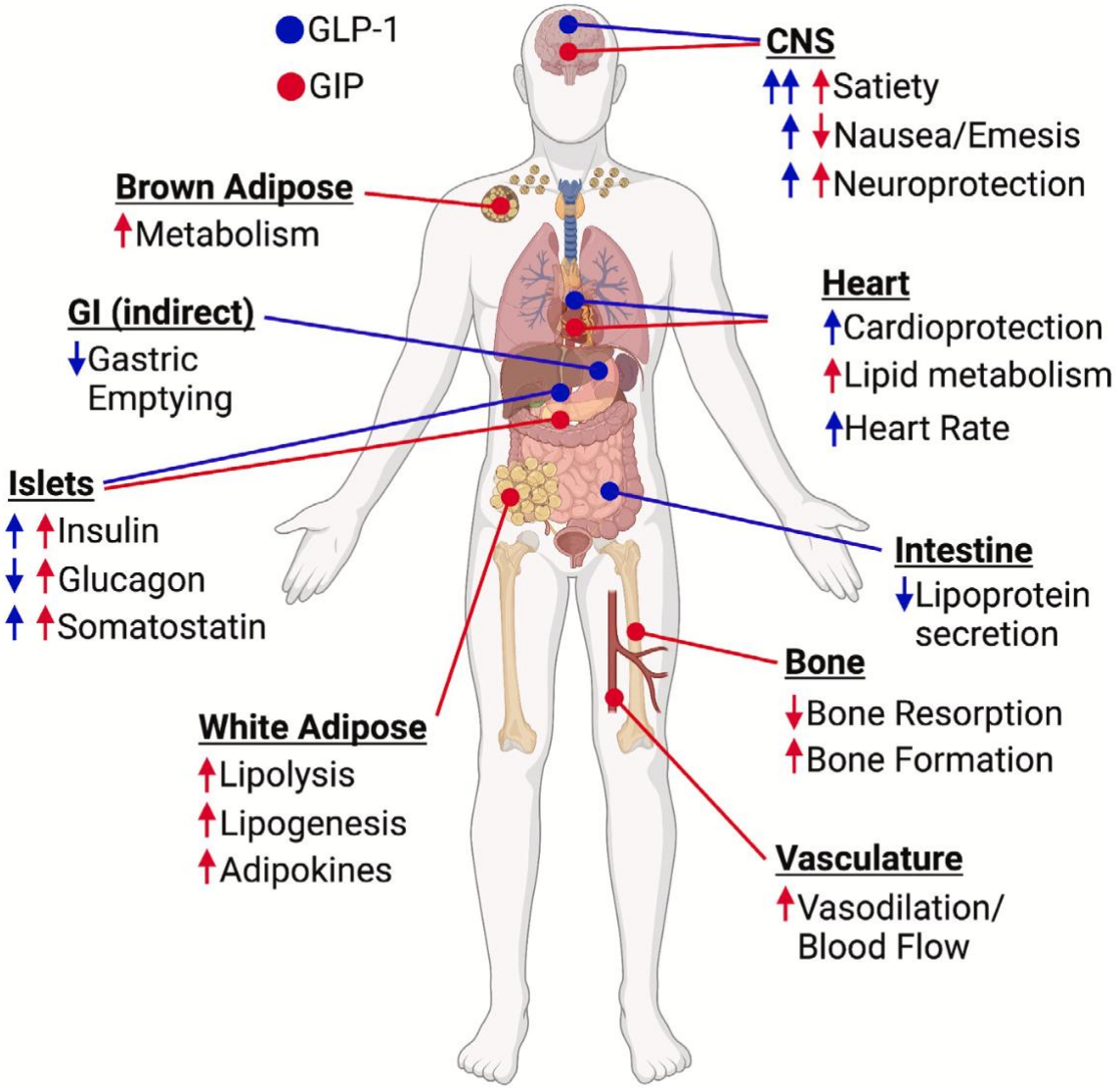
Obesity medications and precision nutrition: synergistic interventions and integrated approach in obesity management

Alessandra Feraco[1,2] · Elisabetta Camajani[1,2] · Giovanna Muscogiuri[3,4,5] · Luigi Barrea[4,6] · Annamaria Colao[3,4,5] · Massimiliano Caprio[1,2]

Received: 7 January 2026 / Accepted: 16 February 2026
© The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2026

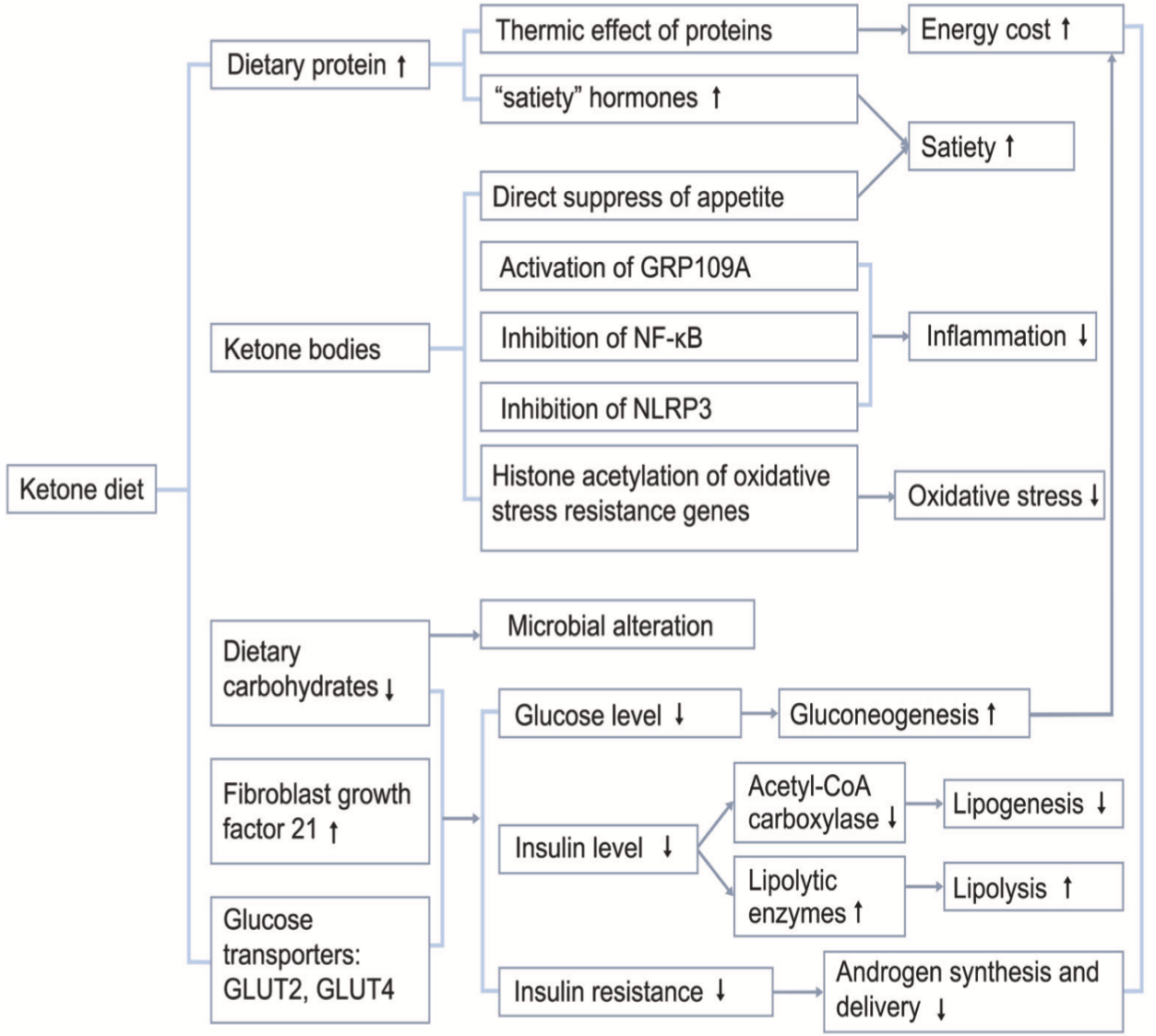


Key metabolic sites of action for GLP-1 (blue) and GIP (red)



Campbell JE, et al. Cell Metab. 2023 Sep 5;35(9):1519-1529. doi: 10.1016/j.cmet.2023.07.010.

Possible mechanisms whereby the ketogenic diet ameliorates metabolic disorders

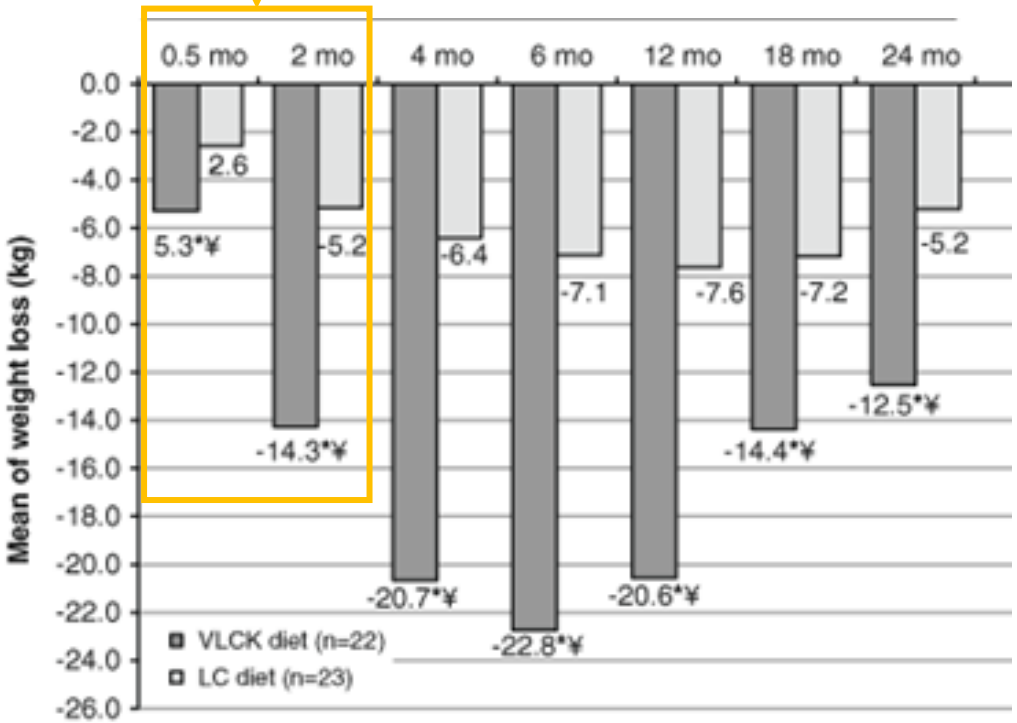


Zhu H, et al. Signal Transduct Target Ther. 2022 Jan 17;7(1)

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

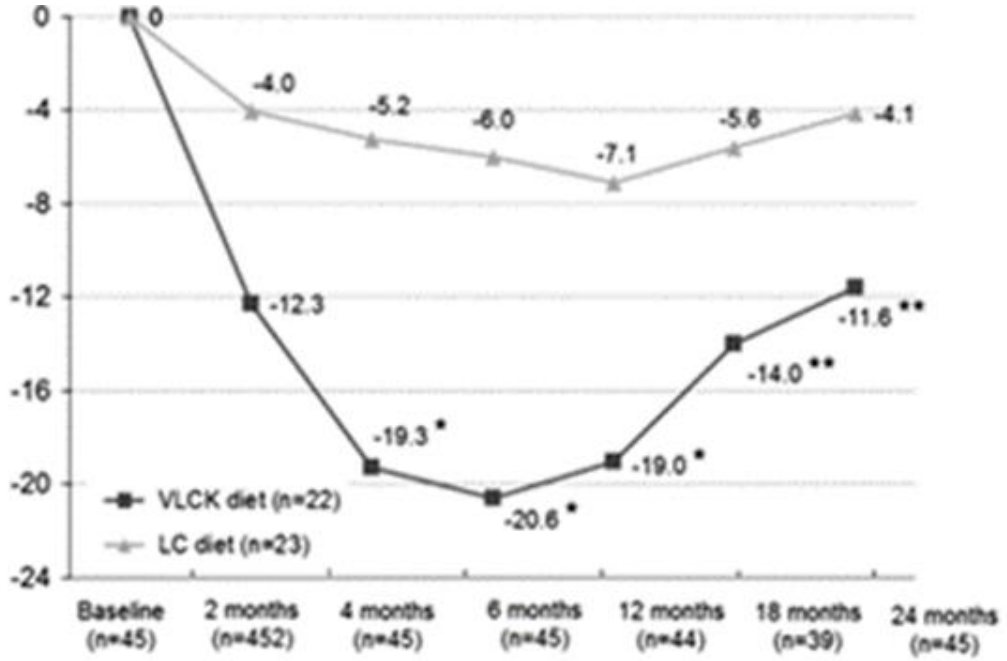
Ketosis

Weight loss



Obesity medicatiosn

Change in waist



Moreno B et al. Endocrine 2016

When to propose VLEKT first



BMI 25–26.9 kg/m^2 with abdominal obesity

Overweight/obesity, PMOS and hypogonadism

Overweight/obesity and neurological/neurodegenerative disorders (epilepsy, migraine)

Overweight/obesity and psoriasis

Overweight/obesity with sarcopenia

Rapid weight loss required before elective surgery

Patients with indications to follow a VLEKT, refusing pharmacological therapy

Take-home messages

- Concerns regarding the impact of VLEKT on cardiovascular disease risk and hepatic and renal function are unfounded.

- VLEKT appear to be more effective than other diets in improving glycaemic control and inducing weight loss in the short term (approximately 3–6 months).

- Patients treated with VLEKT often demonstrate enhanced adherence to overall medical care, potentially resulting in improved outcomes. Meal replacement can be used concomitantly with obesity medications for weight management.

- The anorectic effects of novel drugs pose challenges to nutritional adequacy. Real-world evidence demonstrates a high incidence of micronutrient deficiencies and consistently suboptimal dietary intake across key nutrients.

VLEKT can be easily combined with novel anti-obesity therapies, in order to improve nutrition adequacy, clinical outcomes, long-term weight maintenance, adherence to a healthy life-style, and quality of life in patients with obesity.

A NEW ERA OF NOVEL MULTI-DISCIPLINARY THERAPEUTIC OPPORTUNITIES!

"To repair is twenty times more difficult than to prevent."

Henri-Frédéric Amiel (1821-1881)

Thank you for the attention!

ADMIRE
ALDOSTERONE-MINERALOCORTICOID RECEPTOR
NETWORK

Andrea Armani
Elisabetta Camajani
Alessandra Feraco
Stefania Gorini
Eleonora Bellucci
Vincenzo Marzolla
Luigi Procaccio
Caterina Mammi
Eleonora Moriconi
Marco Infante
Giulia Fiorentini
Chiara Quattrini
Claudia Mattioli
Martina Galasso



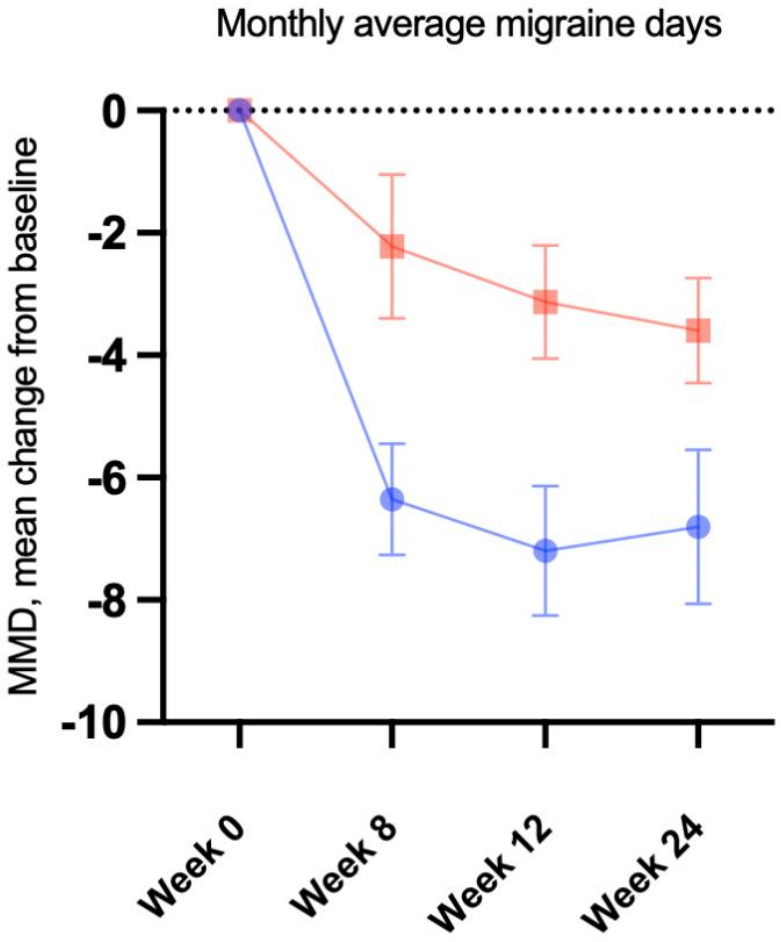


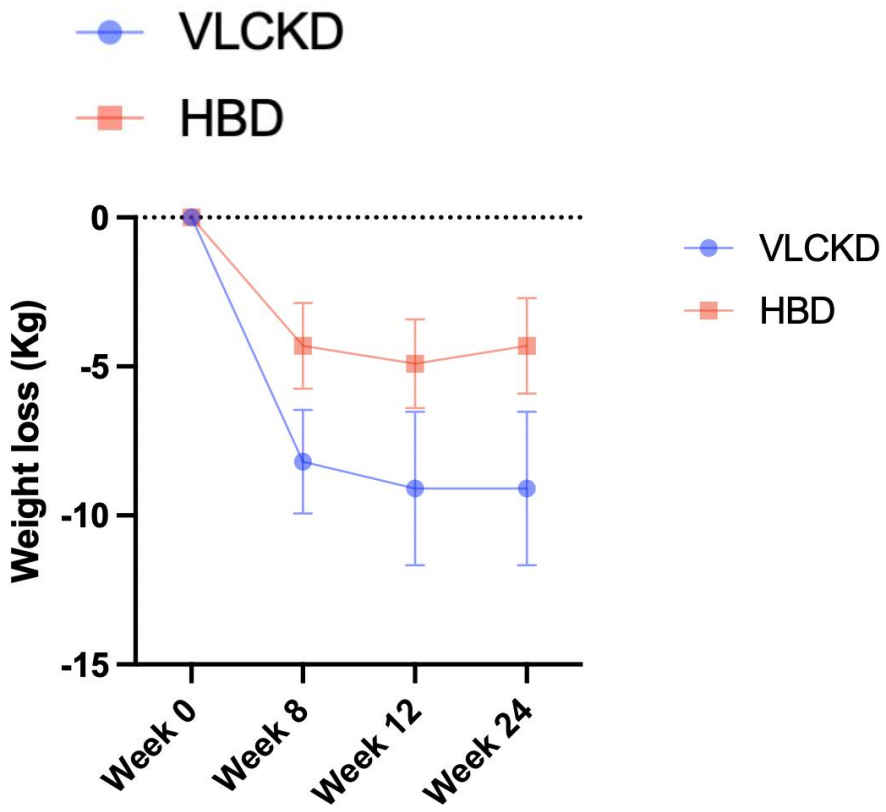


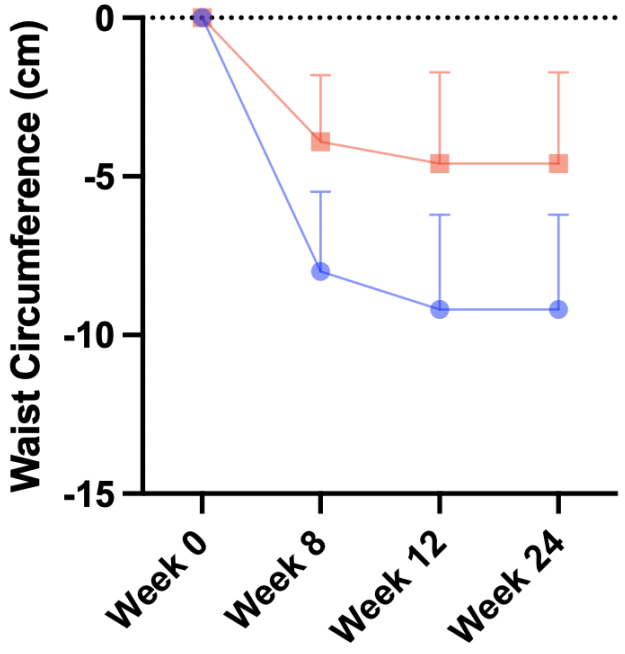
Università San Raffaele Roma

IRCCS San Raffaele

VLCKD in the Prevention of High-Frequency Episodic Migraine in subjects with overweight/obesity: the EMIKETO Randomized, Controlled Trial

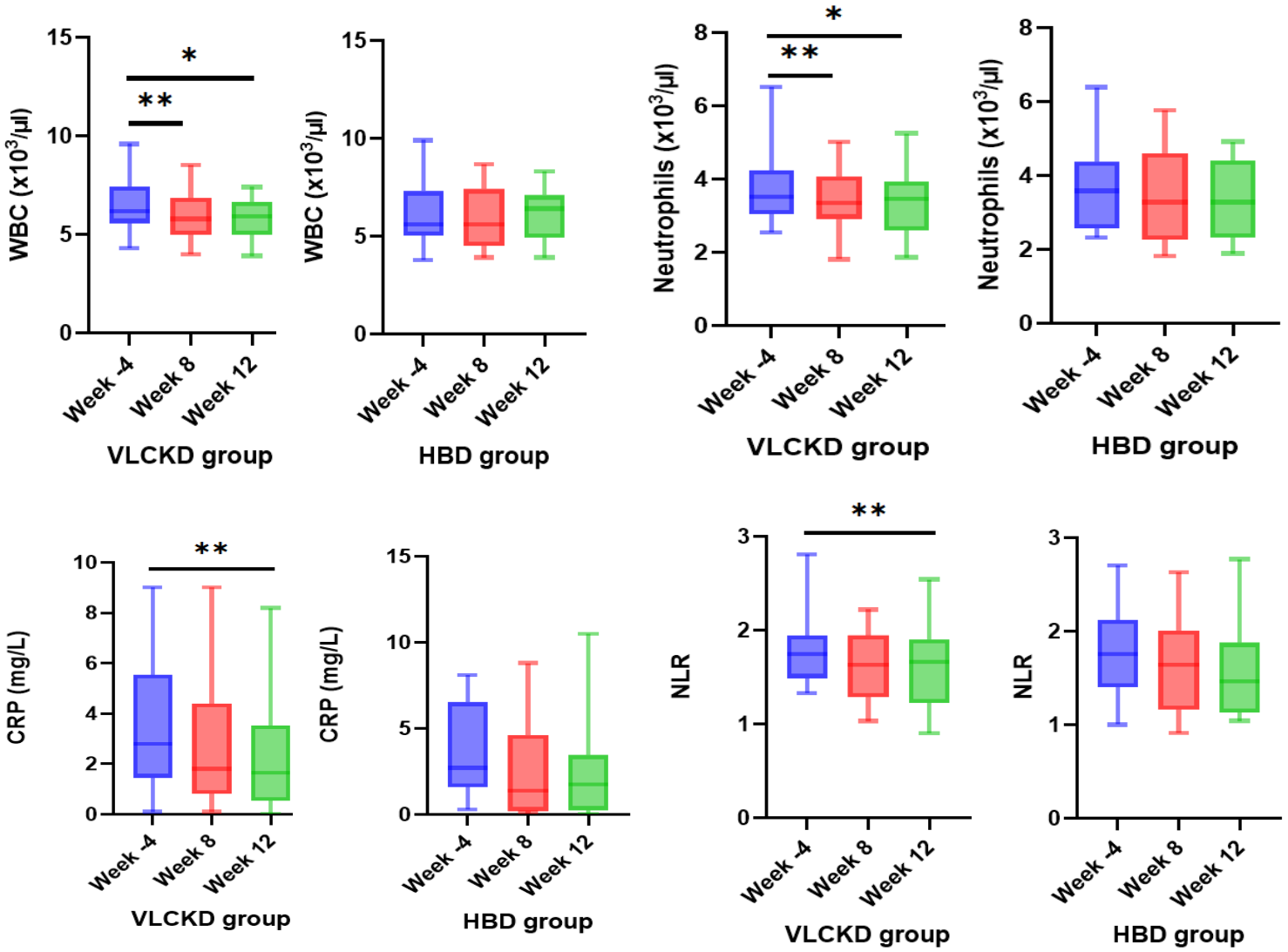


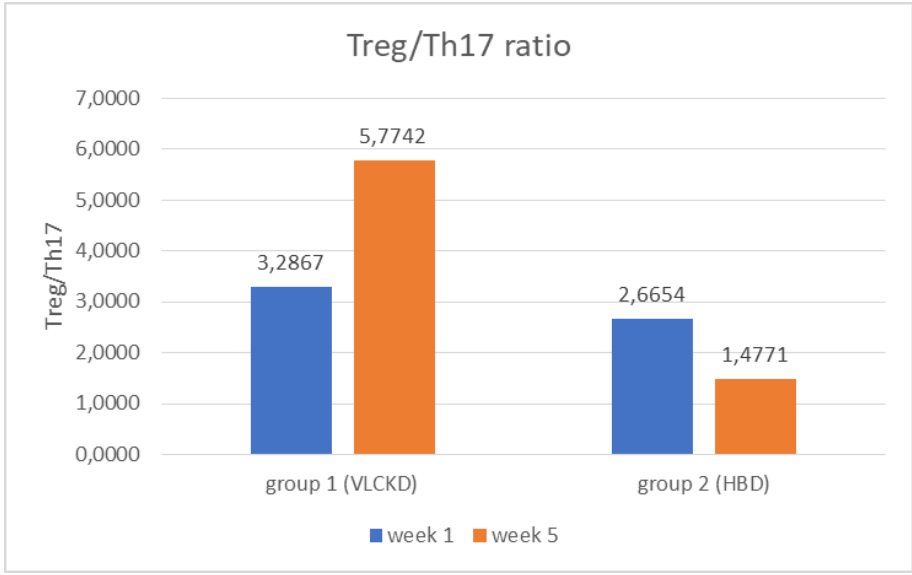




Caprio M, Moriconi E et al. JTM 2023

VLCKD reduces several serum Inflammatory markers at weeks 8 and 12

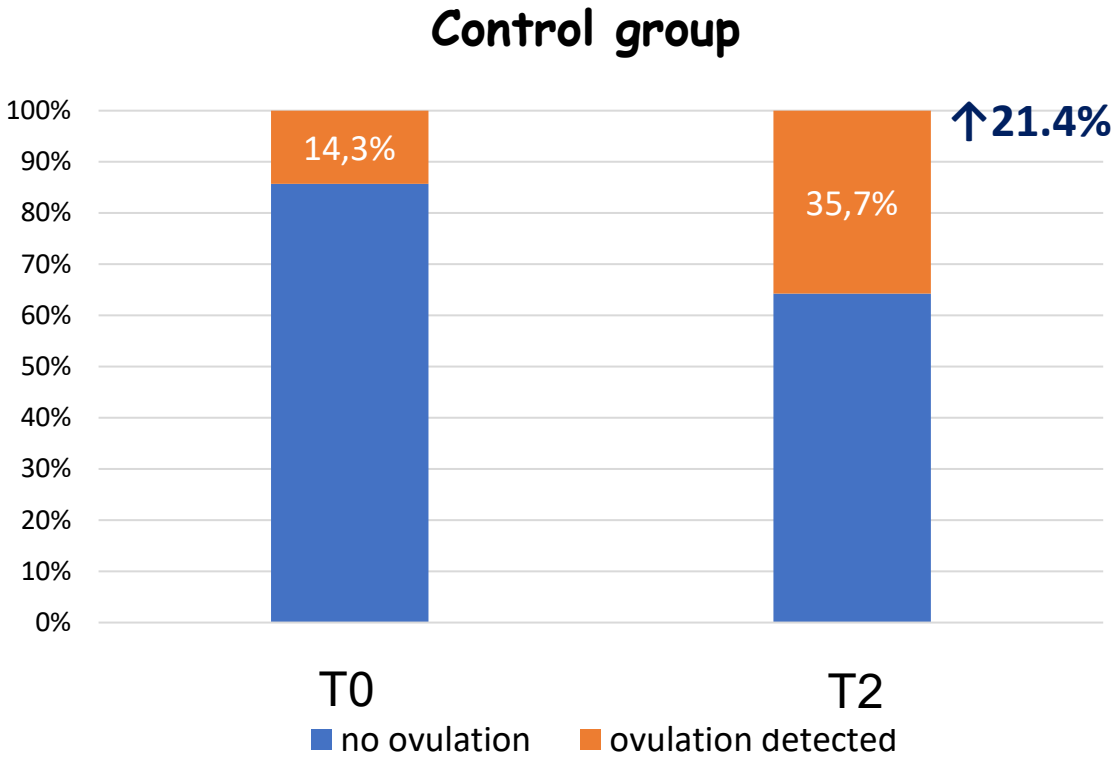


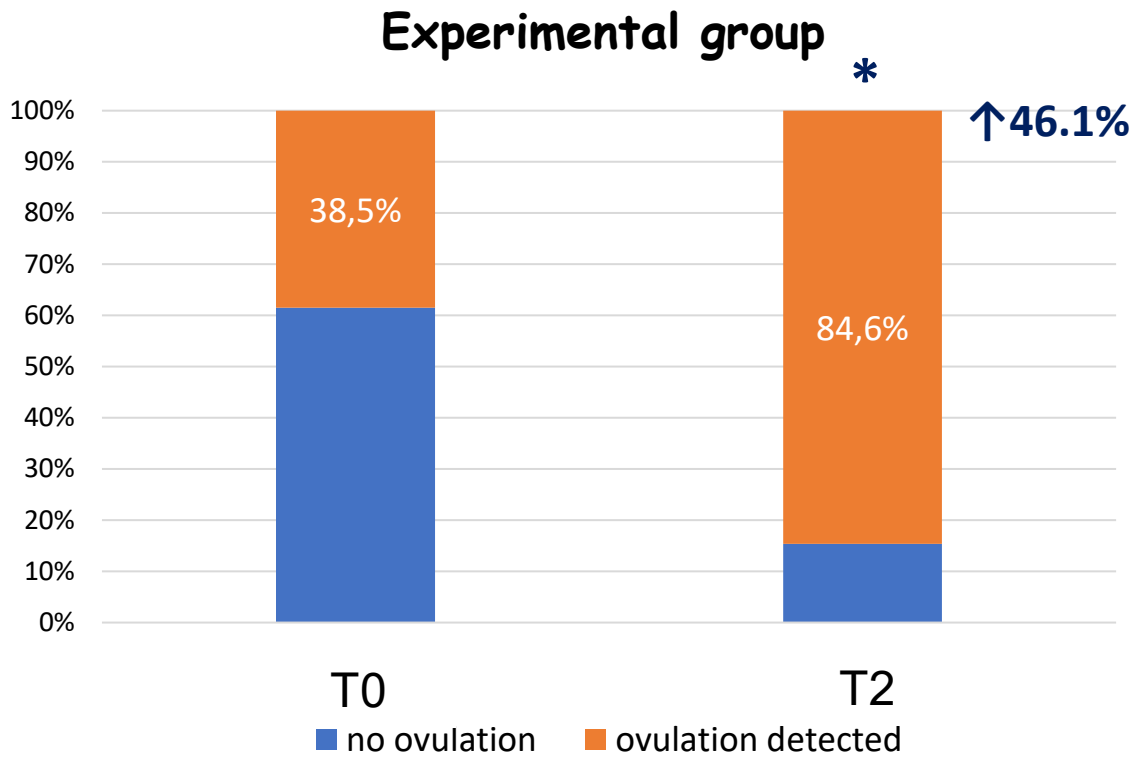


Caprio M, Moriconi E et al. JTM 2023

Efficacy of VLCKD in Obese PCOS: a Randomized Controlled Trial

Ovulation: dominant follicle with a diameter higher than 12mm or corpus luteum seen on pelvis US scanning, and P >8ng/mL or E2 >100pg/mL





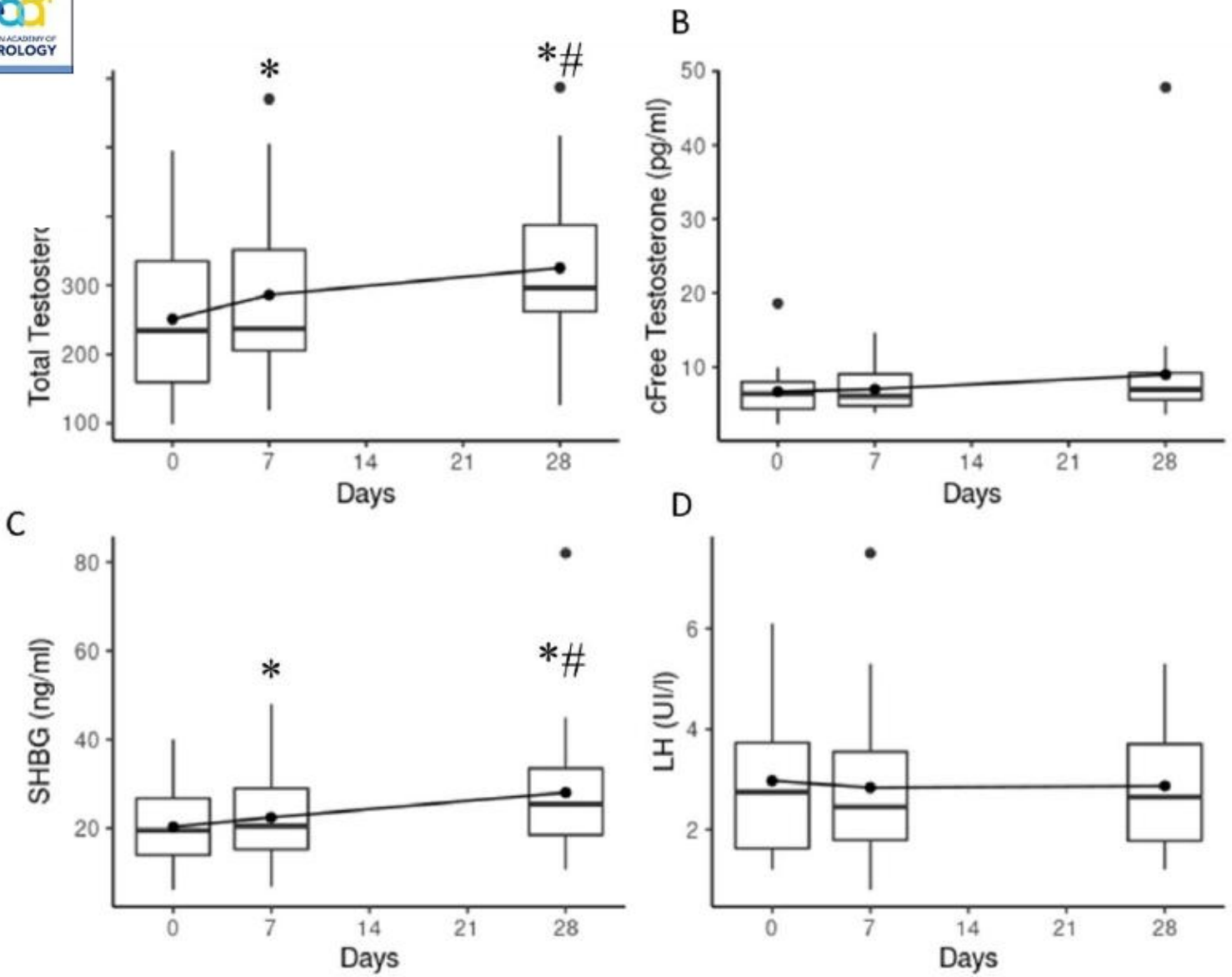
Ovulation occurrence at baseline was similar in the two groups, but it differed significantly by the end of the study (*P* = 0.018). At the end of the study, ovulation occurrence improved significantly in the experimental group, while the change in the control group wasn't significant

*p<0.05, McNemar test

Gambineri et al. Endocr Connect 2023

ANDROLOGY

Very low-calorie ketogenic diet rapidly augments testosterone levels in non-diabetic obese subjects



Cignarelli et al. Andrology 2023

Cignarelli A et al. Andrology 2023



Ridotta tolleranza ai farmaci incretinici
Ridotta risposta in termini di calo ponderale
Programmazione di una gravidanza

Expert Opinion

VLEKT + TERAPIA INCRETINICA → **TERAPIA INCRETINICA** → **DIETA NORMOCALORICA +/- TERAPIA INCRETINICA**



Expert Opinion