



Congresso Regionale AMD - SID Abruzzo/Molise

Il Diabete paradigma di cronicità, coniugare
eccellenza e prossimità dell'assistenza

Auditorium Centro Studi e Tecnologie Avanzate –
CAST

Chieti, 12 novembre 2022

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Università Federico II di Napoli

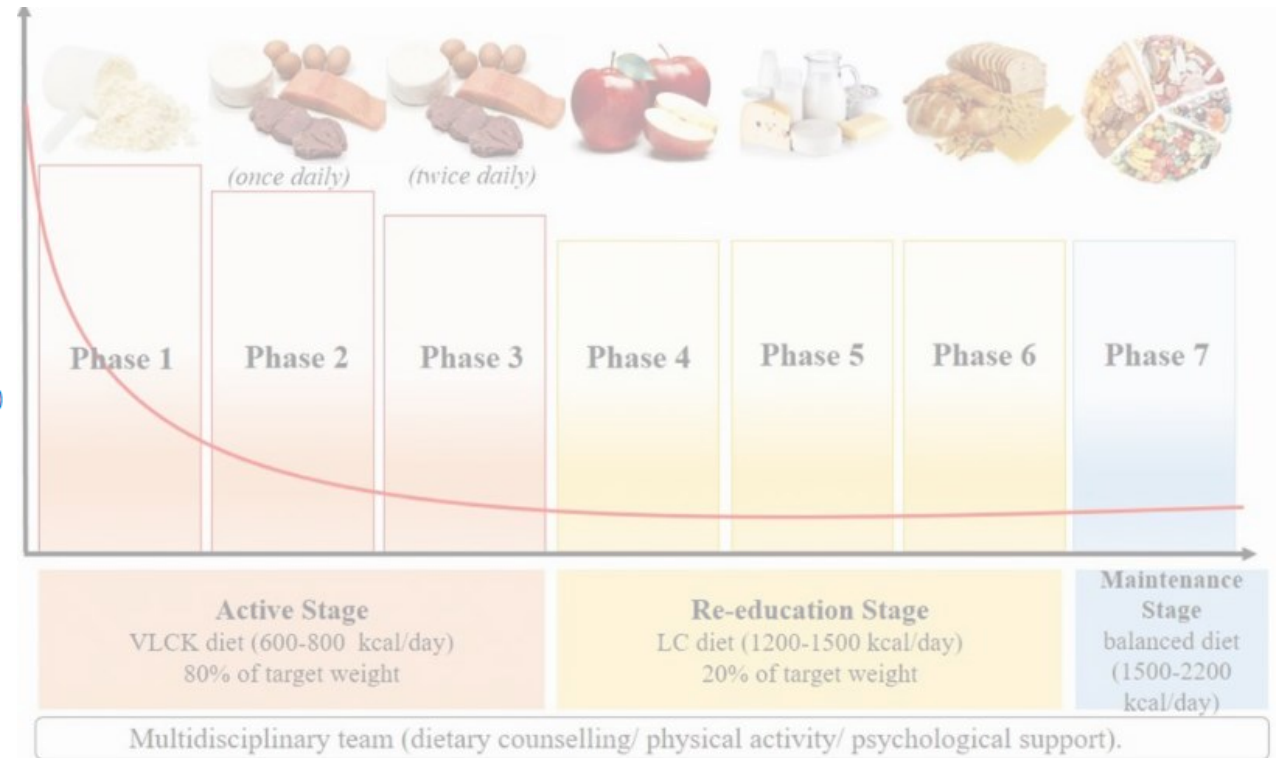
**Very Low Calorie Ketogenic Diet
(VLCKD) strumento utile per la
gestione del DM2?**

Diabetes



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

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Obesity Management Task Force (OMTF) of the European Association for the Study of Obesity (EASO)



Results: Of the 645 articles retrieved, 15 studies met the inclusion criteria and were reviewed, revealing 4 main findings. First, the VLCKD was shown to result in a significant weight loss in the short, intermediate, and long terms and improvement in body composition parameters as well as glycemic and lipid profiles. Second, when compared with other weight loss interventions of the same duration, the VLCKD showed a major effect on reduction of body weight, fat mass, waist circumference, total cholesterol and triglyceridemia as well as improved insulin resistance.

Gu Y et al., Beneficial effects of an 8-week, very low carbohydrate diet intervention on **obese subjects**. Evid Based Complement Alternat Med. 2013

Results: HOMA IR and HOMA β significantly decreased while whole body insulin sensitivity index (WBISI) increased.

Svendsen PF et al., The effect of a very low calorie diet on insulin sensitivity, beta cell function, insulin clearance, incretin hormone secretion, androgen levels and body composition in **obese young women**. Scand J Clin Lab Invest, 2012

Results: Whole body (HOMA-IR) insulin sensitivity increased significantly, while GIP increased after the dietary intervention. A significant increase in insulin clearance was observed.

Demol S et al., Low-carbohydrate (low & high-fat) versus high-carbohydrate low-fat diets in the treatment of **obesity in adolescents**. Acta Paediatr. 2009

Results: Insulin level and HOMA IR decreased significantly in the two low carbohydrate diet groups.

Partsalaki I et al., Metabolic impact of a ketogenic diet compared to a hypocaloric diet in **obese children and adolescents**. J Pediatr Endocrinol Metab. 2012

Results: Both groups significantly reduced fasting insulin and HOMA IR, but the reduction was greater in the ketogenic group.

Severe type 2 diabetes (T2D) remission using a very low-calorie ketogenic diet (VLCKD)

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Luana Barboza Carloto¹, Maitane Nuñez-García², Ignacio Sajoux², Sidney Senhorini³

The reported case is a 35-year-old man with obesity, dyslipidemia, and T2D for 5 years. Despite the use of five antidiabetic medications, including insulin, HbA1c was 10.1%. A VLCKD through a commercial multidisciplinary weight loss program (PnK method) was prescribed and all medications were discontinued. The method is based on high-biological-value protein preparations and has 5 steps, the first 3 steps (active stage) consist of a VLCKD (600-800 kcal/d) that is low in carbohydrates (<50 g daily from vegetables) and lipids. The amount of proteins ranged between 0.8 and 1.2 g/kg of ideal body weight.



After only 3 months, the patient lost 20 kg with weight normalization and diabetes remission, and after 2 years of follow-up, the patient remained without the pathologies.

	Basal	30 days	60 days	90 days	1 year	2 years
Weight	98	90	82	78	79	80
BMI	30.2	27.8	25.3	24.1	24.4	24.7
FG	132	126	92	77	91	86
HbA1c	10.1	8.1	6.8	5.3	5.4	5.2
Uric acid	6.2	5.4	4.4	4.3	4.4	4.9
Creatinine	0.8	0.9	0.7	0.7	0.9	1.0
AST	55	37	37	32	27	34
GGT	90	43	45	24	19	12
TC	132	145		153	145	142
TG	81	114		90	130	80
HDL	43	51		51	44	44
LDL	73	71		84	75	82
Microalbuminuria	89.6			28.0	25.2	22.3

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 Bellido⁴, I Sajoux⁵, A B Crujeiras^{6 3}, B Burguera^{7 8}, P P García-Luna⁹,
A Oleaga¹⁰, B Moreno¹¹, F F Casanueva^{6 3}

Objective: Evaluating the short-term safety and tolerability of a VLCK diet (<50 g of carbohydrate daily) in an interventional weight loss program including lifestyle and behavioral modification support (Diaprokai Method) in subjects with T2DM.

Methods: Eighty-nine men and women, aged between 30 and 65 years, with T2DM and body mass index between 30 and 35 kg m⁻² participated in this prospective, open-label, multi-centric randomized clinical trial with a duration of 4 months. Forty-five subjects were randomly assigned to the interventional weight loss (VLCK diet), and 44 to the standard low-calorie diet.

HIGH FAT, LOW CARB, MODERATE PROTEIN

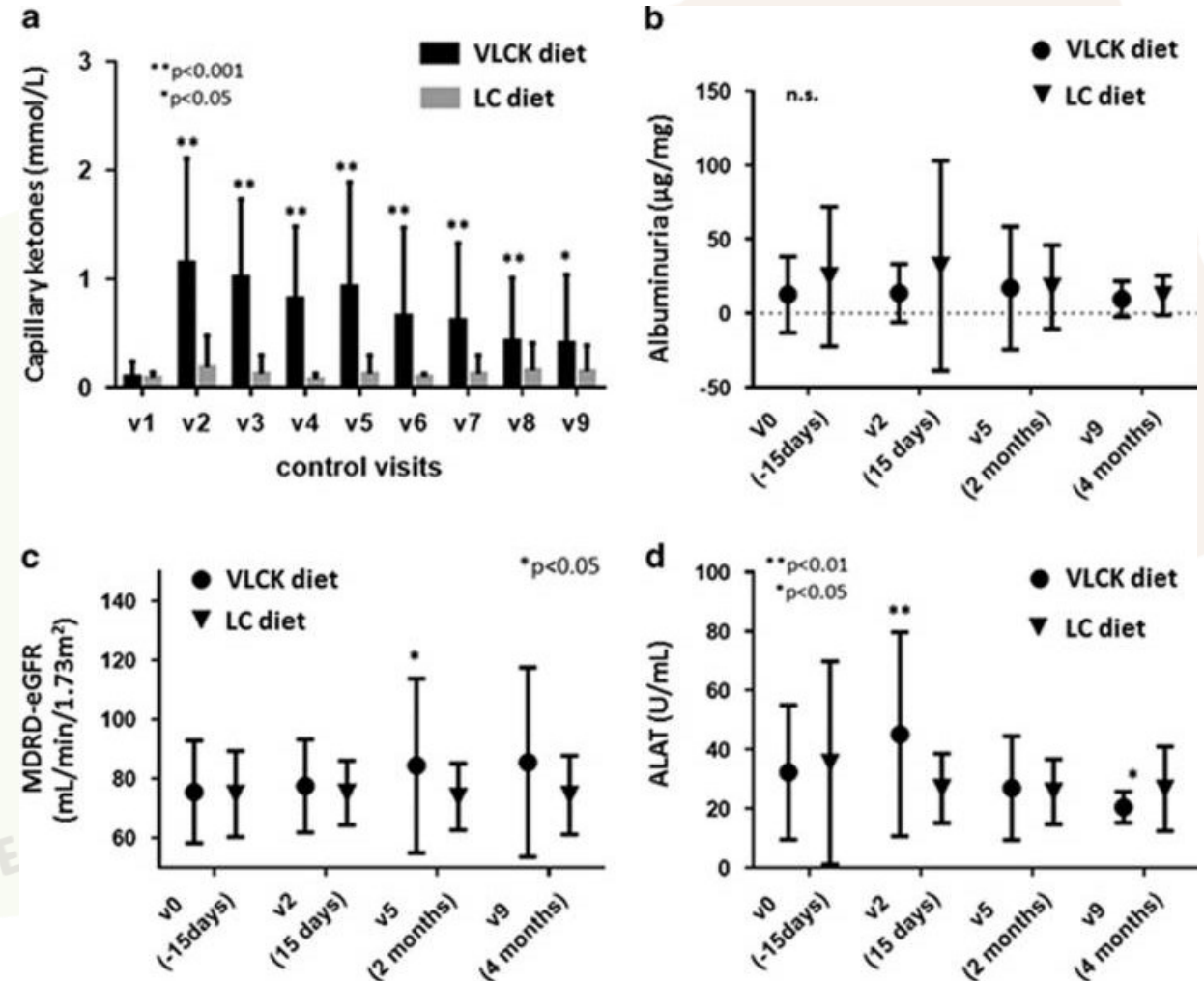
LOW CALORIE DIET

VS

3000KCAL DAILY DEFICIT

Diet-induced changes in safety parameters

Results: No significant differences in the laboratory safety parameters were found between the two study groups.



Diet-induced changes in safety parameters

No serious adverse events were reported and mild adverse events in the VLCKD group declined at last follow-up.

Symptoms ^a	V2 (15 days)			V9 (4 months)		
	VLCK diet group (n=45)	LC diet group (n=44)	P-value	VLCK diet group (n=45)	LC diet group (n=44)	P-value
Asthenia	7	0	0.0092	1	0	0.3396
Headache	9	1	0.0124	2	0	0.1739
Nausea	9	0	0.0028	3	0	0.0936
Vomiting	7	0	0.0092	1	0	0.3396
Constipation	2	0	0.1772	8	0	0.0046
Cramps	1	0	0.3429	0	0	–
Myalgia	1	0	0.3429	1	0	0.3396
Muscular weakness	1	1	0.9328	0	0	–
Heaviness and tiredness of legs	1	1	0.9328	0	0	–
Hair loss	1	0	0.3429	2	0	0.1739
Orthostatic hypotension	0	0	–	6	0	0.0155
Edema	0	0	–	1	0	0.3396
Others ^{b,c}	20	4	0.0004	5	8	0.0731
<i>Patients lost</i>						
Due to side-effects	0	0		1	0	
Voluntary dropout	0	4		4	4	
Total dropout	–	–		5	8	

Diet-induced changes in efficacy parameters

Results: Weight loss and reduction in waist circumference in the VLCKD group were significantly larger than in control subjects (both $P < 0.001$). The decline in HbA1c and glycemic control was larger in the VLCKD group ($P < 0.05$).

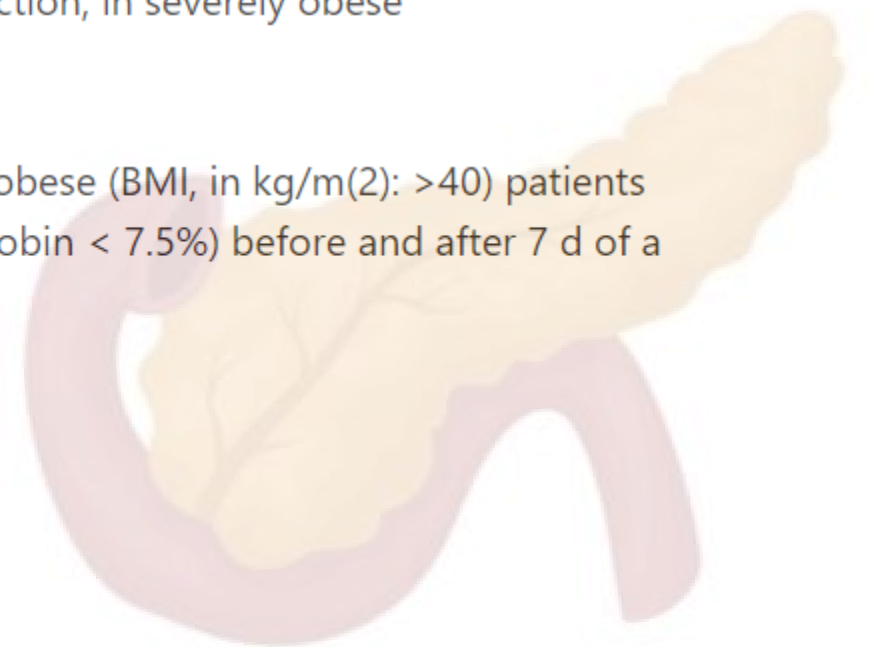
	VLCK diet group (n=45)			LC diet group (n=40)		
	Baseline	4 months	P-value ^a	Baseline	4 months	P-value ^a
<i>Body weight</i>						
Body weight (kg)	91.5 (11.4)	76.8 (9.1)	<0.0001	90.0 (11.3)	84.95 (13.6)	0.5960
Weight lost > 5% of weight	–	40 (97.6%)	–	–	18 (50.0%) [†]	–
Weight lost > 10% of weight	–	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
<i>Glycemic control</i>						
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
<i>Lipid profile</i>						
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

Very-low-calorie diet: a quick therapeutic tool to improve β cell function in morbidly obese patients with type 2 diabetes

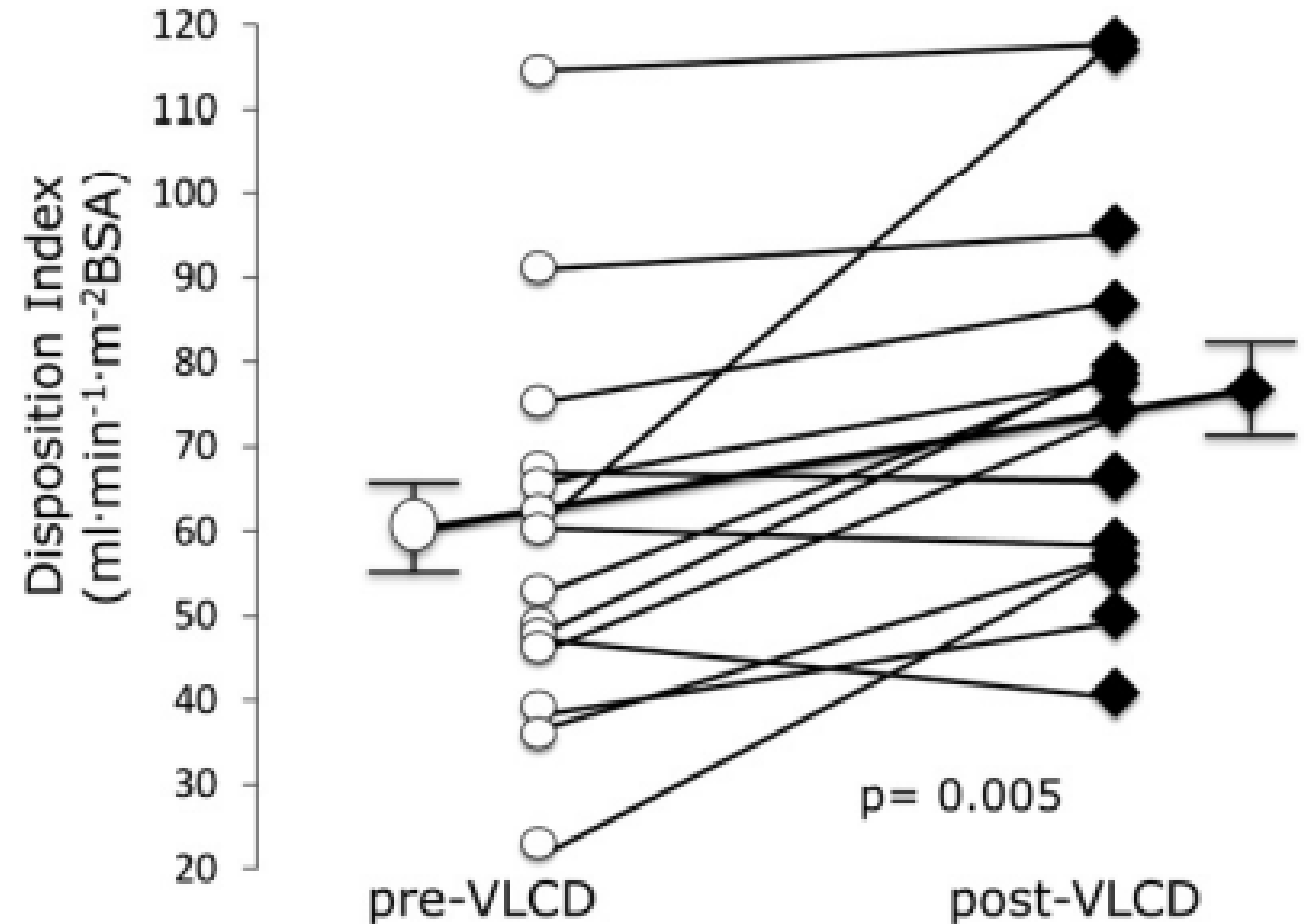
Ilaria Malandrucco ¹, Patrizio Pasqualetti, Ilaria Giordani, Dario Manfellotto, Federica De Marco, Filippo Alegiani, Anna Maria Sidoti, Fabiana Picconi, Alessandra Di Flaviani, Gaetano Frajese, Riccardo C Bonadonna, Simona Frontoni

Objective: The objective was to study the relative contributions of insulin sensitivity, insulin secretion, or both to improvement in glucose metabolism, after 1 wk of caloric restriction, in severely obese diabetic patients.

Design: Hyperglycemic clamps were performed in 14 severely obese (BMI, in kg/m²: >40) patients with type 2 diabetes in good glucose control (glycated hemoglobin < 7.5%) before and after 7 d of a VLCD (400 kcal/d).



Results: the Disposition Index, which measures the body's capability to dispose of a glucose load, significantly increased because of improvements in indexes of both first- and second-phase insulin secretion ($P=0.02$), but with no changes in insulin sensitivity ($P=0.33$).



The gut microbiome as possible mediator of the beneficial effects of very low calorie ketogenic diet on type 2 diabetes and obesity: a narrative review

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AMD-SID-SIEDP-Lifestyle Study Group Lazio; A Bellia, O Bitterman, D Lauro, D Mora, E Santarelli

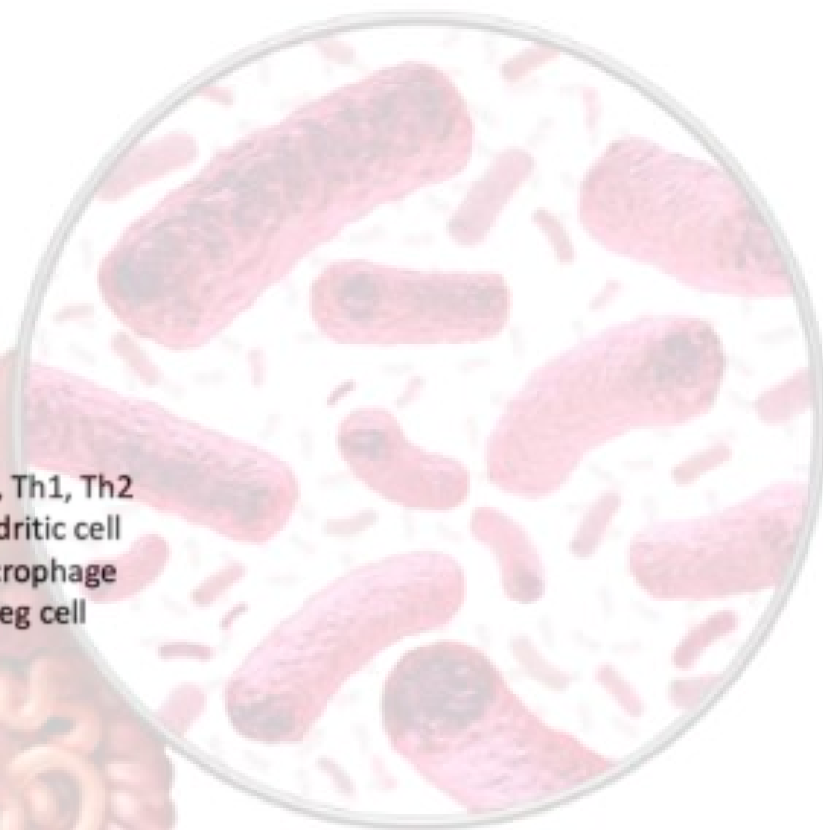
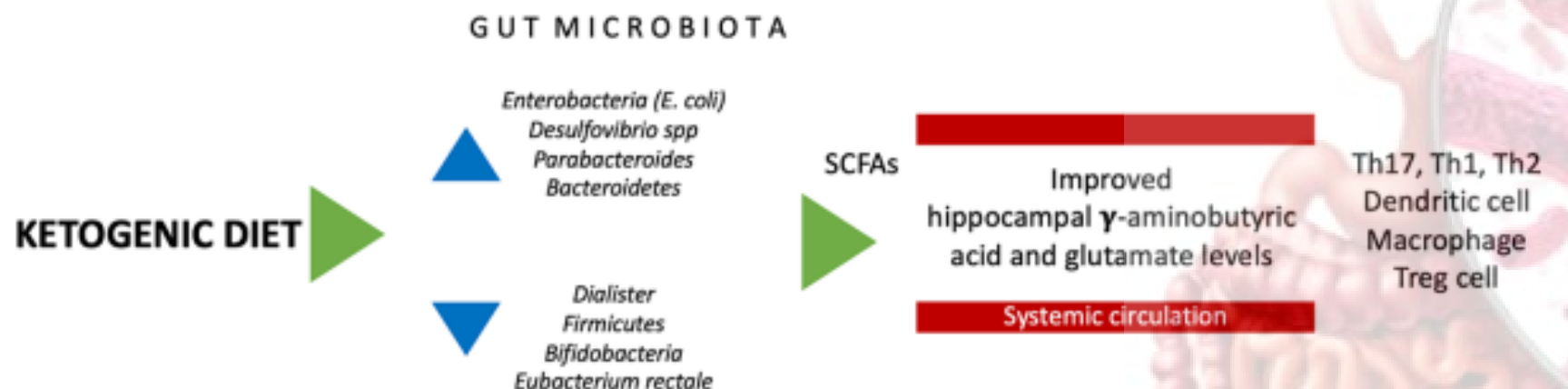
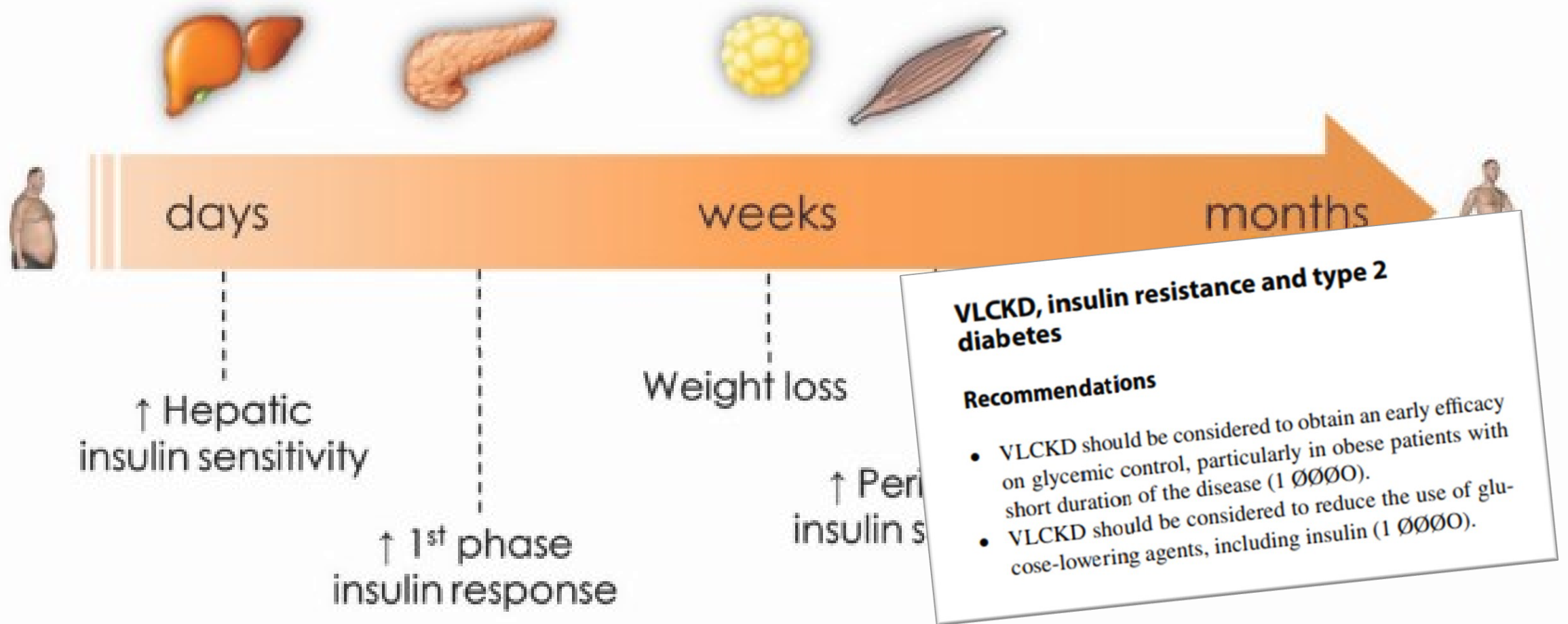


Table 1 Detailed effects of VLCKDs on gut microbiota as observed in patients with T2DM and/or obesity

Authors, year (References)	Type of study	Results
Luo et al. [59]	Sixteen adult patients, who followed a 52 weeks weight-loss program including low calorie diet, exercise and behavioral therapy, selected according to their weight-loss course	Weight reduction in the obese is accompanied with an increased fecal expression of Akkermansia. Metabolic co-morbidities are associated with a higher Firmicutes/Bacteroidetes ratio
Basciani et al. [60]	This is a randomized controlled trial Forty-eight patients with obesity (19 males and 29 females, homeostatic model assessment (HOMA) index ≥ 2.5 , age 56.2 ± 6.1 years, body mass index [BMI] 35.9 ± 4.1 kg/m ²) were randomly assigned to three 45 days isocaloric VLCKD regimens (≤ 800 kcal/day) containing whey, plant, or animal protein	VLCKDs lead to significant weight loss and a striking improvement in metabolic parameters over a 45-day period. VLCKDs (whey or vegetable proteins) showed a safer profile and a healthier microbiota composition than those containing animal proteins
Gutierrez-Repiso et al. [61]	This is a randomized, single-blind, parallel-design trial was conducted in 33 obese patients on a weight-loss program (PnK-Method) including a VLCKD followed by a low-calorie diet (LCD). Subjects were randomly allocated to three groups: one supplemented with synbiotics, a second group supplemented with a placebo during the VLCKD and synbiotics during the LCD phase, and a control group given a placebo	No effects on microbial diversity; Odoribacter and Lachnospira increase with symbiotic administration. The administration of Bifidobacterium animalis subsp. lactis and prebiotics fiber during the LCD is significantly associated with the percentage of weight loss and change in glucose, C-reactive protein and lipopolysaccharide-binding protein
Gutierrez-Repiso et al. [62]	Sixty-one subjects on 1, a hypocaloric Mediterranean diet (MedDiet; $n=21$), 2, a (VLCKD; $n=18$) and 3, sleeve gastrectomy bariatric surgery (BS; $n=22$)	Weight loss is not associated with a specific pattern of gut microbiota changes and changes in gut microbiota occur according to type of weight loss intervention
Ang et al. [63]	Metagenomic and metabolomic analyses of stool samples were performed from an 8 weeks inpatient study on 17 men consuming a baseline diet for 4 weeks followed by an isocaloric ketogenic diet (KD) for another 4 weeks and conducted experimental studies using germ-free and gnotobiotic mice randomly assigned to experimental groups and allotted to either ketogenic or high fat diet (KDs or HFDs, respectively)	Ketone bodies selectively inhibited bifidobacterial growth. Mono-colonizations and human microbiome transplantations into germ-free mice showed that the KD-associated gut microbiota reduces the levels of intestinal pro-inflammatory Th17 cells

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

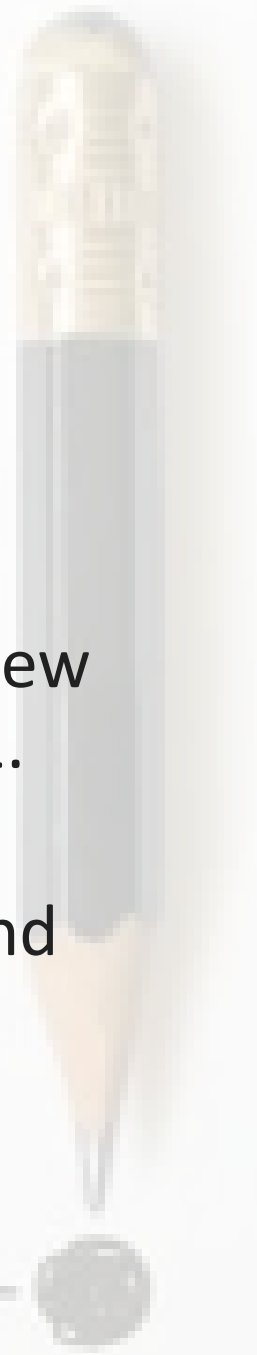


Take home messages

Obesity and type 2 diabetes are conditions that share key pathophysiological mechanisms.

VLCKD is a well-established tool for the treatment of obesity, but new evidence suggests a promising role also in the treatment of DM2.

Further well-designed studies are needed to clarify the efficacy and safety of VLCKD in DM.





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Grazie!

