

On July 5, 2022 research was posted to the National Library of Medicine by the Frontiers in Nutrition titled “Fad Diets: Facts and Fiction”

I’m going to extract the information in this article and dissect it for you to help you better understand why no single diet works for fat loss in the long-term.

An excerpt from the article:

Worldwide obesity has tripled from 1975 to 2016, while childhood obesity is increasing dramatically¹. Excessive calories from fats and sugars, large portions of food, routinely junk food intake, availability of fast foods at the doorstep and limited physical activity are some of the contributing factors to obesity². Being obese or overweight puts a person at greater risk of developing cardiovascular diseases, hypertension, insulin resistance, diabetes, reproductive issues, liver and kidney diseases³.

Despite the growing global prevalence of obesity, there is always a group that is highly obsessed with dieting. The global interest in dieting has increased in the last two decades. A study indicated that internet searches related to weight loss queries had immensely increased between the years 2004 to 2018⁴. In the meantime, people rush toward certain fad diets (FD), assuming them as a magic bullet for their long-term problems. FD is not a scientific terminology but rather a popular or trendy dietary pattern that is known to be a quick fix for obesity⁵.

According to the study, Fad Diets can be easily differentiated from a healthy and balanced diet based on its characteristics features:

1. *Promises of rapid weight loss*
2. *Absence of physical activity guidelines*
3. *Promotes short-term changes rather than achieving lifelong sustainable goals*
4. *Focuses on one type of food or eliminates any food group*
5. *Cannot be maintained for life long period*
6. *Nutritional adequacy is questionable*
7. *Fails to provide health warnings for those with chronic diseases*
8. *Lacks scientific evidence to support the claims⁶.*

¹ World Health Organization [WHO]. WHO Obesity and Overweight. (2021). Available online at: <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight/> (Accessed September 12, 2021).

² Wright SM, Aronne LJ. Causes of obesity. *Abdom Imaging*. (2012) 37:730–2. 10.1007/s00261-012-9862-x

³ Uzogara SG. Obesity epidemic, medical and quality of life consequences: a review. *Int J Public Health Res*. (2017) 5:1–12.

⁴ Teng Y, Huang S, Li Z, Xie Q, Zhang M, Lou Q, et al. Seasonal variation and trends in the internet searches for losing weight: an epidemiological study. *Obes Res Clin Pract*. (2020) 14:225–33. 10.1016/j.orcp.2020.04.001

⁵ Gui G. Fad diets, fats & weight management. *Singapore Fam Physician*. (2008) 34:14–9.

⁶ Bastin S. *Fad Diets*. Lexington, KY: University of Kentucky; (2004).

Aim of the study:

A wide range of FDs has been proposed to date, ranging from low carbohydrate diets to low-fat diets, high-fats to high-protein diets, those with detoxification claims, and others of Mediterranean or Paleolithic origin. These diets are followed blindly but are associated with certain negative health outcomes as one size does not fit all. This review article will explore the current evidence related to the health impacts of some popular diets, including Atkins diet, ketogenic diet, Paleolithic diet, Mediterranean diet, vegetarian diet, intermittent fasting, and detox diet.

Atkins Diet (AD)

In the 1970s, a low carbohydrate, high protein (LCHP) regimen was developed by cardiologist Dr. Robert Atkins, which was published in his book “Dr. Atkins’ New Diet Revolution”⁷. This diet was promoted as a quick weight loss plan based on a lifetime change in eating habits. Atkins believed that metabolic imbalance resulting from carbohydrate consumption is the major cause of obesity. He claimed that this is the easiest, high-energy diet that mobilizes fats more than any other diet for weight loss maintenance. The AD involves an extreme reduction of carbohydrates, i.e., less than 5% of total calorie intake, ad libitum intake of proteins and fats, adequate fluid intake with vitamin and mineral supplementation, and regular exercise⁸.

AD Effectiveness

According to this research, there is substantial evidence suggesting that the Atkins Diet promotes more weight loss than conventional diets. One of the first AD research was published in The New England Journal of Medicine in 2003. Brehm et al.⁹ in a study allocated 53 healthy, obese women to two groups, i.e., low carbohydrate ketogenic diet (LCKD) or energy-restricted low-fat diet (LFD) (carbs: 55%, protein: 15%, fats: 30%). Over 6 months, the LCKD subjects lost 8.5 kg versus 4.2 kg in the LFD group.

In another randomized trial, 132 severely obese individuals (43% had metabolic syndrome while 39% had type 2 diabetes) were assigned to two groups. One group followed AD and the other followed LFD for 6 months. The results showed that LCD individuals lost 3.8 kg more weight than those on LFD. No significant difference was observed in both groups after 12 months¹⁰.

⁷ In the 1970s, a low carbohydrate, high protein (LCHP) regimen was developed by cardiologist Dr. Robert Atkins, which was published in his book “Dr. Atkins’ New Diet Revolution”.

⁸ Apovian C, Brouillard E, Young L. Clinical Guide to Popular Diets. New York: CRC Press; (2018).

⁹ Brehm BJ, Seeley RJ, Daniels SR, D’alessio DAA. Randomized trial comparing a very low carbohydrate diet and a calorie-restricted low fat diet on body weight and cardiovascular risk factors in healthy women. J Clin Endocrinol Metab. (2003) 88:1617–23. 10.1210/jc.2002-021480

¹⁰ Samaha FF, Iqbal N, Seshadri P, Chicano KL, Daily DA, McGrory J, et al. Low-carbohydrate as compared with a low-fat diet in severe obesity. N Engl J Med. (2003) 348:2074–81. 10.1056/NEJMoa022637

Several meta-analyses and systemic reviews reported the promising effects of low carbohydrate diets on weight loss and cardiometabolic risk factors. Mansoor et al.¹¹ demonstrated that the LCD group ...had a greater weight loss and TG reduction in contrast to those following LFD. Hashimoto et al.¹² reported that LCD resulted in a greater reduction of body weight and body fat mass than the control diet. LCD was linked with moderately more significant advancement in weight loss... compared to LFD¹³.

Naude et al.¹⁴ concluded that both LCD and balanced diets had shown weight loss. After 2 years of follow-up, there was no significant difference between the diets in terms of cardiovascular and diabetes risk factors. Bueno et al.¹⁵ found that after 12 months or more, the individuals that followed an energy-restricted very low carbohydrate diet (VLCD) (carbs: <50 g/day or 10%) compared to LFD (fats: <30%) had a more significant improvement in HDL-c, LDL-c, TG and diastolic blood pressure (DBP) as well as the reduction in body weight. Hu et al.¹⁶ compared LCD and LFD and concluded that both diets were efficient at reducing waist circumference, body weight, total cholesterol (TC), total to HDL-c ratio, LDL-c, TG, blood glucose, serum insulin, and blood pressure. LCD showed a greater decrease in TG, and less reduction in LDL-c and TC but increased HDL-c in comparison with LFD.

Problems with AD

Atkins diet has not been extensively studied while those studies that have been mentioned earlier have high dropout rates and are sometimes non-conclusive. Despite the rapid weight reduction, there are some concerns for those with comorbidities. There are some considerable potential complications associated with LCHP diets. There is conflicting evidence on the urinary stone formation tendency of LCHP diets¹⁷. A short-term study showed that healthy subjects followed the LCHP diet for 6 weeks, decreased urine pH, increased urinary-acid excretion, and decreased calcium balance was observed in them. Therefore, they had a greater risk of stone

¹¹ Mansoor N, Vinknes KJ, Veierød MB, Retterstøl K. Effects of low-carbohydrate diets v. low-fat diets on body weight and cardiovascular risk factors: a meta-analysis of randomized controlled trials. *Br J Nutr.* (2016) 115:466–79. 10.1017/S0007114515004699

¹² Hashimoto Y, Fukuda T, Oyabu C, Tanaka M, Asano M, Yamazaki M, et al. Impact of low-carbohydrate diet on body composition: meta-analysis of randomized controlled studies. *Obes Rev.* (2016) 17:499–509. 10.1111/obr.12405

¹³ Sackner-bernstein J, Kanter D, Kaul S. Dietary intervention for overweight and obese adults: comparison of low-carbohydrate and low-fat diets. A meta-analysis. *PLoS One.* (2015) 10:e0139817. 10.1371/journal.pone.0139817

¹⁴ Naude CE, Schoonees A, Senekal M, Young T, Garner P, Volmink J. Low carbohydrate versus isoenergetic balanced diets for reducing weight and cardiovascular risk: a systematic review and meta-analysis. *PLoS One.* (2014) 9:e100552. 10.1371/journal.pone.0100652

¹⁵ Bueno NB, de Melo SIV, De Oliveira SL, da Rocha Ataíde T. Very-low-carbohydrate ketogenic diet v. low-fat diet for long-term weight loss: a meta-analysis of randomized controlled trials. *Br J Nutr.* (2013) 110:1178–87. 10.1017/S0007114513000548

¹⁶ Hu T, Mills KT, Yao L, Demanelis K, Eloustaz M, Yancy WS, et al. Systematic reviews and meta- and pooled analyses effects of low-carbohydrate diets versus low-fat diets on metabolic risk factors: a meta-analysis of randomized controlled clinical trials. *Am J Epidemiol.* (2012) 176:S44–54. 10.1093/aje/kws264

¹⁷ Nouvenne A, Ticinesi A, Morelli I, Guida L, Borghi L, Meschi T. Fad diets and their effect on urinary stone formation. *Transl Androl Urol.* (2014) 3:303–12. 10.3978/j.issn.2223-4683.2014.06.01

formation¹⁸. A prospective cohort study was conducted in Iran, involving 1,797 participants that were followed up for almost 6 years. Results showed that a higher tertile of LCHP diet correlates with a greater risk of chronic kidney disease (CKD)¹⁹.

Metabolic acidosis is a common complication of LCHP diets. A case of 40 years old obese woman was reported, who was presented with nausea, vomiting, dehydration, and dyspnea. Investigations revealed that she was following AD, lost 9 kg in 1 month, and laboratory findings were consistent with ketoacidosis Chen et al.²⁰. Pregnant and lactating mothers should be cautious when following such a diet as there is a reported case of LCD-associated ketoacidosis in a non-diabetic lactating mother²¹. AD provides several benefits including weight reduction and cardio-metabolic health improvement, but limited evidence exists as compliance is the major barrier to this dietary regimen. Strict supervision by health professionals is advised as adverse metabolic sequelae can result from this type of diet.

Ketogenic Diet (KD)

In 1923, Dr. Russell Wilder designed the classic KD for the treatment of epilepsy. Also known as the “keto diet”, the classic keto is a strict regime of a 4:1 ratio, which means one part of carbs and proteins combined for four parts of fats. The use of KD for treating different diseases has increased over the past few decades. All the currently available versions are modified forms of classic KD. There are five types of KD published in the medical literature:

1. Classic Keto
2. Modified Keto
3. Medium-Chain triglycerides oil
4. Low glycemic index treatment
5. Modified Atkins diet

The macronutrient ratio is the major difference between these diets. In a nutshell, KD is a VLCD (Very-low carbohydrate diet) that relies on a moderate amount of proteins, high fat, and low carbohydrates that provide approximately 5–10% of calories from carbohydrates, 20–25% of

¹⁸ Reddy ST, Wang C, Sakhaee K, Brinkley L, Pak CYC. Effect of low-carbohydrate high-protein diets on acid-base balance, stone-forming propensity, and calcium metabolism. *Am J Kidney Dis.* (2002) 40:265–74. 10.1053/ajkd.2002.34504

¹⁹ Farhadnejad H, Asghari G, Emamat H, Mirmiran P, Azizi F. Low-carbohydrate high-protein diet is associated with increased risk of incident chronic kidney diseases among Tehranian adults. *J Ren Nutr.* (2018) 29:343–9. 10.1053/j.jrn.2018.10.007

²⁰ Chen T, Smith W, Rosenstock JL, Lessnau KA. Life-threatening complication of atkins diet. *Lancet.* (2006) 367:958. 10.1016/S0140-6736(06)68394-3

²¹ von Geijer L, Ekelund M. Ketoacidosis associated with low-carbohydrate diet in a non-diabetic lactating woman: a case report. *J Med Case Rep.* (2015) 9:224–6. 10.1186/s13256-015-0709-2

calories from proteins, and 65–80% of calories from fats²². KD includes fasting, proper hydration, physical activity, and intake of electrolytes and nutritional supplements²³.

The KD works by bringing certain metabolic changes to the body. Glucose is the body's primary energy source. Carbohydrate deprivation resulting from KD causes a metabolic shift toward gluconeogenesis and ketogenesis. The preliminary shortage is managed by endogenous production of glucose from glycerol, glutamine, alanine, and lactic acid (gluconeogenesis). To keep up with the needs of the body, ketone bodies come into play and serve as an alternate energy source for the body (ketogenesis). At this stage due to low blood glucose feedback, secretion of insulin is also low, which further reduces the stimulus for fat and glucose storage. This ketotic state remains active until the body's carbohydrates needs are fulfilled²⁴.

Effectiveness of Ketogenic Diet

KD is known for its neuroprotective action in various neurological illnesses like Alzheimer's disease, amyotrophic lateral sclerosis, Parkinson's disease, ischemic brain injury, traumatic brain injury, depression, autism, and narcolepsy²⁵. In the modern era, KD is recognized as a weight loss intervention but studies suggest mixed findings. A study compared the weight loss, appetite, and hunger responses of obese men who were fed a medium carbohydrate (35%) non-ketogenic diet (MCNKD) and low carbohydrates (4%) ketogenic diet (LCKD) in a crossover manner. After 4 weeks period, significantly greater weight loss and lower ad libitum energy intake were observed in the LCKD group because of reduced hunger²⁶.

A meta-analysis concluded that KD contributes to greater long-term weight loss than LFD²⁷. Another study compared the impact of KD and hypocaloric diet (HCD, also known as low-calorie diet) on metabolic parameters in obese subjects. Fifty-eight subjects followed either of the two diets for 6 months. Greater differences in fat mass, weight, waist circumference, and fasting insulin were observed in the KD group as compared to the HCD group... The mechanism behind successful weight loss by KD is still a scientific debate. However, certain mechanisms have been hypothesized including appetite reduction due to the action of appetite-regulating hormones, fulfilling the effect of proteins, or appetite suppressing effect of ketone bodies

²² Gershuni VM, Yan SL, Medici V. Nutritional ketosis for weight management and reversal of metabolic syndrome. *Curr Nutr Rep.* (2018) 7:97–106. 10.1007/s13668-018-0235-0

²³ Neal EG, Zupec-kania B, Pfeifer HH. Carnitine, nutritional supplementation and discontinuation of ketogenic diet therapies. *Epilepsy Res.* (2012) 100:267–71. 10.1016/j.epilepsyres.2012.04.021

²⁴ Dąbek A, Wojtala M, Pirola L, Balcerczyk A. Modulation of cellular biochemistry, epigenetics and metabolomics by ketone bodies. implications of the ketogenic diet in the physiology of the organism and pathological states. *Nutrients.* (2020) 12:788–801. 10.3390/nu12030788

²⁵ Stafstrom CE, Rho JM. The ketogenic diet as a treatment paradigm for diverse neurological disorders. *Front Pharmacol.* (2012) 3:59. 10.3389/fphar.2012.00059

²⁶ Johnstone AM, Horgan GW, Murison SD, Bremner DM, Lobley GE. Effects of a high-protein ketogenic diet on hunger, appetite, and weight loss in obese men feeding ad libitum. *Am J Clin Nutr.* (2008) 87:44–55. 10.1093/ajcn/87.1.44

²⁷ Johnstone AM, Horgan GW, Murison SD, Bremner DM, Lobley GE. Effects of a high-protein ketogenic diet on hunger, appetite, and weight loss in obese men feeding ad libitum. *Am J Clin Nutr.* (2008) 87:44–55. 10.1093/ajcn/87.1.44

(^{28, 29, 30, 31}). Weight loss can also be due to the increase in lipolysis, reduction in lipogenesis, and ease in utilizing fats due to the increased metabolic efficiency as indicated by a reduction in the respiratory quotient at rest (^{32, 33, 34, 35}). The KD group lost 10–15% of body weight, had a reduction in inflammatory markers like hsCRP, decreased WBCs, and increased TGs, HDL-c, and LDL-c³⁶. A recent review summarized that despite the efficacy of KD for rapid weight reduction and improved HbA1c values, KD raise LDL-c and had no superiority over other diets in terms of safety, effectivity, and sustainability³⁷.

Problems with Ketogenic Diet

Short-term minor side effects of KD are quite common, that include vomiting, nausea, gastrointestinal discomfort, fatigue, dizziness, feeling faint, decreased energy, and heartbeat alterations³⁸. KD initiation mostly results in hypoglycemia and lethargy³⁹. KD should be initiated with caution in combination with other treatments. A case report showed that the use of Valproate along with KD resulted in the development of hepatic dysfunction in a patient. The hepatotoxic effect was completely reversible as discontinuation of Valproate normalized the liver enzymes⁴⁰. A recent case report demonstrated KD induced severe hyperlipidemia in an

²⁸ Veldhorst M, Smeets A, Soenen S, Hochstenbach-Waelen A, Hursel R, Diepvens K, et al. Protein-induced satiety: effects and mechanisms of different proteins. *Physiol Behav.* (2008) 94:300–7. 10.1016/j.physbeh.2008.01.003

²⁹ Westerterp-Plantenga MS, Nieuwenhuizen A, Tome D, Soenen S, Westerterp KR. Dietary protein, weight loss, and weight maintenance. *Annu Rev Nutr.* (2009) 29:21–41. 10.1146/annurev-nutr-080508-141056

³⁰ Sumithran P, Prendergast LA, Delbridge E, Purcell K, Shulkes A, Kriketos A, et al. Ketosis and appetite-mediating nutrients and hormones after weight loss. *Eur J Clin Nutr.* (2013) 67:759–64. 10.1038/ejcn.2013.90

³¹ Cahill GF. Fuel metabolism in starvation. *Annu Rev Nutr.* (2006) 26:1–22. 10.1146/annurev-nutr.26.061505.111258

³² Veldhorst MA, Westerterp-plantenga MS, Westerterp KR. Gluconeogenesis and energy expenditure after a high-protein, carbohydrate-free diet. *Am J Clin Nutr.* (2009) 90:519–26. 10.3945/ajcn.2009.27834.1

³³ Paoli A, Cenci L, Fancelli M, Parmagnani A, Fratter A, Cucchi A, et al. Ketogenic diet and phytoextracts comparison of the efficacy of mediterranean, zone and Tisanoreica diet on some health risk factors. *Agro Food Ind Hi Tech.* (2010) 21:24–9.

³⁴ Paoli A, Grimaldi K, Bianco A, Lodi A, Cenci L, Parmagnani A. Medium term effects of a ketogenic diet and a mediterranean diet on resting energy expenditure and respiratory ratio. *BMC Proc.* (2012) 6:37. 10.1186/1753-6561-6-S3-P37

³⁵ Tagliabue A, Bertoli S, Trentani C, Borrelli P, Veggiotti P. Effects of the ketogenic diet on nutritional status, resting energy expenditure, and substrate oxidation in patients with medically refractory epilepsy: a 6-month prospective observational study. *Clin Nutr.* (2012) 31:246–9. 10.1016/j.clnu.2011.09.012

³⁶ Hallberg SJ, Mckenzie AL, Williams PT, Bhanpuri NH, Peters AL, Campbell WW, et al. Effectiveness and safety of a novel care model for the management of type 2 diabetes at 1 year: an open-label, non-randomized, controlled study. *Diabetes Ther.* (2018) 9:583–612. 10.1007/s13300-018-0373-9

³⁷ O'Neill B, Raggi P. The ketogenic diet: pros and cons. *Atherosclerosis.* (2020) 292:119–26. 10.1016/j.atherosclerosis.2019.11.021

³⁸ Bostock ECS, Kirkby KC, Taylor BV, Hawrelak JA. Consumer reports of “Keto Flu” associated with the ketogenic diet. *Front Nutr.* (2020) 7:20. 10.3389/fnut.2020.00020

³⁹ Lin A, Turner Z, Doerr SC, Stanfield A, Kossoff EH. Complications during ketogenic diet initiation: prevalence, treatment and influence on seizure outcomes. *Pediatr Neurol.* (2017) 68:35–9. 10.1016/j.pediatrneurol.2017.01.007

⁴⁰ Stevens CE, Turner Z, Kossoff EH. Hepatic dysfunction as a complication of combined valproate and ketogenic diet. *Pediatr Neurol.* (2016) 54:82–4. 10.1016/j.pediatrneurol.2015.10.006

overweight 41 year old male. In increasing his carbohydrate intake for 2 weeks, his blood lipid panel showed a big improvement:⁴¹ A retrospective cohort study showed that those on KD therapy had low normal bone mineral density, 8.8% of study subjects got kidney stones and 8.8% got a fracture during treatment⁴². A newly recognized complication of KD is hypercalcemia. A series of case studies described the development of acute hypercalcemia about 2.1 years after initiating KD. Out of 14 patients, 13 had low levels of 1, 25-dihydroxyvitamin D, while all had low parathyroid hormone levels. Moreover, low alkaline phosphate (ALP) levels were noted in all subjects except the two oldest, while seven had impaired renal function⁴³.

Paleolithic Diet (PD)

Also known as the “paleo diet” The PD also referred to as the Stone Age, caveman, or hunter-gatherer diet was initially introduced in 1985 by Eaton and Konner, and published by Dr. Loren Cordain in 2010⁴⁴. It is marketed with the claims to improve health and cure diseases like obesity, cardiovascular disease, diabetes, cancer, and osteoporosis. Proponents of this dietary pattern believe that the modern diet (mainly processed foods, dairy products, grains, and legumes) is the cause of modern diseases and the obesity epidemic. Moreover, humans have evolved before agricultural development while the human diet has revolutionized more rapidly than our genetics; thus Paleolithic foods are more suited to our genetic makeup than the current modern diet (⁴⁴, ⁴⁵). Apart from this theory, anthropological research provides evidence that Paleolithic people used to eat a varied diet comprising of plants, grains, legumes, and game meats (⁴⁶, ⁴⁷).

Cordain’s PD has a basic set of rules, i.e., there is no restriction on the consumption of lean meats, fruits, and non-starchy vegetables while dairy products, legumes, cereals, and processed foods are strictly restricted. There is little to no focus on portions, and calories. There are three adherence levels to the PD: entry-level, maintenance level, and maximal weight loss level (Table 3). One has a choice not to advance to the next level if satisfied with the results of this level⁴⁴.

<p>Table 2: Foods in the Paleolithic Diet</p>
--

⁴¹ Swaid B. Severe hyperlipidemia with LDL cholesterol of 393 Milligrams per decilitre after 7 months of high fat ketogenic diet: a rare case report. J Endocr Soc. (2021) 5:A37–8. 10.1210/jendso/bvab048

⁴² Draaisma JMT, Hampsink BM, Janssen M, van Houdt NBM, Linders ETAM, Willemsen MA. The ketogenic diet and its effect on bone mineral density: a retrospective observational cohort study. Neuropediatrics. (2019) 50:353–8. 10.1055/s-0039-1693059

⁴³ Hawkes CP, Roy SM, Dekelbab B, Frazier B, Grover M, Haidet J, et al. hypercalcemia in children using the ketogenic diet: a multicenter study. J Clin Endocrinol Metab. (2021) 106:e485–95. 10.1210/clinem/dgaa759

⁴⁴ Cordain L. The Paleo Diet. Hoboken: John Wiley & Sons; (2010).

⁴⁵ Eaton SB, Konner MJ, Cordain L. Diet-dependent acid load, paleolithic nutrition, and evolutionary health promotion. Am J Clin Nutr. (2010) 91:295–7. 10.3945/ajcn.2009.29058.Am

⁴⁶ Katz SH, Weaver WW. Game. New York: Scribner; (2003).

⁴⁷ Eisenstein M. Evolution: the first supper. Nature. (2010) 468:S8–9. 10.1038/468S8a

Food groups	Foods allowed/ restricted	Reference
Lean Meat	<ul style="list-style-type: none"> About half of daily calories from lean animal foods are encouraged 	44
Eggs	<ul style="list-style-type: none"> 6-12 per week 	
Fruits	<ul style="list-style-type: none"> All fruits are allowed Obese should be mindful of calories from high-sugar fruits 	
Vegetables	<ul style="list-style-type: none"> All non-starchy vegetables are allowed 	
Drinks and beverages	<ul style="list-style-type: none"> Mainly water Sugary beverages should be avoided Limited consumption of alcoholic beverages (i.e. two 4-oz servings of wine, 12-oz serving of beer, or one 4-oz serving of spirits daily) No tea or coffee 	
Fats, oils and nuts	<ul style="list-style-type: none"> Unsaturated fats are allowed in moderation 4 Tbsp of oils per day 4 oz of nuts per day 	
Vitamin and mineral supplements	<ul style="list-style-type: none"> Can be taken as per needed 	

Table 3: Levels of Paleolithic Diet		
Levels	Description	Reference
Level 1: Entry Level	<ul style="list-style-type: none"> 3 open meals* / week Addition of some transitional foods for sake of improving compliance 	48
Level 2: Maintenance Level	<ul style="list-style-type: none"> 2 open meals / week No transitional foods allowed 	

⁴⁸ Apovian C, Brouillard E, Young L. Clinical Guide to Popular Diets. New York: CRC Press; (2018).

Level 3: Maximal	● 1 open meal/ week	
<p>*Open meal; flexible meals including foods from not avoid list, intended to improve the adherence to diet</p> <p>** transitional foods; foods items that don't meet Paleo rules</p>		

Effectiveness of Paleolithic Diet

Metabolic syndrome and insulin resistance are the prime focused areas in most of the literature related to PD. It does provide benefits but only to specific groups, i.e., eliminating dairy products can help people with digestive disorders. 'Liberal consumption of fruits and vegetables can have a preventive effect for inflammatory bowel diseases (IBD). At the same time, this diet being high in meat may increase the risk of IBD⁴⁹.

Paleolithic diet is powerful at advancing weight reduction for the time being, even at the point when the weight reduction is unintentional (^{50, 51, 52}). Initially, weight loss is due to the loss of water weight as this diet is low in carbohydrates. Previous studies suggest that the study participants lost 4–6% of total body weight within 10–12 weeks (^{53, 54}). Most of the studies are based on short-term interventions and there is only one study that followed the subjects for over 2 years. In a randomized trial, 70 postmenopausal obese women were divided into the ad libitum PD group or Nordic Nutrition Recommendations (NNR) diet group. After 24 months, the reductions in waist circumference, fat mass, and weight were observed in both groups irrespective of the dietary regimen followed⁵⁵.

⁴⁹ Hou JK, Abraham B, El-serag H. Dietary intake and risk of developing inflammatory bowel disease: a systematic review of the literature. *Am J Gastroenterol.* (2011) 106:563–73. 10.1038/ajg.2011.44

⁵⁰ Osterdahl M, Kocturk T, Koochek A, Wandell PE. Effects of a short-term intervention with a paleolithic diet in healthy volunteers. *Eur J Clin Nutr.* (2008) 62:682–5. 10.1038/sj.ejcn.1602790

⁵¹ Boers I, Muskiet FAJ, Berkelaar E, Schut E, Penders R, Hoenderdos K, et al. Favourable effects of consuming a palaeolithic-type diet on characteristics of the metabolic syndrome: a randomized controlled pilot-study. *Lipids Health Dis.* (2014) 13:160–72. 10.1186/1476-511X-13-160

⁵² Masharani U, Sherchan P, Schloetter M, Stratford S, Xiao A, Sebastian A, et al. Metabolic and physiologic effects from consuming a hunter-gatherer (paleolithic)-type diet in type 2 diabetes. *Eur J Clin Nutr.* (2015) 69:944–8. 10.1038/ejcn.2015.39

⁵³ Lindeberg S, Jönsson T, Granfeldt Y, Borgstrand E, Soffman J, Sjöström K, et al. Palaeolithic diet improves glucose tolerance more than a mediterranean-like diet in individuals with ischaemic heart disease. *Diabetologia.* (2007) 50:1795–807. 10.1007/s00125-007-0716-y

⁵⁴ Smith MM, Trexler ET, Sommer AJ, Starkoff BE, Devor ST. Unrestricted paleolithic diet is associated with unfavorable changes to blood lipids in healthy subjects. *Int J Exerc Sci.* (2014) 7:128–39.

⁵⁵ Mellberg C, Sandberg S, Ryberg M, Eriksson M, Brage S, Larsson C, et al. Long-term effects of a palaeolithic-type diet in obese postmenopausal women: a 2-year randomized trial. *Eur J Clin Nutr.* (2014) 68:350–7. 10.1038/ejcn.2013.290

Most of the studies reported the TC reduction properties of this diet while there are mixed results for HDL-c (^{51, 52, 54, 56}). A study was conducted to evaluate the physiological and metabolic impacts of PD in healthy adults. After 10 days of intervention, reduction in TC, LDL-c, TG, and mean arterial pressure were observed⁵⁶. In another trial, participants were randomized to PD and reference diet groups. After 2 weeks of intervention, there were greater reductions in TC, TG, and diastolic blood pressure in the PD group⁵¹.

In another study, healthy subjects followed this dietary intervention for 10 weeks, which resulted in increased LDL-c, TC, TC:HDL-c, along with a decline in HDL-c values⁵⁴. No significant changes in fasting blood glucose were seen in most studies (^{55, 56}). While, some studies were short-term, where HbA1c was not measured as per protocol⁵⁷. Modest reduction, i.e., 3–4 mmHg in systolic or diastolic blood pressure was reported in most studies (^{50, 51, 56, 57}). No significant change in inflammatory markers (CRP) was reported (^{51, 57}).

Problems with Paleoethic Diet

According to the researchers, the PD not only requires a big budget but is also very challenging to follow as compared to other diets (^{58, 59}). Despite weight reduction and some favorable impact on cardiometabolic profile, this diet can have long-term consequences. Some studies suggest that this diet is not nutritionally balanced as it discourages certain food groups like whole grains, legumes, and dairy products. The micronutrient deficiencies can have long-term adverse outcomes. Those who follow PD have inadequate calcium intake. A study was conducted to check the nutritional adequacy of this diet. In addition to a low intake of carbs, fats, and total calories that could have promoted weight loss, this diet provided about 50% less calcium than the daily requirement⁵⁰.

Decreased HDL-c has also been observed among healthy adults and those with comorbidities. In a study comprising 28 type 2 diabetic patients, 14 followed the PD and 10 followed the American Diabetes Association (ADA) guidelines. Results showed that there was a significant reduction in HDL-c in the PD group⁵². In another study, healthy subjects followed this dietary intervention for 10 weeks, which resulted in increased LDL-c, TC, TC:HDL-c, along with a decline in HDL-c values⁵⁴. More randomized trials need to be done to highlight the consequences of such diets that eliminate one or more food groups. PD is powerful at advancing weight reduction for the time being but its efficacy in cardiovascular events is not well established as limited long-term data is available.

⁵⁶ Frassetto LA, Schloetter M, Mietus-Synder M, Morris RC, Sebastian A. Metabolic and Physiologic Improvements from Consuming a Paleolithic, Hunter-Gatherer Type Diet. *Eur J Clin Nutr.* (2009) 63:947–55. 10.1038/ejcn.2009.4

⁵⁷ Jönsson T, Granfeldt Y, Åhrén B, Branell U-C, Pålsson G, Hansson A, et al. Beneficial effects of a paleolithic diet on cardiovascular risk factors in type 2 diabetes: a randomized cross-over pilot study. *Cardiovasc Diabetol.* (2009) 8:35–48. 10.1186/1475-2840-8-35

⁵⁸ Jönsson T, Granfeldt Y, Lindeberg S, Hallberg A. Subjective satiety and other experiences of a paleolithic diet compared to a diabetes diet in patients with Type 2 diabetes. *Nutr J.* (2013) 12:105–11. 10.1186/1475-2891-12-105

⁵⁹ Manheimer EW, Van Zuuren EJ, Fedorowicz Z, Pijl H. Paleolithic nutrition for metabolic syndrome: systematic review and meta-analysis. *Am J Clin Nutr.* (2015) 102:922–32. 10.3945/ajcn.115.113613.1

Mediterranean Diet (MD)

The concept of the MD emerged in the 1950s by Dr. Ancel Keys. In one of the first research that related diet and heart health, it was revealed that CVDs associated mortality rates are different in Westerners and Europeans. Lower mortality rates were observed in Europeans, even though they typically consume a moderately high-fat diet⁶⁰. Their dietary pattern can be linked to lower mortality and incidence of CVDs⁶¹.

In 1975, Ancel Keys described this diet in his book as a complex of dietary choices followed by those living in Mediterranean regions. Whole grains, legumes, fruits, vegetables, olive oil, fish, and nuts are key components of this diet with a moderate allowance of alcohol, dairy products, and meat⁶². Traditionally, this diet derives its most calories from fish and plant-based foods. Fats account for 30% of calories which are mostly polyunsaturated fatty acid (PUFA) and monounsaturated fatty acids (MUFA), while carbohydrates provide 50–55% of calories from low glycemic index carbohydrates and proteins provide 15–20% of calories⁶³.

Effectiveness of Mediterranean Diet

The Mediterranean diet is the most extensively studied diet to date. In a previous review, it has been summarized that MD is nutritionally adequate for the general public and may have the potential of preventing micronutrient deficiencies⁶⁴. Research shows that it has preventive and therapeutic potential for many chronic diseases like non-alcoholic fatty liver disease (NAFLD), CVDs, metabolic syndrome, and certain cancers like colorectal and breast cancer⁶⁵. In a 2-year trial, weight loss by LFD, AD, and MD was compared and results showed that the AD (Atkins diet) group had the highest mean weight loss, i.e., -4.7 ± 6.5 kg, while the MD group stood second with a mean weight loss of -4.4 ± 6 kg and LFD (low-fat diet) group lost -2.9 ± 4.2 kg. Following changes were recorded in the MD group: increased molecular adiponectin reduced serum leptin, and CRP levels (76⁶⁶).

In another controlled trial, 259 subjects were randomly allocated to the American Diabetic Association (ADA) diet, traditional MD, or low carbohydrate Mediterranean diet (LCM) group.

⁶⁰ Keys A, Grande F. Role of dietary fat in human nutrition. *Am J Public Health.* (1957) 47:1520–30. 10.2105/ajph.47.12.1530

⁶¹ Martinez-Gonzalez MA, Sanchez-Villegas A. The emerging role of mediterranean diets in cardiovascular epidemiology: monounsaturated fats, olive oil, red wine or the whole pattern? *Eur J Epidemiol.* (2004) 19:9–13. 10.1023/b:ejep.0000013351.60227.7b

⁶² Keys AB. *How to Eat Well and Stay Well the Mediterranean Way.* New York, NY: Doubleday; (1975).

⁶³ Kromhout D, Keys A, Aravanis C, Buzina R, Fidanza F, Giampaoli S, et al. Food Consumption Patterns in the 1960s in Seven Countries. *Am J Clin Nutr.* (1989) 49:889–94. 10.1093/ajcn/49.5.889

⁶⁴ Castro-Quezada I, Román-Viñas B, Serra-Majem L. The mediterranean diet and nutritional adequacy: a review. *Nutrients.* (2014) 6:231–48. 10.3390/nu6010231

⁶⁵ Romagnolo DF, Selmin OI. Mediterranean diet and prevention of chronic diseases. *Nutr Today.* (2017) 52:208–22. 10.1097/NT.0000000000000228

⁶⁶ Shai I, Schwarzfuchs D, Henkin Y, Shahar DR, Witkow S, Greenberg I, et al. Weight loss with a low-carbohydrate, mediterranean, or low-fat diet. *N Engl J Med.* (2008) 359:229–41. 10.1056/NEJMoa0708681

After 12 months, the LCM group had the highest weight reduction, increased HDL-c, improved LDL-c, TG and HbA1c (77). Another study described the effectiveness of MD in the primary prevention of CVDs [Estruch et al. (78)]. A study investigated the protective effect of MD against cancer and found that greater compliance with MD patterns reduces the risk of non-tobacco linked cancers in both men and women (79).

Most MD studies are short-duration studies, only a few studies focused on the long-term impacts of following MD. In a study, non-diabetic elderly subjects (n = 3,541) at higher risk of CVD were randomized to three intervention groups: control diet, MD with nuts or MD with extra virgin olive oil. New cases of diabetes were recorded after regular intervals (median follow-up duration = 4.1 years) and results showed that MD with extra virgin olive oil was associated with a reduced risk of diabetes (80). In another 5 years clinical trial, subjects (n = 7,447) who were type 2 diabetics or those with risk factors of CVDs, were randomized to three intervention groups: control diet, MD with nuts, or MD with extra virgin olive oil. After the specified period, there was no significant weight reduction in all the groups, while the MD group had a significant reduction in central obesity [Estruch et al. (81)].

Problems with Mediterranean Diet

No evidence of adverse effects associated with MD is available in the literature. Rather, MD has preventive and therapeutic potential for many chronic diseases. It is highly suitable for the general public for the prevention of micronutrient deficiencies and specifically for those patients who are more health-conscious than just weight loss oriented.

Vegetarian Diet (VD)

The VD is a dietary pattern characterized by no consumption of meat and meat products, seafood, poultry, and sometimes other animal products like eggs, animal milk, and honey. Some studies have linked meat intake with an increased risk of chronic diseases, while others indicate a positive association between low meat intake and life expectancy (^{67, 68}). VD are of four main types:

1. *Lacto-ovo-vegetarian*: does not consume any meat product but consumes eggs and dairy products.
2. *Lactovegetarian*: does take dairy products but does not consume eggs and meat products.
3. *Ovo-vegetarian*: does not eat meat products and dairy products and is free to consume eggs.

⁶⁷ Singh PN, Sabaté J, Fraser GE. Does low meat consumption increase life expectancy in humans? Am J Clin Nutr. (2003) 78:S526–32. 10.1093/ajcn/78.3.526S

⁶⁸ Sinha R, Cross AJ, Graubard BI, Leitzmann MF, Schatzkin A. Meat intake and mortality: a prospective study of over half a million people. Arch Intern Med. (2009) 169:562–71. 10.1001/archinternmed.2009.6.Meat

4. *Vegan*: does not consume any animal products, including meat, eggs, dairy products, and honey⁶⁹.

Vegan diets include different subtypes: raw vegan, vegan (general), and whole-food vegan. Each subtype has its own set of foods allowed and restricted with one thing in common, i.e., meat products restriction. This dietary pattern is gaining much popularity in the general population, especially in the Western world ⁷⁰. There are various reasons for adopting this dietary profile, including religious beliefs, ethical motivation, cultural aspects, and health considerations (^{70, 71}).

Effectiveness of Vegetarian Diet

Several epidemiological studies reported a lower cardiometabolic risk in the vegan population. A study concluded that non-vegetarians have a higher type 2 diabetes prevalence (7.6%) than vegetarians (2.9%). While the prevalence rate also varies with the type of VD, i.e., 3.2% in lacto-ovo vegetarians, 4.8% in pesco-vegetarians and 6.1% in semi-vegetarians. This can be explained by the low-glycemic-response associated with these diets as vegetarian diets typically include foods that have a low glycemic index such as beans, legumes, nuts, some fruits and vegetables⁷². Glycemic control via a VD is quite controversial, as these are high carbohydrate diets. Some studies have shown that vegetarians also have increased life expectancy⁶⁷. Generally, vegetarians are more health-conscious and have lower BMI than the general population⁷³. The Seventh Day Adventist study showed a lower mean BMI, i.e., 23.6 kg/m² in the vegan population⁷⁴. In a 5-year prospective study, 22,000 subjects having different dietary patterns were checked for their weight gain during this period. Vegans had the lowest weight gain as compared to meat-eaters and fish eaters⁷⁵.

Red meat and poultry intake were most strongly linked to increased risk of esophageal adenocarcinoma and gastric cardia or non-cardia adenocarcinoma, respectively⁷⁶. On the other

⁶⁹ Marsh K, Zeuschner C, Saunders A. Health implications of a vegetarian diet: a review. *Am J Lifestyle Med.* (2012) 6:250–67. 10.1177/1559827611425762

⁷⁰ Leitzmann C. Vegetarian nutrition: past, present, future. *Am J Clin Nutr.* (2014) 100:S496–502. 10.3945/ajcn.113.071365.496S

⁷¹ Craig WJ. Health effects of vegan diets. *Am J Clin Nutr.* (2009) 89:S1627–33. 10.3945/ajcn.2009.26736N

⁷² Tonstad S, Yan R, Butler T, Fraser GE. Type of vegetarian diet, body weight, and prevalence of type 2 diabetes. *Diabetes Care.* (2009) 32:791–6. 10.2337/dc08-1886

⁷³ Bedford JL, Barr SI. Diets and selected lifestyle practices of self-defined adult vegetarians from a population-based sample suggest they are more “health conscious”. *Int J Behav Nutr Phys Act.* (2005) 2:4–14. 10.1186/1479-5868-2-4

⁷⁴ Roberts SB, Urban LE, Das SK. Effects of dietary factors on energy regulation: consideration of multiple- versus single-dietary-factor models. *Physiol Behav.* (2014) 134:15–9. 10.1016/j.physbeh.2014.04.024

⁷⁵ Rosell M, Appleby P, Spencer E, Key T. Weight gain over 5 years in 21966 meat-eating, fish-eating, vegetarian, and vegan men and women in EPIC-Oxford. *Int J Obes.* (2006) 30:1389–96. 10.1038/sj.ijo.0803305

⁷⁶ Silvera SAN, Mayne ST, Risch H, Gammon MD, Vaughan TL, Chow W-H, et al. Food group intake and risk of subtypes of esophageal and gastric cancer. *Int J Cancer.* (2008) 123:852–60. 10.1002/ijc.23544

hand, lower rates of heart diseases and cancers have been observed in vegetarians in comparison with those following other dietary patterns (^{77, 78}). A better cardiometabolic risk profile is generally present in vegetarians, i.e., lower BMI, TC, and LDL-c [Chen et al.⁷⁹; De Biase et al.⁸⁰]. A cross-sectional study investigated the lipid profile of fish-eaters, meat-eaters, and vegetarians. Not only the vegans have a lower BMI but also favorable serum lipid levels: lower LDL-c, TC, and apolipoproteins⁸¹.

In a study, out of 26,346 participants, 1,079 cases of prostate cancer were identified and results showed the protective effect of vegan diets against prostate cancer in the white population⁸². This protective effect against prostate cancer may be due to the higher fiber intake. Some other studies are either short-term or have a very small sample size, showing mixed findings related to colorectal cancer and breast cancer. In a study, 2,304 patients from 10 European countries were assessed for their dietary intake to find the impact of diet on the risk of cancers. Not poultry but red meat intake was found to be associated with an increased risk of esophageal cancer and upper aerodigestive tract (UADT) cancer. Furthermore, vegetable and fruit intake are significantly associated with a reduced risk of UADT cancer⁸³.

Another study showed a significant association between consumption of vegetables and risk of esophageal adenocarcinoma. Elimination of potentially harmful dietary components like animal protein, saturated fats, and cholesterol can be the reason for these benefits. These benefits can also be due to the addition of dietary fiber, phytochemicals, and antioxidants rich in beneficial dietary components like whole grains, legumes, nuts, fruits, and vegetables⁸⁴.

Problems with Vegetarian Diet

This diet is associated with fluctuations in micronutrients intake because of the day-to-day variation in the menu. Depending upon the type of VD, vegetarians are potentially at increased risk of micronutrient deficiencies such as calcium, zinc, iron, vitamin E, vitamin B12, essential

⁷⁷ Bosetti C, Negri E, Franceschi S, Pelucchi C, Talamini R, La Montelle M, et al. Diet and ovarian cancer risk: a case-control study in Italy. *Int J Cancer*. (2001) 93:911–5. 10.1002/ijc.1422

⁷⁸ Norat T, Bingham S, Ferrari P, Slimani N, Jenab M, Mazuir M, et al. Meat, fish, and colorectal cancer risk: the European prospective investigation into cancer and nutrition. *J Natl Cancer Inst*. (2005) 97:906–16. 10.1093/jnci/dji164

⁷⁹ Chen CW, Lin YL, Lin TK, Lin CT, Chen BC, Lin CL. Total cardiovascular risk profile of taiwanese vegetarians. *Eur J Clin Nutr*. (2008) 62:138–44. 10.1038/sj.ejcn.1602689

⁸⁰ de Biase SG, Fernandes SFC, Gianini RJ, Duarte JLG. Vegetarian diet and cholesterol and triglycerides levels. *Arq Bras Cardiol*. (2007) 88:32–6. 10.1590/S0066-782X2007000100006

⁸¹ Bradbury KE, Crowe FL, Appleby PN, Schmidt JA, Travis RC, Key TJ. Serum concentrations of cholesterol, apolipoprotein A-I and apolipoprotein B in a total of 1694 meat-eaters, fish-eaters, vegetarians and vegans. *Eur J Clin Nutr*. (2014) 68:178–83. 10.1038/ejcn.2013.248

⁸² Cross AJ, Ferrucci LM, Risch A, Graubard BI, Ward MH, Park Y, et al. Large prospective study of meat consumption and colorectal cancer risk: an investigation of potential mechanisms underlying this association. *Cancer Res*. (2010) 70:2406–14. 10.1158/0008-5472.CAN-09-3929.A

⁸³ Lagiou P, Talamini R, Samoli E, Lagiou A, Ahrens W, Pohlabein H, et al. Diet and upper-aerodigestive tract cancer in Europe: the ARCAGE study. *Int J Cancer*. (2009) 124:2671–6. 10.1002/ijc.24246

⁸⁴ Silvera SAN, Mayne ST, Risch H, Gammon MD, Vaughan TL, Chow W-H, et al. Food group intake and risk of subtypes of esophageal and gastric cancer. *Int J Cancer*. (2008) 123:852–60. 10.1002/ijc.23544

fatty acids, docosahexaenoic acid (DHA), and eicosapentaenoic acid (EPA)⁸⁵. A study reported that half of the vegan participants were micronutrient deficient as compared to omnivores⁸⁶. Vegetarians have lower serum vitamin B12 levels as plant sources are deficient in this vitamin (^{86, 87}). As VD is generally low in calcium due to the suboptimal intake of dairy, vegetarians are at greater risk of bone fractures due to the lower bone mineral density⁸⁸.

Thus supplementation of certain vitamins like vitamin B12 and vitamin D is needed to avoid these deficiencies among vegetarians⁸⁹. VD can be nutritionally adequate, so it may be helpful in chronic disease prevention and treatment. Benefits and harms depend upon the dietary choices so the individualized plan fulfilling the micronutrient requirements must be carefully developed by a professional.

Intermittent Fasting (IF)

The IF is gaining much popularity and is widely adopted as an effective weight loss intervention. Contrary to the conventional weight loss programs that are based on calorie restriction, IF is more about scheduled eating. Some of the key features of IF are abstinence from food for a certain period, followed by a period of normal eating. There are various versions of IF but the most popular of these are alternate day fasting (ADF), 5:2 diet or periodic fasting (PF), and time-restricted feeding (TRF). The frequency and duration of fast cycles may differ among all types (Table 4).

Table 4: Types of Intermittent Fasting				
Types	Description	Fasting Definition	Normal Eating	Reference
Alternate day fasting	<ul style="list-style-type: none"> Fasting alternated with a day of normal eating 	<ul style="list-style-type: none"> 0-25% of total caloric needs 	<ul style="list-style-type: none"> <i>Ad libitum</i> 	⁸⁹
5:2 diet or periodic fasting	<ul style="list-style-type: none"> Fasting for 2 days with normal eating for 5 days 	<ul style="list-style-type: none"> 0-25% of total caloric needs 	<ul style="list-style-type: none"> <i>Ad libitum</i> 	
Time-restricted feeding	<ul style="list-style-type: none"> Normal eating within a 	–	<ul style="list-style-type: none"> <i>Ad libitum</i> 	

⁸⁵ Craig W.J., Mangels A.R. Position of the American dietetic association: vegetarian diets. J Am Diet Assoc. (2009) 109:1266–82. 10.1016/j.jada.2009.05.027

⁸⁶ Gilsing A.M.J., Crowe F.L., Lloyd-Wright Z., Sanders T.A.B., Appleby P.N., Allen N.E., Key T.J. Serum concentrations of vitamin B12 and folate in British male omnivores, vegetarians, and vegans: results from a cross-sectional analysis of the EPIC-oxford cohort study. Eur J Clin Nutr. (2011) 64:933–9. 10.1038/ejcn.2010.142.Serum

⁸⁷ Allen L.H. How common is vitamin B-12 deficiency? Am J Clin Nutr. (2009) 89:S693–6. 10.3945/ajcn.2008.26947A

⁸⁸ Ho-Pham L.T., Nguyen P.L.T., Le T.T.T., Doan T.A.T., Tran N.T., Le T.A., Nguyen T. V. Veganism, bone mineral density, and body composition: a study in buddhist nuns. Osteoporos Int. (2009) 20:2087–93. 10.1007/s00198-009-0916-z

⁸⁹ Freire R. Scientific evidence of diets for weight loss: different macronutrient composition, intermittent fasting, and popular diets. Nutrition. (2020) 69:110549–59. 10.1016/j.nut.2019.07.001

Effectiveness of Intermittent Fasting

The alternate-day fasting (ADF) approach has been tested for its metabolic effects. In a study, healthy young men ($n = 8$) were subjected to ADF for 20 h/day for 15 days. After the specified study period, weight remained unchanged (86.4 ± 2.3 kg) while the increase in glucose uptake, i.e., 7.3 ± 0.3 mg/kg/min that was previously 6.3 ± 0.6 mg/kg/min, and prominent increase in lipolysis of adipose tissues were observed⁹⁰. Another study showed that when non-obese subjects (8 women and 8 men) fasted for 22 days on alternate days, they lost $4 \pm 1\%$ of their initial fat mass and $2.5 \pm 0.5\%$ of their initial body weight. However, a decrease in fasting insulin and non-significant change in glucose and ghrelin were also reported⁹¹.

A randomized crossover trial was conducted to evaluate the fasting-induced acute changes in biomarkers. Healthy volunteers ($n = 30$) were randomized into two groups: (i) normal eating for 28 ± 4 h then water-only fasting for 28 ± 4 h (ii) 28 ± 4 h of water-only fasting then 28 ± 4 h of normal eating. Blood samples were drawn and analyzed at baseline, day 1 and day 2. Laboratory findings suggested that the fasting intervention acutely increased hemoglobin, hematocrit, red blood cell count, human growth hormone, and HDL-c; on the other hand, decreased body weight, bicarbonates, and TGs, as compared to the normal eating day. Moreover, cholesterol and human growth hormone returned to baseline after 48 h⁹².

Night-time fasting (NTF) has been linked to lower energy intake, consequently resulting in weight loss. In a study, twenty-nine healthy young men were subjected to 9 h of NTF for 2 weeks, then 1 week washout period followed by 2 weeks of controlled conditions. Results showed that the participants had less total calorie intake in the NTF phase as compared to controlled conditions. Significant differences in weight change were also reported, i.e., -0.4 kg for NTF and $+0.6$ kg for control⁹³.

In a randomized trial of 3 months, young overweight premenopausal women ($n = 107$) were randomly assigned to two groups: two consecutive days of fasting (25% energy restriction)/week or fasting for all days of the week. Both interventions were found to be equally good at a weight and showed improvement in risk markers of CVDs, cancer, and diabetes for

⁹⁰ Halberg N., Henriksen M., Söderhamn N., Stallknecht B., Ploug T., Schjerling P., Dela F. Effect of intermittent fasting and refeeding on insulin action in healthy men. *J Appl Physiol.* (2005) 99:2128–36. 10.1152/japplphysiol.00683.2005

⁹¹ Heilbronn LK, Smith SR, Martin CK, Anton SD, Ravussin E. Alternate-day fasting in nonobese subjects: effects on body weight, body composition, and energy metabolism. *Am J Clin Nutr.* (2005) 81:69–73. 10.1093/ajcn/81.1.69

⁹² Horne BD, Muhlestein JB, Lappe DL, May HT, Carlquist JF, Galenko O, et al. Randomized cross-over trial of short-term water-only fasting: metabolic and cardiovascular consequences. *Nutr Metab Cardiovasc Dis.* (2013) 23:1050–7. 10.1016/j.numecd.2012.09.007

⁹³ LeCheminant JD, Christenson E, Bailey BW, Tucker LA. Restricting night-time eating reduces daily energy intake in healthy young men: a short-term cross-over study. *Br J Cancer.* (2013) 110:2108–13. 10.1017/S0007114513001359

example reduction in leptin, leptin to adiponectin ratio, inflammatory markers, fasting insulin, insulin resistance, blood pressure, and lipids⁹⁴.

Fasting also impacts the appetite by influencing the appetite-regulating hormones (^{94, 95}). A previous systematic review summarized that IF may have the potential to provide metabolic benefits in terms of improving insulin resistance, thus providing better glycemic control as IF showed a significant decline in fasting glucose levels as compared to controls. Moreover, IF was associated with a decline in BMI, fat mass, and leptin while an increase in adiponectin⁹⁶. Headland et al.⁹⁷ evaluated the effectiveness of intermittent energy restriction (IER) in improving weight and biological markers in long-term studies. Irrespective of duration, IER was associated with weight loss. However, IER was not found to be superior to continuous energy restriction (CER) in terms of weight loss, blood lipids, glucose, and insulin levels.

Problems with Intermittent Fasting

Some short-term studies highlighted the potential harms posed by IF among normal-weight subjects. IF induces lipolysis, resulting in increased free fatty acids (FFA). So whether it be ADF, periodic fasting, or else, a prolonged course of fasting can lead to large fluctuations in FFA in normal-weight individuals. A study showed that these fluctuations were three times greater than those typically seen after an overnight fast. Furthermore, it induced reductions in insulin sensitivity and acute glucose-stimulated insulin response⁹⁸. Despite the effectiveness of IF in weight loss as indicated by several studies, the current evidence is inconclusive. The prime focus of available literature is weight loss but little is known about its sustainability and long-term health effects. More long-term trials should be conducted to draw a clear conclusion.

Detox Diets (DD)

The popularity of detoxification dates back to Greek, Roman, Indian, and Native American cultures. Many effective approaches that are still used for the removal of toxins include fasting, saunas, herbs, rebounding, dry brush, water, rest, exercise, and meditation⁹⁹. However, detoxification or DD are interventional diets specifically designed for toxins elimination, health

⁹⁴ Harvie MN, Pegington M, Mattson MP, Frystyk J, Dillon B, Evans G, et al. The effects of intermittent or continuous energy restriction on weight loss and metabolic disease risk markers : a randomized trial in young overweight women. *Int J Obes.* (2011) 35:714–27. 10.1038/ijo.2010.171

⁹⁵ Hodgey KK, Gibbons C, Kroeger CM, Trepanowski JF, Barnosky A, Bhutani S, et al. Changes in hunger and fullness in relation to gut peptides before and after 8 weeks of alternate day fasting. *Clin Nutr.* (2016) 35:1380–5. 10.1016/j.clnu.2016.03.011

⁹⁶ Cho Y, Hong N, Kim K, Cho SJ, Lee M, Lee Y, et al. The effectiveness of intermittent fasting to reduce body mass index and glucose metabolism: a systematic review and meta-analysis. *J Clin Med.* (2019) 8:1645–55. 10.3390/jcm8101645

⁹⁷ Headland M, Clifton PM, Carter S, Keogh JB. Weight-loss outcomes: a systematic review and meta-analysis of intermittent energy restriction trials lasting a minimum of 6 months. *Nutrients.* (2016) 8:354–65. 10.3390/nu8060354

⁹⁸ Salgin B, Marcovecchio ML, Humphreys SM, Hill N, Chassin LJ, Lunn DJ, et al. Effects of prolonged fasting and sustained lipolysis on insulin secretion and insulin sensitivity in normal subjects. *Am J Physiol Endocrinol Metab.* (2009) 296:E454–61. 10.1152/ajpendo.90613.2008

⁹⁹ Khalil MT. Impact of a detox diet paradigm in weight management. *Izzivi Prihodnosti.* (2017) 2:237–55.

promotion, and weight management. These short-term dietary interventions involve multiple approaches, including total calorie restriction, dietary modification, or juice fasts, and often involve the use of additional minerals, vitamins, diuretics, laxatives, or cleansing foods. Some commercial DDs have been listed in Table 5. These are most commonly prescribed by naturopathic doctors to prevent or treat a number of conditions like gastrointestinal disorders, inflammation, autoimmune disorders, chronic fatigue syndrome, fibromyalgia, and weight loss¹⁰⁰.

Table 5: Commercial Detox Diets

Diet type	Duration	Foods allowed	Proposed claims	References
Liver cleansing diet	<ul style="list-style-type: none"> 8 weeks 	<ul style="list-style-type: none"> Plant-based Dairy-free Low-fat High fiber Unprocessed foods are allowed Epsom salt and liver tonics are also consumed 	<ul style="list-style-type: none"> Improved energy levels and liver function Toxins removal Improved immune response Efficient metabolism of fats Better weight control 	¹⁰¹
Lemon detox	<ul style="list-style-type: none"> 10 days 	<ul style="list-style-type: none"> A liquid only diet based on purified water, lemon juice, tree syrup and cayenne pepper. A mild laxative herbal tea and sea salt water is also incorporated 	<ul style="list-style-type: none"> Toxins removal Shiny hair Glowing skin Strong nails Weight loss 	¹⁰²
The clean cleanse	<ul style="list-style-type: none"> 21 days 	<ul style="list-style-type: none"> Breakfast and dinner comprise probiotic capsules, cleanse supplements and cleanse shakes A solid meal in lunch while avoiding gluten, dairy, corn, soy, pork, beef, refined sugars, some fruits and vegetables 	<ul style="list-style-type: none"> Toxins removal Improved energy Improved digestion Improved sleep Improved mental health Reduction in joint pain Reduction in headaches Reduction in constipation Reduction in bloating 	¹⁰³

¹⁰⁰ Allen J, Montalto M, Lovejoy J, Weber W. Detoxification in naturopathic medicine: a survey. J Altern Complement Med. (2011) 17:1175–80. 10.1089/acm.2010.0572

¹⁰¹ Cabot S. The Liver Cleansing Diet: Love Your Liver and Live Longer. Phoenix, AZ: SCB International; (2014).

¹⁰² Woloshyn T. The Complete Master Cleanse: A Step-by-Step Guide to Maximizing the Benefits of The Lemonade Diet. Berkeley: Ulysses Press; (2021).

¹⁰³ Junger A. Clean: The Revolutionary Program to Restore the Body's Natural Ability to Heal Itself. New York, NY: HarperOne; (2009).

Martha's vineyard detox diet	<ul style="list-style-type: none"> • 21 days 	<ul style="list-style-type: none"> • Herbal teas • Vegetable soups & juices • Specially formulated tablets, powders, and digestive enzymes are on the menu 	<ul style="list-style-type: none"> • Weight loss up to 9.5kg • Toxins removal • Improved energy levels 	104
Weekend wonder detox	<ul style="list-style-type: none"> • 48 h 	<ul style="list-style-type: none"> • Protein-rich meals • Salads • Detox promoting super foods & beverages • Healthy lifestyle • Spa treatments • Herbal remedies 	<ul style="list-style-type: none"> • Toxins removal • Improved organs' function • Strengthen body • Enhance beauty 	105
Fat flush	<ul style="list-style-type: none"> • 2 weeks 	<ul style="list-style-type: none"> • Large meals are replaced with dilute cranberries, hot water with lemon, pre-prepared cocktails, supplements & small meals 	<ul style="list-style-type: none"> • Toxins removal • Reduced stress • Weight loss • Improved liver function 	106
Blueprint cleanse	<ul style="list-style-type: none"> • 3 days 	<ul style="list-style-type: none"> • Consumption of 6 pre-prepared vegetable and fruit juices is allowed per day 	<ul style="list-style-type: none"> • Toxins removal 	107
The Hubbard purification rundown	<ul style="list-style-type: none"> • Several weeks 	<ul style="list-style-type: none"> • Niacin doses along with sustained consumption of vitamin-A, B, C, D, and E • Daily exercise with balanced meals • Restriction of alcohol and drugs • Sitting in a sauna ≤5h each day 	<ul style="list-style-type: none"> • Toxins removal from fat stores • Improved memory and intelligence quotient • Better blood pressure and cholesterol levels 	108

The DDs have not been extensively investigated; however, the handful of available studies have methodological limitations like sampling bias, small sample sizes, relying on self-reporting, and absence of control groups. Despite the emerging popularity, these diets fail to identify the mechanisms of eliminating toxins or even the specific toxins removed by a particular diet. Detox

¹⁰⁴ Deluz R, Hester J, Beard H. 21 Pounds in 21 Days: The Martha's Vineyard Diet Detox. New York, NY: Harper Collins; (2009).

¹⁰⁵ Cook MS. Weekend Wonder Detox: Quick Cleanses to Strengthen Your Body and Enhance Your Beauty. New York, NY: Da Capo Lifelong Books; (2014).

¹⁰⁶ Gittleman AL. The New Fat Flush Plan. New York, NY: McGraw Hill; (2016).

¹⁰⁷ Sakoutis Z, Huss E. The 3-Day Cleanse: Your BluePrint for Fresh Juice, Real Food, and a Total Body Reset. New York, NY: Grand Central Life & Style; (2010).

¹⁰⁸ Hubbard LR. Clear Body Clear Mind: The Effective Purification Program. Los Angeles: Bridge Publications; (2002).

approaches defy the general principles of human physiology as the liver and kidneys are quite efficient in removing both exogenous and endogenous toxins from our body, along with extra-renal excretion of toxins in sebum and sweat¹⁰⁹.

Effectiveness of Detox Diets

Currently, there is no clinical evidence confirming or negating the effectiveness of commercially available detox regimes for losing weight. Because of its emerging popularity, this area needs attention. So, in the absence of scientific evidence, results can be extrapolated from other closely related studies. It is known that the success rate of dieting, in general, is only 20%¹¹⁰. This may be possible because humans and animals have natural mechanisms to counter weight loss as starvation can have negative health consequences like reduced fertility and even death. Calorie restriction alters the neuropeptides' expression in the hypothalamus; which reduces metabolic rate and stimulates appetite, resulting in a weight loss plateau¹¹¹.

Furthermore, studies in mice have shown binge eating followed by a period of energy restriction, though this phenomenon is not established in humans yet¹¹². A study conducted by Mazurak et al.¹¹³ showed that fasting raised cortisol levels in young healthy women. Another study reported an increase in stress hormone levels in females due to the restricted intake of 1,200 kcal/day¹¹⁴. There is considerable evidence that stress stimulates appetite, thus promoting weight gain via elevations of cortisol¹¹⁵.

Many of the DD are liquid-based, low-calorie, and nutrient-poor. For example, a part of BluePrint Cleanse, Excavation Cleanse, provides only 19 g protein and 860 kcal/day which is far below the actual requirement. Food and Agriculture Organization (FAO) recommends a minimum of 0.83 g/kg body weight of high-quality protein and 1,680 kcal/day for an adult (¹¹⁶, ¹¹⁷). Based on

¹⁰⁹ Genuis SJ, Birkholz D, Rodushkin I, Beesoon S. Blood, urine, and sweat (BUS) study: monitoring and elimination of bioaccumulated toxic elements. *Arch Environ Contam Toxicol*. (2011) 61:344–57. 10.1007/s00244-010-9611-5

¹¹⁰ Wing RR, Phelan S. Long-term weight loss maintenance. *Am J Clin Nutr*. (2005) 82:S222–5. 10.1093/ajcn/82.1.222s

¹¹¹ Sainsbury A, Zhang L. Role of the arcuate nucleus of the hypothalamus in regulation of body weight during energy deficit. *Mol Cell Endocrinol*. (2010) 316:109–19. 10.1016/j.mce.2009.09.025

¹¹² Pankevich DE, Teegarden SL, Hedin AD, Jensen CL, Bale TL. Caloric restriction experience reprograms stress and orexigenic pathways and promotes binge eating. *J Neurosci*. (2010) 30:16399–407. 10.1523/JNEUROSCI.1955-10.2010

¹¹³ Mazurak N, Gunther A, Grau FS, Muth ER, Pustovoyt M, Bischoff SC, et al. Effects of a 48-h fast on heart rate variability and cortisol levels in healthy female subjects. *Eur J Clin Nutr*. (2013) 67:401–6. 10.1038/ejcn.2013.32

¹¹⁴ Tomiyama AJ, Mann T, Vinas D, Hunger JM, DeJager J, Taylor SE. Low calorie dieting increases cortisol. *Psychosom Med*. (2010) 72:357–64. 10.1097/PSY.0b013e3181d9523c.Low

¹¹⁵ Torres SJ, Nowson CA. Relationship between stress, eating behavior, and obesity. *Nutrition*. (2007) 23:887–94. 10.1016/j.nut.2007.08.008

¹¹⁶ Joint WHO/FAO/UNU Expert Consultation. Protein and Amino Acid Requirements in Human Nutrition. Geneva: World Health Organization; (2007).

¹¹⁷ Food and Agriculture Organization [FAO]. FAO Methodology for the Measurement of Food Deprivation: Updating the Minimum Dietary Energy Requirements. (2008). Available online at:

the previous work, DD may induce stress, raise cortisol levels and increase appetite, resulting in difficulty in losing weight, followed by binge eating and weight gain (¹¹⁸, ¹¹⁹, ¹²⁰).

It is quite alarming that the components of detox products may not be according to the labels as there is no regulatory authority that approves such products. A case was reported in Spain that a 50 year old man with no history of relevant medical illness, presented with diffuse abdominal pain, lethargy, profuse diarrhea, and vomiting after ingesting Epsom salt during a liver cleansing diet. That person died within 72 h from the onset of symptoms. Forensic and clinical investigations concluded that instead of magnesium sulfate heptahydrate, the supplier had mistakenly added hydrated manganese sulfate resulted in manganese intoxication¹²¹.

Energy-restricted DDs are capable of short-term weight loss. But still, there is a high likelihood of health risks from detox products because of their nutritional inadequacy. As no convincing evidence exists in this domain, such diets and products need to be discouraged by health professionals and must be subjected to regulatory review and monitoring.

Conclusion of Study

Fad diets facilitate fast and easy weight loss, improve appearance, and do not require a longer time to achieve the results. These diets are effective in improving health to some extent. However, compliance is always a significant concern because of the unrealistic combinations and nutritional inadequacy due to the complete elimination of one or more essential food groups. Despite the rapid weight reduction, there are some concerns for those with comorbidities. All these diets have not been extensively studied while those studies that have been mentioned in the literature have high dropout rates and are sometimes non-conclusive. More randomized controlled trials of prolonged duration need to be done to establish the safety of FDs for the public and to make people aware of the possible consequences of long-term adherence to such dietary patterns.

Calorie Counting Diets

https://www.fao.org/fileadmin/templates/ess/documents/food_security_statistics/metadata/undernourishment_methodology.pdf (Accessed June 20, 2021).

¹¹⁸ Pankevich DE, Teegarden SL, Hedin AD, Jensen CL, Bale TL. Caloric restriction experience reprograms stress and orexigenic pathways and promotes binge eating. *J Neurosci.* (2010) 30:16399–407. 10.1523/JNEUROSCI.1955-10.2010

¹¹⁹ Mazurak N, Gunther A, Grau FS, Muth ER, Pustovoyt M, Bischoff SC, et al. Effects of a 48-h fast on heart rate variability and cortisol levels in healthy female subjects. *Eur J Clin Nutr.* (2013) 67:401–6. 10.1038/ejcn.2013.32

¹²⁰ Tomiyama AJ, Mann T, Vinas D, Hunger JM, DeJager J, Taylor SE. Low calorie dieting increases cortisol. *Psychosom Med.* (2010) 72:357–64. 10.1097/PSY.0b013e3181d9523c.Low

¹²¹ Sanchez B, Casals-Casado J, Quintana S, Arroyo A, Martin-Fumadoc C, Galtes I. Fatal manganese intoxication due to an error in the elaboration of epsom salts for a liver cleansing diet. *Forensic Sci Int.* (2012) 223:e1–14. 10.1016/j.forsciint.2012.07.010

The old school approach for fat loss is the calorie counting diet where a client consumes less calories than they burn. While this approach does theoretically work, it's been shown to be ineffective in long-term fat loss specifically because it's not a sustainable way of eating.

“On the basis of national survey data, the average calorie intake among women and men older than 19 years old are estimated to be between 1,785 and 2,640 calories per day. While these estimates do not appear to be excessive, the numbers are difficult to interpret because survey respondents, especially individuals who are overweight or obese, often underreport dietary intake. Well-controlled studies suggest that the actual number of calories consumed may be higher than these estimates.

The majority of people do not understand calorie counting and caloric restriction. Why would anyone want to measure their food in cups, grams or anything else for that matter? I don't think most people understand how miserable of an experience this is until they go to a restaurant and are counting the number of croutons in their salad while they devour a burger, fries, a

Furthermore, there are many variables that need to be accounted for to actually lose body fat without losing any muscle mass. I've personally never had long-term success on caloric restriction because it's a miserable experience. I was always hungry and eating less calories didn't teach me the habits necessary to develop a healthy relationship with eating.

“The total number of calories a person needs each day varies depending on a number of factors, including the person's age, gender, height, weight, and level of physical activity. In addition, a desire to lose, maintain, or gain weight affects how many calories should be consumed. Estimates range from 1,600 to 2,400 calories per day for adult women and 2,000 to 3,000 calories per day for adult men, depending on age and physical activity level. Within each age and gender category, the low end of the range is for sedentary individuals; the high end of the range is for active individuals. As adults get older, their basal metabolic rate (BMR), generally decreases thereby decreasing their daily caloric needs.”