LIFESTYLE MEDICINE AND TYPE 1 DIABETES

Can Type 1 Diabetes Patients Benefit from a Whole-Food, Plant-Based Diet? A review and critique of a patient story in the film PlantWise

Saadia Alvi, MD, Aysha Inankur, MD, FACE, dipABLM, and George Guthrie, MD, MPH, CDCES

Current research has demonstrated many potential benefits for individuals with type 1 diabetes who adopt a whole-food, plant-based diet. One of these individuals was featured in the film *PlantWise*. Her case serves to illustrate many of the benefits that a person with type 1 diabetes may experience by adopting a whole-food, plant-based lifestyle.

This paper is divided into three parts. The first section contains the patient story told in her own words. The second section will examine the efficacy of including both type 1 and type 2 diabetes patients in a popular documentary film about lifestyle change. The third section will examine the scientific support for a whole-food, plant-based diet and its effects on diseases such as type 1 and type 2 diabetes.

PART 1: Karene's Story

The following is a first-person narrative of Karene B.

"I had a really wonderful childhood. I grew up in the country on three acres, and I have two wonderful parents who are loving and nurturing. I spent a lot of time outdoors and playing in the barn with the animals. I grew up as a vegetarian and very rarely ate meat. However, we ate a lot of cheese and eggs instead of meat, and processed foods like boxed cereals.

"I started having health issues shortly after I got married. It started with my thyroid. I was working the night shift as a nurse in the labor and delivery unit and began having fatigue. I did fine after I got on thyroid medication and didn't have any issues besides that until later. My health status began to change when I got pregnant with our first child.

"At the 27-week mark in the pregnancy, the doctor ordered a glucose tolerance test. I failed my test quite significantly. They told me I had gestational diabetes, and I was going to have to see an endocrinologist and do food

counseling. They said, 'But don't worry; it will go away. You'll just have to be careful. But if you exercise and keep yourself healthy, you'll be just fine.'

"But the opposite happened. I had terrible muscle weakness. Our daughter would be hungry and crying, and I would be struggling to open the baby food jars. Then I started having intermittent blurred vision. My eye doctor suggested my diabetes could have come back.

"One night I had an experience that was a definitive moment for me. Our daughter was fussy, and my husband said, 'On the nights you work, I drive through the takeout at the coffee shop and get a frozen coffee. I take our daughter on a little drive and she's quiet and sleeps.' So we shared a frozen coffee together and went back home, but I was a mess. I couldn't sleep. I was having hot flashes. I was profusely sweaty and shaky. About midnight or one in the morning when I was still awake and feeling nauseated and sick, I checked my blood sugar. It was very high, between 350 and 400. I went to my doctor, who told me, 'You have type 1 diabetes. Your body simply does not produce enough insulin anymore.' It was very disheartening, and I went through a lot of denial. I was truly grieving a loss. I was losing my health, which is a part of what all of us have the right to enjoy in life.

"For a while, my health journey was a rollercoaster. You hear of yo-yo dieting, but I was really having a yo-yo life, until I discovered plant-based eating. Then all of that stopped. I'm incredibly grateful to the medical professionals that helped me address some of the issues I was dealing with. Sometimes you hear the negative side of the medical profession and people who just want to give you a pill and send you out the door. But there are medical professionals out there who have studied lifestyle medicine and who can help you make changes to be at your best.

"When I made the switch to a whole-food, plantbased lifestyle, I started experiencing significant changes rather quickly. Within six months, I lost 40 pounds. I went to my doctor and told him, 'I'm really starting to feel dizzy.' He said, 'Well, your blood pressure is quite low. I think we're going to have to take you off your blood pressure medication.' My cholesterol was dropping too. He said, 'I don't think you will need your cholesterol medication anymore.'

"My acid reflux went away, along with all the allergy issues I was struggling with, so I was able to stop taking those medications as well. In fact, I was able to get off the majority of my medications.

"What I was left with was the core chronic diseases of my diabetes and my thyroid. But even they improved. My doctor was able to lower my medication doses. Previously, I was using 50 to 60 units of insulin a day with my type 1 diabetes, and now I take around 20 units. As you can imagine, these improvements drastically changed and revolutionized my whole life.

"I thought I was free, but I didn't really understand what freedom was until I changed my lifestyle. You have more energy, you're more vibrant, you're happier. When you really decide you're going to change your lifestyle and you stand firm with that decision, it will radically change your life for the better, and you'll never want to go back."

"Type 1 diabetes, without a doubt, has its challenges. It's not always easy to be the person who has to excuse themselves to take an injection or explain why you wear a piece of machinery on your hip. It comes with highs and lows, literally and not so literally.

"Carb counting, finger sticks, blood sugar monitoring, supplies, and doctors' visits are among the many day-to-day routines we face. A person with type 1 diabetes makes hundreds of decisions every day, so why not make a decision that will make all the other decisions so much easier, by eating a whole-food, plant-based diet? My journey led me not only to physical healing, but mental and spiritual healing as well, and it all began with changing the way I eat. The hidden blessing comes not only from feeling whole but being whole. There is hope!"

PART 2: Why Include Type 1 and Type 2 Patients in the Same Film?

Documenting Health Transformation

Karene's story was featured in the documentary film *PlantWise*. *PlantWise* follows the stories of six individuals struggling with debilitating health conditions, the lifestyle medicine approaches they took, and the results achieved. They learn that the Standard American Diet is often the culprit in creating or exacerbating their condition. High in saturated fat, sugar, and salt. Low in fiber and nutrients. It's wreaking havoc and contributing to chronic illnesses in much of our society. With hope, they discover that this epidemic of diseases—including heart disease, type

2 diabetes, obesity, and high blood pressure—is largely preventable and oftentimes reversible.

The six individuals, including Karene, discover the benefits of a whole-food, plant-based diet and choose to wholeheartedly embrace it. They greatly reduce their chronic conditions and experience a health transformation. They find renewed energy and vitality they thought they had lost forever. The film also includes many nationally recognized experts from fourteen different disciplines discussing the benefits of lifestyle medicine in general and a whole-food, plant-based diet in particular. Their conclusion: it is the choices we make every day that often determines our health destiny.

Why a Type 1 Diabetes Story?

Many may wonder, why a person with type 1 diabetes is included in a film where all the rest have type 2 diabetes? Isn't type 1 diabetes irreversible? Is there anything a person with type 1 diabetes can do to help their condition except to take their insulin every day? These may be uncomfortable questions, but they are questions that need to be answered.

Answering An Important Issue

While there is an occasional case report claiming type 1 diabetes reversal,1 it is commonly understood to be irreversible. But the pathophysiology of type 2 diabetes and Metabolic Syndrome may be pushed into remission. In many ways, type 1 diabetes is the opposite of type 2 diabetes. In type 1 diabetes, the pancreas is failing to make enough insulin and, in its "clean" form, there is commonly very little or no insulin resistance, so the body's need for insulin is close to normal pancreatic secretion, i.e. the equivalent of around 20-30 units per day. Type 1 is commonly caused by an autoimmune reaction in which the body attacks and incapacitates the cells that make insulin. Persons with type 1 diabetes tend to be thinner. Persons with Type 2, on the other hand, tend to be "thick." Earlier in the disease they also have higher-than-normal insulin production by the pancreas that is necessary for overcoming the insulin resistance in the liver, muscles, and other tissues. We have known for a long time that this insulin resistance and, more recently, many of the other physiologic problems identified as "metabolic syndrome" in type 2 diabetes can be reversed with lifestyle change. But the damage to the pancreas from autoimmune action as is seen in type 1 diabetes is much less reversible. Type 1 diabetes is not considered reversible at this time although researchers are working hard at making progress in this area.

The film *PlantWise* never says or intends to imply that type 1 diabetes can be reversed with healthy lifestyle choices. Rather, by sharing Karene's personal story, *Plant-Wise* demonstrates that a plant-based diet coupled with

exercise can lead to overall health improvements and possible reductions in medication even in an individual with an incurable condition. Karene developed gestational diabetes. This is diabetes that occurs when the hormones of pregnancy worsen insulin resistance. This happens frequently in persons who have already developed a bit of insulin resistance from poor nutrition on top of a sedentary lifestyle. This person likely had early type 1 diabetes that was undiagnosed when she became pregnant. Her pancreatic function was already under stress from an attacking personal immune system (type 1 diabetes), her weakening pancreas was not identified during the pregnancy, and her sugars were managed with diet. Her underlying type 1 diabetes was then diagnosed after the pregnancy, and she was appropriately started on insulin.

Many persons with type 1 diabetes who are placed on insulin actually go on to develop metabolic syndrome. When insulin is started, it is common practice to add extra food within the meal or through snacking in order to avoid low blood sugar reactions. The extra calories then lead to an increase in weight and, in time, even to liver insulin resistance, one of the key hallmarks of type 2 diabetes. This combination of increased insulin and excess calories defines the metabolic milieu that creates the metabolic syndrome basis of type 2 diabetes. When present with type 1 diabetes it can be reasonably understood as a combination of both types. This also magnifies the negative features of both types of diabetes and combines the problems of both: high cholesterol, overweight/obesity, high blood pressure, vascular inflammation, neuropathy, kidney failure, low insulin, and very difficult-to-control blood sugars.

Karene's lifestyle change led to a resolution of her metabolic syndrome and what remained was her type 1 diabetes, which would then be much easier to treat and manage. When basal long-acting insulin is just the right amount to keep the liver from making extra sugar, and a person learns how to match the short-acting insulin to the food intake, a long healthy life can be expected. Once someone adopts a healthy lifestyle and is able to safely lower their insulin needs (and use) the metabolic syndrome can go away, the patient feels better, and they are often able to reduce their medications. The disease is not managing them, and they feel in control of the disease. But individuals with type 1 diabetes will always need insulin. This is exactly what happened with Karene. Getting rid of her metabolic syndrome is what her story is about.

Quality of Life Improvement

We consider it very appropriate to have a person with type 1 diabetes include their story in *PlantWise* because important components of their health and quality of life were improved with lifestyle changes. Type 1 diabetes is not a condemnation to a life of misery. Karene's story il-

lustrates the significant improvement in the management of an irreversible disease (type 1 diabetes) that is available through effectively addressing the lifestyle causes of this common secondary disease, metabolic syndrome. When no longer having to address the problems with blood pressure, weight, and heart disease risk factors, Karene found that her blood sugars were much more in control, and she needed much less insulin and other medications. Her life became much less stressful when it became much more predictable. She became healthier and was much more in control of the unchangeable dimensions of type 1 diabetes. If you have type 1 diabetes, we trust that Karene's story will be an encouragement to you and start you on the path to living a happier and healthier life in spite of the presence of a potentially devastating autoimmune disease.

PART 3: Scientific Support for Addressing Type 1 and Type 2 Diabetes with a Whole-Food, Plant-Based Lifestyle

The scientific literature gives evidence that a whole-food, plant-based diet supplies some very helpful tools for those with type 1 diabetes.

High Plant Diets Associated with Decreased Risk of Getting Type 1 Diabetes

A high whole-plant diet may help prevent type 1 diabetes in those families predisposed to autoimmune diseases. The high fiber intake that comes from a whole-food, plant-based diet supports good bacteria in the colon. The fiber itself is called a prebiotic because the good bacteria of the colon thrive on it. There is evidence that the presence of the good bacteria in the gut that make short chain fatty acids decreases the risk of a child getting type 1 diabetes.² In a study of food choices that looked for correlation with autoimmune disease risk, the TEENDIAB study looked at children with a first-degree relative with type 1 diabetes.3 Those that got an autoimmune disease such as type 1 diabetes had intakes of vitamin D, iodine, folate, and plant-based foods considerably below the official recommendations. They also had intakes of vitamin K, sodium, protein, meat products, and sweets/snacks above the recommended amounts.

Persons who carry excess weight have a higher risk of developing type 1 diabetes. Rapid weight gain during infancy⁴ and obesity during childhood are linked with increased risk of type 1 diabetes.⁵ Some forms of type 1 diabetes develop in adulthood and are slowly progressive.⁶ Adults who are overweight or obese are at increased risk of developing this later-onset autoimmune diabetes.⁷

Plant-based diets may help prevent type 1 diabetes throughout the lifespan by helping persons maintain a healthy body weight. Systematic reviews and meta-analyses of clinical trials conducted in persons with and without type 2 diabetes showed plant-based diets resulted in weight reduction.^{8,9} A person with type 1 diabetes who adopted a diet of whole plant foods was reported to experience significant weight loss, and this weight loss was sustained over subsequent years on the diet.¹⁰ A plant-based meal, compared to a meal of meat and cheese, induced higher levels of the gut hormone amylin in men with and without type 2 diabetes and obesity.¹¹ Amylin increases satiety and may be one reason for the weight-reducing effects of plant-based diets.

High Plant Fiber Improves Blood Sugar Control

In a recent review, gut dysbiosis in diabetes mellitus is associated with decreased short-chain fatty acid production and epithelial barrier disruption. Microbial-derived toxins move across the "leaky gut" and induce systemic inflammation and insulin resistance. In children, gut dysbiosis has been associated with risk of developing type 1 diabetes mellitus. ¹² In animal models, the obesity state is transferable via microbiota transplantation. Plantbased, low-protein diets and certain anti-diabetic drugs have been associated with positive microbiome effects. Clinical trials with prebiotics and probiotics have yielded mixed results. The authors conclude that further studies are needed to evaluate the gut microbiome as a potential therapeutic target for both prevention and management of diabetes. ¹³

An analysis of six randomized clinical trials showed A1c reduced 0.4% on plant-based diets compared with conventional diets in persons with type 2 diabetes. 14 This A1c reduction may be due to higher fiber content in the plant-based diets. Fiber-rich foods are known to reduce post-meal blood sugars in patients with type 1 and type 2 diabetes. 15,16 A second way plant-based diets may lower blood sugars in persons with type 1 diabetes relates to their low content of saturated fat. The Diabetes Control and Complications Trial (DCCT) followed 532 persons with type 1 diabetes for 5 years. In the patients in this trial, diets higher in saturated fat and lower in carbohydrate were associated with worse blood sugar management regardless of exercise or body mass index (BMI).17 Persons consuming plant-based diets have a lower intake of saturated fat compared to persons on omnivore diets. 18,19 Naturally high in fiber and low in saturated fat, plant-based diets effectively lower blood sugars.

High-Fiber Diet Protects Against Harmful Substances

Those who eat a low-fiber diet have bacteria in their colons that tend to make more TMAO, a substance associated with increased risk of cancer and some neurologic diseases.²⁰ The substrates for TMAO are the sulfur-containing amino acids that are high in animal proteins. In a randomized controlled trial of four different weight-loss

diet interventions in 504 overweight or obese adults, restriction of dietary choline and L-carnitine was associated with decreased blood TMAO and improved insulin sensitivity at 2 years.²¹ TMAO is another reason for persons with metabolic syndrome to increase their whole-plant and fiber intake while decreasing the amount of animal protein they consume.

High Plant Fiber Diet Improves Sugar Control and Heart Disease Risk in Individuals with Diabetes

It has also been noted that vegetarian dietary patterns improve glycemic control, LDL-C, non-HDL-C, and body weight/adiposity in individuals with diabetes, supporting their inclusion for diabetes management.²² Whole-food, plant-based dietary patterns that release smaller amounts of sugar slowly result in small important improvements in sugar control, cholesterol numbers, weight, blood pressure, and even inflammation that go beyond that obtained from diabetes medications including insulin. This is true in adults with moderately controlled type 1 and type 2 diabetes. The available evidence provides a good indication of the significant benefit for these individuals.²³ Research continues in this area.

High Protein Accelerates Kidney Disease; High Plant Intake Protects

Both types of diabetes place a stress on the kidneys and increase the risk of kidney failure.24 There has been evidence for some time that decreasing animal proteins may protect the kidneys.²⁵ Increased fruit and vegetable dietary patterns seemed to protect against the kidney damage.26 There are reasonable physiologic mechanisms to explain the observation.27 A PLAnt-DOminant, low-protein (PLADO) diet, which restricts protein intake to 0.6 to 0.8 g/kg body weight per day and with >50% protein from plants provided protection against kidney damage in persons without diabetes.²⁸ Furthermore, there is evidence that substituting plant proteins for animal proteins decreases mortality.²⁹ Further study is needed to establish benefit in diabetes but enough evidence exists to encourage those with either type 1 or type 2 diabetes to move in the direction of eating more plants and less animal protein.

High Plant Food Diet Decreases Risk of Diabetic Eye Disease and Diabetic Nerve Disease

Diabetic retinopathy is estimated to affect 86% of persons with type 1 diabetes in the United States.³⁰ Diets low in plant foods were linked with a risk factor for retinopathy progression in children and adolescents with type 1 diabetes.³¹ Children and adolescents with type 1 diabetes eating diets low in plant foods experienced widening of the venules (small veins that join capillaries to larger veins), a risk factor for retinopathy. This study suggests diets high

in plant foods may be protective against diabetic eye disease.

Diabetic neuropathy is projected to affect 20% of persons with type 1 diabetes 20 years after diagnosis.³² Diabetic neuropathy has improved through use of plant-based diets,³³ and plant-based diets combined with exercise.³⁴ This improvement is thought to be mediated through increased blood flow to nerve cells.³⁵

Plant-Based Diets May Reduce Risk of Eating Disorders

Persons with type 1 diabetes are more likely than persons without diabetes to develop an eating disorder.³⁶ Disordered eating significantly affects the quality and length of life in persons with type 1 diabetes as it is linked with poorer blood sugar management and decreased survival.³⁷ Among youths with type 1 diabetes, being overweight or obese increases the odds of developing disordered eating.³⁸ With significant benefits toward weight reduction,³⁹ plant-based diets may be an important tool to help prevent disordered eating in persons with type 1 diabetes.

Conclusion

Current research has demonstrated that there are many potential benefits to be gained by individuals with type 1 diabetes who adopt a whole-food, plant-based lifestyle. For Karene B., a patient featured in the film *PlantWise*, the benefits included weight loss, normalization of blood pressure and cholesterol allowing her to stop both medications, elimination of acid reflux and allergy problems, and a reduction of insulin intake. Her case illustrates many of the benefits that a person with type 1 diabetes may experience by adopting a whole-food, plant-based lifestyle. Her experience demonstrates the importance of telling stories of both type 1 and type 2 diabetes patients to provide inspiration and hope to patients and their families.

Endnotes

- Chowdhury BR. Reversal of type 1 diabetes using plant-based diet: A case study. Biomed Res. 2019;30(3):513-515. doi:10.35841/bio-medicalresearch.30-19-182.
- 2. Vatanen T, Franzosa EA, Schwager R, et al. The human gut microbiome in early-onset type 1 diabetes from the TEDDY study. *Nature*. 2018;562(7728):589-594. doi:10.1038/s41586-018-0620-2.
- Weber KS, Raab J, Haupt F, et al. Evaluating the diet of children at increased risk for type 1 diabetes: first results from the TEEN-DIAB study. *Public Health Nutr.* 2015;18(1);50-58. doi:10.1017/ s1368980013003406.
- Hyppönen E, Kenward MG, Virtanen SM, et al. Infant feeding, early weight gain, and risk of type 1 diabetes. Childhood Diabetes in Finland (DiMe) Study Group. *Diabetes Care*. 1999; 22(12):1961-1965. doi:10.2337/diacare.22.12.1961.
- Verbeeten KC, Elks CE, Daneman D, Ong KK. Association between childhood obesity and subsequent Type 1 diabetes: a systematic review and meta-analysis. *Diabet Med* 2011;28:10–18. doi:10.1111/ j.1464-5491.2010.03160.x.

Author Bios

- SAADIA ALVI, MD, is a board-certified specialist in endocrinology, diabetes, and metabolism. Dr. Alvi earned her medical degree at the respected American University of Integrative Sciences. She undertook her internal medicine residency at Advocate Illinois Masonic Medical Center in Chicago and Saint Joseph Mercy Hospital, followed by her endocrinology fellowship at the University of Texas Medical Branch in Galveston. Dr. Alvi practices endocrinology at the AdventHealth Diabetes Institute.
- AYSHA INANKUR, MD, FACE, dipABLM, holds triple board certification in endocrinology, lifestyle medicine, and internal medicine.

 Dr. Inankur finished medical school and her internal medicine residency at Loma Linda University. She completed her chief residency at Kettering Medical Center and endocrinology fellowship at the University of Kentucky. She holds memberships in the Endocrine Society, the American Association of Clinical Endocrinologists, and the American College of Lifestyle Medicine.

 Dr. Inankur practices adult endocrinology and lifestyle medicine at Wildwood Lifestyle Center in Georgia.
- GEORGE E. GUTHRIE, MD, MPH, CDCES, CNS, FAAFP, FACLM, is a board-certified family medicine physician and a member of the family medicine team at AdventHealth's academic practice in Winter Park, Florida, where he trains medical residents. He received certification from the Board for Certification of Nutrition Specialists (BCNS), is a Certified Diabetes Care and Education Specialist (CDCES), and has a special interest in lifestyle management for those with type 2 diabetes, hypertension, obesity, and coronary heart disease. He is a past president of the American College of Lifestyle Medicine.
- Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2021. Diabetes Care 2021;44 (Supplement_1): S15– S33. doi:10.2337/dc21-s002.
- Hjort R, Ahlqvist E, Carlsson PO, et al. Overweight, obesity and the risk of LADA: results from a Swedish case-control study and the Norwegian HUNT Study. *Diabetologia*. 2018;61(6):1333-1343. doi:10.1007/s00125-018-4596-0.
- Barnard ND, Levin SM, Yokoyama Y. A systematic review and meta-analysis of changes in body weight in clinical trials of vegetarian diets. *J Acad Nutr Diet* 2015;115(6):954-969. doi:10.1016/j. jand.2014.11.016.

- Viguiliouk E, Kendall CW, Kahleova H, et al. Effect of vegetarian dietary patterns on cardiometabolic risk factors in diabetes: A systematic review and meta-analysis of randomized controlled trials. Clin Nutr. 2019;38(3):1133-1145. doi:10.1016/j.clnu.2018.05.032.
- Kahleova H, Carlsen B, Berrien Lopez R, Barnard ND. Anti-diabetic, haematinic and anti-cholesterolmic effects of wheat (*Triticum aestivum Linn.*) grass juice metabolites to cure alloxan monohydrate induced type-1 diabetes in albino rats. *J Diab Metab.* 2020;11:847. doi:10.35248/2155-6156.20.11.847.
- 11. Klementova M, Thieme L, Haluzik M, et al. A Plant-Based Meal Increases Gastrointestinal Hormones and Satiety More Than an Energy- and Macronutrient-Matched Processed-Meat Meal in T2D, Obese, and Healthy Men: A Three-Group Randomized Crossover Study. Nutrients. Jan 2019;11(1):157. doi:10.3390/nu11010157.
- Vatanen T, Franzosa EA, Schwager R. et al. The human gut microbiome in early-onset type 1 diabetes from the TEDDY study. *Nature*. 2018:562, 589–594. doi:10.1038/s41586-018-0620-2.
- Lau WL, Tran T, Rhee CM, Kalantar-Zadeh K, Vaziri ND. Diabetes and the Gut Microbiome. Semin Nephrol. 2021;41(2):104-113. doi:10.1016/j.semnephrol.2021.03.005.
- 14. Yokoyama Y, Barnard ND, Levin SM, Watanabe M. Vegetarian diets and glycemic control in diabetes: a systematic review and meta-analysis. *Cardiovasc Diagn Ther.* 2014;4(5):373-382. doi:10.3978/j. issn.2223-3652.2014.10.04.
- Riccardi G, Rivellese AA, Giacco R. Role of glycemic index and glycemic load in the healthy state, in prediabetes, and in diabetes. Am J Clin Nutr. 2008;87(1):269S-274S. doi 10.1093/ajcn/87.1.269S.
- Wolfram, T. and Ismail-Beigi, F. Efficacy of High-Fiber Diets in the Management of Type 2 Diabetes Mellitus. *Endocrine Practice*, 2011;17(1):132-142. doi:10.4158/EP10204.RA.
- Delahanty LM, Nathan DM, Lachin JM, et al. Association of diet with glycated hemoglobin during intensive treatment of type 1 diabetes in the Diabetes Control and Complications Trial. Am J Clin Nutr. 2009;89(2):518-24. doi:10.3945/ajcn.2008.26498.
- Roshanai F, Sanders TA. Assessment of fatty acid intakes in vegans and omnivores. Hum Nutr Appl Nutr. 1984;38(5):345–354. PMID:6526681.
- Sobiecki JG, Appleby PN, Bradbury KE, Key TJ. High compliance with dietary recommendations in a cohort of meat eaters, fish eaters, vegetarians, and vegans: results from the European Prospective Investigation into Cancer and Nutrition-Oxford study. *Nutr Res.* 2016;36(5):464–477. doi:10.1016/j.nutres.2015.12.016.
- Janeiro MH, Ramírez MJ, Milagro FI, Martínez JA, Solas M. Implication of Trimethylamine N-Oxide (TMAO) in Disease: Potential Biomarker or New Therapeutic Target. *Nutrients*. 2018;10(10):1398. doi:10.3390/nu10101398.
- 21. Heianza Y, Sun D, Li X, et al. Gut microbiota metabolites, amino acid metabolites and improvements in insulin sensitivity and glucose metabolism: the POUNDS Lost trial. *Gut.* 2019;68(2):263-270. doi:10.1136/gutjnl-2018-316155.
- Viguiliouk E, Kendall CW, Kahleova H, et al. Effect of vegetarian dietary patterns on cardiometabolic risk factors in diabetes: A systematic review and meta-analysis of randomized controlled trials. Clin Nutr. 2019;38(3):1133-1145. doi:10.1016/j.clnu.2018.05.032.
- Chiavaroli L, Lee D, Ahmed A, et al. Effect of low glycaemic index or load dietary patterns on glycaemic control and cardiometabolic risk factors in diabetes: systematic review and meta-analysis of randomised controlled trials. *BMJ*. 2021;374:n1651. doi:10.1136/bmj. n1651.
- 24. Hansen H, Tauber-Lassen E, Jensen BR, Parving H. Effect of di-

- etary protein restriction on prognosis in patients with diabetic nephropathy. *Kidney Int.* 2002;62(1):220-228. doi:10.1046/j.1523-1755.2002.00421.x.
- Ihle BU, Becker GJ, Whitworth JA, Charlwood RA, Kincaid-Smith PS. The effect of protein restriction on the progression of renal insufficiency. N Engl J Med. 1989;321(26):1773-1777. doi:10.1056/ nejm198912283212601.
- Keel S, Itsiopoulos C, Koklanis K, et al. Dietary patterns and retinal vascular calibre in children and adolescents with type 1 diabetes. *Acta Ophthalmol*. 2016;94(5):e345-52. doi:10.1111/aos.12941.
- Sellmeyer DE, Stone KL, Sebastian A, Cummings SR. Study of Osteoporotic Fractures Research Group, A high ratio of dietary animal to vegetable protein increases the rate of bone loss and the risk of fracture in postmenopausal women. *Am J Clin Nutr.* 2001;73(1):118-22. doi:10.1093/ajcn/73.1.118.
- Kalantar-Zadeh K, Joshi S, Schlueter R, et al. Plant-dominant low-protein diet for conservative management of chronic kidney disease. *Nutrients*. 2020:12(7):1931. doi:10.3390/nu12071931.
- Hansen H, Tauber-Lassen E, Jensen BR, Parving H. Effect of dietary protein restriction on prognosis in patients with diabetic nephropathy. *Kidney Int.* Jul; 62(1):220-228. doi:10.1046/j.1523-1755.2002.00421.x.
- Roy MS, Klein R, O'Colmain BJ, Klein BEK, Moss SE, Kempen JH.
 The prevalence of diabetic retinopathy among adult type 1 diabetic persons in the United States. Arch Ophthalmol. 2004;122(4):546–551. doi:10.1001/archopht.122.4.546.
- 31. Keel S, Itsiopoulos C, Koklanis K, et al. Dietary patterns and retinal vascular calibre in children and adolescents with type 1 diabetes. *Acta Ophthalmol.* 2016;94(5):e345-e352. doi:10.1111/aos.12941.
- Tesfaye S, Chaturvedi N, Eaton SE, et al. for EURODIAB Prospective Complications Study Group. Vascular risk factors and diabetic neuropathy. N Engl J Med. 2005;352(4):341-50. doi:10.1056/NEJ-Moa032782.
- Bunner AE, Wells CL, Gonzales J, Agarwal U, Bayat E, Barnard ND. A dietary intervention for chronic diabetic neuropathy pain: a randomized controlled pilot study. *Nutr Diabetes*. 2015;5(5): e158. doi:10.1038/nutd.2015.8.
- Crane MG, Sample C. Regression of diabetic neuropathy with total vegetarian (vegan) diet. J Nutr Med. 1994;4:431-439. doi:10.3109/13590849409003592.
- McCarty MF. Favorable impact of a vegan diet with exercise on hemorheology: implications for control of diabetic neuropathy. *Med Hypotheses*. 2002;58(6):476-86. doi:10.1054/mehy.2001.1456.
- Goebel-Fabbri AE. Disturbed eating behaviors and eating disorders in type 1 diabetes: clinical significance and treatment recommendations. Curr Diab Rep. 2009 Apr;9(2):133-9. doi:10.1007/s11892-009-0023-8
- 37. Neumark-Sztainer D, Patterson J, Mellin A, et al. Weight control practices and disordered eating behaviors among adolescent females and males with type 1 diabetes: associations with sociodemographics, weight concerns, familial factors, and metabolic outcomes. *Diabetes Care*. 2002;25(8):1289-96. doi:10.2337/diacare.25.8.1289.
- Tse J, Nansel TR, Haynie DL, Mehta SN, Laffel LM. Disordered eating behaviors are associated with poorer diet quality in adolescents with type 1 diabetes. *J Acad Nutr Diet*. 2012;112(11):1810-4. doi:10.1016/j.jand.2012.06.359.
- Huang RY, Huang CC, Hu FB, Chavarro JE. Vegetarian diets and weight reduction: a meta-analysis of randomized controlled trials. J Gen Intern Med. 2016;31(1):109-116. doi:10.1007/s11606-015-3390-7.