



Disclosure

No financial interest in any of the products or research presented.

Diabetes in US

CDC 2015

- 30 million with diabetes
 - 9.4% of population
- 8 million do not know they have DM
- 84 million have pre-diabetes
- 7th leading cause of death

Diabetes...It's a Big Deal

- One of the leading causes of blindness in the U.S. for persons 20–74 years of age.
- Prevalence DR
 - **35% worldwide**
 - **28.5% US**
 - **10% VTDR worldwide**
 - **4.4% VTDR**
- Greater severity associated with lower general and vision-specific quality of life.

Preferred Practice Patterns AAO 2017

A1C

Glycated Hemoglobin (A1C)

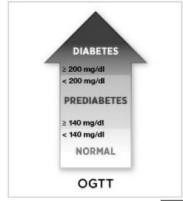
- Does NOT require fasting, indicates average blood sugar level for past two to three months.
- Measures the percentage of BS attached to hemoglobin (oxygen-carrying protein in RBC).
- A1C level of 6.5 percent or higher on two separate tests indicates that you have diabetes.
- A1C between 5.7 and 6.4 percent indicates prediabetes.
- Below 5.7 is considered normal.

FPG

Blood Sugar Test

- **Random Blood Sugar Test**
 - 200 (mg/dL) — 11.1 (mmol/L) or higher suggests diabetes.
- **Fasting Blood Sugar Test**
 - BS taken after an overnight fast.
 - Fasting BS level < 100 mg/dL (5.6 mmol/L) is normal.
 - Fasting BS level from 100 to 125 mg/dL (5.6 to 6.9 mmol/L) considered prediabetes.
 - Fasting BS 126 mg/dL (7 mmol/L) or higher on two separate tests is considered diabetes.

Oral Glucose Tolerance Test



- Fasting BS level measured typically in morning.
- Drink sugary liquid and levels tested periodically for two hours.
- BS < 140 mg/dL (7.8 mmol/L) is normal.
- More than 200 mg/dL (11.1 mmol/L) after two hours indicates diabetes.
- Reading between 140 and 199 mg/dL (7.8 mmol/L and 11.0 mmol/L) indicates prediabetes.

CLIA and Laboratory Testing

WHAT IS A LABORATORY?

- Under CLIA
- A laboratory is defined as a facility that performs testing on materials derived from the human body for the purpose of providing information for the diagnosis, prevention, or treatment of any disease or impairment of, or assessment of the health of, human beings.

Point-of-care testing (POCT)

- POCT is an analysis or test that employs an analytical method and is used in a diagnostic setting that is remote from a centralized laboratory facility.
- Glucometers
- At home A1C meters for monitoring or screening, not diagnosing

CLIA Waiver

Simple tests that carry a low risk for an incorrect result.

For waived testing, CLIA requires:

- Enroll in the CLIA program by obtaining a certificate;
- Pay the certificate fee every two years (\$150.00)
- Follow the manufacturers' instructions for the waived tests you are performing;
- Notify your State Agency of any changes in ownership, name, address or director within 30 days, or if you wish to add tests that are more complex; and
- Permit inspections by CMS agent, such as a surveyor from the State Agency. Laboratory is not subject to a routine survey or inspection.

Glucometers

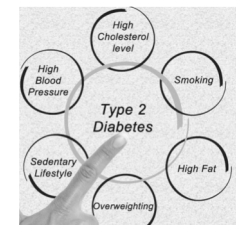
- 99% of blood glucose measurements within 20% of lab results
- 95% of blood glucose measurements within 15% of lab results

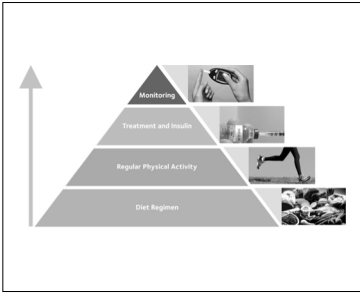


"I'm Pre-Diabetic"

Who to Screen?

- **Anyone with BMI > 25 (23 for Asian-Americans), regardless of age, with additional risk factors** (HBP, abnormal cholesterol, sedentary lifestyle, polycystic ovary syndrome, heart disease, close relative with diabetes).
- **Anyone > 45 years** advised to receive an initial blood sugar screening, if the results are normal, to be screened every 3 years.
- **Any woman with gestational diabetes** advised to be screened for diabetes every 3 years.
- **Anyone diagnosed with prediabetes** is advised to be tested every year.





How is Diabetes Treated?

- Nutrition
- Exercise
- Medication

Glucose Control

- **The Diabetes Control and Complications Trial**
- Intensive glucose control in patients with **type 1 diabetes** decreases incidence and progression of diabetic retinopathy.
- Risk reductions ranged from 35 to 75% (median 7% A1C)
- Secondary analysis showed strong relationships between risks of developing complications and glycemic exposure over time.
- **Continuous reduction in complications as glycemic levels approached normal range.**

Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 329:977-986, 1993

Reichard P, Nilsson BY, Rosenqvist V. The effect of long-term intensified insulin treatment on the development of microvascular complications of diabetes mellitus. *N Engl J Med* 320:304-309, 1989

POSITION STATEMENT

Implications of the United Kingdom Prospective Diabetes Study

AMERICAN DIABETES ASSOCIATION

- **United Kingdom Prospective Diabetes Study (UKPDS):**
- 10 years (70's – 90's)
- Newly diagnosed **T2D** and reduction CV and microvascular events
- Retinopathy, nephropathy, and neuropathy benefited by lowering BG with **intensive therapy** to achieve median HbA_{1c} 7.0% compared with conventional therapy of median HbA_{1c} of 7.9%.
- Tight vs "less tight" BP control

UKPDS

- Intensive glycemic control
 - Reduced microvascular complications 12%
 - **Reduced progression of retinopathy 25%**
- Intensive blood pressure control (140 vs. 180 mm Hg)
 - Reduced microvascular complications 37%
 - **Reduced progression retinopathy 34%**
 - Reduced moderate vision loss 47%
- 1% reduction in HbA_{1c} reduced the risk for retinopathy by 31%.
- 10 mmHg reduction in SBP reduced photocoagulation or vitreous hemorrhage by 11%.

Legacy Effect

- Metabolic memory
- 10 years after UKPDS trial stopped
- Continued to be reduced by 24% in those previously assigned to tight glycemic control vs. standard glycemic control

ADVANCE Trial

- Action in Diabetes and Vascular Disease: Preterax and Diamicon MR Controlled Evaluation (ADVANCE)
- Aim: whether intensifying glucose control to achieve A1C <6.5% would provide additional benefit in reducing risk of micro and macrovascular disease.
- AND whether BP lowering in T2D with routine BP-lowering therapy produced additional benefits in macro and microvascular disease (irrespective of baseline BP) and added benefits produced by other CV therapies (ACE inhibitors)

ADVANCE Study

- A1C fell progressively in the intensive group to 6.5% after 2–3 years.
- Systolic BP significantly lower in individuals in intensive glucose control group.
- Intensive strategy with conventional agents can achieve mean A1C levels of 6.5% safely with no increase in mortality
- No significant effect in reducing macrovascular disease
- Reduces microvascular disease - diabetic nephropathy by ~20%.



ADA recommends all patients with diabetes (T2 and T1) strive to maintain glycated hemoglobin levels of less than 7% to prevent or minimize long-term complications

ADA

- Glycemic, blood pressure and lipid control
- A1C < 7%
- BP < 140/80 mmHg
- LDL < 100 mg/dL; triglycerides < 150 mg/dL; HDL > 40 mg/dL (men) and > 50 mg/dL (women)
- Achieve and maintain body weight goal
- Delay or prevent complications
- Provide tools for success (meal planning, positive message, personal preferences/culture)

Biguanides

- Lower BG by decreasing amount of glucose produced by liver
- Muscle tissue more sensitive to insulin
- Metformin (Glucophage)
- Taken 2-3 times day with food
- Side effect: diarrhea (very common)

Biguanides and B12

- Malabsorption of B-12 in digestive track
- Metformin-induced Cbl deficiency (MCD): Chronic metformin use results in vitamin B12 deficiency in 30% of patients.
- Exhaustion of vitamin B12 stores usually after 12-15 years of absolute vitamin B12 deficiency.



Biguanides and B12

- B12 deficiency may be misdiagnosed as diabetic neuropathy.
- Poor circulation in hands and toes resulting in numbness, tingling sensation and difficulty in walking.
- Palpitations, vision problems, depression and constipation.
- Vitamin B12: 200-500mcg/day

Nutrition Facts
Serving size: 1 Tablespoon (5g)
Servings Per Container: 25

Amount Per Serving	
Calories 20	
	% Daily Value*
Total Fat 0g	0%
Sodium 0mg	0%
Total Carbohydrate 2g	1%
Dietary Fiber 1g	4%
Protein 3g	

Iron 2% *Thiamine (B1) 180%
Riboflavin (B2) 160% *Niacin (B3) 70%
Pyridoxine (B6) 140% *Folic Acid 40%
Vitamin B12 40% *Pantothenic Acid 30%
Zinc 6% *Selenium 10%

Not a significant source of calories from fat, trans fat, saturated fat, cholesterol, sugar, vitamin A, Vitamin C or Calcium.
*% Daily Value based on 2,000 calorie diet.

Foods with B12

- Liver and organ meats
- Seafood: clams, sardines, tuna, trout, salmon
- Beef
- Eggs
- Dairy
- Nutritional yeast * (vegetarians)

Biguanides Nutrient Depletions

- COQ10
 - Ubiquitous
 - Highest in organs with high rates of metabolism: heart, kidney, and liver
 - Cofactor in ETC in series of redox reactions involved in the synthesis of ATP.
 - Essential for the health of virtually all human tissues and organs.
 - Lipid antioxidant prevents free radicals and modifications of proteins, lipids, and DNA.
- Deficiencies:
 - Muscle weakness, fatigue, kidney failure and slowed cognition.
 - Sustained HBP due to CoQ10 depletion may lead to congestive heart failure.
- COQ10 (30-200mcg) - organ meats (liver), beef, pork, chicken and fatty fish

Biguanides Nutrient Depletions

Folic Acid:

- Vital for making red blood cells and synthesis and repair of DNA and RNA.
- Deficiencies:
 - Reduction in oxygen carrying capacity which can cause anemia and weakness.
 - Cardiovascular disease due to chronic folic acid deficiency.
 - Pregnant women more likely to have serious birth defects.
- Folic Acid: 400mcg/day
- Pulses (dry peas, beans, lentils and chickpeas)

Meglitinides

- Stimulate insulin release from pancreas
- Repaglinide (Prandin), nateglinide (Starlix)
- Taken 3 times day before each meal
- Side effect: hypoglycemia
- May cause depletion of coenzyme Q10

Thiazolidinediones (TZDs or Glitazones)

- Rosiglitazone (Avandia), pioglitazone (ACTOS)
- Make body produce new fat cells which are more sensitive to insulin.
- Improve insulin function and reduces glucose production in liver.
- Liver problems, may increase risk congestive heart failure, macular edema.
- ACTOS: Bladder cancer - lawsuits and FDA review, still prescribed in U.S. but banned in Germany, France and India.
- Side effects: edema (fluid retention), anemia, weight gain

In June 2011, the Type 2 Diabetes drug Actos (pioglitazone) had its sales suspended by medical regulators in France and Germany because of a possible bladder cancer risk. The French and German decisions to ban the drug came after a study commissioned by the French Medicines Agency found that people taking Actos were more likely to develop bladder cancer, an aggressive form of cancer.

Sulfonylureas

- Cause insulin release from the pancreas
- Second generation smaller doses:
 - Glipizide (Glucotrol and Glucotrol XL)
 - Glimepiride (Amaryl),
 - Glyburide (Diabeta, Glynase, Micronase)
 - Tolbutamide (Ornase)
- Once or twice daily with food
- Common side effects: low blood sugar, weight gain, upset stomach, liver (rare) watch for jaundice
- May cause depletion of coenzyme Q10 vitamin B12, folic Acid

T2D and Diabetic Retinopathy

- T2D over 30 years age with diabetes < 5 years with DR:
 - 40% on insulin
 - 24% not on insulin
- T2D over 30 years age with diabetes up to 19 years with DR:
 - 84% on insulin
 - 53% not on insulin
- PDR
 - T2D < 5 years 2%
 - T2D for 25 years or more 25%

Managing Retinopathy

- Early Treatment Diabetic Retinopathy Study (ETDRS):** laser surgery for ME reduces incidence of moderate visual loss from 30% to 15% over a 3-year period.
- Diabetic Retinopathy Study:** Scatter PRP reduces the risk of severe visual loss (< 5/200) by more than 50%.
- Diabetes Control and Complications Trial:** Maintaining HbA1c level in 6-7% optimal for management of diabetes and substantially reduces diabetic retinopathy.
- Diabetic Retinopathy Clinical Research Network (DRCR.net):**
 - Ranibizumab with prompt or deferred focal/grid laser treatment achieved superior visual acuity and OCT outcomes compared with focal/grid laser treatment alone.
 - Ranibizumab groups approx. 50% eyes substantial improvement (10 or more letters) and 30% gained 15 or more letters.
 - Intravitreal triamcinolone combined with focal/grid laser did not result in superior visual outcomes compared with laser alone but did have a visual acuity benefit similar to ranibizumab in pseudophakic eyes.

Anti-VEGF

- Ranibizumab's indication for DR was expanded in 2017 to include all NPDR and PDR with OR without DME.
- Diabetic Retinopathy Clinical Research Network's (DRCR.net) Protocol 5 study:** Ranibizumab therapy in comparison with PRP in DR with or without DME.
- Retinopathy improved in patients in the ranibizumab group, either with or without DME.
- Aflibercept approved for diabetic retinopathy with DME in March 2015 following VISTA^{DM} and VIVID^{DM}.
 - Achieved primary endpoint successfully were 41.6% and 31.1% versus 7.8% (P < 0.0001) in VISTA
 - 32.4% and 33.3% versus 9.1% (P < 0.0001) in VIVID.
- Bevacizumab commonly used to treat DME at a much lower cost alternative.

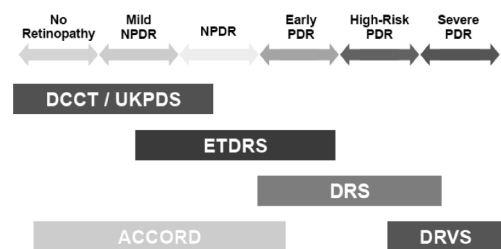
Anti-VEGF

- DRCR.net clinical trial:**
 - Comparing Eylea (aflibercept), Lucentis (ranibizumab), and Avastin (bevacizumab) for DME
 - Aflibercept greater visual improvement than other 2 drugs for VA 20/50 or worse.
 - All 3 achieved similar average improvement for VA 20/40 to 20/32.
 - No major differences in safety
 - Aflibercept and ranibizumab reduced swelling of the macula more than bevacizumab.
 - Smaller percentage of participants on aflibercept (36%) had laser treatment for persistent edema that did not resolve with anti-VEGF treatment alone compared with participants on bevacizumab (56%) or ranibizumab (46%).

Long-Term Monitoring

- F/U frequency dictated by baseline stage of retinopathy.
- Only 5% of patients with mild NPDR progress to PDR in 1 year without follow-up care, monitoring these patients every 6-12 months is appropriate.
- Up to 27% of patients with moderate NPDR progress to PDR in 1 year and these patients should be seen every 4 to 8 months.
- More than 50% with severe NPDR progress to PDR in 1 year without F/U care and 75% develop high-risk characteristics within 5 years; follow-up care every 2 to 3 months to ensure prompt recognition and treatment.
- Any stage associated with DME should be treated promptly with laser and observed closely (every 1-2 mos.)

Diabetic Retinopathy National Institutes of Health-supported Clinical Trials



Obesity in America



- Over 1/3 of U.S. adults (~36%) are obese
- Approximately 12.5 million children and adolescents aged 2-19 (17%) are obese
- Obesity affects all ethnic backgrounds, income and education levels.
- The highest overall obesity rates found amongst racial and ethnic minorities, lower levels of education, lower income levels and in rural populations

The Cost of Obesity



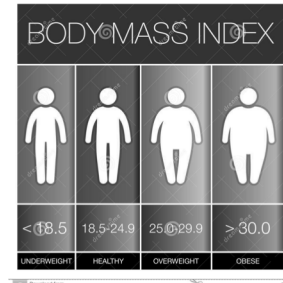
- Direct medical costs **100% higher than healthy weight adults**
- Medical spending \$147 billion annually for adults and \$14.3 billion annually for children.
- Productivity costs (absenteeism, disability, premature mortality) as high as \$66 billion annually for the US.
- Economic impacts (transportation costs and human capital accumulation costs) are significant.
- Overall economic impact of obesity in US is substantial in excess of **\$215 billion**.

Center for Disease Control and Prevention

- Adults
 - Age 20 years and over with obesity: 37.9% (2013-2014)
 - Age 20 years and over with overweight including obesity: 70.7% (2013-2014)
- Children
 - Adolescents age 12-19 years with obesity: 20.6% (2013-2014)
 - Children age 6-11 years with obesity: 17.4% (2013-2014)
 - Children age 2-5 years with obesity: 9.4% (2013-2014)

BMI

- Body Mass Index is a measure of body fat based on height and weight
- Weight (kg) / height(m)²
 - <19: Underweight
 - 19-24: Normal
 - 25-29: Overweight
 - >30: Obese



Obesity and T2DM: "Diabesity"

- Hyperinsulinemia leads to insulin resistance and impaired glucose tolerance
- Obesity is the greatest risk factor for type 2 diabetes

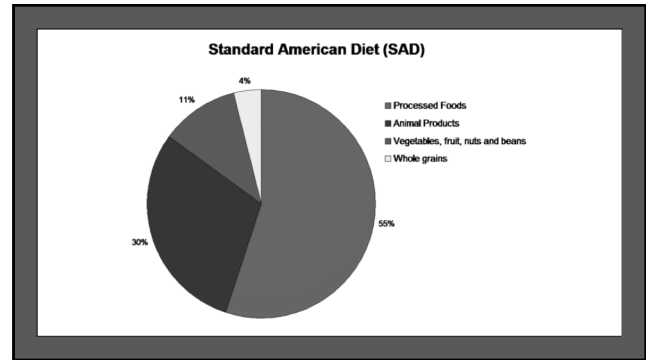
BLOOD GLUCOSE CHART			
Mg/DL	Fasting	After Eating	2-3 hours After Eating
Normal	80-100	170-200	120-140
Impaired Glucose	101-125	190-230	140-160
Diabetic	126+	220-300	200 plus

Diabetes and Weight Loss

- Reducing energy intake while maintaining a healthful eating pattern
- Ten (10%) weight loss improvement in diabetic control
- Modest weight loss correlates with clinical benefits; improved glycemic control, blood pressure and lipid profiles
- May be able to remove or reduce medications

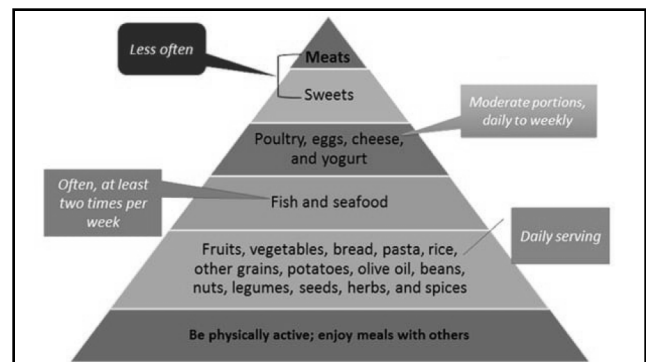
Diabetes and Macronutrients

- Carbohydrate intake has a direct effect on postprandial glucose levels and is the primary macronutrient of concern.
- GI and GL
- No ideal/prescriptive percentages, but on average:
 - Carbohydrates 45%
 - Protein 16%-18%
 - Fat 36%-40%
- Mediterranean eating pattern reported with largest improvement in A1C at 1 year



Mediterranean Diet

- Primarily plant-based foods, such as fruits and vegetables, whole grains, legumes and nuts
- Replacing butter with healthy fats (olive oil and canola oil)
- Using herbs and spices instead of salt to flavor
- Limiting red meat to no more than a few times a month
- Eating fish and poultry at least twice a week
- Enjoying meals with family and friends
- Drinking red wine in moderation (resveratrol)
- Getting plenty of exercise



Mediterranean Diet

- Compare the effects of a low-carbohydrate Mediterranean-style (<50% carb) OR a low-fat diet (<30%) on the need for antihyperglycemic drug therapy in patients with newly diagnosed type 2 diabetes
 - N=100
- After 4 years, 44% of patients in the Mediterranean-style diet group and 70% in the low-fat diet group required treatment. (95% CI and P < 0.001).
- Participants on Mediterranean-style diet lost more weight and experienced greater improvements in some glycemic control and coronary risk measures than did those assigned to the low-fat diet.

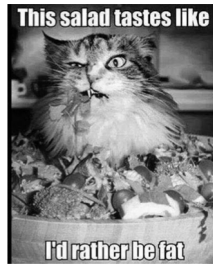
Esposito K, et al. Ann Intern Med. 2009 Sep 1;151(5):1305-14. Effects of a Mediterranean-style diet on the need for antihyperglycemic drug therapy in patients with newly diagnosed type 2 diabetes: a randomized trial.

AHEAD Study

- Action for Health in Diabetes (Look AHEAD): randomized trial on Intensive Lifestyle Intervention (ILI) focusing on weight loss through healthy eating and increased physical activity VS. control condition of Diabetes Support and Education (DSE) in overweight and obese individuals with Type 2 DM.
- Look AHEAD Extension (LA-E) whether ILI provided for 10 years
- Primary aims of LA-E: ILI relative to DSE has long term effects on increased lifespan and reduced health care costs.
- Secondary aims: ILI relative to DSE has long-term effects on healthy aging: less frailty, reduced diabetic microvascular complications, and improved quality of life.
- LA-E will also compare long-term trajectories of weight, physical activity, fat and lean mass, and bone density.

What Works?

- Look AHEAD: At 10 years mean weight loss from baseline was 6% in intervention group and 3.5% in control group.
- Mediterranean-style eating pattern largest improvement in A1C at 1 year.
- Look AHEAD study intensive intervention (healthy eating and physical activity) next largest improvement.



Exercise Works!



- Insulin action in muscle and liver can be modified by exercise
- Acute state: aerobic exercise increases muscle glucose uptake 5-fold
- After exercise:
 - Glucose uptake remains elevated up to 48 hours following prolonged bouts
 - Shorter bouts of exercise (high intensity) glucose uptake remains elevated for up to 24 hours
 - Low intensity 60 minutes enhances insulin action in obese, insulin resistant adults.

Recommendations

- Focus on quality of carbohydrate (GI/GL)
 - Replace sucrose (table sugar) for starch – both affect blood glucose but want food to be nutrient dense
- Fructose in fruit results in better glycemic control compared to sucrose and starch without affecting triglycerides
 - Obesity and diabetes rates were low when total fructose intake was in the range of 25–40 g/d.
- Add fiber and whole grain



Recommendations

- No specific vitamin or supplement recommendations by ADA for diabetics.
- Use general population recommendations for vitamin and essential fatty acid intake.
- Fats
 - Increase monounsaturated fats (Mediterranean diet)
 - Increase EPA and DHA (fatty fish) and ALA for beneficial effects on lipoproteins, prevention of heart disease
 - Decrease saturated and trans fats

Diabetes Month, *Synch Obes*, 2018 Jul 12;11:345-355. doi: 10.2147/DMSO.S165586. eCollection 2018.

Weight outcome after 2 years of a diet that excludes six processed foods: exploratory study of the "1,2,3 diet" in a moderately obese population.

Corone R¹, Colvard J^{1,2}, Lattas P^{1,3}, Harsel B¹, Nivenu S^{1,3}, Dagher P³, Trancharat L^{1,3}.

Author information

Abstract
BACKGROUND: The Paleolithic diet, a diet devoid of food-processing procedure, seems to produce a greater decrease in weight compared to healthy reference diets but its limited food choices make it difficult to implement in our modern times where refined food is dominant.

OBJECTIVE: To evaluate the effects of a 2-year diet that excludes only six refined foodstuffs implicated in obesity. Professional contact was kept minimal to approximate the approach used by most dieters.

DESIGN: Single-arm, open-label, exploratory study.

SETTING: One academic medical center, outpatient setting.

PATIENTS: One hundred and five subjects with a mean age of 50 (SD, 14 years) and mean body mass index of 30.5 kg/m² (SD, 4 kg/m²). Thirty-nine percent had type 2 diabetes.

INTERVENTION: An ad libitum diet that excludes six refined foodstuffs (margarine, vegetable oils, butter, cream, processed meat, and sugary drinks) called the "1,2,3 diet".

OUTCOMES: Weight at 2 years was the primary outcome. Secondary outcomes included number of patients who lost more than 5% of initial body weight, glycated hemoglobin (HbA_{1c}) level, and changes in dietary behavior.

RESULTS: Average weight loss was 4.8 kg (p<0.001), representing 5.6% of their initial body weight. Among completers (51%), the average weight loss was 5.5 kg (p<0.001), and 56% had a reduction of at least 5% of their initial body weight. Among diabetics, weight loss was similar to nondiabetics, and mean HbA_{1c} level decreased by 1% (p<0.001) without modification in glucose-lowering medications. A higher intake of bread, dairy products, chocolate, and fresh fruits was the typical trend in dietary changes reported by completers.

CONCLUSION: In this exploratory study, there was a significant long-term weight loss with the "1,2,3 diet" despite minimal professional contact. Given the lack of a control group and high attrition rate, further evaluation of this diet is warranted.

Plant-Based Eating

- Diet absent or low in animal-based products - beneficial in the prevention of diabetes and microvascular complications such as DR.
- Vegetarian and vegan diets avoid some or all animal-based products but may not include avoidance of high levels of fat, sugar or processed foods.
- Encourages increased intake of fruits, vegetables, legumes, seeds and nuts (in small portions), while avoiding high levels of fat, processed foods and sugars.

The Adventist Health Study 2 (AHS-2)

- N = 96,000 throughout the US and Canada between 2002 and 2007.
- 7.7% vegan, 29.2% lacto-ovo-vegetarian, 9.9% pesco-vegetarian, 5.4% semi-vegetarian and 47.7% non-vegetarian
- Vegetarian diets associated with lower BMI values, lower prevalence of hypertension, lower prevalence of the metabolic syndrome, lower prevalence and incidence of diabetes, and lower all-cause mortality.
- **Vegetarians approximately half the risk of developing diabetes as non-vegetarians.**

Vegetarian diets in the Adventist Health Study 2: a review of initial published findings¹⁻⁴

Michael J. Orlich and Gary E. Fraser

Plant Based Eating and Diabetes?

- Vang et al discovered that non-vegetarians 74% more likely to develop diabetes over a 17-year period.
- Tonstad et al found prevalence of diabetes in vegans to be 2.9% vs. 7.6% in non-vegans.

Plant-Based Eating

- Tanaka, et al
 - Investigated fruit intake and DR evaluated the diets of 978 patients in the Japan Diabetes Complication Study found a correlation between fruit intake and risk of diabetic retinopathy.
 - An intake range of 23 gm/day – 253 g/day, those that consumed an average of 253 g/day of fruit had a 50% **lower risk** of retinopathy than those with a lower intake.
 - Exhibited better A1C, BMI, triglycerides and systolic blood pressure control.

Plant-Based Eating

- Uribarri J 2010
 - AGEs higher levels in animal-derived foods and increased further through cooking at high heat with low moisture.
 - Investigated 549 foods offered within a Northeastern Metropolis area of the US and found the group highest in AGEs were beef and cheeses, as well as poultry, pork, fish and eggs.
 - Grains, legumes, breads, vegetables, fruits and low-fat milk were among the lowest in AGEs.

Schwingshackl et al Meta-Analysis

- Association of T2D with major food groups; whole grains, refined grains, vegetables, fruits, nuts, legumes, eggs, dairy, fish, red meat, processed meat and sugar-sweetened beverages on T2D.
- Optimal consumption of risk-reducing foods of 2 servings/day whole grains, 2-3 servings/day vegetables, 2-3 servings/day fruits, 3 servings/day dairy
- Resulted in 42% reduction of T2D with the greatest reduction seen for whole grains 50 g/day.

Schwingshackl et al Meta-Analysis

- Foods that increased the risk were: red meat 2 servings/day, processed meat 4 servings/day, sugar-sweetened beverages 3 servings/day and eggs 1 serving/day associated with a three-fold increase in the risk for T2D.
- Foods posing the greatest risk were red and processed meats and sugar-sweetened beverages.
- Avoidance of these foods would reduce the risk by 70%.
- Eating the optimal consumption proposed was found to reduce the risk by 80%.

BMR

- Basal metabolic rate (BMR) – activities of the body when individual is at rest but not asleep
 - Slightly lower than RMR
- Resting metabolic rate (RMR) – measured at any time of the day
 - Body size (80% metabolic rates)
 - Thyroid
 - Nutritional status (undernutrition slows RMR)
 - Genetics
 - Age, race, gender
- Overweight/obese individuals have higher RMR than those that are not obese



Diabetes and MPOD

- MPOD is lower in patients with diabetes and even lower in patients with diabetic retinopathy
- Higher serum zeaxanthin/lutein is associated with 2/3 lower risk of developing type 2 diabetes and early NPDR
- Should measure and optimize MPOD in patients with DM and at-risk for diabetes



Invest Ophthalmol Vis Sci. 2010 Nov;51(11):5840-5

Diabetic Retinopathy and Vitamin D

- Vitamin D status has been hypothesized to protect against development of diabetic retinopathy via its anti-inflammatory and anti-angiogenic properties.
- Studies suggest vitamin D favorably influences blood pressure and blood glucose control, which are strong risk factors for diabetic retinopathy.

Look at Serology

Table 1: Serum 25-Hydroxyvitamin D [25(OH)D] Concentrations and Health* [1]

nmol/L**	ng/mL*	Health status
<30	<12	Associated with vitamin D deficiency, leading to rickets in infants and children and osteomalacia in adults
30 to <50	12 to <20	Generally considered inadequate for bone and overall health in healthy individuals
≥50	≥20	Generally considered adequate for bone and overall health in healthy individuals
>125	>50	Emerging evidence links potential adverse effects to such high levels, particularly >150 nmol/L (>60 ng/mL)

* Serum concentrations of 25(OH)D are reported in both nanomoles per liter (nmol/L) and nanograms per milliliter (ng/mL).

** 1 nmol/L = 0.4 ng/mL

NIH Website

Table 2: Recommended Dietary Allowances (RDAs) for Vitamin D [1]

Age	Male	Female	Pregnancy	Lactation
0–12 months*	400 IU (10 mcg)	400 IU (10 mcg)		
1–13 years	600 IU (15 mcg)	600 IU (15 mcg)		
14–18 years	600 IU (15 mcg)	600 IU (15 mcg)	600 IU (15 mcg)	600 IU (15 mcg)
19–50 years	600 IU (15 mcg)	600 IU (15 mcg)	600 IU (15 mcg)	600 IU (15 mcg)
51–70 years	600 IU (15 mcg)	600 IU (15 mcg)		
>70 years	800 IU (20 mcg)	800 IU (20 mcg)		

* Adequate Intake (AI)

NIH Website

Diabetes and Vitamin D

- Participants in the Atherosclerosis Risk in Communities (ARIC) study with
- N = 1339 (906 Caucasians, 433 African Americans)
- Serum 25-hydroxyvitamin (25(OH)D) concentrations assessed and non-mydratric retinal photographs taken to assess retinopathy.
- **Conclusion:**
- 25(OH)D concentrations ≥ 75 nmol/L were associated with lower odds of any retinopathy assessed 3 years later.

Millen A, et al. Adequate vitamin D status is associated with the reduced odds of prevalent diabetic retinopathy in African Americans and Caucasians. *Cardiovasc Diabetol* 2016; 15:128

Diabetic Retinopathy & Vitamin D

- Two groups: N= 139 and 144 patients with and without retinopathy. (Advanced diabetic complications were excluded)
- 25-Hydroxy-vitamin D₃ (25(OH)D) concentrations and vitamin D deficiency were associated with the presence of diabetic retinopathy.
- Patients with more advanced stages of retinopathy had lower concentrations of 25(OH)D and were more frequently vitamin D deficient compared with patients without eye complication.
- **Conclusion:** Association of vitamin D deficiency with the presence and severity of diabetic retinopathy in type 2 diabetes.

Alcubierre N, et al. *Journal of Diabetes Research*. Vol 2015 (2015) Vitamin D Deficiency is Associated with the Presence and Severity of Diabetic Retinopathy in Type 2 Diabetes Mellitus.

J Clin Endocrinol Metab, 2017 Sep 1;102(9):3097-3110. doi: 10.1210/clinem.2017-01024

The Effect of Improved Serum 25-Hydroxyvitamin D Status on Glycemic Control in Diabetic Patients: A Meta-Analysis.

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Abstract

BACKGROUND: Type 2 diabetes is a global health concern, with an increased prevalence and high cost of treatment.

OBJECTIVE: The aim of this systematic review and meta-analysis was to determine the effect of vitamin D supplementation and improved vitamin D status on glycemia and insulin resistance in type 2 diabetic patients.

DATA SOURCE: We searched PUBMED/Medline, Cumulative Index to Nursing and Allied Health, and Cochrane Library (until January 2017).

STUDY SELECTION: Prospective clinical trials were selected evaluating the impact of vitamin D supplementation on glycosylated hemoglobin (HbA1c), serum fasting plasma glucose (FPG), and homeostatic model assessment of insulin resistance (HOMA-IR) in diabetic patients.

DATA EXTRACTION AND SYNTHESIS: We used a random-effects model to synthesize quantitative data, followed by a leave-one-out method for sensitivity analysis. The systematic review registration was CRD42017059555. From a total of 844 entries identified via literature search, 24 controlled trials (1528 individuals diagnosed with type 2 diabetes) were included. The meta-analysis indicated a significant reduction in HbA1c [mean difference: -0.30%; 95% confidence interval (CI): -0.45 to -0.15, P < 0.001], FPG [mean difference: -4.9 mg/dL (-0.27 mmol/L), 95% CI: -8.1 to -1.6 (-0.45 to -0.09 mmol/L), P = 0.003], and HOMA-IR (mean difference: -0.66; 95% CI: -1.06 to -0.26, P = 0.001) following vitamin D supplementation and significant increase in serum 25-hydroxyvitamin D levels [overall increase of 17.2 ± 2.4 nmol/L (67.2 ± 8.9 nmol/L)].

CONCLUSIONS: Vitamin D supplementation, a minimum dose of 100 µg/d (4000 IU/d), may significantly reduce serum FPG, HbA1c, and HOMA-IR index, and helps to control glycoemic response and improve insulin sensitivity in type 2 diabetic patients.

1. **Sunlight** – 5–30 minutes of sun exposure at least twice per week (over 100 percent DV)

2. **Cod Liver Oil** – 1 tablespoon: 1,360 IU (over 100 percent DV)

3. **Wild-Caught Salmon** – 3 ounces: 447 IU (over 100 percent DV)

4. **Mackerel** – 3 ounces: 306 IU (76 percent DV)

5. **Tuna Fish** – 3 ounces: 154 IU (39 percent DV)

6. **Fortified Milk** – 1 cup: 124 IU (31 percent DV)

7. **Sardines** – 2 sardines: 47 IU (12 percent DV)

8. **Beef Liver** – 3 ounces: 42 IU (11 percent DV)

9. **Eggs** – 1 egg: 41 IU (10 percent DV)

10. **Fortified Cereal** – 1 cup: 40 IU (10 percent DV)

11. **Caviar** – 1 tablespoon: 37 IU (9 percent DV)

12. **Mushrooms** – 1 cup: 2 IU (1 percent DV)

BE PROACTIVE ABOUT THE A1C

- Hemoglobin A1c (A1c) is the standard test to measure blood sugar in patients with diabetes.
- Elevated A1c levels are strongly correlated with development of retinopathy.
- Encourage patients to control A1c to significantly reduce the rate of progression of microvascular complications.
- Ask patients to know their A1c level at every visit.
- Patients should aim to keep their A1c level below 7.0%, which is considered diagnostic for diabetes.



ENCOURAGE A HEALTHY LIFESTYLE

- Educate patients on ways to manage modifiable risk factors.
- Though genetics plays a role in the development of T2D, large-scale population studies suggest that excess weight, lack of exercise, unhealthy diet, smoking, and alcohol use might be the most important determinants in the development of diabetes and subsequent complications.
- Encourage patients to take ownership of their lifestyle.