# Finding Freedom: Overcoming Type 2 Diabetes

Diabetes Free Zone Scott Stoll, MD, FABPMR

## Overview

Causes of insulin resistance
 Review dietary research
 Why plant based nutrition
 Practical application







## **Multifactorial Disease**

#### Epigenetic

Environmental Microbiome Medications Food desert Culture

Lifestyle Diet Exercise Stress Habits

# Responds to Multimodal Intervention











# Terry

- Discontinued 18 medications
- Discontinued wheelchair
- Pain resolved and discontinued opioids
- heart disease in remission
- Lost 140 pounds
- Became and inspiration

"Our Findings showed that the increased intake of certain foods and not enough of others was associated with nearly half of all deaths in the US due to heart disease, stroke, and diabetes."

Renata Micha, PhD, RD Lead Author, Jama Study 2017

Micha, Renata, et al. "Association between dietary factors and mortality from heart disease, stroke, and type 2 diabetes in the United States." *Jama* 317.9 (2017): 912-924.



© 2008 Diabetes Health

#### **Current Status of Type 2 Diabetes**

#### 21 million diagnosed

- 9.3% population
- 8.1 million undiagnosed
- 1/3 Caucasian 1/2 ethnic develop DM II
- 100 million by 2050

## 84 million people with pre-diabetes in the US

#### 9/10 don't know they have pre diabetes

Worldwide double by 2030 India: 100 million, 25% family income spent on adult with DM 1 out of 2 have diabetes or prediabetes

#### \$327 billion

- Direct and indirect costs
- 50% higher all cause risk of death
- 2x medical cost-single largest cost is hospital admission for long term complications

Centers for Disease Control and Prevention. National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States, 2017



IDF	2013	2035	INCREASE
REGION	MILLIONS	MILLIONS	%
Africa	19.8	41.4	109%
Middle East and North Africa	34.6	67.9	<b>96</b> %
South-East Asia	72.1	123	71%
South and Central America	24.1	38.5	<mark>60</mark> %
<ul> <li>Western Pacific</li> </ul>	138.2	201.8	46%
North America and Caribbean	36.7	50.4	37%
Europe	56.3	68.9	22%
World	381.8	591.9	55%

#### Lifestyle: Pivot Point

- >90% of the increase in type 2 diabetes in 2<sup>nd</sup> half of the 20<sup>th</sup> century linked to lifestyle
- Children born after 2000: 33% men and 39% women will develop type 2 diabetes
- Type 2 diabetes is largely preventable with lifestyle intervention
- Type 1 diabetes is optimized with lifestyle intervention
- Remission of type 2 diabetes can be achieved with lifestyle intervention



#### **Epigenetics Type 2 DM**

- Maternal diet influences the methylation status of a promoter region (RXRA) strongly correlated with adiposity and metabolic syndromes
- Gestational diabetes mellitus
  - Offspring have a 2-4 four fold increase risk of developing diabetes, metabolic syndrome and obesity
- Epigenetic alleles such as PGC-1α that increase susceptibility to T2D-Chinese, Japanese, Korean, Iranian, and some Europeans like Danish, Italians

#### Insulin Resistance



## **Origins of Insulin Resistance**



![](_page_18_Picture_0.jpeg)

One meal, multiple sites of injury

## NF-kB Inflammatory initiation/Free radicals

![](_page_19_Figure_1.jpeg)

#### Intramyocellular Lipid

![](_page_20_Picture_1.jpeg)

# **Normal Insulin Sensitivity**

![](_page_21_Figure_1.jpeg)

# **Multi-Site Disruption**

![](_page_22_Figure_1.jpeg)

# **Insulin Resistance**

![](_page_23_Figure_1.jpeg)

# **Dietary Intervention Trials**

![](_page_24_Picture_1.jpeg)

#### **Intensive Medication Intervention**

On February 6, 2008 the National Heart, Lung, and Blood Institute (NHLBI) stopped the intensive arm of the ACCORD study (Action to Control Cardiovascular Risk in Diabetes)

"A thorough review of the data shows that the medical treatment strategy of intensively reducing blood sugar below current clinical guidelines causes harm in these especially high-risk patients with type 2 diabetes."

Elizabeth G. Nabel, M.D., director, NHLBI

#### Need to individualize the intervention strategy

https://www.nhlbi.nih.gov/news/press-releases/2008/for-safety-nhlbi-changes-intensive-blood-sugar-treatment-strategy-in-clinical-trial-of-diabetes-and-cardiovascular-disease

# Is Weight Loss the Primary Mechanism?

High Carbohydrate, High Fiber Diet

- 16 day Interventional trial with a plant based diet (HCF)
  - Patients on insulin for type 2 diabetes
  - maintained weight during the study, no weight loss during the study
- Average decrease in insulin dosing 15 units/day
- Insulin dosing was discontinued in 9 patients taking 15-20 u/day and 2 patients taking 32 u/day (approx. 50% of patients)

# **High Fat Diet and IMCL**

- Normal Fat Diet 30% fat, 55% as carbohydrate, and 15% as protein vs. HF diet, 60% fat, 25% as carbohydrate, and 15% as protein.
  - Prescribed physical activity that was 1.6-1.7x metabolic level
  - High fat diet: 54% increase in IMCL with increased molecular adaptations that favor storage of fat
- 4-5 weeks of HF diet: 86-130% increase in IMCL
- High fat, high carbohydrate: induced endotoxemia and disruptions in Toll-like receptor 4 and cytokine signaling 3 involved in insulin signaling
  - High fruit diet did not induce any of these changes

## **Composition of Plant Based Diet**

- Low fat vegan diet with lower saturated and trans fats resulted in greater insulin sensitivity
  - Changes in fatty acid composition were associated with changes in insulin resistance and secretion
- Interventional trials substituting unsaturated fatty acids for saturated fatty acids lowers plasma fatty acids and improves insulin sensitivity
- Plant based diets have been shown to be higher in linoleic acid and improve insulin sensitivity

Fig 1. Pooled hazard ratios (95% CIs) for type 2 diabetes according to deciles of the overall, healthful, and unhealthful plant-based diet indices.

![](_page_29_Figure_1.jpeg)

Satija A, Bhupathiraju SN, Rimm EB, Spiegelman D, Chiuve SE, et al. (2016) Plant-Based Dietary Patterns and Incidence of Type 2 Diabetes in US Men and Women: Results from Three Prospective Cohort Studies. PLOS Medicine 13(6): e1002039. https://doi.org/10.1371/journal.pmed.1002039 https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002039

# **Broad Study**

- Interventional trial of 12 weeks with 1 year follow up
  - Unlimited plant based diet vs. control
  - No exercise intervention
  - Greatest sustained weight loss to date in study with diet alone
  - High satiety levels
  - Improved A1C's in all intervention subjects with 2 reversals (2/32)
  - 29% reduction in medications over 12 months

# Plant Based Diet and Beta Cell Function

- Lifestyle Intervention: Diet and exercise
  - Insulin secretion increased due to increased beta cell function
  - "We demonstrate for the first time that changes in insulin secretion after lifestyle intervention may be mediated via alterations in GIP secretion from intestinal K-cells."
- 16 week interventional trial: Low fat vegan diet significant improvement in beta cell function and insulin sensitivity.
  - Related to loss of visceral fat but independent of changes in BMI

# 24 Week Intervention PBD + Exercise

Conclusion: "We found that a calorie-restricted vegetarian diet increased insulin sensitivity, reduced volume of visceral fat and improved plasma concentrations of adipokines and oxidative stress markers more than a conventional diet in patients with Type 2 diabetes over 24 weeks. The addition of exercise training further augmented the improved outcomes with our vegetarian diet."

# **Dietary Research**

- NIH study:
- 49 participants on PBD vs
- 50 participants on ADA 2002 recommendations
  - No modification of exercise

	PBN	ADA
A1C	↓1.23 points	<b>↓</b> 0.38 points
LDL	<b>↓</b> 21.2%	<b>↓</b> 10.7%
Weight	<b>↓</b> 14.3 lbs	<b>↓</b> 6.8 lbs
Medications Req.	<b>↓</b> 43%	<b>↓</b> 26%

#### **Dietary Research**

Vegetarian vs American Diabetes Association (ADA) diet

![](_page_34_Figure_2.jpeg)

# What about keto/paleo diets?

![](_page_35_Picture_1.jpeg)

# High Protein/Low Carbohydrate

- Systematic review and meta-analysis of dietary carbohydrate restriction in patients with type 2 diabetes.
  - "The greater the carbohydrate restriction, the greater glucose lowering, a relationship that has not been demonstrated earlier. Apart from this lowering of HbA1c over the short term, there is no superiority of low-carbohydrate diets in terms of glycemic control, weight, or LDL cholesterol."

# Studies that depict reduction in IMCL--imaging

- IMCL proportions can be readily imaged clinically using ultrasound and magnetic resonance spectroscopy (MRS)
- 2018 Systematic Review and Meta-Analysis
  - "high-fat diets and diets with caloric intake increased above the amount required to maintain BMI with carbohydrates, and short-term starvation diets are associated with increases in IMF (intramyocellular fat) content"
  - Added sucrose/fructose beverages increased IMF content

## High Protein, Low Carb Diets

#### Lancet NIH funded Meta-analysis

"Low carbohydrate dietary patterns favouring 2 animal-derived protein and fat sources, from sources such as lamb, beef, pork, and chicken, were associated with higher mortality, whereas those that favoured plant-derived protein and fat intake, from sources such as vegetables, nuts, peanut butter, and whole-grain breads, were associated with lower mortality, suggesting that the source of food notably modifies the association between carbohydrate intake and mortality."

# Risks of High Protein/Low Carbohydrate

- Elevated cholesterol
- Renal disease due to acid load
- Increased risk of cancer
- Increased calcium loss
- Can contribute to long term insulin resistance
- Endothelial injury
- Disruption of the microbiome

#### Dietary Research: Meat Consumption and Type 2 DM Risk

- European
   Prospective
   Investigation into
   Cancer and
   Nutrition-EPIC study
  - 16, 835 subcohort on type 2 DM
  - Every 5% of calories from animal protein resulted in a 30% increased risk of diabetes
  - Vegetable protein was not associated with increased risk of DM

![](_page_40_Figure_5.jpeg)

# **Dietary Research: Eggs**

- Nurses Health Study, Health Professionals Follow-up Study and Physicians Health Study:
  - Persons with diabetes consuming more than 1 egg a day double their risk of cardiovascular disease compared to those that ate less than 1 per week
- Eating more than 5 eggs per week was associated with an increased risk of developing diabetes

# Microbiome

#### Humans are an Elaborate Vessel for Bacteria:

![](_page_42_Figure_2.jpeg)

#### Altered Microbiome

"analysis showed that patients with type 2 diabetes were characterized by a moderate degree of gut microbial dysbiosis, a decrease in the abundance of some universal butyrateproducing bacteria and an increase in various opportunistic pathogens" Diet and Lifestyle can restore microbiome

# Microbiome

- Plant based diets for 1 year positively impacted the microbiome by enhancing protective species that produce butyrate and other SCFA and metabolites
  - Improved diversity of bacteria and prevalence of positive strains like Prevotella
  - A1c levels improvement correlated with greater diversity and abundance
  - Greater insulin sensitivity
  - Increased short chain fatty acids that enhance insulin sensitivity and mineral absorption, 
     cholesterol,
     glycolysis in the liver, improved satiety

# Improved Microbiome

- Dietary fiber increases short chain fatty acid producing bacterial strains.
- Improved diversity of bacteria and prevalence of positive strains
- A1C levels improvement correlated with greater diversity and abundance

# Angiogenesis

#### Normal process

- Delicate balance of angiogeneic, (such as VEGF FGF) and angiostatic (angiostatin) factors
- Hyperglycemia disrupter
- Hyperinsulinemia stimulates angiogenesis
- Contributes to macro/microvascular complications

![](_page_46_Picture_6.jpeg)

# **Angiogenesis and Diabetes**

#### Increased risk:

- Poor wound healing
- Peripheral neuropathy
- Diabetic retinopathy
- Renal disease-tubule and glomerulus
- Cancer
- Cardiovascular
- Placenta
  - Hyperglycemia associated with embryonic vasculopathy

![](_page_47_Figure_10.jpeg)

## Dietary Sources That Optimize Angiogenesis

Kale	Blackberries	Sea cucumber
Bok Choy	Blueberries	Pomegranate
Broccoli	Strawberries	Olives
Cauliflower	Cranberries	Maitake mushrooms
Brussels sprouts	Cherries	Onion
Asparagus	Red grapes	Garlic
Parsley	Oranges	Tumeric
Artichokes	Lemons	Ginger
Soy beans	Grapefruit	Сосоа
Tomatoes	Apple	Ginseng
Pumpkin	Pineapple	Green Tea

#### **Diabetes: DPN**

Reduced pain of diabetic peripheral neuropathy

20 week trial: significant reduction pain scores (8.2) and improved quality of life scores Nutrition & Diabetes volume 5, page e158 (2015)

 25 day inpatient intervention: 17/21 or 81% reported a significant improvement in symptoms including numbness in just 4-16 days
 2 weeks Insulin requirement decreased in 50% of patients
 14<sup>th</sup> day fasting blood glucose decreased 35%
 4 year follow-up 71% maintained on the diet, 16/17 reported no return of symptoms

Crane, Milton G., and Clyde Sample. "Regression of diabelic neuropathy with total vegetarian (vegan) diet. Journal of Nutritional and Environmenta Medicine 4.4 (1994): 431-439.

#### **Reversal of DPN**

Iran: Interventional Trial 2018: lifestyle vs control

- Patients with severe pain: All reported improvement and only mild to moderate pain at the end of the study
- 6 with mild symptoms had complete resolution
- 13 people with moderate neuropathy
  - 5 complete resolution
  - 8 reported mild pain at the end of the trial
  - All in the control group same or worse

#### Intensive Lifestyle Intervention: Diabetic Retinopathy

![](_page_51_Picture_1.jpeg)

February 1954

March 1956

![](_page_51_Picture_4.jpeg)

#### **Geisinger Health**

![](_page_52_Picture_1.jpeg)

"We should be investing in people and processes, not hospitals."

Dr. David Feinberg, CEO

#### So they did...

### FreshFood Farmacy<sup>™</sup> Geisinger

![](_page_53_Picture_2.jpeg)

Identified patients with T2DM (A1c >8) and who self identified with food insecurity Food insecurity: 14% pop, 23% children Claims data revealed \$8000-\$12000 per month expenses

#### **Pilot Study:**

- 37 patients for 12 months
- Pre A1c 9.6%, Post 7.5%
- corresponds to 40% decrease in risk of death and serious consequences
- Mean healthcare costs decreased by 80%
- From \$240,000/member/year to \$48,000/member/year

![](_page_54_Picture_6.jpeg)

![](_page_54_Picture_7.jpeg)

#### Lifestyle Intervention: Nutrition

- Epigenetic effect-potential generational effect
- Normalize angiogenesis reducing comorbid disease
- Lower total caloric intake resulting in weight loss, improved A1C, leptin adiponectin levels
- Independent of weight loss, WFPBD improves insulin sensitivity
- Anti-inflammatory diet, both by addition and subtraction, improving insulin sensitivity
- Lower overall endothelial cell injury, oxidative stress and inflammatory cascade NF-Kβ, JNK

#### Lifestyle Intervention

#### Protection of β cells

- Normalization of lipid profile
- Normalization of leptin/adiponectin pathway
- Down regulation of cytokine inflammatory cascade
- Down regulation of NF-Kβ
- Normalization of glucose protects against apoptosis
- Stabilizes immune system via multitude of pathways

Intensive Lifestyle Intervention with a WFPBD: Comprehensive Solution

### Diabetes

![](_page_57_Figure_2.jpeg)

Macular Degeneration

Alzheimer's

No matter how far you traveled down one road, You're only one step awa from choosing a new direction.

![](_page_59_Picture_0.jpeg)

![](_page_60_Picture_0.jpeg)

![](_page_60_Picture_1.jpeg)

www.PlantricianProject.org WWW.IJDRP.org <u>www.PBNHC.com</u> <u>www.plantbaseddocs.com</u> <u>www.nutritionfacts.org</u>

# Thank You

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