

The Virta Health Clinic Reversing Type 2 Diabetes

Stephen Phinney MD, PhD

**Prof of Medicine, emeritus
UC Davis**

CMO, Virta Health

Disclosures

Commercial Interest

What Received

Role

Virta Health Corp

Ownership Interest

Chief Medical Officer
Co-founder

Beyond Obesity, LLC

Book Royalties

Author

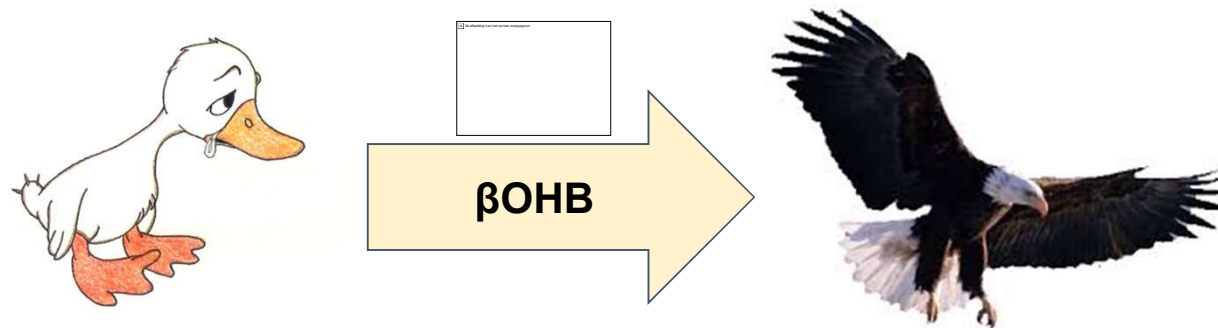
Atkins Nutritionals, Inc

Honorarium

Science Advisor

Introduction to Nutritional Ketosis

- Until recently, much of what is taught about ketones to health care providers is flawed or outright wrong
 - Most physicians still do not differentiate between physiological ketones as a fuel source and the pathophysiology of DKA
- In the past 5 years, our perspective and appreciation of β OHB have changed radically
 - Superior energy supply
 - Hormone-like activity regulating oxidative stress and inflammation

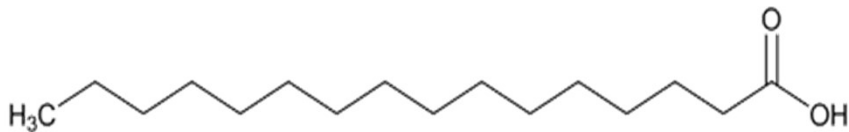


Ketones: NOT a “Toxic” Accident of Metabolism



STORED ENERGY

Palmitate = 16-carbon Saturated Fat

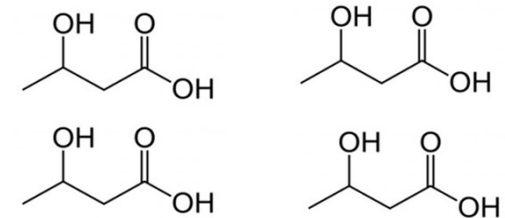


versus



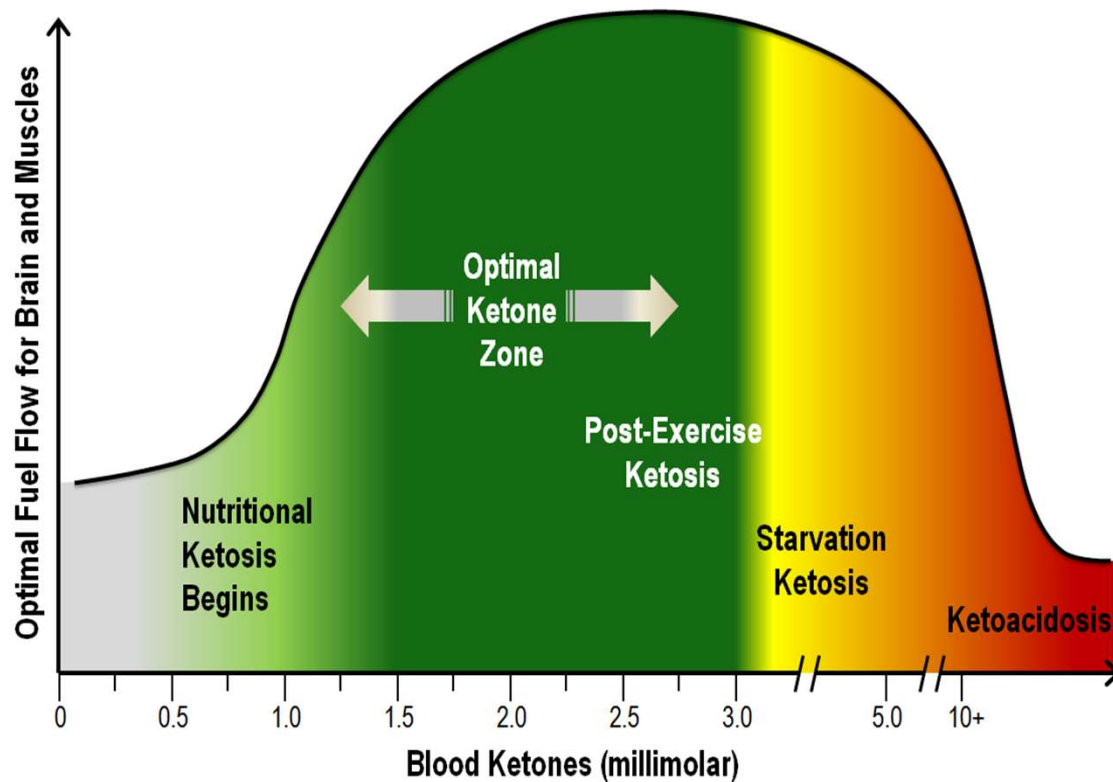
USEABLE ENERGY

4 x βOHB = 4-carbon Carboxylic Acid



- Firewood is NOT just “broken logs”
- Ketones are NOT “toxic breakdown products of fat” → they are made on **PURPOSE**

The Ketone Zone: Nutritional Ketosis versus DKA



State	Ketones (mmol/L)	
Moderate-carbohydrate diet (fed state)	<0.1	10X
Moderate-carbohydrate diet (fasted state)	0.1 to 0.3	
Fasting (weeks)	5 to 7	
Very low-carbohydrate diet (<50 g/day)	0.5 to 3.0	10X
Very low-carbohydrate diet (post-exercise)	1.0 to 5.0	
Keto-acidosis (insulin insufficiency)	10 to 20+	

The New Science of BOHB

Reduced
oxidative
stress
reduces
aging and
inflammation

Suppression of Oxidative Stress by β -Hydroxybutyrate, an Endogenous Histone Deacetylase Inhibitor

Tadahiro Shimazu^{1,2}, Matthew D. Hirschey^{1,2}, John Newman^{1,2}, Wenjuan He^{1,2}, Kotaro Shirakawa^{1,2}, Natacha Le Moan³, ...

+ See all authors and affiliations

Science 11 Jan 2013;
Vol. 339, Issue 6116, pp. 211-214
DOI: 10.1126/science.1227166





Diabetes Research and Clinical Practice

Volume 106, Issue 2, November 2014, Pages 173-181

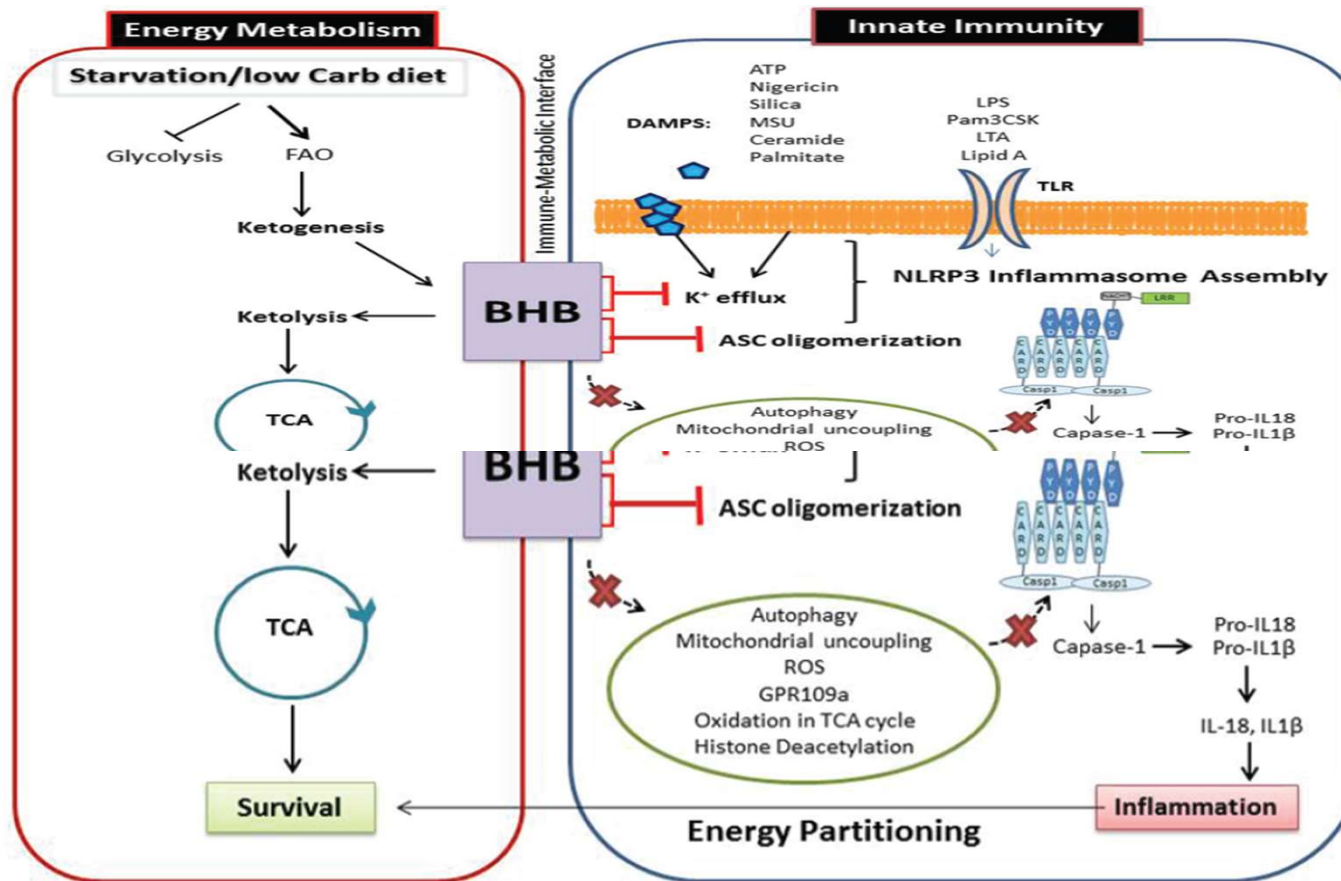
Invited Review

β -hydroxybutyrate: Much more than a metabolite

John C. Newman^{a, b}, Eric Verdin^b  

Possible
direct effects
on insulin
resistance

β OHB Inhibits Inflammatory Gene Expression



- β OHB does not just reduce isoprostane production (prostaglandin-like compounds formed by ROS-peroxidation of essential fatty acids like ARA)
- It intervenes at the regulatory level by blocking NLRP3 inflammasome-mediated inflammatory disease

Source: Youm et al.; "Ketone body β -hydroxybutyrate blocks the NLRP3 inflammasome-mediated inflammatory disease"; Nature Medicine (2015)

Inflammation and Type 2 Diabetes

Type 2 diabetes as an inflammatory disease

Marc Y. Donath and Steven E. Shoelson#*

www.nature.com/reviews/immunol

FEBRUARY 2011 | VOLUME 11

The Journal of Clinical Investigation

REVIEW SERIES: METABOLISM AND INFLAMMATION

Series Editors: Alan R. Saltiel and Jerrold M. Olefsky

Inflammatory mechanisms linking obesity and metabolic disease

Alan R. Saltiel and Jerrold M. Olefsky

Department of Medicine, UCSD, La Jolla, California, USA.

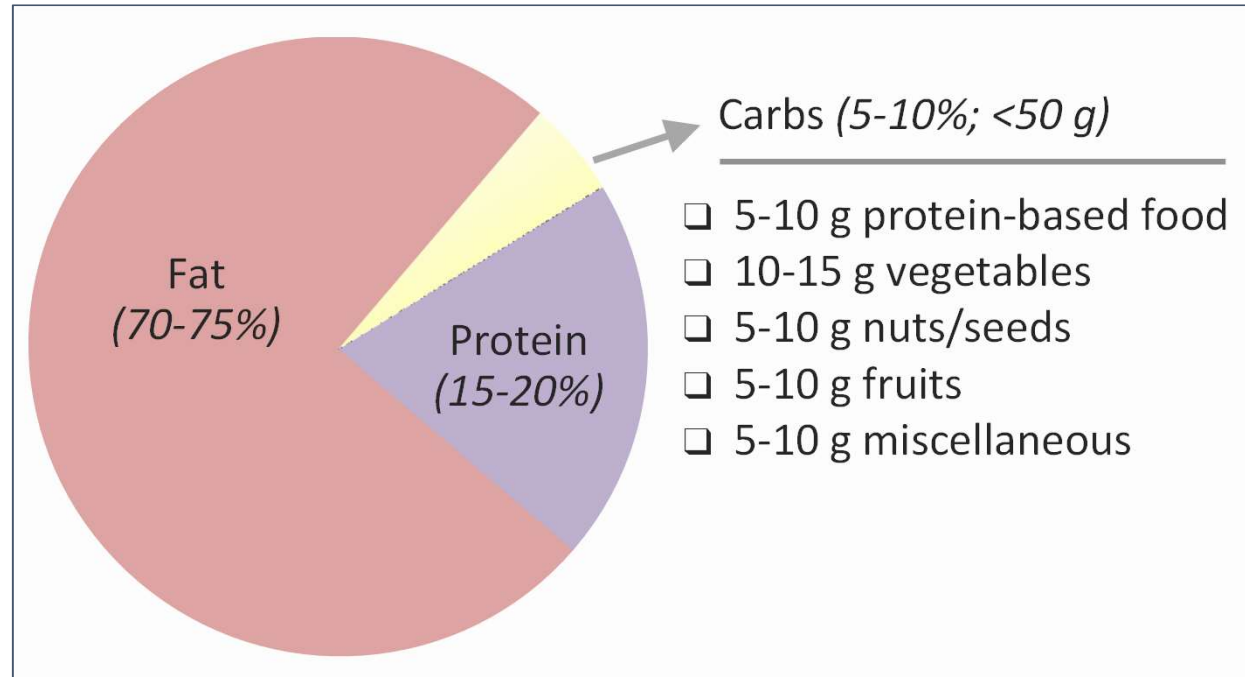
jci.org

Volume 127

Number 1

January 2017

What Goes into a WFKD?



Study: LFD versus LCD for Metabolic Syndrome (2009)

Lipids

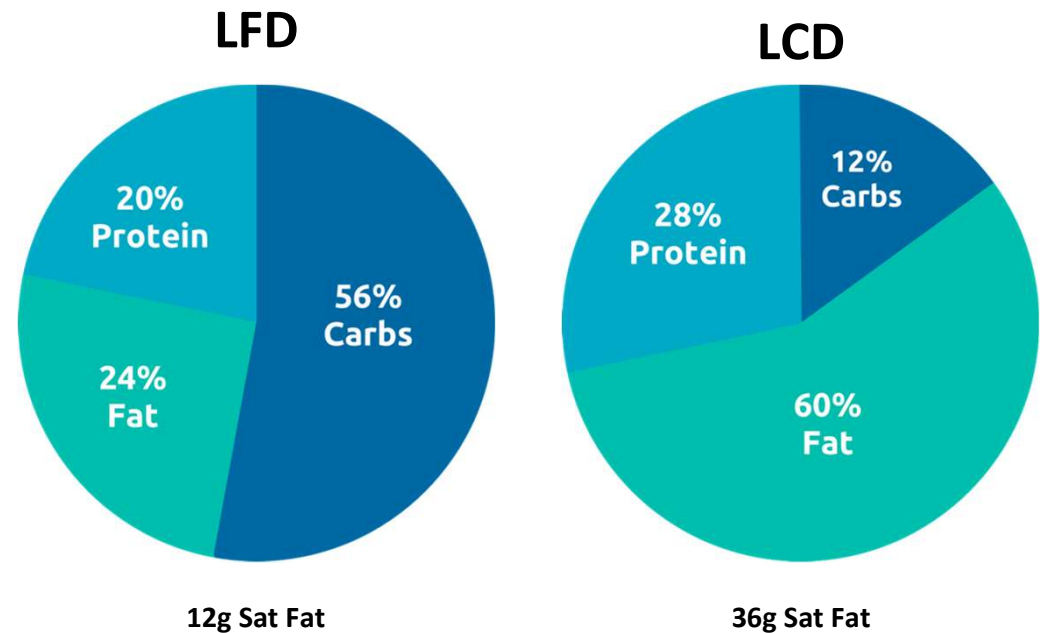
N = 40

Demographics:

- 40 overweight subjects with atherogenic dyslipidemia
- Age: 18 – 55 years
- BMI > 25 kg/m²

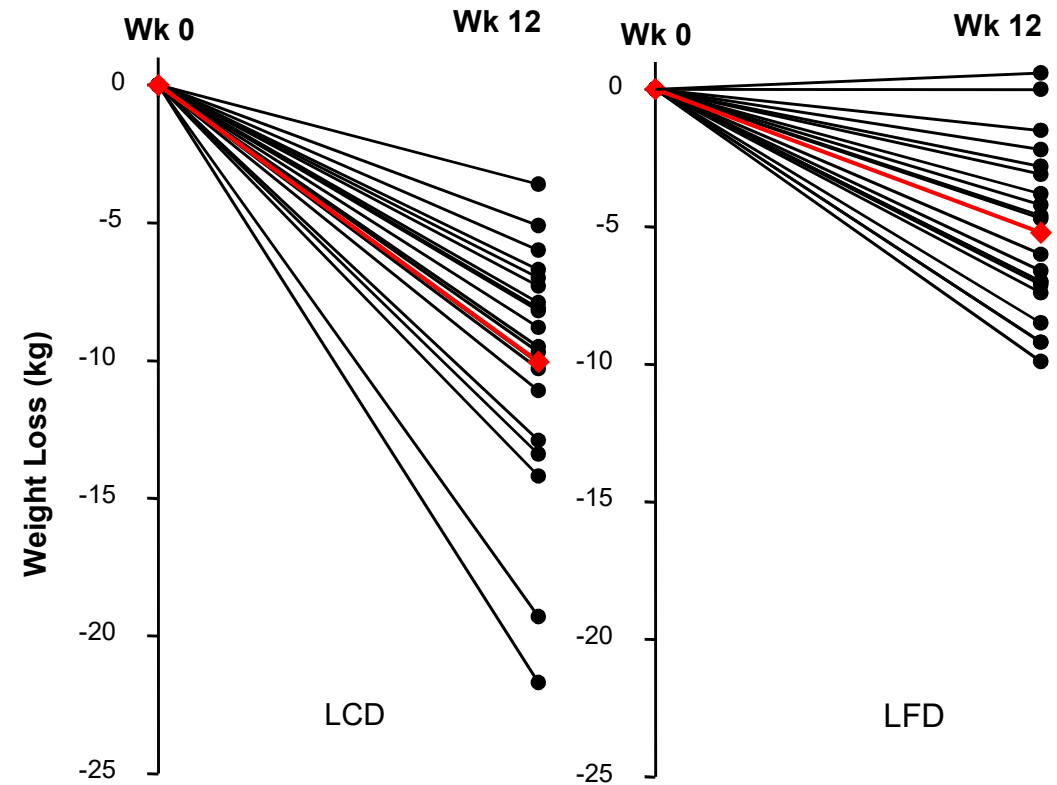
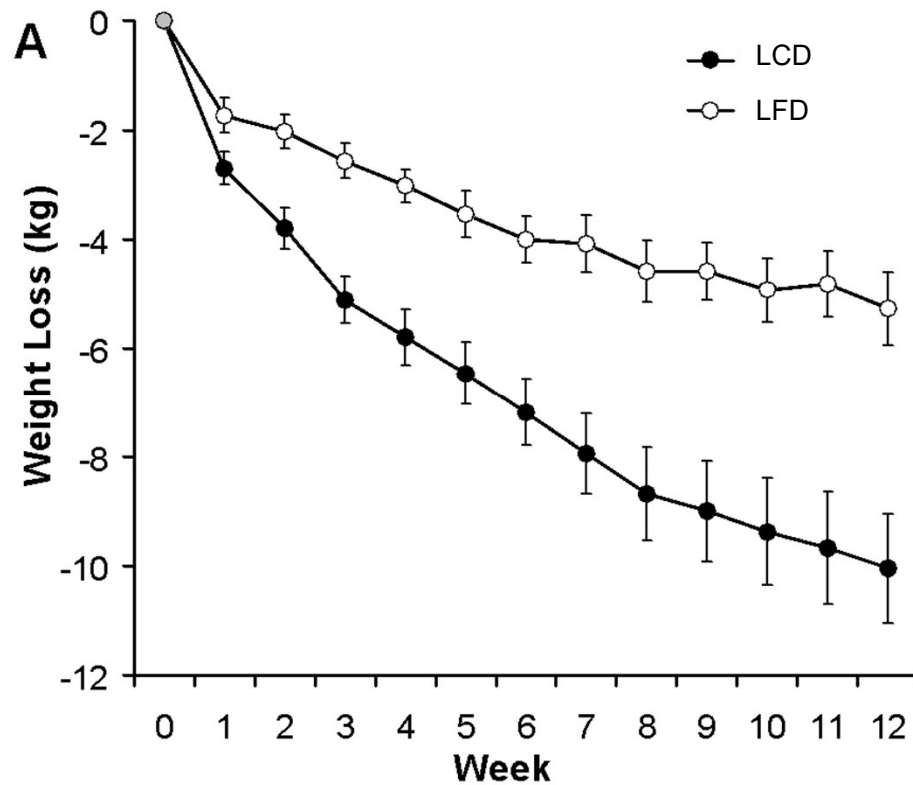
Method:

- Outpatient for 12 weeks
- Two randomly assigned groups:
 - LCD: eaten to satiety (reported 1500 kcal); 12% carb, 59% fat, 28% protein
 - Hypocaloric LFD: 1,500 kcal, 56% carb; 24% fat; 20% protein



Source: Forsythe et al.; "Carbohydrate Restriction has a More Favorable Impact on the Metabolic Syndrome than a Low Fat Diet"; Lipids (2009)

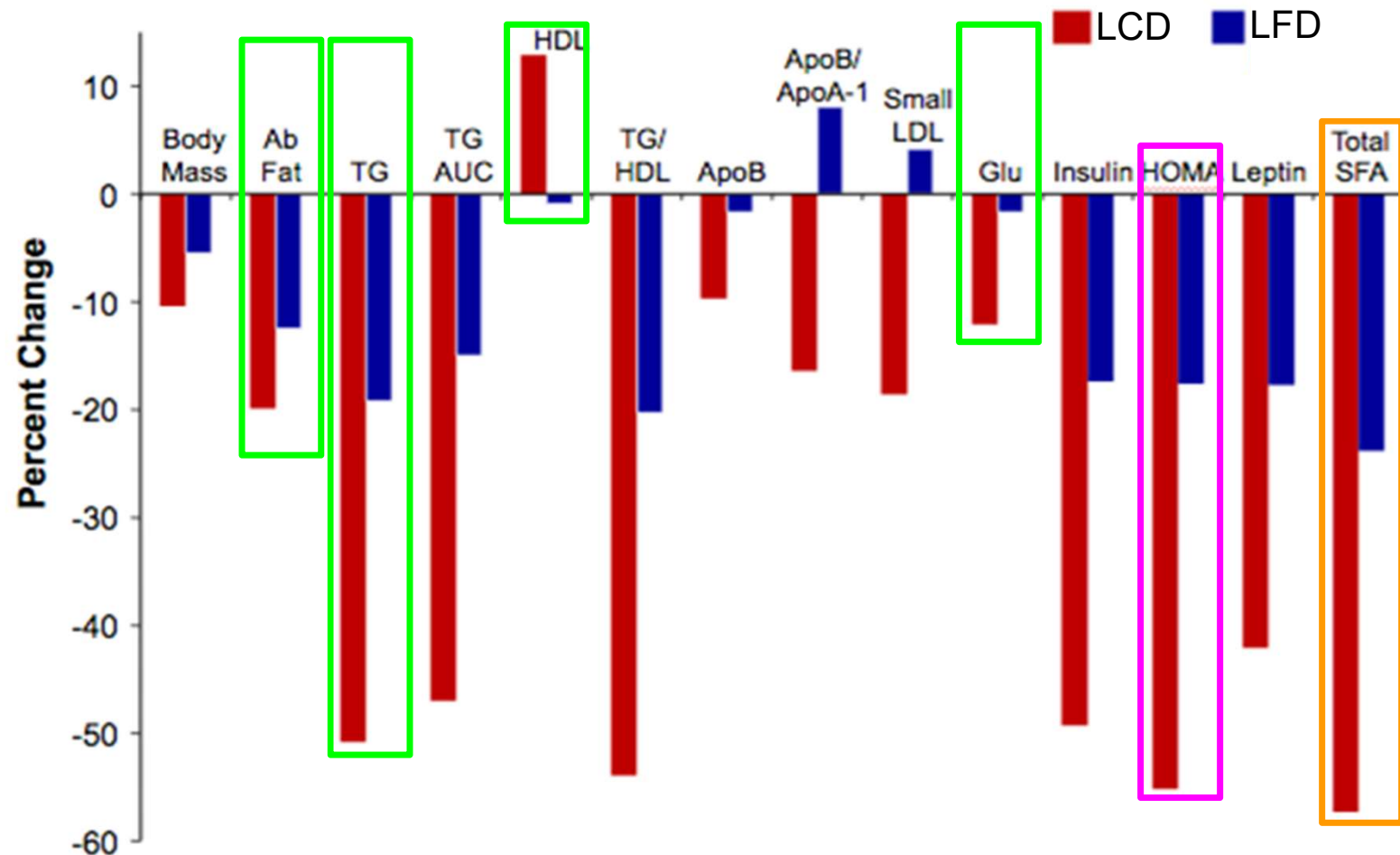
Results: LFD versus LCD for Metabolic Syndrome (2009)



- While both groups continue weight loss at 12-weeks, **LCD weight loss significantly greater**

Forsythe et al.; "Carbohydrate Restriction has a More Favorable Impact on the Metabolic Syndrome than a Low Fat Diet"; Lipids (2009)

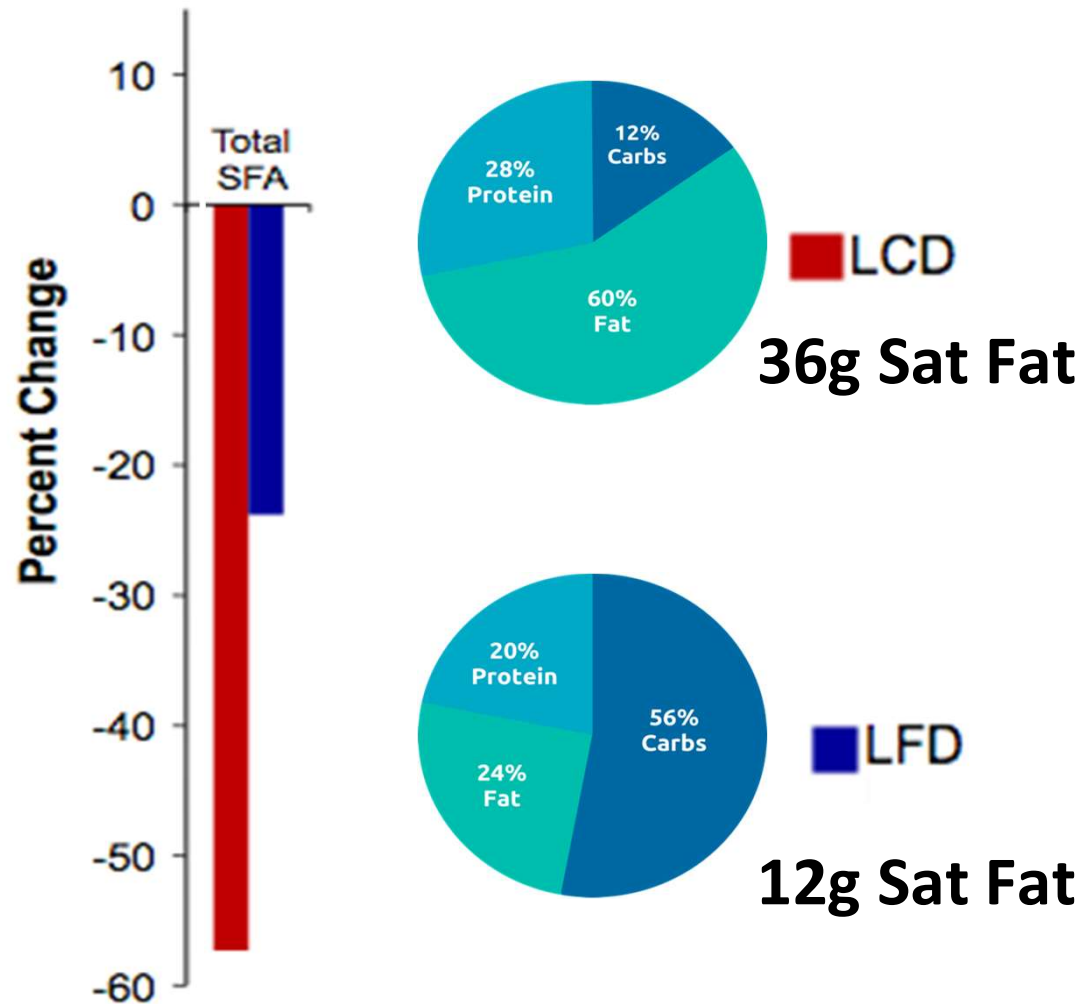
Results: LFD versus LCD for Metabolic Syndrome (2009)



- All the **markers of MetS improved**, significantly better in LC than LF
 - Except BP (not shown)
- **Marker of insulin resistance (HOMA-IR)** improved dramatically for LC than LF
- **Total SFA** was dramatically lower in LC than LF in serum, even though dietary intake was 3x higher
 - Likely because patients are so much better at oxidizing it

Source: Forsythe et al.; "Carbohydrate Restriction has a More Favorable Impact on the Metabolic Syndrome than a Low Fat Diet"; Lipids (2009)

Conclusions: LFD versus LCD for Metabolic Syndrome (2009)

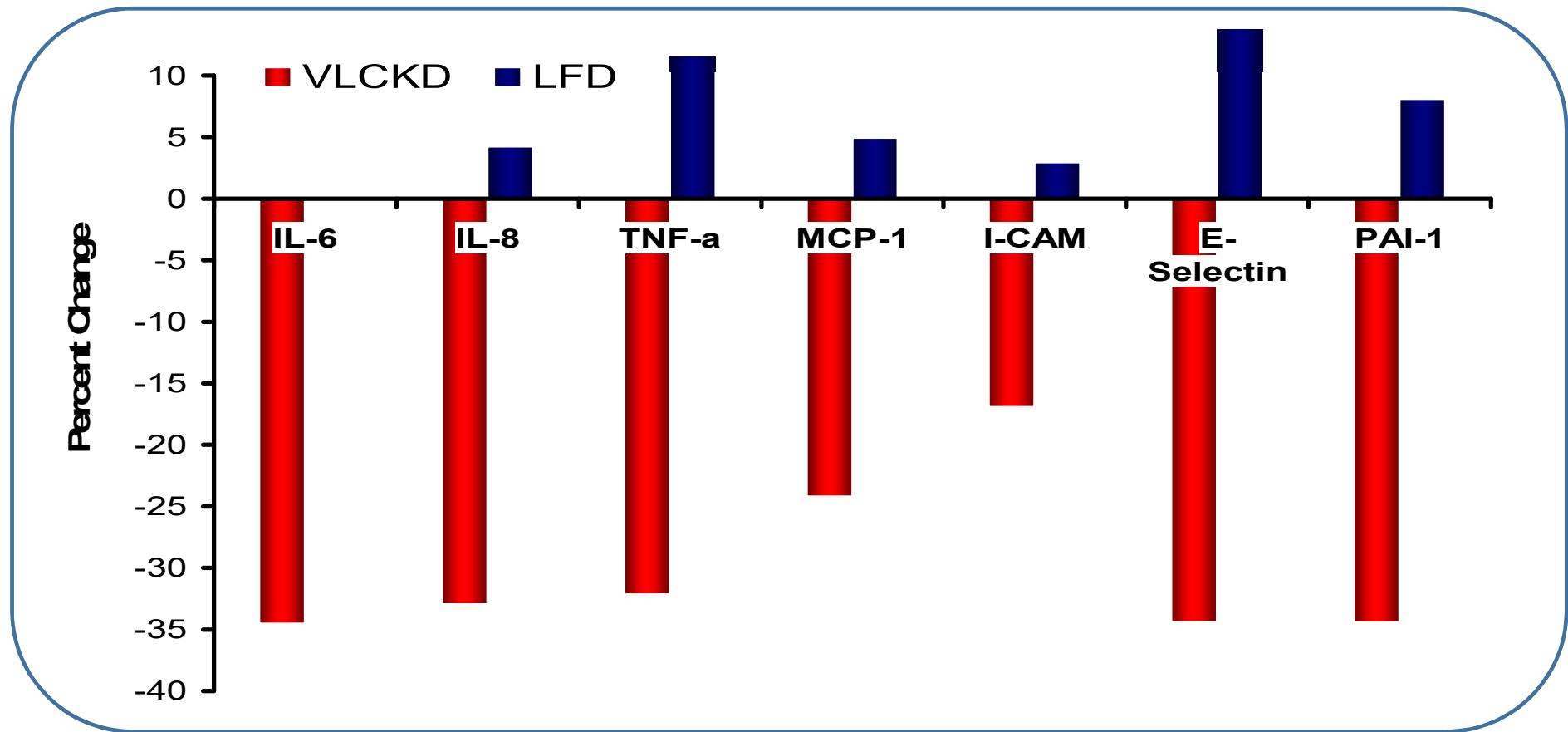


- This study was on MetS, which is essentially the same as Pre-D
 - Showed significant improvements in LCD over LFD for both lipid profiles and insulin resistance
- “You are NOT what you eat”
 - Eating a lot of saturated fat on a WFKD is not dangerous!

Source: Forsythe et al.; “Carbohydrate Restriction has a More Favorable Impact on the Metabolic Syndrome than a Low Fat Diet”; Lipids (2009)

A ketogenic diet has potent anti-inflammatory effects

LCD vs LFD: 7 of 14 inflammation biomarkers significantly reduced



Study: First Published Diabetes Reversal (1976)



N = 7

Demographics:

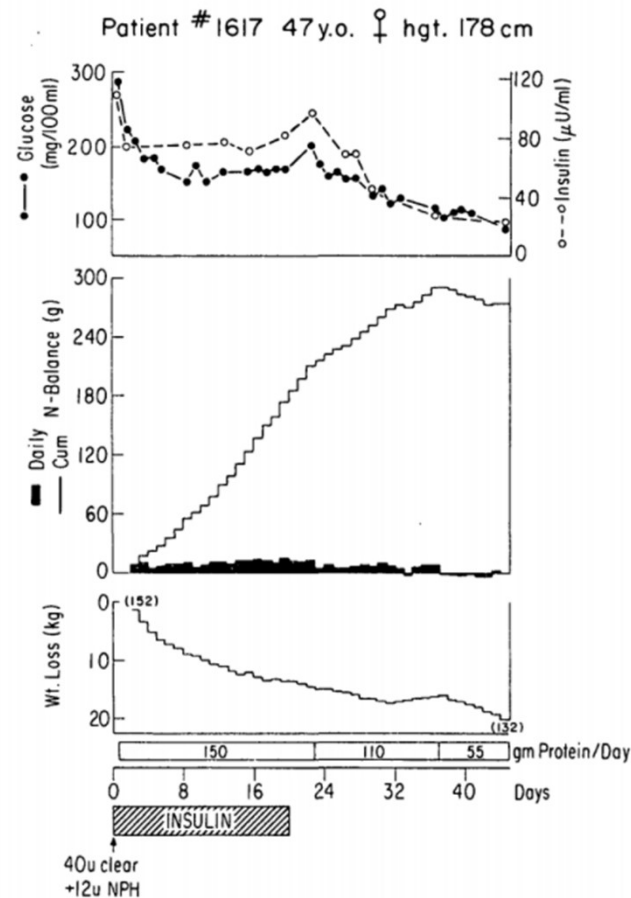
- Obese T2D patients, all on insulin
- Age: 47 – 63 years; 5/7 female

Method:

- Inpatient (6/7) in metabolic ward to ensure adherence (1.5-4 months)
 - Then followed as outpatients (1.5-12 months)
- Treated with a **ketogenic PSMF** = protein-sparing modified fast
 - Extreme caloric restriction = 350-750 cal/day
- Included vitamin/mineral supplements (K⁺, Ca⁺, Na⁺, Fe⁺)

Results:

- Weight Loss: 5/7 maintained 9-74 kg weight loss after 12 months
- Insulin: withdrawn within 0-19 days for all patients



→ This is the **FIRST** modern use of a ketogenic diet to reverse T2D, and it worked in **EVERY** patient (7/7)

FIG. 1. Acute effects on selected biochemical and clinical parameters of a PSMF in patient 1.

Study: The Prompt Action of a WFKD Against T2D (Boden, 2005)

Annals of Internal Medicine

ESTABLISHED IN 1927 BY THE AMERICAN COLLEGE OF PHYSICIANS

N = 10

Demographics:

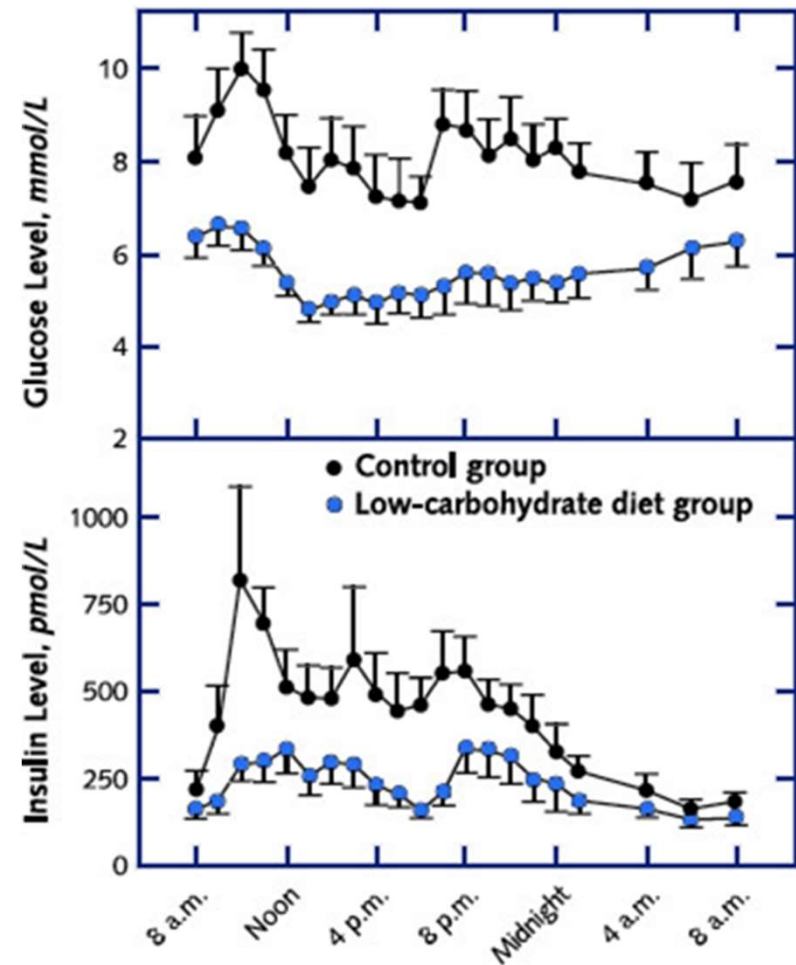
- Obese T2D patients
- Age: 51 ± 9.5 (36–64)
- BMI: 40.3 ± 5.7 (33–52)

Method:

- Inpatient, metabolic ward for 3 weeks
- Fed SAD 7 days, then low carb (<21 g/d) diet for 14 days
 - No calorie restriction - buffet-style eating, all food weighed

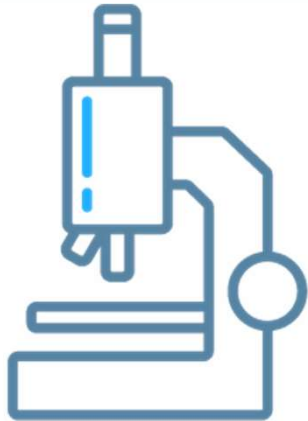
Results:

- Fasting BG: $7.5 \rightarrow 6.3$ mmol/L
- HbA1c: $7.3 \rightarrow 6.8\%$
- Insulin sensitivity: increased ~75% (euglycemic hyperinsulinemic clamp)
- Meds reduced
- Plasma triglycerides: decreased 35%
- Plasma cholesterol: decreased 10%
- Hunger reduced



Source: Boden et al.; "Effect of a Low-Carbohydrate Diet on Appetite, Blood Glucose Levels, and Insulin Resistance in Obese Patients with Type 2 Diabetes"; Ann Intern Med. (2005)

Virta's Two Innovations



Science



Technology

Technology



BIOMARKER TRACKING

- Weight
- Glucose
- Finger-stick BOHB



PATIENT





**BIOMARKER
TRACKING**



Coach continually monitors data

PATIENT



HEALTH COACH

Provide daily input
and support

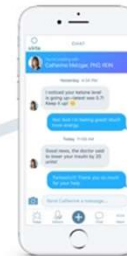


**BIOMARKER
TRACKING**



Coach continually monitors data

PATIENT



HEALTH COACH

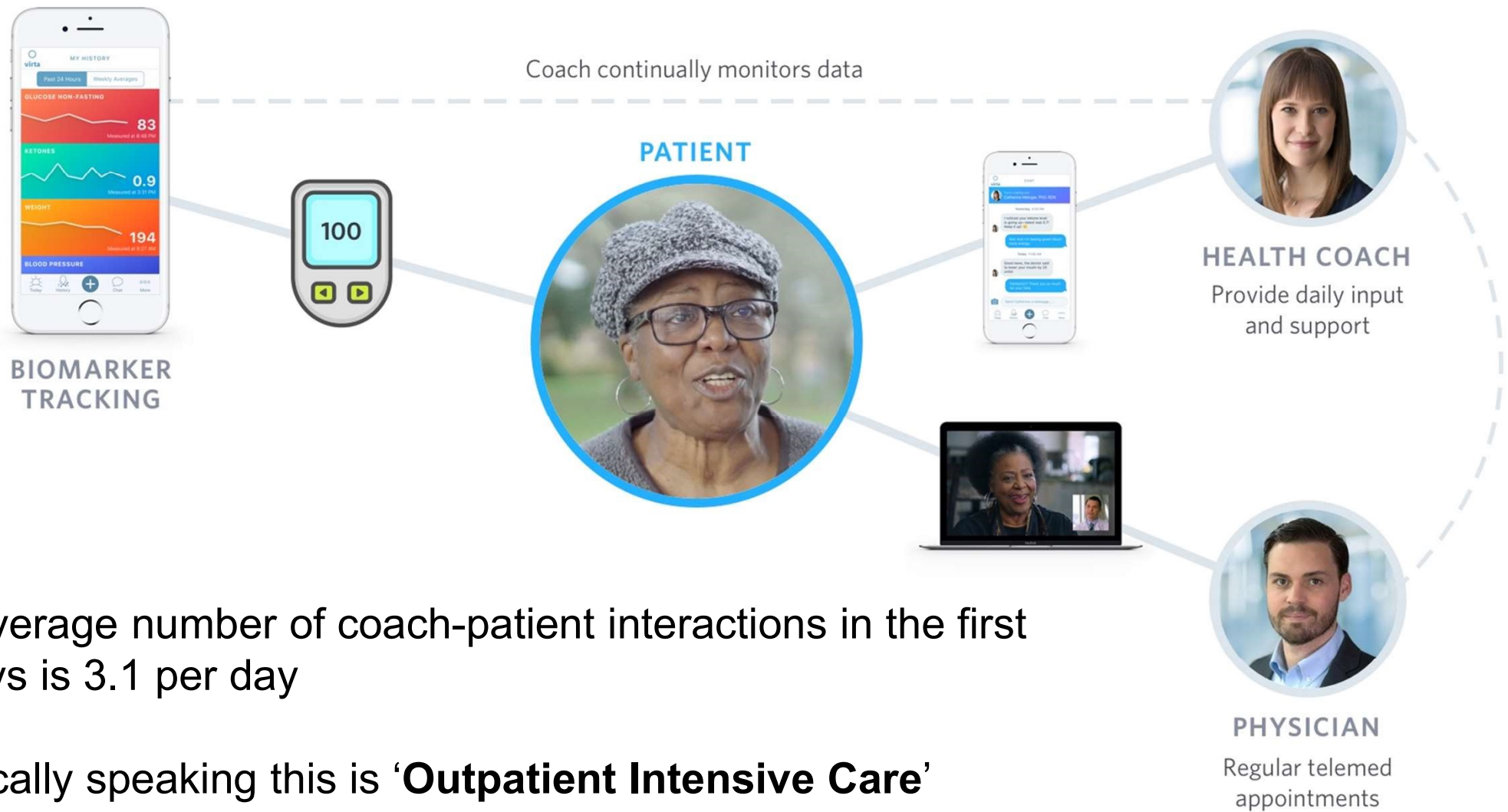
Provide daily input
and support



PHYSICIAN

Regular telemed
appointments

Licensed to practice tele-medicine in 50 states



The average number of coach-patient interactions in the first 70 days is 3.1 per day

Practically speaking this is '**Outpatient Intensive Care**'
Necessary for safe diabetes medication management

Coach continually monitors data

PATIENT



BIOMARKER TRACKING



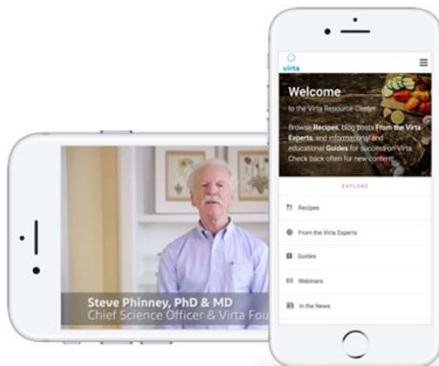
HEALTH COACH

Provide daily input and support



PHYSICIAN

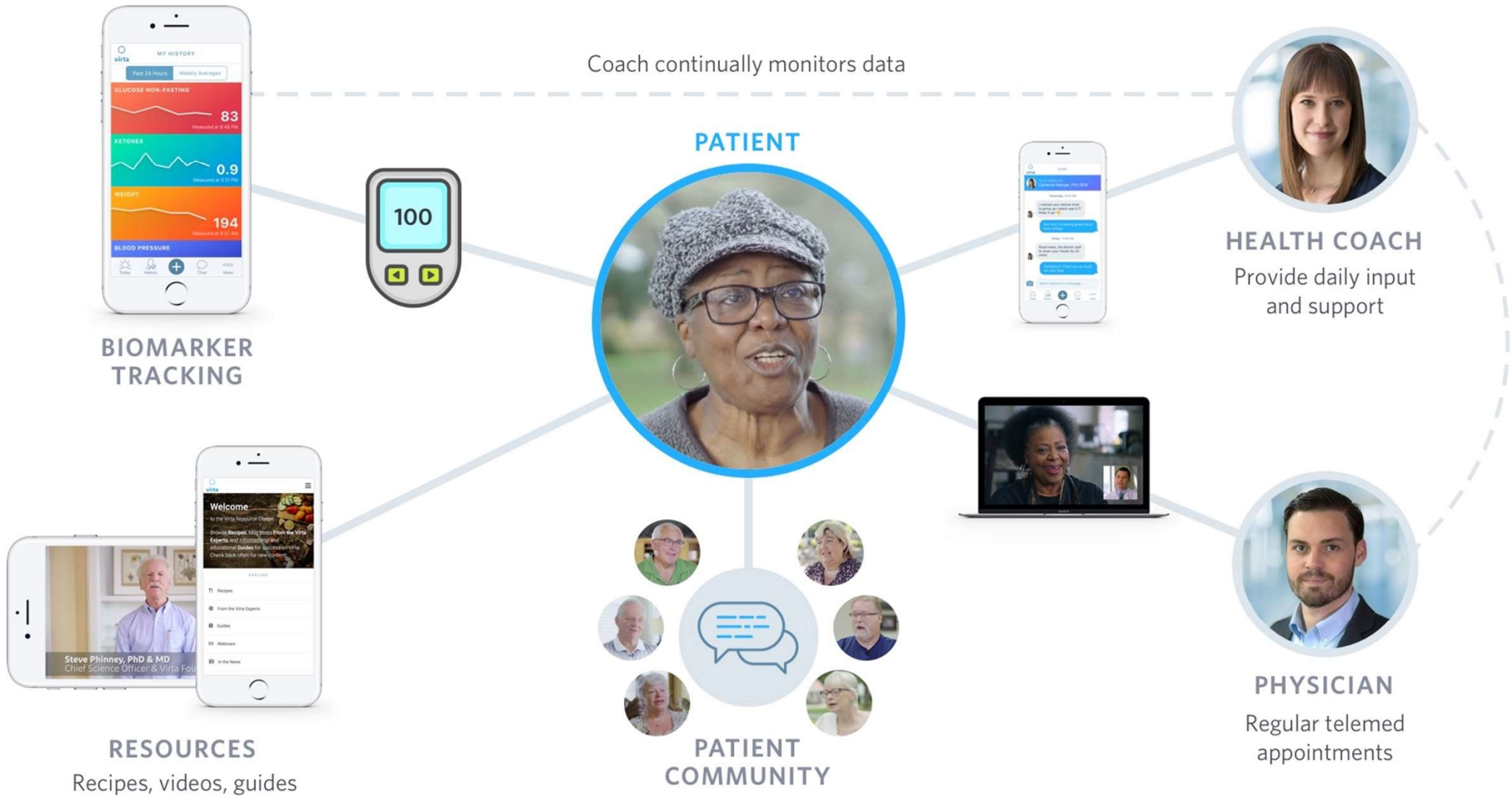
Regular telemed appointments



RESOURCES

Recipes, videos, guides





THE IUH CLINICAL TRIAL
Principal Investigator
Dr. Sarah Hallberg

Our Patients

N = 262 with T2D, 67% female

Location: Central Indiana

Mean Age: 54

Mean Starting BMI: 41

Mean Starting Weight: 117 kg

Our Diet (real foods)

30 g/d carbs

Moderate protein

Added fat to satiety



New Study: The Virta Ongoing IUH Clinical Trial (2017)

A Novel Intervention Including Individualized Nutritional Recommendations Reduces Hemoglobin A1c Level, Medication Use, and Weight in Type 2 Diabetes

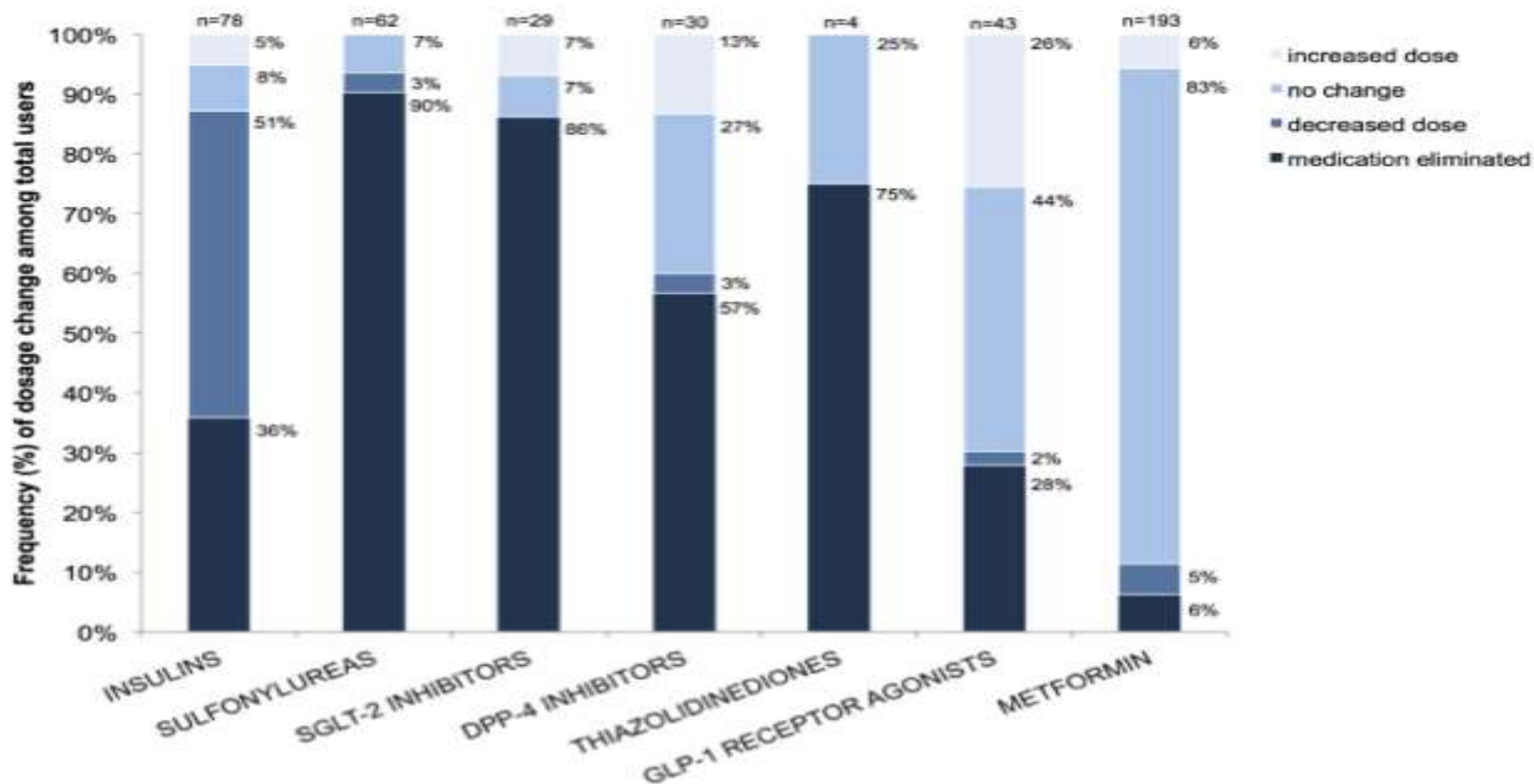
Amy L McKenzie¹, PhD; Sarah J Hallberg^{1,2}, DO, MS; Brent C Creighton¹, PhD; Brittanie M Volk¹, RD, PhD; Theresa M Link¹, RD, CDE; Marcy K Abner¹, RD; Roberta M Glon¹, RN, BSN; James P McCarter¹, MD, PhD; Jeff S Volek¹, RD, PhD; Stephen D Phinney¹, MD, PhD

¹Virta Health, San Francisco, CA, United States

²Indiana University Health Arnett, Medically Supervised Weight Loss, Lafayette, IN, United States

JMIR Diabetes 2017;2(1):e5 <http://diabetes.jmir.org/2017/1/e5/>

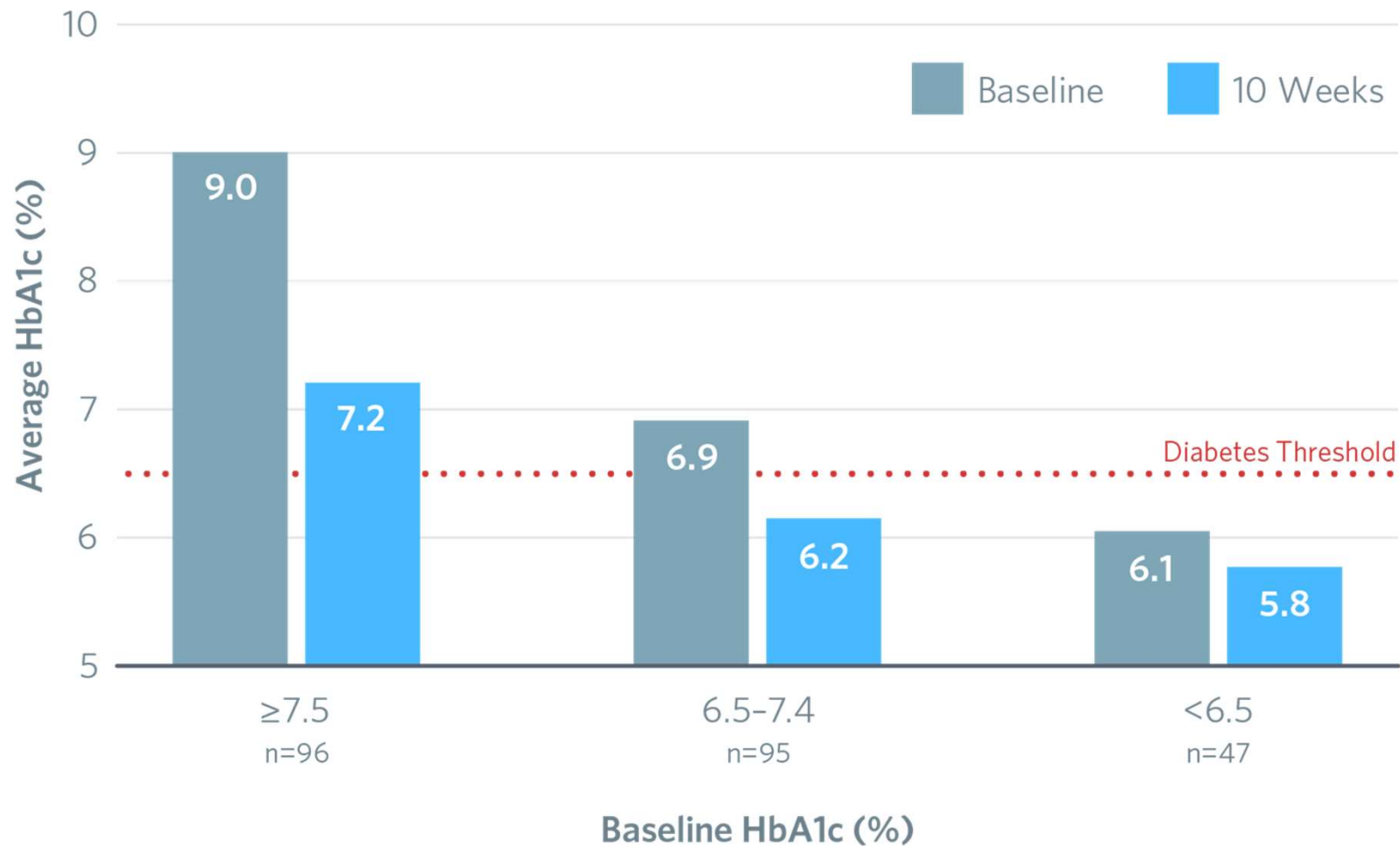
Medication changes in 232 people with type 2 diabetes after 10 weeks on a well-formulated ketogenic diet



McKenzie et al. JMIR Diabetes, 2017

AFTER 10 WEEKS

Significant Decreases in HbA1c



HbA1c decreased by 1.0 from 7.5% to 6.5%

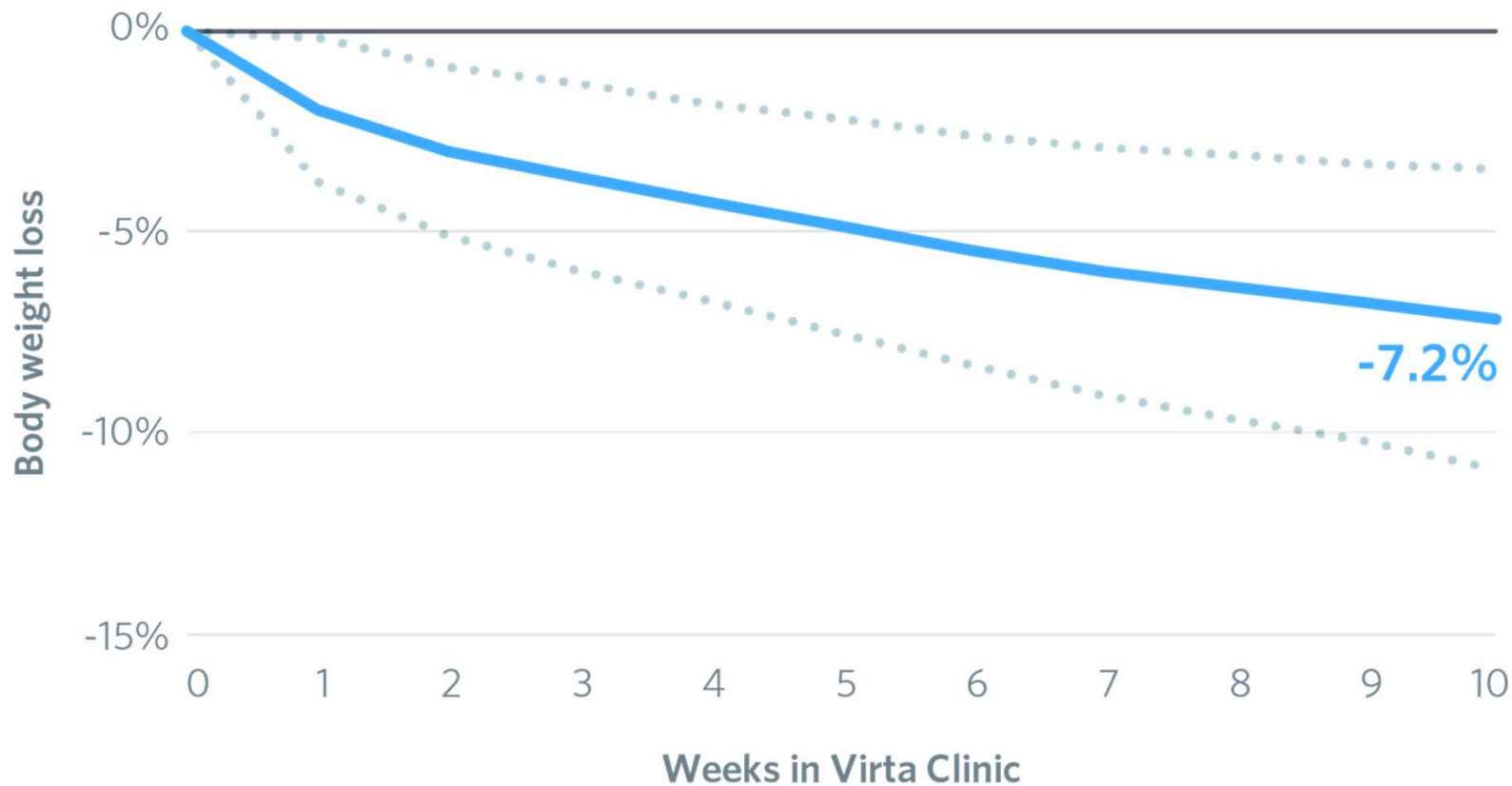
56% below diabetic threshold (6.5%)

Serum BOHB 0.6 mM at 10 weeks

Preliminary 6 month data: avg HbA1c = 6.1%

AFTER 10 WEEKS

71% of patients achieved clinically significant weight loss (>5%)



Preliminary
6 month data
shows no regain,
with a mean 12%
weight loss

Nutritional Ketosis in the Management of T2D?

PROS

- BOHB is an excellent fuel (brain, heart, skeletal muscle) at physiologic concentrations
- Potent epigenetic signal regulating oxidative stress, inflammation, and insulin resistance
- **Outpatient nutritional ketosis is admittedly difficult to sustain** in the face of usual dietary habits and social pressure (mean of 0.6 mM across first 10 weeks)
- However given intensive education and support, it appears to be feasible in the majority (238 of 262) of an outpatient cohort with T2D

CONS

- Given the rapid reduction in medication requirement, **close monitoring and prompt physician attention to medication dosage is essential for safety**
- Longer term (1-2 year) data are required to demonstrate a lasting effect on T2D biomarkers and disease progression.



Welcome to Steve's Inuit Bed and Breakfast

Low Weekend Rates, Free Air Conditioning