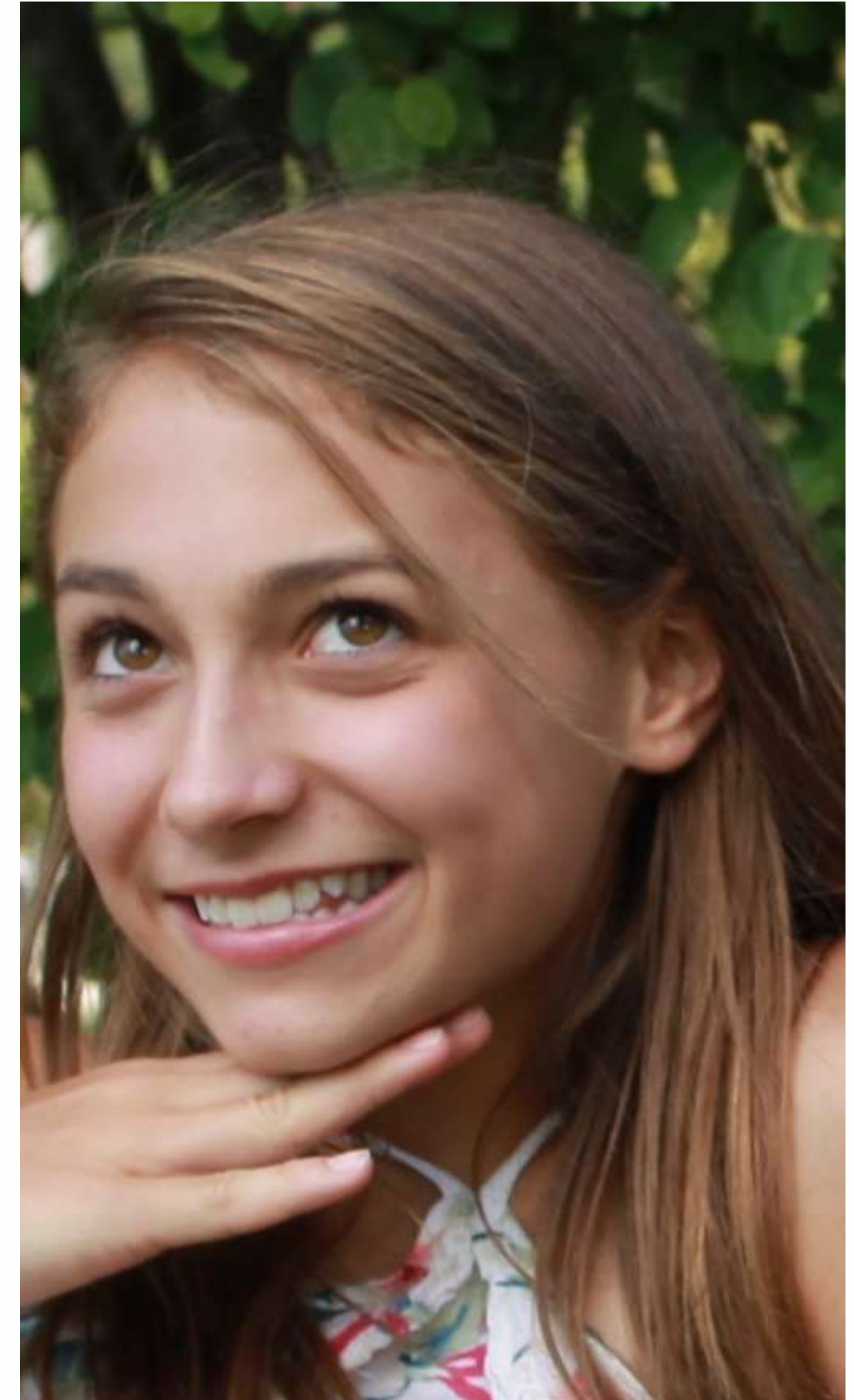


Ketogenic Diet for Type 2 Diabetes

Dr. Sarah Hallberg DO, MS

Disclosures

1. Virta Health Corp
Ownership interest
2. Atkins Corp
Honorarium for advisory role



Purpose

1. Examine the current treatment limitations for patients with type 2 diabetes
2. Ongoing study at Indiana University Health

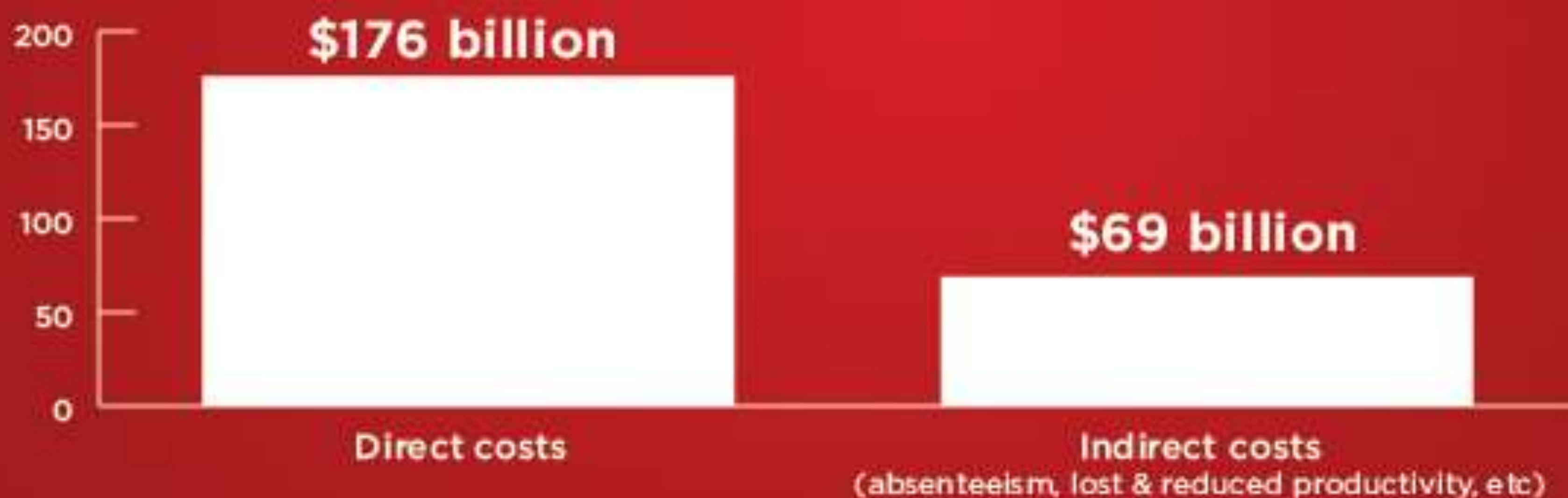
The Problem

As of 2012:

- 14.3% of all adults had diabetes
- 38% have pre-diabetes
- Now OVER 50% (52.3%) have diabetes or pre-diabetes

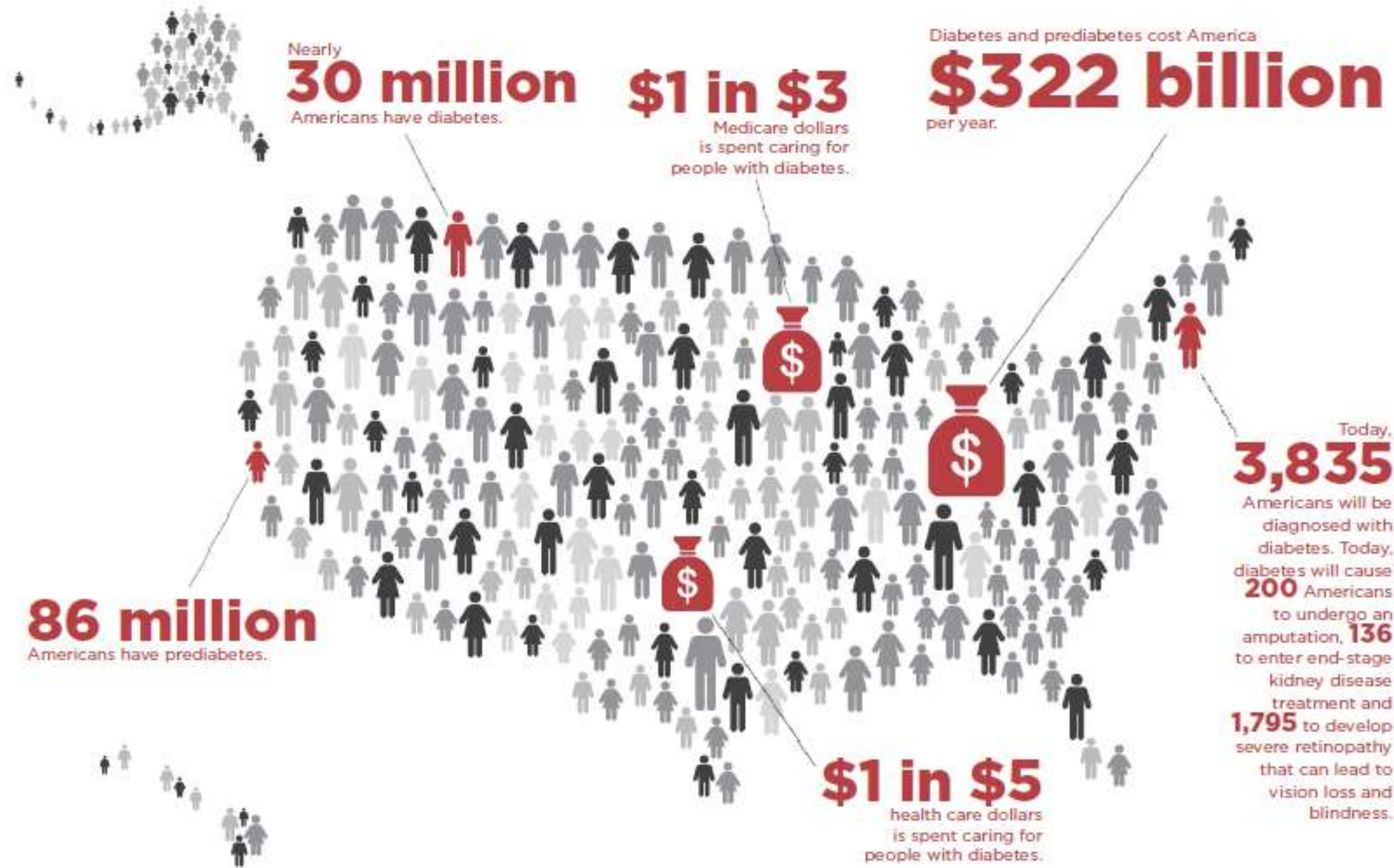
\$245 BILLION

TOTAL COST OF DIAGNOSED DIABETES IN THE UNITED STATES IN 2012.



Sources: American Diabetes Association

THE STAGGERING COSTS OF DIABETES IN AMERICA



Learn how to fight this costly disease at diabetes.org/congress



The Solution...

THE JOURNAL OF CLINICAL AND APPLIED RESEARCH AND EDUCATION

VOLUME 41 | NUMBER 1

Diabetes Care

WWW.DIABETES-CARE.EDU

JANUARY 2018

CONTENTS
1

AMERICAN DIABETES ASSOCIATION

STANDARDS OF MEDICAL CARE IN DIABETES—2018



1900 2018



Evidence suggests that there is not an ideal percentage of calories from carbohydrate, protein and fat for all people with diabetes. Therefore, macronutrient distribution should be based on an individualized assessment of current eating patterns, preferences, and metabolic goals.

Evidence E

Carbohydrates

“Studies examining the ideal amount of carbohydrate intake for people with diabetes are inconclusive, although monitoring carbohydrate intake for people and considering the blood glucose response to dietary carbohydrates are key for improving postprandial glucose control.”

“Carbohydrate intake has a direct effect on postprandial glucose levels in people with diabetes and is the primary macronutrient of concern in glycemic management”

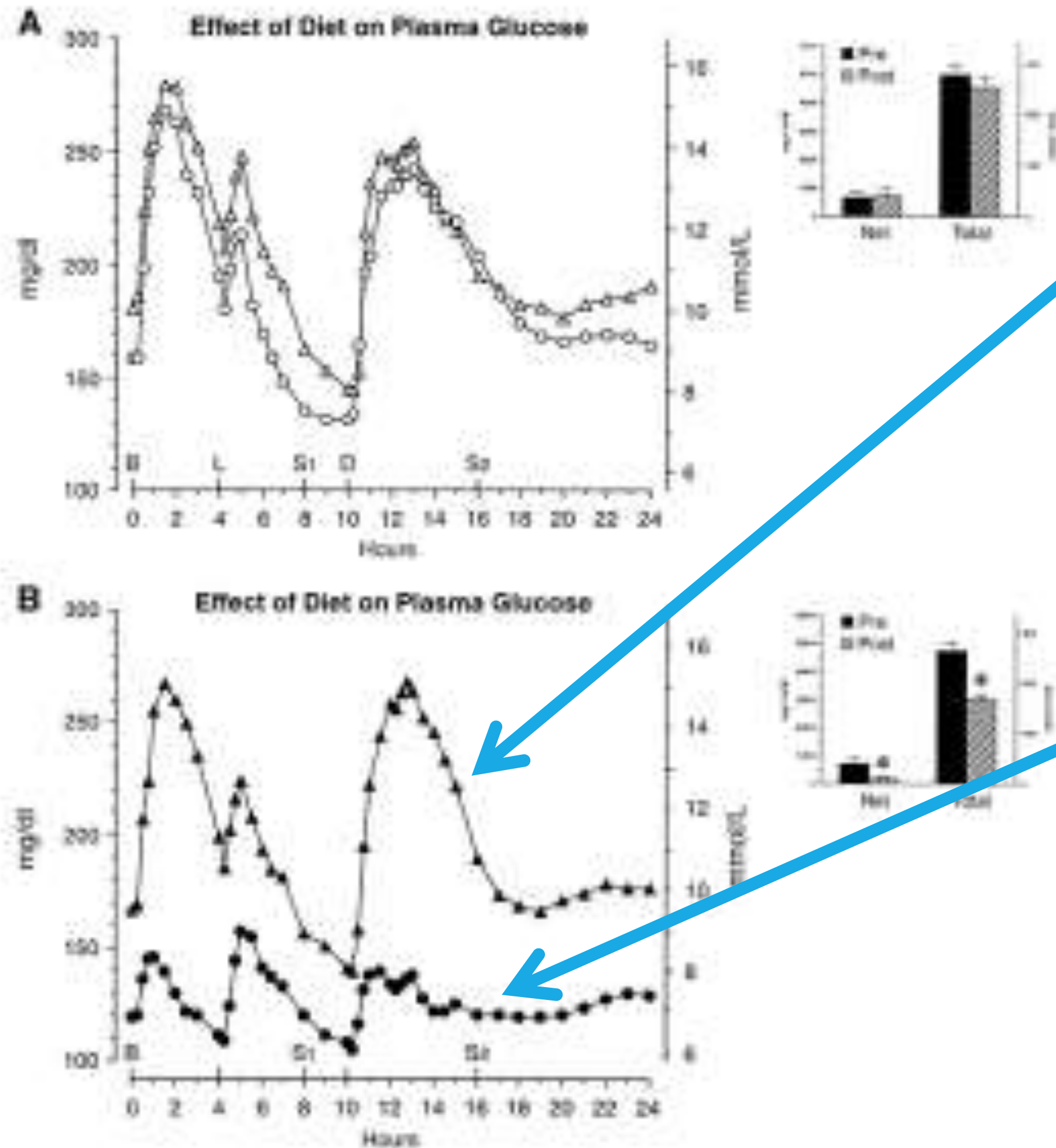
Carbohydrates will cause blood sugar to rise.

ADA Nutrition Guidelines 2017

“Couple insulin administration
with carbohydrate intake”

ok...

Mean plasma glucose concentration before (Δ) and after (\circ) 5 weeks on the control diet.



Control diet couples with LOTS of insulin
carbohydrate:protein:fat ratio was 55:15:30

Test diet - does NOT couple with a lot of insulin
Ratio was 20:30:50

ADA Nutrition Guidelines 2017

“For people whose meal schedules or carbohydrate consumption is variable, regular counseling to help them understand the *complex relationship between carbohydrate intake and insulin needs is important*”

Complex??

Eat carbs.

Blood sugar rises.

Insulin needs to go up.

Simple.

Proteins

ADA Nutrition Guidelines 2017

Some research has found successful management of type 2 diabetes with meal plans including slightly higher levels of protein (20–30%), which may contribute to increased satiety.

Fats

ADA Nutrition Guidelines 2018

“The ideal amount of dietary fat for individual with diabetes is controversial. The IOM has defined an acceptable macronutrient distribution for total fat for ALL adults to be 20–35% of energy.”

Dietary Patterns - for management

Evidence B

1. Mediterranean
2. DASH
3. Plant-based

Mediterranean/MUFA 2018 Standards of Care

2 studies cited that show a Mediterranean diet can improve A1c.

- 1 was on need for meds in newly diagnosed T2D
- An opinion piece that reference back to the Standards of Care

Mediterranean/MUFA

Nutrition Therapy Recommendations for the Management of Adults with Diabetes 2014

6 RCT that included people with diabetes reported improved glycemic control

- 2 showed no difference
- 1 looked at only new diagnosis improvements
- 1 did not have glycemic control as a primary endpoint
- 1 showed that the low carb mediterranean is superior to both traditional mediterranean and ADA standard
- 1 showed low carb had better A1c improvements than Mediterranean and low fat.

DASH

2018 Standards of Care

2 studies cited that show a DASH diet can improve A1c.

- 1 was on need healthy eating patterns and incidence of T2D
- 1 was an opinion piece that reference back to the Standards of Care
- 1 was non-systemic review

DASH EVIDENCE IN DIABETES - A SINGLE STUDY OF 31 PEOPLE

DASH

Nutrition Therapy Recommendations for the Management of Adults with Diabetes 2014

ONLY CITES THE SINGLE STUDY OF 31 PEOPLE

- Limited evidence exists on the effects of the DASH eating plan on health outcomes specifically in individuals with diabetes; however, one would expect similar results to other studies using the DASH eating plan.

Plant-based 2018 Standards of Care

2 studies cited

- 1 was a review of evidence supporting the Canadian Diabetes Association recommendations
 - Study cited was meta-analysis and of the 6 reviewed only 2 showed improvements
 - total of 27 patients
 - 1 additional study
- 1 was non-systemic review
 - Cited meta-analysis above
 - Cited a study that said no difference after accounting for weight loss

Plant-based Nutrition Therapy Recommendations for the Management of Adults with Diabetes 2014

6 studies reviewed

- Diets did not consistently improve glycemic control or CVD risk factors except when energy intake was restricted and weight was lost.

The 2014 Nutrition review did look at low carb as an eating pattern

- 11 studies reviewed
- 7 showed clear advantage for low carb
- 4 did not show a difference
 - 2 showed greater med reduction in LC: “These limited data suggest that changes in medication may have masked a potential in the low-carb dietary advice group to have m a more positive impact on glycemic control”
 - 1 study was on its with and without diabetes and there was a statistically significant advantage within the patients with diabetes
 - 1 was tried to do low fat and low carb

The 2018 Standard of Care discusses low carb

- Confusion due to definition of low-carb
- Benefits tend to be short term and effects are not maintained
- Ketogenic diets may be effective but only for 3 - 4 months as little long term research citing benefit or harm

Nutrition Therapy Recommendations for the
Management of Adults with Diabetes

“total amount of carbohydrate
eaten is the primary predictor of
glycemic response.”

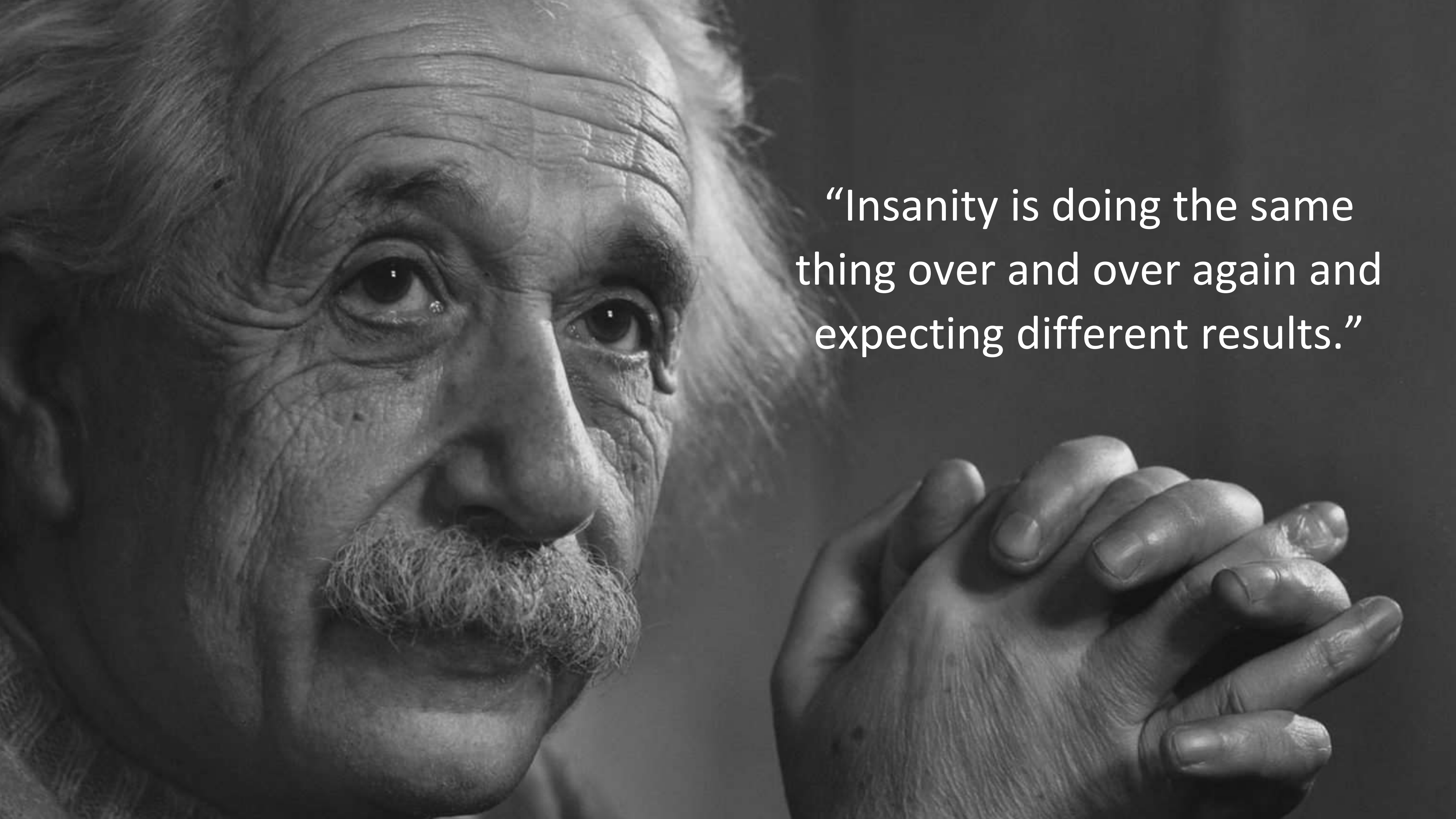
American Association of Diabetes Educators

Healthy Eating Patterns

- My Plate
- DASH
- Mediterranean
- Vegetarian or Vegan

Common Thread

Low Fat

A black and white close-up portrait of Albert Einstein, showing his characteristic wild hair and mustache. He is looking slightly to the right of the camera with a thoughtful expression. His hands are clasped together in front of him. The background is dark and out of focus.

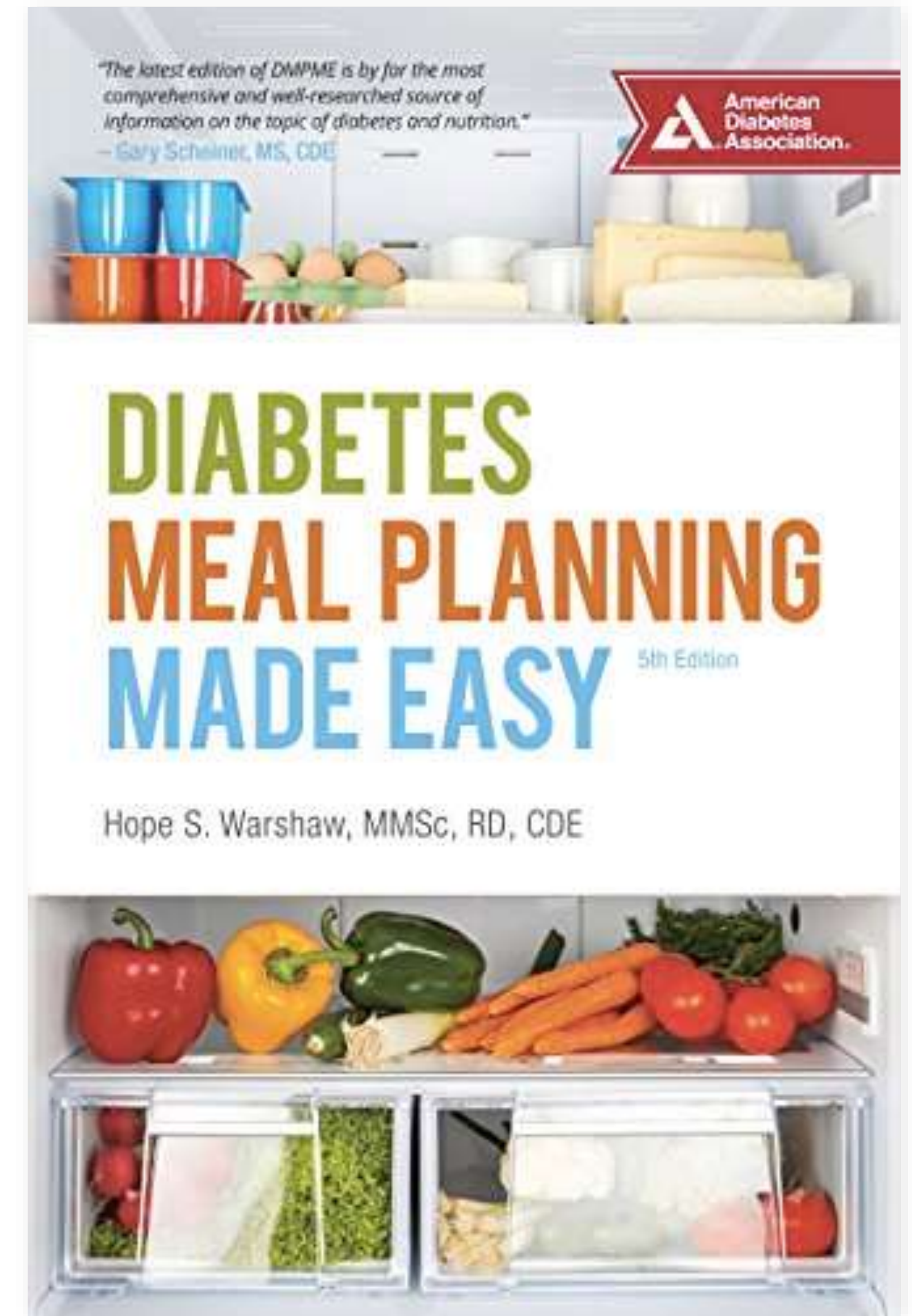
“Insanity is doing the same thing over and over again and expecting different results.”

Macronutrients

1. Fat: low
2. Protein: ??
3. Carbs: must be high(er)

In general, the ADA recommends an eating plan in which about 45–65% of your total daily calories come from carbohydrate. The exact grams of carbohydrate you eat will vary depending on your total calorie goal and a number of other factors.

“total amount of carbohydrate eaten is the primary predictor of glycemic response”





From ADA Website
(March 2017)

How Much Carbohydrate?

How much carbohydrate you eat is very individual. Finding the right amount of carbohydrate depends on many things including how active you are and what, if any, medicines you take. Some people are active and can eat more carbohydrate. Others may need to have less carbohydrate to keep

How Much Carbohydrate?

How much carbohydrate you eat is very individual. Finding the right amount of carbohydrate depends on many things including how active you are and what, if any, medicines you take. Some people are active and can eat more carbohydrate. Others may need to have less carbohydrate to keep their blood glucose in control.

Finding the balance for yourself is important so you can feel your best, do the things you enjoy, and lower your risk of diabetes complications.

A place to start is at about 45-60 grams of carbohydrate at a meal. You may need more or less carbohydrate at meals depending on how you manage your diabetes.

You and your health care team can figure out the right amount for you. Once you know how much carb to eat at a meal, choose your food and the portion size to match.



American Diabetes Association

Thank you for your comments. How much carbohydrate to eat is a very individual decision, and not every recipe is going to suit everyone's meal plan. A general guideline is to have 45-60 grams of carbohydrate at each meal and 15-20 grams of carbohydrate for a snack. A dietitian or diabetes educator can work with you to make a personalized plan; you may require more or less carbohydrate based on your needs and your diabetes management plan.

2 hours ago · Like · Reply

“The discovery of insulin was a severe setback to the advancement of the science and art of nutrition”

Louis Newburgh, 1936

Oops is right!



“The high-carb diet I put you on 20 years ago gave you diabetes, high blood pressure, and heart disease. Oops.”

And the science says...



Ongoing study at Indiana University Health

- 400 treatment patients: All treated with a ketogenic diet. Blood ketones obtained initially daily then decreasing frequency.
 - 200 patients treated “live” in the clinic with weekly group meetings for the first 3 months then decreasing frequency over 2 years
 - 200 patients treated “virtually” with all education being done via portal. Follow ups only at 3 months, 1yr and 2yrs or as needed
- 100 controls
 - Treated by the IU Health dietitians with ADA protocol



Ongoing study at Indiana University Health

- All treatment patients given health coach
- Biomarker tracking in “app”
- Medication adjustment by supervising physician based on daily blood glucose and blood pressure levels
- Online support community



Indiana University Health

Ongoing study at Indiana University Health

Primary Outcomes

- Body Weight
- Metabolic Syndrome Criteria
- Type 2 Diabetes Status



Ongoing study at Indiana University Health

Secondary Outcomes

- Carotid intima media thickness (cIMT) will be measured by ultrasound 3 times over 2 years (baseline, 12, and 24 months).
- Serum lipids analyzed by NMR to determine LDL particle size and number
- Full Body DEXA
- Banked Samples

Key Results from McKenzie et al., JMIR Diabetes, 2017.

For the N=262 T2DM participants at 10 weeks. Intent to treat analysis & completers analysis.

1.0 Average reduction in HbA1c (from 7.6 to 6.6)

87% Eliminated or reduced insulin

48% Reduced HbA1c < 6.5*

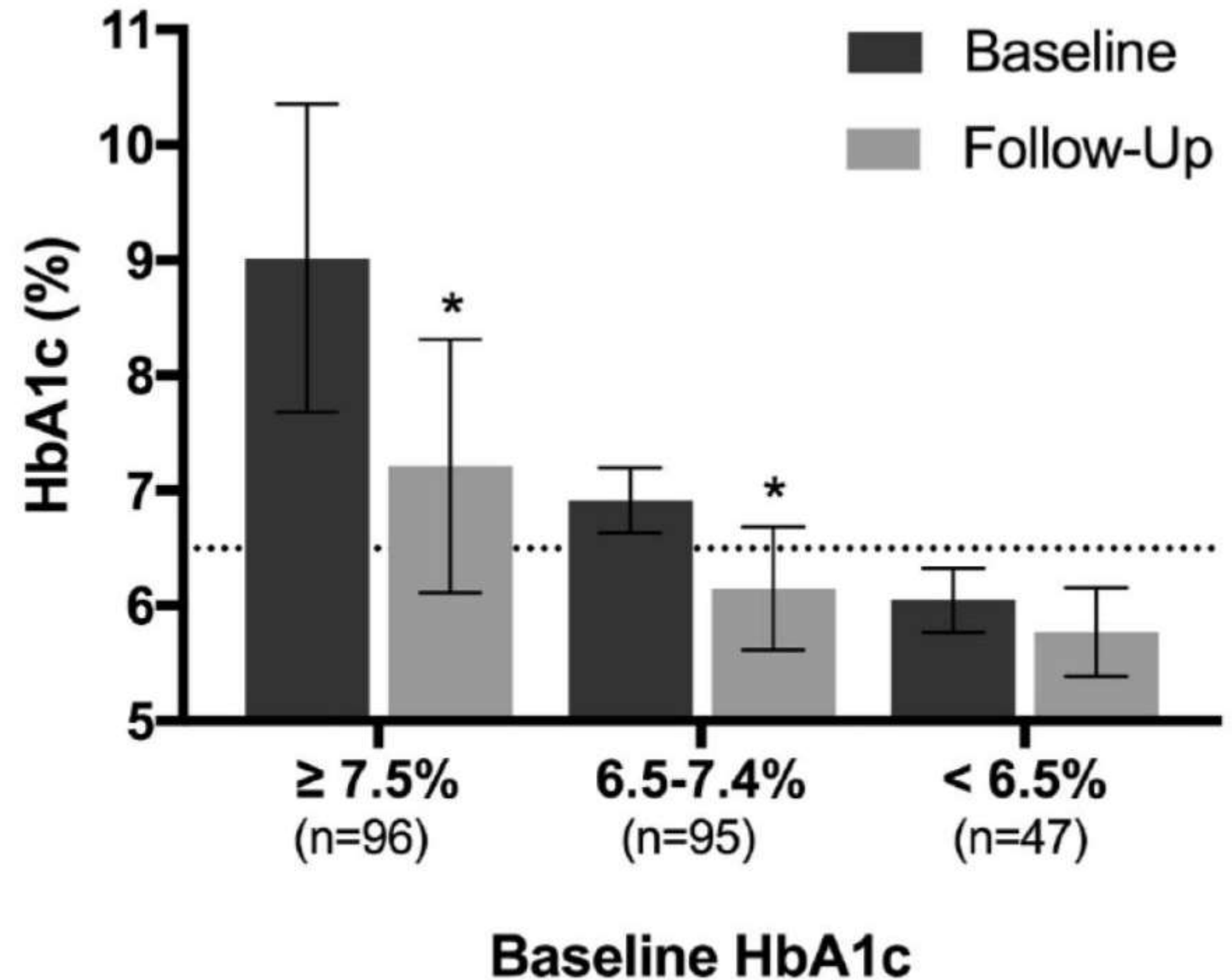
75% Of completers experienced clinically significant weight loss of >5%

91% Completed protocol

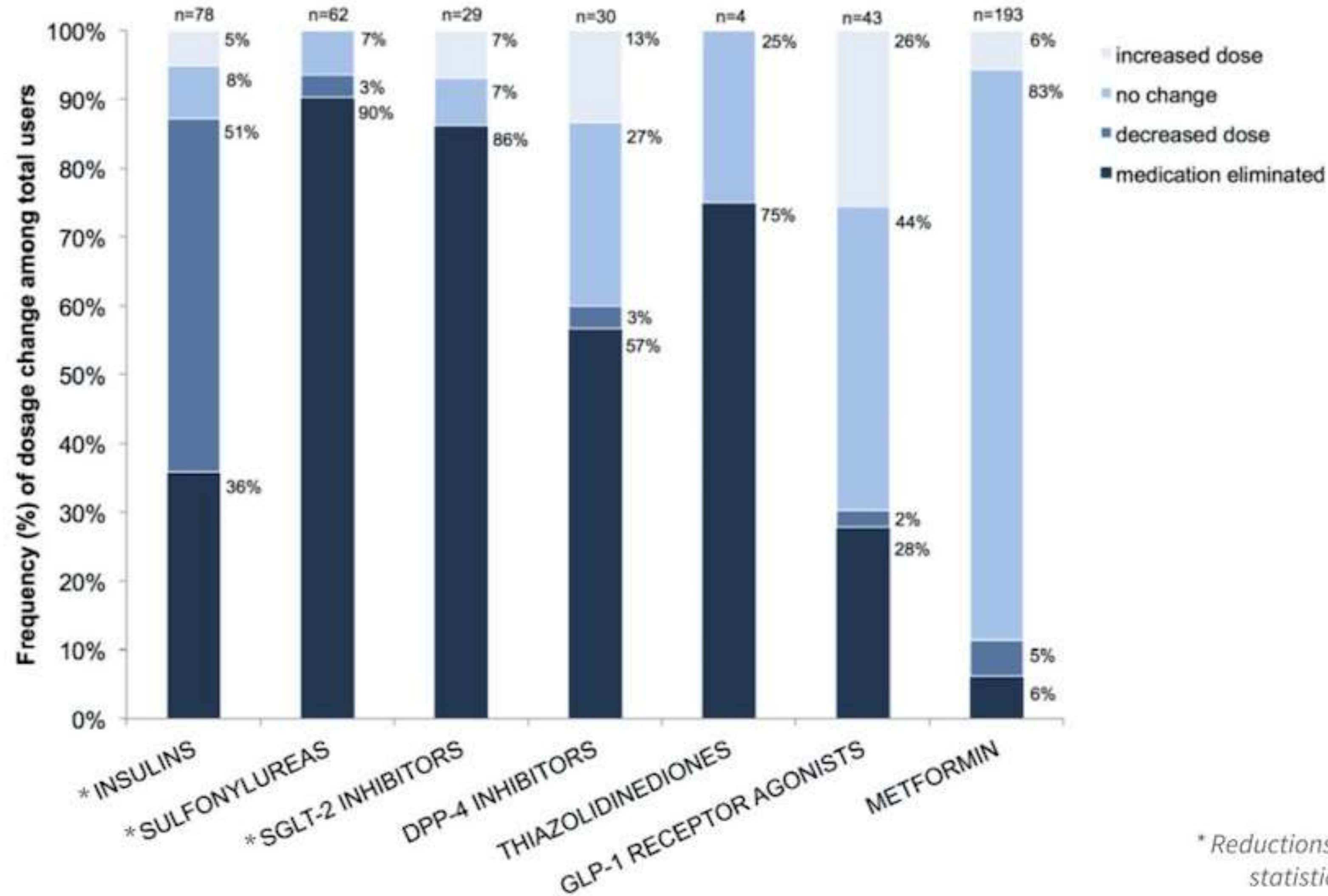
20% Average reduction in triglycerides

Trial at 70 days: HbA1c is Substantially Reduced

- Completers improved HbA1c by $1.1 \pm 1.1\%$ in the first 10–11 weeks, from $7.6 \pm 1.5\%$ at baseline to $6.5 \pm 1.0\%$ ($P < 0.001$)
- This is a dramatic reduction in HbA1c, while withdrawing medications



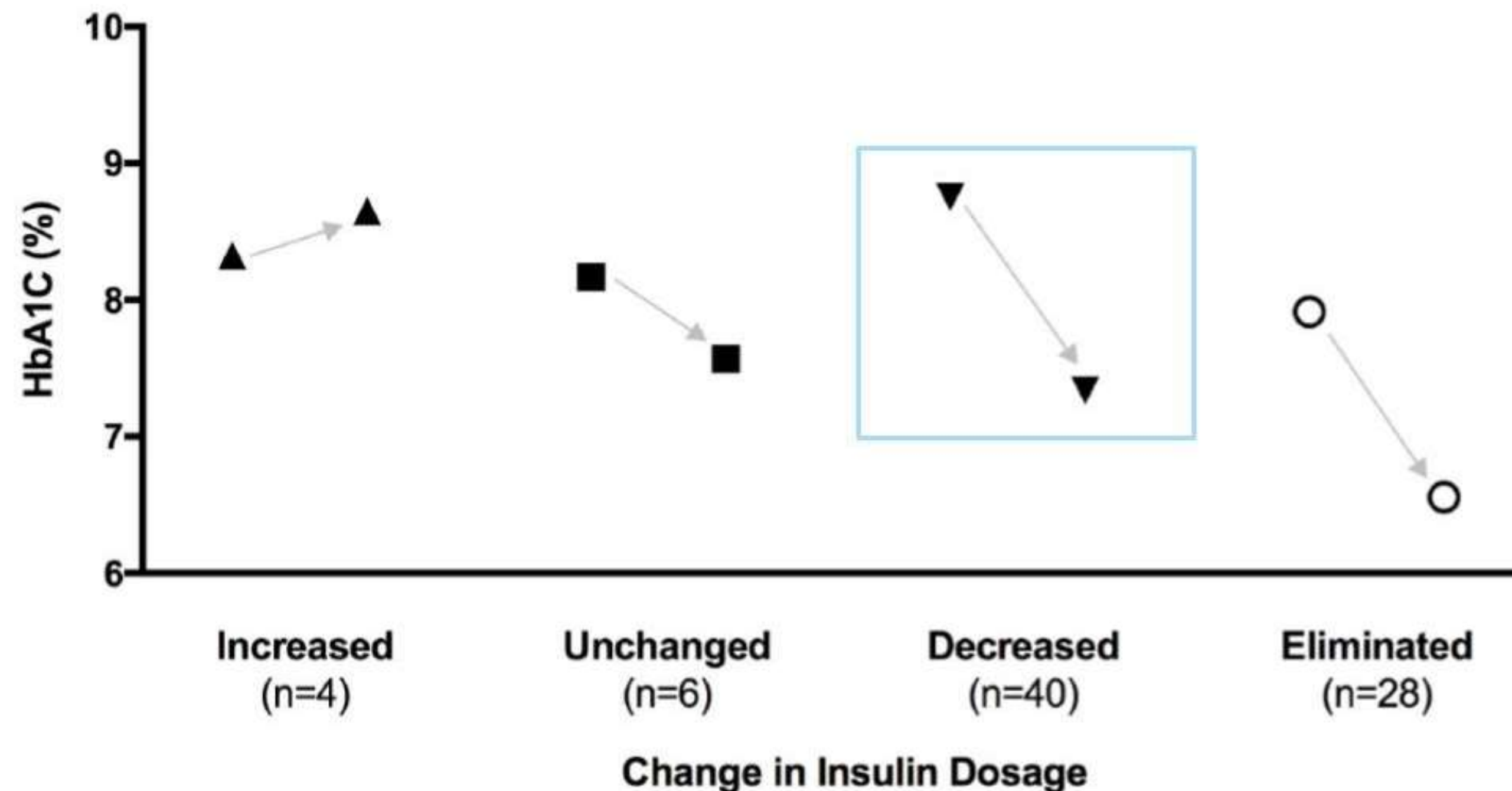
Trial at 70 days: Medications are Substantially Reduced & Eliminated



Trial at 70 days: A1c and Medications Reductions were Concurrent

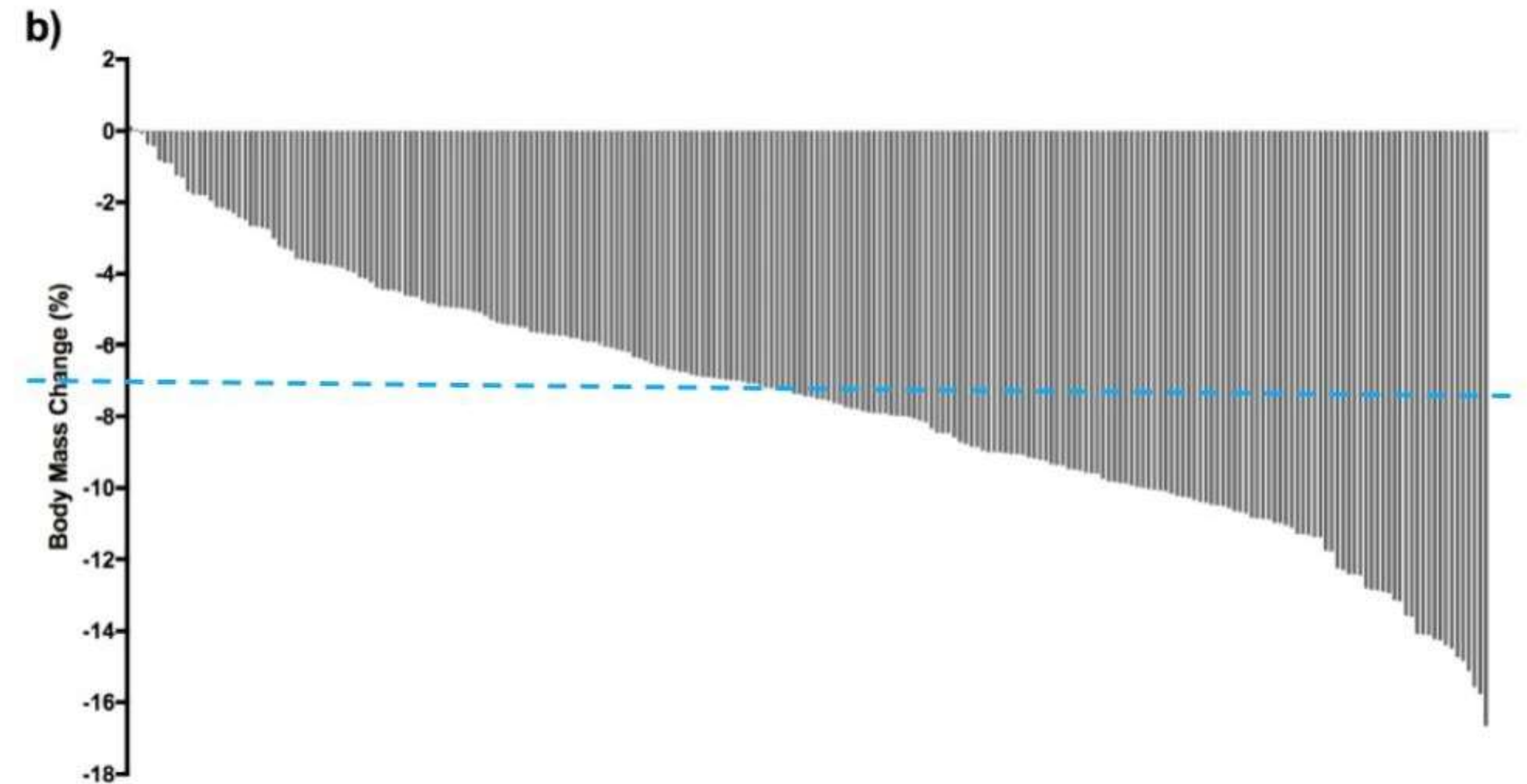
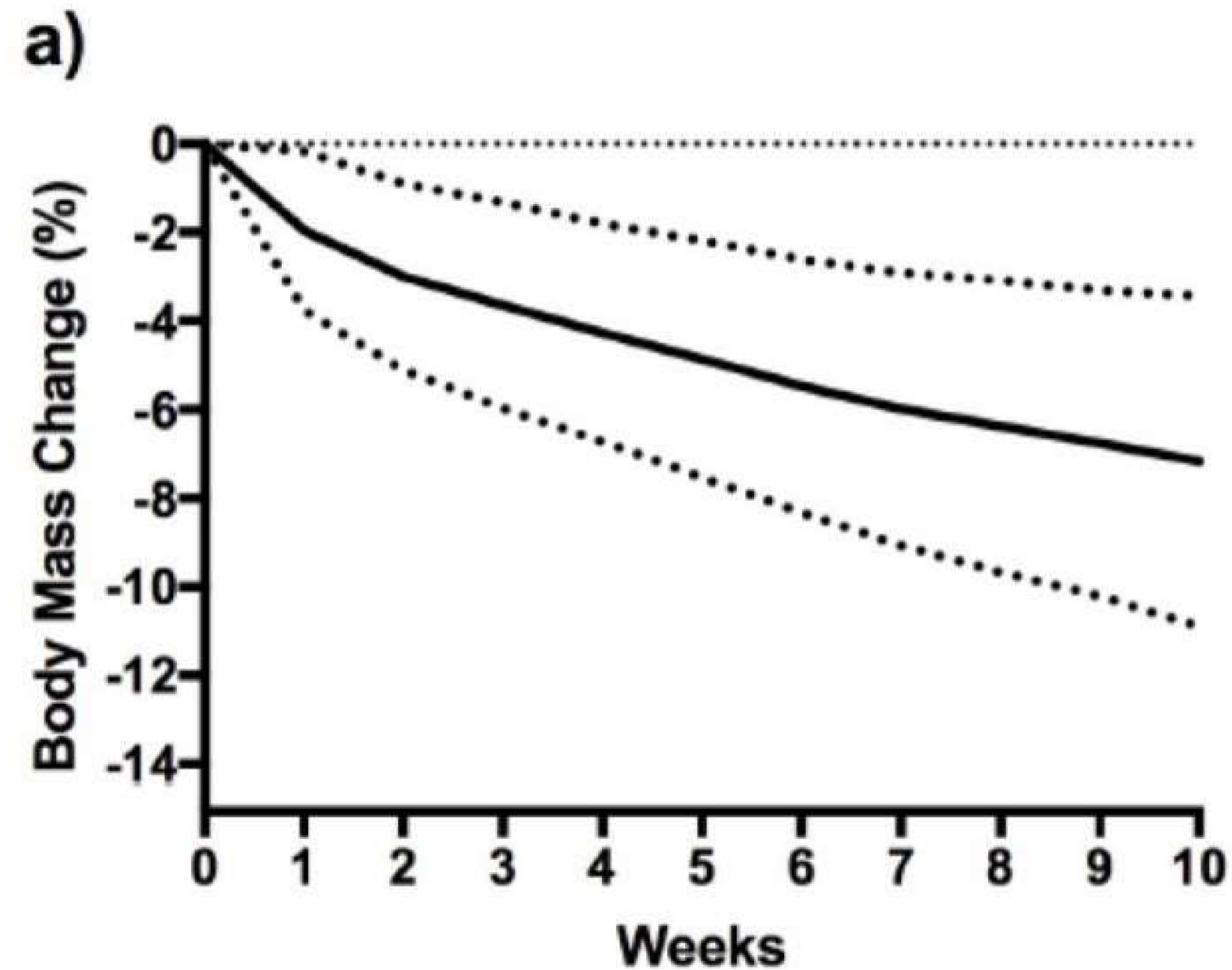
Table 2. Change in prescription of medication class or dose between baseline and follow-up.

Change in medication prescription or dose between baseline and follow-up	n	HbA _{1c} ^a <6.5% at follow-up, n (%)	Baseline HbA _{1c} (%), mean (SD)	Follow-up HbA _{1c} (%), mean (SD)
Increase	13	4 (31)	8.5 (2.0)	7.4 (1.4)
No change	88	57 (65)	7.2 (1.2)	6.5 (1.0)
Decrease	112	47 (42)	8 (1.6)	6.8 (1.1)
Complete elimination of medications	21	17 (81)	6.7 (0.9)	6.1 (0.5)
No medications prescribed	28	22 (79)	7.3 (1.3)	6.3 (1.1)

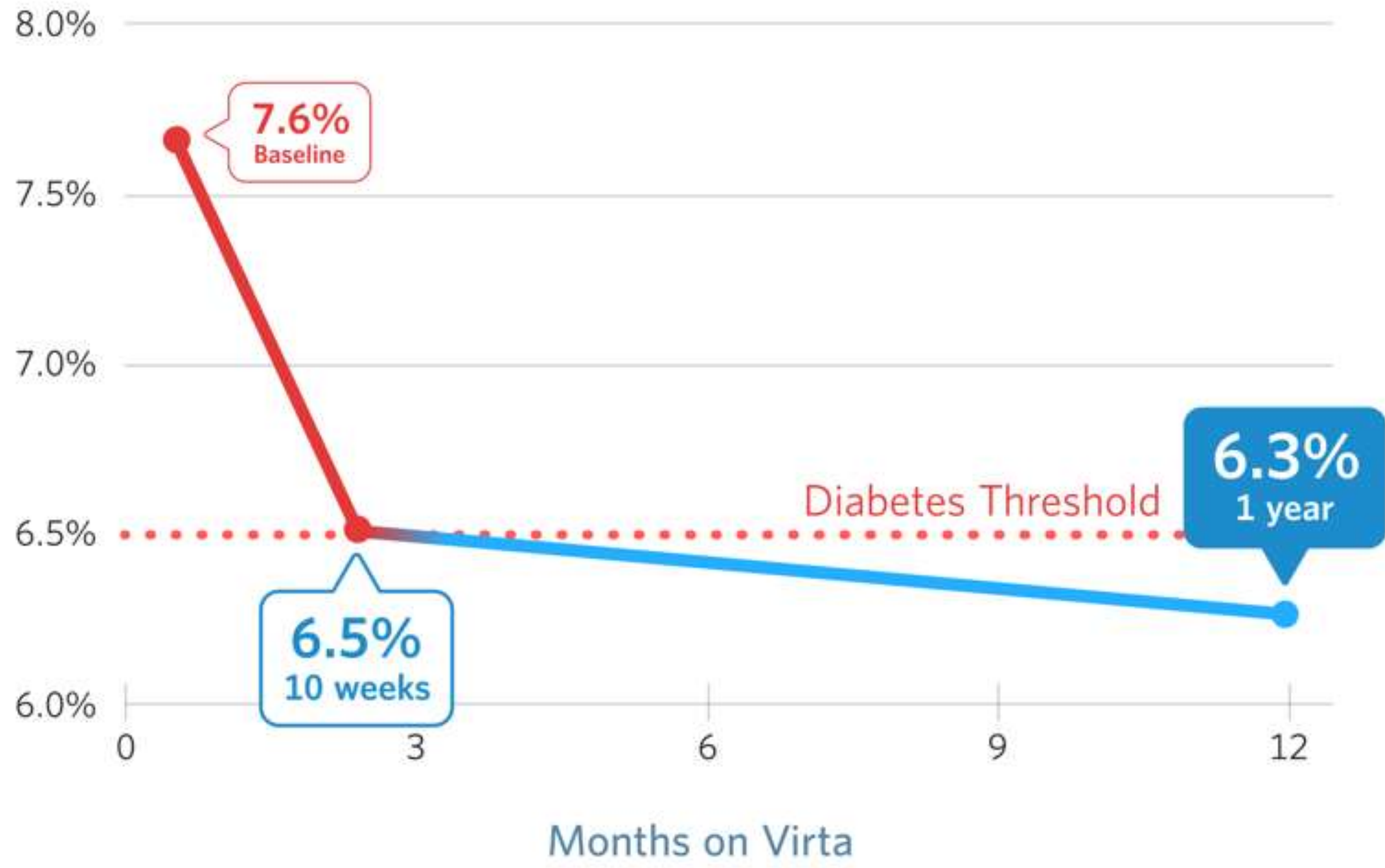


The most common pattern was a decline in A1c concurrent with decreased medication use.

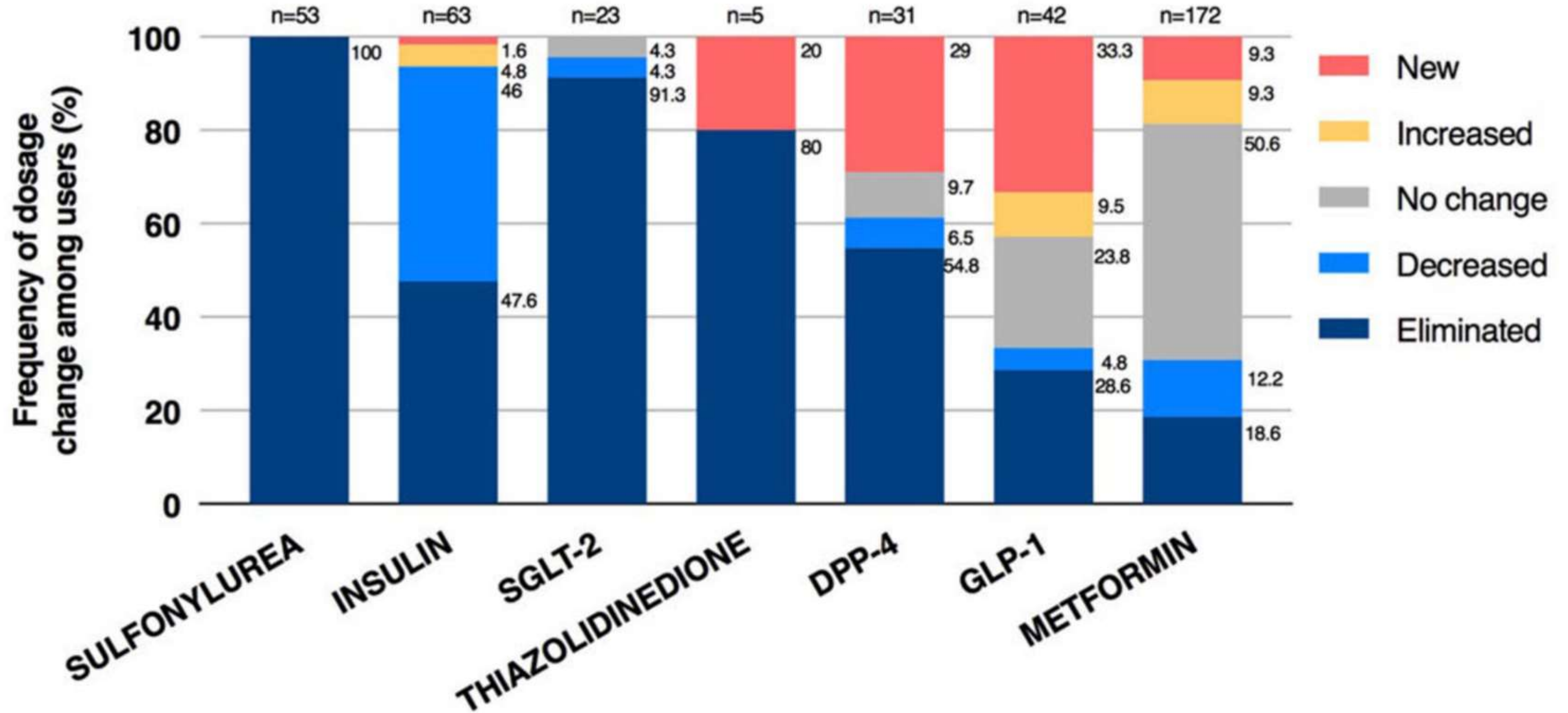
Trial at 70 days: Weight Loss is Significant at 10 weeks.
Rate of loss is modest at ~2 lbs/week



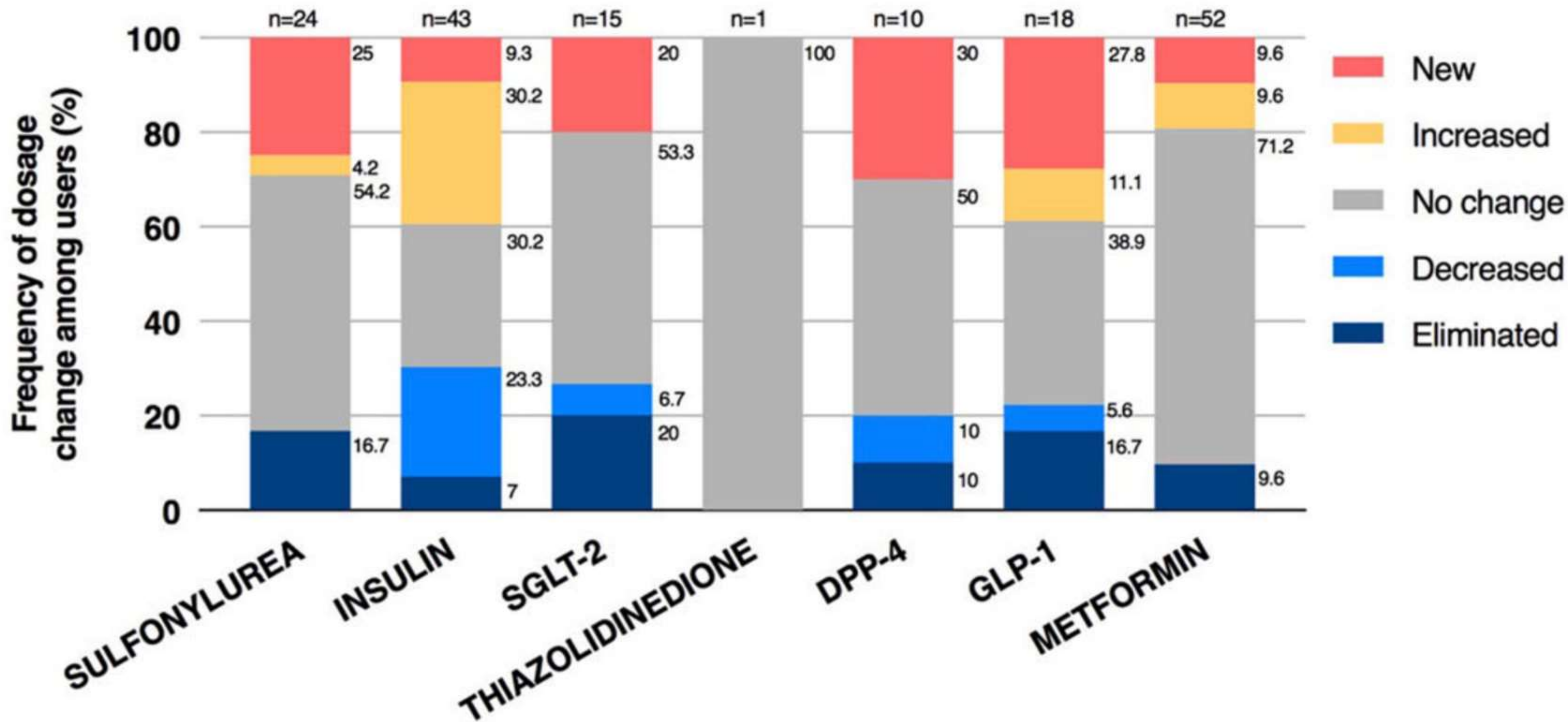
- Mean weight loss of 7.2% (~19 lbs by 10 weeks)
- 75% of completers experienced clinically significant weight loss of >5%
- Only 5 of 262 subjects registered a weight gain (2 completers, 3 non-completers)



Continuous Care Intervention



Usual Care



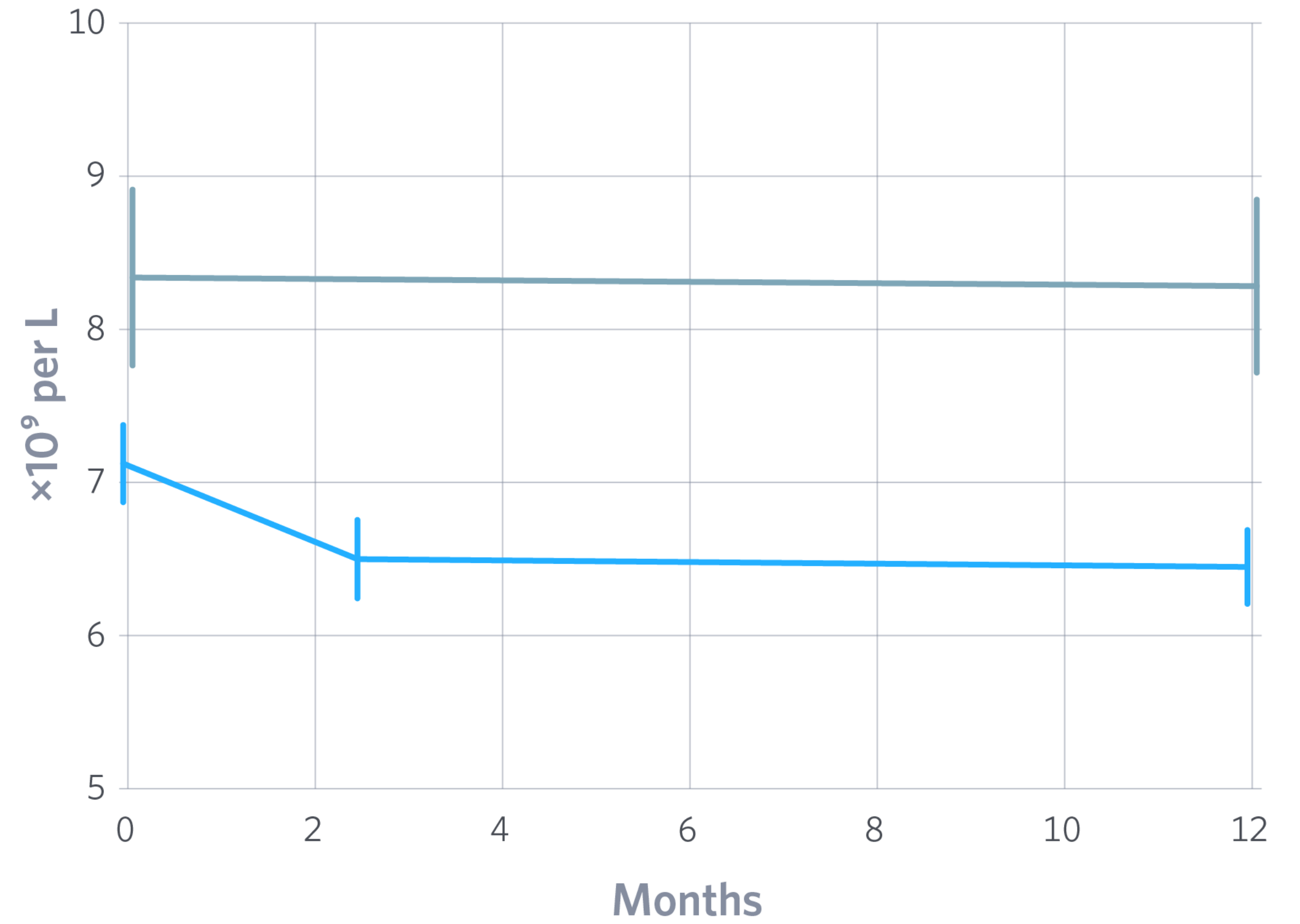
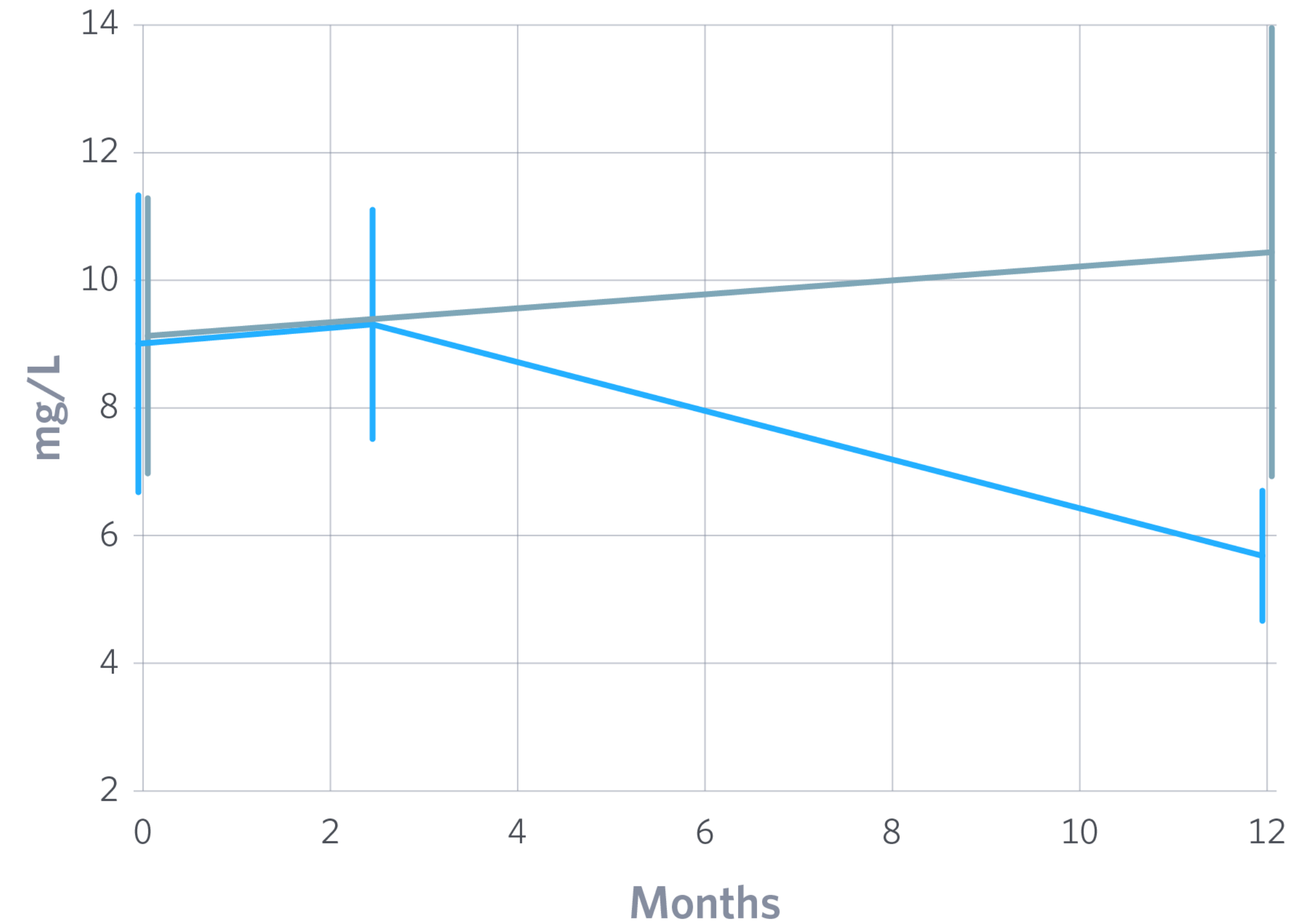
Liver Function Outcomes After 1 Year

	Virta	Usual Care
ALT	▼ -29%	▼ -2%
AST	▼ -20%	▲ +3%

Inflammation Responses to a Well-Formulated Ketogenic Diet

C-Reactive Protein

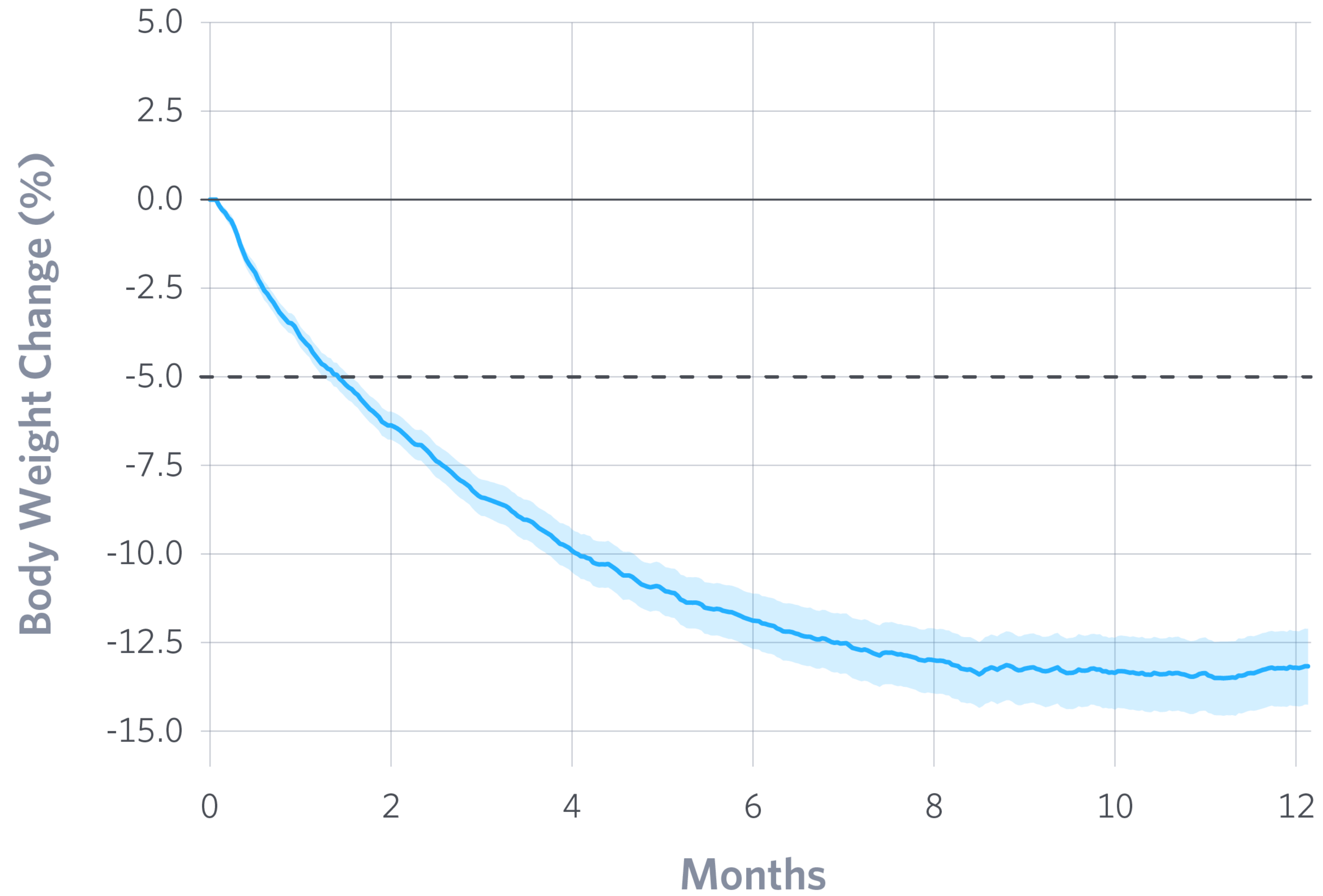
White Blood Cell Count



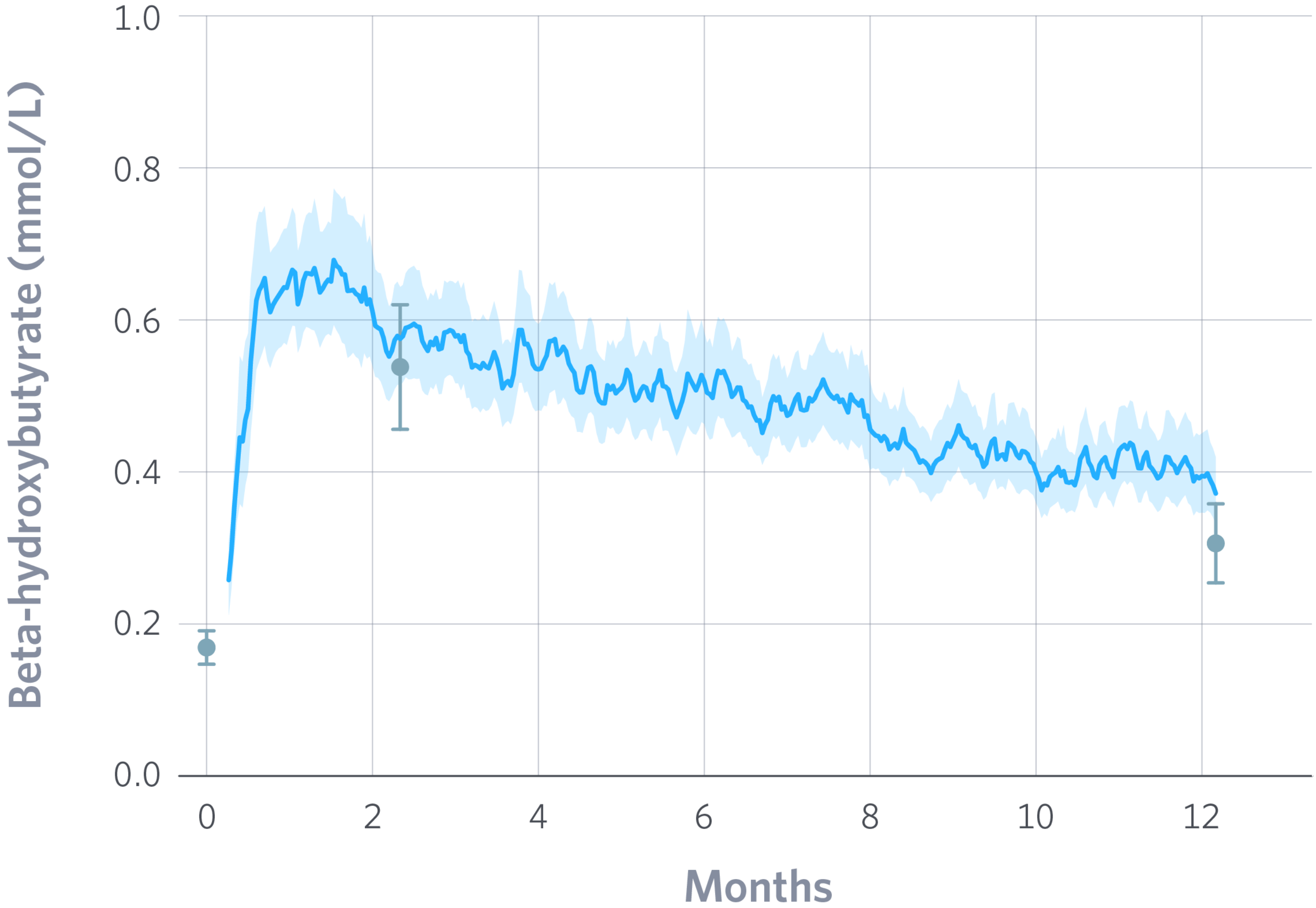
Virta intervention
n=193

Usual care control
n=70

Weight Change

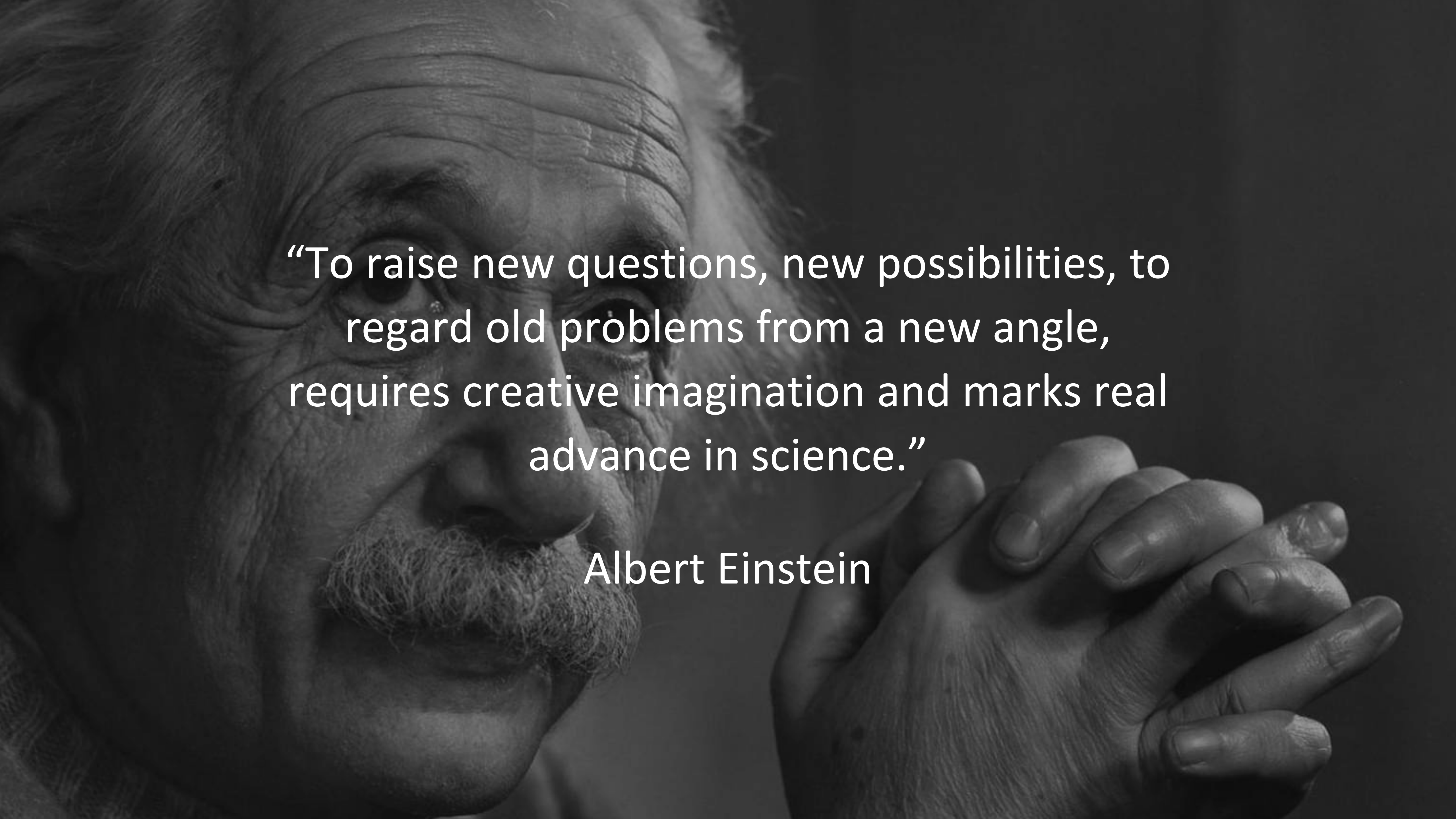


Ketones



From: Hallberg SJ, et al. Diabetes Therapy. 2018; <https://doi.org/10.1007/s13300-018-0373-9>

Time for a Paradigm Change

A black and white photograph of Albert Einstein. He is shown from the chest up, looking slightly to the right of the camera. His hands are clasped together in front of him. The lighting is dramatic, highlighting the texture of his skin and the details of his hands. The background is dark and out of focus.

“To raise new questions, new possibilities, to regard old problems from a new angle, requires creative imagination and marks real advance in science.”

Albert Einstein

The Nutrition Coalition

A non-profit and non industry funded organization working to ensure that our dietary guidelines are evidence-based and apply to all Americans

