# Evidence for a new category of diabetes care: Reversal

James McCarter MD PhD, Head of Research, Virta Health

September 20, 2018



# Why "manage" when you can reverse type 2 diabetes without medication or surgery?

# Nate is typical of Thousands of Virta patients

24 years with type 2 diabetes and taking 290 units of insulin

With the Virta treatment ...

- A1c down 1.4% off insulin
- BP down off BP meds
- 70 pounds weight loss
- Restored metabolic health



Nate, before and after Virta

# Nate is typical of Thousands of Virta patients

24 years with type 2 diabetes and taking 290 units of insulin

With the Virta treatment ...

- A1c down 1.4% off insulin
- BP down off BP meds
- 70 pounds weight loss
- Restored metabolic health



Nate, before and after Virta

"When I first stopped my medicines, I was scared, but I trusted my coach and personal doctor's guidance. First, I cut back the insulin and then my blood pressure meds by half. Then, I got the news not to take insulin injections or the blood pressure meds at all. As I loaded my needle the morning after getting the news, it dawned on me that I didn't have to do that anymore. After so long using insulin as a crutch to control my glucose, now I just looked at the bottles and needles sitting there. They reminded me that I'm conquering diabetes. I have hope!"

# High Level Context

Outcomes

Patient Experience

Enterprise Experience

Conclusion



# High Level Context

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# THE STAGGERING COSTS OF **DIABETES**



More than

30 MILLION

Americans have diabetes



Health care costs for Americans with diabetes are

2.3X greater than those without diabetes



Diagnosed diabetes costs America

\$327 BILLION

per year





\$1 IN \$7

Health care dollars is spent treating diabetes and its complications



Today, **4,110** Americans will be diagnosed with diabetes. Additionally, diabetes will cause **295** Americans to undergo an amputation and **137** will enter end-stage kidney disease treatment.

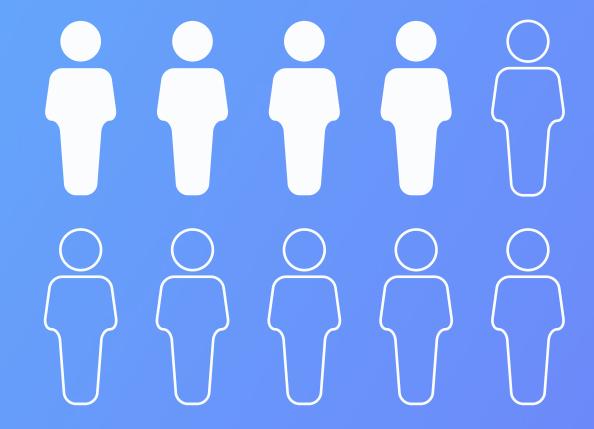


Learn how to fight this costly disease at diabetes.org/congress

# Over 30 million Americans with diabetes costing \$327 billion annually ADA 2018 estimates

#### Nearly 4 in 10 US Adults have

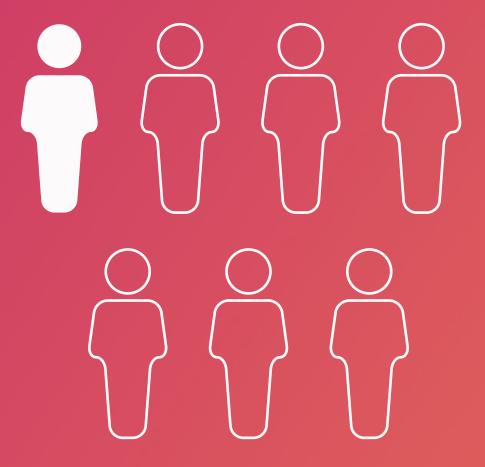
**PRE-DIABETES** 



38.0% of US Adults

1 in 7 US Adults have

**TYPE-2 DIABETES** 

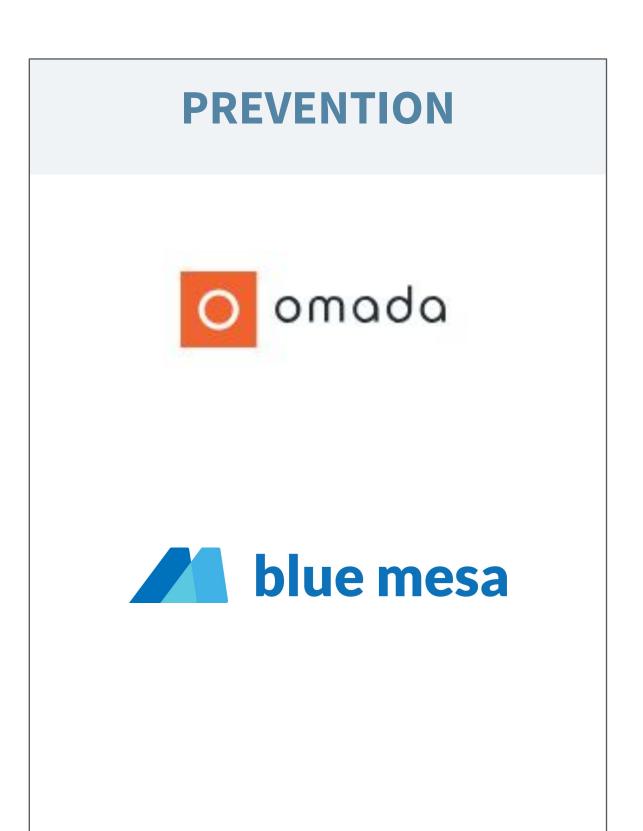


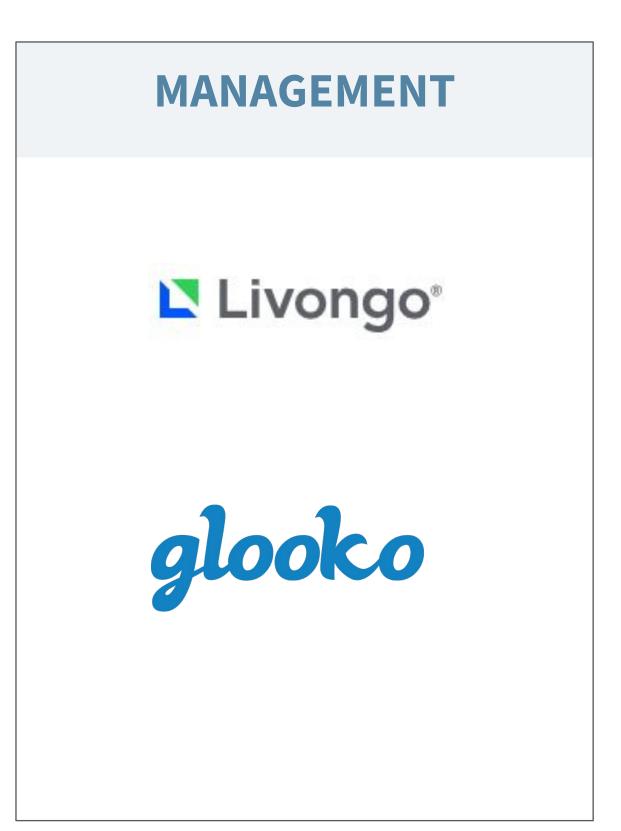
14.3% of US Adults

# **Redefining Categories of Care with Outcomes**

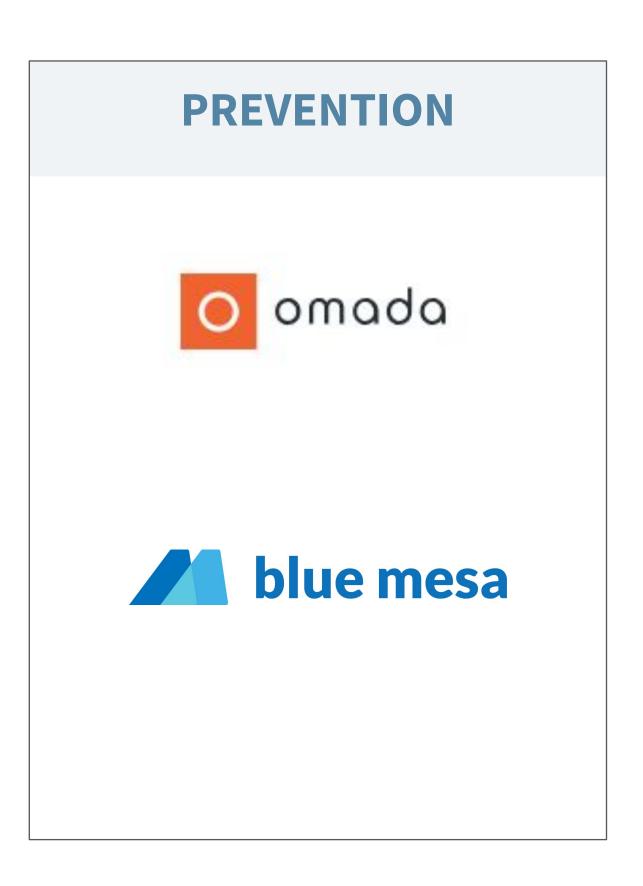
# **PREVENTION** omada **blue mesa**

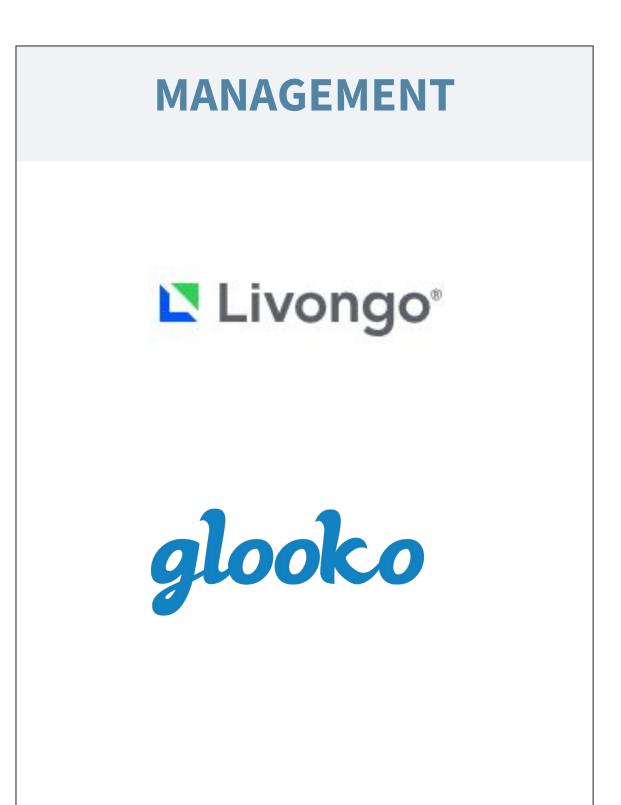
### **Redefining Categories of Care with Outcomes**

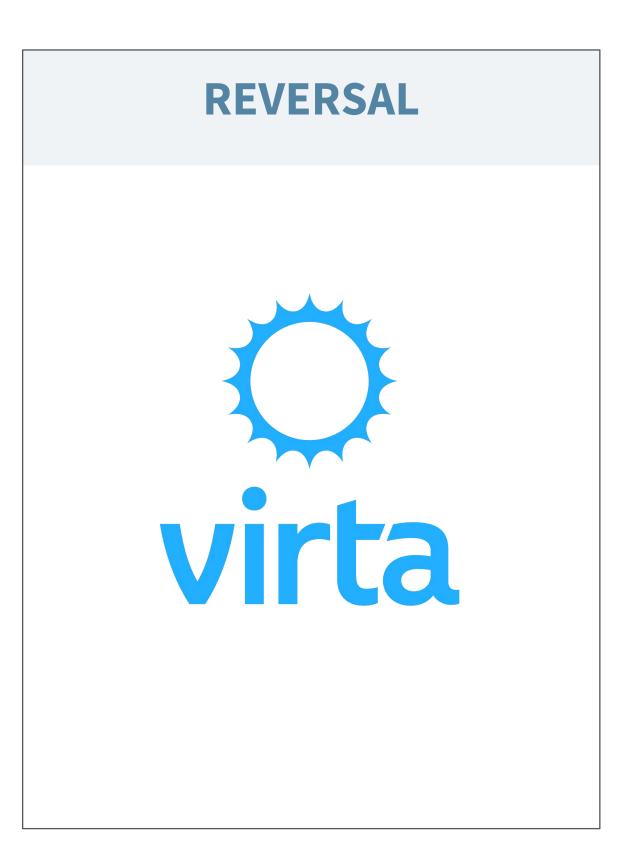




#### **Redefining Categories of Care with Outcomes**







### What does not have evidence of Diabetes Reversal?

# Usual Care

# "0.1% diabetes remission rate"



Diabetes Care 2014 Sep; DC\_140874.





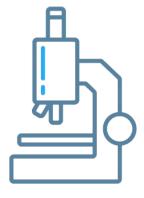


Proven type 2 diabetes reversal





Proven type 2 diabetes reversal

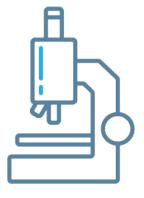


Improves 4 other chronic diseases





Proven type 2 diabetes reversal



Improves 4 other chronic diseases



Superior, peer-reviewed, published outcomes

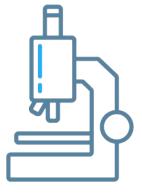




Proven type 2 diabetes reversal



High activation (30%) & retention (90%) at 1 year

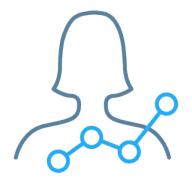


Improves 4 other chronic diseases



Superior, peer-reviewed, published outcomes

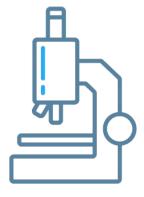




Proven type 2 diabetes reversal



High activation (30%) & retention (90%) at 1 year



Improves 4 other chronic diseases



Licensed medical provider in all 50 states with continuous remote care

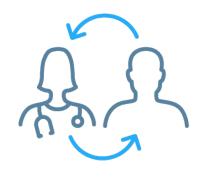


Superior, peer-reviewed, published outcomes

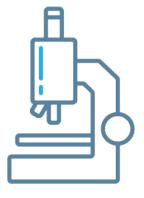




Proven type 2 diabetes reversal



High activation (30%) & retention (90%) at 1 year



Improves 4 other chronic diseases



Licensed medical provider in all 50 states with continuous remote care



Superior, peer-reviewed, published outcomes



Fees at risk based on results

# High Level Context

# Outcomes

Patient Experience

Enterprise Experience

Conclusion



# Virta-IUH Clinical Trial

- 5 year, non-randomized prospective controlled study
- 465 participants recruited
   Aug 2015 Mar 2016
- Active arm n=378, of which n=262 T2DMs
- Usual care arm n=87
- Central Indiana
- Mean age: 54
- Mean BMI: 40.3
- Mean weight: 257 lbs.
- Mean Yrs. T2D: 8.4
- 67% female



of completing patients reverse diabetes Glycemic Control without use of diabetes-specific medications



60% of completing patients reverse diabetes Glycemic Control without



#### **Blood Glucose Improvement**

1.3% average HbA1c reduction, 70% below 6.5%85% decrease at least 0.2%



Hallberg et al. *Diabetes Therapy*, 2018. Bhanpuri et al. *Cardiovascular Diabetology*, 2018.

use of diabetes-specific

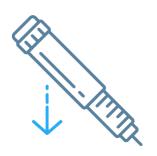
medications

60% of completing patients reverse diabetes Glycemic Control without



#### **Blood Glucose Improvement**

1.3% average HbA1c reduction, 70% below 6.5%



#### **Medication Reduction**

94% of insulin users reduced or eliminated usage

57% of all diabetes-specific prescriptions discontinued



use of diabetes-specific

medications

60% of completing patients reverse diabetes Glycemic Control without



#### **Blood Glucose Improvement**

1.3% average HbA1c reduction, 70% below 6.5%



#### **Medication Reduction**

94% of insulin users reduced or eliminated usage



#### **Weight Loss**

12% average weight loss (30 pounds)

**86%** of patients lost >5%



use of diabetes-specific

medications

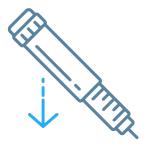
60% of completing patients reverse diabetes

Glycemic Control without use of diabetes-specific medications



#### **Blood Glucose Improvement**

1.3% average HbA1c reduction, 70% below 6.5%



#### **Medication Reduction**

94% of insulin users reduced or eliminated usage



#### **Weight Loss**

12% average weight loss (30 pounds)



#### **CVD Risk Improvement including Dyslipidemia**

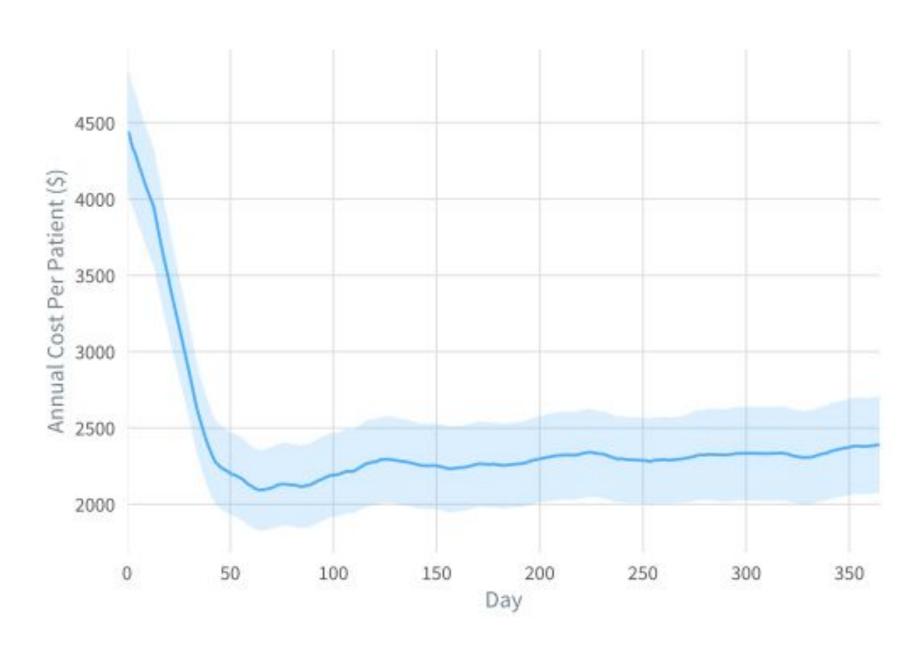
12% improvement in 10-year ASCVD Risk Score

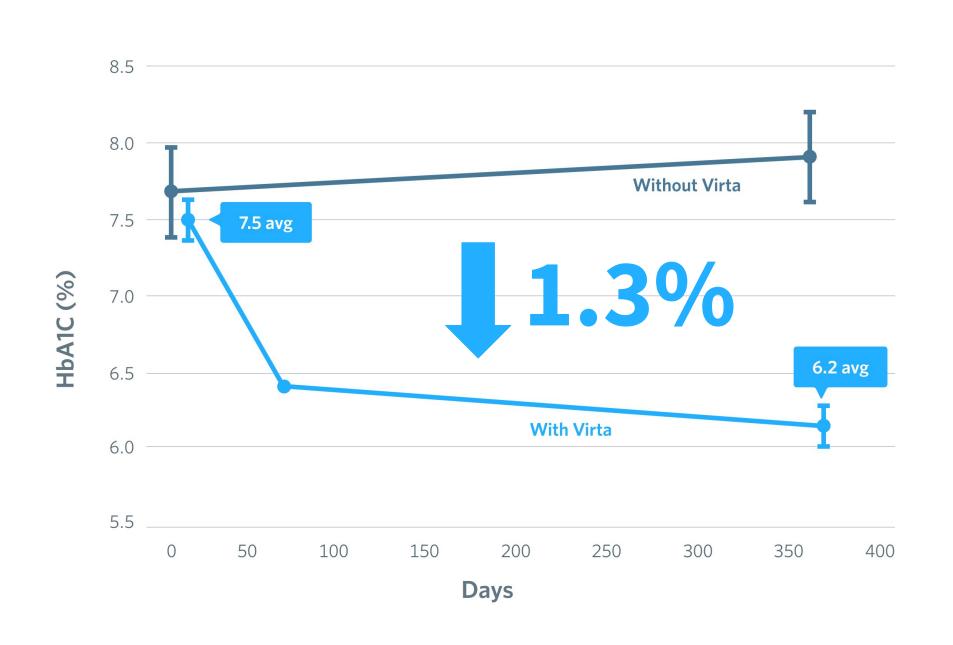
22 of 26 risk factors show significant improvement

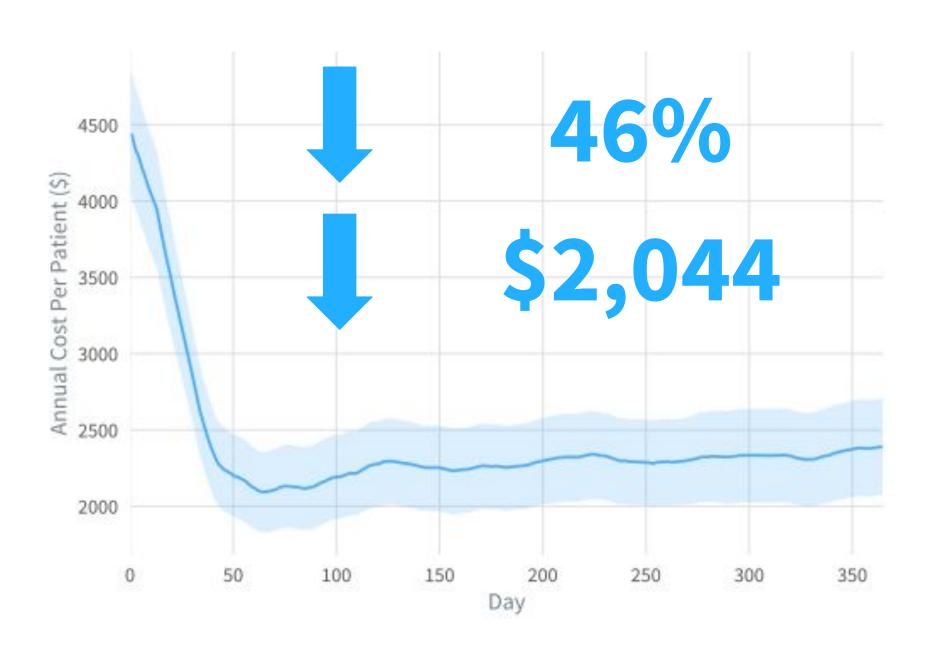


Hallberg et al. *Diabetes Therapy*, 2018. Bhanpuri et al. *Cardiovascular Diabetology*, 2018.

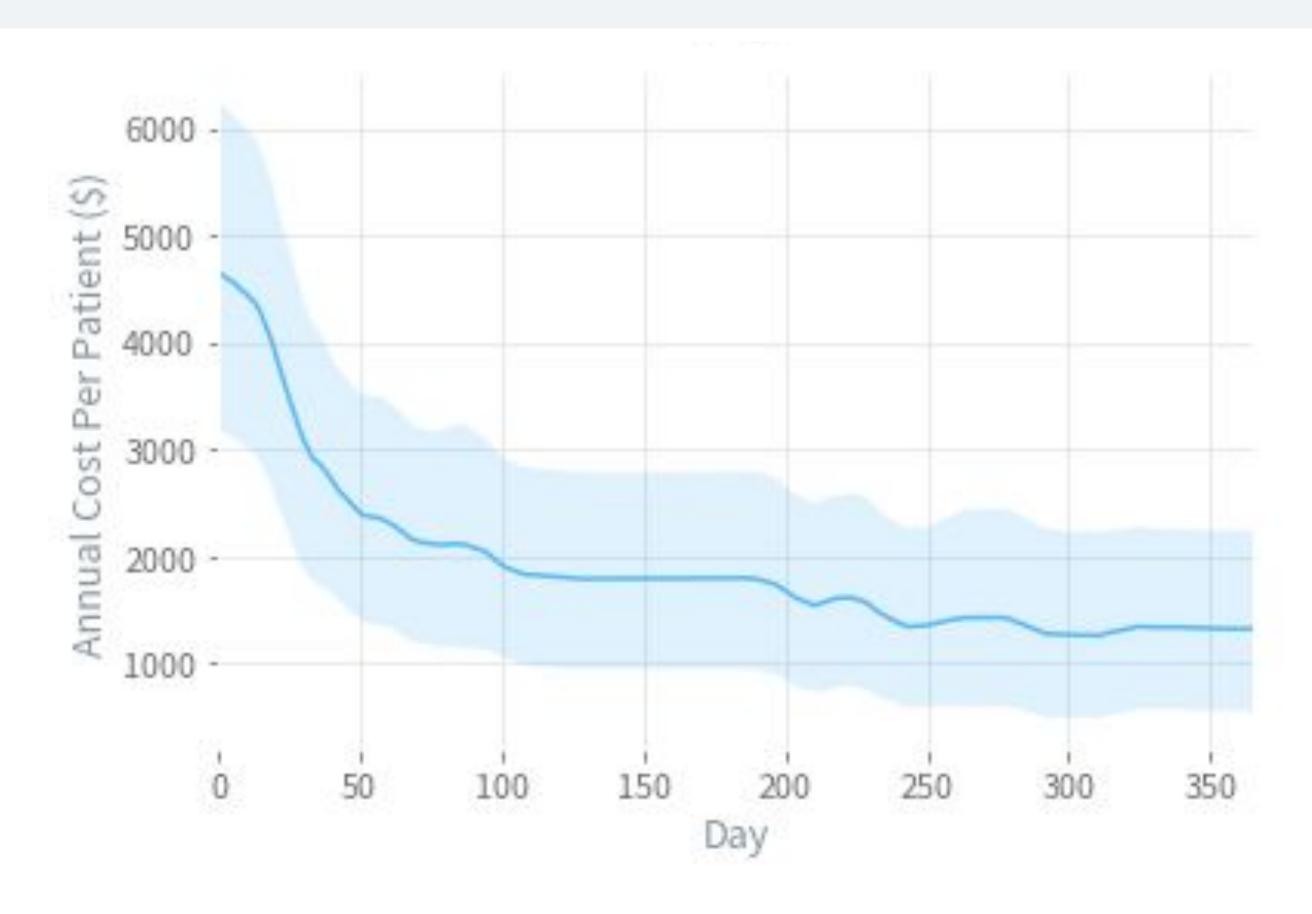








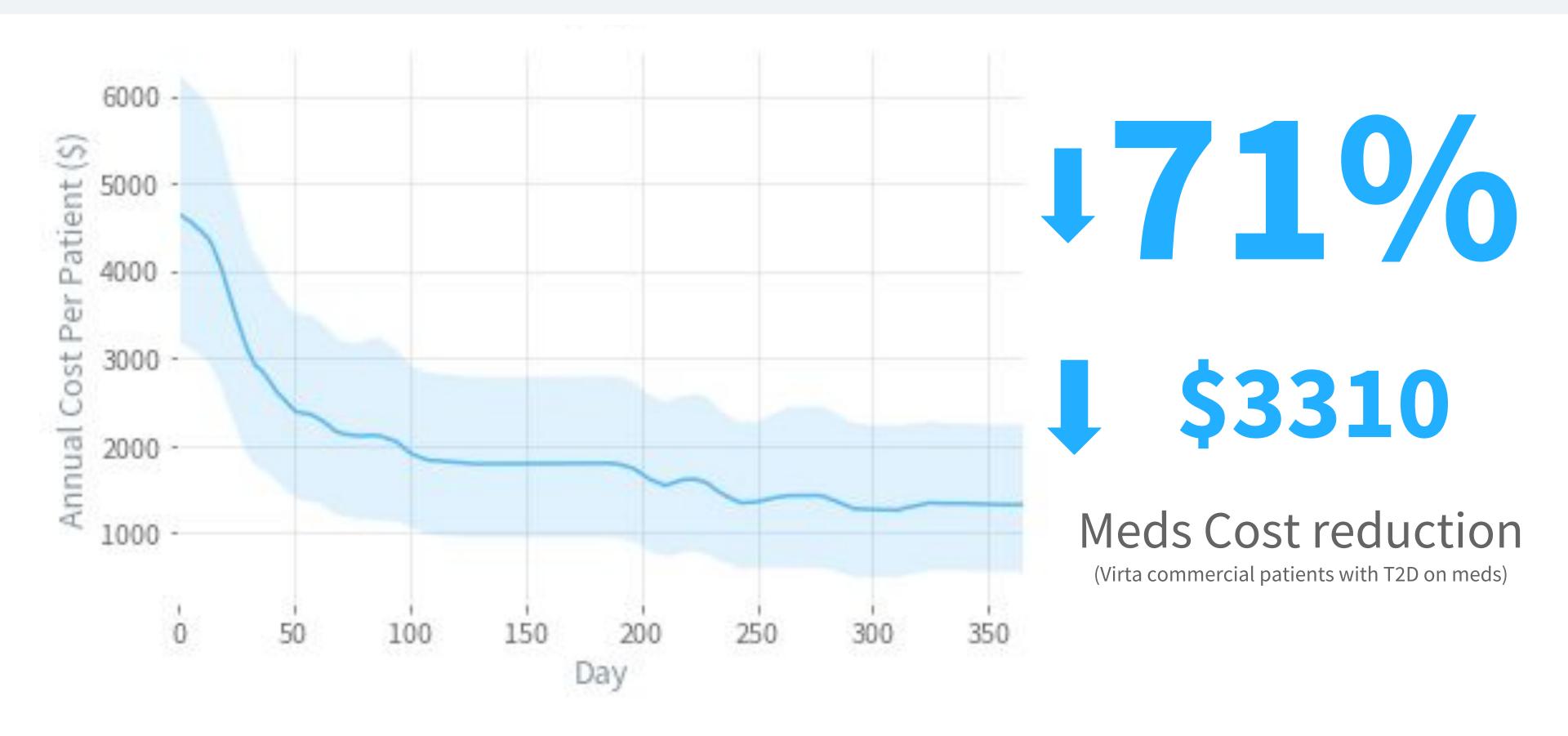
#### In Commercial populations, even more dramatic drug cost savings



# Meds Cost reduction

(Virta commercial patients with T2D on meds)

#### In Commercial populations, even more dramatic drug cost savings



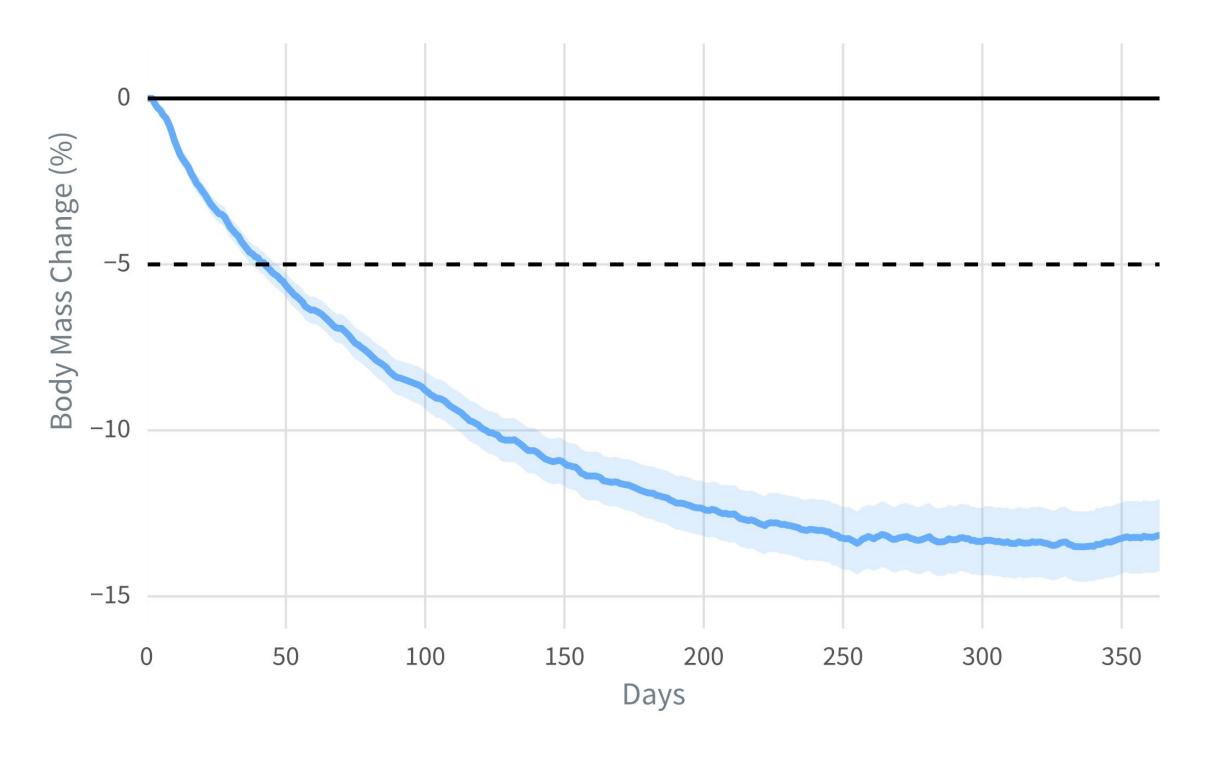
## Per Patient Average Medical Cost Savings alone Nearly \$10,000 in first 2 years<sup>1</sup>





<sup>&</sup>lt;sup>1</sup>Does not include consideration of Virta fees
Virta internal analysis - Economic Impact Model built using Virta clinical results and published estimates of medical & pharmacy costs by A1c level and BMI from Li et. al., The Economic Burden of Obesity by Glycemic Stage in the United States; PharmacoEconomics (2015) 33:735–748; publication pending

#### Clinical Trial Outcomes - Weight Loss Averaged 12%, Sustained At 1 Year





86% of patients lost > 5% 61% of patients lost > 10%

Intent-to-treat  $P < 1.0 \times 10^{-16}$ 

Examining all available cardiovascular risk biomarkers,

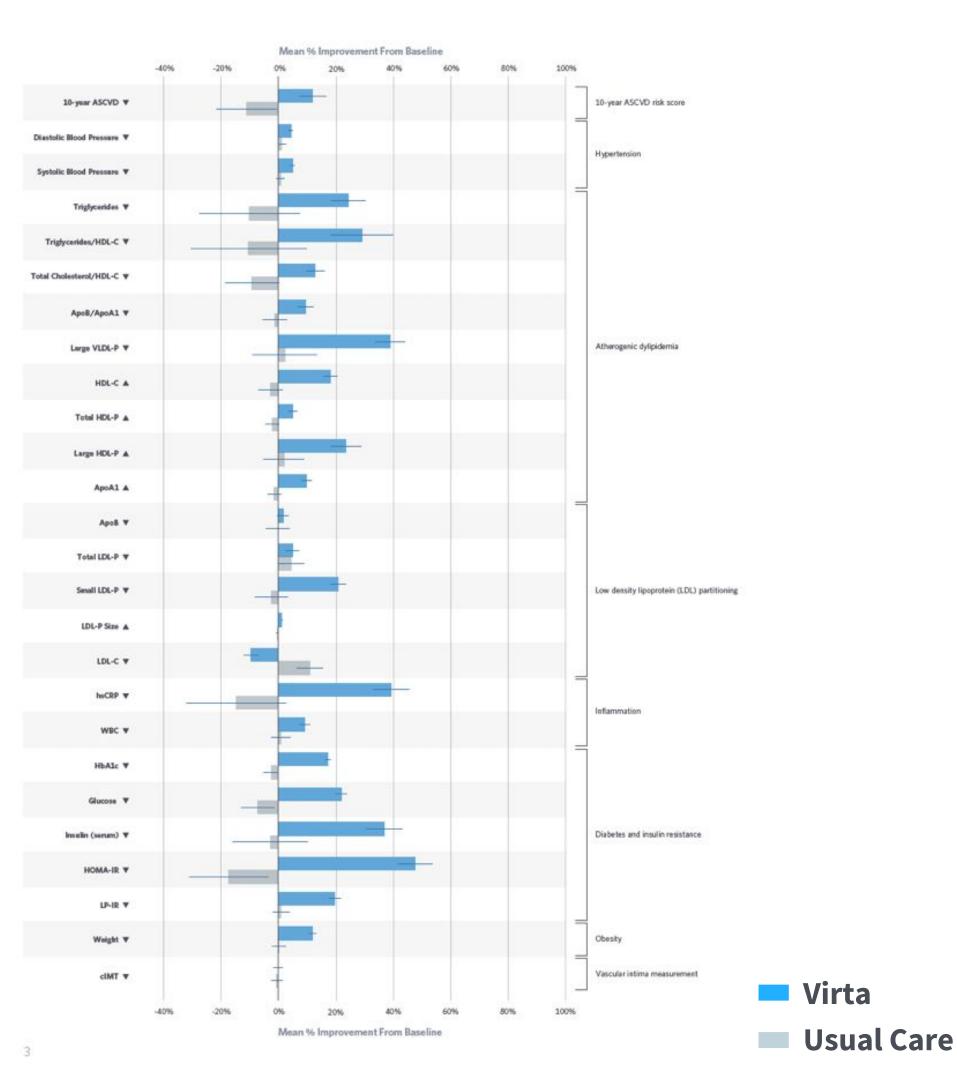
22 of 26 in Virta Treatment

show statistically significant improvement versus

0 of 26 for Usual Care

Intent-to-treat For 22 significant changes P < 0.0019

Hallberg et al. *Diabetes Therapy*, 2018. Bhanpuri et al. *Cardiovascular Diabetology*, 2018.



Examining all available cardiovascular risk biomarkers,

#### 22 of 26 in Virta Treatment

show statistically significant improvement versus

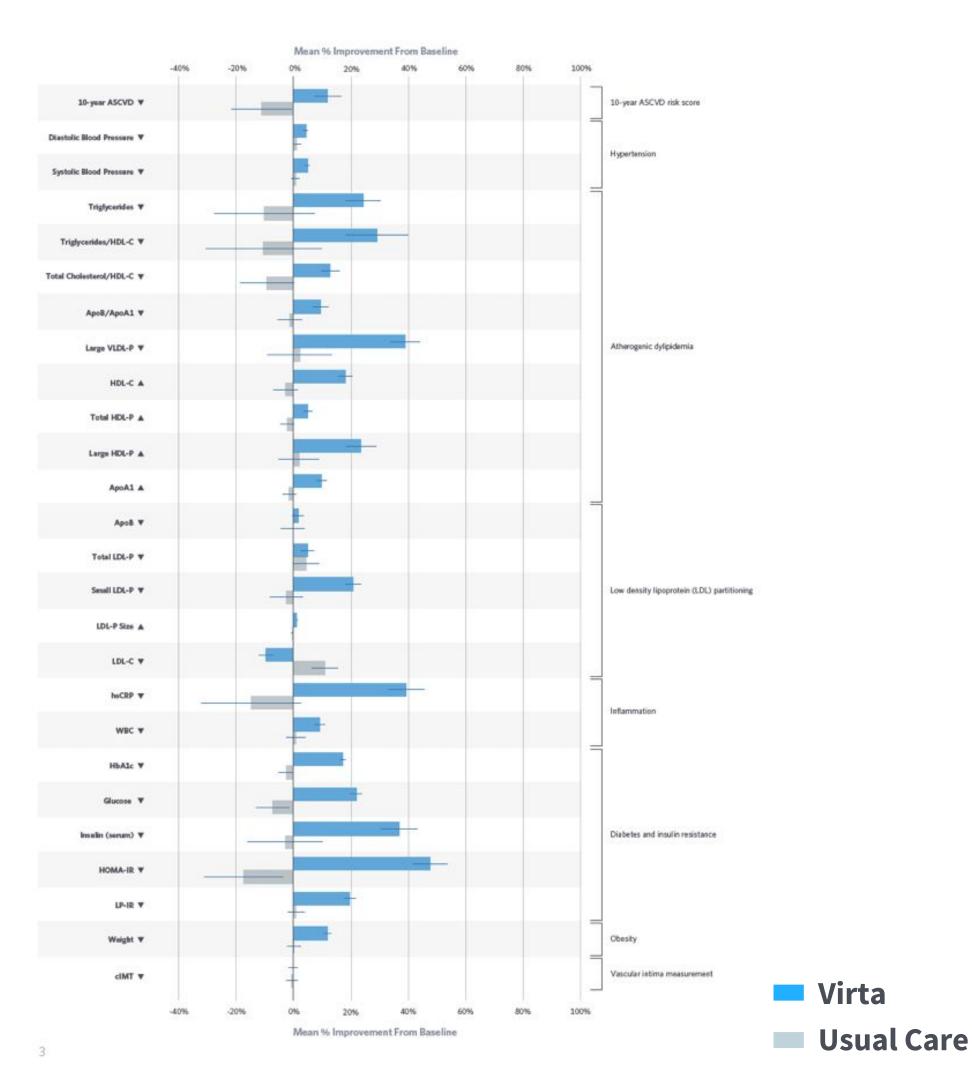
## 0 of 26 for Usual Care

including

- hypertension
- atherogenic dyslipidemia
  - fatty liver disease
  - chronic inflammation

Intent-to-treat For 22 significant changes P < 0.0019

Hallberg et al. *Diabetes Therapy*, 2018. Bhanpuri et al. *Cardiovascular Diabetology*, 2018.



# Papers Published on 70 day and 1 yr T2D & CVD Outcomes

Diabetes Ther https://doi.org/10.1007/sE3300-018-0373-9



#### ORIGINAL RESEARCH

#### Effectiveness and Safety of a Novel Care Model for the Management of Type 2 Diabetes at 1 Year: An Open-Label, Non-Randomized, Controlled Study

Sarah J. Hallberg · Amy L. McKenzie · Paul T. Williams ·

Nasir H. Bhanpuri - Anne L. Peters - Wayne W. Campbell - Tamara L. Hazbun

Brittanie M. Volk · James P. McCarter · Stephen D. Phinney

Jeff S. Volek

Received: December 28, 2017

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#### ABSTRACT

Introduction: Carbohydrate restriction markedly improves glycemic control in patients with type 2 diabetes (T2D) but necessitates prompt medication changes. Therefore, we assessed the effectiveness and safety of a novel care model providing continuous remote care with medication management based on biometric feedback combined with the metabolic approach of nutritional ketosis for T2D management.

Enhanced content To view enhanced content for this article go to https://doi.org/10.6084/m9.figshare. 5903119.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s13300-018-0373-9) contains supplementary material, which is available to authorized users.

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P. T. Williams Independent Consultant, Lafayette, CA, USA

A. L. Peters Keck School of Medicine, University of Southern California, Los Angeles, CA, USA Methods: We conducted an open-label, nonrandomized, controlled, before-and-after 1-year study of this continuous care intervention (CCI) and usual care (UC). Primary outcomes were glycosylated hemoglobin (HbA<sub>3c</sub>), weight, and medication use. Secondary outcomes included fasting serum glucose and insulin, HOMA-IR, blood lipids and lipoproteins, liver and kidney function markers, and high-sensitivity C-reactive protein (hsCRP).

Results: 349 adults with T2D enrolled: CCI: n = 262 [mean (5D); 54 (8) years, 116.5 (25.9) kg, 40.4 (8.8) kg m<sup>2</sup>, 92% obese, 88% prescribed T2D medication]; UC: n = 87 (52 (10) years, 105.6 (22.15) kg, 36.72 (7.26) kg m<sup>2</sup>, 82% obese, 87% prescribed T2D medication]. 218 participants (83%) remained enrolled in the CCI at 1 year. Intention-to-treat analysis of the CCI (mean  $\pm$  SE) revealed HbA<sub>1c</sub> declined from

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Published online: 07 February 2018

Bhanpuri et al. Cardiovasc Diabetol (2018) 17:56 https://doi.org/10.1186/s12933-018-0698-8

Cardiovascular Diabetology

#### ORIGINAL INVESTIGATION

Open Access

Cardiovascular disease risk factor responses to a type 2 diabetes care model including nutritional ketosis induced by sustained carbohydrate restriction at 1 year: an open label, non-randomized, controlled

Study

Nasir H. Bhanpuri<sup>1\*</sup>

Sarah J. Hallberg<sup>1,2</sup>, Paul T. Williams<sup>3</sup>, Amy L. McKenzie<sup>1</sup>, Kevin D. Ballard<sup>4</sup>,

Wayne W. Campbell<sup>5</sup>, James P. McCarter<sup>1,6</sup>, Stephen D. Phinney<sup>1</sup> and Jeff S. Volek<sup>1,7</sup>

#### Abstract

**Background:** Cardiovascular disease (CVD) is a leading cause of death among adults with type 2 diabetes mellitus (T2D). We recently reported that glycemic control in patients with T2D can be significantly improved through a continuous care intervention (CCI) including nutritional ketosis. The purpose of this study was to examine CVD risk factors in this cohort.

Methods: We investigated CVD risk factors in patients with T2D who participated in a 1 year open label, non-randomized, controlled study. The CCI group (n = 262) received treatment from a health coach and medical provider. A usual care (UC) group (n = 87) was independently recruited to track customary T2D progression. Circulating biomarkers of cholesterol metabolism and inflammation, blood pressure (BP), carotid intima media thickness (cIMT), multi-factorial risk scores and medication use were examined. A significance level of P < 0.0019 ensured two-tailed significance at the 5% level when Bonferroni adjusted for multiple comparisons.

Results: The CCI group consisted of 262 participants (baseline mean (SD): age 54 (8) year, BMI 40.4 (8.8) kg m $^{-2}$ ). Intention-to-treat analysis (% change) revealed the following at 1-year: total LDL-particles (LDL-P) (-4.9%, P=0.02), small LDL-P (-20.8%,  $P=1.2\times10^{-12}$ ), LDL-P size (+1.1%,  $P=6.0\times10^{-12}$ ), Apo8 (-1.6%, P=0.37), ApoA1 (+9.8%,  $P<10^{-16}$ ), Apo8/ApoA1 ratio (-9.5%,  $P=1.9\times10^{-3}$ ), triglyceride/HDL-C ratio (-29.1%,  $P<10^{-16}$ ), large VLDL-P (-38.9%,  $P=4.2\times10^{-15}$ ), and LDL-C (+9.9%,  $P=4.9\times10^{-5}$ ). Additional effects were reductions in blood pressure, high sensitivity C-reactive protein, and white blood cell count (all P<1 ×  $10^{-3}$ ) while cIMT was unchanged. The 10-year atherosclerotic cardiovascular disease (ASCVD) risk score decreased -11.9% ( $P=4.9\times10^{-5}$ ). Antihypertensive medication use was discontinued in 11.4% of CCI participants ( $P=5.3\times10^{-5}$ ). The UC group of 87 participants (baseline mean (SD): age 52 (10) year, BMI 36.7 (7.2) kg m $^{-2}$ ) showed no significant changes. After adjusting for baseline differences when comparing CCI and UC groups, significant improvements for the CCI group included small LDL-P, ApoA1, triglyceride/HDL-C ratio, HDL-C, hsCRP, and LP-IR score in addition to other biomarkers that were previously reported. The CCI group showed a greater rise in LDL-C.

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JMIR DIABETES McKenzie et al

#### Original Paper

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

Amy L McKenzie<sup>1</sup>, PhD; Sarah J Hallberg<sup>1,2</sup>, DO, MS; Brent C Creighton<sup>1</sup>, PhD; Brittanie M Volk<sup>1</sup>, RD, PhD; Theresa M Link<sup>1</sup>, RD, CDE; Marcy K Abner<sup>1</sup>, RD; Roberta M Glon<sup>1</sup>, RN, BSN; James P McCarter<sup>1</sup>, MD, PhD; Jeff S Volek<sup>1</sup>, RD, PhD; Stephen D Phinney<sup>1</sup>, MD, PhD

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#### Abstract

Background: Type 2 diabetes (T2D) is typically managed with a reduced fat diet plus glucose-lowering medications, the latter often promoting weight gain.

Objective: We evaluated whether individuals with T2D could be taught by either on-site group or remote means to sustain adequate carbohydrate restriction to achieve nutritional ketosis as part of a comprehensive intervention, thereby improving glycemic control, decreasing medication use, and allowing clinically relevant weight loss.

Methods: This study was a nonrandomized, parallel arm, outpatient intervention. Adults with T2D (N=262, mean age 54, SD 8, years, mean body mass index 41, SD 8, kg m<sup>-2</sup>, 66.8% (175/262) women) were enrolled in an outpatient protocol providing intensive mutrition and behavioral counseling, digital coaching and education platform, and physician-guided medication management. A total of 238 participants completed the first 10 weeks. Body weight, capillary blood glucose, and beta-hydroxybutyrate (BOHB) levels were recorded daily using a mobile interface. Hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) and related biomarkers of T2D were evaluated at baseline and 10-week follow-up.

Results: Baseline HhA<sub>1c</sub> level was 7.6% (SD 1.5%) and only 52/262 (19.8%) participants had an HbA<sub>1c</sub> level of <6.5%. After 10 weeks, HbA<sub>1c</sub> level was reduced by 1.0% (SD 1.1%; 95% CI 0.9% to 1.1%, P<.001), and the percentage of individuals with an HbA<sub>1c</sub> level of <6.5% increased to 56.1% (147/262). The majority of participants (234/262, 89.3%) were taking at least one diabetes medication at baseline. By 10 weeks, 133/234 (56.8%) individuals had one or more diabetes medications reduced or eliminated. At follow-up, 47.7% of participants (125/262) achieved an HbA<sub>1c</sub> level of <6.5% while taking metformin only (n=86) or no diabetes medications (n=39). Mean body mass reduction was 7.2% (SD 3.7%; 95% CI 5.8% to 7.7%, P<.001) from baseline (117, SD 26, kg). Mean BOHB over 10 weeks was 0.6 (SD 0.6) mmol·L<sup>-1</sup> indicating consistent carbohydrate restriction. Post hoc comparison of the remote versus on-site means of education revealed no effect of delivery method on change in HbA<sub>1c</sub> (F<sub>1.260</sub>=1.503, P=22).

Conclusions: These initial results indicate that an individualized program delivered and supported remotely that incorporates nutritional ketosis can be highly effective in improving glycemic control and weight loss in adults with T2D while significantly decreasing medication use.

(JMIR Diabetes 2017;2(1):e5) doi:10.2196/diabetes 6981

http://diahetes.junic.org/2017/1/e5/

JMIR Dishetes 2017 | vol. 2 | iss. 1 | e5 | p.1 (page number not for citation purposes)

Papers submitted or in progress on 1 yr NAFLD/NASH, 1 yr sleep, 2 yr T2D, 2 yr Pre-D, etc.

# High Level Context

Outcomes

# Patient Experience

Enterprise Experience

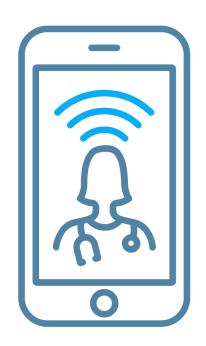
Conclusion



## Virta's Practice - Two Key Pillars



## Virta's Practice - Two Key Pillars

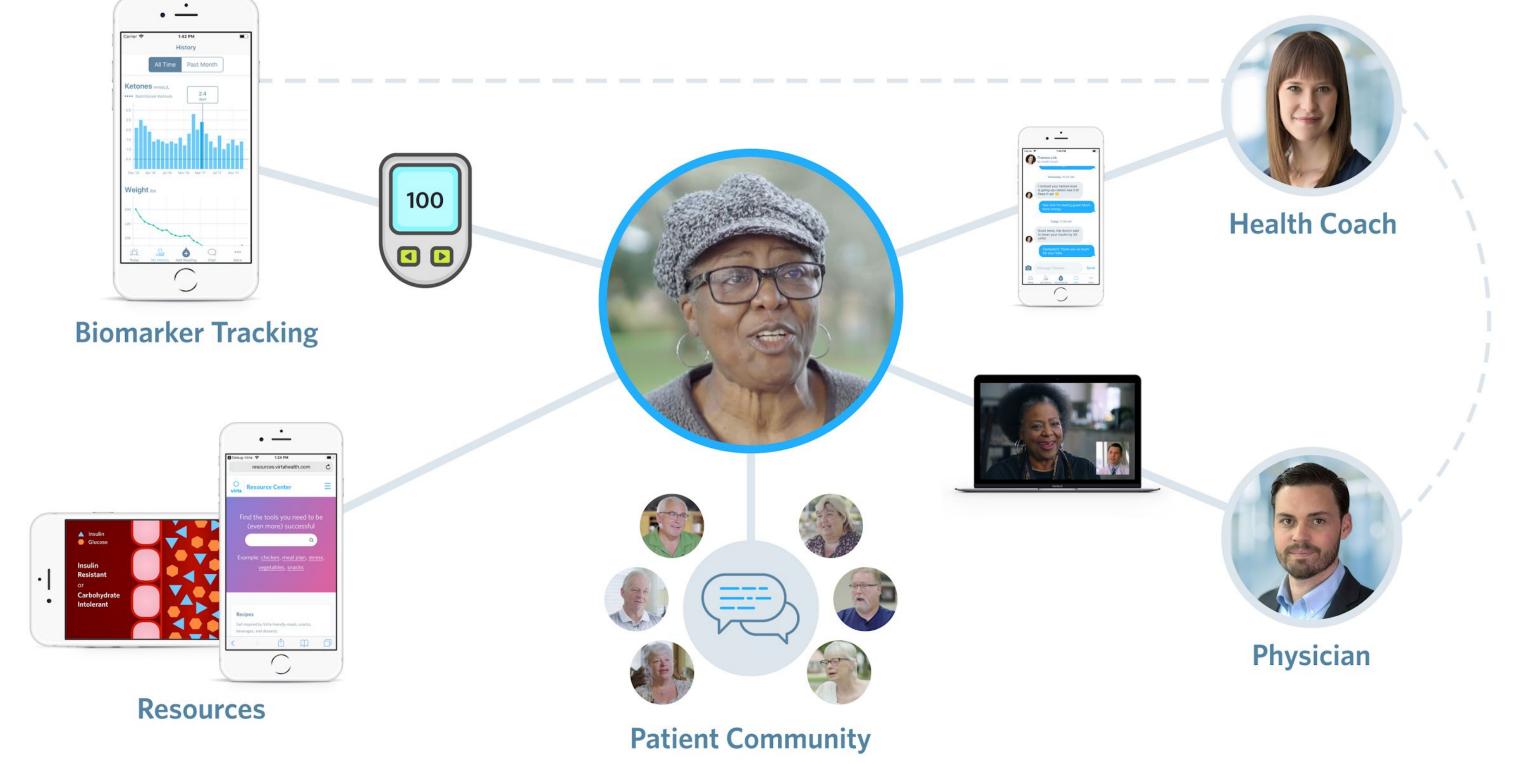


#### **Continuous Remote Care**

Telemedicine platform for 'in your pocket', personalized physician and coach care

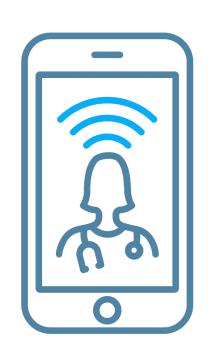


## Virta's Continuous Remote Care Platform



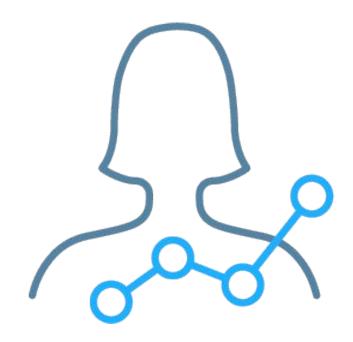


## Virta's Practice - Two Key Pillars



#### **Continuous Remote Care**

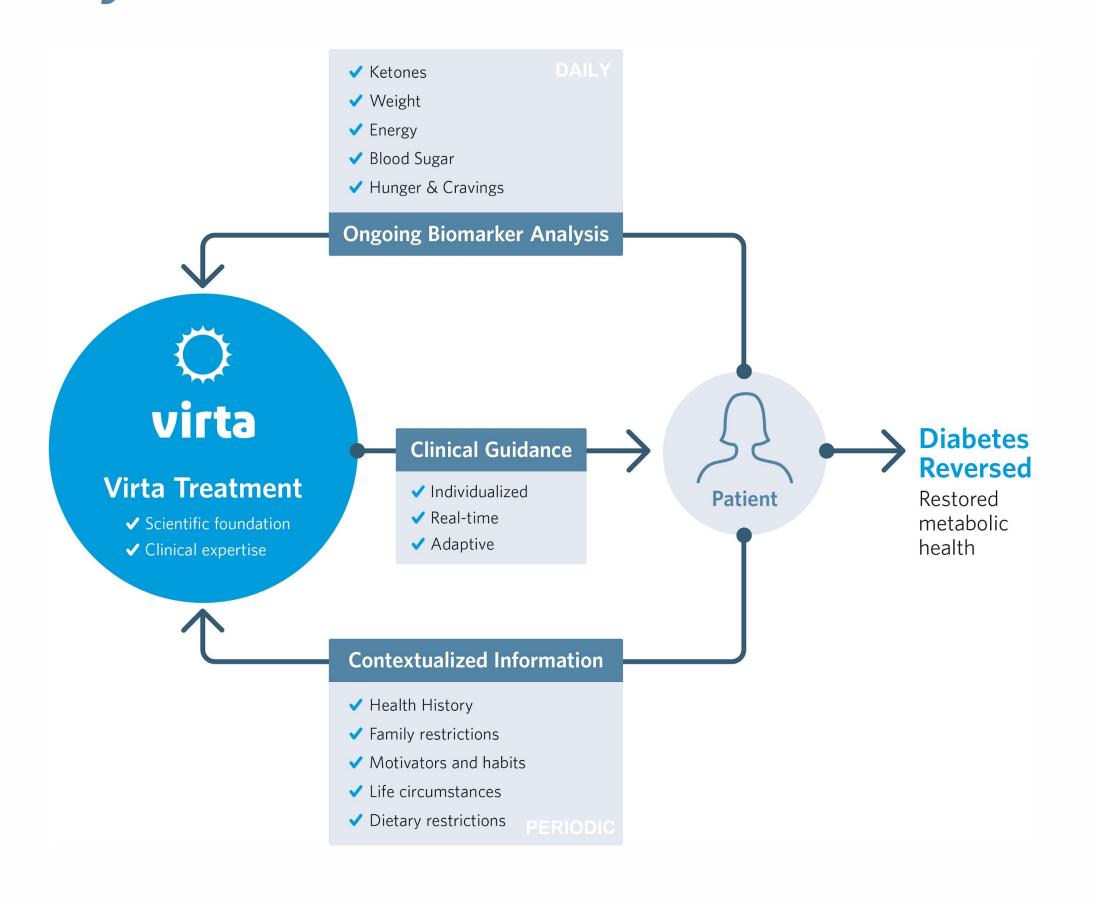
Telemedicine platform for 'in your pocket', personalized physician and coach care



## **Proprietary Virta Protocol**

Med Management and Patient lifestyle guidance, with a focus on nutritional ketosis

## Individualized protocol behind Virta Treatment is very complex and can only be delivered with data and software at scale



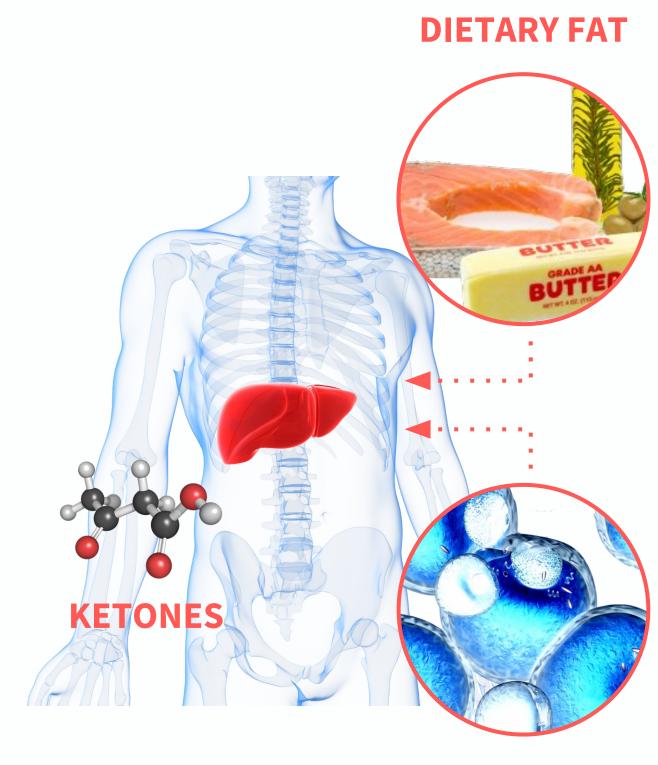


## What is nutritional ketosis and why is it beneficial?

- Nutritional ketosis is a metabolic state in which the body is predominantly fueled by fats from diet or body fat
- Ketone bodies are natural products of liver metabolism
   & preferred fuel for the brain
- Ketone bodies increase when dietary carbohydrates are limited to < 30 g/day with moderate protein</li>

#### Benefits of ketosis arise from ...

- Alternative energy source with decreased reliance on glucose/insulin "rollercoaster"
- Hormonal properties of ketones reduce inflammation & oxidative stress



**BODY FAT** 

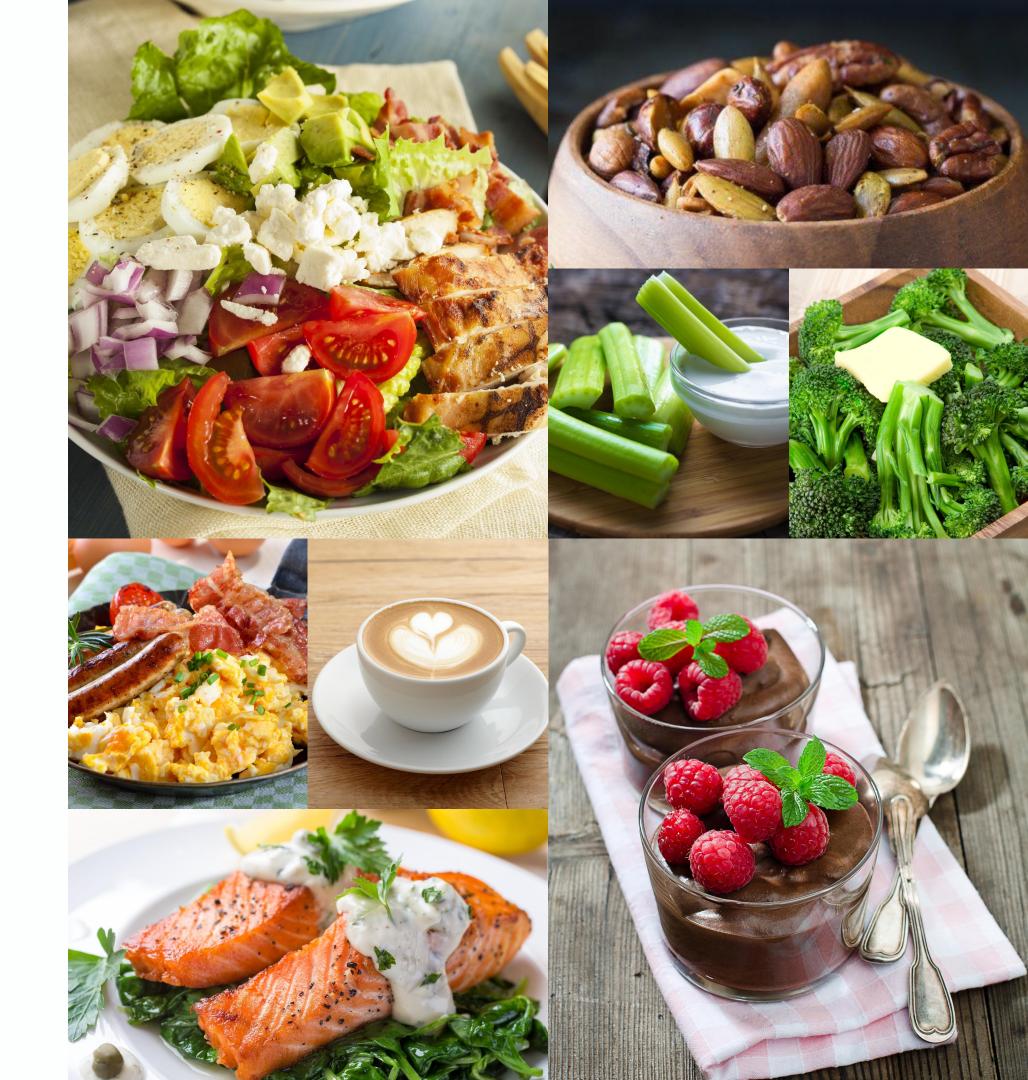
## Nutritional Ketosis -Individualized Guidance

Carb restriction to achieve nutritional ketosis (initially 30 grams)

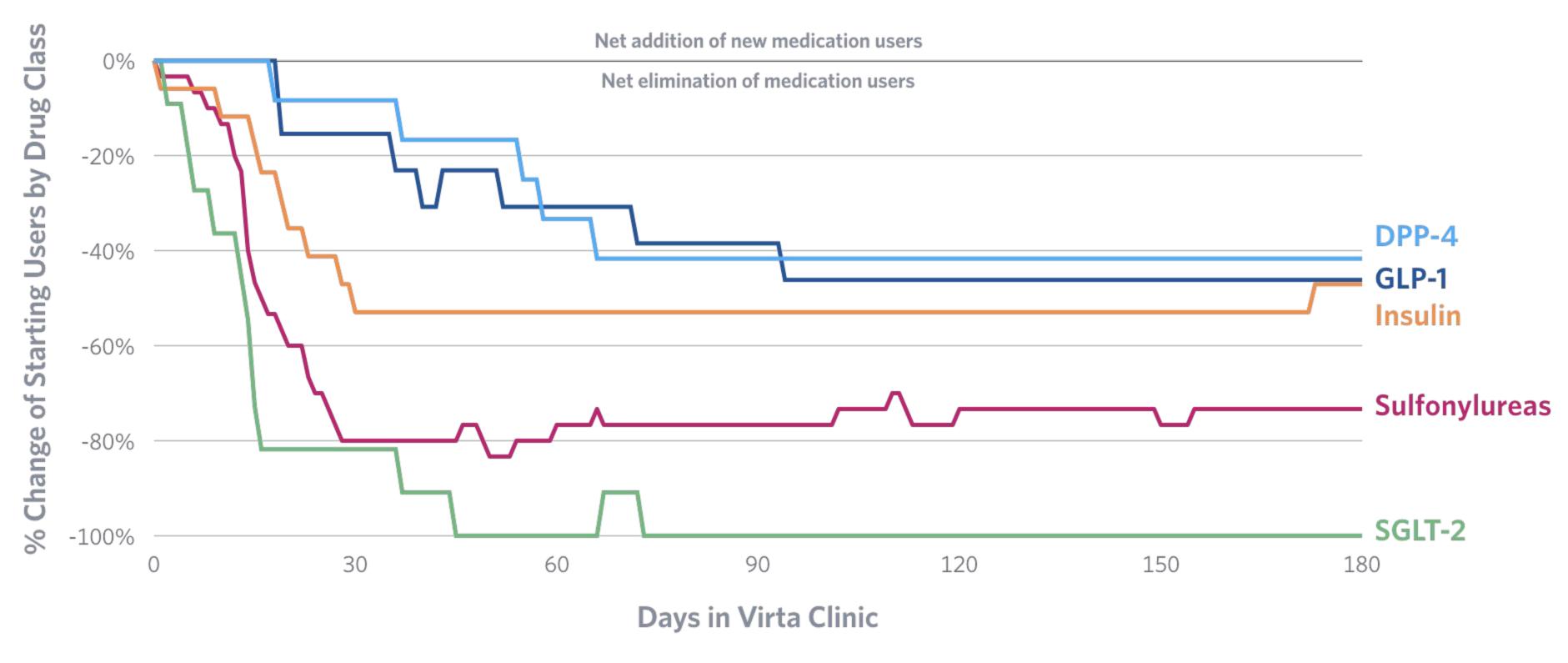
Highly personalized (socio-economic, cultural, religious)

Education & problem solving, not meal delivery/replacement

Eat delicious, real foods until satisfied, no calorie counting



#### **Commercial Outcomes - Medication Reductions are Individualized and Rapid**

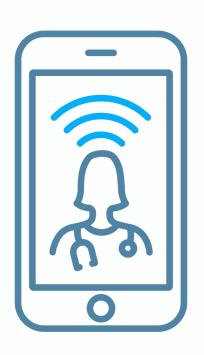


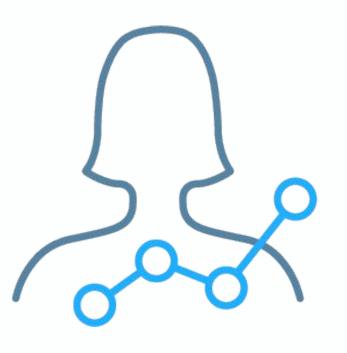
Graph depicts the change from baseline in percent of medication users by class over time. Negative values on y axis indicate a net elimination of medication users; positive values indicate a net addition of new medication users.

**Source:** Virta Health Registry for Remote Care of Chronic Conditions, enterprise patients with type 2 diabetes, outcomes as of May 31, 2018. Excludes metformin as it is recommended for treatment of prediabetes and in conditions such as PCOS. Not patient was prescribed a thiazolidinedione.

#### Are the Virta Treatment outcomes sustainable?

- The Virta treatment is aimed at lifelong changes in nutrition and behavior.
   (Patients can stay under Virta's care long-term.)
- The Virta-IUH clinical trial has been extended to five years.
- Favorable two year results are in preparation for publication.
- Some patients enjoy staying in nutritional ketosis long-term.
- Some patients use improved insulin sensitivity to enjoy greater dietary flexibility while still staying generally on the lower spectrum of carbohydrate consumption.
- Virta is not a cure for diabetes and we do not advise a return to high carbohydrate consumption.





## High Level Context

Outcomes

Patient Experience

## Enterprise Experience

Conclusion



## Virta Patient Marketing

#### Nielsen Launch: March 14, 2017

#### **Campaigns**

- Newsletter email
- Direct mailers
- Text
- Posters
- Brochures

#### Purdue Launch: April 10, 2017

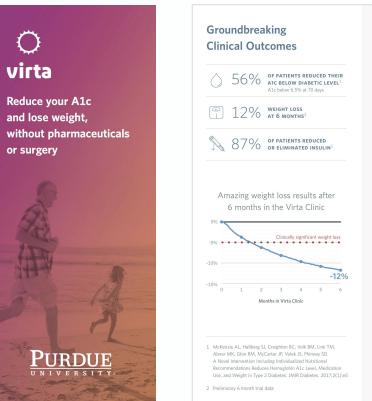
#### **Campaigns**

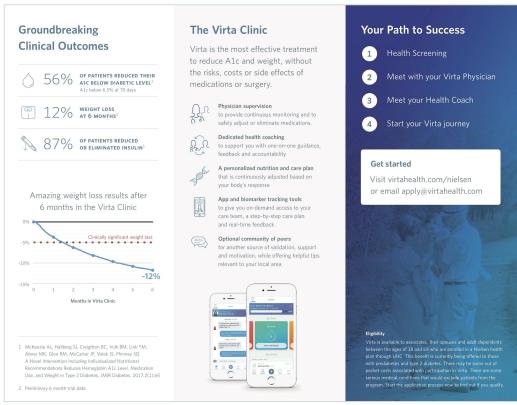
- Direct emails
- Direct mailers
- On-site events
- Posters
- Brochures

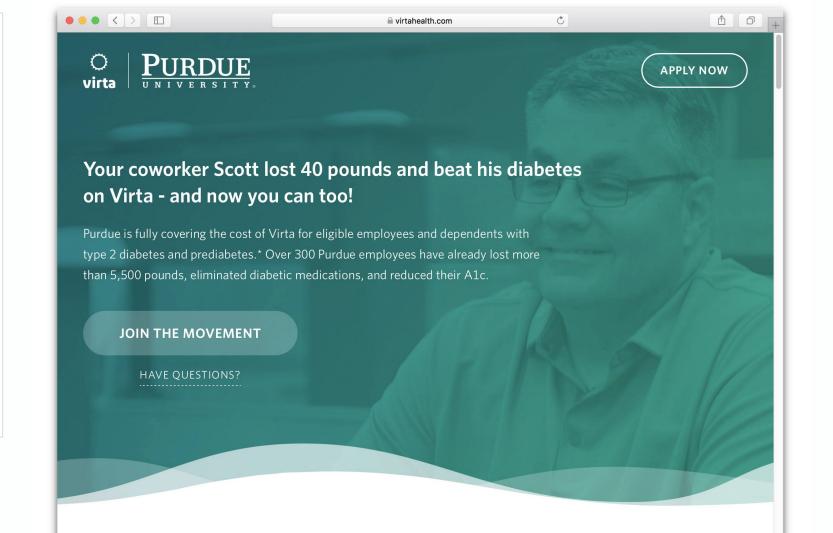


virtahealth.com/nielsen

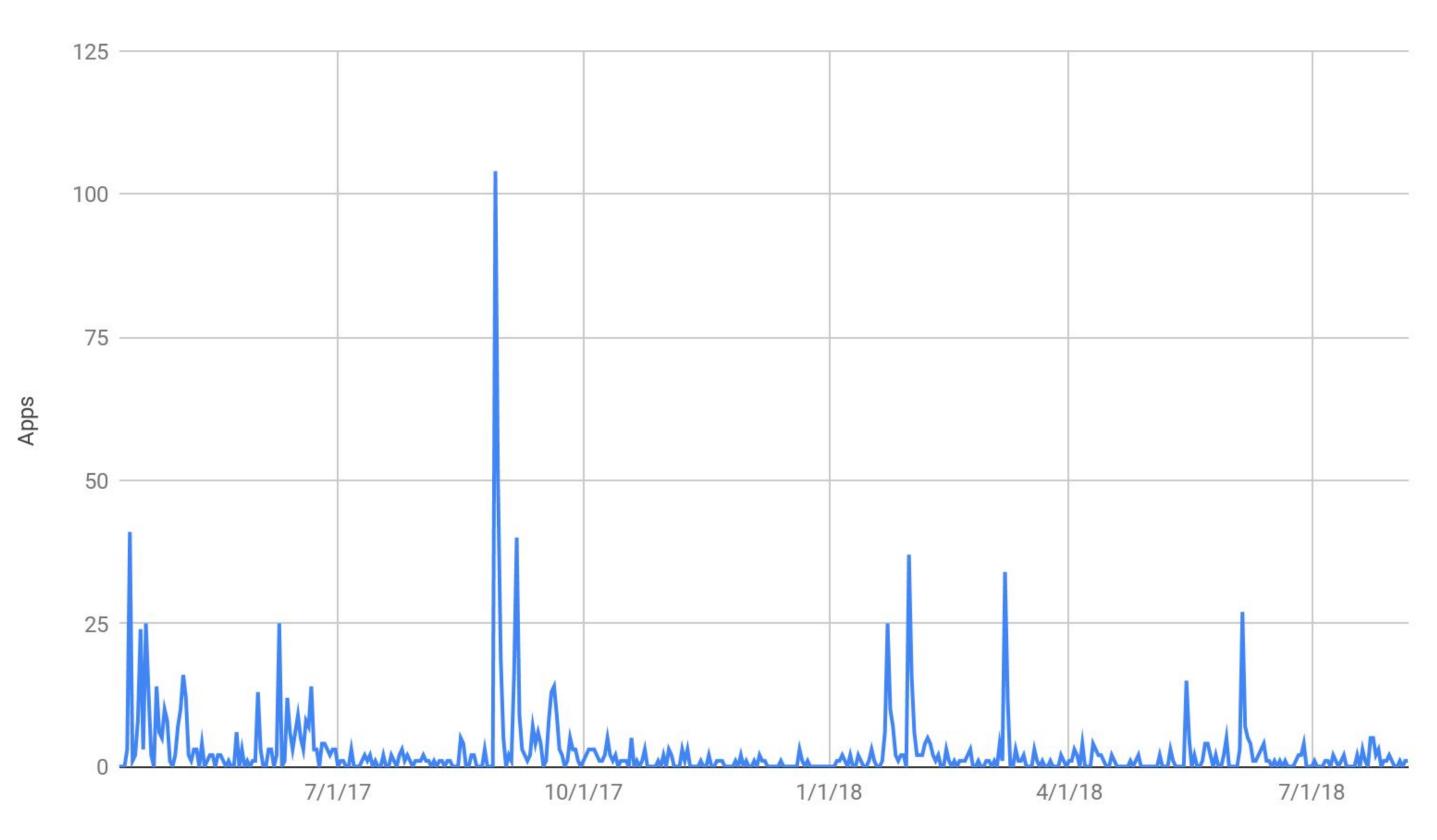
employees and dependents with type 2 diabe and prediabetes. See website for eligibility. virta







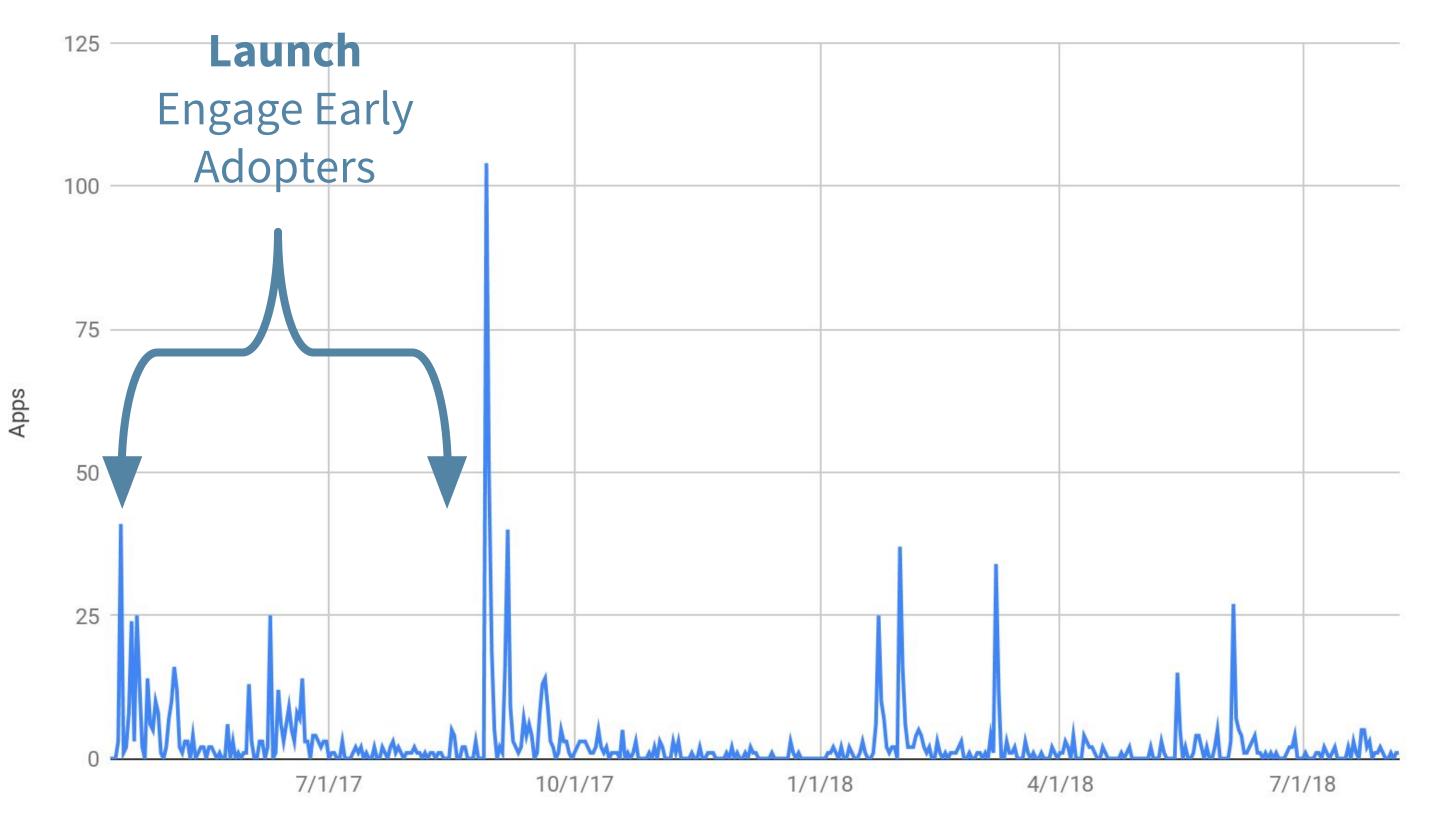
% of target T2D population applied



% of target T2D population applied

**15%** 

0-3 month launch



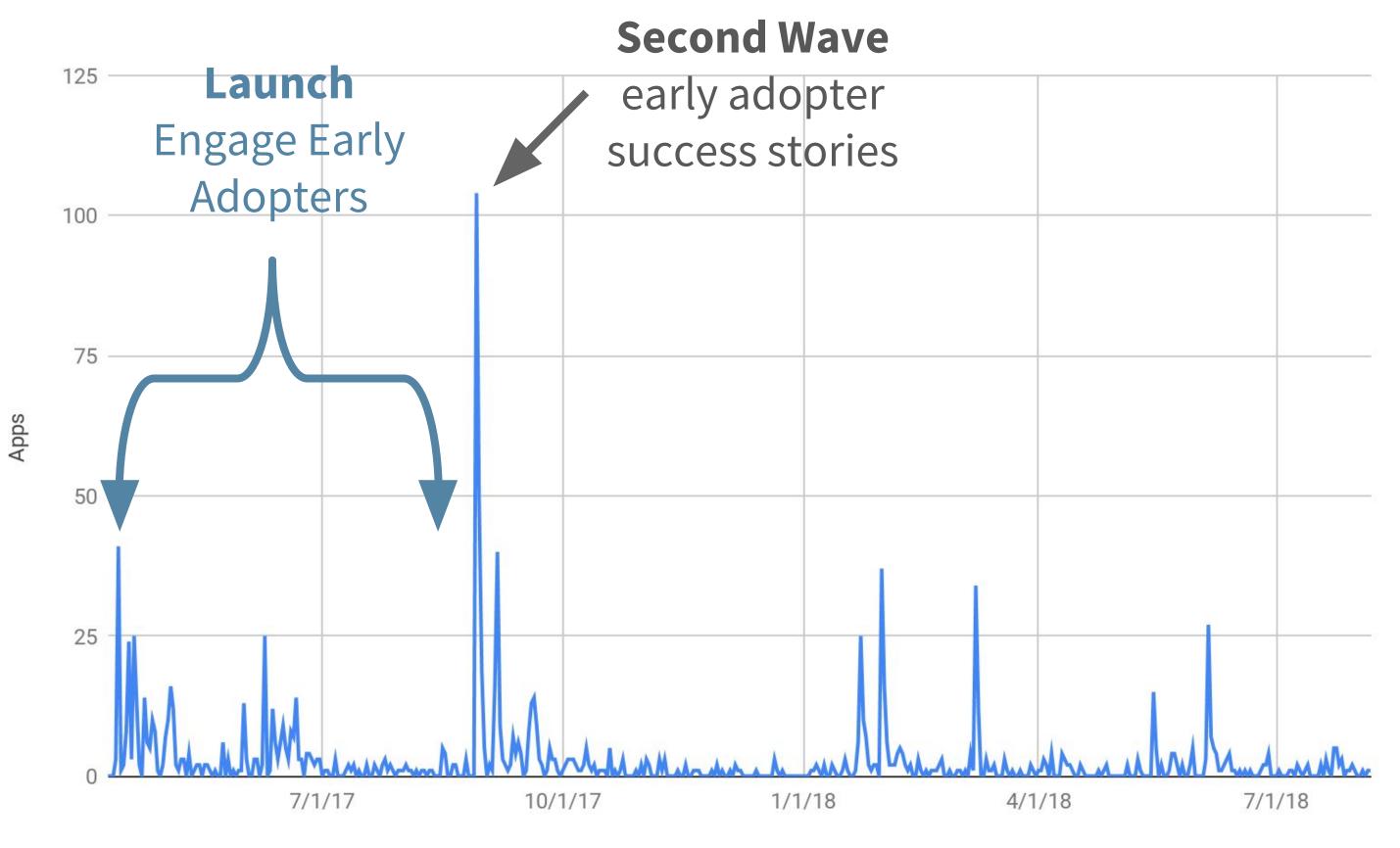
% of target T2D population applied

**15%** 

0-3 month launch

25%

2nd wave, 3-9 months



% of target T2D population applied

**15%** 

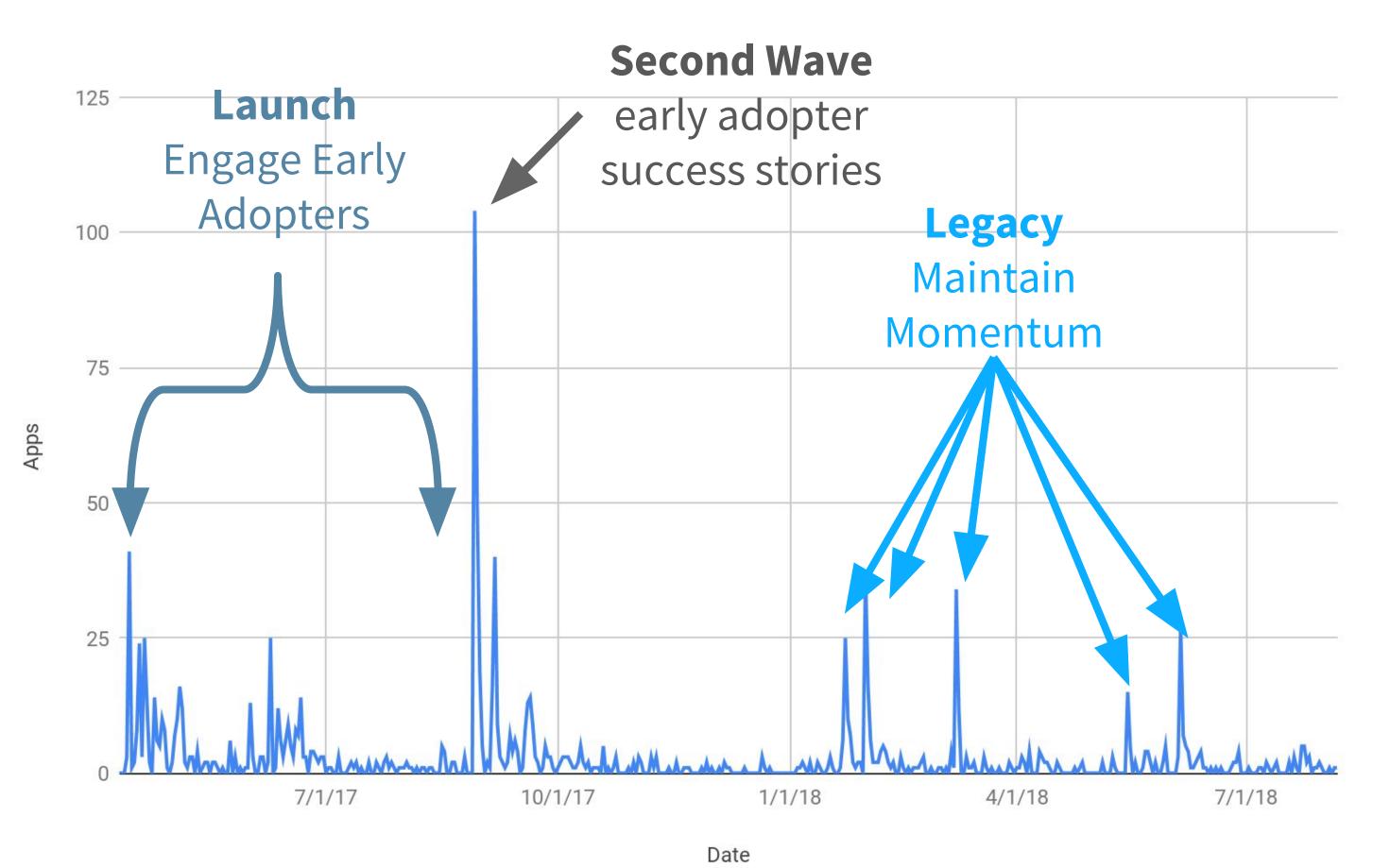
0-3 month launch

25%

2nd wave, 3-9 months

40%

>9 months





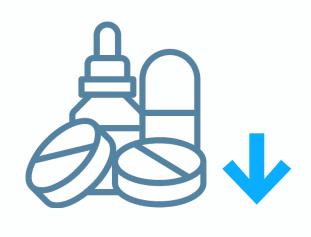
Virta Patient
Net Promoter Score

# Integration with Existing Providers

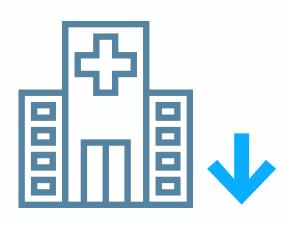
- Virta is a Metabolic Health Expert doing work PCPs and Endos don't have time/access to do
- We report patient outcomes to PCPs periodically and provider physician-to-physician consultations as needed
- We typically reverse T2 diabetes "in between" PCP visits



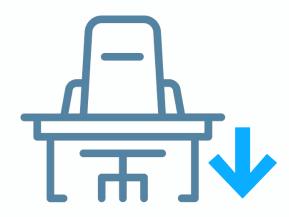
## Virta Drives a Variety of Savings



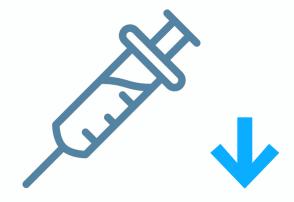
**Medications** 



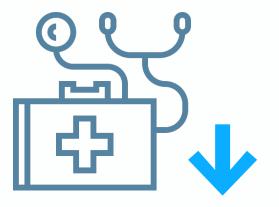
**ER/Hospital Visits** 



Workplace Absenteeism



Medical Equipment



**Specialized Visits** 



Workers' Comp Claims





## High Level Context

Outcomes

Patient Experience

Enterprise Experience

Conclusion



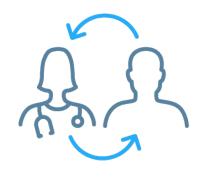
# Why "manage" when you can reverse type 2 diabetes without medication or surgery?



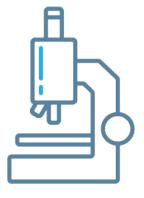
## The Virta Treatment is different from anything else



Proven type 2 diabetes reversal



High activation (30%) & retention (90%) at 1 year



Improves 4 other chronic diseases



Licensed medical provider in all 50 states with continuous remote care



Superior, peer-reviewed, published outcomes



Fees at risk based on results

## Thank you!



#### Links to further information

www.virtahealth.com

@virtahealth, @jpmccarter

jim @ virtahealth.com