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# Clinical Trial Update: 6 month outcomes in patients with type 2 diabetes

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# Clinical Trial Update: 6 month outcomes in patients with type 2 diabetes

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Nearly 30 million Americans<sup>1</sup> and over 400 million people worldwide<sup>2</sup> live with type 2 diabetes (T2D), a condition that is considered chronic and progressive with no cure<sup>3</sup>. While capable of improving glycemic control, pharmacological therapy and bariatric surgery are often accompanied by side effects<sup>4</sup>, reduced quality of life<sup>5</sup>, and economic burden<sup>6</sup>, highlighting the critical need for interventions with better outcomes without the negative impact.

Intensive lifestyle interventions and nutritional medicine often improve health outcomes for people living with diabetes in the short term, but evidence for their sustainability over the long term is limited.<sup>7</sup> Another challenge for treatment of chronic conditions is the need for continuous care, which is difficult to provide in an outpatient setting.<sup>8</sup>

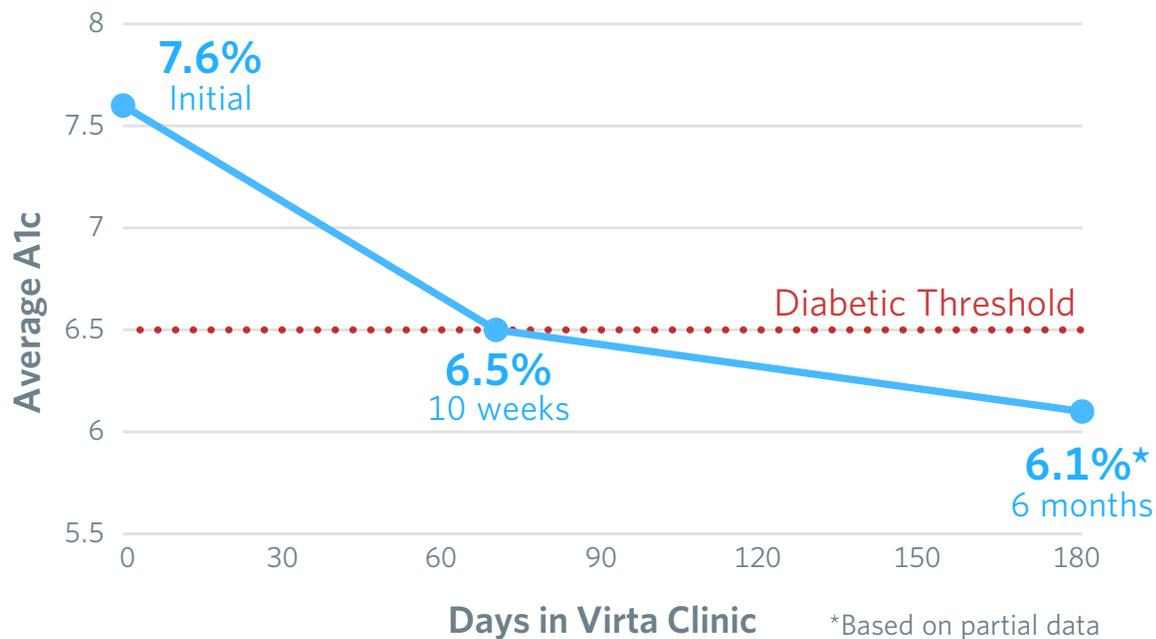
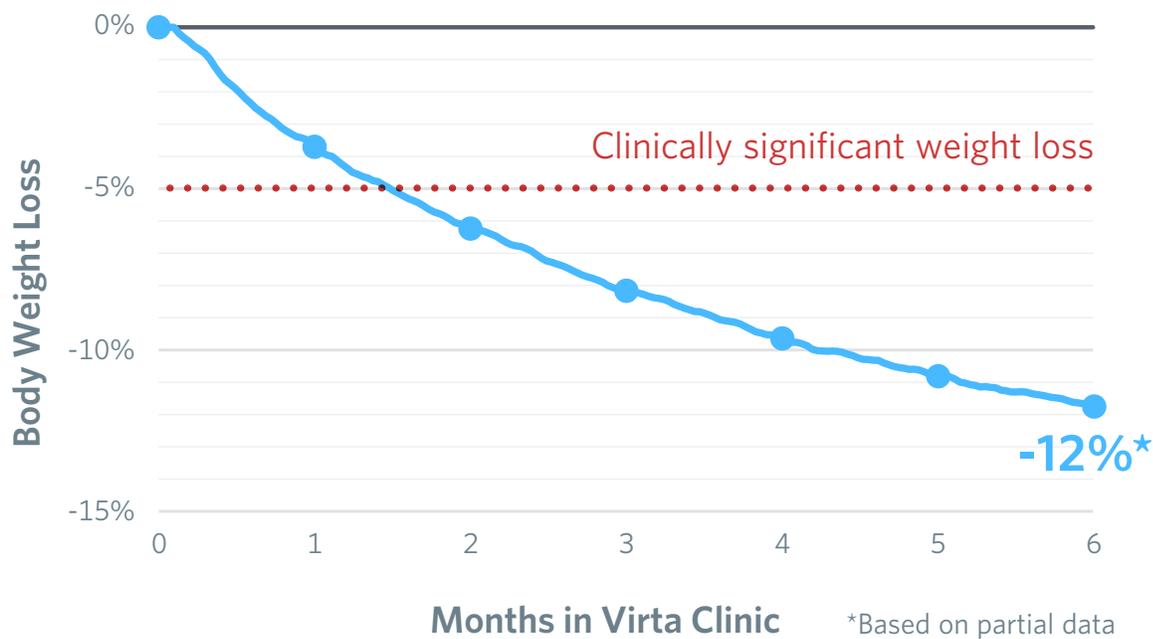
At the Virta Clinic, we hope to address these challenges by providing patients with intensive, personalized interventions backed by continuous support from our remote care team of health coaches and physicians. Our research efforts will evaluate the efficacy, safety, sustainability, and economic impact of care within the Virta Clinic for people living with T2D. Our ongoing research will allow us to continuously improve our personalized care plans to positively impact health outcomes for patients.

In partnership with Indiana University Health Arnett, we have undertaken a clinical trial to evaluate the efficacy of the personalized care plans utilized at the Virta Clinic for 262 patients with a diagnosis of T2D (baseline characteristics, mean $\pm$ SD—age: 54 $\pm$ 8 y, body mass: 117 $\pm$ 26 kg, BMI: 41 $\pm$ 9 kg·m<sup>-2</sup>, 66.8% (175/262) women, HbA1c: 7.6 $\pm$ 1.5%, with 89% prescribed at least 1 glycemic control medication). At the Virta clinic, each patient receives an individualized plan for nutritional ketosis, behavioral and social support, biomarker tracking tools, and ongoing care from a health coach with medication management by a physician.

Recently, we published short-term, 10 week health outcomes for these patients.<sup>9</sup> On average, patients reduced their HbA1c 1.1% from 7.6% at enrollment with 91% retention. Fifty-six percent (147 of 262) of participants achieved an HbA1c <6.5% at follow up, and 97% (143 of 147) of those participants achieved this without an increase in the number or dosage of diabetic medications. Further, 64% of insulin, sulfonylurea, SGLT-2 inhibitor, DPP-4 inhibitor, and thiazolidinedione prescriptions were

eliminated in 10 weeks. The average patient lost 7.2% of their body weight—75% of completers attained clinically significant weight loss during this time (more than 5% of their body weight).

After 6 months, 89% of participants were still enrolled in the study. Glycosylated hemoglobin was reduced to  $6.1 \pm 0.7\%$  from  $7.5 \pm 1.3\%$  in a sample of 108 participants who elected to test HbA1c at 6 months. Twenty-two of the 108 started with a HbA1c  $< 6.5\%$ , and at 6 months, 82 of 108 (76%) reduced their HbA1c below the threshold for diabetes diagnosis (6.5%). Patients lost  $11.5 \pm 8.8\%$  of their body weight; 81% (212 of 262) patients attained clinically significant weight loss. Most medication eliminations were maintained through 6 months concurrently with reduced HbA1c and weight.



## Discussion

Improvements in glycemic control and lipid profiles in adults with T2D have been associated with weight loss of greater than 5%<sup>10</sup>, making weight loss a desired component of many T2D treatment plans. The assumption in this paradigm is often that weight loss leads to the improvements in glycemic control, but it's possible that improvements in glycemic control occur simultaneously with or before significant weight loss is achieved. In our 10 week outcomes, weight and HbA1c reduction seemingly occur simultaneously, but with significant reductions in HbA1c occurring even before the full life cycle of red blood cells (approximately 100 days). Other research demonstrates improvements in glycemic control occur prior to significant weight loss. Patients with T2D who consumed a low carbohydrate (21g per day) diet had significantly improved insulin sensitivity concurrent with significantly lower plasma glucose and HbA1c, but only 2kg (1.8%) weight loss after two weeks<sup>11</sup>. This early improvement in glycemic control is further highlighted by how quickly insulin and some oral anti-diabetic medications must be reduced or eliminated when a low carbohydrate diet is begun, with most reductions and eliminations occurring in the first 3 weeks<sup>11,12</sup>. This suggests weight loss may not be the driver of improved glycemic control, but rather a positive side effect that is achieved concurrently with a well-formulated, very low carbohydrate diet.

Glycosylated hemoglobin and weight changes after 6 and 12 months were evaluated in a systematic review and meta-analysis of 11 studies involving intensive lifestyle interventions for adults with T2D who were also overweight or obese<sup>10</sup>. HbA1c was not evaluated at 6 months in any of these studies, but at 1 year, changes in HbA1c ranged from +0.2% to -1.2% with only 4 interventions eliciting a reduction greater than 0.5%. Interventions utilizing meal replacements, reduced energy intake, and a diet containing <25% of caloric intake from carbohydrates helped patients lose more than 5% of their weight in 6 months. In all but 2 studies, patients regained weight between 6 and 12 months; weight loss was maintained within 0.1% in the remaining 2 investigations. Published earlier this year, a small RCT evaluated 32 week (8 month) health outcomes following the online delivery of a low-carbohydrate intervention with lifestyle recommendations compared to the American Diabetes Association's "Create Your Plate" diet in adults with T2D who were "ready to change" and "conscientious", as defined by the researchers.<sup>13</sup> After 8 months, participants in the low carbohydrate intervention group reduced HbA1c by 0.8% from 7.1% at enrollment and reduced body weight 11.6% from 110 kg at baseline. In summary, most interventions were not successful at achieving clinically significant weight loss in 6 months and were accompanied by a range of responses in HbA1c. However, the online program utilizing a low carbohydrate diet<sup>13</sup> was the most impactful on both HbA1c and body weight in this timeframe.

It's important to note that reductions in HbA1c and weight were achieved in these studies through the delivery of special programs or intensive interventions with patients, not from one-time instruction. However, none of these programs are available outside of research studies to help adults with T2D

follow through on clinical advice. On the other hand, commercially available weight loss programs have recently been adapted specifically for adults with T2D; one such program was compared to the standard of care in an RCT.<sup>14</sup> At 6 months, this program helped patients reduce HbA1c 0.7% and lose 4% of body weight, compared to only 2% weight loss and no change in HbA1c in the standard of care control group. Although it is difficult to compare our results directly to interventions in separate RCTs, patients with T2D receiving care at the Virta Clinic lost nearly three times as much weight in 6 months, with a loss of 11.5%, compared to this commercially available program, and over 5 times as much as the standard of care group in this study.

Maintaining these health outcomes is a known and ongoing challenge for many intensive interventions. The team at Virta is focused on evaluating long-term outcomes and sustainability in our patients, committed to learning from our research and the research of others, and constantly evolving care plans to meet individual patient goals and needs. While six months is early in long-term maintenance, we look forward to sharing our 1- and 2- year outcomes and learnings in the peer-reviewed literature as the data become available.

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