
Virta publishes full two-year results (n=262) in *Frontiers of Endocrinology*: 54% diabetes "reversal," granularity on med elimination - June 6, 2019

Mean insulin dose down 81% in Virta group vs. 13% increase in comparator; SUs completely eliminated, SGLT-2s down significantly; 7% complete diabetes remission (A1c <5.7% without meds), 18% partial (A1c <6.5% without meds)

Virta [published](#) two-year outcomes from their low-carb + continuous remote care intervention, expanding on topline results from [Obesity Week 2018](#). Participants in the Virta arm achieved 10% mean weight loss (~12 kg; 26.5 lbs) and a ~0.9 absolute A1c reduction (baseline: 7.7%). These figures are roughly aligned with those seen at [one year](#). Meanwhile, the standard care control arm (n=87) saw A1c increase significantly (+0.4% from baseline 7.9%), with no change from baseline weight.

At two years, 7% of the Virta group had achieved "complete diabetes remission" (A1c <5.7% without medication); "partial remission" (A1c <6.5% without medication), was 18%. 54% had achieved "diabetes reversal" (A1c <6.5% and no medications apart from metformin).

The number of Virta users on a diabetes medication (besides metformin) dropped from 56% at baseline to 27% at two years. Most notably, the mean insulin dose among Virta participants decreased by 81% at 2 years (from 81.9 to 15.5 U/day) vs. a 13% increase in the standard care control arm (from 96.6 to 109.3 U/day). Importantly, this reduction was not entirely driven by a subgroup of users who discontinued; for those who remained on insulin at two years, mean dose fell by 61% in the Virta group (81.9 to 15.5 U/day) vs. growing 19% in the comparator (103.8 to 123.5 U/day).

Cost savings for insulin-users were estimated at "nearly \$5,000 annually". At [one year](#), Virta has estimated cost savings at ~\$9,600 per participant per two years (primarily from medication discontinuation), and this number includes all Virta participants regardless of baseline insulin use to our understanding. Of note, this estimate would just about cover the original first-year expenses of Virta (\$4,940 total: \$500 upfront, \$370/month) and save significant money in the time after (\$199/month). Since Virta began tying 100% of its fees at risk in [November 2018](#), we have less clarity on the cost-effectiveness of the program, though representatives did assure us that the new structure is designed to assure quicker savings to partners. We'd also love to see a breakdown of the savings, i.e. out-of-pocket reductions vs. savings for the employer/health plan.

From a cardiovascular health perspective at two years, systolic and diastolic blood pressure were down 6 mmHg (baseline: 132 mmHg) and 3 mmHg (baseline: 82 mmHg), respectively, HDL was up 8 mg/dl (baseline: 42 mg/dl), and triglycerides were down 44 mg/dl (baseline: 197 mg/dl). Total LDL cholesterol was elevated by 11 mg/dl (baseline: 104 mg/dl), but Dr. McCarter noted that in published one-year outcomes, LDL particle number trended down and that large, buoyant particles prevail (a lower risk phenotype) - it's not clear if that composition is reflected in two year data. The intent-to-treat analysis shows that mean beta-hydroxybutyrate (blood ketone) levels remain stable from year one to year two (both ~0.27 mmol/L), signifying continued degree of adherence to the ketogenic diet.

Some other highlights specific to medication discontinuation (see table below, full numbers in the published [appendix](#)):

- **Sulfonylurea use was reduced from 24% at baseline to 0% at one and two years with Virta, while growing 5% over two years in the comparator group.** We would love to see how this affected hypoglycemia between the two groups.
- **SGLT-2 inhibitor use was significantly reduced over two years with Virta (10.3% down to 3.1%).** Seeing as this novel class is one of the more expensive on the market, we would love to

know how much it attributed to overall cost savings. Further, we'd love to know the estimated cost savings for all drug classes.

- **Use of any diabetes medication besides metformin rose significantly in the comparator group, from 66.7% to 79.3 % (p=0.004).**

	Baseline	1-year	2-year	p-value (2-year vs. baseline)
Any diabetes medication, excluding metformin	Virta: 56.9% Comparator: 66.7%	28.0% 75.6%	26.8% 79.3%	1.3x10 ⁻¹¹ 0.004
Sulfonylureas	Virta: 23.7% Comparator: 24.1%	0% 25.6%	0% 29.3%	4.2x10 ⁻¹² 0.23
Insulin	Virta: 29.8% Comparator: 46.0%	14.7% 51.3%	11.3% 55.2%	9.1x10 ⁻⁹ 0.23
TZDs	Virta: 1.5% Comparator: 1.2%	0.5% 1.3%	2.6% 6.9%	0.73 0.25
SGLT-2 Inhibitors	Virta: 10.3% Comparator: 14.9%	0.9% 16.7%	3.1% 13.8%	0.01 0.69
DPP-4 Inhibitors	Virta: 9.9% Comparator: 8.1%	6.4% 11.5%	6.7% 8.6%	0.42 0.99
GLP-1 Agonists	Virta: 13.4% Comparator: 16.1%	15.1% 20.5%	10.8% 27.6%	0.42 0.18
Metformin	Virta: 71.4% Comparator: 60.9%	64.2% 60.3%	63.9% 63.8%	0.05 0.18

- **Virta built out its diabetes reversal and remission data, giving us the full picture of outcomes at two years (new data highlighted in yellow below).** Of course, "reversal" as a category is slightly problematic, as it'd be difficult to argue that an individual who is only taking metformin and has an A1c of 6.6% is not benefitting.

Intent-to-Treat Analysis for Type 2 Patients	<u>Ten Week Results</u>	<u>One Year Results</u>	Two Year Results
Diabetes Reversal	56%	60%	54%
Diabetes Remission (complete or partial)	--	--	18%
Complete Diabetes Remission	--	--	7%
Retention Rate	91%	83%	74%

Body Weight Reduction (115 kg baseline)	8 kg	14 kg	12 kg
A1c Reduction (7.7% baseline)	-1.0%	-1.3%	-0.9%
Percent Taking Diabetes Medications	81%	30%	27%

- As a reminder, we learned at [Obesity Week](#) that Virta also plans to publish data at 3.5 years and five years to compliment [already published one-year-data](#), [one year CVD biomarker data](#), and [this two-year data](#). The study is scheduled to last five years. Two-year data from the prediabetes cohort (n=116) was also expected to be submitted by early 2019, though we have not heard of any progress on this front since Obesity Week. Also this year, we're expecting a paper that explores predictors of patient success (frequency of contact, adherence, etc.), according to Virta advisor Dr. James McCarter. Seeing as, in the second year, topics of conversation between the patient and coach shift to more of a focus on life events and overall health (exercise, sleep, self-care, mindfulness, family) and less on basic nutrition, we're eager to see the results.

--by Peter Rentzepis, Brian Levine, and Kelly Close