
Virta Health publishes full one-year results (n=262) in Diabetes Therapy showing 60% type 2 diabetes "reversal," 1.3% A1c reduction, 12% bodyweight loss - February 9, 2018

Executive Highlights

- **This week, Virta Health [announced](#) the publication of positive full results (n=262 type 2s on Virta vs. 87 type 2s under usual care) from its one-year, non-randomized, controlled trial in [Diabetes Therapy](#).** Impressively, 60% of patients in the Virta arm achieved reversal of diabetes, defined as an A1c <6.5% and the elimination of all medications except metformin (which, as a sidenote, we think everyone with prediabetes should be taking even though it is not yet approved for prediabetes). On average, patients using Virta achieved an astounding 1.3% A1c reduction (baseline: 7.6%), and a quite incredible 12% weight loss (~30 lbs), and improvements in HDL and triglycerides. An impressive 94% of patients on insulin (n=63) eliminated or reduced their insulin therapy and a resounding 100% of Virta patients on sulfonylureas (n=53) eliminated the medication at one year. Those that continued with their usual treatment (the control group) reported no significant changes in any of the measured parameters.
- **This ongoing study of Virta's low-carb/high-fat ketogenic diet (<30 grams of carbs per day), and tech-enabled remote care reported a strong 83% retention rate,** indicating a favorable value:burden tradeoff for patients. This is the number one criticism of ketogenic diets (can people stick to them?) and encouraging data is now in at one year for Virta. Importantly, participants could select whether to receive the majority of their education in-person or online, and there were no significant differences in any of the outcomes between these two modalities - there were about half on each.
- **In a call with Virta's management, we learned that the program is available to patients both out of pocket (~\$370/month) and through select employers and health plans.** When going the B2B2C route, Virta places 50% of its fees at risk based on clinical outcomes (primarily A1c reductions) for each patient treated. Mr. Sytsma also shared that Virta, which is now licensed in all 50 states, is currently working with Purdue and Nielsen in addition to other as-yet unnamed employers.

Yesterday, Virta Health [announced](#) publication of highly-anticipated one-year data in [Diabetes Therapy](#) testing a low-carb/high-fat diet (to induce nutritional ketosis) and tech-enabled remote care. The non-randomized, controlled study, conducted in collaboration with Indiana University Health Arnett, compared 262 people with type 2 diabetes on the [Virta Health program](#) vs. 87 self-selected type 2 patients continuing with usual care. Notably, this study is actually 2.5 years in (out of five years planned), but data has only been peer-reviewed out to one year - to this point, the program continues to look very effective, building on the data shared at [ADA 2017](#)! As UCSF cardiologist Dr. Ethan Weiss is quoted in the [press release](#): "This is highly unusual." The key one-year results:

- **60% of Virta patients achieved diabetes reversal** defined as an A1c <6.5% and elimination of all medications except metformin.
- **94% of Virta patients on insulin (n=63) eliminated or reduced their insulin therapy,** and a resounding 100% of Virta patients on sulfonylureas (n=53) eliminated the medication by the study's end, the latter an extremely positive outcome considering the unacceptable rates of hypoglycemia seen in patients using SFUs.
- **Virta users saw a 1.3% A1c reduction** (baseline: 7.6%).

- **Virta drove 12% body weight loss** (~30 lbs), though as the graph below indicates, the variability is astounding - some saw <5% weight loss, most were in the 10%-15% range, and some lost 30%-40% of their body weight.

The control group did not see significant reductions in A1c, weight loss, or medication usage.

Based on these improvements, Virta estimates that its program saves ~\$9,600 per patient per two years (~\$4,800 per patient per year), which would cover the ~\$370/month cost. Longer-term we would expect to see greater savings, but this is hard to estimate.

Patients in the Virta arm, but not those in usual care, also saw improvements in metrics of other chronic diseases: A 24% reduction in triglycerides, an 18% improvement in HDL, a 55% reduction in insulin resistance, a 39% decrease in C-reactive protein (a marker of inflammation), and improvements in blood pressure. This will help counter the big misconception that a low-carb, high-fat diet increases the risk of heart disease; in fact, CVD metrics almost always improve on ketogenic diets.

Promisingly, the study reported 83% patient retention at one year, meaning ~45 of the initial 262 discontinued. Strong retention, along with a very favorable net promoter score of 69 (presumably this was votes from n=217 - we're checking this), is a very good sign that Virta is delivering outcomes and providing a strong perceived ratio of value:burden for this group of patients. Then again, this is a clinical trial, presumably aimed at those open to ketogenic diets, so it will be interesting to see real-world data as Virta rolls the program out to employers/payers. We'd be interested to know who stayed in the trial and ate more carbs than 30 per day but benefited in an outsized way from other elements of the Virta Health Clinic. In other words, what was adherence beyond staying in the study?

These full results align well with preliminary data (n=111) [presented at ADA 2017](#), in which 58% of enrolled patients met the criteria for diabetes reversal. The improvement appears quite rapidly: Even at [10 weeks](#) (the company's first publication [last March](#)), 56% of the same 262 patients had already achieved remission. While there will always be questions of scale, cost-effectiveness, durability, and generalizability, data from this trial of Virta's clinic continues to look very encouraging.

Virta Marketing Lead Mr. Paul Sytsma confirmed that the program is available to patients both cash-pay (at \$370/month) and through select employers and health plans (price not disclosed but presumably lower). The direct-to-consumer (DTC) pricing is down slightly from the ~\$400/month rate announced when [Virta first launched](#) in March 2017 (or the team may have simply been more specific this time around). **We learned that Virta places 50% of its fees at risk based on clinical outcomes (primarily A1c reductions) for each patient treated. We're impressed to see Virta moving to value-based health care; clearly, elimination/reduction of costly medications helps with the value proposition. Mr. Sytsma shared that Virta is currently working with Purdue and Nielsen as well as other unnamed employers.** Virta hopes to eventually generate data supporting improvements for other chronic metabolic diseases to sweeten the pitch to payers and employers.

We've noticed an uptick in virtual clinic/coaching approaches recently - in addition to Virta, Onduo [launched last week](#), Dexcom/United Healthcare [are ramping up a pilot](#) in 10,000 type 2s, [Hygieia just reported very positive outcomes](#), Medtronic Turning Point, among others (Livongo, One Drop, etc.). How will these various approaches compare? What programs will offer the most cost savings? What devices are essential vs. optional? How will "coaching" approaches stack up in terms of human touch, medication management, and interfacing with the healthcare system? How receptive are payers? Will HCPs be a driver (referrals) or a roadblock (trust concerns)? Will any of these scale to developing markets?

Read more paper details, new updates on Virta, and questions below.

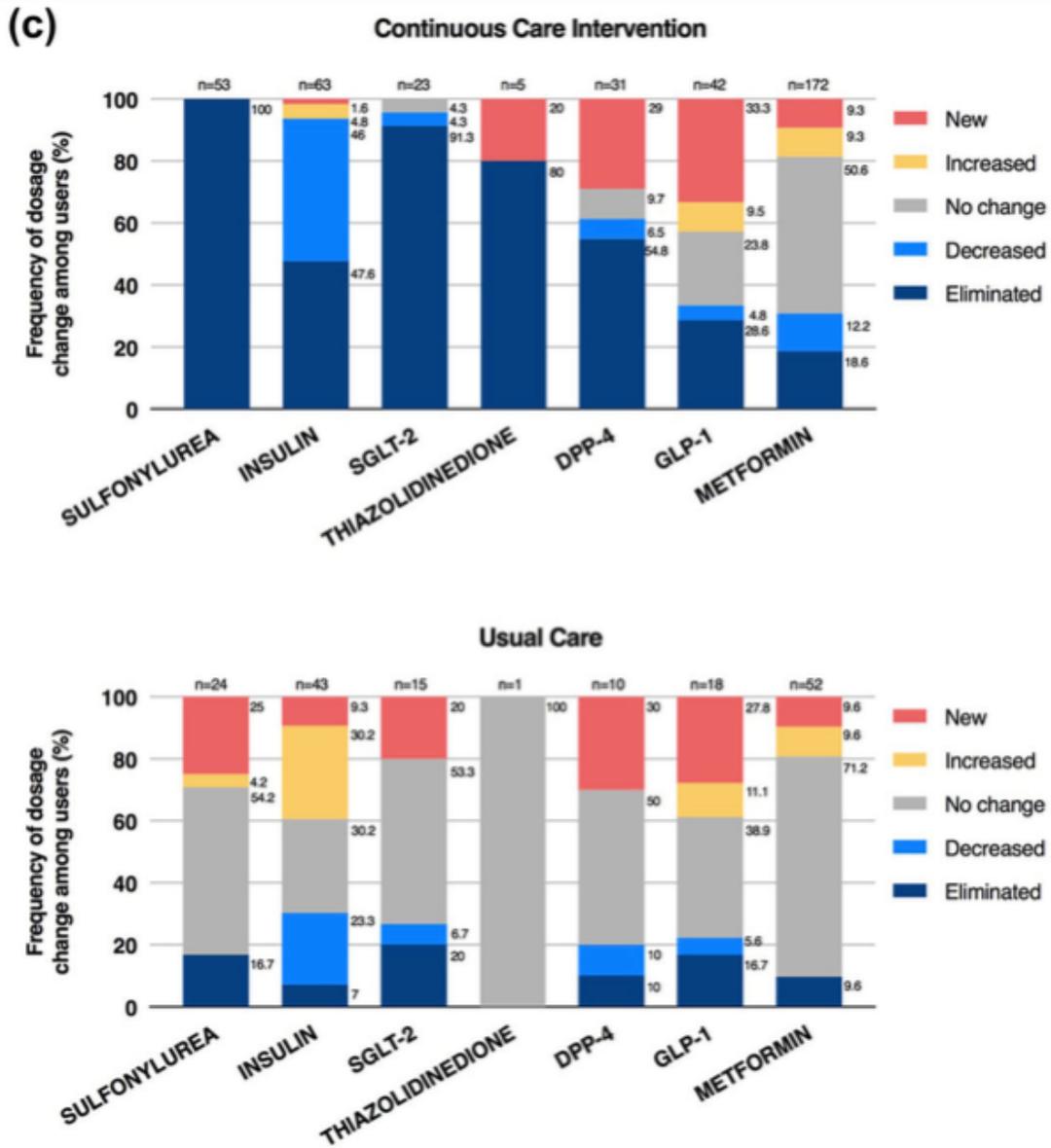
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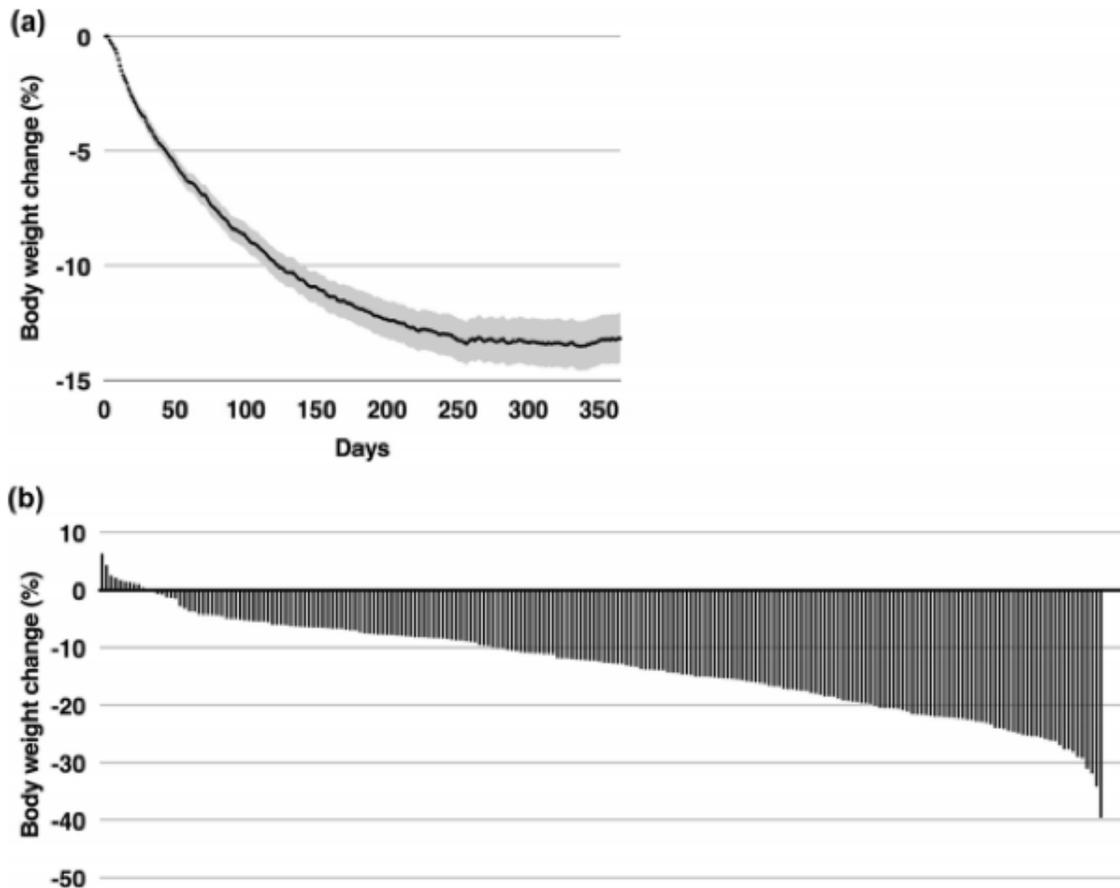
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Key Figures - Medication Changes and Weight Loss





* In the bottom-most figure, each bar represents an individual patient. Bars above the line signify weight gain and bars below the line signify weight loss. This means four patients lost 30%-40% of their body weight after a year with Virta, and the majority lost over 10% of their body weight.

Additional Study Details

- The authors point out that the majority of study participants are Caucasian, and that socioeconomic and psychosocial status and genetic data were not collected - how generalizable were these findings?** The average Virta participant age was ~54 years; 67% were female; average diabetes duration was ~8 years; and 7% were African American (percent white wasn't shared beyond "majority"). According to the article, future studies could include a multi-site RCT with "greater racial and ethnic diversity, broader age range, and greater disease severity."

Participants in the treatment arm self-selected how they would receive their education: (i) via on-site group education classes that met weekly for 12 weeks, bi-weekly for 12 weeks, and monthly for six months (n=136); or (ii) via web-based, recorded educational content viewed independently through the app (n=126). **There were no significant differences between the two modalities for any of the outcomes - a promising sign that the program could be scaled through the app.**
- An additional 116 people with prediabetes are currently enrolled in the Virta arm - bringing the total intervention group to 378 people - but were not included in the publication.** We're dying to know how this cohort fared in terms of prediabetes "reversal" and progression to type 2 diabetes, as preventing diabetes could be a big strategic move that broadens an already wide potential market for Virta. For the moment, management emphasizes the company has no plans for prediabetes and is "laser-focused" on diabetes.

- **The business model around prediabetes could be the biggest nut to crack.** While Virta in type 2 diabetes can show reductions in costly medications and price based on outcomes, the immediate cost of providing the Virta program in prediabetes might add cost to the system short-term (though obviously save in the long term). Would a payer/ employer cover the cost in prediabetes? How might the business model change?
- **According to the [Clinicaltrials.gov listing](#), the study will continue out to five years!** The primary purpose of the research is to investigate the efficacy of nutritional ketosis plus remote coaching over two years in treating/preventing metabolic syndrome. The additional three years were scheduled to determine if there is a difference in outcomes between onsite vs. web-based education delivery, explore relationships between change in LDL cholesterol and carotid intima media thickness (a marker of atherosclerotic vascular disease, even when pre-symptomatic), to evaluate the sustainability of health outcomes, and to quantify economic impact.
 - **Launching a company with controlled data of this quality already is a big win.** Virta Founder/CEO Mr. Sami Inkinen previously co-founded Trulia, which was acquired by Zillow in 2015 for \$2.5 billion, and the company is well-funded by the likes of Venrock and Redmile Group; \$37 million in funding was announced [last March](#). An advantage Virta had was extensive literature showing the benefits of the ketogenic diet, much of it driven by CMO Dr. Stephen Phinney. Still, building out the tech/remote care component is expensive, and selling into the healthcare system is never easy. We wonder how much investment Virta needs in the next year or two and what would drive more confidence - More sustained outcomes? Big employer/payer contracts? What can other young digital health companies learn from Virta? How much is Virta continuing to iterate the software/ app and educational content? Virta's board is terrific - we'd love to learn more about what they are doing, how much they are meeting, etc. For example, Dexcom's board is a BOD known to be incredibly active and where joining is a major commitment - we'd love to know what the Virta board is like (it's actually not clear to us who is on the scientific advisory board vs. the Board of Directors).
 - **The decision to explore the impacts of Virta on cardiovascular health is a very strategically smart and we are thrilled to see this.** At this point, there are [two drugs on the US market](#) that FDA has granted CV indications (Novo Nordisk's GLP-1 agonist Victoza and Lilly/BI's SGLT-2 inhibitor Jardiance and undoubtedly more will come. While looking at carotid intima media thickness is not the same as a full-on CVOT, it could lend credence that Virta's intervention may cardioprotective effects (as one would expect given its impact on A1c and weight). This will also help counter the misconception that a high-fat diet increase CVD risk - a myth based on years of poor US Dietary Guidelines. At some point, it would be fascinating to compare effective and sustainable digital lifestyle interventions and pharmaceutical interventions on the basis of A1c reductions, weight loss, cardiovascular endpoints, and health economics. We would love to see a major CVOT put together where there were multiple therapies and approaches and some with both - we receive ridicule when we suggest this but we maintain it would be an outstanding investment.
- **To our delight, the great Dr. Anne Peters (USC Keck School of Medicine) is listed as the fifth author on the study.** She was not on the [10-week publication](#), and the authorship section of the paper indicates she was involved in "writing-review and editing." This represents a strong endorsement of the program and data from one of the smartest and most respected leaders in the field. At a higher level, we're noticing that Dr. Peters, known herself for tirelessly reviewing patient data uploads at home outside of clinic hours, is demonstrating an increasing interest in the remote, digital, and virtual. In addition to authorship on this paper, Dr. Peters is also a Physician Expert for the "site-less" clinical trial company [Science 37](#) and often appears on Omada Health's papers. We, too, see remote care as a must in chronic conditions like diabetes, and are very encouraged by all work to increase enrollment and reduce cost of clinical studies. Particularly given

Dr. Peters increased visibility and her reputation as someone for whom patients at the lower ends of the socioeconomic spectrum represent a major priority, we will be very interested to hear her impressions.

Virta Health Program Specifics

- **Virta is now a licensed provider in 50 states.** We're not sure how long this took or how difficult it was, but it will surely help Virta achieve one of its goals of continued expansion through employers and health plans in 2018. Other goals for 2018 are to "release additional research" and to "have some presence at ADA."
- **The full Virta treatment includes the starter kit, access to Virta physicians and health coaches, digital tools (BGM and ketone monitoring devices), plus additional resources.** Currently, the program is device-agnostic, but biomarker input is still manual and there is no connectivity with fitness trackers or apps like Apple HealthKit or Google Fitness (yet?). In this study, participants received biomarker tracking tools including a cellular-connected body weight scale, Abbott's Precision Xtra blood glucose and ketone meter, and an Omron blood pressure cuff (if hypertension was diagnosed). Mr. Sytsma referred to Virta as an "outsourced metabolic specialist," with which patients interact on a daily, if not multiple-daily basis depending on the individual need. He emphasized that while medication changes are communicated to the patient through a health coach, all treatment alterations are physician-initiated from Virta's in-house MD team. We wonder how Virta (and other virtual clinics) integrate with a patient's established care team - are there ever conflicting recommendations and if so, are patients alerted to the differing opinions or presented with one final treatment plan? In the study, care coordination between the PCP and the Virta provider occurred "as needed" - in general, how do providers feel about companies offloading some/much of their care duties? While HCPs are overburdened and a successful intervention would make their lives easier, do they view it as an invasion? Do they get paid significantly less? Do they resent not being in the loop all of the time?
 - **We've always been curious if Virta will scale dramatically, especially given the 24-hour access to coaches and [bold mission](#) of reversing type 2 diabetes in 100 million people by 2025.** For context, 100 million people with type 2 diabetes would require hitting half of the global diagnosed population, which strikes us as a very, very bold target to hit only seven years from now. Much of this would be in China and India, requiring a pretty radical change in language and potentially implementation of the ketogenic diet. What kind of resources and program changes would support 100 million individuals?
 - **Management was vague on our call, but confirmed that Virta does not intend for users to stay with the program forever.** However, the suggested absolute minimum duration is one year. Another big question is how health outcomes track after enrollees leave Virta - after a minimum of 12 months with a provider in your pocket, will things continue as the training wheels are removed? In the best-case scenario, the 12 months could be habit-forming and continue after someone leaves the Virta clinic. Perhaps Virta could be used similarly to intermittent CGM, used when needed but not continuously over time. When we heard that people would not be "on the program" forever, we also wondered if they could take part in the Virta Health Clinic but possibly not be following a ketogenic diet.
- **While Virta's program centers around helping users identify foods that promote nutritional ketosis, Mr. Sytsma emphasized that Virta coaches work to create personalized recommendations for each individual's life circumstances and preferences.** The individualization and flexibility of the program is likely a key contributor to the impressive 83% retention rate. As an example, 10 sugar-free, low-carb holiday recipes were recently featured on [Virta's blog](#) - this was terrific to see and we will be asking our food experts what they

think of these offerings! We particularly enjoyed the [accompanying piece](#) providing 15 useful hacks for navigating the holiday season, such as focusing on what you can eat as opposed to items to avoid, keeping your hands busy, and making the best decision in the moment, even if it's not the perfect one.

Other Type 2 Diabetes Remission Excitement

- **While Virta is tackling its [bold mission of reversing type 2 diabetes](#) using nutritional ketosis (very low-carb, high-fat ketogenic diet) coupled with digital health coaching, behavioral support, biometric feedback, and online peer support, the [DiRECT trial](#) is also demonstrating promising diabetes remission results from intensive weight loss intervention (very low calorie diet). [At IDF](#), Dr. Mike Lean presented one-year data (n=298) showing that 46% of those who received the intensive weight loss intervention achieved diabetes remission. 24% of participants in the treatment arm achieved ≥ 15 kg (~33 lbs) weight loss, and of those, a striking 86% saw diabetes remission. For DiRECT, intensive weight loss consisted of withdrawal of anti-diabetic and anti-hypertensive drugs, total diet replacement with an ~800 calorie/day meal plan for three-five months, stepped food reintroduction for two-eight weeks, and structured support for long-term weight maintenance. While Virta's outcomes reporting 60% of users to achieve diabetes remission appear superior to DiRECT, the studies aren't directly comparable. An advantage of Virta's approach is it doesn't require carb counting, and those on ketogenic diets typically report less hunger. Cost comparison between the programs is not clear, though presumably Virta will get cheaper over time as more of the program is delivered digitally. The DiRECT intervention was delivered by modestly-trained usual care providers. All in all, both of these approaches offer plenty of cause for optimism - will we see a day in the future where mainstream diabetes remission clinics pop up?**

Close Concerns Questions

Q: How long is the typical patient enrolled in Virta's program? Is it possible to take part in the "clinic" and not the diet?

Q: When will the 2.5-year data be published, and how does it look in terms of outcomes and retention?

Q: Does real-world data with Purdue, Nielsen, and other Virta clients etc. align with results seen in this study?

Q: How generalizable are these findings, given the low ethnic diversity?

Q: How will Virta's outcomes differ based on diabetes duration, if at all? The average diabetes duration going into this study was ~eight years?

Q: How effective has Virta been in preventing progression from prediabetes to type 2 diabetes?

Q: How much will this five-year study cost when all is said and done? Is the new-normal in digital health for companies with missions as bold as Virta's? How big of a barrier is this kind of seed financing to digital health startups looking for investors?

Q: How many providers and coaches does Virta currently employ? How many patients are using Virta? What is the ratio of Virta providers:patients?

Q: Where does Virta stand in terms of financing? Will it announce a funding round in the next year?

Q: How much does Virta typically cost employers/payers - is it the same as the ~\$370/month for the direct-to-consumer version? How frequently does Virta meet its A1c-based outcomes milestones for reimbursement?

Q: What is the split between cash-pay patients and patients enrolled through employers and health systems? Is the cash price of ~\$370/month sustainable for the business, or is it a loss leader for Virta (i.e., funded by higher pricing in the payer/employer market)?

Q: What are the characteristics of patients who drop out of Virta? Of those who don't see diabetes reversal (~10 patients in the Virta arm actually saw weight gain, and 40% didn't meet criteria for reversal)?

Q: How frequently does the typical patient engage with Virta coaches/providers? How long do these engagements typically last? Is there a correlation between engagement volume and outcomes?

Q: How does Virta interface with the health system? Are providers happy to have companies offload patient care, or do they view it as invasive and less reimbursement for themselves?

Q: To what extent will remote care approaches complement vs. threaten the established pharma industry in type 2 diabetes? Certainly, they could complement the field if they help drive safer and more effective use of drugs - this is our expectation, and we believe as more drugs are taken by those with pre-diabetes, combination approaches may work well for many patients (not that therapy would be funded at this stage). As Virta, Hygieia, Dexcom, and others talk about reducing costly medications, this pharma will certainly be reduced; if it can be reduced and patients can stay healthy or become healthier while at the same time stay engaged with the Virta Health Clinic approach, that will be an overall positive from a population health perspective.

-- by Maeve Serino, Brian Levine, Adam Brown, and Kelly Close