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Clinical effectiveness and cost-impact after 2 years of a ketogenic diet and virtual coaching intervention for patients with diabetes

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Abstract

Aim: We previously evaluated the impacts at 5 months of a digitally delivered coaching intervention in which participants are instructed to adhere to a very low carbohydrate, ketogenic diet. With extended follow-up (24 months), we assessed the longer-term effects of this intervention on changes in clinical outcomes, health care utilization and costs associated with outpatient, inpatient and emergency department use in the Veterans Health Administration.

Materials and Methods: We employed a difference-in-differences model with a waiting list control group to estimate the 24-month change in glycated haemoglobin, body mass index, blood pressure, prescription medication use, health care utilization rates and associated costs. The analysis included 550 people with type 2 diabetes who were overweight or obese and enrolled in the Veterans Health Administration for health care. Data were obtained from electronic health records from 2018 to 2021.

Results: The virtual coaching and ketogenic diet intervention was associated with significant reductions in body mass index [−1.56 (SE 0.390)] and total monthly diabetes medication usage [−0.35 (SE 0.054)]. No statistically significant differences in glycated haemoglobin, blood pressure, outpatient visits, inpatient visits, or emergency department visits were observed. The intervention was associated with reductions in per-patient, per-month outpatient spending [−USD286.80 (SE 97.175)] and prescription drug costs (−USD105.40 (SE 30.332)].

Conclusions: A virtual coaching intervention with a ketogenic diet component offered modest effects on clinical and cost parameters in people with type 2 diabetes and with obesity or overweight. Health care systems should develop methods to assess participant progress and engagement over time if they adopt such interventions, to ensure continued patient engagement and goal achievement.

KEYWORDS
dietary intervention, health economics, type 2 diabetes, real-world evidence

1 | INTRODUCTION

Veterans have a disproportionately high prevalence of diabetes mellitus (DM). DM is diagnosed in about 25% of Veterans, compared with 20% of the general population.[1,2] The cost and consequences of diabetes care, including medication costs, make it important for the Veterans Health Administration (VHA) to consider potential non-pharmacological treatment options as an adjunct to medications. As weight management is a cornerstone of lifestyle modifications for patients with DM, the VHA recently explored the efficacy and cost impacts of a ketogenic diet and virtual coaching intervention among patients with DM.

Virtual dietary coaching programmes have been proposed as interventions for short-term weight loss and improving glucose levels in patients with DM.[3–12] While reduced calorie diets per se are the mainstay of weight-loss programmes, some have suggested that coaching programmes that include a carbohydrate-reduced diet, which produces mild ketosis, may facilitate tapering DM medications.[13] Despite these claims, there is limited evidence that ketogenic-focused, virtual coaching programmes can sustain clinical effectiveness beyond a relatively short timeframe.[4,14,15] Furthermore, there is virtually no long-term evidence as to their impact on associated changes in health care utilization and spending.

We evaluated 2-year outcomes among Veterans enrolled in a digitally delivered coaching intervention in which participants are encouraged to adhere to a very low carbohydrate, ketogenic nutrition programme (Virta Health). In a previous report we observed significant changes in clinical outcomes after 5 months of the intervention.[12] To determine if changes are sustained for 2 years after programme initiation, we employed a quasi-experimental design to evaluate clinical outcomes, health care utilization and costs associated with pharmacy, outpatient, inpatient and emergency department (ED) use. The overarching goal of this research is to determine whether a virtual coaching intervention and ketogenic diet might be an effective, longer-term treatment strategy for Veterans with type 2 DM (T2D) and overweight or obesity.

2 | MATERIALS AND METHODS

2.1 | Study design

We employed a difference-in-differences study design with a cohort of Veterans with T2D who applied to participate in the virtual coaching and ketogenic diet programme. A treatment group was created from the Veterans with T2D who were given access to the programme on a first-come-first-serve basis, and a control group was created from Veterans with T2D who applied to participate but were unable to enrol after programme capacity was reached in October of 2019.

An initial evaluation of the impact of the programme was conducted at a 5-month follow-up interval.[12] The present study extends the follow-up to 24 months. During that period, 40 patients who were initially on the wait list were offered access to the programme. Those patients are excluded from the present analyses, and additional details on their characteristics can be found in Appendix A. The study was reviewed and considered exempt research by the VA Boston Healthcare System Institutional Review Board (R&D #3317-X).

2.2 | Intervention

The programme is a virtual coaching intervention in which participants are instructed to eat a ketogenic diet.[16] The intervention adheres to the standard definition of a ketogenic diet, which typically comprises a maximum of 50 g or 5-10% of carbohydrates daily. Participants are provided with guidance and resources, including suggested meal plans, to help them adhere to this carbohydrate limit. The intervention also includes educational components and regular medication management counselling, including medication adjustments. Participants receive dietary advice regularly from certified nutritionists and dietitians who are part of the intervention team. This guidance is provided both at the onset and throughout the programme in scheduled sessions and as needed based on participant progress. Medication management counselling is provided online to participants, facilitated by clinicians associated with the intervention platform. This is separate from the guidance provided by their primary care physicians, although coordination between both is encouraged to ensure optimal patient care. Medication adjustments are informed by an algorithm that considers blood glucose levels, weight and other relevant clinical parameters. The intervention application allows participants to log these metrics, making them available to counsellors in real-time. This facilitates timely and personalized medication management.

Participants were required to meet specific inclusion criteria: enrolment in benefits through VHA, a current T2D diagnosis [glycated haemoglobin (HbA1c) ≥6.5%] confirmed by their primary care provider, overweight or obese body mass index (BMI) categories, at least one current prescription for diabetes medication other than, or in addition to, metformin, and enrolled in the VHA for health care. Exclusion criteria included active-duty status, type 1 diabetes, end stage renal disease, heart failure and active chemotherapy treatment. The target enrolment for the programme was 450 participants, and was based on the VHA's contract with Virta Health for the pilot phase of the intervention.

2.3 | Data

Data for this study came from the VHA Corporate Data Warehouse, which contains administrative records on sociodemographic characteristics as well as electronic health records documenting health status, prescription medications and health care utilization. Virta Health provided the name, address, social security number and telephone number for all programme and wait list patients to the research team. These data were used to match participants to their VHA administrative records. Data on health care costs were obtained from the VA's Managerial Cost Accounting System, which contains costs of outpatient visits, inpatient hospitalizations and dispensed outpatient prescriptions.

2.4 | Dependent variables

We examined 13 outcomes related to diabetes care, health care utilization and health care costs. Health outcomes included HbA1c, weight, BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), number of insulin prescriptions and number of all diabetes prescriptions. Utilization outcomes were the number of outpatient visits, number of inpatient hospitalizations and number of ED visits. Cost outcomes included outpatient costs, inpatient costs, prescription costs and total costs. In these data, total costs are the sum of outpatient and inpatient costs. Prescription costs are a subset of outpatient costs. All outcomes were captured up to 24 months after the application date to the programme. Because control participants do not have a treatment date, we used the application month as the relevant post-period comparison for both the treatment and the control groups.

2.5 | Independent variables

The primary independent variable of interest was the effect of participation in the virtual coaching and ketogenic diet programme and is operationalized as the interaction term between a dichotomous variable for treatment status and a dichotomous variable for the post-application period. Additional covariates included baseline sociodemographic characteristics (i.e. sex, age, race/ethnicity and urban/rural residence), Charlson comorbidity index[17] and VHA enrolment priority status, which is a proxy for service-connected disability and socio-economic status. All models included dichotomous variables for individual months (fixed effects), a standard approach in difference-in-differences analyses.

2.6 | Statistical analyses

We compared baseline characteristics of treatment and control groups using t-tests for binary or continuous variables and chi-squared tests for categorical variables. Differences in outcomes were estimated using difference-in-differences equations using the following specification:

$$y_{it} = \alpha + \beta_1 T_i + \beta_2 Post_{it} + \boldsymbol{\beta_3}(T \times Post)_{it} + \theta X_i' + \gamma_t + \varepsilon_{it} \qquad (1)$$

where y_{it} is one of 13 outcomes for individual, *i*, in month, *t*; β_3 is the change in outcome associated with receiving the treatment, T_i, in the post-period, $Post_{it}$. X_i are covariates and γ_t are month fixed effects. Huber-White robust standard errors were calculated at the patient level.[18]

We conducted sensitivity analyses to examine the potential for differential missingness of data between treatment and control outcomes for three outcomes: HbA1c, BMI and SBP/DBP (combined). The purpose of this analysis was to detect any potential documentation bias in the administrative health records that was specifically related to programme participation. We created a dichotomous indicator variable for outcome-specific missingness and regressed this indicator on the variables included in Eqn (1) to indicate the percentage point probability that programme participation was associated with missingness for any of the three outcomes. For outcomes with evidence of differential missingness, we tested specifications weighting the observations using the inverse of the probability of having a non-missing outcome in the post-application period.[19]

Additional sensitivity analyses were conducted to investigate whether simultaneous changes in weight loss medications, in particular GLP-1 receptor agonists, could explain any observed changes in BMI. In particular, we examined the impact of treatment on changes in days' supply of GLP-1 receptor agonists.

3 | RESULTS

3.1 | Baseline characteristics

The baseline characteristics of the treatment and control groups are presented in Table 1. Treatment group participants were less likely to be male and more likely to be white, non-Hispanic relative to patients in the control group. The treatment group had slightly lower HbA1c and monthly insulin prescriptions and were more likely to have participated in the VA intramural weight loss programme (MOVE!) at baseline. All other measures of baseline socio-demographic characteristics, health care utilization, health status and prescription patterns were balanced between the treatment and control groups.

3.2 | Impacts of the treatment programme on diabetes outcomes and health care utilization

The difference-in-differences estimates comparing health outcomes before and after application dates to the treatment programme are reported in Table 2. Treatment was associated with a significant reduction in absolute weight {−8.89 kg [standard error (SE): 2.83]} and BMI [−1.56 (SE: 0.39)] during the 24-month study period. Significant reductions were also detected in monthly insulin prescriptions [−0.21 (SE: 0.04)] and all monthly diabetes-related medications [−0.35 (SE: 0.05)]. No significant changes in HbA1c, DBP or SBP were detected. Similarly, no significant changes were detected in outpatient, inpatient or emergency department utilization rates.

3.3 | Impacts of the treatment programme on costs

The 24-month changes in diabetes costs for people with T2D in the treatment and control groups before and after application

TABLE 1 Baseline characteristics of Veterans enrolled in the ketogenic diet virtual coaching programme and in the wait list control group, 2018-2022.

Baseline variables	Treatment (n = 275)	Control (n = 275)	*p*-Value
Socio-demographic characteristics			
Males, %	85.8	92.7	.009***
Age, avg.	58.1 (7.88)	58.0 (7.66)	.512
Urban resident, %	66.2	71.3	.198
Race/ethnicity, %			
Black, non-Hispanic	13.8	20.4	.032*
White, non-Hispanic	68.4	56.4	
Hispanic	7.3	10.9	
Other, non-Hispanic	7.3	10.2	
Missing	3.3	2.2	
Priority status, %			
1-3	73.5	72.0	.900
4-6	16.4	17.8	
7-8	10.2	10.2	
VA utilization			
Outpatient visits, monthly avg.	2.2 (2.3)	2.1 (2.2)	.050
Emergency Department visits, monthly avg.	0.07 (0.31)	0.08 (0.31)	.771
VA *MOVE!* Participation, %[a]	13.1	7.3	.024*
Inpatient admissions, monthly avg.	0.02 (0.003)	0.01 (0.003)	.810
Health status			
Comorbidity index, avg.	1.0 (1.34)	1.2 (1.29)	.207
BMI, kg/m^2; avg.[b]	35.2 (6.08)	34.7 (6.44)	.778
HbA1c, %; avg.	8.8 (1.71)	9.2 (1.94)	.006**
SBP	132.9 (15.31)	132.0 (16.09)	.451
DBP	79.0 (8.7)	77.9 (9.69)	.102
Prescriptions, Rx			
Metformin, %	73.1	66.9	.114
Insulin, monthly avg. prescriptions	0.5 (0.87)	0.6 (0.90)	.028*
Diabetes medications, monthly avg. prescriptions	1.1 (1.23)	1.2 (1.32)	.568
Total no. of non-metformin prescriptions, monthly avg.	6.2 (4.15)	6.5 (4.35)	.367

Note: p-values were computed using two-sample t-tests for differences in continuous variables, and chi-squared tests for categorical variables. ***$p < .001$, **$p < .01$, *$p < .05$. For calculation of average BMI, there were 260 non-missing subjects. For calculation of average SBP and DBP, there were 272 non-missing treated and 269 non-missing control subjects. Standard deviations for continuous variables are reported in parentheses.
Abbreviations: avg., average; BMI, body mass index; DBP, diastolic blood pressure; HbA1c, glycated haemoglobin; SBP, systolic blood pressure; VA, Veterans Administration.
[a]VA *MOVE!* participation indicates whether a Veteran has previously participated in a formal VA sponsored weight loss programme.
[b]Number of observations for BMI are smaller because of missingness in the variable. Sample size for this metric is presented in parentheses next to group averages.

dates are presented in Table 3. The treatment programme was associated with a significant reduction in per-patient, per-month outpatient costs [−USD286.80 (SE: 97.175)] and a −USD105.40 (SE: 30.332) per-patient, per-month reduction in prescription drug costs. There were no statistically significant differences in overall costs or inpatient costs between treatment and control groups at 24 months.

3.4 | Sensitivity analyses

We conducted tests for differential missingness in outcomes between treatment and control groups for several clinical outcomes, HbA1c, BMI and SBP/DBP (Appendix B). Two outcomes, BMI and BP, showed evidence of differential attrition. Treatment group patients were 6% and 4% more likely to have a missing BMI and BP measurement,

TABLE 2 24-month changes in diabetes outcomes for Veterans in the ketogenic diet virtual coaching treatment and control groups, before and after application dates.

	Outcomes									
Variables	HbA1c, %	Body mass index	Weight, kg	Systolic blood pressure, mmHg	Diastolic blood pressure, mmHg	Outpatient visits, no.	Inpatient Admissions, no.	ED visits, no.	Insulin prescriptions, no.	Any diabetes prescriptions, no.
Treatment × Post (DiD Estimator)	−0.20 (0.149)	−1.56*** (0.390)	−8.89** (2.827)	−1.01 (1.050)	−0.88 (0.561)	−0.14 (0.118)	−0.0049 (0.005)	−0.016 (0.014)	−0.21*** (0.038)	−0.35*** (0.054)
Treatment group indicator	−0.28 (0.154)	0.88 (0.630)	6.28 (4.573)	−0.23 (1.257)	0.77 (0.675)	0.25 (0.211)	−0.0049 (0.005)	−0.00059 (0.015)	−0.047 (0.051)	0.011 (0.062)
Post-period indicator	−0.59*** (0.155)	−0.29 (0.524)	−3.13 (3.669)	0.50 (1.311)	0.24 (0.684)	0.46* (0.189)	−0.0030 (0.006)	−0.0017 (0.015)	−0.0087 (0.038)	0.021 (0.062)
Observations	3051	4096	4096	4913	4913	17 050	17 050	17 050	17 050	17 050
R^2	0.072	0.064	0.111	0.024	0.105	0.071	0.005	0.008	0.036	0.028

Note: The treatment × post-period difference-in-difference (DiD) indicator estimates the impact of treatment. All regression models included time fixed effects and individual-level controls (age, sex, comorbidity index, urban, past MOVE! participation, race/ethnicity and priority status) not shown here. Number of observations are reported at the patient-month level. ***$p < .001$, **$p < .01$, *$p < .05$.

Abbreviations: ED, Emergency Department; HbA1c, glycated haemoglobin.

respectively, relative to the patients in the control group. However, results from sensitivity analyses using inverse-probability weighted models were not meaningfully different from the results presented in the primary specifications (Appendix C). We also examined whether or not the intervention was associated with changes in the days' supply of GLP-1 receptor agonists (Appendix D). Indeed, we find that the intervention slightly reduced the days' supply of GLP-1 receptor agonists for patients in the treatment group relative to patients in the control group. Relative to changes in the days' supply of insulin medications or all diabetes medications in general, we interpret this as a small change. Nonetheless, we do not believe use of GLP-1 receptor agonists are the primary mechanism driving our findings.

4 | DISCUSSION

In this analysis of the 2-year outcomes of a virtual coaching and ketogenic diet programme, we found that treatment was associated with a 4% reduction in BMI in the treatment group at 24 months. This compares with a 3% change observed at 5 months of follow-up of the same cohort. A full comparison of percentage changes at months 5 and 24 can be found in Appendix E. While the observed changes in BMI were statistically significant, they did not meet standard criteria for clinically meaningful changes, typically defined as weight loss exceeding 5% of the initial body weight.[20–22] Although significant reductions in HbA1c and BP were observed at the 5-month follow-up period,[12] there were no significant differences in HbA1c or BP outcomes at 24 months. This inability to sustain improvements in health outcomes is consistent with many dietary interventions for DM, which typically find that health benefits diminish or return to baseline as patient adherence to dietary recommendations wanes over time.[23]

We used electronic health data to examine the impacts of the virtual coaching and ketogenic diet intervention on diabetes medication usage, health care utilization and health care costs. We found that the intervention led to significant, sustained differences in monthly diabetes-related medications. Treatment participants received 0.21 fewer insulin prescriptions per month and 0.35 fewer prescription fills for all diabetes medications per month, representing a 32.5% reduction in medication usage relative to baseline. The magnitude of this change is similar to those reported in other virtual diabetes programmes.[4–7,10] The sustained nature of these changes is probably reflective of the fact that the virtual coaching intervention includes medication management as a prominent component. It may be viewed as a somewhat positive finding that fewer diabetes medications were needed to maintain similar levels of HbA1c. However, clinical programmes for DM management should impact HbA1c levels and possibly other clinical biomarkers to be considered successful.

No statistically significant changes in health care utilization were noted for outpatient, inpatient or ED care at 24 months. We did observe a USD286 difference in per-patient, per-month outpatient costs and a USD105 reduction in per-patient, per-month diabetes prescription drug costs probably because of fewer pharmacy and primary care visits. It is unclear if these changes reflect actual clinical

TABLE 3 24-month changes in diabetes costs for Veterans in the ketogenic diet virtual coaching treatment and control groups, before and after application dates.

	Outcomes			
Variables	Total cost, USD	Outpatient cost, USD	Rx cost, USD	Inpatient cost, USD
Treatment × Post (DiD Estimator)	−484.4 (283.553)	−286.8** (97.175)	−105.4*** (30.332)	−197.6 (266.501)
Treatment group indicator	156.0 (159.329)	117.3 (114.143)	34.7 (56.012)	38.7 (99.741)
Post-period indicator	339.3 (267.863)	337.7** (112.922)	66.1 (47.087)	1.63 (231.455)
Observations	17 050	17 050	17 050	17 050
R^2	0.002	0.037	0.011	−0.000

Note: The treatment × post-period difference-in-difference (DiD) indicator estimates the impact of treatment. All regression models included time fixed effects and individual-level controls (age, sex, comorbidity index, urban, past MOVE! participation, race/ethnicity and priority status) not shown here. Number of observations are reported at the patient-month level. ****p* < .001, ***p* < .01, **p* < .05.

improvements among the participants or merely a shifting of care management and costs from VHA to the virtual coaching component of the intervention. The extent to which the costs of the intervention offset these spending reductions depends on the monthly price of the intervention and whether reduced medication usage and outpatient visits can be sustained over time.

Several limitations of the study are worth mentioning. This was not a randomized controlled trial. Although a difference-in-differences approach with a wait-list control offers the advantage of quasi-experimental evidence, the results of our study should be interpreted cautiously. While our results are consistent with many long-term evaluations of virtual dietary interventions, future randomized trials could provide a more definitive perspective. In particular, all patients expressed interest in participating in the programme, those in the control group were offered a chance to receive treatment, and some patients eventually elected to participate in the intervention. Although patients who switched to the treatment group were excluded from the analyses and appeared similar to patients in the control group, they were slightly younger, had higher BMI and lower HbA1c relative to patients in the control group who did not switch into treatment (Appendix A). We are unable to determine intervention intensity and/or attrition for those who enrolled in the treatment group, and therefore all results should be interpreted as intent-to-treat estimates. Although we are unable to report how many patients maintained contact with the intervention for 24 months, from a cost-estimation standpoint this approach aligns with the fact that VHA paid the vendor regardless of patients' usage of programme resources. In addition, as dietary preferences would probably vary based on patients' personal and cultural preferences, we are unable to determine which of the programme components is most important or valued by patients.

5 | CONCLUSIONS

Although health improvements were observed for participants receiving a virtual coaching and ketogenic diet intervention after 5 months, these effects were diminished after 2 years. With respect to the findings that were sustained (lower BMI and reduced diabetes medication use), it remains unclear whether these effects can be attributed to personalized coaching, a ketogenic diet, some combination of these two, or other unknown factors. These health outcome and cost results suggest that health plans and health care delivery systems considering the adoption of virtual dietary coaching programmes should review participants' progress, participation and outcome measures on a periodic basis, with continued participation being conditional on patient engagement and goal achievement.

AUTHOR CONTRIBUTIONS

KLS, SDP and ABF conceived the idea for the study. KLS, JL, SDP and ABF contributed to the study design and analysis plan. KLS and JL conducted the statistical analysis. All authors contributed to and approved the final manuscript. KLS takes responsibility for the contents of the article.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

PEER REVIEW

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DATA AVAILABILITY STATEMENT

Data from the Department of Veterans Affairs are not publicly available.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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