Check for updates

Diabetes, Obesity and Metabolism

WILEY

ORIGINAL ARTICLE OPEN ACCESS

Effectiveness of Telehealth Low-Carbohydrate Intervention in Preventing Chronic Kidney Disease: A Real-World, Retrospective, Matched Cohort Study

Shaminie J. Athinarayanan[1] | Petter Bjornstad[2] | Priya V. Shanmugam[1] | Thomas Weimbs[3] | Adam J. Wolfberg[1] | Jeff S. Volek[4] | Jonathan Himmelfarb[5] | Richard J. Johnson[6]

[1]Research Department, Virta Health, Denver, Colorado, USA | [2]Kidney Research Institute and Division of Metabolism, Endocrinology and Nutrition, Department of Medicine, University of Washington, Seattle, Washington, USA | [3]Department of Molecular, Cellular, and Developmental Biology, University of California, Santa Barbara, California, USA | [4]Department of Human Sciences, College of Education and Human Ecology, The Ohio State University, Columbus, Ohio, USA | [5]Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, New York, USA | [6]Division of Renal Diseases and Hypertension, Department of Medicine, University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA

Correspondence: Shaminie J. Athinarayanan (shaminie@virtahealth.com)

Received: 11 May 2026 | **Revised:** 24 June 2026 | **Accepted:** 30 June 2026

Handling Editor: Richard Donnelly

Keywords: carbohydrate reduction | chronic kidney disease | ketosis | obesity | telemedicine | type 2 diabetes

ABSTRACT

Background: Lifestyle interventions targeting metabolic health may influence chronic kidney disease (CKD) risk, particularly among adults with type 2 diabetes and obesity. We evaluated real-world associations between a telehealth-delivered, individualized nutrition therapy program (VINT) and CKD incidence and progression compared with usual care.

Methods: We conducted a retrospective, propensity score–matched cohort study using the Komodo Healthcare Map, a longitudinal U.S. administrative claims database. Adults enrolled in a telehealth-delivered nutrition therapy emphasising carbohydrate reduction, VINT ($n = 11\,077$) were matched 1:1 to usual-care controls on demographic, clinical, and medication covariates, over 5 years of follow-up. Primary outcomes were new-onset CKD, CKD stage ≥ 3, and CKD stage ≥ 4. Secondary outcomes included renal safety events. Cox proportional hazards and Poisson regression models were used to estimate hazard ratios (HRs) and incidence rate ratios (IRRs).

Results: VINT participation was associated with a lower incidence of new-onset CKD (10.1 vs. 15.6 per 1000 person-years; HR 0.64, 95% CI 0.53–0.77; $p < 0.001$), CKD stage ≥ 3 (HR 0.57, 95% CI 0.45–0.73; $p < 0.001$), and CKD stage ≥ 4 (HR 0.38, 95% CI 0.18–0.79; $p = 0.009$). No increased risk of kidney stones, metabolic acidosis, diabetic ketoacidosis, or gout was observed in VINT compared with the UC group.

Conclusions: In this large, real-world matched cohort, participation in a telehealth-delivered nutrition therapy emphasising carbohydrate reduction was associated with lower CKD incidence and progression without increased renal adverse events. These findings suggest that individualized nutrition therapy may be a safe and scalable approach to CKD prevention and management in adults with metabolic disease, warranting further prospective investigation.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2026 Virta Health and The Author(s). *Diabetes, Obesity and Metabolism* published by John Wiley & Sons Ltd.

1 | Introduction

The prevalence of chronic kidney disease (CKD) has risen sharply, particularly among individuals with type 2 diabetes (T2D) [1, 2]. CKD carries profound consequences, including reduced quality of life, elevated cardiovascular risk, and increased morbidity and mortality [2–4]. Although recent therapeutic advances including sodium-glucose cotransporter 2 inhibitors (SGLT2i) [5, 6], nonsteroidal mineralocorticoid receptor antagonists [7], and GLP1 receptor agonists (GLP1-RA) [8, 9] offer benefit, medical therapy remains the foundation of standard care, and these agents are costly, may cause adverse effects, and leave substantial residual risk of CKD progression [1, 2, 10]. Accordingly, lifestyle interventions, particularly dietary strategies, remain critical as complementary approaches either alone or in combination with pharmacotherapy.

High-protein diets accelerate CKD progression in animals [11, 12], prompting investigators to study protein restriction as an intervention [13]. However, benefits were modest or limited to subgroups, and extreme restriction was found to have deleterious effects on overall morbidity and mortality [13]. Current guidelines therefore recommend avoiding high protein intake but emphasise only modest restriction (0.6–1.0 g/kg/day) for individuals with moderate CKD [14]. In contrast, the 2020 KDOQI guidelines recommend more stringent protein restriction (as low as 0.55–0.60 g/kg/day in metabolically stable patients), highlighting ongoing uncertainty and debate regarding the optimal level of dietary protein intake in CKD [15]. Similarly, caloric restriction may confer some benefit in CKD linked to metabolic syndrome or diabetes [16]. Despite investigation, dietary therapy has not been established as a disease-modifying standard of care for CKD. Evidence, however, implicates high carbohydrate intake in CKD progression. Carbohydrate excess contributes to metabolic syndrome and diabetes, and experimental studies demonstrate that diets high in sugar or fructose can accelerate CKD [17, 18].

We studied a remotely administered, digitally supported nutrition and lifestyle program developed primarily for individuals with type 2 diabetes and obesity/overweight that focuses on carbohydrate reduction leading to varying degrees of nutritional ketosis [19, 20]. This intervention is delivered in the context of usual medical care; however, adherence to the program is associated with a high rate of type 2 diabetes remission, often accompanied by complete medication deprescription [19, 20]. Post hoc analyses of clinical trial data from this intervention also demonstrated a reversal of eGFR slope decline, with a significant increase in eGFR from baseline to 2 years, corresponding to a slope of +0.91 mL/min/1.73 m^2/year [21]. The multimodal intervention, integrating personalised carbohydrate reduction with continuous remote care, individualized treatment, and real-time clinical support, likely achieved these effects by addressing multiple interrelated mechanisms rather than isolated pathways. Beyond eGFR benefits, both clinical trials and real-world studies show improvements in glycemia [19, 20, 22], weight [19, 20, 22], and blood pressure [23]. Kidney-specific benefits include durable reductions in urinary albumin-to-creatinine ratio (UACR) among patients with stage 2–3 albuminuria, sustained for up to 2 years [24].

In this claims-based analysis, we evaluated associations between participation in a multimodal, carbohydrate-reduced lifestyle intervention delivered alongside usual care and the development and progression of CKD, compared with matched individuals receiving usual care alone. Given the limitations of claims data without linked laboratory data, this analysis was designed to be exploratory and hypothesis-generating, intended to estimate associations and effect sizes rather than establish causality. Outcomes included incidence of new CKD diagnoses, including albuminuria, and the occurrence of advanced CKD stages during follow-up. Safety outcomes included kidney stone, gout, and acidosis including diabetic ketoacidosis (DKA) diagnoses. Finally, we explored whether metabolic response, defined by ketone levels, weight loss, and A1c change, was associated with CKD risk within the VINT cohort and stability or regression of existing CKD.

2 | Materials and Methods

2.1 | Data Source

This study used the Komodo Healthcare Map, a longitudinal U.S. claims database covering ~330 million individuals across Medicare, Medicaid, and commercial payers [25]. Program participant data were linked to claims to enable longitudinal follow-up. A control cohort was drawn from the same database and aligned to the treated cohort on key characteristics. Analyses were conducted within the Komodo Sentinel environment (data version: April 19, 2026). Additional details are provided in the Supporting Information.

2.2 | Study Population and Design

The study included adults enrolled in the Virta Individualized Nutrition Therapy (VINT) program with type 2 diabetes, overweight, or obesity. VINT consisted of continuous remote care integrating individualized nutrition therapy, medication management, and health coaching. Each participant in VINT works with a health coach who monitors dietary adherence and supports behavioural change, while an assigned clinician oversees medical management, including addressing clinical concerns and adjusting medications as needed. Further details are provided in the Supporting Information.

Eligible participants in both VINT and usual care (UC) cohorts were required to have ≥ 1 year of continuous pre-index claims coverage and ≥ 6 months of claims follow-up. Sequential exclusions removed individuals with conditions incompatible with the VINT or likely to confound CKD outcomes (e.g., type 1 diabetes, severe comorbid illness, or non-CKD kidney diseases). Those with any baseline CKD and albuminuria were excluded as well.

The control cohort was constructed by assigning index dates aligned to the treated cohort's enrollment distribution and applying identical inclusion and exclusion criteria. UC control was matched 1:1 to VINT participants using propensity scores based on demographic, clinical, and healthcare utilisation variables.

The primary analysis cohort included all eligible VINT participants with available closed claims data and their matched UC controls, regardless of program duration, to enhance generalizability. A secondary cohort was constructed by restricting the

14631326, 2026, 10, Downloaded from https://dom-pubs.onlinelibrary.wiley.com/doi/10.1111/dom.71086, Wiley Online Library on [03/09/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

analysis to participants with ≥6 months of continuous VINT participation and rematching UC controls using the same matching approach as the primary analysis. The secondary cohort was used for exploratory analyses to evaluate outcomes among participants with sufficient exposure to VINT. Outcomes were assessed from the index date in both cohorts. Full eligibility criteria and matching specifications are detailed in the Supporting Information.

2.3 | Intervention and Medication Management

VINT delivered continuous remote care via telemedicine, combining personalised carbohydrate reduction, medication management, and ongoing health coaching, with regular monitoring of biomarkers to guide individualized adjustments.

Medications were actively managed by clinicians, with early reductions in hypoglycemia-prone drugs and ongoing adjustments based on patient response and real-time data. Comprehensive details on VINT and medication management are provided in the Supporting Information.

2.4 | Baseline Characteristics

Baseline variables included demographics, comorbidities, medication use, and healthcare utilisation, defined using administrative claims (ICD-10-CM and drug codes). These variables were selected a priori and incorporated into the matching process. Detailed descriptions and definitions are provided in Tables S1–S3 and Supporting Information.

2.5 | Study Outcomes

The primary outcomes were time to first occurrence of: (1) incident chronic kidney disease (CKD), defined as a new diagnosis of CKD stage 1–5, end-stage kidney disease (ESKD), renal dialysis, or albuminuria among participants without CKD or albuminuria at baseline; and (2) incident CKD stage 3 or higher, defined as a first diagnosis of CKD stage 3a, stage 3b, stage 4, stage 5, ESKD, or renal dialysis during follow-up. An exploratory outcome was incident CKD stage 4 or higher, defined as a first diagnosis of CKD stage 4, stage 5, ESKD, or renal dialysis during follow-up. Participants were censored at loss of continuous claims coverage or study end.

Stage-specific outcomes were defined to capture progression to more advanced CKD stages; individuals developing lower stages during follow-up were censored at the time lower stage occurred and not counted as events.

The secondary outcomes were the occurrence of kidney stones, acidosis including diabetic ketoacidosis, and gout during follow-up. Exploratory outcomes included: (1) assessment of predictors associated with new-onset CKD diagnosis in the VINT group from the secondary matched cohort, and (2) evaluating CKD stage trajectories; we constructed a separate matched cohort of participants with baseline CKD and/or albuminuria. Among those with at least one follow-up CKD diagnosis prior to censoring, we assessed CKD stage transitions, including regression, stability, and progression, in both the VINT and UC groups. Detailed ICD-10-CM diagnosis codes used to define CKD outcomes are provided in Table S1. Additional ICD-10-PCS (International Classification of Diseases, Tenth Revision, Procedure Coding System), CPT (Current Procedural Terminology), and HCPCS (Healthcare Common Procedure Coding System) procedure codes used to identify different exclusion criteria and advanced kidney disease ascertainment are provided in Table S2.

2.6 | Statistical Analysis

A full description of the statistical methods is provided in the Supporting Information and Methods. The study design, conduct, and reporting adhered to STROBE guidelines [26].

Categorical variables were summarised using counts and percentages, and continuous variables using means and standard deviations. UC controls were matched 1:1 to VINT participants using nearest-neighbour propensity score matching without replacement based on demographic, clinical, medication, and healthcare utilisation variables, with other comorbidities (e.g., type 2 diabetes, obesity, index year, relevant medications, etc.) enforced as exact matches. Additional details regarding the matching procedure and balance assessment are provided in the Supporting Information. Outcomes were assessed from the index date.

For primary outcomes, Cox proportional hazards regression was used to estimate hazard ratios (HRs) with 95% confidence intervals (CIs). Models were adjusted for age, sex, race/ethnicity, and baseline comorbidities. Different modelling strategies were applied to assess robustness: (1) a base model without medication adjustment; (2) models additionally adjusting for follow-up medication use (modelled as ever/never and proportion of days covered); and (3) models incorporating medication use as a time-varying covariate. Additional sensitivity analyses using marginal structural models with inverse probability weighting were conducted to account for time-varying confounding and potential mediation by medication use. Outcomes were assessed in both the primary and secondary cohorts, as defined in the study outcomes. As a further robustness check, inverse probability of treatment weighting (IPTW) was applied, retaining all eligible VINT participants and UC. Given the potential for mortality to act as a competing event for CKD outcomes, we also evaluated all incident CKD outcomes using Fine–Grey subdistribution hazard models. In addition, mortality was assessed as a separate outcome within the study cohort. Incidence rates were also calculated as the number of events per 1000 person-years of follow-up. Person-years were based on total observed follow-up time from the index date and were used for descriptive purposes only. Additional details are provided in the Supporting Information.

Analyses of secondary safety outcomes and exploratory endpoints, including adverse events, predictors of CKD, and CKD stage transitions, are summarised in the Supporting Information. Statistical significance was defined as a two-sided α of 0.05. All analyses were conducted using R.

14631326, 2026, 10, Downloaded from https://dom-pubs.onlinelibrary.wiley.com/doi/10.1111/dom.71086, Wiley Online Library on [03/09/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

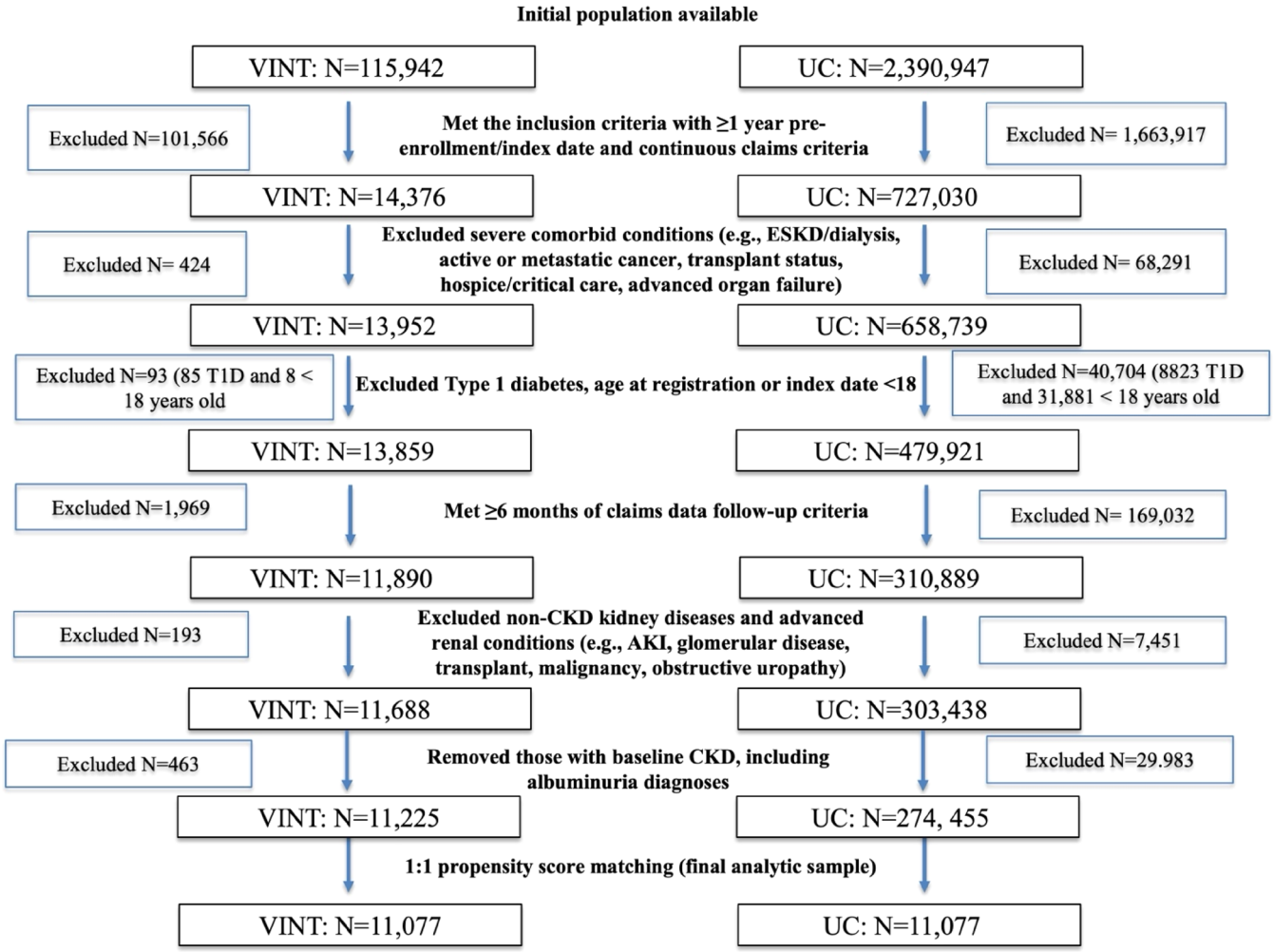

FIGURE 1 | Patient attrition flowchart from the initial population in the Komodo Healthcare Sentinel working environment to the final analytic sample after 1:1 matching.

3 | Results

3.1 | Study Participant Flow

A total of 115 942 VINT participants and 2.39 million controls were identified in the Komodo Sentinel database (Figure 1; Table S4). After applying inclusion criteria, 11 890 VINT and 310 889 UC participants remained. Following exclusions and after removing those with baseline CKD or albuminuria diagnosis, 11 255 VINT participants (after removing duplicates) and 274 455 UC controls were eligible for propensity score matching.

Using a stringent (Tier 3) 1:1 propensity score–matching approach, the final analytic sample included 11 077 VINT participants and 11 077 matched UC.

3.2 | Baseline Characteristics

Baseline characteristics were well balanced between groups in the primary matched cohort, with all standardised mean differences (SMDs) <0.1 (Tables 1 and 2). The mean age was 51 years, with a female-to-male ratio of approximately 3:2. Mean follow-up was 1.8 years for VINT and 1.9 years for UC. Control index dates were aligned with VINT enrollment years to account for temporal trends (Figure S1). The matched VINT cohort was broadly representative of excluded VINT participants (Table S5), with baseline characteristics largely balanced (SMDs <0.1), except for minor differences in race/ethnicity and enrollment index year, which were addressed in matching. Similarly, baseline characteristics in the secondary matched cohort were also well balanced between groups, with all SMDs <0.1 (Table S6).

3.3 | Primary Outcomes

During follow-up, incidence rates of new-onset CKD, CKD stage ≥ 3, and CKD stage ≥ 4 were lower among VINT participants compared with UC. Incidence rates were 10.1 versus 15.6 per 1000 person-years for new-onset CKD, 5.7 versus 9.7 per 1000 person-years for CKD stage ≥ 3, and 0.5 versus 1.3 per 1000 person-years for CKD stage ≥ 4 (Table 3; Figure 2A).

In Cox proportional hazards models adjusted for age, sex, and race/ethnicity, VINT participation was associated with significantly lower risk of all CKD outcomes compared with UC (Figure 2B–D; Table 3). These associations remained consistent after additional adjustment for medication use, including GLP-1

14631326, 2026, 10, Downloaded from https://dom-pubs.onlinelibrary.wiley.com/doi/10.1111/dom.71086, Wiley Online Library on [03/09/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 1 | Baseline demographics, disease trajectory as assessed by cost, and area level variables of propensity score 1:1 matched cohort of VINT and UC.

	Unmatched dataset			Matched dataset		
	VINT ($n = 11\,235$)	UC ($n = 303\,438$)		VINT ($n = 11\,077$)	UC ($n = 11\,077$)	
Variables	Mean (SD) or *n* (%)	Mean (SD) or *n* (%)	SMD	Mean (SD) or *n* (%)	Mean (SD) or *n* (%)	SMD
Demographics and characteristics						
Age (years)	50.7 (10.2)	53.3 (16.0)	0.20	50.7 (10.2)	50.7 (10.4)	0.01
Follow duration (years)	1.9 (1.1)	1.6 (1.1)	0.27	1.9 (1.1)	1.8 (1.1)	0.08
Gender			0.04			< 0.001
Female	6722 (59.9)	160 582 (58.5)		6653 (60.1)	6653 (60.1)	
Male	4433 (39.5)	111 443 (40.6)		4371 (39.5)	4371 (39.5)	
Unknown	70 (0.6)	2430 (0.9)		53 (0.5)	53 (0.5)	
Race and Ethnicity			0.14			0.06
White	5657 (61.5)	134 755 (57.5)		5591 (61.6)	5229 (59.7)	
African American	1214 (13.2)	34 461 (14.7)		1192 (13.1)	1144 (13.1)	
Hispanic or Latino	938 (10.2)	30 947 (13.2)		923 (10.2)	888 (10.1)	
Asian or Pacific Islander	351 (3.8)	8436 (3.6)		349 (3.8)	372 (4.2)	
Other	235 (2.6)	8386 (3.6)		228 (2.5)	227 (2.6)	
Unknown	803 (8.7)	17 193 (7.3)		790 (8.7)	899 (10.3)	
Thiazolidine	195 (1.7)	2942 (1.1)	0.06	184 (1.7)	170 (1.5)	0.01
Other T2D medications	3266 (29.1)	46 767 (17.0)	0.29	3167 (28.6)	3245 (29.3)	0.02
Baseline area level variables						
Region			0.48			0.04
Midwest	4191 (37.3)	73 652 (26.8)		4156 (37.5)	4082 (36.9)	
Northeast	999 (8.9)	70 130 (25.6)		982 (8.9)	1110 (10.0)	
South	4680 (41.7)	91 298 (33.3)		4605 (41.6)	4539 (41.0)	
West	1355 (12.1)	39 371 (14.3)		1334 (12.0)	1346 (12.2)	
Area deprivation index (ADI) quintiles			0.29			
ADI 1	1840 (16.4)	70 001 (25.5)		1811 (16.3)	1887 (17.0)	
ADI 2	4704 (41.9)	85 152 (31.0)		4650 (42.0)	4617 (41.7)	
ADI 3	2832 (25.2)	64 178 (23.4)		2788 (25.2)	2786 (25.2)	
ADI 4	1168 (10.4)	34 275 (12.5)		1153 (10.4)	1119 (10.1)	
ADI 5	681 (6.1)	20 844 (7.6)		675 (6.1)	668 (6.0)	
Index year			0.56			< 0.001
2011	0 (0.0)	383 (0.1)		0 (0.0)	0 (0.0)	
2012	0 (0.0)	490 (0.2)		0 (0.0)	0 (0.0)	
2013	0 (0.0)	1550 (0.6)		0 (0.0)	0 (0.0)	

(Continues)

14631326, 2026, 10, Downloaded from https://dom-pubs.onlinelibrary.wiley.com/doi/10.1111/dom.71086, Wiley Online Library on [03/09/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 1 | (Continued)

	Unmatched dataset			Matched dataset		
	VINT ($n=11235$)	UC ($n=303438$)		VINT ($n=11077$)	UC ($n=11077$)	
Variables	Mean (SD) or *n* (%)	Mean (SD) or *n* (%)	SMD	Mean (SD) or *n* (%)	Mean (SD) or *n* (%)	SMD
2014	0 (0.0)	832 (0.3)		0 (0.0)	0 (0.0)	
2015	3 (0.0)	1484 (0.5)		3 (0.0)	3 (0.0)	
2016	3 (0.0)	2601 (0.9)		3 (0.0)	3 (0.0)	
2017	12 (0.1)	6252 (2.3)		12 (0.1)	12 (0.1)	
2018	19 (0.2)	5144 (1.9)		18 (0.2)	18 (0.2)	
2019	201 (1.8)	13814 (5.0)		186 (1.7)	186 (1.7)	
2020	521 (4.6)	19707 (7.2)		497 (4.5)	497 (4.5)	
2021	812 (7.2)	28003 (10.2)		792 (7.1)	792 (7.1)	
2022	1768 (15.8)	41983 (15.3)		1731 (15.6)	1731 (15.6)	
2023	1856 (16.5)	41482 (15.1)		1829 (16.5)	1829 (16.5)	
2024	5108 (45.5)	71585 (26.1)		5091 (46.0)	5091 (46.0)	
2025	922 (8.2)	39145 (14.3)		915 (8.3)	915 (8.3)	

Note: Standardised mean differences (SMDs) were computed as the absolute difference in means (or proportions for categorical variables) between groups divided by the pooled standard deviation. SMDs were calculated using both the TableOne and MatchIt packages to cross-validate covariate balance estimates. To evaluate covariate balance between matched groups, SMD ≤ 0.1 was used as the criterion for acceptable balance. Unlike *p* values, which are influenced by sample size and may indicate statistically significant differences that are not clinically meaningful in large samples, SMD provides a sample size–independent measure of balance that quantifies the magnitude of difference between groups. Therefore, SMDs were used as the primary metric for assessing post-matching balance, whereas *p* values were reported descriptively.
Abbreviations: UC, usual care; VINT, individualized nutrition therapy (intervention) program.

receptor agonists and SGLT2 inhibitors, regardless of whether medication exposure was modelled as categorical use, proportion of days covered, or time-varying covariates (Table 3; Figure S2; Table S7). Similarly, in marginal structural models accounting for time-varying confounding and potential mediation by medication use, VINT participation remained significantly associated with lower risk of incident CKD outcomes (Table 3; Figure S2). Results were also consistent in Fine–Grey subdistribution hazard models accounting for mortality as a competing event, in which VINT participation remained associated with a significantly lower risk of incident CKD (sHR 0.67, 95% CI 0.55–0.81; $p<0.001$). In addition, VINT participation was associated with significantly lower mortality risk compared with matched controls (aHR 0.40, 95% CI 0.21–0.76; $p<0.01$). The consistency of findings across Cox, marginal structural, and competing-risk models suggests effect estimates were largely unchanged, supporting the robustness of the observed associations.

In a secondary cohort restricted to participants with ≥ 6 months of VINT participation, associations were similar to and generally stronger than those observed in the primary cohort across all CKD outcomes (Table 3; Figure S2; Tables S7 and S8). Findings remained consistent after adjustment for medication use.

Results from IPTW-weighted Cox models were directionally consistent with the primary analyses, further supporting the robustness of the findings across alternative analytic approaches (Table S9).

3.4 | Secondary and Exploratory Outcomes

Detailed results are provided in the Supplementary Results. In brief, rates of kidney stones, gout, and diabetic ketoacidosis were similar between VINT and usual care, with no statistically significant differences observed. Metabolic acidosis occurred less frequently among VINT participants.

Exploratory analyses suggested that higher mean beta-hydroxybutyrate levels were associated with a lower risk of incident CKD (Figure S3), whereas weight loss and HbA1c change were not significantly associated with CKD risk. Among participants with baseline CKD and follow-up claims data, CKD regression or stability occurred more frequently in VINT participants than UC (83.2% vs. 73.3%; $p=0.03$). In adjusted logistic regression models, VINT participants had a significantly less likelihood of CKD progression compared with controls (OR = 0.51, 95% CI: 0.25–0.99, $p=0.04$).

Additional details, including medication use patterns (Table S10), are reported in the Supporting Information Results.

4 | Discussion

Our findings demonstrate that participation in the VINT program was significantly associated with a lower risk of incident claims-based CKD compared with a matched control cohort.

14631326, 2026, 10, Downloaded from https://dom-pubs.onlinelibrary.wiley.com/doi/10.1111/dom.71086, Wiley Online Library on [03/09/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 2 | Baseline comorbidities and medication use of propensity score 1:1 matched cohort of VINT and UC, including those not used in the matching.

	Unmatched dataset			Matched dataset		
	VINT ($n = 11\,235$)	UC ($n = 274\,455$)		VINT ($n = 11\,077$)	UC ($n = 11\,077$)	
Variables	**Mean (SD) or *n* (%)**	**Mean (SD) or *n* (%)**	**SMD**	**Mean (SD) or *n* (%)**	**Mean (SD) or *n* (%)**	**SMD**
Baseline comorbidities						
Type 2 diabetes	4086 (36.4)	63 283 (23.1)	0.30	3976 (35.9)	3976 (35.9)	< 0.001
Obesity	6135 (54.7)	125 775 (45.8)	0.18	6082 (54.9)	6082 (54.9)	< 0.001
Chronic kidney disease	0 (0.0)	0 (0.0)	< 0.001	0 (0.0)	0 (0.0)	< 0.001
Kidney stones	179 (1.6)	5525 (2.0)	0.03	133 (1.2)	133 (1.2)	< 0.001
Heart failure	87 (0.8)	8874 (3.2)	0.18	83 (0.7)	91 (0.8)	0.01
Hyperlipidemia	4957 (44.2)	126 180 (46.0)	0.04	4868 (43.9)	4978 (44.9)	0.02
Hypertension	4757 (42.4)	126 826 (46.2)	0.08	4671 (42.2)	4637 (41.9)	0.01
Stroke	153 (1.4)	10 059 (3.7)	0.15	147 (1.3)	139 (1.3)	0.01
Coronary artery disease	484 (4.3)	23 203 (8.5)	0.17	475 (4.3)	420 (3.8)	0.03
Cardiovascular disease	66 (0.6)	3968 (1.4)	0.09	65 (0.6)	65 (0.6)	< 0.001
Smoking	364 (3.2)	17 622 (6.4)	0.15	353 (3.2)	420 (3.8)	0.03
Baseline medications						
SGLT2i	908 (8.1)	11 301 (4.1)	0.17	842 (7.6)	842 (7.6)	< 0.001
Incretin mimetics	1993 (17.8)	31 395 (11.4)	0.18	1908 (17.2)	1908 (17.2)	< 0.001
RAASi	3701 (33.0)	92 801 (33.8)	0.02	3620 (32.7)	3620 (32.7)	< 0.001
MRA and nonMRA	289 (2.6)	7960 (2.9)	0.02	241 (2.2)	241 (2.2)	< 0.001
Diuretic	2014 (17.9)	60 152 (21.9)	0.10	1961 (17.7)	1998 (18.0)	0.01
Beta blocker	1224 (10.9)	47 955 (17.5)	0.19	1192 (10.8)	1164 (10.5)	0.01
Calcium blocker	1282 (11.4)	43 893 (16.0)	0.13	1248 (11.3)	1175 (10.6)	0.02
Other antihypertensive medications	230 (2.0)	9051 (3.3)	0.08	221 (2.0)	209 (1.9)	0.01
Insulin	605 (5.4)	10 047 (3.7)	0.08	578 (5.2)	673 (6.1)	0.04
Sulfonylureas	339 (3.0)	4901 (1.8)	0.08	322 (2.9)	344 (3.1)	0.01
DPP4i	384 (3.4)	5022 (1.8)	0.10	368 (3.3)	414 (3.7)	0.02
Thiazolidine	195 (1.7)	2942 (1.1)	0.06	184 (1.7)	170 (1.5)	0.01
Other T2D medications	3266 (29.1)	46 767 (17.0)	0.29	3167 (28.6)	3245 (29.3)	0.02
Baseline cost and trajectory						
Total cost of care	11773.0 (24464.4)	10649.2 (22926.6)	0.05	11689.2 (24507.1)	11603.19 (23553.7)	0.004
Outpatient cost	904.5 (7410.2)	1157.1 (7761.8)	0.03	899.8 (7396.0)	921.3 (6062.6)	0.003
Inpatient cost	3638.8 (12464.6)	3214.3 (12949.7)	0.03	3557.3 (12448.5)	3726.7 (11220.6)	0.01
Pharmacy cost	7227.6 (17690.8)	6271.3 (14965.2)	0.06	7229.9 (17773.8)	6949.3 (17712.9)	0.02

(Continues)

14631326, 2026, 10, Downloaded from https://dom-pubs.onlinelibrary.wiley.com/doi/10.1111/dom.71086, Wiley Online Library on [03/09/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 2 | (Continued)

Variables	Unmatched dataset			Matched dataset		
	VINT ($n = 11\,235$)	UC ($n = 274\,455$)		VINT ($n = 11\,077$)	UC ($n = 11\,077$)	
	Mean (SD) or *n* (%)	Mean (SD) or *n* (%)	SMD	Mean (SD) or *n* (%)	Mean (SD) or *n* (%)	SMD
Variables not included in the matching						
Other baseline comorbidities						
Cancer	446 (4.0)	15 953 (5.8)	0.09	442 (4.0)	470 (4.2)	0.01
Afib	172 (1.5)	11 163 (4.1)	0.15	171 (1.5)	186 (1.7)	0.01
Glaucoma	444 (4.0)	16 377 (6.0)	0.09	438 (4.0)	440 (4.0)	0.001
MASLD	655 (5.8)	14 058 (5.1)	0.03	625 (5.6)	655 (5.9)	0.01
MASH	55 (0.5)	1385 (0.5)	0.002	51 (0.5)	65 (0.6)	0.02
Liver fibrosis	25 (0.2)	419 (0.2)	0.02	25 (0.2)	16 (0.1)	0.02
GERD	1566 (14.0)	48 361 (17.6)	0.10	1544 (13.9)	1917 (17.3)	0.09
Osteoarthritis	1427 (12.7)	48 113 (17.5)	0.14	1409 (12.7)	1649 (14.9)	0.06
Sleep disorder	2751 (24.5)	56 551 (20.6)	0.09	2698 (24.4)	2465 (22.3)	0.05
PAD	167 (1.5)	14 450 (5.3)	0.21	163 (1.5)	267 (2.4)	0.07
Diabetes Neuropathy	387 (3.4)	10 895 (4.0)	0.03	375 (3.4)	498 (4.5)	0.06
Schizophrenia	18 (0.2)	2307 (0.8)	0.10	18 (0.2)	73 (0.7)	0.08
Bipolar disorder	127 (1.1)	5544 (2.0)	0.07	124 (1.1)	243 (2.2)	0.08
Common mental health	2490 (22.2)	62 832 (22.9)	0.02	2463 (22.2)	2726 (24.6)	0.06
Other mental health conditions	814 (7.3)	17 270 (6.3)	0.04	807 (7.3)	795 (7.2)	0.004
Other baseline medications						
Anticoagulant	227 (2.0)	13 181 (4.8)	0.15	226 (2.0)	324 (2.9)	0.06
Antiplatelet	291 (2.6)	13 536 (4.9)	0.12	284 (2.6)	448 (4.0)	0.08
Statin	3577 (31.9)	91 963 (33.5)	0.04	3487 (31.5)	3674 (33.2)	0.04
PCSK9i	531 (4.7)	13 553 (4.9)	0.01	35 (0.3)	34 (0.3)	0.002
Other lipid lowering medications	37 (0.3)	1152 (0.4)	0.02	511 (4.6)	613 (5.5)	0.04
Sacubitril	15 (0.1)	1241 (0.5)	0.06	15 (0.1)	21 (0.2)	0.01
Neuropathy medications	1548 (13.8)	51 526 (18.8)	0.14	1518 (13.7)	2103 (19.0)	0.14
Antidepressant	2944 (26.2)	76 229 (27.8)	0.04	2902 (26.2)	3337 (30.1)	0.09
Antipsychotic	197 (1.8)	10 793 (3.9)	0.13	193 (1.7)	466 (4.2)	0.15

Note: Standardised mean differences (SMDs) were computed as the absolute difference in means (or proportions for categorical variables) between groups divided by the pooled standard deviation. SMDs were calculated using both the TableOne and MatchIt packages to cross-validate covariate balance estimates. To evaluate covariate balance between matched groups, SMD ≤ 0.1 was used as the criterion for acceptable balance. Unlike *p* values, which are influenced by sample size and may indicate statistically significant differences that are not clinically meaningful in large samples, SMD provides a sample size–independent measure of balance that quantifies the magnitude of difference between groups. Therefore, SMDs were used as the primary metric for assessing post-matching balance, whereas *p* values were reported descriptively.

Abbreviations: Afib, atrial fibrillation; CKD, chronic kidney disease; DPP4i, dipeptidyl peptidase-4 inhibitor; GERD, gastro-oesophageal reflux disease; MASH, metabolic dysfunction-associated steatohepatitis; MASLD, metabolic dysfunction-associated steatotic liver disease; MRA, mineralocorticoid receptor antagonist (steroidal); non-MRA, non-steroidal mineralocorticoid receptor antagonist (e.g., finerenone); PAD, peripheral artery disease; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor; RAASi, renin–angiotensin–aldosterone system inhibitor (e.g., ACEi/ARB/ARNI); SGLT2i, sodium–glucose cotransporter-2 inhibitor; T2D, type 2 diabetes; UC, usual care; VINT, individualized nutrition therapy (intervention) program.

14631326, 2026, 10, Downloaded from https://dom-pubs.onlinelibrary.wiley.com/doi/10.1111/dom.71086, Wiley Online Library on [03/09/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 3 | Association of VINT participation with CKD outcomes in primary and secondary cohorts.

Outcome		Number of events	Number at risk	Person-years	Incidence rate
All new-onset CKD	VINT	210	11 077	20462.9	10.1 (8.9, 11.7)
	UC	303		19391.7	15.6 (13.9, 17.5)
CKD stage 3+	VINT	117	11 077	20462.9	5.7 (4.7, 6.9)
	UC	189		19391.7	9.7 (8.4, 11.2)
CKD stage 4+	VINT	10	11 077	20462.9	0.5 (0.2, 0.9)
	UC	26		19391.7	1.3 (0.9, 2.0)

Cox regression models including base model and models with sequential and alternative medication adjustments

		Primary cohort		Secondary cohort	
	Models	aHR (95% CI)	*p*	aHR (95% CI)	*p*
All new-onset CKD	Base cox	0.64 (0.53–0.77)	< 0.001	0.58 (0.47–0.70)	< 0.001
	Medication adj (categorical)	0.67 (0.55–0.81)	< 0.001	0.58 (0.47–0.70)	< 0.001
	Medication adj (continuous PDC)	0.68 (0.56–0.82)	< 0.001	0.61 (0.50–0.74)	< 0.001
	Time-varying categorical	0.69 (0.58–0.82)	< 0.001	0.60 (0.50–0.72)	< 0.001
	Time-varying PDC	0.69 (0.58–0.90)	< 0.001	0.60 (0.50–0.72)	< 0.001
	MSM	0.74 (0.61–0.82)	0.002	0.61 (0.51–0.74)	< 0.001
CKD stage 3+	Base Cox	0.57 (0.45–0.73)	< 0.001	0.51 (039–0.66)	< 0.001
	Medication adj (categorical)	0.60 (0.47–0.77)	< 0.001	0.51 (0.40–0.66)	< 0.001
	Medication adj (continuous PDC)	0.60 (0.47–0.77)	< 0.001	0.52 (0.40–0.68)	< 0.001
	Time-varying categorical	0.62 (0.49–0.78)	< 0.001	0.53 (0.41–0.66)	< 0.001
	Time-varying PDC	0.62 (0.50–0.79)	< 0.001	0.53 (0.41–0.66)	< 0.001
	MSM	0.70 (0.54–0.90)	0.006	0.55 (0.43–0.71)	< 0.001
CKD stage 4+	Base Cox	0.45 (0.21–0.97)	< 0.05	0.39 (0.19–0.83)	< 0.05
	Medication adj (categorical)	0.50 (0.23–0.98)	< 0.05	0.43 (0.20–0.91)	< 0.05
	Medication adj (continuous PDC)	0.43 (0.20–0.91)	< 0.05	0.37 (0.18–0.78)	< 0.05
	Time-varying categorical	0.44 (0.21–0.92)	< 0.05	0.39 (0.19–0.80)	< 0.05
	Time-varying PDC	0.44 (0.21–0.92)	< 0.05	0.39 (0.19–0.80)	< 0.05
	MSM	0.42 (0.18–0.94)	< 0.05	0.43 (0.20–0.92)	< 0.05

Note: All models were adjusted for age, sex, and race/ethnicity. The Base Cox model included demographic covariates only (age, sex, and race/ethnicity). Medication-adjusted models additionally included follow-up use of ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; ACEI/ARB, angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker; SGLT2i, sodium–glucose cotransporter-2 inhibitor; incretin mimetics including GLP-1 receptor agonists (GLP-1RA); MRA, mineralocorticoid receptor antagonist; non-MRA, non-steroidal mineralocorticoid receptor antagonist (e.g., finerenone); NSAID, nonsteroidal anti-inflammatory drug use and baseline diagnosis of T2D and obesity. Categorical medication models adjusted for medication use as binary indicators, whereas continuous medication models adjusted for medication exposure using proportion of days covered (PDC). Time-varying models incorporated medication use as time-dependent covariates during follow-up, modelled either categorically or using PDC. Marginal structural models (MSMs) used stabilised inverse probability weighting to account for time-varying medication exposure and potential time-dependent confounding.
Abbreviations: MSM, marginal structural model; PDC, proportion of days covered.

In this large, longitudinal, claims-based analysis, VINT was associated with a reduced risk of new-onset CKD (~30% reduction), including diagnoses at advanced stages such as stage 3 and beyond (~43% reduction), with a trend toward reduced incidence of stage 4 and beyond (~50% reduction) during follow-up. These results provide novel real-world evidence that a digitally delivered lifestyle intervention emphasising carbohydrate reduction can meaningfully alter the course of CKD, a condition typically considered progressive and irreversible [27].

Importantly, real-world data analyses such as this extend the relevance of clinical research by capturing outcomes in routine care settings, complementing traditional trials, and informing policy and practice decisions [28]. The observation that even advanced-stage CKD diagnoses were prevented, together with

14631326, 2026, 10, Downloaded from https://dom-pubs.onlinelibrary.wiley.com/doi/10.1111/dom.71086, Wiley Online Library on [03/09/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

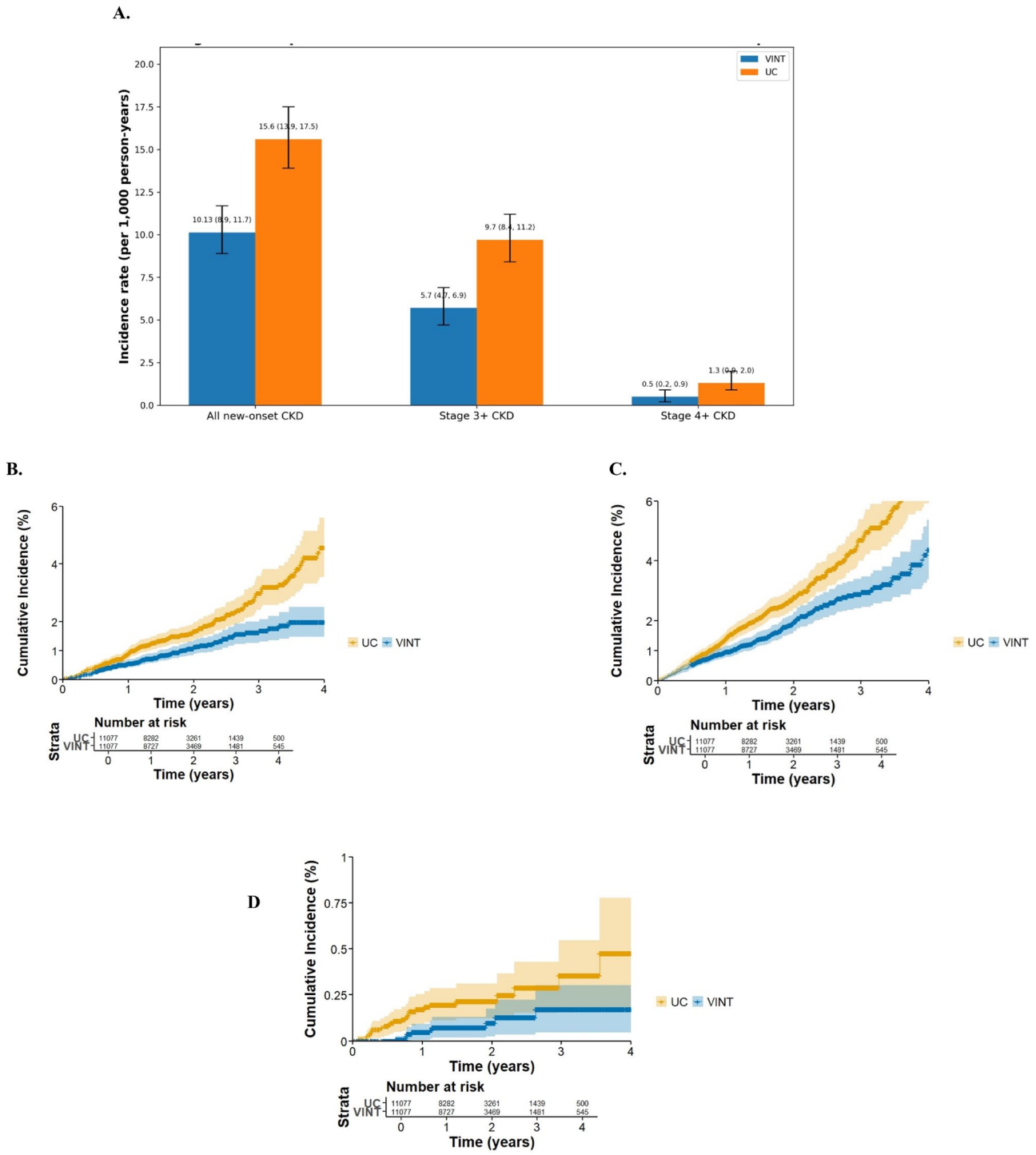

FIGURE 2 | (A) Comparison of CKD Incidence Rates Between VINT and UC Groups. Cumulative incidence curves for (B) new-onset CKD (including albuminuria), (C) new-onset stage ≥ 3 CKD, and (D) new-onset stage ≥ 4 CKD during follow-up, comparing VINT participants with matched controls (UC). Curves are displayed up to 4 years to aid interpretability, given the decreasing sample size late in follow-up, though all analyses were conducted using the full 5-year observation window with standard right-censoring. At-risk tables are shown below each panel, and steps in the curves reflect incident events. Estimates toward the right tail should be interpreted with caution due to smaller denominators.

findings from exploratory analyses showing a significantly greater likelihood of stage maintenance and regression among participants with baseline CKD in the treated group compared with matched controls, reinforces the potential to improve kidney function in at-risk patients through nutritional and lifestyle interventions.

Telemedicine and digital health interventions, including mobile apps, remote monitoring, and web-based counselling, have been shown to improve diet quality, blood pressure, renal function, and quality of life in adults with CKD [29, 30]. Beyond clinical outcomes, telehealth improves access, reduces cost and travel burden, and enhances multidisciplinary

14631326, 2026, 10, Downloaded from https://dom-pubs.onlinelibrary.wiley.com/doi/10.1111/dom.71086, Wiley Online Library on [03/09/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

collaboration, key advantages in CKD care where specialist access is limited. Broader reviews of telenephrology have similarly demonstrated high patient satisfaction, adherence, and scalability [31–33]. Integrating these evidence-based digital strategies into a continuous remote care model, the present intervention has previously been shown to reverse and manage T2D and obesity, major CKD risk factors. In this claims-based study, we extend these findings to CKD prevention and progression, suggesting that this approach could be scaled for broader renal care delivery.

The observed reduction in CKD incidence may reflect the unique metabolic effects of nutritional ketosis. Carbohydrate restriction improves insulin sensitivity, inflammation, visceral adiposity, and glycaemic and blood pressure control [19–24, 34], all central to CKD pathogenesis [35]. Prior analyses of the same intervention in type 2 diabetes demonstrated stabilisation or reversal of eGFR decline [21] and reductions in UACR [24], independent of pharmacologic therapy. In this larger real-world cohort, the protective effect of VINT persisted across multiple modelling approaches, including models that adjusted for medication use as confounders and models that treated medications as mediators, suggesting benefits beyond drug management. Other clinical and real-world evidence supports these findings, with carbohydrate restriction improving eGFR, UACR, and cystatin C [36–40] and lowering risks of kidney failure and mortality [41, 42], whereas high energy-dense carbohydrate intake is associated with a threefold higher CKD risk [43]. Unlike traditional low-protein diets, which did not slow CKD progression in the MDRD trial [13, 44], nutritional ketosis targets multiple metabolic pathways simultaneously, offering a more comprehensive disease-modifying strategy.

Consistent with prior studies, participants with mean βHB ≥ 0.5 mmol/L during the first 6 months had a significantly lower risk of developing new-onset CKD. In the primary cohort, which included all participants regardless of program duration, effect estimates were modestly attenuated but remained significant, likely reflecting greater heterogeneity in engagement. In contrast, the secondary cohort restricted to ≥ 6 months of continuous participation showed slightly stronger associations, particularly for more advanced CKD stages, underscoring the importance of sustained exposure. As the ≥ 6-month definition reflects adherence and metabolic response, these findings are considered exploratory and may be subject to selection or survivor bias. Nevertheless, consistent directionality across cohorts supports the robustness of the association. Sustained carbohydrate restriction, reflected by higher BHB levels, may contribute to these observed benefits. These findings are consistent with prior work demonstrating a dose–response relationship between ketosis and improvements in eGFR slope [21], as well as with Liu et al. which linked higher βHB levels to improved renal survival and reduced ESRD risk [45]. Potential mechanisms include modulation of inflammation, oxidative stress, fibrosis, and renal metabolism [22]. Although long-term ketosis trajectories could not be fully assessed, the observed consistency supports the potential role of nutritional ketosis as a kidney-protective strategy, paralleling effects observed with SGLT2 inhibitors [46, 47] and supported by evidence from ADPKD studies showing improved eGFR and reduced kidney volume with greater ketosis [48, 49].

Concerns regarding kidney-related safety of ketogenic interventions have historically focused on kidney stones [22, 50, 51] and metabolic acidosis [52, 53]. In this analysis, kidney stone risk in VINT participants was comparable to matched controls across incidence, prevalence, and recurrence, suggesting no increased risk despite theoretical concerns related to altered urinary calcium, uric acid, and citrate excretion. These findings are consistent with evidence that, under medical supervision with dietary guidance and adequate hydration, nephrolithiasis risk is not elevated [21]. Safety outcomes extended beyond nephrolithiasis. Although ketogenic diets are often perceived as high in protein, this intervention employed moderate protein intake, and VINT participants had lower rates of acidosis, potentially reflecting preserved kidney function, particularly in advanced CKD [21, 53]. Given overlap in ICD-10 coding for acidosis and diabetic ketoacidosis (DKA), DKA was evaluated separately, with no increased risk observed in the VINT group, likely reflecting improved glycemic control and renal function. These findings reinforce that physiologic nutritional ketosis remains distinct from pathologic ketoacidosis [54]. Finally, despite concerns regarding gout and renal urate handling, including transient increases during initiation [55], no increase in incident or prevalent gout was observed. Mechanistic evidence further suggests that β-hydroxybutyrate may mitigate gout flares via inhibition of the NLRP3 inflammasome [56].

4.1 | Strengths and Limitations of Study

This study has several strengths, including use of a large external claims' dataset with up to 5 years of follow-up, robust propensity score–based matching, and confirmation of findings across complementary analytic approaches, including inverse probability of treatment weighting. Although modest differences in kidney-relevant medication use were observed between cohorts, these therapies were addressed using categorical, continuous, and time-varying models that treated medications as confounders and, in separate analyses, as potential mediators. Associations between the VINT and reduced CKD risk were consistent across analytic approaches, supporting the robustness of the findings.

Several limitations should also be considered. Reliance on closed claims data without linkage to electronic health records or laboratory measures limited follow-up to a subset of the eligible population and precluded direct assessment of kidney function or disease progression using quantitative biomarkers. Outcomes were defined using ICD-10 diagnostic codes, which may introduce misclassification and limit assessment of disease timing, progression, or subclinical changes. Some cases classified as advanced CKD may have reflected pre-existing disease, and analyses focused on incident CKD onset rather than progression of established disease.

Analyses in the secondary cohort, restricted to participants with at least 6 months of program participation, demonstrated larger effect sizes, suggesting that greater engagement and sustained adherence may enhance the observed benefits of VINT. This extended exposure window also enables exploratory analyses of beta-hydroxybutyrate and weight change within the VINT cohort. These analyses were intended to characterize patterns of adherence and metabolic response over time and to inform the

14631326, 2026, 10, Downloaded from https://dom-pubs.onlinelibrary.wiley.com/doi/10.1111/dom.71086, Wiley Online Library on [03/09/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

design of future studies, rather than to provide causal estimates at enrollment.

Finally, residual confounding related to secular treatment trends, health-seeking behaviours, physical activity, weight loss motivation, digital access, and unmeasured lifestyle or socioeconomic factors cannot be excluded. Dietary intake in the matched control cohort was not captured, and it is therefore unknown whether some individuals in the control group were following similar dietary patterns (e.g., low-carbohydrate or ketogenic diets), which could bias effect estimates toward the null. In addition, VINT represents a multifaceted care model that includes an initial clinical assessment, medication review and adjustment at enrollment, and ongoing medication management in addition to nutritional guidance. Although we incorporated medication-adjusted and time-varying models to account for differences in treatment during follow-up, the independent contribution of baseline clinical assessment and early medication optimization cannot be fully disentangled from the effects of nutritional ketosis. As such, the observed associations likely reflect a combination of metabolic and care-delivery effects. Additionally, the follow-up period may be insufficient to capture longer-term kidney outcomes. No formal sample size calculation was performed, as analyses were exploratory and hypothesis generating. These findings support the need for future randomised and prospective studies integrating claims, electronic health record, and laboratory data to more definitively assess kidney-related effects of carbohydrate reduction and nutritional ketosis.

5 | Conclusions

Although RCTs remain the gold standard, our findings provide complementary real-world evidence that extends generalizability to broader, more heterogeneous patient populations and demonstrates effectiveness in routine care settings, offering timely insights to inform clinical guidelines, payer decisions, and health policy [28]. These results suggest that the program may offer benefits beyond type 2 diabetes reversal and weight loss, functioning as a comprehensive metabolic intervention with potential relevance to kidney disease risk and progression, an area that merits further investigation. This treatment approach, already established as an evidence-based model for achieving diabetes reversal and sustained weight loss, integrates continuous remote monitoring, medication management, and individualized dietary support focused on carbohydrate restriction. Delivered digitally, this model represents a scalable, nonpharmacologic strategy to help address the growing burden of CKD among metabolically at-risk populations and warrants careful evaluation in patients with more advanced CKD through appropriately designed RCTs.

Author Contributions

S.J.A. drafted the manuscript, and contributed to the study concept and design, critically reviewed and revised the manuscript, and approved the final version. S.J.A. performed the statistical analyses. S.J.A. and P.V.S. acquired and curated the data. R.J.J., P.B., A.J.W., T.W., J.H., and J.S.V. provided clinical and scientific oversight and interpretation of the findings. All authors reviewed and revised the manuscript. R.J.J. supervised the study and is the guarantor. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Funding

The authors have nothing to report.

Disclosure

Dissemination: The findings of this study will be disseminated to the public through social media, blogs, and professional networks to enhance accessibility and public understanding. For research transparency and early feedback, the manuscript has been uploaded as a preprint https://www.medrxiv.org/content/10.1101/2025.10.17.25338238v.3 Once the study is published, we plan to share a summary of the results through digital platforms and academic forums. The study and its findings will also be used to support future research proposals and grant applications aimed at expanding this work and evaluating long-term kidney outcomes in broader populations. Reporting guidelines: This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for cohort studies. A completed STROBE checklist was prepared and submitted with the manuscript.

Ethics Statement

The study was determined to be exempt from institutional review board (IRB) review, as it relied solely on retrospectively collected, de-identified data and did not involve any additional contact or intervention with human subjects.

Conflicts of Interest

Three authors (S.J.A., P.V.S., A.W.) are employees of Virta Health and offered stock options. One author (J.S.V.) is a co-founder and shareholder of the company. Virta Health provides a remote care intervention including individualized nutrition therapy for people with type 2 diabetes and related metabolic conditions. These authors and other coauthors contributed to the study design, data analysis, interpretation, and manuscript preparation. All other authors declare no conflicts of interest.

Data Availability Statement

The datasets analyzed in this study are not publicly available because they were obtained through a commercial license from the data vendor. Access to these data is restricted, and they were used solely under the terms of the license granted for this study.

Peer Review

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/dom.71086.

References

1. X. Ding, X. Li, Y. Ye, J. Jiang, M. Lu, and L. Shao, "Epidemiological Patterns of Chronic Kidney Disease Attributed to Type 2 Diabetes From 1990–2019," *Frontiers in Endocrinology* 15 (2024): 1383777, https://doi.org/10.3389/fendo.2024.1383777.

2. A. Francis, M. N. Harhay, A. C. M. Ong, et al., "Chronic Kidney Disease and the Global Public Health Agenda: An International Consensus," *Nature Reviews. Nephrology* 20, no. 7 (2024): 473–485, https://doi.org/10.1038/s41581-024-00820-6.

3. L. Deng, S. Guo, Y. Liu, et al., "Global, Regional, and National Burden of Chronic Kidney Disease and Its Underlying Etiologies From 1990 to 2021: A Systematic Analysis for the Global Burden of Disease Study 2021," *BMC Public Health* 25 (2025): 636, https://doi.org/10.1186/s12889-025-21851-z.

4. M. van der Velde, K. Matsushita, J. Coresh, et al., "CKD Prognosis Consortium. Lower Estimated Glomerular Filtration Rate and Higher Albuminuria Are Associated With All-Cause and Cardiovascular Mortality: A Collaborative Meta-Analysis of High-Risk Population

14631326, 2026, 10, Downloaded from https://dom-pubs.onlinelibrary.wiley.com/doi/10.1111/dom.71086, Wiley Online Library on [03/09/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Cohorts," *Kidney International* 79, no. 12 (2011): 1341–1352, https://doi.org/10.1038/ki.2010.536.

5. V. Perkovic, M. J. Jardine, B. Neal, et al., "Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy," *New England Journal of Medicine* 380, no. 24 (2019): 2295–2306.

6. M. E. Cooper, S. E. Inzucchi, B. Zinman, et al., "Glucose Control and the Effect of Empagliflozin on Kidney Outcomes in Type 2 Diabetes: An Analysis From the EMPA-REG OUTCOME Trial," *American Journal of Kidney Diseases* 74, no. 5 (2019): 713–715.

7. G. L. Bakris, R. Agarwal, S. D. Anker, B. Pitt, and L. M. Ruilope, "FIDELIO-DKD Investigators. Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes," *New England Journal of Medicine* 383, no. 23 (2020): 2219–2229, https://doi.org/10.1056/NEJMoa2025845.

8. M. JFE, D. D. Ørsted, and J. B. Buse, "Liraglutide and Renal Outcomes in Type 2 Diabetes," *New England Journal of Medicine* 377, no. 22 (2017): 2197–2198, https://doi.org/10.1056/NEJMc1713042.

9. V. Perkovic, K. R. Tuttle, P. Rossing, K. W. Mahaffey, and M. JFE, "FLOW Trial Committees and Investigators. Effects of Semaglutide on Chronic Kidney Disease in Patients With Type 2 Diabetes," *New England Journal of Medicine* 391, no. 2 (2024): 109–121, https://doi.org/10.1056/NEJMoa2403347.

10. G. M. Chertow, R. Correa-Rotter, K. U. Eckardt, et al., "Projecting the Clinical Burden of Chronic Kidney Disease at the Patient Level (Inside CKD): A Microsimulation Modelling Study," *EClinicalMedicine* 72 (2024): 102614, https://doi.org/10.1016/j.eclinm.2024.102614.

11. T. H. Hostetter, T. W. Meyer, H. G. Rennke, and B. M. Brenner, "Chronic Effects of Dietary Protein in the Rat With Intact and Reduced Renal Mass," *Kidney International* 30, no. 4 (1986): 509–517, https://doi.org/10.1038/ki.1986.216.

12. R. Sharma and J. H. McNeill, "Effect of High-Protein Feeding on Progression of Renal Failure in Rats," *Journal of Laboratory and Clinical Medicine* 90, no. 2 (1977): 212–219.

13. S. Klahr, A. S. Levey, G. J. Beck, et al., "The Effects of Dietary Protein Restriction and Blood-Pressure Control on the Progression of Chronic Renal Disease," *New England Journal of Medicine* 330, no. 13 (1994): 877–884, https://doi.org/10.1056/NEJM199403313301301.

14. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group, "KDIGO 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease," *Kidney International* 98, no. 4S (2020): S1–S115, https://doi.org/10.1016/j.kint.2020.06.019.

15. T. A. Ikizler, J. D. Burrowes, L. D. Byham-Gray, et al., "KDOQI Clinical Practice Guideline for Nutrition in CKD: 2020 Update," *American Journal of Kidney Diseases* 76, no. 3 Suppl 1 (2020): S1–S107.

16. L. U. Lavenburg, D. E. Schaubel, A. M. Chao, P. P. Reese, and J. B. Cohen, "The 10-Year Effects of Intensive Lifestyle Intervention on Kidney Outcomes," *Kidney Medicine* 6, no. 5 (2024): 100814, https://doi.org/10.1016/j.xkme.2024.100814.

17. R. J. Johnson, L. G. Sánchez-Lozada, P. Andrews, and M. A. Lanaspa, "Fructose, but Not Dextrose, Accelerates the Progression of Chronic Kidney Disease," *American Journal of Physiology. Renal Physiology* 292, no. 1 (2007): F423–F431, https://doi.org/10.1152/ajprenal.00181.2007.

18. A. Andres-Hernando, D. J. Orlicky, C. Cicerchi, et al., "High Fructose Corn Syrup Accelerates Kidney Disease and Mortality in Obese Mice With Metabolic Syndrome," *Biomolecules* 13, no. 5 (2023): 780, https://doi.org/10.3390/biom13050780.

19. S. J. Hallberg, A. L. McKenzie, P. T. Williams, et al., "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," *Diabetes Therapy* 9, no. 2 (2018): 583–612.

20. S. J. Athinarayanan, R. N. Adams, S. J. Hallberg, et al., "Long-Term Effects of a Novel Continuous Remote Care Intervention Including Nutritional Ketosis for the Management of Type 2 Diabetes: A 2-Year Non-Randomized Clinical Trial," *Frontiers in Endocrinology* 10 (2019): 348, https://doi.org/10.3389/fendo.2019.00348.

21. S. J. Athinarayanan, C. G. P. Roberts, S. D. Phinney, T. Weimbs, A. N. Friedman, and J. S. Volek, "Effects of a Continuous Remote Care Intervention Including Nutritional Ketosis on Kidney Function and Inflammation in Adults With Type 2 Diabetes: A Post-Hoc Latent Class Trajectory Analysis," *Frontiers in Nutrition* 12 (2025): 1609737, https://doi.org/10.3389/fnut.2025.1609737.

22. S. J. Athinarayanan, C. G. P. Roberts, C. Vangala, et al., "The Case for a Ketogenic Diet in the Management of Kidney Disease," *BMJ Open Diabetes Research & Care* 12, no. 2 (2024): e004101, https://doi.org/10.1136/bmjdrc-2024-004101.

23. S. J. Athinarayanan, C. G. P. Roberts, and G. K. Shetty, "Hypertension Management in Individuals Participating in Carbohydrate-Restricted Nutrition Therapy," *Diabetes* 73 (2024): 1595-P.

24. P. V. Shanmugam, S. J. Athinarayanan, R. CGP, G. K. Shetty, R. N. Adams, and A. R. Zoller, "Impact of Carbohydrate-Restricted Nutrition Therapy on Urinary Albuminuria in Insulin-Resistant Individuals With CKD Over Two Years," *Diabetes* 73 (2024): 1860-LB.

25. T. Khan, C. Kim, and A. Druet, "High Burden, Low Priority? Iron Deficiency Anemia in U.S. Women and the Challenges of Data Gaps With Over-The-Counter Treatments," (2023), Komodo Insights, https://www.komodohealth.com/insights/high-burden-low-priority-iron-deficiency-anemia-in-u.s-women-and-the-challenges-of-data-gaps-with-over-the-counter-treatment.

26. E. von Elm, D. G. Altman, M. Egger, et al., "The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for Reporting Observational Studies," *BMJ* 335, no. 7624 (2007): 806–808, https://doi.org/10.1136/bmj.39335.541782.AD.

27. K. Kalantar-Zadeh, T. H. Jafar, D. Nitsch, B. L. Neuen, and V. Perkovic, "Chronic Kidney Disease," *Lancet* 398, no. 10302 (2021): 786–802, https://doi.org/10.1016/S0140-6736(21)00519-5.

28. A. B. Abbasi, L. H. Curtis, and R. M. Califf, "The Promise of Real-World Data for Research—What Are We Missing?," *New England Journal of Medicine* 393, no. 4 (2025): 318–321, https://doi.org/10.1056/NEJMp2416479.

29. S. J. Schrauben, A. Inamdar, C. Yule, et al., "Effects of Dietary App-Supported Tele-Counseling on Sodium Intake, Diet Quality, and Blood Pressure in Patients With Diabetes and Kidney Disease," *Journal of Renal Nutrition* 32, no. 1 (2022): 39–50, https://doi.org/10.1053/j.jrn.2021.08.006.

30. R. Santosh, Y. N. Mohammed, Z. Rahaman, and S. Khurana, "The Role of Telemedicine in Enhancing Chronic Kidney Disease (CKD) Management and Dialysis Care," *Cureus* 16, no. 3 (2024): e55816, https://doi.org/10.7759/cureus.55816.

31. T. Ellis, A. J. Kwon, and M. Y. Hong, "The Effectiveness of Telehealth Intervention on Chronic Kidney Disease Management in Adults: A Systematic Review," *Mayo Clin Proc Digit Health* 3, no. 1 (2025): 100181, https://doi.org/10.1016/j.mcpdig.2024.11.002.

32. D. Adair, "Telehealth and Kidney Care: Helping Patients Understand and Access Telemedicine," *Journal of Renal Nutrition* 31, no. 5 (2021): e1–e6, https://doi.org/10.1053/j.jrn.2020.12.005.

33. S. A. Greenwood, Y. HML, J. Briggs, et al., "Evaluating the Effect of a Digital Health Intervention to Enhance Physical Activity in People With Chronic Kidney Disease (Kidney BEAM): A Multicentre, Randomised Controlled Trial in the UK," *Lancet Digital Health* 6, no. 1 (2024): e23–e32, https://doi.org/10.1016/S2589-7500(23)00204-2.

34. S. J. Hallberg, N. E. Dockter, J. Kushner, and S. J. Athinarayanan, "Improving the Scientific Rigor of Nutritional Recommendations for Adults With Diabetes: A Comprehensive Review of the American Diabetes Association Guidelines Recommended Eating Patterns," *Diabetes, Obesity and Metabolism* 21 (2025): 1769, https://doi.org/10.1111/dom.13736.

14631326, 2026, 10, Downloaded from https://dom-pubs.onlinelibrary.wiley.com/doi/10.1111/dom.71086, Wiley Online Library on [03/09/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

35. V. Vallon and R. Komers, "Pathophysiology of the Diabetic Kidney," *Compr Physiol* 1 (2011): 1175–1232.

36. A. N. Friedman, L. G. Ogden, G. D. Foster, et al., "Comparative Effects of Low-Carbohydrate High-Protein Versus Low-Fat Diets on the Kidney," *Clinical Journal of the American Society of Nephrology* 7, no. 7 (2012): 1103–1111.

37. A. Tirosh, R. Golan, I. Harman-Boehm, et al., "Renal Function Following Weight Loss Dietary Strategies," *Diabetes Care* 36, no. 8 (2013): 2225–2232.

38. A. N. Friedman, M. Chambers, L. M. Kamendulis, and J. Temmerman, "Short-Term Changes After a Weight Reduction Intervention in Advanced Diabetic Nephropathy," *Clinical Journal of the American Society of Nephrology* 8, no. 11 (2013): 1892–1898.

39. A. Bruci, D. Tuccinardi, R. Tozzi, et al., "Very Low-Calorie Ketogenic Diet: A Safe and Effective Tool for Weight Loss in Patients With Obesity and Mild Kidney Failure," *Nutrients* 12, no. 2 (2020): 333.

40. D. Unwin, J. Unwin, D. Crocombe, et al., "Renal Function in Patients Following a Low-Carbohydrate Diet for Type 2 Diabetes," *Current Opinion in Endocrinology, Diabetes, and Obesity* 28, no. 5 (2021): 469–479.

41. F. S. Facchini and K. L. Saylor, "A Low-Iron-Available, Polyphenol-Enriched, Carbohydrate-Restricted Diet to Slow Progression of Diabetic Nephropathy," *Diabetes* 52, no. 5 (2003): 1204–1209.

42. Q. Ren, Y. Zhou, H. Luo, et al., "Associations of Low-Carbohydrate With Mortality in Chronic Kidney Disease," *Renal Failure* 45, no. 1 (2023): 2202284, https://doi.org/10.1080/0886022X.2023.2202284.

43. B. Gopinath, D. C. Harris, V. M. Flood, G. Burlutsky, J. Brand-Miller, and P. Mitchell, "Carbohydrate Nutrition Is Associated With the 5-Year Incidence of Chronic Kidney Disease," *Journal of Nutrition* 141, no. 3 (2011): 433–439, https://doi.org/10.3945/jn.110.134304.

44. V. Menon, J. D. Kopple, X. Wang, et al., "Effect of a Very Low-Protein Diet on Outcomes: Long-Term Follow-Up of the Modification of Diet in Renal Disease (MDRD) Study," *American Journal of Kidney Diseases* 53, no. 2 (2009): 208–217, https://doi.org/10.1053/j.ajkd.2008.08.009.

45. K. Liu, Q. Yang, Y. Lang, et al., "Ketogenic Diet, Serum Ketone Bodies and Risk of End-Stage Renal Disease in Patients With Diabetic Kidney Disease: A Multi-Cohort Study," *Journal of Diabetes* 17, no. 8 (2025): e70140, https://doi.org/10.1111/1753-0407.70140.

46. H. A. Kim, H. N. Jang, S. H. Kong, et al., "Ketonuria as an Indicator of Improvement of Renal Function in Patients With Type 2 Diabetes Receiving SGLT2 Inhibitor Treatment," *Endocrinology and Metabolism* 39, no. 4 (2024): 653–658, https://doi.org/10.3803/EnM.2024.1919.

47. I. Tomita, S. Kume, S. Sugahara, et al., "SGLT2 Inhibition Mediates Protection From Diabetic Kidney Disease by Promoting Ketone Body-Induced mTORC1 Inhibition," *Cell Metabolism* 32 (2020): 404.

48. S. Cukoski, A. Kühn, C. H. Lindemann, et al., "Ketosis Moderates the Effect on Kidney Volume in Dietary Interventions for ADPKD—More Insights on the KETO ADPKD Trial," *Nephrology, Dialysis, Transplantation* 39 (2024): gfae06907382160, https://doi.org/10.1093/ndt/gfae069.738.

49. S. Cukoski, C. H. Lindemann, S. Arjune, et al., "Feasibility and Impact of Ketogenic Dietary Interventions in Polycystic Kidney Disease: KETO-ADPKD—A Randomized Controlled Trial," *Cell Reports Medicine* 4 (2023): 101283.

50. P. Acharya, C. Acharya, C. Thongprayoon, et al., "Incidence and Characteristics of Kidney Stones in Patients on Ketogenic Diet: A Systematic Review and Meta-Analysis," *Diseases* 9, no. 2 (2021): 39.

51. E. H. Kossoff, P. L. Pyzik, S. L. Furth, et al., "Kidney Stones, Carbonic Anhydrase Inhibitors, and the Ketogenic Diet," *Epilepsia* 43, no. 10 (2002): 1168–1171.

52. N. Tangri, V. Mathur, N. L. Reaven, et al., "Association of Serum Bicarbonate With Kidney Stones in Patients With Chronic Kidney Disease: A Retrospective Cohort Study," *Clinical Kidney Journal* 16, no. 7 (2023): 1113–1121.

53. F. Pazos Pérez, "Uric Acid Renal Lithiasis: New Concepts," *Contributions to Nephrology* 192 (2018): 116–124.

54. R. CGP, S. J. Athinarayanan, R. E. Ratner, and G. E. Umpierrez, "Illnesses Associated With Ketosis Including Diabetic Ketoacidosis During Very Low-Carbohydrate and Ketogenic Diets," *Diabetes, Obesity & Metabolism* 27 (2025): 2531, https://doi.org/10.1111/dom.16252.

55. T. Hu, J. Zhang, Y. Liu, et al., "Effects of a Ketogenic Diet in Women With Polycystic Ovary Syndrome With Different Uric Acid Concentrations," *Diabetes, Metabolic Syndrome and Obesity* 15 (2022): 2333–2342, https://doi.org/10.2147/DMSO.S37292.

56. E. L. Goldberg, J. L. Asher, R. D. Molony, et al., "β-Hydroxybutyrate Deactivates Neutrophil NLRP3 Inflammasome to Relieve Gout Flares," *Cell Reports* 18, no. 9 (2017): 2077–2087, https://doi.org/10.1016/j.celrep.2017.02.004.

Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Figure S1:** Distribution of index dates among VINT participants and matched UC controls. Bars represent the count of participants initiating follow-up on a given index date, plotted separately for VINT (red) and UC (blue). The figure illustrates the temporal overlap in cohort enrollment, showing increasing accrual over time with peaks corresponding to more recent years. The overlap between VINT and UC participants across the study period reduces the potential for confounding by calendar time or seasonal effects. **Figure S2:** Risk of CKD outcomes by model adjustment. Forest plot of hazard ratios (HRs) and 95% confidence intervals for new-onset chronic kidney disease (CKD), CKD stage 3 or higher, and CKD stage 4 or higher among VINT participants compared with matched UC controls in the primary and secondary cohorts. Estimates are shown across different adjusted Cox proportional hazards models, including adjustment for demographics only, categorical medication use, continuous medication exposure modelled as proportion of days covered (PDC), and time-varying medication exposure, as well as marginal structural models (MSMs) accounting for time-varying confounding. Points indicate HRs and horizontal lines indicate 95% confidence intervals; the dashed vertical line denotes the null value (HR = 1.0). **Figure S3:** Cumulative incidence curves for new-onset CKD during follow-up stratified by mean 6-month beta-hydroxybutyrate (BHB) concentration (< 0.5 mmol/L vs. ≥ 0.5 mmol/L). Participants with CKD at baseline were excluded. Curves are displayed through 4 years to improve visualisation, although all analyses were conducted using the full 5-year follow-up period with standard right-censoring. Shaded areas represent 95% confidence intervals. Numbers at risk are shown below each panel. Estimates at later time points should be interpreted with caution because of the decreasing number of participants remaining under observation. **Table S1:** ICD-10 code sets for identifying primary, exploratory and safety outcomes assessed in the study. **Table S2:** ICD-10 code sets for identifying baseline comorbidities and other follow-up comorbidities used for matching or matching assessment. **Table S3:** List of drug names used to identify prescription drug use at baseline and during follow-up. **Table S4:** Cohort Selection Process, Inclusion and Exclusion Criteria, and Final Analytic Sample for VINT and Usual Care Cohorts. **Table S5:** Demographics and treatment characteristics of matched VINT participants used in this analysis versus unmatched VINT participants or those without closed claims. **Table S6:** Baseline characteristics of unmatched and propensity score matched secondary cohorts of VINT (with at least 6 m VINT tenure) and UC. **Table S7:** Cox regression models for all new-onset of chronic kidney disease (CKD) and stage 3 CKD and beyond, presenting the effect estimates after covariate adjustment in the primary 1:1 matched cohort analysis of VINT and UC. **Table S8:** Cox regression models for all new-onset of chronic kidney disease (CKD) and stage 3 CKD and

14631326, 2026, 10, Downloaded from https://dom-pubs.onlinelibrary.wiley.com/doi/10.1111/dom.71086, Wiley Online Library on [03/09/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

beyond, presenting the effect estimates after covariate adjustment in the secondary 1:1 matched cohort analysis of VINT and UC where VINT participants with ≥ 6 months of program engagement. **Table S9:** Cox regression models for all new-onset of chronic kidney disease (CKD) and stage 3 CKD and beyond, presenting the effect estimates after covariate adjustment in VINT and UC sensitivity analyses (IPTW-weighted model). **Table S10:** Comparison of Medication Use Between VINT Participants and Matched UC Controls Among Those with CKD diagnosis at follow-up with available prescription claims follow-up before censoring.

14631326, 2026, 10, Downloaded from https://dom-pubs.onlinelibrary.wiley.com/doi/10.1111/dom.71086, Wiley Online Library on [03/09/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License