Supplementary Table 1. Summary of clinical and observational studies assessing the effect of low carbohydrate on kidney function and disease

Study	Study Details	Details on Carbohydrate Restriction and Protein Intake	Kidney Function Findings
Clinical Trials including post-hoc analyses			
Tay J et al., 2015 [113]	Randomized controlled trial (RCT) comparing a very low-carbohydrate, high-unsaturated fat/low-saturated fat diet (LC, carbohydrate <50g/day; 14% energy) vs. a high-carbohydrate, low-fat diet (LF) on glycaemic control and CVD risk factors in T2D. Both diets were energy matched Follow-up duration 52 weeks Study included overweight and obese adults with type 2 diabetes (T2D) Baseline eGFR (mL/min/per 1.73m^2) was normal in both groups (LC, 96 and LF, 92)	Carbohydrate intake in LC stayed significantly lower than the LF group. Carbohydrate intake in the LC increased gradually from weeks 0-12 to weeks 37-52. Self-reported protein level and protein intake estimated from 24 hours urinary urea excretion was higher in LC (1.2g/kg/day) group versus LF (0.9g/kg/day).	**No negative effect on kidney function** Both intervention groups experienced non-significant decreases in eGFR (LC,- 4%; LF, -2%) and albuminuria (LC,-42%; LF, -33%) with no difference between groups. The 2-4% decrease in eGFR is consistent with age-related change in T2D and at 52 weeks, the mean eGFR was still in normal range
Tirosh A et al., 2013 [116]	RCT comparing 3 diets. Low fat (LF, restricted calorie with only 30% of the calories from fat), Mediterranean (M, moderate fat, restricted calorie diet) Low carbohydrate (LC, non-restricted calorie diet, with 20g carbohydrate per day during the first 2 month of induction phase and 120g carbohydrate per day during the maintenance phase) Follow-up duration 24 months Study included participants with BMI ≥	The LC intervention arm had significantly lower intake of carbohydrate and higher intake of protein than the other two intervention arms (LF and M) Only 8.3% of the LC arm participant had detectable urinary ketone at 24 mos (4.8% LF and 2.8% M participants had detectable urinary ketones)	**Beneficial effect on kidney function** All three intervention groups reported significant increase in eGFR from baseline but no significant difference between groups. LC, +5.3%; M, +5.2%; LF, +4.0% Among 23 participants who met microalbuminuria criteria at baseline, all three intervention

	27kg/m^2 and 14% of them had T2D Baseline eGFR (mL/min/per 1.73m^2) in all three intervention groups (LC, 71.1; M, 70.2 and LF, 70.3)		arms had a non -significant decrease in albumin (LC, -37.0 mg/dL; M, -0.4 mg/dL and LF, -52.7mg/dL) Subgroup analysis among those with moderate CKD stage III at baseline also reported significant increase in eGFR from baseline in the LC and M intervention arms. LC, +10.0%; M, +6.0%; LF, +5.4%
Brinkworth GD et al., 2010 [114]	RCT comparing energy-restricted very low carbohydrate diet (LC) and isocaloric conventional high carbohydrate diet (HC) Follow-up duration 52 weeks Baseline eGFR (mL/min/per 1.73m^2) was normal in both groups (LC, 90 and HC, 83.8)	The LC group consumed significantly less carbohydrate and more protein than the HC arm.	**No negative effect on kidney function** No significant changes in serum creatinine and eGFR from baseline to 1 year in both intervention arms
Friedman AN et al., 2012 [93]	RCT comparing low carbohydrate, high protein (LC) and energy restricted low fat (LF) groups. Follow-up duration 24 months Study included participants with BMI ranging from 30 to 40 kg/m^2 without T2D	The first 12 weeks, the LC arm limited carbohydrate intake <20g per day. After 12 weeks, participants gradually increased carbohydrate intake at a rate of 5g/d per week.	**Beneficial effect on kidney function only at 3 and 12 months** LC reported significant decrease in serum creatinine and cystatin C at 3 months and relative increase in creatinine clearance at 3 months that lasted up to 12 months. Both intervention arms had a significant decrease in urinary albumin excretion at 24 months

Zainordin NA et al., 2021 [115]	RCT comparing very low carbohydrate plus low protein diet (VLCBD) with standard low protein/low salt (Control) diet groups. Follow-up duration 12 weeks Study included individuals with T2D and stable CKD stages 2 or 3 Baseline eGFR (mL/min/per 1.73m^2) were 71.7 in VLCBD arm and 65.0 in control arm	The VLCBD group had significantly lower carbohydrate count and higher daily intake of protein at 6 and 12 weeks compared to control.	**No negative effect on kidney function** No significant decrease in eGFR and worsening of serum creatinine in both intervention group (with no difference between groups) There was a greater decrease in urine microalbumin in the VLCBD group (not significant from baseline) but no change in the control group.
Facchini FS et al., 2003 [117]	RCT compared a carbohydrate-restricted, low iron available, polyphenol enriched (CR-LIPE) diet with a control group prescribed a standard protein restricted diet. Mean follow-up duration 3.9 ± 1.8 years (approximately 4 years) Study included individuals with T2D with different levels of renal failures including albuminuria. Baseline eGFR (mL/min) were 64.0 in CR-LIPE arm and 62.0 in control arm.	The CR-LIPE restricted carbohydrate up to 30% and had a protein intake of 25 to 30% (2 to 2.4g/day) of the energy. vs Control diet restricted protein up to 10% (0.8g/day) and had a carbohydrate intake of 65% of the energy	**Beneficial effect on all-cause mortality and kidney endpoints** 191 patients were enrolled, and 170 patients met the outcome or completed the last follow-up. Doubling of serum creatinine reported in 19 patients on CR-LIPE (21%) and in 31 control patients (39%), relative risk (RR) 0.53 (95% CI 0.33-0.86, p<0.01) All-cause mortality occurred in 8 patients on CR-LIPE (8.8%) and in 14 control subjects (17.7%), RR 0.5 (95% CI 0.2-1.12). Dialysis or renal replacement therapy occurred in 10 patients on CR-LIPE (11.0%) and in 17

			control subjects (21.5%)
Bruci A et al., 2020 [119]	A single arm, prospective real-life follow-up study on individuals following a very low-calorie ketogenic diet (VLCKD) Follow-up duration 3 months Study included individuals with obesity. Baseline eGFR (mL/min/per 1.73m^2) was 94.5	Ketosis was confirmed each week by measuring urinary ketone levels.	**No negative overall effect on kidney function but positive effect observed in individuals with diminished renal function at baseline.** No significant change in eGFR from baseline to 3 months in the whole cohort In the subgroup analysis after stratifying individuals into normal kidney function, NKF (eGFR≥90) and mild chronic kidney disease, MCKD (eGFR between 60 to 89) - no significant increase in eGFR reported in the NKF but the MCKD group had a significant 7.7% increase in eGFR at 3 months. 27.7% of the participants in the MCKD group normalized their eGFR (eGFR≥90) at 3 months
Friedman AN et al., 2013 [118]	A single arm, observational prospective follow-up on individuals following very low calorie ketogenic diet Study only included individuals with known diabetes nephropathy with baseline eGFR <40 mL/min/per 1.73m^2 and urine albumin excretion >30g/day (only six individuals included) Follow-up duration 12 weeks	Carbohydrate intake was restricted to less than 50g/day	**Beneficial effect on kidney function** A significant 12% reduction in serum creatinine and cystatin C. A significant increase in eGFR There was a non-significant 36% decrease in urine albumin excretion

Observational studies			
Unwin D et al., 2021 [120]	A retrospective chart analysis of routine clinical data from a suburban GP practice where a low carbohydrate diet is prescribed routinely. n=143 included in the analysis who persisted in the diet and with available data. Average follow-up duration 30 months Baseline eGFR (mL/min/per 1.73m^2) was 85.5	Participants confirmed maintaining the low carbohydrate diet lifestyle	**Beneficial effect on kidney function** A significant increase in eGFR (2.8%) and decrease in urine albumin creatinine ratio. Serum creatinine also significantly decreased with 88% of individuals showing improvement in the creatinine levels
Mitchell NS et al., 2021 [121]	A retrospective cohort study of an outpatient ketogenic diet provider clinic. Included only patients who had at least two visits with the keto diet provider. Change in kidney function assessed at 1 year n=2004 included in the final analysis, which includes n=823 with baseline eGFR ≥ 90 (E1) n= 881 with baseline eGFR 60-89 (E2) n=300 with baseline eGFR 30-59 (E3) Baseline eGFR (mL/min/per 1.73m^2) of the overall cohort was 84.0	Recommended to restrict carbohydrate <20g and no restriction in protein and fat intake. No details on adherence reported in the paper.	**Beneficial effect observed in individuals with diminished renal function at baseline.** Among those in the E1 category with or without T2D, eGFR decreases approximately 4-6 mL/min/1.73m^2 regardless of weight loss categories. Among those in the E2 category without T2D, eGFR improves approximately 3-4 mL/min/1.73m^2 regardless of weight loss categories. Those in the E2 category and with T2D, eGFR improves 1-2 mL/min/1.73m^2 regardless of weight loss categories. For those in E3 category without T2D, with at least 5% weight

			loss, the eGFR improves 3 mL/min/1.73m^2 and without any weight loss, the eGFR improves 1 mL/min/1.73m^2 For those in E3 category and with T2D, no changes in eGFR regardless of degree of weight loss
Wilmsen N et al., 2022 [122]	A retrospective observational cohort study of participants who enrolled in the Reverse Diabetes 2Now program. Participants with baseline eGFR<70 mL/min/1.73m^2 were included in the final analysis (n=45) Baseline median eGFR (mL/min/per 1.73m^2) of those included in the analysis and with available data is 62.0.	Reverse Diabetes 2Now program aims to improve diet quality, sleep and physical activity. Participants were prescribed a restricted carb Mediterranean diet, rcMD. It is not very clear how low carbohydrate was restricted in the intervention.	**Beneficial effect on kidney** A significant increase in median eGFR from 62.0 at baseline to 69.0 at 6 months (an average increase of 8.1%). At 12 months (n=22 with available data), median eGFR (63.5) remains stable with no difference from baseline. No changes in urinary albumin creatinine ratio (UACR) at 6 and 12 months. The median UACR was within normal range at baseline, 6 and 12 months