

PMID	First Author	Title	Year	Study Type	CVD	RF by CQ	Country	Setting	Blinding	Int Length	Total Study Duration	Main Study Objective	Total N	Target Population	Eligibility Criteria	Patient Characteristics	Int. n at Baseline (n at Final Follow-up)	Int Type	Specific Intervention	Control n at Baseline (n at Final Follow-up)	Specific Control	Outcomes Measured	Results/CI	Significance S (p<0.05 or non-overlapping CI); S* (p<0.01); NS (p>0.05 or overlapping CI)	Safety and Adverse Events	Additional Findings	Summary	Main Reported Findings by Critical Question	
8621870	Wheeler ML	Controlled portions of presweetened cereals present no glycemic penalty in persons with insulin-dependent diabetes mellitus	1996	RCT (crossover)	None	Q10 (RF6)	USA	Clinical	None	1 d	13 d Includes 3 72-hr washout periods	Determine metabolic responses to commercially sweetened flaked corn cereal, unsweetened flaked corn cereal, glucose, and sucrose in teenagers and young adults with insulin-dependent diabetes mellitus	24	Pediatric/Young Adults	Insulin-dependent diabetes mellitus Exclusions: > 120% desirable weight Fasting TG > 2.3 mmol/L Questionable insulin dependence (C-peptide > 0.3 nmol/L)	14-25 yr Mean age (SD):19.8 yr (3.5) Males: 16 White: 20 Non-white: 4 Mean duration of diabetes: 7.0 yr (4.2)	24 (NR)	Behavioral	Intervention 1: Commercially sweetened corn flake cereal 42% CHO energy derived from sucrose Intervention 2: Unsweetened corn flake cereal 3% CHO energy derived from sucrose Intervention 3: Sucrose Intervention 4: Glucose Meals in each crossover intervention arm provided CHO amount of 50 g/1.73 m ² of body surface area	N/A	N/A	Primary: AUC plasma glucose [mmol/L x hr (SD)] Mean free insulin [pmol/L (SD)] Mean TG [mmol/L (SD)]	Primary: Glucose: 21.6 (3.99) Sweetened cereal: 19.30(5.80) Unsweetened corn cereal: 19.02(3.84) Sucrose: 17.29(4.77) No difference between groups Secondary: No difference between groups	S (p<0.05 or non-overlapping CI); S* (p<0.01); NS (p>0.05 or overlapping CI)	None described	Glycemic response greater for glucose than for any other intake at all times until 180 mins post meal. Cereals differed little as the sugar/starch contents do not vary much	In children with T1DM, a glucose load produced greater post meal response in plasma glucose than sucrose.	Q10. Glucose produced greater post meal response in plasma glucose than sucrose. This result does not address any CQ.	
1177207	Jones KL	Effect of metformin in pediatric patients with type 2 diabetes: a randomized controlled trial	2002	RCT	None	Q10 (RF6, RF8) Q13 (RF5)	USA, Russia, Ukraine, Belarus, Poland	Clinical	Double	16 wk	Approx. 15 mo Includes open-label phase	Evaluate the safety and efficacy of metformin in children with type 2 diabetes	82	Pediatric/Young Adults	8-16 yr Type 2 diabetes FPG levels 7.0-13.3 mmol/L HbA1c ≥ 7.0% Stimulated C-peptide ≥ 0.5 ng/ml BMI > 50 th percentile for age Exclusions: ≥ 1 positive immune marker for type 1 diabetes Diabetic ketoacidosis ≤ 8 wk before screening Renal insufficiency	Mean age (SD): Arm 1: 13.9 yr (1.8) Control Arm: 13.6 yr (1.8) Males: Arm 1: 12 Control Arm: 13 White: Arm 1: 17 Control Arm: 13 Black: Arm 1: 11 Control Arm: 13 Asian/Pacific Islander: Arm 1: 3 Control Arm: 1 Hispanic/Latino: Arm 1: 9 Control Arm: 9 Other race: Arm 1: 2 Control Arm: 4	42 (19)	Pharmacologic	Arm 1: Metformin 500 mg bid + counseling (MET) 500 mg tablets titrated at 1 wk intervals beginning with 2 tablets/d to a maximum of 4 tablets/d Counseling on diet and exercise at each visit	40 (3)	Control Arm: Placebo + counseling (CON) Counseling on diet and exercise at each visit	Primary: Adjusted mean change in fasting plasma glucose [mmol/L (95% CI)] Mean fasting plasma glucose [mmol/L (95% CI)] Secondary: Mean HbA1c [% (SD)] Adjusted mean HbA1c [% (95% CI)] Mean change in TC [mg/dL] Mean change in LDL-C [mg/dL] Adjusted mean change in HDL-C [mg/dL] Mean change in TG [mg/dL] Mean change in weight [kg] Mean change in BMI [kg/m ²] Simulated C-peptide	Primary: MET: -2.4 (CI:-3.5,-1.3);CON:+1.2(CI: 0.1, 2.3) MET: 7.0(2.2); CON: 11.5(4.5) MET: 8.2(1.3) to 7.2 (1.2); CON:8.9(1.4) to 8.9 (1.6) MET: 7.5 (CI: 7.2, 7.8);CON: 8.6 (CI: 8.3, 9.0) MET: -0.25(-0.7); CON:+0.01(0.7) MET:-0.11(-4.2); CON:+0.10(+4.0) No change in any of these variables	S** S** S** S* S p=0.053 NS for all	Adverse events occurred in 70% of MET subjects vs 60% of placebo group.	Decrease in glucose seen after only 2 weeks of treatment.	Metformin improves glycemic control in adolescents with DM2.	Q10. Metformin improves glycemic control in adolescents with DM2.	
15043687	Cavallo A	Blood pressure response to melatonin in type 1 diabetes	2004	RCT (crossover)	None	Q13 (RF4)	USA	Clinical	Double	1 wk	22 d Includes 1 wk washout	Determine whether melatonin affects BP during sleep of normotensive adolescents with type 1 diabetes	11	Pediatric/Young Adults	14-18 yr Type 1 diabetes ≥ 1 yr Stable diabetes (no documented nocturnal hypoglycemia or ketoadosis in 6 mo) Exclusions: Medical history of hypertension Use of anti-hypertensive medications Microalbuminuria or diagnosed renal disease Immune deficiency	Mean age (SD): Arm 1: 16.0 yr (1.6) Males: 8 Mean duration of diabetes: 7.0 yr (3.5)	11 (10)	Pharmacologic	Intervention: Melatonin 5 mg (NT) Taken 0.5 h before bedtime each night of the treatment wk 10 healthy controls matched by age and sex were used as a reference group	11 (10)	Control: Placebo 5 mg (CON) Taken 0.5 h before bedtime each night of the treatment wk Mean Sleep SBP [mmHg (SD)] Mean Sleep DBP [mmHg (SD)] Decline in mean SBP from wake to sleep interval [mmHg (SD)] Decline in mean DBP from wake to sleep interval [mmHg (SD)]	Primary: Mean 24 h SBP [mmHg (SD)] Mean 24 h DBP [mmHg (SD)] Mean Sleep SBP [mmHg (SD)] Mean Sleep DBP [mmHg (SD)] Decline in mean SBP from wake to sleep interval [mmHg (SD)] Decline in mean DBP from wake to sleep interval [mmHg (SD)] Secondary: Sleep Interval (hours) Awakenings (number per night)	Primary: No difference between groups No difference between groups No difference between groups INT: 14.7(4.4); CON: 16.8(5.9) INT: 17.8(4.4); CON: 16.0 (3.0) Secondary: No difference between groups INT T1: 3.2 (2.6) vs INT T2: 0.9 (1.1)	NS NS NS NS S*	Rare and not different between groups.	In children with T1DM, melatonin significantly increased nighttime DBP.	Q13. In children with T1DM, melatonin significantly increased nighttime DBP.		
16818571	MacKenzie KE	Folate and vitamin B6 rapidly normalize endothelial dysfunction in children with type 1 diabetes mellitus	2006	RCT	FMD	Q2 (RF6) Q13 (RF4, RF5, RF7)	Australia	Clinical	Double	8 wk	8 wk	Evaluate the effect of folate and vitamin B6 on endothelial function in children with type 1 diabetes mellitus	124	Pediatric/Young Adults	Type 1 diabetes for ≥ 1 yr Normotensive No clinically detectable microvascular disease Exclusions: Cellac disease Active smokers Taking supplemental vitamins, including multivitamins	Mean age (SD): Arm 1: 14.3 yr (2.6) Arm 2: 14.1 yr (2.6) Arm 3: 14.3 yr (2.9) Control Arm: 13.6 yr (2.8) Males: Arm 1: 23 Arm 2: 16 Arm 3: 14 Control Arm: 18 Mean duration of diabetes (SD): Arm 1: 5.8 yr (3.65) Arm 2: 5.5 yr (4.46) Arm 3: 5.9 yr (4.06) Control Arm: 4.2 yr (2.84) Elevated cotinine levels: 5	Arm 1: 31 (31) Arm 2: 31 (31) Arm 3: 30 (30)	Dietary Supplements	Arm 1: Folate 5 mg qd + vitamin B6 placebo qd Arm 2: Vitamin B6 100 mg qd + folate placebo qd Arm 3: Folate 5 mg qd + vitamin B6 100 mg qd	32 (30)	Control Arm: Folate placebo + vitamin B6 placebo	Primary: Immediate mean change in FMD [% (SD)] FMD at 8 weeks [% (SD)] Change in FMD (%) from baseline	Primary: Folate: 1.88 (3.93) to 10.46 (8.12); B6: 4.7 (4.94) to 8.36 (4.31) CON: 6.16(3.56) to 5.90(4.34) Folate: 2.6 (4.27) to 9.67 (6.00); B6: 3.5 (4.02) to 8.31 (4.21); Combo: 2.79 (3.45) to 10.48 (4.39) No difference between groups at any time. All 3 INT groups increased, no change for placebo	S** S* NS S** S** NS between groups.	None	Baseline FMD independently determined by resting diameter and LDL. All 3 treatment groups had increased FMD at 8 weeks vs no change in CON. Change in FMD correlated with RBC folate, serum folate and B6.	In adolescents with T1DM, folate and B6 increase FMD to near control levels beginning within 2 hrs of treatment and persisting to 8 wks. If conformed and sustained, this finding in pilot with known compromised endothelial function has the potential for long-term beneficial effects on vascular outcomes.	Q10. In adolescents with T1DM, folate and B6 increase FMD to near control levels beginning within 2 hrs of treatment and persisting to 8 wks. If conformed and sustained, this finding in pilot with known compromised endothelial function has the potential for long-term beneficial effects on vascular outcomes.	
17763007	Davis JN	Feasibility of a home-based versus classroom-based nutrition intervention to reduce obesity and type 2 diabetes in Latino youth	2007	RCT	None	Q10 (RF8) Q13 (RF4, RF5, RF6, RF9, RF14)	USA	Mult settings	None	12 wk	12 wk	Compare the dietary, physiological and metabolic effects of a 12-wk modified carbohydrate nutrition intervention when disseminated in an individualized home-based format versus a group classroom-based format	30	Parental/Family/Caregiver	12-17 yr Female Hispanic origin BMI > 85 th percentile for age and sex Absence of diabetes as determined by an oral glucose tolerance test Not presently taking medications or diseases that could influence dietary intake, body composition and fat distribution, or insulin action and secretion Not involved with any dietary or weight loss program within the previous 6 mo	Mean age (SD): Arm 1: 15.1 yr (1.3) Arm 2: 14.2 yr (1.7) Patient characteristics available only for participants who completed the study	Arm 1: 15 (11)	Behavioral	Arm 1: Individualized home-based dietary intervention Dietary intervention targeted 2 goals: 1) x 10% of total daily calorie intake from added sugar, and 2) ≥ 14 g/1,000 kcal of dietary fiber/d; also encouraged a diet with 45-55% of calories as carbohydrate and 30-35% of calories from fat Diet was not energy restrictive; participants were encouraged to eat to satiety & snack when hungry 90-min weekly sessions for 12 wks; each session included a hands-on cooking activity, a healthy snack, an interactive game, workbook style handouts, review of dietary recall and a goal setting exercise Parents were required to attend at least 4 sessions;other family members were welcome to attend	Arm 2: 15 (12)	Arm 2: Group classroom-based dietary intervention Participants in Arm 2 received an identical intervention to Arm 1 except that the intervention was delivered to a group in a classroom setting, Arm 2 participants engaged in standard 10-15 min goal setting activities each wk rather than motivational interviewing, and Arm 2 families received \$25 worth of grocery gift certificates each wk	Arm 2: 15 (12)	Refined carbohydrate intake [servings/d(SD)] Added sugar intake [kcal] Dietary fiber intake [g/1000 kcal] Sugary beverage intake [serv/d(SD)] Mean BMI z-score (SD) Mean weight [kg (SD)] Mean BMI [kg/m ² (SD)] Mean waist circumference [cm ² (SD)] Mean total fat mass [kg (SD)] Mean percent fat [% (SD)] Mean total lean tissue mass [% (SD)] Mean blood pressure (systolic/diastolic) [mmHg] Mean TC [mg/dL (SD)]	Groups combined - no difference between arms. 4.1(2.8) to 2.7(1.4) 18.6% to 12.5% 8.6g/1000 kcal to 12.4 g/1000 kcal. 1.9(1.7) to 0.6(0.6) CLASS: 2.0(0.4) to 1.9(0.4) vs HOME: 2.1(0.5) to 2.0(0.5) No significant change in either group for this or any other variable below this.	S* S* S* S* S for each group NS for all below this.	None.	This is a feasibility study and may have been underpowered to assess metabolic outcomes. In this small efficacy pilot study, a nutrition intervention delivered in the classroom and one delivered in an intensive, individualized home format both exhibited significant improvements in dietary intake and in BMI z-score with no difference between the interventions. Neither intervention significantly impacted metabolic parameters.	Q10,13. In this small efficacy pilot study, a nutrition intervention delivered in the classroom and one delivered in an intensive, individualized home format both exhibited significant improvements in dietary intake and in BMI z-score with no difference between the two. Neither intervention significantly impacted metabolic parameters.	
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