Supplementary Tables and Figures

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Supplementary Figure 23. Subgroup analyses for addition studies investigating the effect of adding excess calories to the diet in the form of food sources of fructose-containing sugars on fasting blood insulin.

Supplementary Figure 24. Risk of bias (using The Cochrane Collaboration Tool) subgroup analysis for substitution studies investigating the effect of isocaloric exchange of food sources of fructose-containing sugars for other macronutrients on fasting blood insulin.

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Supplementary Figure 26. Publication bias funnel plots for the effect of food sources of fructose-containing sugars on glycemic control in substitution and addition studies.

Supplementary Figure 27. Trim and Fill funnel plot for the effect of food sources of fructose-containing sugars on fasting blood glucose in substitution studies.

Supplementary Table 1. Search strategy for the effect of food sources of fructose-containing sugars on glycemic control.

Database and search terms		
Medline	**Embase**	**The Cochrane library of control studies**
1 exp Fructose/ 2 exp Dietary Sucrose/ 3 HFCS.mp. 4 sugar.mp. 5 sugar* sweetened beverage*.mp. 6 exp Honey/ 7 glyc?em*.mp. 8 exp insulin/ 9 HbA1c.mp or exp hemoglobin A, glycosylated/ 10 fructosamine.mp. 11 exp blood glucose/ 12 gly*albumin.mp. 13 1 or 2 or 3 or 4 or 5 or 6 14 7 or 8 or 9 or 10 or 11 or 12 15 13 and 14 16 limit 15 to animals 17 15 not 16 18 clinical trial.mp. 19 clinical trial.pt. 20 random:.mp. 21 tu.xs. 22 18 or 19 or 20 or 21 23 17 and 22	1 exp Fructose/ 2 exp sucrose/ 3 HFCS.mp. 4 exp sugar/ 5 sugar* sweetened beverage*.mp. 6 exp Honey/ 7 exp glycemic control/ or glyc?em*.mp. 8 exp insulin/ 9 HbA1c.mp or exp hemoglobin A1c/ 10 fructosamine blood level/ or fructosamine.mp. 11 exp glucose blood level/ 12 exp glucosylated albumin/ or gly*albumin.mp. 13 1 or 2 or 3 or 4 or 5 or 6 14 7 or 8 or 9 or 10 or 11 or 12 15 13 and 14 16 limit 15 to animals 17 15 not 16 18 limit 17 to animal studies 19 17 not 18 20 random:.tw. 21 clinical trial:.mp. 22 exp health care quality/ 23 20 or 21 or 22 24 19 and 23	1 Fructose/ 2 Dietary Sucrose/ 3 HFCS.mp. 4 sugar.mp. 5 sugar* sweetened beverage*.mp. 6 Honey/ 7 glyc?em*.mp. 8 Insulin/ 9 HbA1c.mp, hemoglobin A or glycosylated/ 10 fructosamine.mp. 11 blood glucose/ 12 gly*albumin.mp. 13 1 or 2 or 3 or 4 or 5 or 6 14 7 or 8 or 9 or 10 or 11 or 12 15 13 and 14

For all databases, the original search date was November 3rd 2015; updated searches were performed on May 29th 2017 and April 25th 2018 .

Supplementary Table 2. Characteristics of included intervention studies of the effect of food sources of fructose-containing sugars on glycemic control

Study, Year	Participants	Mean Age, years (SD or Range)	Mean BW, units (SD or range)	Mean BMI, kg/m^2 (SD)	Setting	Baseline			Design	Feeding Control[a]	Randomization	Fructose-Containing Sugars Dosage, g/d (% E)[b]	Intervention or comparator	Food source	Diet[c]	Energy Balance[d]	Follow-Up	Funding Sources[e]
						FBG, mmol/L (SD or range)	FBI, pmol/L (SD or range)	HbA1c, % (SD)										
Substitution Studies (Isocaloric comparison)																		
Fruit																		
Agebratt et al. 2016	30 H (18 M, 12 W)	23.5 (3.7)		22.3 (1.9)	OP, Sweden				P	Supp	Yes						8 wk	A
Intervention	15 H (7 M, 8 W)		66.5 kg (8.7)	22.2 (1.6)		5.1 (0.4)	53.7 (21.5)	5.1 (2.4)				25.6 (~3.8)	Fruit	7 cal/kg bw/ day of fruit	NR	Neutral		
Control	15 H (11 M, 4 W)		73.6 kg (9.0)	22.5 (2.3)		5.3 (0.5)	50.6 (20.1)	5.1 (2.5)					Fat	7 cal/kg bw/ day of walnuts				
Basu et al. 2010 (BB)		49.8 (15.3)	-	37.8 (11.2)	OP, USA	-	-	-	P	Supp	Yes				NR	Positive	8 wk	A, I
Intervention	25 MetS (2 M, 23 W)	51.5 (15.0)		38.1 (7.5)								30 (~6) [l]	Fruit	Freeze dried blueberry beverage				
Control	23 MetS (2 M, 21 W)	48.0 (15.8)		37.5 (14.4)									Water	Water				
Basu et al. 2010 (SB)		46.7 (16.6)	102.3 kg (9.5)	37.8 (8.9)	OP, USA	5.1 (0.7)	-	-	P	Supp	Yes					Positive	8 wk	A, I
Intervention	15 MetS (0 M, 15 W)	48.0 (20.5)	102.0 kg (11.6)	39.0 (7.7)		5.2 (0.8)						~14.6 (~3.2) [f]	Fruit	Freeze dried strawberry beverage	45:37:13			
Control	12 MetS (2 M, 10 W)	45.0 (10.4)	102.7 kg (6.6)	36.4 (10.4)		5.0 (0.7)							Water	Water	46:35:15			
Christensen et al. 2013		58 (12)	91.8 kg (16.9)	32 (5.5)	OP, Denmark	6.6 (1.1)	-	-	P	DA	Yes				NR	Negative	12 wk	NR
Intervention	32 DM2 (18 M, 14 W)	59 (12)	92.4 kg (17)	32 (5)		6.74 (1.2)						~23.1 (~4.6) [f]	Fruit	Incorporate ≥ 2 fruit/d into diet				
Control	31 DM2 (13 M, 18 W)	57 (12)	91.2 kg (17)	32(6)		6.53 (1.1)							Mixed Comparator	Incorporate ≤ 2 fruit/d into diet				
Conceição de Oliveira et al. 2003		44.0 (4.5)		-	OP, Brazil	5.2 (0.9)	74.7 (57.3)	-	P	Supp	Yes				55:30:15	Negative	12 wk	I
Interventiengin on	26 OW/OB, HCL (0 M, 26 W)	43.7 (4.8)	77.7 kg (10.8)			5.3 (1.0)	85.4 (62.5)					Apple, 22.8 (~5.6) ; pear, 19.2 (~3.8)	Fruit	300 g/d apple, 300g/d pear				
Control	9 OW/OB, HCL (0 M, 9 W)	45.0 (3.8)	78.9 kg (9.7)			5.1 (0.6)	43.8 (17.4)						Mixed Comparator	Oat Cookie				
Hegde et al. 2013		58.0 (9.2)	-	24.9 (3.9)	OP, India	8.3 (2.5)	-	8.0 (1.4)	P	DA	No				NR	Positive	3 mo	A
Intervention	60 DM2	58.5 (9.6)		24.4 (3.9)		7.9 (1.5)		8.0 (1.3)				~16.5 (~3.3) [f]	Fruit	Incorporate 2 fruit/d into regular diet				
Control	63 DM2	57.5 (8.9)		25.3 (3.9)		8.6 (3.1)		8.0 (1.5)					Mixed Comparator	Regular diet				
Kolehmainen et al. 2012		51.7 (6.5)			OP, Finland	6.0 (0.7)	103.5 (64.7)	-	P	Supp	Yes					Neutral	8 wk	A
Intervention	15 MetS (5 M, 10 W)	53 (6)	85.4 kg (12.1)	31.4 (4.7)		6.1 (0.9)	100.7 (70.8)					~18.8 (~4.0) [g]	Fruit	200 g/d bilberry puree and 40 g/d dried bilberries equivalent to 400 g/d fresh bilberries	~52:31:17			
Control	12 MetS (3 M, 9 W)	50 (7)	93.1 kg (10.8)	32.9 (3.4)		5.8 (0.4)	107.0 (59.0)						Starch	Other Carbohydrates	~50:34:16			
Lehtonen et al. 2010		42.9 (35-52)	-		OP, Finland	5.0 (0.4)	57.3 (27.9)	5.3 (0.2)	P	Supp	Yes					Neutral	20 wk	A, I
Intervention	28 OW (0 M, 28 W)			29.3 (2.2)		5.1 (0.4)	55.6 (27.1)	5.3 (0.2)				~14.7 (~3.3) [g]	Fruit	163 g/d fresh berries	~50:32:17			
Control	22 OW (0 M, 22 W)			29.5 (1.8)		4.9 (0.4)	59.0 (29.2)	5.2 (0.2)					Mixed comparator	Snacks	~46:35:19			
Madero et al. 2011	131 OW/OB (29 M, 102 W)	38.3 (8.8)	80.9 kg (13.4)	32.4 (4.5)	OP, Mexico	5.0 (1.2)	125.1 (70.8)	-	P	DA	Yes				50:30:15	Negative	6 wk	A
Intervention	65 OW/OB (15 M, 50 W)	40.2 (8.1)	79.1 kg (13.4)	32.8 (4.5)		4.9 (1.2)	125.5 (71.1)					~60 (~14)	Fruit	Fruits				
Control	66 OW/ OB (14 M, 52 W)	37.6 (9.3)	82.7 kg (13.3)	32.9 (4.5)		5.1 (1.2)	124.7 (71.1)					<10-20	Starch	Low fructose diet substituted with cereal products				
Moazen et al. 2013	36 DM2 (13 M, 23 W)	51.6 (11.1)			OP, Iran	10.0 (4.1)	-	7.3 (1.7)	P	Supp	Yes					Neutral	6 wk	A, I
Intervention	19 DM2	51.9 (8.3)	75.8 kg (9.3)	27.3 (3.3)		8.9 (2.8)		7.2 (1.6)				~14.6 (~3.2)	Fruit	Freeze dried strawberry beverage equivalent to 500 g fresh strawberries				
Control	17 DM2	51.2 (13.9)	73.0 kg (11.8)	28.7 (4.2)		11.2 (5.0)		7.5 (1.9)					Lactose	Sugar-free strawbery flavored beverage with lactose				
Rodriguez et al. 2005		32.6 (5.8)			OP, Spain	5.1 (0.5)	46.1 (44.3)	-	P	DA	Yes				55:30:15	Negative	8 wk	A
Intervention	7 OB (0 M, 7 W)		91.6 kg (6.0)	34.2 (2.6)		5.2 (0.5)	52.8 (59.0)					~45.0 (13.8)	Fruit	High fruit diet				
Control	8 OB (0 M, 8 W)		91.1 kg (13.0)	35.6 (3.3)		5.0 (0.5)	40.3 (29.2)					~12.6 (4.0)	Starch	Low fruit diet with substitution for other carbohydrates				
Singh et al. 1997		50.5 (8.5)		-	OP, India	6.1 (0.6)	-	-	P	Supp	Yes					Neutral	24 wk	NR
Intervention	52 HTN, HCL (43 M, 9 W)	49.1 (7.5)	67.8 kg (9.6)			6.1 (0.6)						~36.8 (~7) [f]	Fruit	412 g/d guava	63:23:14			
Control	49 HTN, HCL (45 M, 4 W)	52.0 (9.2)	69.2 kg (11.4)			6.2 (0.7)							Mixed comparator	Refined CHO, saturated fat and cholesterol	57:29:14			

Supplementary Table 2. (Continued)

Study, Year	Participants	Mean Age, years (SD or Range)	Mean BW, units (SD or range)	Mean BMI, kg/m^2 (SD)	Setting	Baseline			Design	Feeding Control[a]	Randomization	Fructose-Containing Sugars Dosage, g/d (% E)[b]	Intervention or comparator	Food source	Diet[c]	Energy Balance[d]	Follow-Up	Funding Sources[e]
						FBG, mmol/L (SD or range)	FBI, pmol/L (SD or range)	HbA1c, % (SD)										
Dried Fruit																		
Anderson et al. 2014		60.6			OP, USA	5.3 (0.6)	-	5.9 (0.4)	P	Supp	Yes				NR	Neutral	12 wk	I
Intervention	31 MetS (12 M, 19 W)	60.3	86.3 kg (12.2)	30.0 (2.8)		5.3 (0.7)		5.9 (0.4)				~60 (~12)	Fruit	84 g/d raisins				
Control	15 MetS (9 M, 6 W)	61.1	85.2 kg (12.4)	29.2 (2.3)		5.2 (0.3)		5.8 (0.5)					Mixed comparator	Processed snacks				
Bays et al. 2015		58.4			OP, USA	8.5 (1.8)	88.6 (93.8)	7.4 (0.9)	P	Supp	Yes				NR	Neutral	12 wk	I
Intervention	27 DM2 (17 M, 10 W)	58	-	34 (5)		9.0 (1.9)	97.2 (111.1)	7.6 (1.0)				~60 (~12)	Fruit	84 g/d raisins				
Control	19 DM2 (10 M, 9 W)	59	-	37 (7)		7.8 (1.5)	76.4 (62.5)	7.1 (0.6)					Mixed comparator	Processed snacks				
Kaliora et al. 2016	55 NAFLD (23 M, 32 W)				OP, Greece				P	DA	YES				50:30:20	Neutral	24 wk	I
Intervention	28 NAFLD (13 M, 15 W)	50.7 (10.9)	85.7 (14.3)	29.7 (22.2)		5.3 (0.7)	109.7 (50.0)	5.8 (0.5)				36 (7.5)	Fruit	36 g/d currant				
Control	27 NAFLD (10 M, 17 W)	51.6 (9.4)	82.0 (3.0)	29.1 (21.8)									Diet alone	Diet alone				
Kanellos et al. 2014		63.4 (7.3)		-	OP, Greece	7.8 (1.9)	-	6.7 (0.8)	P	Supp	Yes				NR	Neutral	24 wk	A, I
Intervention	26 DM2 (15 M, 11 W)	63.7 (6.3)	83.4 kg (13.8)			7.7 (1.3)		6.5 (0.6)				~24.5 (~4.9)	Fruit	36 g/d raisins				
Control	22 DM2 (10 M, 12 W)	63.0 (8.5)	81.2 kg (14.3)			7.9 (2.4)		6.9 (0.9)					Mixed Comparator	Snacks				
Fruit Juice																		
Ribeiro et al. 2017	78 OB (24 M, 54 W)	36 (1.0)	-	33 (3.0)	OP, Brazil	4.8 (0.5)	104.2 (41.7)	-	P	Supp	Yes	44 (~8.8)						
Intervention	39 OB	37 (1.0)		33 (3.0)		4.8 (0.6)	104.2 (41.7)						Fruit	Orange Juice	NR	Negative	12 wk	A,I
Control	39 OB	33 (1.0)		35 (4.0)		4.7 (0.3)	104.2 (41.7)						Mixed comparator	Energy equivalent food item				
SSBs																		
Aeberli et al. 2011 (HD)	29 H (29 M, 0 W)	26.3 (6.6)	73.7 kg (8.8)	22.4 (1.9)	OP, Switzerland	4.5 (0.5)	-	-	C	Supp	Yes	80 (~13)				Neutral	3 wk	A, I
Intervention													Fructose, sucrose	Fructose SSB, sucrose SSB	~55:32:13			
Control													Glucose	Glucose SSB	~57:31:13			
Aeberli et al. 2011 (MD)	29 H (29 M, 0 W)	26.3 (6.6)	73.7 kg (8.8)	22.4 (1.9)	OP, Switzerland	4.5 (0.5)	-	-	C	Supp	Yes	40 (~7)				Neutral	3 wk	A, I
Intervention													Fructose	Fructose SSB	~51:35:14			
Control													Glucose, starch	Glucose SSB, low fructose diet	~49:35:15			
Aeberli et al. 2013	9 H (9 M, 0 W)	22.8 (1.7)	-	22.6 (1.4)	OP, Switzerland	-	-	-	C	Supp	Yes	80 (~14)				Neutral	3 wk	A
Intervention													Fructose, sucrose	Fructose SSB, sucrose SSB	~55:31:15			
Control													Glucose	Glucose SSB	54:31:14			
Beck-Nielsen et al. 1980	15 H	(21-25)		-	OP, Denmark	5.5 (0.6)	37.5 (29.8)	-	P	Supp	Yes				44:38:18	Positive	7 d	A, I
Intervention			61.5 kg (9.9)			5.2 (0.6)	27.8 (19.6)					250 (~33)	Fructose	Fructose dissolved in water				
Control			60.9 kg (7.4)			5.8 (0.5)	48.6 (36.7)						Glucose	Glucose dissolved in water				
Heden et al. 2014 (AJCN-H)	20 H (9 M, 11 W)	18.3 (1.5)	70.5 kg (11.3)	23.9 (3.3)	OP, USA	-	-	-	C	Supp	Yes	50 (~10)			NR	Positive	2 wk	A
Intervention													Fructose	Fructose SSB				
Control													Glucose	Glucose SSB				
Heden et al. 2014 (AJCN-OW/OB) (XX)	20 OW/ OB (11 M, 9 W)	17.4 (1.7)	88.0 kg (16.7)	30.8 (6.1)	OP, USA	-	-	-	C	Supp	Yes	50 (~10)			NR	Positive	2 wk	A
Intervention													Fructose	Fructose SSB				
Control													Glucose	Glucose SSB				
Heden et al. 2015	7 OW/ OB (3 M, 4 W)	18 (1.1)	93.6 kg (10.6)	34.6 (4.2)	OP, USA	-	-	-	C	Supp	Yes	50 (~10)			NR	Positive	2 wk	A
Intervention													Fructose	Fructose SSB with walking (≥12000 steps per day)				
Control													Glucose	Glucose SSB with walking (≥12000 steps per day)				

Supplementary Table 2. (Continued)

Study, Year	Participants	Mean Age, years (SD or Range)	Mean BW, units (SD or range)	Mean BMI, kg/m^2 (SD)	Setting	Baseline			Design	Feeding Control [a]	Randomization	Fructose-Containing Sugars Dosage, g/d (% E)[b]	Intervention or comparator	Food source	Diet [c]	Energy Balance [d]	Follow-Up	Funding Sources [e]
						FBG, mmol/L (SD or range)	FBI, pmol/L (SD or range)	HbA1c, % (SD)										
Jin et al. 2014	21 OW (11 M, 10 W)	13.5 (2.5)		-	OP, USA	5.3 (1.1)	234.5 (176.4)	-	P	Supp	Yes				NR	Neutral	4 wk	A
Intervention	9 OW (3 M, 6 W)	14.2 (2.6)	82.3 kg (5.6)			5.5 (0.8)	211.1 (89.4)					99 (~20)	Fructose	Fructose SSB				
Control	12 OW (8 M, 4 W)	13.0 (2.5)	82.0 kg (4.27)			5.0 (1.3)	252.1 (233.5)						Glucose	Glucose SSB				
Johnston et al. 2013 (T1)	32 OW (32 M, 0 W)	34 (9.9)			OP, UK	4.6 (0.3)	112.1 (38.5)	-	P	Met	Yes				55:30:15	Neutral	2 wk	A
Intervention	15 OW (15 M, 0 W)	35 (11)	96.8 kg (7.4)	30.0 (1.4)		4.5 (0.2)	124.3 (35.4)					~221 (25)	Fructose	Fructose dissolved in water				
Control	17 OW (17 M, 0 W)	33 (9)	93.9 kg (8.7)	28.9 (1.7)		4.7 (0.4)	101.4 (38.9)						Glucose	Glucose dissolved in water				
Johnston et al. 2013 (T2)	32 OW (32 M, 0 W)	34 (9.9)			OP, UK	4.6 (0.3)	112.1 (38.5)	-	P	Supp	Yes				NR	Positive	2 wk	A
Intervention	15 OW (15 M, 0 W)	35 (11)	96.8 kg (7.4)	30.0 (1.4)		4.5 (0.2)	124.3 (35.4)					~221 (25)	Fructose	Fructose dissolved in water				
Control	17 OW (17 M, 0 W)	33 (9)	93.9 kg (8.7)	28.9 (1.7)		4.7 (0.4)	101.4 (38.9)						Glucose	Glucose dissolved in water				
Koivisto and Yki-Järvinen 1993	10 DM2 (4 M, 6 W)	61 (10)	81.9 kg (15.4)	27.5 (4.1)	IP, Finland				C	Met	Yes				50:30:20	Neutral	4 wk	A, I
Intervention			82.0 kg (15.8)			9.7 (3.2)	83 (44.3)	9.0 (1.6)				~55 (~10)	Fructose	Fructose dissolved in water				
Control			81.8 kg (15.8)			10.0 (2.5)	89 (60.1)	9.5 (1.9)					Glucose	Glucose dissolved in water				
Maersk et al. 2012	22 OW/OB (9 M, 13 W)	38 (8)	96.2 kg (13.8)	31.6 (2.8)	OP, Denmark	5.4 (0.7)	74.2 (59.3)	-	P	Supp	Yes				NR	Neutral	6 mo	A, I
Intervention	10 OW/OB (6 M, 4 W)	39 (6)	97.8 kg (12.5)	31.3 (2.9)		5.4 (0.6)	54.3 (26.7)					~106 (~21)	Sucrose	Cola				
Control	12 OW/OB (3 M, 9 W)	38 (9)	94.7 kg (15.3)	31.9 (2.8)		5.4 (0.8)	92.6 (74.9)						Lactose	Semi-skim milk				
Mark et al. 2014	73 OW (0 M, 73 W)	39.7 (8.6)	92.0 kg (12.6)	32.7 (4.3)	OP, Denmark	5.5 (0.6)	58.9 (40.2)	-	P	Supp	Yes				~20:45:34	Neutral	4 wk	A
Intervention	35 OW (0 M, 35 W)					5.4 (0.4)	58.2 (43.6)					60 (~13.6)	Fructose	Fructose dissolved in water				
Control	38 OW (0 M, 38 W)					5.5 (0.4)	62.6 (36.3)						Glucose	Glucose dissolved in water				
McAteer et al. 1987	10 DM2	64.4 (54-71)	59.3 kg (5.4)	-	OP, Ireland	-	-	-	C	Supp	No				42:38:20	Neutral	4 wk	I
Intervention												43.7 (11.6)	Fructose	Fructose dissolved in water with lemon or orange flavor				
Control												10.6 (2.8)	Starch	Starch containing foods				
Ngo Sock et al. 2010	11 H (11 M, 0 W)	24.6 (2)	71.9 kg (5.3)	(19-25)	OP, Switzerland	5.0 (0.4)	54.0 (11.9)	-	C	Met	Yes				55:30:15	Positive	7 d	A
Intervention												~214 (35)	Fructose	20% fructose solution				
Control													Glucose	20% glucose solution				
Schwarz et al. 2015	8 H (8 M, 0 W)	42 (8.5)	-	24.4 (4.5)	IP, USA	4.3 (0.3)	34.7 (33.4)	-	C	Met	No				50:35:15	Neutral	9 d	A
Intervention												~112.5 (~22.5)	Fructose	Fructose SSB				
Control													Starch	Isocaloric exchange of fructose for CCHO				
Silbernagel et al. 2011	20 H (12 M, 8 W)	30.5 (8.9)		25.9 (2.3)	OP, Germany	4.85 (0.3)	47.9 (29.2)	-	P	Supp	Yes				50:35:15	Positive	4 wk	A
Intervention	10 H (7 M, 3 W)	32.8 (9.3)	80.3 kg (9.1)	25.5 (2.2)		4.8 (0.3)	45.4 (36.7)					150 (~22)	Fructose	Fructose dissolved in water				
Control	10 H (5 M, 5 W)	28.2 (8.4)	80.7 kg (7.5)	26.2 (2.4)		4.9 (0.2)	50.6 (20.9)						Glucose	Glucose dissolved in water				
Stanhope et al. 2011 (AJCN)	32 OW/OB (16 M, 16 W)	53.7 (8.1)	85.9 kg (10.5)	29.3 (2.9)	IP/ OP, USA	4.9 (0.2)	99.2 (45.0)	-	P	Met/ Supp	No					Positive	8 wk	A
Intervention	17 OW/ OB(9 M, 8 W)	52.5 (9.3)	85.8 kg (10.7)	29.3 (2.6)		4.9 (0.2)	99.2 (45.0)					158 (25)	Fructose	Fructose SSB	~55:30:15			
Control	15 OW/OB (7 M, 8 W)	55.1 (6.6)	86.1 kg (10.6)	29.4 (3.2)		4.9 (0.4)	104.1 (55.9)						Glucose	Glucose SSB	~55:30:15			
Stanhope et al. 2011 (JCEM)	48 (27 M, 21 W)	27.6 (7.1)	76.0 kg (13.1)	25.5 (4.0)	IP/OP, USA	4.9 (0.4)	96.6 (55.0)	-	P	Met/ Supp	No				55:30:15	Neutral	2 wk	A
Intervention	32 (18 M, 14 W)	27.9 (7.1)	75.6 kg (12.8)	25.2 (4.3)		4.9 (0.4)	96.0 (64.4)					~125 (25)	Fructose, HFCS	Fructose SSB, HFCS SSB				
Control	16 (9 M, 7 W)	27.0 (7.2)	76.8 kg (14.1)	26.2 (3.6)		4.9 (0.4)	97.9 (30.4)						Glucose	Glucose SSB				
Swarbrick et al. 2008	7 OW/OB (0 M, 7 W)	(50-72)	75.7 kg (24.3)	29.1 (5.8)	IP, USA	4.6 (1.1)	58 (48)	-	C	Met	No				55:30:15	Neutral	10 wk	A
Intervention												~125 (25)	Fructose	Fructose SSB (12 % solution flavored with unsweetened drink mix)				
Control													Starch	Complex CHO sources (bread, rice, pasta)				
Vaisman et al. 2006	25 DM2	62.3 (10.1)			OP, Israel	11.47 (3.6)	348.3 (231.8)	8.47 (0.8)	P	Supp	Yes	22.5 (~5)			NR	Neutral	3 mo	NR
Intervention	12 DM2	65.4 (10.7)	82.9 kg (10.9)	29.5 (3.9)		11.3 (3.6)	357.0 (319.5)	8.6 (0.9)					Fructose	Fructose dissolved in water				
Control	13 DM2	59.5 (9.1)	83.4 kg (17.6)	30.5 (5.2)		11.7 (3.7)	340.3 (117.4)	8.4 (0.8)					Maltodextrin	Maltodextrin dissolved in water				
Sweetened Low-Fat Milk																		
Lowndes et al. 2015-Fructose	95 OW/ OB (43 M, 52 W)	36.0 (11.5)	74.3 kg (12.5)	26.0 (3.5)	OP, USA	5.0 (0.4)	55.1 (40.8)	-	P	Supp	Yes					Neutral	10 wk	I
Intervention	30 OW/OB (16 M, 14 W)	35.6 (10.4)	74.3 kg (13.1)	26.0 (3.8)		4.9 (0.4)	55.6 (31.9)					~49.5 (9)	Fructose	Fructose sweetened milk	~52:29:20			
Control	65 OW/OB (27 M, 38 W)	36.2 (12.0)	74.3 kg (12.3)	26.1 (3.4)		5.0 (0.4)	54.9 (44.6)						Glucose, lactose	Glucose sweetened milk, unsweetened milk	~52:30:19			

Supplementary Table 2. (Continued)

Study, Year	Participants	Mean Age, years (SD or Range)	Mean BW, units (SD or range)	Mean BMI, kg/m^2 (SD)	Setting	Baseline			Design	Feeding Control [a]	Randomization	Fructose-Containing Sugars Dosage, g/d (% E)[b]	Intervention or comparator	Food source	Diet [c]	Energy Balance [d]	Follow-Up	Funding Sources [e]
						FBG, mmol/L (SD or range)	FBI, pmol/L (SD or range)	HbA1c, % (SD)										
Lowndes et al. 2015-Sucrose	92 OW/ OB (36 M, 56 W)	35.2 (11.5)	72.5 kg (13.1)	26.0 (3.5)	OP, USA	5.0 (0.4)	58.5 (35.9)	-	P	Supp	Yes					Neutral	10 wk	I
Intervention	61 OW/OB (26 M, 35 W)	35.2 (11.1)	72.7 kg (13.6)	26.0 (3.5)		4.9 (0.4)	60.6 (36.2)					sucrose, HFCS: ~109.7 (18)	Sucrose, HFCS	Sucrose or HFCS sweetened milk (18% E)	~55:28:18			
Control	31 OW/OB (10 M, 21 W)	35.3 (12.5)	72.3 kg (12.2)	26.0 (3.5)		5.0 (0.4)	54.2 (35.4)						Diet alone	Unsweetened milk (9% E)	~49:32:20			
Baked Goods, Desserts and Sweets																		
Behall et al. 1980 (non-OC)	6 (0 M, 6 W)	(19-25)	63 kg	-	OP, USA			-	C	Met	No	~214 (~43)			51:36:13	Neutral	4 wk	A
Intervention						4.4 (0.4)	141.7 (35.7)						Sucrose	Sucrose Pattie				
Control						4.4 (0.3)	147.2 (66.3)						Starch	Starch Pattie				
Behall et al. 1980 (OC)	6 (0 M, 6 W)	(19-25)	64 kg	-	OP, USA			-	C	Met	No	~214 (~43)			51:36:13	Neutral	4 wk	A
Intervention						4.4 (0.4)	132.6 (42.5)						Sucrose	Sucrose Pattie				
Control						4.8 (0.7)	179.9 (42.5)						Starch	Starch Pattie				
Claesson et al. 2009	25 H (11 M, 14 W)	23.4 (2.7)	68.0 kg (6.7)	22.2 (1.7)	OP, Sweden	4.7 (0.4)	26 (13)	-	P	Supp	Yes					Positive	2 wk	A
Intervention	12 H (5 M, 7 W)	23.2 (3.5)	67.3 kg (7.6)	22.2 (1.4)		4.7 (0.5)	27 (11)					278 (~37)	Sucrose	Candy	65:21:10			
Control	13 H (6 M, 7 W)	23.6 (1.8)	68.7 kg (6.1)	22.2 (2.0)		4.7 (0.3)	24 (15)					92 (~12)	Fat	Peanuts	32:48:18			
Costa et al. 2005	10 DM1 (7 M, 3 W)	(14-18)	58.5 kg (11.8)	21.7 (3.2)	OP, Brazil	-	-	8.3	C	DA	No					Neutral	4 mo	I
Intervention												~37.5 (~6.2)	Sucrose	Sweets	50:30:20			
Control													Starch	Other CHO sources	48:32:21			
Hallfrisch et al. 1983 HI	12 HI (12 M, 0 W)	39.5 (7.3)	81.4 kg (8.0)	-	IP/OP, USA	-	164.6 (19.0)	-	C	Met	No				43:42:15	Neutral	5 wk	NR
Intervention												~50.6 (7.5), ~101.3 (15) [h]	Fructose	Fructose wafer				
Control													Starch	Starch wafer				
Hallfrisch et al. 1983 H	12 H (12 M, 0 W)	39.8 (8.3)	80.5 kg (11.1)	-	IP/OP, USA	-	145.2 (19.2)	-	C	Met	No				43:42:15	Neutral	5 wk	NR
Intervention												~50.6 (7.5), ~101.3 (15) [h]	Fructose	Fructose wafer				
Control													Starch	Starch wafer				
Jones et al. 2014		26.2 (7.2)	69.0 kg (16.0)	23.6 (3.7)	OP, USA			-	P	Supp	Yes				NR	Neutral	12 wk	I
Intervention	25 H					4.8 (0.3)	59.4 (46.3)					6 (~1.2)	Sucrose [i]	Honey roasted peanuts				
Control	25 H					4.8 (0.5)	48.7 (30.4)						Fat	unsalted peanuts				
Kelsay et al. 1974	8 H (0 M, 8 W)	(18-23)	(43.6-65.3 kg)	-	OP, USA	-	-	-	C	Met	Yes			Sucrose	50:38:12	Neutral	4 wk	NR
Intervention												~212.5 (~42)	Sucrose	Uncooked fondant pattie made with fat and sucrose				
Control													Glucose	Uncooked fondant pattie made with fat and glucose				
Malerbi et al. 1996	16 DM2 (7 M, 9 W)	54.2 (9.2)	65.7 kg (8.1)	25.6 (2.8)	OP, Brazil	7.2 (1.5)	57.9 (41.3)	7.5 (1.0)	C	Met	No					Neutral	4 wk	I
Intervention												63.2 (20)	Fructose	85% of fructose incorporated into a papaya frozen cream sorbet, remaining 15% from natural sources such as fruits and vegetables	55:30:15			
Control													Starch	Starch contianing foods	50:35:15			
Reiser et al. 1989 (HI)	10 HI (10 M, 0 W)	47.4	85 kg	25.7	IP/OP, USA	-	-	-	C	Met	No				51:36:13	Neutral	5 wk	NR
Intervention												168 (20)	Fructose	Fructose fondant				
Control													Starch	Starch muffin				
Reiser et al. 1989 (H)	11 H (11 M, 0 W)	38.10	79 kg	24.4	IP/OP, USA	-	-	-	C	Met	No				51:36:13	Neutral	5 wk	NR
Intervention												168 (20)	Fructose	Fructose fondant				
Control													Starch	Starch muffin				
Added Sweeteners																		
Abdulrhman et al. 2013	20 DM1 (10 M, 10 W)	11.4 (4.2)	105 % IBW (12.1)	-	OP, Egypt	9.4 (1.1)	-	7.2 (0.8)	C	Supp	Yes				NR	Neutral	12 wk	NR
Intervention												~26.6 (~4.0)	Honey	Honey added to diet				
Control													Diet alone	Regular diet				
Bantle et al. 2000	24 H (12 M, 12 W)	41.3 (13.5)		25.1 (2.4)	OP, USA	5.1 (0.5)	-	-	C	Met	Yes	~85 (17)			55:30:15	Neutral	6 wk	A
Intervention			74.1 kg (7.3)										Fructose	Baked goods, beverages, breakfast cereals				
Control			74.1 kg (6.9)										Glucose	Baked goods, beverages, breakfast cereals				
Despland et al. 2017	8 H (8 M 0 W)	-	73.7 kg (5.7)	23.8 (2.3)	IP/ OP, Switzerland	-	-	-	C	Met	Yes				55:30:15	Neutral	7-8 d	A,I
Intervention												~150 (30)	Honey, HFCS	25% starch substituted for robinia honey or fructose+glucose solution comparable to honey composition				
Control													Starch	Starch				

Supplementary Table 2. (Continued)

Study, Year	Participants	Mean Age, years (SD or Range)	Mean BW, units (SD or range)	Mean BMI, kg/m^2 (SD)	Setting	Baseline			Design	Feeding Control[a]	Randomization	Fructose-Containing Sugars Dosage, g/d (% E)[b]	Intervention or comparator	Food source	Diet[c]	Energy Balance[d]	Follow-Up	Funding Sources[e]
						FBG, mmol/L (SD or range)	FBI, pmol/L (SD or range)	HbA1c, % (SD)										
Emanuele et al. 1986	5 DM2, HLP (5 M, 0 W)	59 (6.7)	117 % IBW (14.5)	-	OP, USA				C	Met	Yes					Neutral	4 wk	NR
Intervention			93 kg (24.6)			13.2 (3.2)	187.5 (155.3)	-				220 (~39)	Sucrose	220 g/d sucrose added to beverages and cereals, gelatin desserts, artificially flavored beverages, jelly spreads	63:22:15			
Control			94 kg (22.4)			10.4 (3.1)	145.8 (77.6)	-				≤ 3 (~≤0.5)	Mixed comparator	Isocaloric low sucrose (≤ 3 g/d), low CHO diet	38:39:22			
Grigoresco et al. 1988	8 DM2 (5 M, 3 W)	40 (6.9)	74.3 kg (12.4)	26.1 (3.3)	OP, France	8.0 (1.4)	168.1 (95.2)	6.8 (1.6)	C	Supp	Yes				50:30:20	Neutral	8 wk	A, I
Intervention												30 (8)	Fructose	30 g powdered fructose packs added to food and beverages				
Control													Starch	Fructose exchanged for 30 g starch				
Jellish et al. 1984		59.5 (9.6)	92.6 kg (19.2)	-	IP, USA	11.7 (4.0)	166.7 (106.2)	-	P	Met	Yes					Neutral	4 wk	NR
Intervention	18 DM2 (18 M, 0 W)	60.7 (8.9)	92.4 kg (19.4)									120 (~21), 220 (~39)[h]	Sucrose	Hot beverages, cereals, gelatin desserts, jelly spreads, beverages	50:35:15, 65:21:14[m]			
Control	8 DM2 (8 M, 0 W)	59.5 (9.6)	92.6 kg (19.2)									≤ 3 (~1)	Mixed comparator	Isocaloric low sucrose diet	37:41:22			
Koh et al. 1988 (IGT)	9 IGT (3 M, 6 W)	54 (18)	74.5 kg (15)	-	OP, USA	-	-	-	C	Supp	No					Neutral	4 wk	NR
Intervention												~64 (15)	Fructose	Fructose packets added to Fruit juice, milk, water or baked goods	~53:32:16			
Control													Glucose	Glucose packets added to Fruit juice, milk, water or baked goods				
Koh et al. 1988 (NGT)	9 H (3 M, 6 W)	50 (15)	65.9 kg (13.6)	-	OP, USA	-	-	-	C	Supp	No					Neutral	4 wk	NR
Intervention												~78.5 (15)	Fructose	Fructose packets added to Fruit juice, milk, water or baked goods	~53:32:16			
Control													Glucose	Glucose packets added to Fruit juice, milk, water or baked goods				
Lock et al. 1980	18 (18 M, 0 W)	(31-62)	-	-	OP, England	-	-	-	C	Supp	No					Neutral	12 mo	NR
Intervention												60 (~10.2)	Sucrose	Crystalline and powdered sucrose	41:42:13			
Control													Glucose	Crystalline and powdered dried glucose syrup	42:41:14			
Malerbi et al. 1996	16 DM2 (7 M, 9 W)	54.2 (9.2)	65.7 kg (8.1)	25.6 (2.8)	OP, Brazil	7.2 (1.5)	57.9 (41.3)	7.5 (1.0)	C	Met	No					Neutral	4 wk	I
Intervention												77.8 (19)	Sucrose	Sucrose used to sweeten fruits, milk, beverages and coffee	55:30:15			
Control													Starch	Starch contianing foods	50:35:15			
Osei et al. 1987	18 DM2 (3 M, 15 W)	57 (8.6)	82.7 kg (13.5)	-	OP, USA	12.7 (3.2)	-	11.51 (2.5)	P	Supp	Yes				50:35:15	Neutral	12 wk	A, I
Intervention	9 DM2 (2 M, 7 W)	57 (8.7)	82.8 kg (15.6)			12.4 (4.0)		11.5 (1.5)				60 (~10)	Fructose	Crystalline fructose added to cereals and non-alcoholic beverages				
Control	9 DM2 (1 M, 8 W)	57 (9.0)	82.5 kg (12.0)			12.9 (2.3)		11.5 (3.3)					Starch	ADA recommended diet - mostly CCHO as souce of carbohydrates				
Osei et al. 1989	13 DM2 (5 M, 8 W)	54 (11)		29.6 (9.4)	OP, USA		-		C	Supp	Yes				50:35:15	Neutral	6 mo	A, I
Intervention			87.7 kg (27.4)			12.6 (4.0)		11.3 (1.4)				60 (15)	Fructose	Crystalline fructose incorporated into cereals and non-alcoholic beverages				
Control			88.3 kg (20.9)			11.0 (0.4)		10.4 (2.5)					Starch	ADA recommended diet - mostly CCHO as souce of carbohydrates				
Mixed Sources																		
Abraira et al. 1988	18 DM2 (17 M, 1 W)			-	IP, USA	8.7 (3.4)	149.3 (142.6)	-	P	Met	Yes	220 (~38)			50:35:15	Neutral	1 mo	I
Intervention	9 DM2 (9 M, 0 W)	61.4 (4.8)	85.4 kg (22.2)			8.2 (3.0)	132.0 (145.8)						Sucrose	Beverages, gelatin desserts, cereals				
Control	9 DM2 (8 M, 1 W)	61.4 (7.2)	82.6 kg (18.1)			9.2 (3.8)	166.7 (145.8)						Starch	Bread, potatoes, pasta				
Anderson et al. 1989	14 DM2 (14 M, 0 W)	60 (15.0)	112 % DBW (15)	-	IP/OP, USA	11.2 (4.2)	-	10.6 (1.9)	C	Met	No	~55 (12)			55:20:25	Neutral	24 wk	A, I
Intervention													Fructose	Cookies, lemonade-flavored drink, crystalline fructose				
Control													Starch	Starch containing foods				

Supplementary Table 2. (Continued)

Study, Year	Participants	Mean Age, years (SD or Range)	Mean BW, units (SD or range)	Mean BMI, kg/m^2 (SD)	Setting	Baseline			Design	Feeding Control[a]	Randomization	Fructose-Containing Sugars Dosage, g/d (% E)[b]	Intervention or comparator	Food source	Diet[c]	Energy Balance[d]	Follow-Up	Funding Sources[e]
						FBG, mmol/L (SD or range)	FBI, pmol/L (SD or range)	HbA1c, % (SD)										
Bantle et al. 1986 (DM1)	12 DM1 (6 M, 6 W)	23 (15-32)	103 % MRW (82-123)	-	IP, USA	-	-	9.9 (1.8)	C	Met	Yes	~137 (21)			55:30:15	Neutral	8 d	A, I
Intervention													Fructose, sucrose	Baked goods, beverages, breakfast cereals				
Control													Starch	Starch containing foods				
Bantle et al. 1986 (DM2)	12 DM2 (5 M, 7 W)	62 (36-80)	129 % MRW (106-160)	-	IP, USA	-	-	8.5 (2.4)	C	Met	Yes	~137 (21)		Fructose, sucrose	55:30:15	Neutral	8 d	A, I
Intervention													Fructose, sucrose	Baked goods, beverages, breakfast cereals				
Control													Starch	Starch containing foods				
Bantle et al. 1992 (DM1)	6 DM1 (3 M, 3 W)	23 (18-34)	102 % MRW (97-111)	-	IP/OP, USA		-	8.1 (0.3)	C	Met	Yes	~120 (20)			55:30:15	Neutral	28 d	A, I
Intervention						10.6 (4.0)							Fructose	Baked goods, beverages, breakfast cereals				
Control						10.3 (4.2)							Starch	Starch containing foods				
Bantle et al. 1992 (DM2)	12 DM2 (4 M, 8 W)	62 (40-72)	136 % MRW (99-170)	-	IP/OP, USA		-	7.2 (2.1)	C	Met	Yes	~120 (20)			55:30:15	Neutral	28 d	A, I
Intervention						9.3 (2.3)							Fructose	Baked goods, beverages, breakfast cereals				
Control						8.2 (1.4)							Starch	Starch containing foods				
Bantle et al. 1993	12 DM2 (4 M, 8 W)	62 (40-72)		-	OP, USA		-		C	Met	Yes	~114 (19)			55:30:15	Neutral	28 d	A, I
Intervention			86.0 kg (22.5)			8.7 (2.5)		7.2 (1.1)					Sucrose	Baked goods, beverages, breakfast cereals				
Control			86.9 kg (22.2)			8.2 (1.4)		7.2 (1.5)					Starch	Starch containing foods				
Black et al. 2006	13 H (13 M, 0 W)	33 (11)	86.0 kg (12.3)	26.6 (3.2)	OP, UK	4.8 (0.4)	-	5.7 (0.4)	C	Met	Yes	~199 (25)			55:33:12	Neutral	6 wk	A
Intervention													Sucrose	High sucrose diet (25% E)				
Control													Starch	Low sucrose diet (10% E)				
Blayo et al. 1990	14 DM1, 6 DM2	46.9 (13.1)	-	22.6 (1.9)	OP, France	9.8	-	8.8	P	Supp	Yes				55:30:15	Neutral	12 mo	A, I
Intervention	8 DM1, 4 DM2	49.5 (14.1)		23.0 (2.1)		9.4		7.8				~25 (5)	Fructose, sucrose	20-30 g sugar/d in drinks, desserts, meals				
Control	6 DM1, 2 DM2	43.0 (11.0)		22.0 (1.6)		10.4		9.5					Starch	Isocaloric substitution of sugar with starch				
Brymora et al. 2012	28 CKD (17 M, 11 W)	59 (15)	85.8 kg (11.5)	29.9 (4.2)	OP, Poland	5.4 (0.7)	77.8 (42.4)	-	C	DA	No				55:30:15	Neutral	6 wk	A
Intervention												~56 (~10)	Fructose, sucrose	Regualr diet				
Control												12 (~2)	Starch	Isocaloric low fructose diet through reduction of fruits and added sugars				
Brynes et al. 2003	17 OW/ OB (17 M, 0 W)	45 (8)	-	29.3 (4.0)	OP, London	-	-	-	C	Supp	Yes	132 (~22)				Neutral	24 d	I
Intervention													Sucrose	Table sugar	51:33:16			
Control													Fat, starch	Olive oil, instant potato, wholegrain rye bread	~43:39:18			
Buysschaert et al. 1987	10 DM1 (5 M, 5 W)	52 (12.6)	124 % IBW (22)	-	OP, Belgium	-	-	9.5 (1.3)	C	Met	Yes				45:35:20	Neutral	3 mo	NR
Intervention												19 (~5.4)	Sucrose	Sucrose incorporated into desserts and/ or soft drinks				
Control													Starch	Conventional diabetic diet				
Cooper et al 1988	17 DM2 (6 M, 11 W)	62.2 (14.0)	69.1 kg (2.8)	26.0 (3.0)	OP, Australia	8.9 (2.8)	100.0 (50.4)	8.1 (1.7)	C	Supp	Yes				NR	Positive	6 wk	I
Intervention												28 (8.2)	Sucrose	28 g sucrose added to hot beverages, fruit juice, milk, cereals, stewed fruit				
Control													Starch	30 g starch and saccharin added to hot beverages, fruit juice, milk, cereals, stewed fruit				
Coulston et al. 1985	11 DM2 (5 M, 6 W)	62 (6.6)	-	27.8 (2.3)	OP, USA	7.8 (1.7)	-	-	C	Met	No					Neutral	15 d	A
Intervention												~80 (16)	Sucrose	Sucrose added diet	53:29:18			
Control												~5 (1)	Starch	Sucrose free diet	51:30:19			
Dunnigan et al. 1970	8 CND, 1 CAD (6 M, 3 W)	51.8 (8.1)	63.1 kg (10.5)	-	IP, Scotland	-	-	-	C	Met	No				45:40:15	Neutral	4 wk	NR
Intervention												169 (~34)	Sucrose	70% CHO intake as sucrose				
Control													Starch	85% CHO intake as wheat, potato or maize starch				
Fry et al. 1972	19 (19 M, 0 W)	24.7 (20.8-40.8)	76.9 kg (8.4)	-	OP, Antartica	-	-	-	C	Met	No				44:43:13	Neutral		NR
Intervention												97 (~13)	Sucrose	Sucrose-containing diet			18 wk	
Control													Glucose	Sucrose-free diet with glucose syrup and calcium cyclamate			14 wk	

Supplementary Table 2. (Continued)

Study, Year	Participants	Mean Age, years (SD or Range)	Mean BW, units (SD or range)	Mean BMI, kg/m^2 (SD)	Setting	Baseline			Design	Feeding Control [a]	Randomization	Fructose-Containing Sugars Dosage, g/d (% E)[b]	Intervention or comparator	Food source	Diet [c]	Energy Balance [d]	Follow-Up	Funding Sources [e]
						FBG, mmol/L (SD or range)	FBI, pmol/L (SD or range)	HbA1c, % (SD)										
Hendler et al. 1986	6 OB (0 M, 6 W)	(20-44)	(56-126 % IBW)	-	OP, USA	-	-	-	C	Met	No					Negative	15 d	A, I
Intervention												~190 (95)	Sucrose	High sucrose diet	96:04:00			
Control													Protein	High protein diet	96:04:00			
Lewis et al. 2013	13 OW/ OB (9 M, 4 W)	46.1 (6.9)	92 kg (10.5)	31.7 (3.2)	OP, UK	5.2 (0.7)	-	-	C	Met	Yes	~101.8 (15)				Neutral	6 wk	I
Intervention													Sucrose	High sucrose diet (15% E)	~55:33:12			
Control													Starch	Low sucrose diet (5% E)	~55:33:12			
Liu et al. 1984	10 HTG (4 M, 6 W)		-		IP, USA	-	-	-	P	Met	Yes				40:41:19	Neutral	15 d	A
Intervention	5 HTG	52 (4.5)		29.6 (4.5)								~65 (13)	Sucrose	13 % sucrose diet				
Control	5 HTG	55 (4.5)		28.9 (4.0)								~45 (9)	Starch	9 % sucrose diet				
Maki et al. 2015	34 DM2 (17 M, 17 W)	53.8 (12.2)	-	32.2 (4.7)	OP, USA	5.5 (0.5)	56.0 (21.0)	-	C	Supp	Yes					Neutral	6 wk	A, I
Intervention												~92 (~17)	Sucrose	Non-diet soda and non-dairy pudding	57:29:15			
Control													Lactose	2% milk and sugar-free low fat yogurt	47:33:19			
Paganus et al. 1987 (CG)	8 DM1 (3 M, 5 W)	12.3 (10.7-14.8)	-	-	OP, Finland	-	-	-	C	Met	Yes				50:30:20	Neutral	3 wk	I
Intervention												37 (~7.4)	Fructose	Marmalade, grain fruit bar, pure fructose sweetener				
Control													Starch	Isocaloric exchange of fructose for other carbohydrates				
Paganus et al. 1987 (SG)	22 DM1 (9 M, 13 W)	12.2 (8.9-15.9)	-	-	OP, Finland	-	-	-	C	Met	Yes				50:30:20	Neutral	3 wk	I
Intervention												37 (~7.4)	Fructose	Marmalade, grain fruit bar, pure fructose sweetener				
Control													Starch	Isocaloric exchange of fructose for other carbohydrates				
Paineau et al. 2008					OP, France	-	-	-	P	DA	Yes				-	Negative	8 mo	A, I
Intervention	297 (55 M, 242 W)	40.4 (5.3)	66.8 kg (13.5)	24.2 (4.5)								~80.1 (~17.6) j	Sucrose	Reduced fat, increased CCHO				
Control	298 (48 M, 250 W)	40.3 (5.4)	67.3 kg (16.0)	24.6 (5.7)									Starch	Reduced fat, reduced sugar, increased CCHO to maintain isocaloric CHO intake				
Pelkonen et al. 1972	10 DM1 (5 M, 5 W)	25.5 (19-70)	99 % RBW (90-118)	-	IP, Finland	-	-	-	C	Met	No				40:40:20	Neutral	10 d	A
Intervention												75 (15)	Fructose	Fructose incorporated into main meals replacing starch				
Control													Starch	Starch incorporated into main meals				
Peterson et al. 1986 (DM1)	12 DM1 (10 M, 2 W)	52 (11)	-	24.9 (21.2-27.9)	OP, UK	-	-	-	C	DA	Yes				50:30:20	Neutral	6 wk	NR
Intervention												45 (~9.4)	Sucrose	45 g CCHO replaced by sucrose in food				
Control													Starch	British Diabetic Association recommended diet				
Peterson et al. 1986 (DM2)	11 DM2 (7 M, 4 W)	56 (9)	-	24.7 (20.1-28.0)	OP, UK	-	-	-	C	DA	Yes				50:30:20	Neutral	6 wk	NR
Intervention												45 (~9.4)	Sucrose	45 g CCHO replaced by sucrose				
Control													Starch	British Diabetic Association recommended diet				
Porta et al. 1989	16 DM2 (8 M, 8 W)	60 (9.7)	-		OP, Italy	8.5 (2.2)	-	5.8 (1.1)	P	Supp	Yes					Neutral	6 mo	A
Intervention	8 DM2 (4 M, 4 W)	60 (8.5)		27.4 (3.1)		9.3 (2.5)		6.0 (1.4)				~38.1 (10)	Sucrose	10% of starch replaced by sucrose in 2 main meals, coffee, tea, fruit	54:28:18			
Control	8 DM2 (4 M, 4 W)	60 (11.3)		28.2 (2.5)		7.7 (1.7)		5.6 (0.8)					Starch	Traditional diabetic diet	55:28:18			
Rath et al. 1974	6 H (6 M, 0 W)	21.5 (2.7)	65.8 kg (10.2)	-	IP, Prague	-	-	-	C	Met	No					Neutral	24 d	NR
Intervention												400 (52.5)	Sucrose	High sugar diet (400 g/d sugar)	72:16:12			
Control												120 (17.1)	Mixed comparator	Control diet (120 g/d sugar)	50:33:17			
Reiser et al. 1986 (W)	9 H (0 M, 9 W)	(27-48)	-	-	IP/OP, USA	4.9 (1.2)	128.5 (45.8)	-	C	Met	No				50:35:15	Neutral	6 wk	NR
Intervention												141.8 (~21)	Sucrose	High sugar diet (20 %E)				
Control													Starch	Low sugar diet with isocaloric exchange of sugar for CCHO				

Supplementary Table 2. (Continued)

Study, Year	Participants	Mean Age, years (SD or Range)	Mean BW, units (SD or range)	Mean BMI, kg/m^2 (SD)	Setting	Baseline			Design	Feeding Control [a]	Randomization	Fructose-Containing Sugars Dosage, g/d (% E)[b]	Intervention or comparator	Food source	Diet[c]	Energy Balance[d]	Follow-Up	Funding Sources[e]
						FBG, mmol/L (SD or range)	FBI, pmol/L (SD or range)	HbA1c, % (SD)										
Reiser et al. 1986 (M)	10 H (10 M, 0 W)	(24-56)	107 % DBW	-	IP/OP, USA	5.2 (0.6)	123.6 (24.2)	-	C	Met	No				50:35:15	Neutral	6 wk	NR
Intervention												141.8 (~21)	Sucrose	High sugar diet (20 %E)				
Control													Starch	Low sugar diet with isocaloric exchange of sugar for CCHO				
Santacroce et al. 1990	12 DM1 (6 M, 6 W)	27 (16-46)	-	22.3 (19.8-25)	OP, Italy	-	-	6.9 (1.0)	C	Met	Yes				52:31:17	Neutral	2 mo	NR
Intervention								6.8 (1.0)				30 (~6)	Sucrose	Sucrose added to foods and mixed meals				
Control								6.9 (1.0)					Starch	High glycemic index bread				
Souto et al. 2013	33 DM1 (21 M, 12 W)	21.7 (5)	-		OP, Brazil	10.0 (3.8)	-	7.6 (1.6)	P	DA	Yes					Negative	3 mo	NR
Intervention	15 DM1 (8 M, 7 W)			24.0 (2.6)		10.9 (3.6)		8.0 (2.1)				~162 (27)	Sucrose	Sucrose containing foods	58:26:20			
Control	18 DM1 (12 M, 6 W)			22.4 (2.7)		9.4 (3.9)		7.3 (1.1)					Starch	Isocaloric exchange of sucrose for other carbohydrates	53:24:20			
Sunehag et al. 2002 (P1-AD)	12 H (6 M, 6 W)	14.5 (1.1)	55.5 kg (10.7)	20.2 (3.1)	IP/ OP, Italy	-	-	-	C	Met	Yes					Neutral	7 d	A
Intervention												~74.9 (~12.1)	Fructose	High CHO low fat diet (20% CHO from fructose)	60:25:15			
Control												~39.8 (~6.3)	Mixed comparator	Low CHO high fat diet (20% CHO from fructose)	30:55:15			
Sunehag et al. 2002 (P1-PP)	12 H (6 M, 6 W)	8.0 (1.0)	26.1 kg (4.5)	15.7 (1.3)	IP/ OP, Italy	-	-	-	C	Met	Yes					Neutral	7 d	A
Intervention												~50.6 (~12.1)	Fructose	High CHO low fat diet (20% CHO from fructose)	60:25:15			
Control												~27.7 (~6.3)	Mixed comparator	Low CHO high fat diet (20% CHO from fructose)	30:55:15			
Sunehag et al. 2002 P2	12 H (6 M, 6 W)	14.8 (1.3)	60.3 kg (11.1)	21.8 (3.9)	IP/ OP, Italy	-	-	-	C	Met	Yes					Neutral	7 d	A
Intervention												~150.3 (~23.8)	Fructose	High CHO low fat diet (40% CHO from fructose)	60:25:15			
Control												~40.4 (~6.5)	Starch	High CHO low fat diet (10% CHO fructose)	60:25:15			
Sunehag et al. 2008	6 OB (3 M, 3 W)	15.2 (1.2)	98.4 kg (18.4)	35 (4.9)	OP, USA	-	-	-	C	Met	Yes				60:25:15	Neutral	7 d	A, I
Intervention												~149.1 (24)	Fructose	White bread, fruit, fruit juice, canned fruit in heavy syrup, candy, soft drinks				
Control												~38 (6)	Starch	Isocaloric exchange of fructose from other carbohydrates				
Surwit et al. 1997	42 OB (0 M, 42 W)	40.2 (7.6)			OP, England	4.9 (0.6)	-	-	P	Met	Yes					Negative	6 wk	A, I
Intervention	20 OB (0 M, 20 W)	40.6 (8.2)	96.1 kg (13.7)	35.9 (4.8)		5.0 (0.7)						121.2 (58.0)	Sucrose	High-sucrose, low fat diet	73:11:19			
Control	22 OB (0 M, 22 W)	40.3 (7.3)	96.7 kg (12.6)	34.9 (4.4)		4.9 (0.6)						11.8 (6.0)	Starch	Low-sucrose, low fat diet	71:11:20			
Swanson et al. 1992	14 H (7 M, 7 W)	34 (19-60)		-	IP/ OP, USA	5.1 (0.4)	-	5.0 (0.4)	C	Met	Yes			Fructose	55:30:15	Neutral	28 d	A, I
Intervention			68.6 kg (3.1)			4.9 (0.4)		5.1 (0.4)				100 (20)	Fructose	Crystalline fructose added to baked goods, beverages, breakfast cereals, and natural fructose in fruits and vegetables				
Control			68.5 kg (3.0)			5.2 (0.4)		4.9 (0.4)				14 (<3)	Starch	Bread, potatoes, wheat and corn flour, oats				
Szanto et al. 1969	19 H (19 M, 0 W)	28 (21-44)	73.1 kg (58.5-81.5)	-	OP, UK	3.8 (3.4-4.5)	153 (97.2-180.6)	-	C	DA	No				NR	Neutral	2 wk	A
Intervention												438 (~52)	Sucrose	High sucrose diet				
Control													Starch	High starch diet				
Van Meijl et al. 2011	35 OW/OB (10 M, 25 W)	49.5 (13.2)	-	32.0 (3.8)	OP, Netherlands	5.68 (0.6)	-	-	C	Supp	Yes					Neutral	8 wk	I
Intervention												70.2 (~12.8) [l]	Sucrose	Fruit Juice (600 mL), fruit biscuits (43 g)	53:30:16			
Control													Lactose	Low fat milk (500 mL), low fat yogurt (150 g)	46:33:19			
Volp et al. 2007 (G1)	10 H (0 M, 10 W)	22.5 (2.1)			OP, Brazil	-	-	-	P	DA	Yes					Neutral	14 d	A
Intervention	5 H (0 M, 5 W)		54.9 (48.8-64.5) [k]	21.7 (20.2-25.0) [k]								110 (~22)	Sucrose	High sucrose diet	59:28:13			
Control	5 H (0 M, 5 W)		55.8 (48.0-65.6) [k]	21.3 (19.4-24.8) [k]								10 (~2)	Fat	High fat diet	42:45:13			

Supplementary Table 2. (Continued)

Study, Year	Participants	Mean Age, years (SD or Range)	Mean BW, units (SD or range)	Mean BMI, kg/m^2 (SD)	Setting	Baseline			Design	Feeding Control[a]	Randomization	Fructose-Containing Sugars Dosage, g/d (% E)[b]	Intervention or comparator	Food source	Diet[c]	Energy Balance[d]	Follow-Up	Funding Sources[e]
						FBG, mmol/L (SD or range)	FBI, pmol/L (SD or range)	HbA1c, % (SD)										
Volp et al. 2007 (G2)	10 OW (0 M, 10 W)	21.8 (2.8)			OP, Brazil	-	-	-	P	DA	Yes					Neutral	14 d	A
Intervention	5 OW (0 M, 5 W)		73.9	29.1								130 (~23)	Sucrose	High sucrose diet	59:28:13			
Control	5 OW (0 M, 5 W)		72	28.7								10 (2)	Fat	High fat diet	42:45:13			
Volp et al. 2008 (G1)	6 H (0 M, 6 W)	21 (19-24) [k]	-	21.4 (20.2-22.8) [k]	OP, Brazil	5.5 (5.2-5.8)	89.6 (59.7-100.0)	-	C	DA	Yes					Neutral	14 d	AI
Intervention												~81.1 (18.4)	Sucrose	High sucrose diet	65:22:16			
Control												~11.2 (2.6)	Fat	High fat diet	50:36:17			
Volp et al. 2008 (G2)	6 OW/OB (0 M, 6 W)	21 (19-22) [m]	-	28.6 (25.1-32.1) [m]	OP, Brazil	5.9 (5.4-6.0)	124.3 (77.1-157.0)	-	C	DA	Yes					Neutral	14 d	A, I
Intervention												~47.1 (8.8)	Sucrose	High sucrose diet	63:26:15			
Control												~10.5 (2.4)	Fat	High fat diet	53:31:16			
Yudkin et al. 1972	11 (11 M, 0 W)	29 (21-44)	-	-	OP, England	-	-	-	C	DA	No					Neutral		I
Intervention												441 (~53)	Sucrose	Substitute sugar for starch from regular diet	~59:30:10		2 wk	
Control												148 (~18)	Starch	Regular diet	~58:30:10		1 wk	
Addition Studies (Hypercaloric comparison)																		
Fruit																		
Basu et al. 2010 (BB)		49.8 (15.3)	-	37.8 (11.2)	OP, USA	-	-	-	P	Supp	Yes				NR	Neutral	8 wk	A, I
Intervention	25 MetS (2 M, 23 W)	51.5 (15.0)		38.1 (7.5)								30 (~6) [n]	Fruit	Freeze dried blueberry beverage				
Control	23 MetS (2 M, 21 W)	48.0 (15.8)		37.5 (14.4)									Water	Water				
Basu et al. 2010 (SB)		46.7 (16.6)	102.3 kg (9.5)	37.8 (8.9)	OP, USA	5.1 (0.7)	-	-	P	Supp	Yes					Neutral	8 wk	A, I
Intervention	15 MetS (0 M, 15 W)	48.0 (20.5)	102.0 kg (11.6)	39.0 (7.7)		5.2 (0.8)						~14.6 (~3.2) [g]	Fruit	Freeze dried strawberry beverage	45:37:13			
Control	12 MetS (2 M, 10 W)	45.0 (10.4)	102.7 kg (6.6)	36.4 (10.4)		5.0 (0.7)							Water	Water	46:35:15			
Cressey et al. 2014 (DM2)	15 DM2	52.8 (5.23			OP, Thailand			-	C	Supp	No					Positive		A
Intervention			61.8 kg (13.3)	25.8 (4.7)		7.3 (2.5)	97.2 (117.4)					~18.1 (~3.3)[f]	Fruit	1 banana/d (250 g)	~57:25:18		4 wk	
Control			62.3 kg (13.0)	25.9 (4.6)		6.7 (1.7)	117.4 (122.2)						Diet alone	No banana	~53:29:19		8 wk	
Cressey et al. 2014 (H)		36.4 (12.0)	51.3 kg (6.1)	20.2 (2.7)	OP, Thailand	4.6 (0.5)	-	-	P	Supp	Yes					Positive		A
Intervention	7 H	41 (13.7)	54.5 kg (5.6)	21.5 (2.9)		4.7 (0.4)						~36.2 (~9.2) [f]	Fruit	2 banana/d (500 g)	~65:21:14		3 mo	
Control	5 H	30 (5.2)	46.9 kg (3.8)	18.4 (1.0)		4.5 (0.6)							Diet alone	No banana	~52:30:19		3 mo	
Cressey et al. 2014 (HCL HD)	15 HCL	43.1 (7.5)			OP, Thailand			-	C	Supp	No					Positive		A
Intervention			59.6 kg (11.8)	24.0 (3.94)		5.7 (0.4)	22.9 (14.6)					~36.2 (~6.3) [f]	Fruit	2 banana/d (500 g)	~57:26:17		12 wk	
Control			59.3 kg (12.1)	24.1 (4.2)		5.1 (0.4)	19.4 (11.1)						Diet alone	No banana	~49:34:17		8 wk	
Cressey et al. 2014 (HCL LD)	15 HCL	44.8 (10.3)			OP, Thailand			-	C	Supp	No					Positive		A
Intervention			61.5 kg (10.9)	24.8 (4.0)		5.5 (0.4)	21.5 (11.1)					~18.1 (~3.5) [f]	Fruit	1 banana/d (250 g)	~56:27:17		12 wk	
Control			61.5 kg (10.7)	24.8 (4.3)		5.1 (0.5)	29.9 (13.9)						Diet alone	No banana	~47:35:17		8 wk	
Ellis et al. 2011	12 OW/OB	50.9 (15.0)	86.6 kg (12.9)	29.2 (2.3)	OP, USA	-	-	-	C	Supp	No				NR	Positive		A, I
Intervention												~5.9 (~1.2) [f]	Fruit	Freeze dried strawberry beverage equivalent to ~100 g/d fresh strawberries			6 wk	
Control													Diet alone	No beverage			7 d	
Mitsou et al. 2011	22 OW/OB (0 M, 22 W)	31	74.2 kg (9.4)	27.6 (2.7)	OP, Greece	5.1 (0.4)	53.8 (14.6)	-	P	Supp	Yes				NR	Positive	60 d	A, I
Intervention	12 OW/OB (0 M, 12 W)		74.6 kg (11.4)	27.6 (2.9)		5.1 (0.5)	53.5 (15.3)					~17.4 (~3.5) [f]	Fruit	240 g/d Dessert Banana				
Control	10 OW/OB 0 M, 10 W)		73.8 kg (6.9)	27.5 (2.5)		5.0 (0.4)	54.2 (14.6)						Water	Water				
Ravn-Haren et al. 2013	23 H (9 M, 14 W)	36.2 (17.9)	-	22.3 (2.6)	OP, Denmark	-	40.6 (28.2)	-	C	Supp	Yes				NR	Positive	4 wk	A
Intervention												~51 (~10) [l]	Fruit	Polyphenolic and pectin restricted diet with whole apples equivalent to ~550 g/d				
Control													Diet alone	Polyphenolic and pectin restricted diet with apple pomace				
Dried Fruit																		
Puglisi et al. 2008		56.3 (4.6)	78.6 kg (16.0)	27.7 (3.8)	OP, USA	5.4 (0.6)	-	-	P	Supp	Yes					Positive	6 wk	I
Intervention	10 H (5 M, 5 W)	57.8 (5.2)	78.4 kg (15.9)	27.5 (3.8)		5.22 (0.41)						~49.7 (~9.9) [f]	Fruit	Walking + 1 cup raisins/d	57:29:15			
Control	12 H (6 M, 6 W)	55.0 (3.8)	78.7 kg (16.8)	27.9 (3.9)		5.52 (0.7)							Diet alone	Walking	43:40:16			
Fruit Juice																		
Banini et al. 2006			-		OP, USA				P	Supp	Yes				~50:31:19	Positive	28 d	A, I
Intervention	8 H	50 (13)		29.3 (1.4)		5.0 (0.4)	86.8 (88.4)	5.5 (0.3)				~17[l]	fruit	Muscadine grape juice				

Control	15 H	25 (75)		27.5 (1.4)		4.9 (0.8)	75.7 (43.0)	5.5 (1.2)					Diet alone	No beverage				
Hollis et al. 2009		25 (8.1)	78.3 kg (9.3)	27.2 (1.5)	OP, USA	4.5 (0.6)	81.5 (70.1)	-	P	Supp	Yes					Positive	12 wk	I
Intervention	25 OW	22 (4)	79.0 kg (8.4)	27.0 (1.6)		4.4 (0.6)	83.8 (90.4)					82 (~17)	fruit	Concord grape juice	~50:35:15			
Control	25 OW	28 (10)	77.6 kg (10.3)	27.3 (1.5)		4.7 (0.5)	79.2 (43.0)						Diet alone	No beverage	~50:34:16			

Supplementary Table 2. (Continued)

Study, Year	Participants	Mean Age, years (SD or Range)	Mean BW, units (SD or range)	Mean BMI, kg/m^2 (SD)	Setting	Baseline			Design	Feeding Control[a]	Randomization	Fructose-Containing Sugars Dosage, g/d (% E)[b]	Intervention or comparator	Food source	Diet[c]	Energy Balance[d]	Follow-Up	Funding Sources[e]
						FBG, mmol/L (SD or range)	FBI, pmol/L (SD or range)	HbA1c, % (SD)										
Ravn-Haren et al. 2013	23 H (9 M, 14 W)	36.2 (17.9)	-	22.3 (2.6)	OP, Denmark	-	40.6 (28.2)	-	C	Supp	Yes				NR	Positive	4 wk	A
Intervention												~61 (~12.2) [m]	fruit	Polyphenolic and pectin restricted diet with clear or cloudy apple juice (~500 mL/d)				
Control													Diet alone	Polyphenolic and pectin restricted diet				
Fruit Drinks																		
Ellis et al. 2011	12 OW/OB	50.9 (15.0)	86.6 kg (12.9)	29.2 (2.3)	OP, USA	-	-	-	C	Supp	No				NR	Positive		A, I
Intervention												25.9 (~5) total sugar	Sucrose	Strawberry flavored beverage			6 wk	
Control													Diet alone	No beverage			7 d	
Hollis et al. 2009		27 (9)	78.3 kg (10.4)	27.1 (1.5)	OP, USA	4.7 (0.7)	78.9 (36.7)	-	P	Supp	Yes					Positive	12 wk	I
Intervention	26 OW	26 (9)	79.0 kg (10.7)	27.0 (1.5)		4.7 (0.8)	78.6 (30.3)					82 (~17)	sucrose	Grape flavored drink	~48:36:16			
Control	25 OW	28 (10)	77.6 kg (10.3)	27.3 (1.5)		4.7 (0.5)	79.2 (43.0)						Diet alone	No beverage	~50:34:16			
Mitsou et al. 2011	20 OW/OB (0 M, 22 W)	31	71.3 kg (7.6)	26.7 (2.3)	OP, Greece	5.0 (0.3)	48.7 (20.3)	-	P	Supp	Yes				NR	Positive	60 d	A, I
Intervention	10 OW/OB (0 M, 10 W)		68.8 kg (7.7)	25.8 (1.8)		5.0 (0.3)	43.1 (24.3)					50.6 (~10)	Sucrose	Banana flavored drink				
Control	10 OW/OB (0 M, 10 W)		73.8 kg (6.9)	27.5 (2.5)		5.0 (0.4)	54.2 (14.6)						Water	Water				
SSBs																		
Abdel-Sayed et al. 2008	6 H (6 M, 0 W)	24.7 (3.1)	78.3 kg (7.4)	23.1 (2.2)	OP, Switzerland	-	-	-	C	Met	Yes	234 (~47)				Positive	7 d	A
Intervention													Fructose	Fructose dissolved in water	67:22:11			
Control													Diet alone	No beverage	55:30:15			
Beck-Nielsen et al. 1980	10 H	(21-35)		-	OP, Denmark	5.2	21.2	-	P	Supp	Yes				44:38:18	Positive	7 d	A, I
Intervention	8 H		61.5 kg (9.9)			5.2 (0.6)	27.8 (19.6)					250 (~33)	Fructose	Fructose SSB				
Control	2 H		57 kg			5.4	34.7						Diet alone	No beverage				
Koopman et al. 2014		22.2 (2.7)	78.6 kg (8.0)	22.3 (1.7)	OP, Netherlands	4.8 (0.2)	48.0 (24.1)	-	P	Supp	Yes					Positive	6 wk	A
Intervention	15 H (15 M , 0 W)	21.9 (2.6)	79.9 kg (8.3)	22.2 (1.5)		4.8 (0.2)	48.0 (24.1)					~237 (~27)	Sucrose	Sucrose SSB	~57:28:12			
Control	5 H (5 M, 0 W)	23.0 (3.1)	76.6 kg (7.7)	22.6 (2.3)		4.8 (0.4)	45.0 (13.4)						Diet alone	No beverage				
Lê et al. 2006	7 H (7 M, 0 W)	24.7 (3.4)	69.3 kg (6.9)	(19-25)	OP, Switzerland	4.9 (0.3)	50.4 (9.5)	-	C	Supp	No				55:30:15	Positive	4 wk	A
Intervention												~104 (18)	Fructose	20% fructose solution				
Control												<20	Diet alone	No beverage				
Lê et al. 2009 (ODM2)	16 ODM2 (16 M, 0 W)	24.7 (5.2)	-	-	OP, Switzerland	-	-	-	C	Met	Yes	~220 (35)			55:30:15	Positive	7 d	A
Intervention													Fructose	20% fructose solution				
Control													Diet alone	No beverage				
Maersk et al. 2012	35 OW/OB (14 M, 21 W)	39 (7)	97.3 kg (16.5)	32.1 (3.8)	OP, Denmark	5.4 (0.6)	72.5 (42.5)	-	P	Supp	Yes				NR	Positive	6 mo	A, I
Intervention	10 OW/OB (6 M, 4 W)	39 (6)	97.8 kg (12.5)	31.3 (2.9)		5.4 (0.6)	54.3 (26.7)					~106 (~21)	Sucrose	Cola				
Control	25 OW/ OB (8 M, 17 W)	39 (8)	97.1 kg (18.1)	32.5 (4.2)		5.4 (0.6)	79.8 (45.8)						Sweetener, Water	Diet beverage, water				
Silbernagel et al. 2011	10 (7 M, 3 W)	32.8 (9.3)	80.3 kg (9.1)	25.5 (2.2)	OP, Germany	4.8 (0.3)	45.4 (36.7)	-	C	Supp	Yes				50:35:15	Positive		A
Intervention												150 (~22)	Fructose	Fructose dissolved in water			4 wk	
Control													Diet alone	No beverage			2 wk	
Sobrecases et al. 2010 (XX)	8 H (8 M, 0 W)	24.8 (3.2)	-	(19-25)	OP, Switzerland	-	-	-	C	Supp	No				55:30:15	Positive	7 d	A
Intervention												~214 (35)	Fructose	Fructose SSB				
Control													Diet alone	No beverage				
Stanhope et al. 2011 (AJCN)	17 OW/ OB (9 M, 8 W)	52.5 (9.3)	85.8 kg (10.7)	29.3 (2.6)	IP/ OP, USA	4.9 (0.2)	99.2 (45.0)	-	C	Met/ Supp	No				~55:30:15	Positive		A
Intervention												158 (25)	Fructose	Fructose SSB			8 wk	
Control													Diet alone	No beverage			2 wk	
Stanhope et al. 2011 (JCEM FRU)	16 (9 M, 7 W)	28.0 (6.8)	76.8 kg (10.6)	25.4 (3.8)	IP/OP, USA	4.9 (0.4)	102.8 (86.4)	-	C	Met/ Supp	No	~125 (25)			55:30:15	Positive	2 wk	A
Intervention													Fructose	Fructose SSB				
Control													Diet alone	No Beverage				
Stanhope et al. 2011 (JCEM HFCS)	16 (9 M, 7 W)	27.8 (7.60	74.3 kg (14.9)	24.9 (4.8)	IP/OP, USA	4.9 (0.4)	89.1 (31.6)	-	C	Met/ Supp	No	~125 (25)			55:30:15	Positive	2 wk	A
Intervention													HFCS	HFCS SSB				
Control													Diet alone	No Beverage				

Supplementary Table 2. (Continued)

Study, Year	Participants	Mean Age, years (SD or Range)	Mean BW, units (SD or range)	Mean BMI, kg/m² (SD)	Setting	Baseline			Design	Feeding Control [a]	Randomization	Fructose-Containing Sugars Dosage, g/d (% E)[b]	Intervention or comparator	Food source	Diet[c]	Energy Balance [d]	Follow-Up	Funding Sources [e]
						FBG, mmol/L (SD or range)	FBI, pmol/L (SD or range)	HbA1c, % (SD)										
Sweetened Chocolate																		
Njike et al. 2011	39 OW (6 M, 33 W)	52.2 (10.6)			OP, USA		-	-	C	Supp	Yes			Sucrose		Positive	6 wk	A, I
Intervention			81.7 kg (10.7)	30.4 (3.4)		5.1 (0.5)						Sugar-sweetened cocoa, 91 (~18) ; Placebo, 110 (~26) [h]	Sucrose	Sugar-sweetened hot cocoa beverage, placebo beverage	~55:30:15			
Control			81.3 kg (10.9)	30.2 (3.4)		5.1 (0.4)							Sweetener	Sugar-free hot cocoa beverage	~47:35:17			
Baked Goods and Sweets																		
Schwingshandl et al. 1994	24 DM1 (11 M, 13 W)	15.5 (5.5)	-		OP, Australia	-	-	8.7 (1.5)	P	DA	No			Sucrose		Positive		NR
Intervention	11 DM1 (8 M, 3 W)	15.0 (5.4)		20.2 (2.7)				8.5 (1.4)				~25 (5)	Sucrose	≤ 5% E as sucrose incorporated into cakes, ice-cream and snacks	49:36:16		83 d (42-127)	
Control	13 DM1 (3 M, 10 W)	16.0 (5.7)		21.2 (4.5)				8.8 (1.8)					Diet alone	Sucrose free diet	48:35:16		77 d (41-103)	
Added Sweeteners																		
Bahrami et al. 2009	48 DM2 (13 M, 35 W)	57.2 (8.4)	70.8 kg (10.6)	-	OP, Iran	8.0 (2.5)	-	7.1 (1.2)	P	Supp	Yes	~125 (~33)				Positive	8 wk	A
Intervention	25 DM2		71.3 kg (12.7)			8.5 (2.4)		7.1 (1.2)					Honey	Honey added to diet	64:23:15			
Control	23 DM2		70.3 kg (8.1)			7.5 (2.5)		7.1 (1.3)					Diet alone	Regular diet	60:22:15			
Colagiuri et al. 1989	9 DM2 (8 M, 1 W)	66 (5)	70.3 kg (8.1)	26.4 (2.1)	OP, Australia	5.7 (3.3)	-	7.2 (1.1)	C	Supp	No				NR	Positive	6 wk	A, I
Intervention												45 (~9)	Sucrose	Sucrose sachets added to beverages and meals				
Control													Sweetener	Aspartame sachets added to beverages and meals				
Enginyurt et al. 2017 (DM)	32 DM2 (16 M, 16 W)	(18-80)	-	-	OP, Turkey	-	-		P	Supp	Yes				NR	Positive	4 mo	NR
Intervention								6.6 (0.8)				5,10,15	Honey	Honey added to diet at 5,15, 25 g				
Control								7.09 (0.91)					Diet alone	Regular diet				
Enginyurt et al. 2017 (H)	32 H (16 M, 16 W)	(18-80)	-	-	OP, Turkey	-	-		P	Supp	Yes				NR	Positive	4 mo	NR
Intervention								5.4 (0.3)				5,10,15	Honey	Honey added to diet at 5,15, 25 g				
Control								5.15 (0.35)					Diet alone	Regular diet				
Majid et al. 2013		20.1 (0.8)	-	-	IP, Pakistan	5.0 (0.3)	-	-	P	Met	Yes				NR	Positive	4 wk	A
Intervention	32 H (32 M, 0 W)	20.1 (0.1)				5.0 (0.1)						70 (~11)	Honey	Honey dissolved in tap water				
Control	31 H (31 M, 0 W)	20.0 (0.2)				4.9 (0.1)							Diet Alone	No beverage				
Mixed Sources																		
Raben et al. 2011		35.4 (10.6)	82.4 kg (9.0)	28.2 (2.5)	OP, Denmark	4.7 (0.3)	39.5 (17.7)	-	P	Supp	Yes					Positive	10 wk	A, I
Intervention	12 OW	35.3 (9.7)	84.5 kg (8.3)	28.7 (2.4)		4.7 (0.4)	41.8 (18.4)					180 (27)	Sucrose	Sucrose containing food and beverages	56:29:11			
Control	11 OW	35.5 (11.9)	80.1 kg (9.6)	27.6 (2.7)		4.8 (0.3)	37.0 (17.6)					27 (5)	Sweetener	Artificially sweetened food and beverages	47:32:15			
Subtraction Studies (Hypocaloric comparison)																		
SSBs																		
Campos et al. 2015 (G1)	12 OW/OB (3 M, 9 W)	28.3 (6.5)	-	-	OP, Switzerland	5.1 (0.5)	85.8 (40.6)	-	P	Supp	Yes					Negative	12 wk	A
Intervention	6 OW/OB					4.9 (0.5)	104.9 (42.5)						Sweetener	Replace SSB with ASB	~46:38:16			

Control	6 OW/OB					5.2 (0.5)	66.7 (30.6)						86.8 (~15)	Sucrose, HFCS	Habitual SSB consumption (≥ 2 SSB/d)	~51:34:15		

Supplementary Table 2. (Continued)

Study, Year	Participants	Mean Age, years (SD or Range)	Mean BW, units (SD or range)	Mean BMI, kg/m² (SD)	Setting	Baseline			Design	Feeding Control [a]	Randomization	Fructose-Containing Sugars Dosage, g/d (% E)[b]	Intervention or comparator	Food source	Diet [c]	Energy Balance [d]	Follow-Up	Funding Sources [e]
						FBG, mmol/L (SD or range)	FBI, pmol/L (SD or range)	HbA1c, % (SD)										
Campos et al. 2015 (G2)	15 OW/OB (11 M, 4 W)	29.1 (6.9)	-	-	OP, Switzerland	5.5 (0.6)	133.7 (54.5)	-	P	Supp	Yes					Negative	12 wk	A
Intervention	7 OW/OB					5.2 (0.5)	127.1 (60.6)						Sweetener	Replace SSB with ASB	~46:38:16			
Control	8 OW/OB					5.7 (0.5)	140.3 (51.4)					86.8 (~15)	Sucrose, HFCS	Habitual SSB consumption (≥ 2 SSB/d)	~51:34:15			
Hernandez-Cordero et al. 2014	240 OW/OB (0 M, 240 W)				OP, Mexico	5.0 (0.2)	-	5.8 (0.1)	P	Supp	Yes				NR	Negative	9 mo	I
Intervention	120 OW/OB (0 M, 120 W)	33.5 (6.7)	76.9 kg (3.3)	31.0 (1.1)		5.0 (0.2)		5.8 (0.1)					Water	Substitute water for SSBs, general recommendations for healthy eating				
Control	120 OW/OB (0 M, 120 W)	33.4 (6.7)	76.0 kg (3.3)	31.0 (1.1)		5.0 (0.2)		5.8 (0.1)				~73 (19.3)	Sucrose, HFCS	Habitual SSB consumption (≥250 kcal/d), general recommendations for healthy eating				
Tate et al. 2012					OP, USA	5.1 (0.9)			P	Supp, DA	Yes				NR	Negative	6 mo	I
Intervention	213 OW/ OB (35 M, 178 W)	42.2 (10.9)	99.6 kg (18.5)	35.9 (5.7)		5.1 (1.0)	-	-				~33.7 (~8.7)	Sweetener, water	Diet beverage, Water				
Control	105 OW/OB (15 M, 90 W)	41.6 (10.4)	102.6 kg (18.3)	36.8 (6.2)		4.9 (0.6)	-	-				~55.7 (~13.8)	Sucrose, HFCS	Habitual SSB consumption (≥280 kcal/d)				
Mixed Sources																		
Friedman et al. 1970	6 HTG (6 M, 0 W)	45 (4.2)	103.2 kg (16.7)	-	OP, USA	-	-	-	C	DA	No					Negative		A
Intervention												~24 (~6) [m]	No sucrose	Avoid sucrose containing foods from habitual diet	25:45:30		60 d	
Control												~58 (~10) [m]	Sucrose	Habitual diet	29:39:32		7 d	
Ad Libitum Studies (Free feeding comparison)																		
Baked Goods and Sweets																		
Chantelau et al. 1985	10 DM1 (2 M, 8 W)	(25-43)	66.7 kg (7.6)	26.4 (2.1)	OP, Germany	-	-	7.6 (0.4)	C		Yes				52:26:22	Positive	4 wk	NR
Intervention										DA		24 (~5)	Sucrose	Ad libitum sucrose-containing food consumption; sucrose-containing soft drinks discouraged				
Control										Supp			Sweetener	Ad libitum sodium cyclamate tablets and liquids				
Mixed Sources																		
Huttunen et al. 1976	127 H	(13-55)	-	-	OP, Finland	-	-	-	P	Supp	Partial [n]				-	Neutral	18 mo	NR
Intervention	68 H											~72 (~14)	Fructose, sucrose	Ad libitum fructose and sucrose containing foods				
Control	48 H												Sweetener	Ad libitum xylitol containing foods with avoidance of sweet fruits and sucrose containing products				
Markey et al. 2015	50 H (16 M, 34 W)	31.3 (9.6)	69.8 kg (11.4)	24.0 (3.3)	OP, UK	4.9 (0.4)	31.0 (14.3)	-	C	Supp	Yes					Neutral	8 wk	I
Intervention	22 H (7 M, 15 W)	31.6 (10.2)	70.5 kg (13.1)	24.2 (3.3)		5.0 (0.5)	34.0 (16.9)					62 (~12) [o]	Sucose	Exchange ≥1 food portion and ≥1 beverage per day from habitual diet with sugar containing products	54:30:14			
Control	28 (9 M, 19 W)	31.1 (9.2)	69.3 kg (10.1)	23.9 (3.4)		4.8 (0.4)	29.4 (14.7)						Sweetener	Exchange ≥1 food portion and ≥1 beverage per day from habitual diet with sugar reformulated products	48:33:15			
Poppitt et al. 2002					OP, UK	5.7 (0.6)	-	-	P	Partial Met	Yes					Neutral	6 mo	A, I
Intervention	14 MetS (6 M, 8 W)	45.9 (5.0)	89.3 kg (15.7)	30.9 (3.0)		5.6 (0.5)						~165.4 (29) [p]	Sucrose	Ad libitum low-fat SCHO diet	~59:20:22			
Control	25 MetS (6 M, 19 W)	46.1 (5.4)	91.3 kg (9.2)	32.7 (35.2)		5.7 (0.7)							Starch, Mixed comparator	Ad libitum low fat CCHO diet, ad libitum habitual diet	Starch, ~50:26:24; Mixed,			

Supplementary Table 2. (Continued)

Study, Year	Participants	Mean Age, years (SD or Range)	Mean BW, units (SD or range)	Mean BMI, kg/m^2 (SD)	Setting	Baseline			Design	Feeding Control [a]	Randomization	Fructose-Containing Sugars Dosage, g/d (% E)[b]	Intervention or comparator	Food source	Diet [c]	Energy Balance [d]	Follow-Up	Funding Sources [e]
						FBG, mmol/L (SD or range)	FBI, pmol/L (SD or range)	HbA1c, % (SD)										
Raben et al. 2000 (PO)	8 PO (0 M, 8 W)	40 (11.3)	65.4 kg (3.4)	23.5 (1.4)	OP, Denmark			-	C	Met	Yes					Neutral	2 wk	A, I
Intervention						4.6 (0.2)	33 (18)					~156.7 (23)	Sucrose	Ad libitum sucrose diet	59:28:13			
Control						4.8 (0.3)	32 (21)						Starch, fat	Ad libitum starch diet, ad libitum fat diet	Starch, 59:28:13; Fat, 41:46:13			
Raben et al. 2000 (C)	10 H (0 M, 10 W)	38 (9.5)	62.1 kg (4.1)	22.9 (0.9)	OP, Denmark			-	C	Met	Yes					Neutral	2 wk	A, I
Intervention						4.9 (0.1)	32 (13)					~141.6 (23)	Sucrose	Ad libitum sucrose diet	59:28:13			
Control						4.8 (0.4)	34 (23)						Starch, fat	Ad libitum starch diet, ad libitum fat diet	Starch, 59:28:13; Fat, 41:46:13			
Saris et al. 2000					OP, Netherlands	5.4 (0.8)	84.5 (35.2)	-	P	Partial Met	Yes					Neutral	6 mo	A, I
Intervention	76 OW/OB (36 M, 40 W)	41 (9)	90.7 kg (12.7)	30.9 (2.8)								~183 (~29.5) [p]	Sucrose	Ad libitum Low-fat high SCHO diet	~56:26:16			
Control	160 OW/OB (80 M, 80 W)	38 (9)	88.7 kg (12.3)	30.3 (2.7)								Starch, ~ 105.7 (~18.8); Mixed, ~132.5 (~21.4) [p]	Starch, Mixed comparator	Ad libitum low-fat high CCHO diet, Ad libitum control diet	Starch, ~52:28:18 ; Mixed, ~46:37:18			

FBG=fasting blood glucose; FBI=fasting blood insulin; A= agency; AD=Adolescent; ADA= American Diabetes Association; ASB= artificially sweetened beverage; BB=blueberries; bw=body weight; C= controls; CAD= coronary artery disease; cal=calories; CCHO= complex carbohydrate; CG= control group; CHO=carbohydrate; CKD= chronic kidney disease; CND= chronic neurological disease; d=days; DBW= desirable body weight; DM1= Diabetes Mellitus Type 1; DA= dietary advice; DM2=Diabetes Mellitus Type 2; E=energy; EXP 1= experiment 1; EXP 2= experiment 2; G1=group 1; G2=group2; HCL= hypercholesterolemic; HD=high dose; HFCS= high fructose corn syrup; HI=hyperinsulinemic; HLP= hyperlipidemia; HTG = hypertriglyceridemia; HTN=hypertension; I= industry; IBW= ideal body weight; IGT= impaired glucose tolerance; kg=kilograms; M=men; mo=months; MD=moderate dose; OP=outpatient; Met=metabolic; MetS=metabolic syndrome criteria; MRW= mean relative weight; NGT=normal glucose tolerance; NR= not reported; OB= obese; OC= oral contraceptive users; ODM2 = offspring of parent with Type 2 Diabetes; OW= overweight; P1= protocol 1; P2= protocol 2; PCOS= polycystic ovarian syndrome; PO= post-obese; PP=pre-pubertal; RBW= relative body weight; SB= strawberries; SCHO=simple carbohydrates; SG= study group; SSB=sugars-sweetened beverage; Supp=supplemented; TEI= total energy intake; W= women; wk=weeks

[a] Metabolic feeding control included provision of all study foods, supplement feeding control included provision of study supplements only, and dietary advice included dietary counseling without the provision of any dietary foods or supplements.

[b] Doses preceded by "~" represent approximate amounts calculated on the basis of average body weight or energy intake reported by participants. In the absence of this data, an average of 70 kg body weight or 2000 kcal/d was assumed.

[c] Total energy intake in the form of carbohydrate:fat:protein

[d] Positive energy balance included interventions designed to consume excess calories on top of a baseline diet. Negative energy balance included interventions designed to create a caloric deficit compared to the baseline diet. Neutral energy balance included interventions designed to continue habitual caloric intake.

[e] Agency funding included government, not-for profit health agencies or University sources.

[f] Fructose-containing sugars dose estimated based on data from United States Department of Agriculture (USDA) nutrient database

[g] Fructose-containing sugars dose estimated based on data from Finland National Food Composition Database

[h] Fructose-containing sugars was given at 2 different doses.

[i] Although honey roasted peanuts were provided as the intervention, sucrose was the main sugar used to sweeten the study products.

[j] Represents estimated sugar intake excluding underreporters

[k] Values reported as medians and inter-quartile ranges (IQR)

[l] Fructose-containing sugars dose estimated based on the carbohydrate difference between the control diet (no juice) and the treatment diet (muscadine grape juice).

[m] Fructose-containing sugars dose estimated from total sugars used in study products

[n] Half of the participants were assigned to groups according to personal preference, while the other half of the participants were randomly allocated

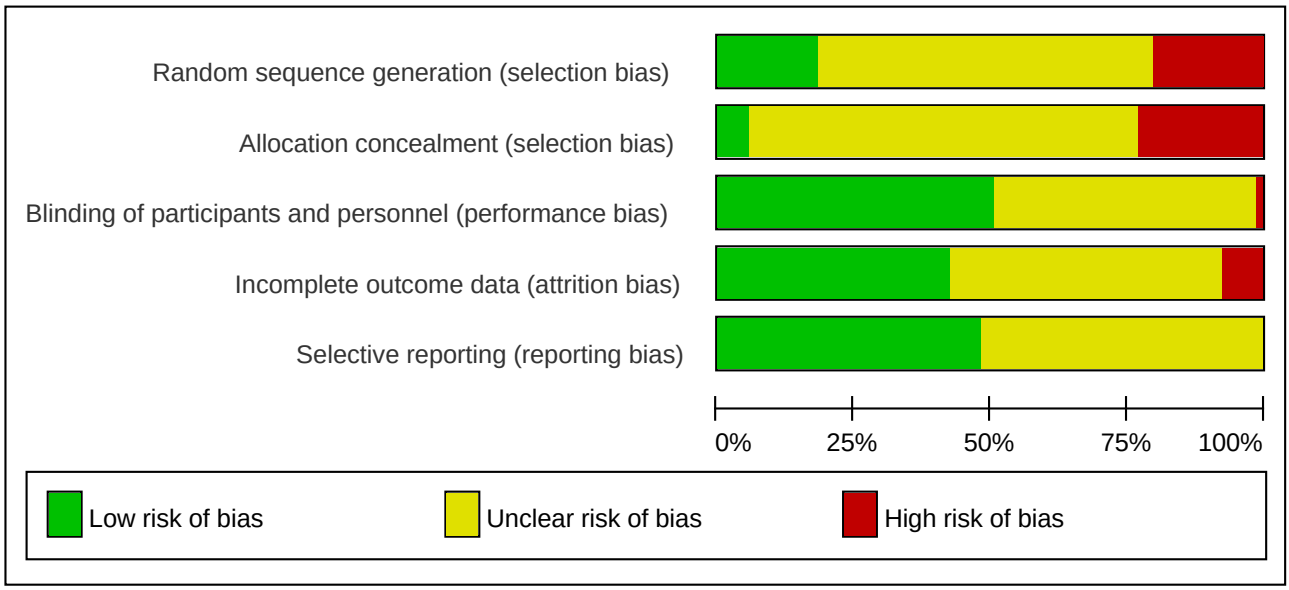
[o] Fructose-containing sugars dose estimated from non-milk extrinsic sugar intake

[p] Fructose-containing sugars dose estimated from simple carbohydrate intake

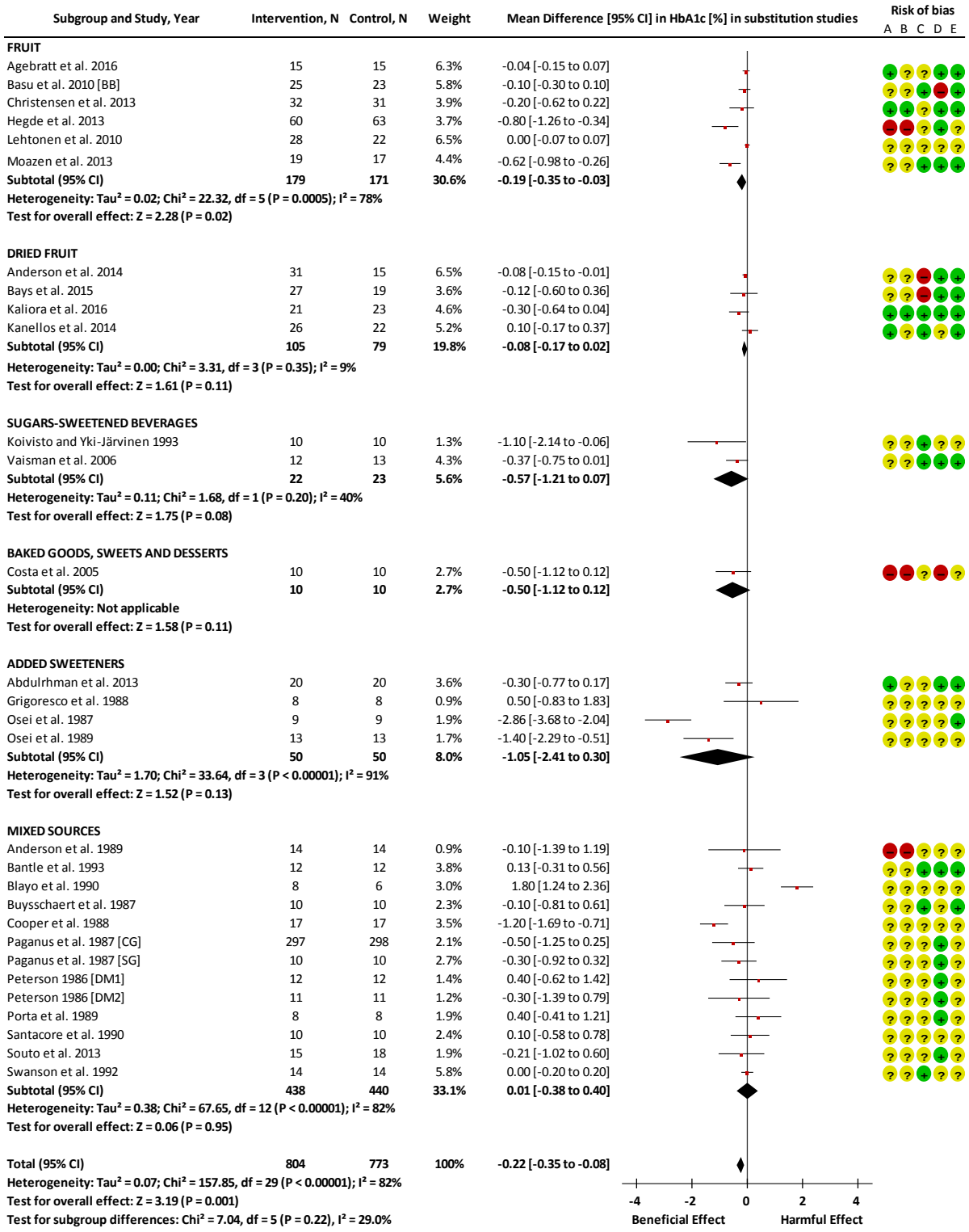
Supplementary Table 3. Select sensitivity analyses in which the systematic removal of an individual study altered the significance of the effect estimate or the evidence for substantial heterogeneity.

Removal of	Intervention N	Control N	Mean Difference MD	95% CI	*P*-value	Heterogeneity I^2	*P*-value
Fasting Blood Glucose							
Addition Studies							
Puglisi et al. 2008	10	12	0.08	[0.00 to 0.15]	0.04	71%	<0.0001
Ellis et al. 2011	12	12	0.08	[0.00 to 0.15]	0.04	71%	<0.0001
Abdel-Sayed et al. 2008	6	6	0.08	[0.00 to 0.15]	0.04	71%	<0.0001
Njike et al. 20011	39	39	0.08	[0.01 to 0.16]	0.03	69%	<0.0001
Bahrami et al. 2009	25	23	0.08	[0.01 to 0.15]	0.03	69%	<0.0001
Majid et al. 2013	32	31	0.09	[0.02 to 0.16]	0.02	67%	<0.0001
Subtraction Studies							
Campos et al. 2015 [G2]	7	8	-0.02	[-0.11 to 0.07]	0.63	0%	0.78
Tate et al. 2012	213	105	0.20	[0.00 to 0.40]	0.05	32%	0.23
Fasting Blood Insulin							
Addition Studies							
Hollis et al. 2009	25	25	3.71	[0.94 to 6.49]	<0.01	42%	0.02
Substitution studies							
Maersk et al. 2012	10	12	2.78	[0.22 to 5.34]	0.03	57%	<0.0001
Koh et al. 1988 - NGT	9	9	2.58	[0.10 to 5.05]	0.04	55%	<0.0001
Subtraction Studies							
Campos et al. 2015 (G2)	7	8	-39.54	[-75.02 to -4.06]	0.03	1%	0.31
Ad Libitum Studies							
Raben et al. 2000 (c)	8	8	5.72	[-1.55 to 12.99]	0.12	0 %	0.51

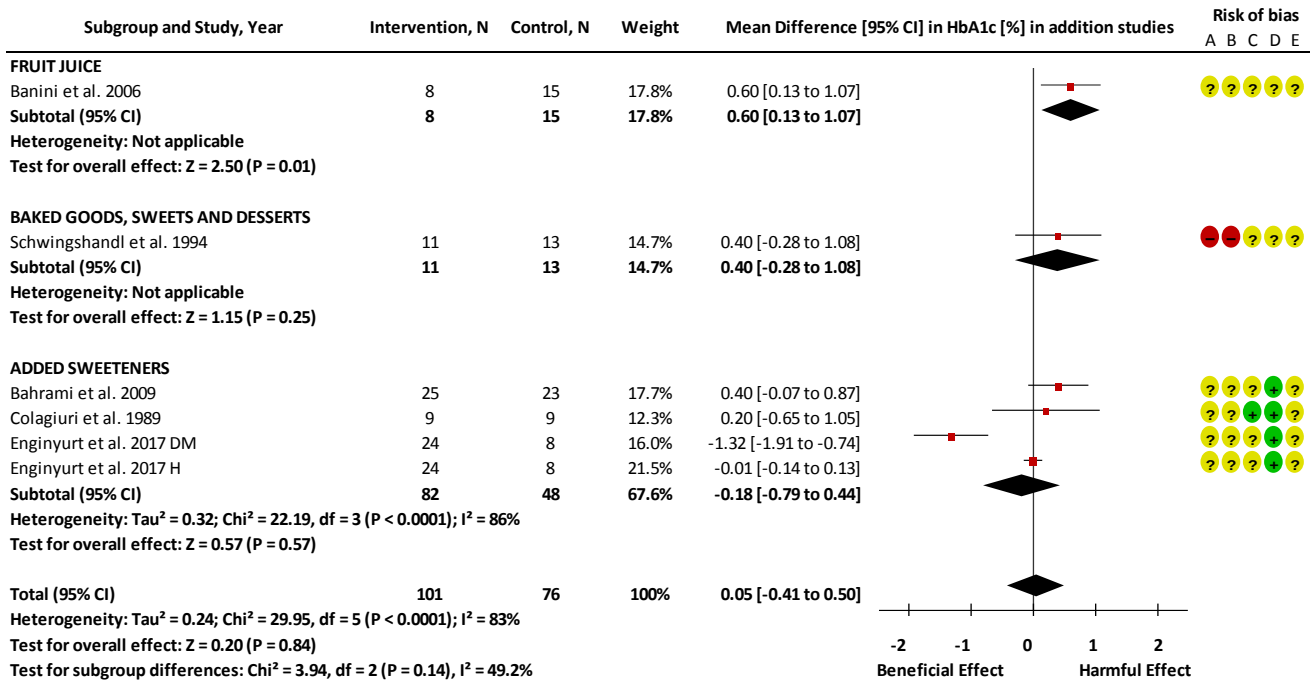
DM= diabetes mellitus; G2= Group 2; ODM2=offspring of people with type 2 diabetes. Data are expressed as mean differences (MD) with 95% CI, using generic inverse-variance random-effects models. Interstudy heterogeneity was tested by using the Cochrane's Q statistic (I^2) at a significance level of $P < 0.10$ and quantified by I^2, levels ≥ 50 % represent substantial heterogeneity. The residual I^2 value indicates the interstudy heterogeneity unexplained by the removal of each study.



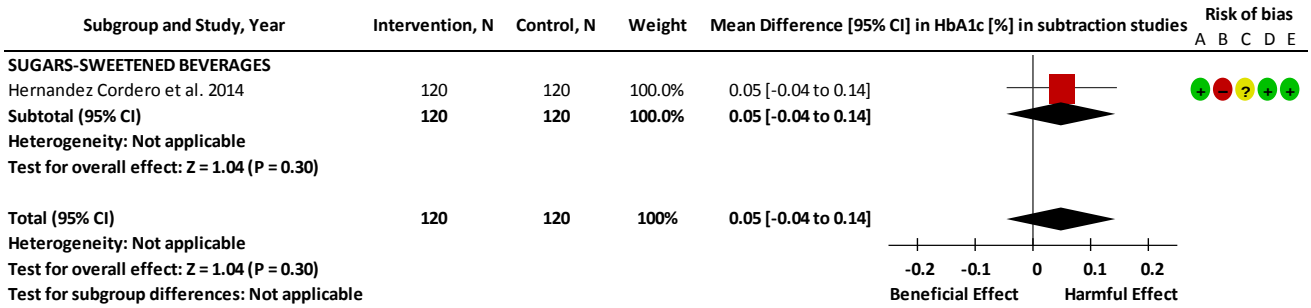
Supplementary Figure 1. Risk of bias summary for the effect of food sources of fructose-containing sugars on glycemic control. Colored bars represent the proportion of studies assessed as low (green), unclear (yellow) or high (red) risk of bias for the 5 domains of bias above according to criteria set by the Cochrane Risk of Bias tool in the 118 included unique studies.



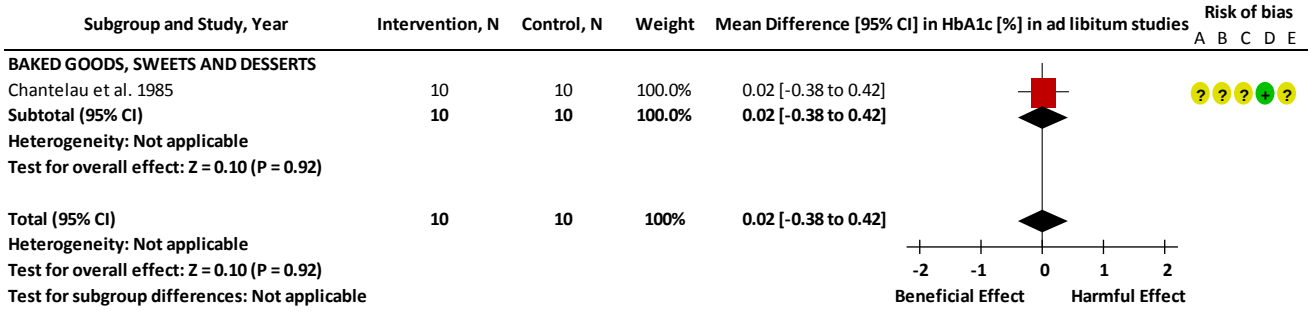
Supplementary Figure 2. Forest plot for substitution studies investigating the effect of isocaloric exchange of food sources of fructose-containing sugars for other macronutrients on HbA1c. Risk of bias: A=random sequence generation; B=allocation concealment; C=blinding of participants and personnel; D=incomplete outcome data; E=selective reporting. CG= control group; SG= study group; df= degrees of freedom; DM1= type 1 diabetes mellitus; DM2= type 2 diabetes mellitus; EXP=experiment; HbA1c= hemoglobin A1c; N= number of participants. Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals (CIs), using the generic inverse-variance method with random effects models. Paired analyses were applied to all crossover studies. Inter-study heterogeneity was tested by the Cochran Q-statistic at a significance level of $p < 0.10$ and quantified by I^2, level of ≥ 50 % represented substantial heterogeneity.



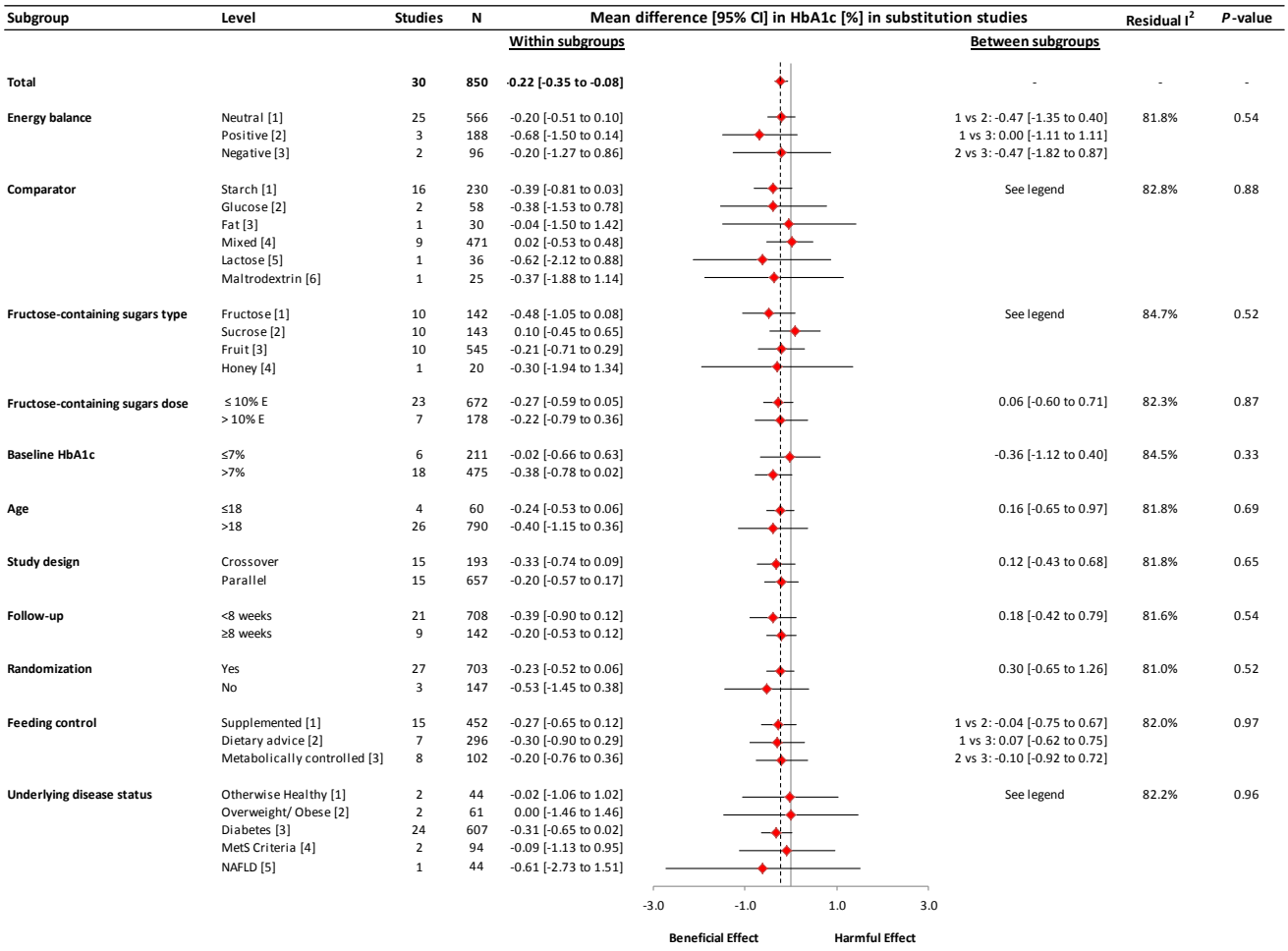
Supplementary Figure 3. Forest plot for addition studies investigating the effect of adding excess calories to the diet in the form of food sources of fructose-containing sugars on HbA1c. Risk of bias: A=random sequence generation; B=allocation concealment; C=blinding of participants and personnel; D=incomplete outcome data; E=selective reporting. BB= blueberries; HbA1c= hemoglobin A1c; N= number of participants; DM=diabetes mellitus; H=healthy. Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals (CIs), using the generic inverse-variance method with random effects models. Paired analyses were applied to all crossover studies. Inter-study heterogeneity was tested by the Cochran Q-statistic at a significance level of $p < 0.10$ and quantified by I^2, level of ≥ 50 % represented substantial heterogeneity.



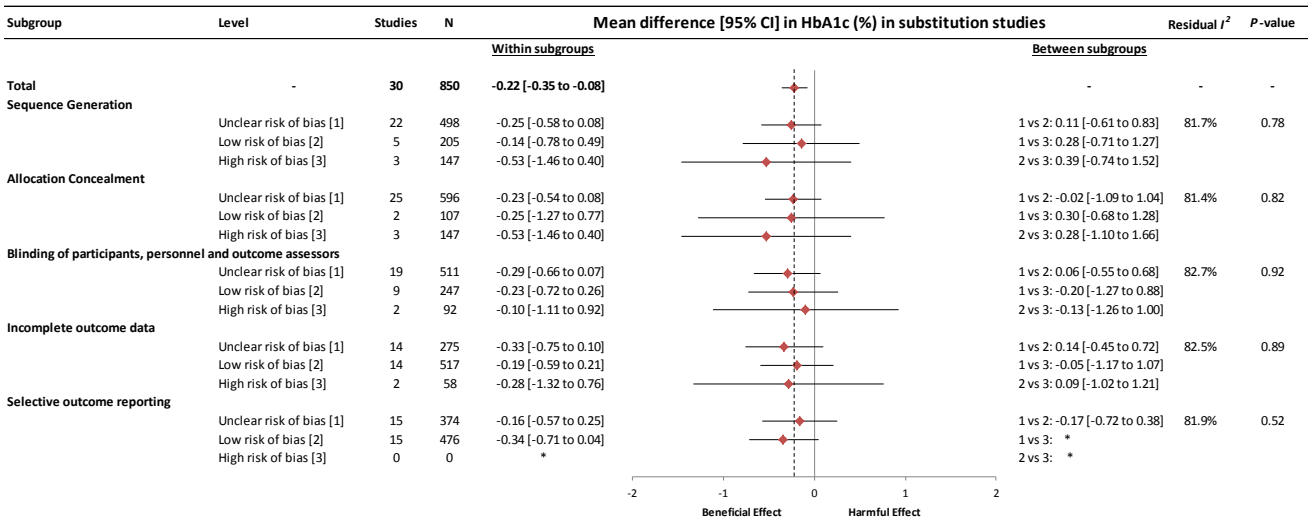
Supplementary Figure 4. Forest plot for subtraction studies investigating the effect of removing calories from the diet in the form of food sources of fructose-containing sugars on HbA1c. Risk of bias: A=random sequence generation; B=allocation concealment; C=blinding of participants and personnel; D=incomplete outcome data; E=selective reporting. HbA1c= hemoglobin A1c; N= number of participants. Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals (CIs), using the generic inverse-variance method with fixed effects models. Paired analyses were applied to all crossover studies. Inter-study heterogeneity was tested by the Cochran Q-statistic at a significance level of $p < 0.10$ and quantified by I^2, level of ≥ 50 % represented substantial heterogeneity.



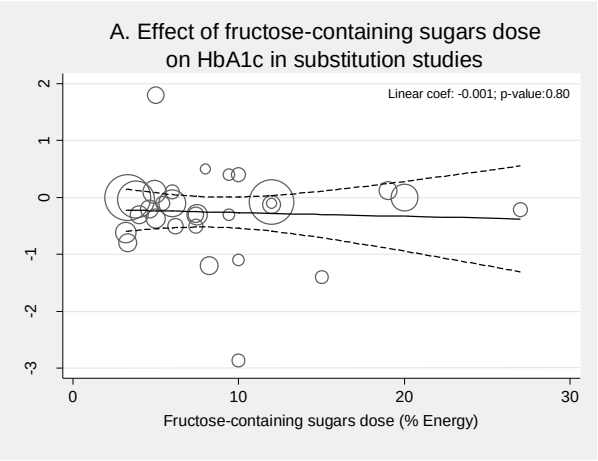
Supplementary Figure 5. Forest plot for ad libitum studies investigating the effect of freely replacing calories from food sources of fructose-containing sugars with other dietary sources on HbA1c. Risk of bias: A=random sequence generation; B=allocation concealment; C=blinding of participants and personnel; D=incomplete outcome data; E=selective reporting. HbA1c= hemoglobin A1c; N= number of participants. Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals (CIs), using the generic inverse-variance method with fixed effects models. Paired analyses were applied to all crossover studies. Inter-study heterogeneity was tested by the Cochran Q-statistic at a significance level of $p < 0.10$ and quantified by I^2, level of ≥ 50 % represented substantial heterogeneity.

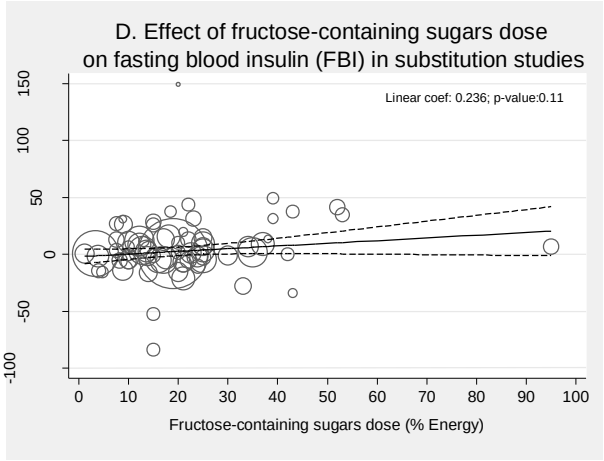


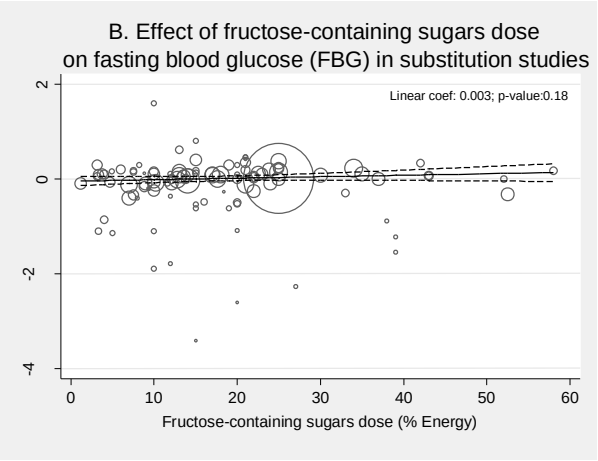
Supplementary Figure 6. Subgroup analyses for substitution studies investigating the effect of isocaloric exchange of food sources of fructose-containing sugars for other macronutrients on HbA1c. E= energy; HbA1c=hemoglobin A1C; MetS= metabolic syndrome; N= number of participants. Pooled effect estimates for each subgroup are represented by the diamonds. The dashed line represents the pooled effect estimate for the overall analysis. The residual I^2 value represents unexplained heterogeneity for each subgroup. Pairwise between-subgroup mean differences (95% CI) for comparator are as follows: 1 vs 2: 0.01 [-1.21 to 1.24]; 1 vs 3: 0.35 [-1.17 to 1.86]; 1 vs 4: 0.37 [-0.29 to 1.02]; 1 vs 5: -0.23 [-1.79 to 1.33]; 1 vs 6: 0.02 [-1.55 to 1.58]; 2 vs 3: -0.34 [-2.19 to 1.52]; 2 vs 4: -0.35 [-1.61 to 0.91]; 2 vs 5: 0.25 [-1.65 to 2.14]; 2 vs 6: -0.01 [-1.90 to 1.89]; 3 vs 4: -0.02 [-1.56 to 1.52]; 3 vs 5: 0.58 [-1.51 to 2.67]; 3 vs 6: 0.33 [-1.77 to 2.43]; 4 vs 5: 0.60 [-0.99 to 2.18]; 4 vs 6: 0.35 [-1.24 to 1.93]; 5 vs 6: -0.25 [-2.38 to 1.88]. Pairwise between-subgroup mean differences (95% CI) for fructose-containing sugars type are as follows: 1 vs 2: 0.58 [-0.21 to 1.37]; 1 vs 3: 0.27 [-0.48 to 1.03]; 1 vs 4: 0.18 [-1.55 to 1.92]; 2 vs 3: 0.31 [-0.44 to 1.06]; 2 vs 4: 0.40 [-1.33 to 2.13]; 3 vs 4: 0.09 [-1.62 to 1.80]. Pairwise between-subgroup mean differences (95% CI) for underlying disease status are as follows: 1 vs 2: -0.02 [-1.81 to 1.77]; 1 vs 3: 0.29 [-0.80 to 1.38]; 1 vs 4: 0.07 [-1.40 to 1.53]; 1 vs 5: 0.59 [-1.77 to 2.95]; 2 vs 3: 0.31 [-1.18 to 1.81]; 2 vs 4: 0.09 [-1.70 to 1.88]; 2 vs 5: 0.61 [-2.68 to 3.91]; 3 vs 4: 0.22 [-0.87 to 1.31]; 3 vs 5: -0.30 [-2.39 to 1.79]; 4 vs 5: 0.52 [-1.83 to 2.88].

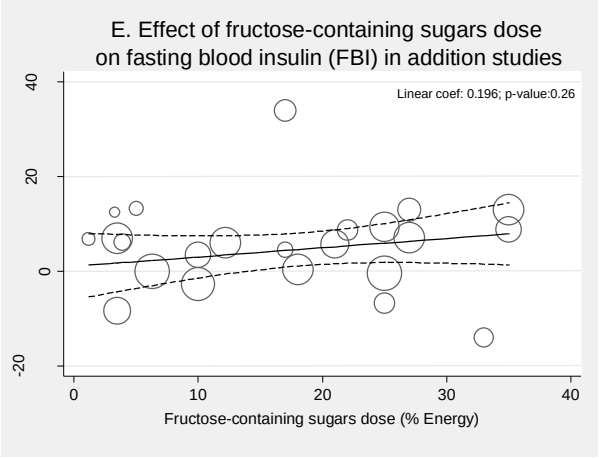


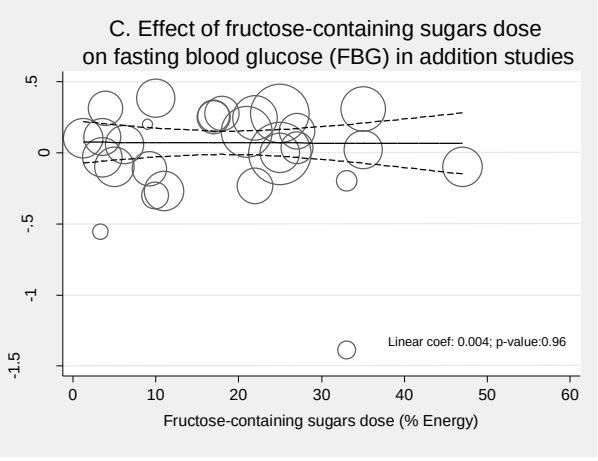
Supplementary Figure 7. Risk of bias (using The Cochrane Collaboration Tool) subgroup analysis for substitution studies investigating the effect of isocaloric exchange of food sources of fructose-containing sugars for other macronutrients on HbA1c. Point estimates for each subgroup level are the pooled effect estimates and are represented by diamonds. The residual I^2 value represents unexplained heterogeneity for each subgroup. HRB=High Risk of Bias, LRB=Low Risk of Bias, URB= Unclear Risk of Bias. *Within and/or between subgroup analysis could not be performed since no values were available for respective HRB/URB/LRB subgroups. Statistically significant pairwise subgroup effect modification by meta-regression analysis ($P< 0.05$).



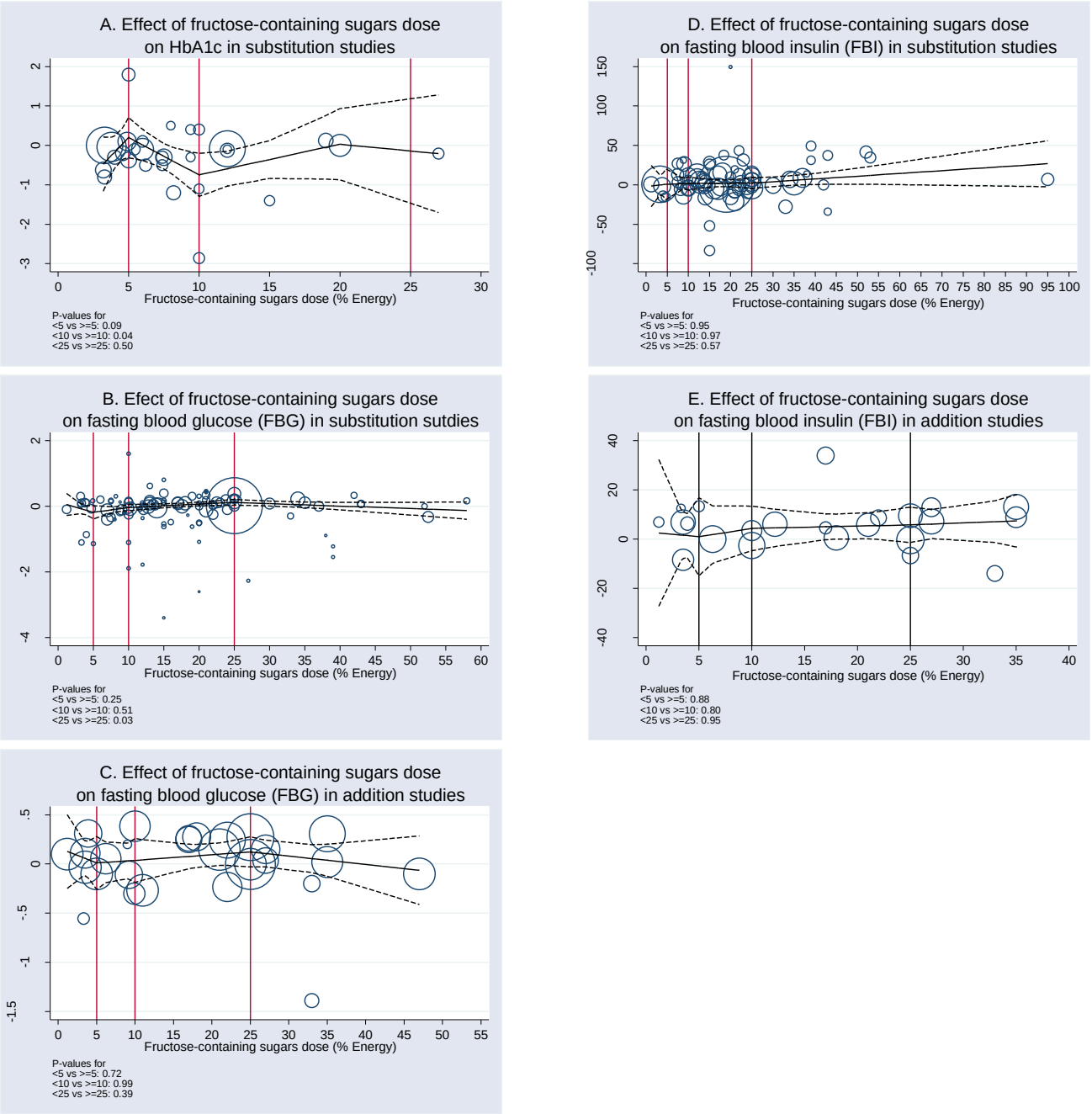




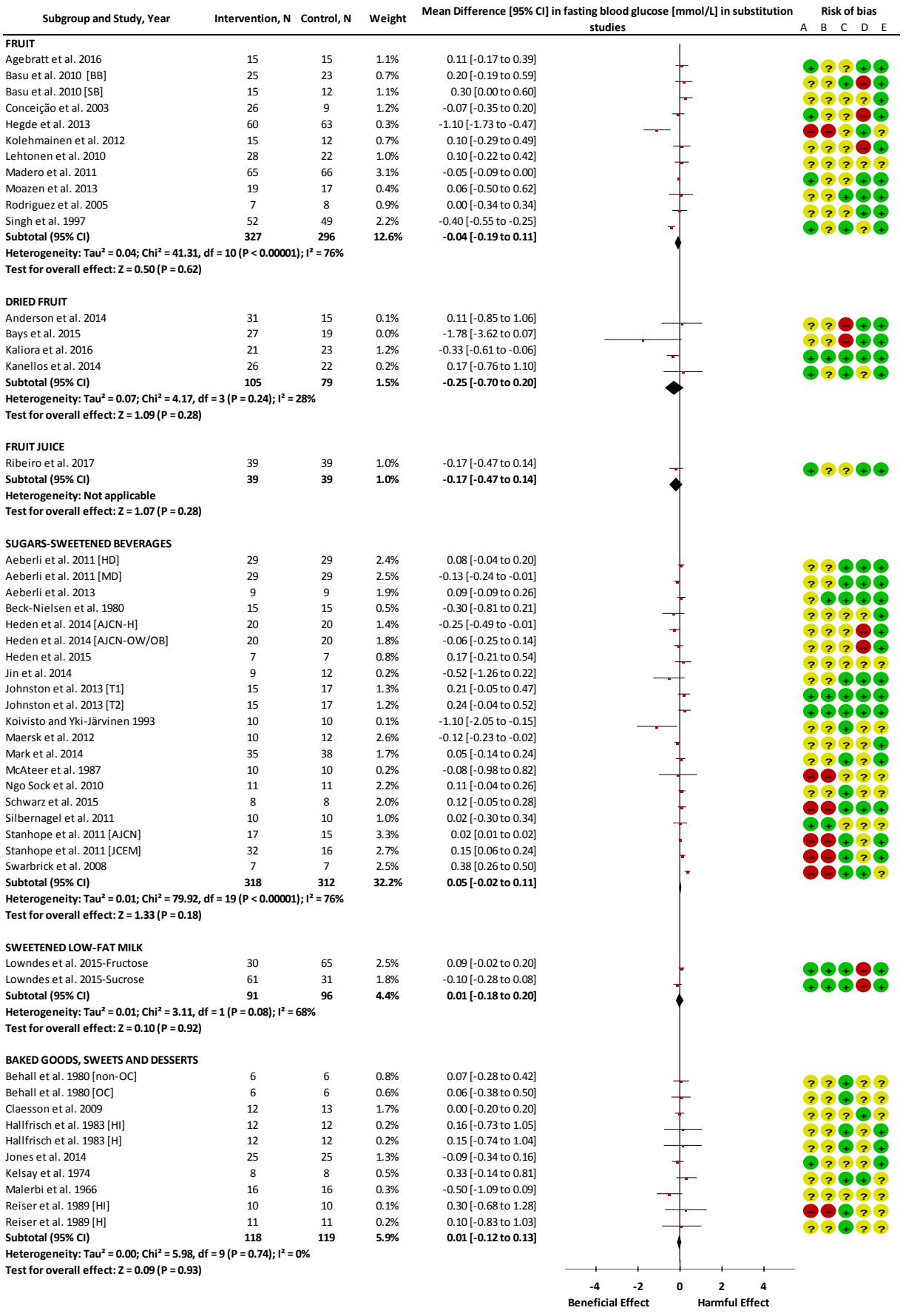




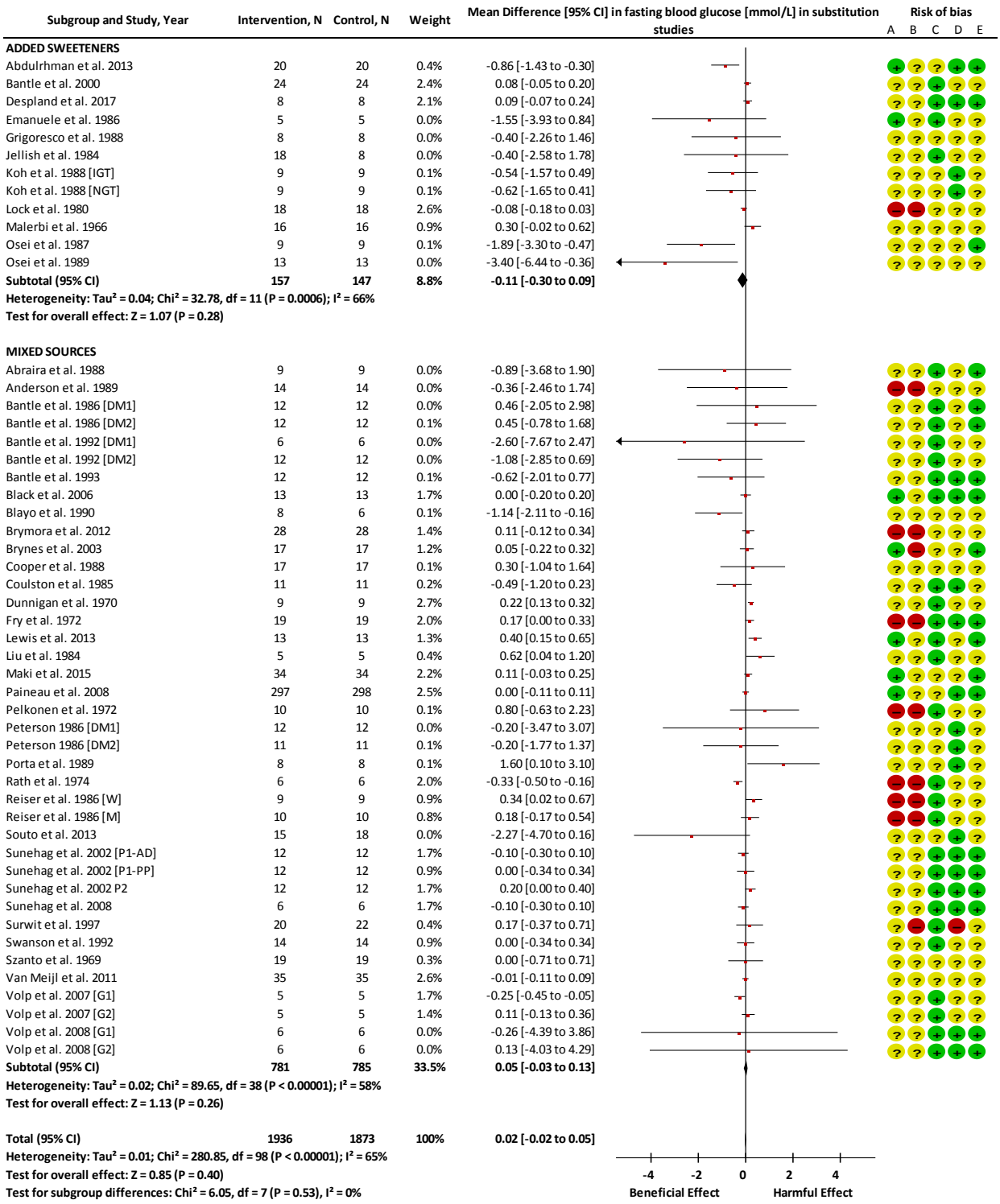
Supplementary Figure 8. Linear meta-regression analyses for the effect of fructose-containing sugars dose (%E) on glycemic control in substitution and addition studies. Individual studies are represented by the circles, with their weight in the overall analysis represented by the size of the circles. The straight line represents the estimate dose response for amount of fructose-containing sugars consumed (% of total energy intake) and the dashed lines represent the upper and lower 95% Confidence Intervals.



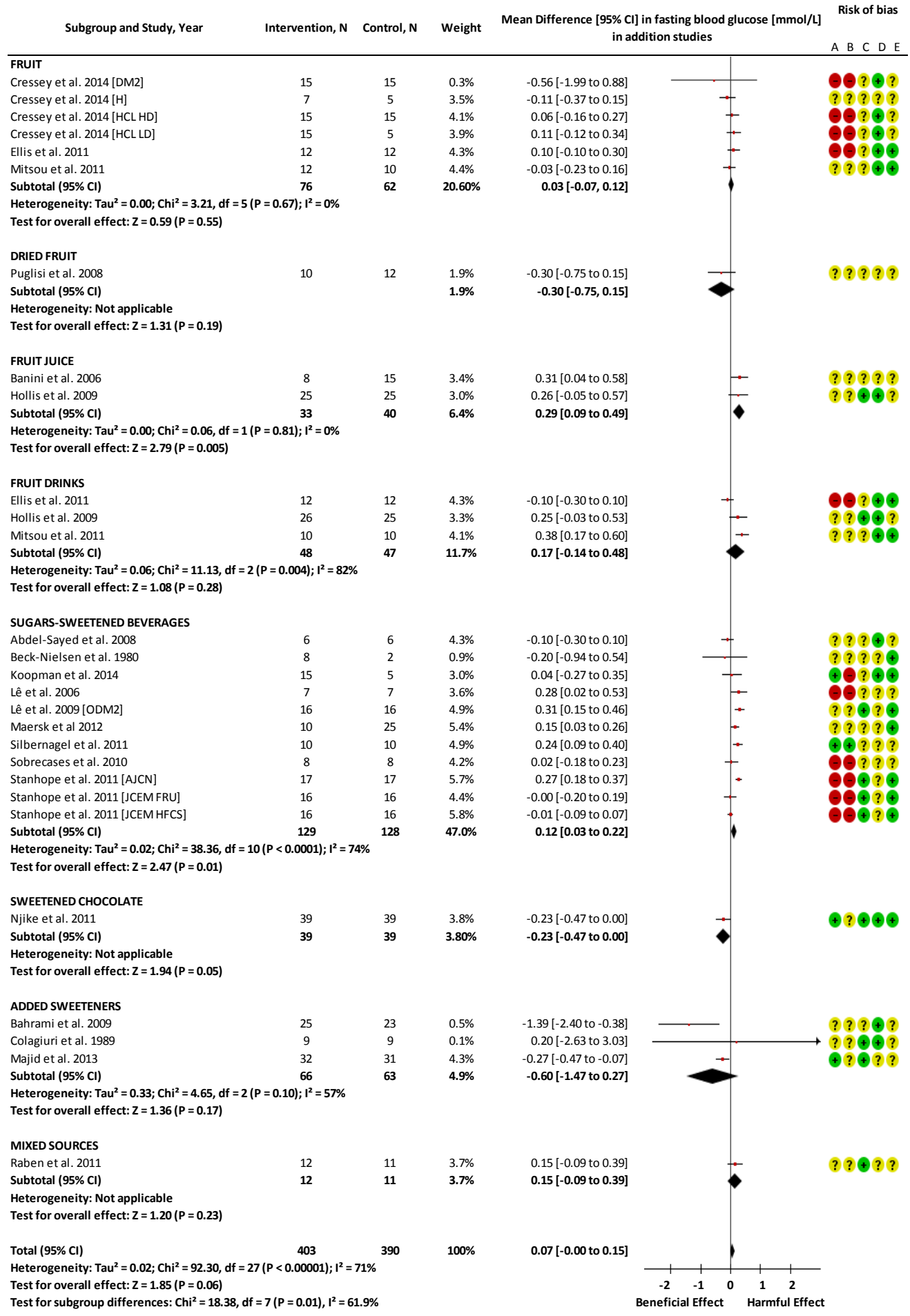
Supplementary Figure 9. Non-linear meta-regression analyses for the effect of fructose-containing sugars dose (% Energy) on glycemic control in substitution and addition studies. Individual studies are represented by the circles, with their weight in the overall analysis represented by the size of the circles. The horizontal straight line represents the estimate dose response for amount of fructose-containing sugars consumed (% of total energy intake), and the dashed lines represent the upper and lower 95% Confidence Intervals. The vertical straight lines represent the threshold knots.



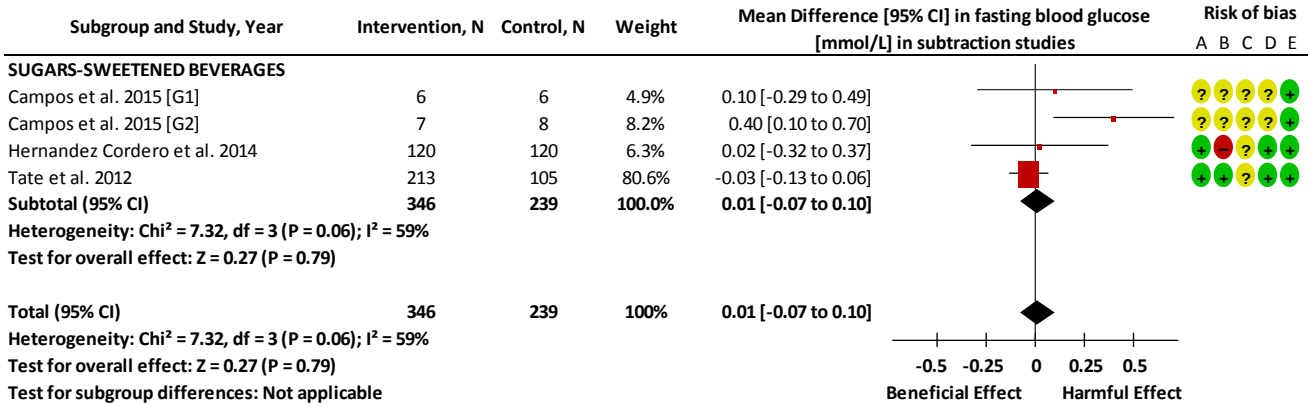
Supplementary Figure 10. Forest plot for substitution studies investigating the effect of isocaloric exchange of food sources of fructose-containing sugars for other macronutrients on fasting blood glucose (continues next page).



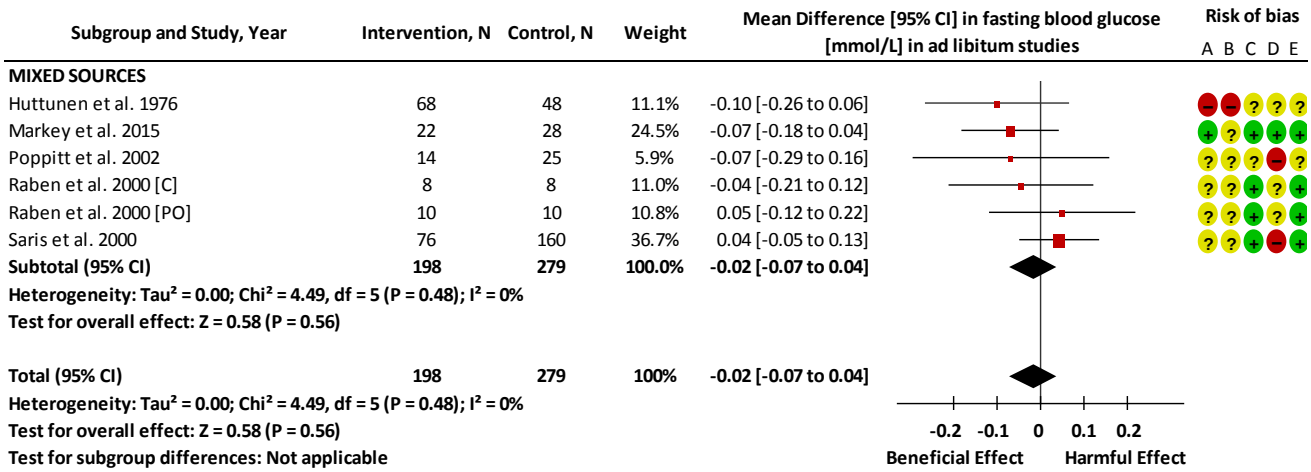
Supplementary Figure 10. (continued). Risk of bias: A=random sequence generation; B=allocation concealment; C=blinding of participants and personnel; D=incomplete outcome data; E=selective reporting. AJCN = American Journal of Clinical Nutrition; DM= diabetes mellitus; EXP1= experiment 1; EXP2= experiment 2; H=healthy; HC= high carbohydrate; HD= high dose; HI=hyperinsulinemic; JPAH= Journal of Physical Activity and Health; JCEM= Journal of Clinical Endocrinology and Metabolism; LC= low carbohydrate; MD= moderate dose; N= number of participants; OC= oral contraceptive users; OW/OB= overweight/obese participants; T1= trial 1; T2=Trial 2. Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals (CIs), using the generic inverse-variance method with random effects models. Paired analyses were applied to all crossover studies. Inter-study heterogeneity was tested by the Cochran Q-statistic at a significance level of $p < 0.10$ and quantified by I^2, level of ≥ 50 % represents substantial heterogeneity.


Subgroup and Study, Year
Intervention, N
Control, N
Weight
Mean Difference [95% CI] in fasting blood glucose [mmol/L] in addition studies
Risk of bias
A B C D E
FRUIT
Cressey et al. 2014 [DM2] 15 15 0.3% -0.56 [-1.99 to 0.88]
Cressey et al. 2014 [H] 7 5 3.5% -0.11 [-0.37 to 0.15]
Cressey et al. 2014 [HCL HD] 15 15 4.1% 0.06 [-0.16 to 0.27]
Cressey et al. 2014 [HCL LD] 15 5 3.9% 0.11 [-0.12 to 0.34]
Ellis et al. 2011 12 12 4.3% 0.10 [-0.10 to 0.30]
Mitsou et al. 2011 12 10 4.4% -0.03 [-0.23 to 0.16]
Subtotal (95% CI) 76 62 20.60% 0.03 [-0.07, 0.12]
Heterogeneity: Tau² = 0.00; Chi² = 3.21, df = 5 (P = 0.67); I² = 0%
Test for overall effect: Z = 0.59 (P = 0.55)
DRIED FRUIT
Puglisi et al. 2008 10 12 1.9% -0.30 [-0.75 to 0.15]
Subtotal (95% CI) 1.9% -0.30 [-0.75, 0.15]
Heterogeneity: Not applicable
Test for overall effect: Z = 1.31 (P = 0.19)
FRUIT JUICE
Banini et al. 2006 8 15 3.4% 0.31 [0.04 to 0.58]
Hollis et al. 2009 25 25 3.0% 0.26 [-0.05 to 0.57]
Subtotal (95% CI) 33 40 6.4% 0.29 [0.09 to 0.49]
Heterogeneity: Tau² = 0.00; Chi² = 0.06, df = 1 (P = 0.81); I² = 0%
Test for overall effect: Z = 2.79 (P = 0.005)
FRUIT DRINKS
Ellis et al. 2011 12 12 4.3% -0.10 [-0.30 to 0.10]
Hollis et al. 2009 26 25 3.3% 0.25 [-0.03 to 0.53]
Mitsou et al. 2011 10 10 4.1% 0.38 [0.17 to 0.60]
Subtotal (95% CI) 48 47 11.7% 0.17 [-0.14 to 0.48]
Heterogeneity: Tau² = 0.06; Chi² = 11.13, df = 2 (P = 0.004); I² = 82%
Test for overall effect: Z = 1.08 (P = 0.28)
SUGARS-SWEETENED BEVERAGES
Abdel-Sayed et al. 2008 6 6 4.3% -0.10 [-0.30 to 0.10]
Beck-Nielsen et al. 1980 8 2 0.9% -0.20 [-0.94 to 0.54]
Koopman et al. 2014 15 5 3.0% 0.04 [-0.27 to 0.35]
Lê et al. 2006 7 7 3.6% 0.28 [0.02 to 0.53]
Lê et al. 2009 [ODM2] 16 16 4.9% 0.31 [0.15 to 0.46]
Maersk et al 2012 10 25 5.4% 0.15 [0.03 to 0.26]
Silbernagel et al. 2011 10 10 4.9% 0.24 [0.09 to 0.40]
Sobrecases et al. 2010 8 8 4.2% 0.02 [-0.18 to 0.23]
Stanhope et al. 2011 [AJCN] 17 17 5.7% 0.27 [0.18 to 0.37]
Stanhope et al. 2011 [JCEM FRU] 16 16 4.4% -0.00 [-0.20 to 0.19]
Stanhope et al. 2011 [JCEM HFCS] 16 16 5.8% -0.01 [-0.09 to 0.07]
Subtotal (95% CI) 129 128 47.0% 0.12 [0.03 to 0.22]
Heterogeneity: Tau² = 0.02; Chi² = 38.36, df = 10 (P < 0.0001); I² = 74%
Test for overall effect: Z = 2.47 (P = 0.01)
SWEETENED CHOCOLATE
Njike et al. 2011 39 39 3.8% -0.23 [-0.47 to 0.00]
Subtotal (95% CI) 39 39 3.80% -0.23 [-0.47 to 0.00]
Heterogeneity: Not applicable
Test for overall effect: Z = 1.94 (P = 0.05)
ADDED SWEETENERS
Bahrami et al. 2009 25 23 0.5% -1.39 [-2.40 to -0.38]
Colagiuri et al. 1989 9 9 0.1% 0.20 [-2.63 to 3.03]
Majid et al. 2013 32 31 4.3% -0.27 [-0.47 to -0.07]
Subtotal (95% CI) 66 63 4.9% -0.60 [-1.47 to 0.27]
Heterogeneity: Tau² = 0.33; Chi² = 4.65, df = 2 (P = 0.10); I² = 57%
Test for overall effect: Z = 1.36 (P = 0.17)
MIXED SOURCES
Raben et al. 2011 12 11 3.7% 0.15 [-0.09 to 0.39]
Subtotal (95% CI) 12 11 3.7% 0.15 [-0.09 to 0.39]
Heterogeneity: Not applicable
Test for overall effect: Z = 1.20 (P = 0.23)
Total (95% CI) 403 390 100% 0.07 [-0.00 to 0.15]
Heterogeneity: Tau² = 0.02; Chi² = 92.30, df = 27 (P < 0.00001); I² = 71%
Test for overall effect: Z = 1.85 (P = 0.06)
Test for subgroup differences: Chi² = 18.38, df = 7 (P = 0.01), I² = 61.9%
-2 -1 0 1 2
Beneficial Effect
Harmful Effect

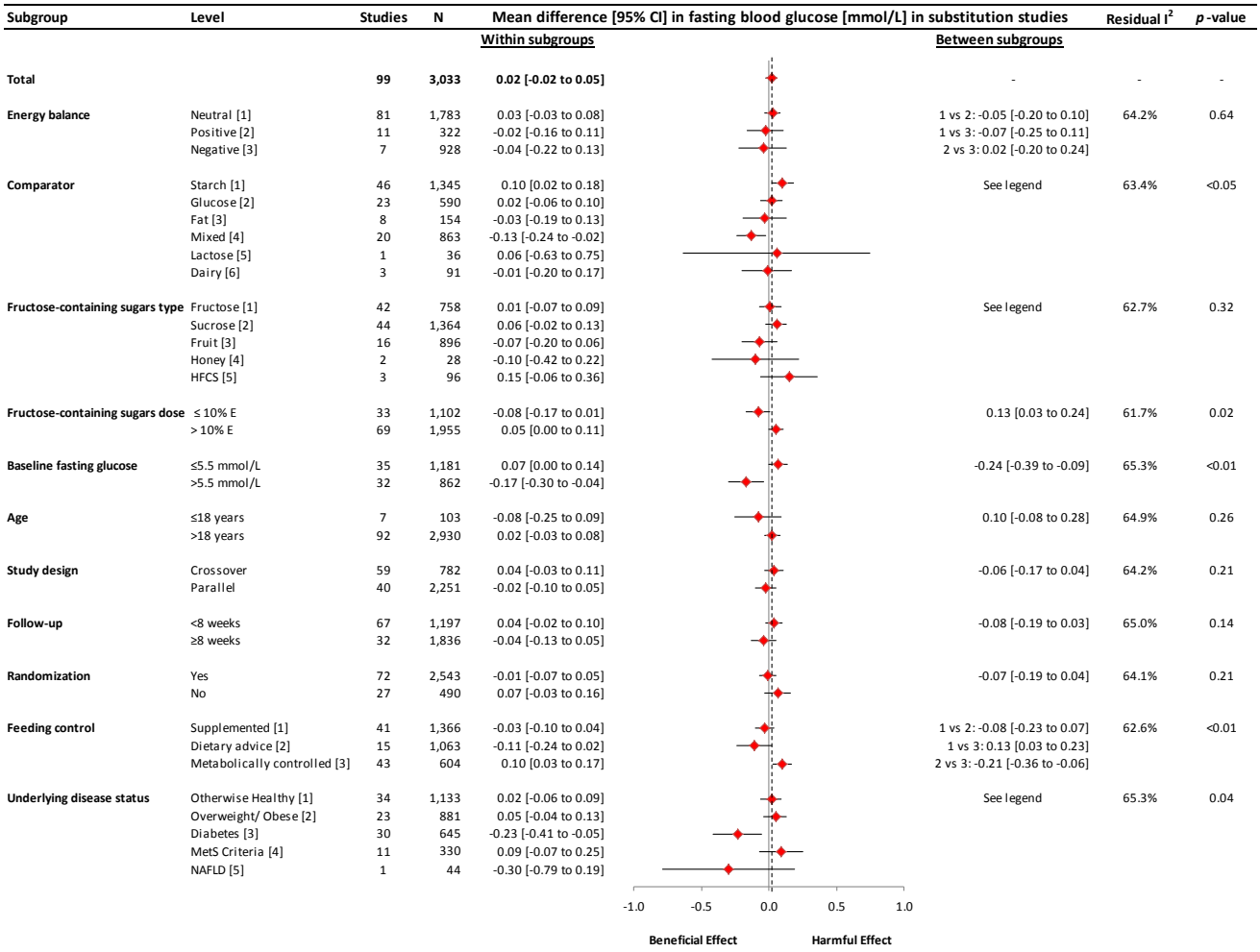
Supplementary Figure 11. Forest plot for addition studies investigating the effect of adding excess calories to the diet in the form of food sources of fructose-containing sugars on fasting blood glucose. Risk of bias: A=random sequence generation; B=allocation concealment; C=blinding of participants and personnel; D=incomplete outcome data; E=selective reporting. AJCN = American Journal of Clinical Nutrition; BB= blueberries; DM2= type 2 diabetes mellitus; EXP2= experiment 2; FRU=fructose; H=healthy; HCL= hypercholesterolemic; HD= high dose; HFCS= high fructose corn syrup; JCEM= Journal of Clinical Endocrinology and Metabolism; LD= low dose; N= number of participants; ODM2= offspring of people with type 2 diabetes; SB= strawberries. Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals (CIs), using the generic inverse-variance method with random effects models. Paired analyses were applied to all crossover studies. Inter-study heterogeneity was tested by the Cochran Q-statistic at a significance level of $p < 0.10$ and quantified by I^2, level of ≥ 50 % represents substantial heterogeneity.



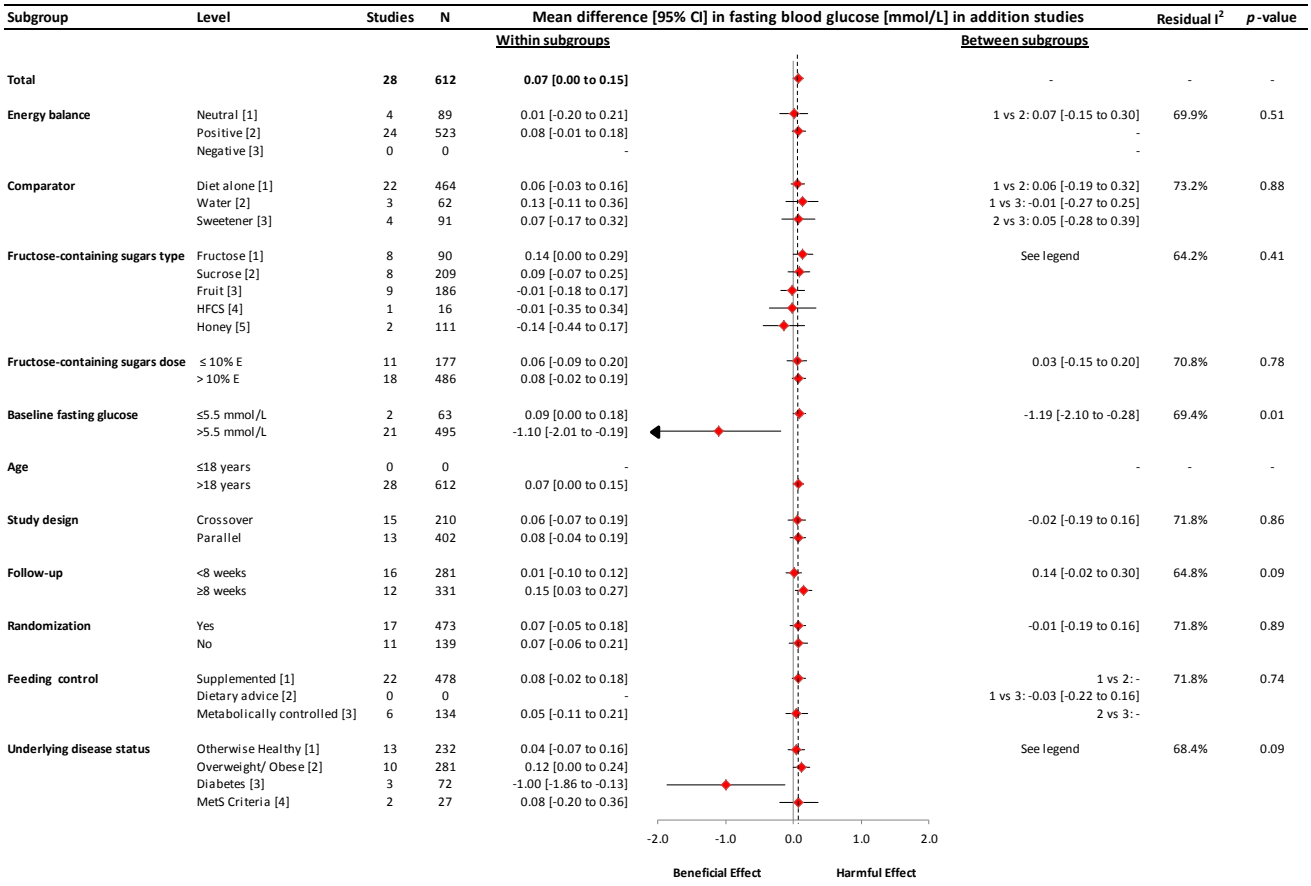
Supplementary Figure 12. Forest plot for subtraction studies investigating the effect of removing calories from the diet in the form of food sources of fructose-containing sugars on fasting blood glucose. Risk of bias: A=random sequence generation; B=allocation concealment; C=blinding of participants and personnel; D=incomplete outcome data; E=selective reporting. G1= group 1; G2= group 2; N= number of participants. Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals (CIs), using the generic inverse-variance method with fixed effects models. Paired analyses were applied to all crossover studies. Inter-study heterogeneity was tested by the Cochran Q-statistic at a significance level of $p < 0.10$ and quantified by I^2, level of ≥ 50 % represents substantial heterogeneity.



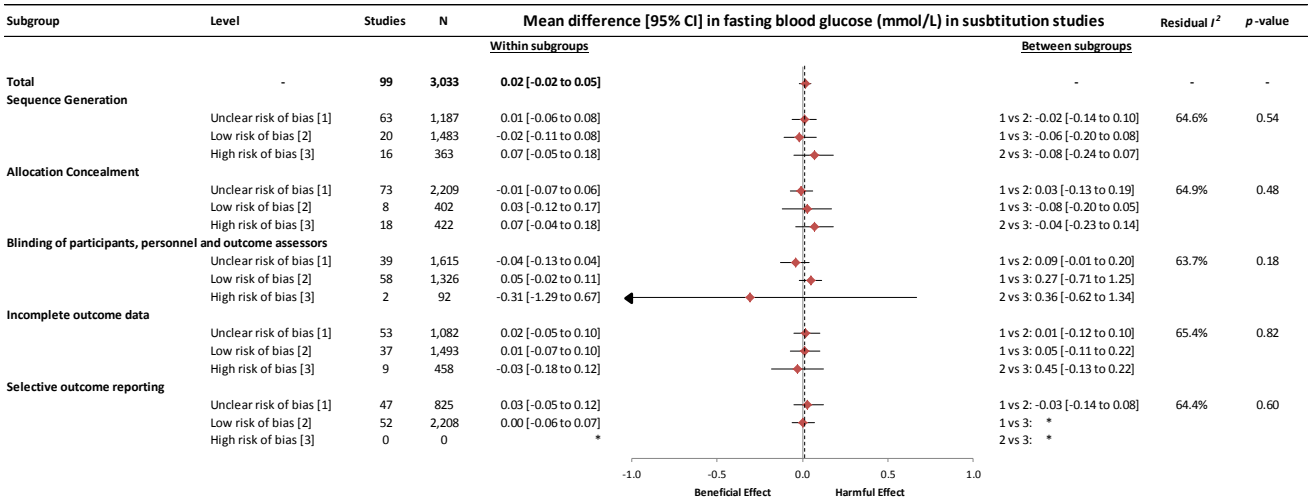
Supplementary Figure 13. Forest plot for ad libitum studies investigating the effect of freely replacing calories from food sources of fructose-containing sugars with other dietary sources on fasting blood glucose. Risk of bias: A=random sequence generation; B=allocation concealment; C=blinding of participants and personnel; D=incomplete outcome data; E=selective reporting. C= controls; N= number of participants; PO= post-obese. Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals (CIs), using the generic inverse-variance method with random effects models. Paired analyses were applied to all crossover studies. Inter-study heterogeneity was tested by the Cochran Q-statistic at a significance level of $p < 0.10$ and quantified by I^2, level of ≥ 50 % represents substantial heterogeneity.



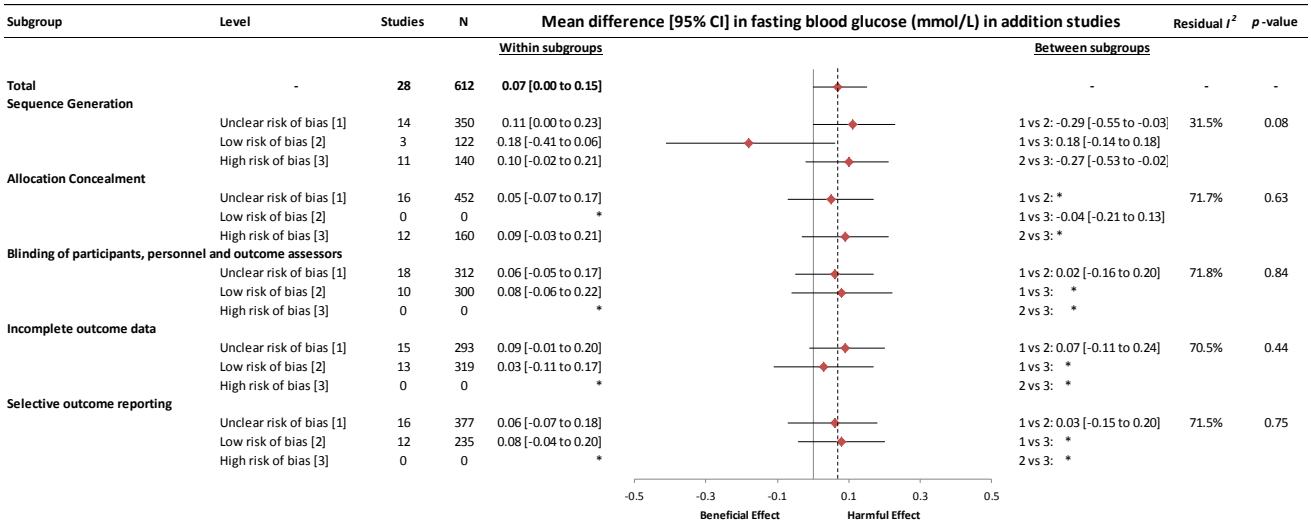
Supplementary Figure 14. Subgroup analyses for substitution studies investigating the effect of isocaloric exchange of food sources of fructose-containing sugars for other macronutrients on fasting blood glucose. E= energy; HFCS= high fructose corn syrup; MetS= metabolic syndrome; N= number of participants. Pooled effect estimates for each subgroup are represented by the diamonds. The dashed line represents the pooled effect estimate for the overall analysis. The residual I^2 value represents unexplained heterogeneity for each subgroup. Pairwise between-subgroup mean differences (95% CI) for comparator are as follows: 1 vs 2: -0.07 [-0.19 to 0.04]; 1 vs 3: -0.13 [-0.31 to 0.06]; 1 vs 4: -0.23 [-0.37 to -0.09]; 1 vs 5: -0.04 [-0.73 to 0.66]; 1 vs 6: 0.11 [-0.31 to 0.09]; 2 vs 3: 0.05 [-0.13 to 0.24]; 2 vs 4: 0.16 [0.02 to 0.29]; 2 vs 5: -0.04 [-0.73 to 0.66]; 2 vs 6: 0.4 [-0.17 to 0.24]; 3 vs 4: 0.10 [-0.09 to 0.30]; 3 vs 5: -0.09 [-0.80 to 0.62]; 3 vs 6: -0.02 [-0.26 to 0.23]; 4 vs 5: -0.19 [-0.89 to -0.50]; 4 vs 6: -0.12 [-0.34 to 0.09]; 5 vs 6: 0.07 [-0.64 to 0.78]. Pairwise between-subgroup mean differences (95% CI) for fructose-containing sugars type are as follows: 1 vs 2: -0.04 [-0.16 to 0.07]; 1 vs 3: 0.08 [-0.07 to 0.24]; 1 vs 4: 0.11 [-0.22 to 0.44]; 1 vs 5: -0.13 [-0.36 to 0.09]; 2 vs 3: 0.13 [-0.02 to 0.28]; 2 vs 4: 0.15 [-0.18 to 0.49]; 2 vs 5: -0.09 [-0.31 to 0.13]; 3 vs 4: 0.03 [-0.32 to 0.38]; 3 vs 5: -0.22 [-0.46 to 0.03]; 4 vs 5: -0.25 [-0.63 to 0.14]. Pairwise between-subgroup mean differences (95% CI) for underlying disease status are as follows: 1 vs 2: -0.03 [-0.15 to 0.08]; 1 vs 3: 0.25 [0.05 to 0.44]; 1 vs 4: -0.07 [-0.25 to 0.11]; 1 vs 5: 0.32 [-0.17 to 0.81]; 2 vs 3: 0.28 [0.08 to 0.48]; 2 vs 4: -0.04 [-0.22 to 0.14]; 2 vs 5: 0.35 [-0.15 to 0.84]; 3 vs 4: 0.32 [0.08 to 0.56]; 3 vs 5: -0.07 [-0.59 to 0.45]; 4 vs 5: 0.39 [-0.12 to 0.90].



Supplementary Figure 15. Subgroup analyses for addition studies investigating the effect of adding excess calories to the diet in the form of food sources of fructose-containing sugars on fasting blood glucose. E= energy; HFCS= high fructose corn syrup; MetS= metabolic syndrome; N= number of participants. Pooled effect estimates for each subgroup are represented by the diamonds. The dashed line represents the pooled effect estimate for the overall analysis. The residual I^2 value represents unexplained heterogeneity for each subgroup. Pairwise between-subgroup mean differences (95% CI) for fructose-containing sugars type are as follows: 1 vs 2: 0.05 [-0.17 to 0.27]; 1 vs 3: 0.15 [-0.08 to 0.38]; 1 vs 4: 0.15 [-0.23 to 0.53]; 1 vs 5: 0.28 [-0.06 to 0.62]; 2 vs 3: 0.10 [-0.14 to 0.34]; 2 vs 4: 0.10 [-0.29 to 0.48]; 2 vs 5: 0.23 [-0.11 to 0.57]; 3 vs 4: 0.00 [-0.39 to 0.39]; 3 vs 5: 0.13 [-0.22 to 0.48]; 4 vs 5: 0.13 [-0.33 to 0.59]. Pairwise between-subgroup mean differences (95% CI) for underlying disease status are as follows: 1 vs 2: -0.08 [-0.24 to 0.09]; 1 vs 3: 1.04 [0.17 to 1.91]; 1 vs 4: -0.04 [-0.134 to 0.26]; 2 vs 3: 1.11 [0.24 to 1.99]; 2 vs 4: 0.04 [-0.27 to 0.34]; 3 vs 4: 1.08 [0.17 to 1.99].

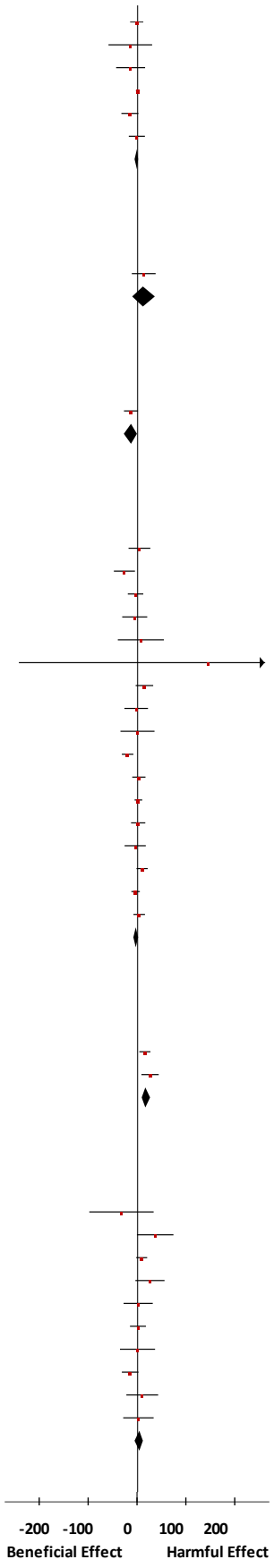


Supplementary Figure 16. Risk of bias (using The Cochrane Collaboration Tool) subgroup analysis for substitution studies investigating the effect of isocaloric exchange of food sources of fructose-containing sugars for other macronutrients on fasting blood glucose. Point estimates for each subgroup level are the pooled effect estimates and are represented by diamonds. The residual I^2 value represents unexplained heterogeneity for each subgroup. HRB=High Risk of Bias, LRB=Low Risk of Bias, URB= Unclear Risk of Bias. *Within and/or between subgroup analysis could not be performed since no values were available for respective HRB/URB/LRB subgroups. Statistically significant pairwise subgroup effect modification by meta-regression analysis (P< 0.05).

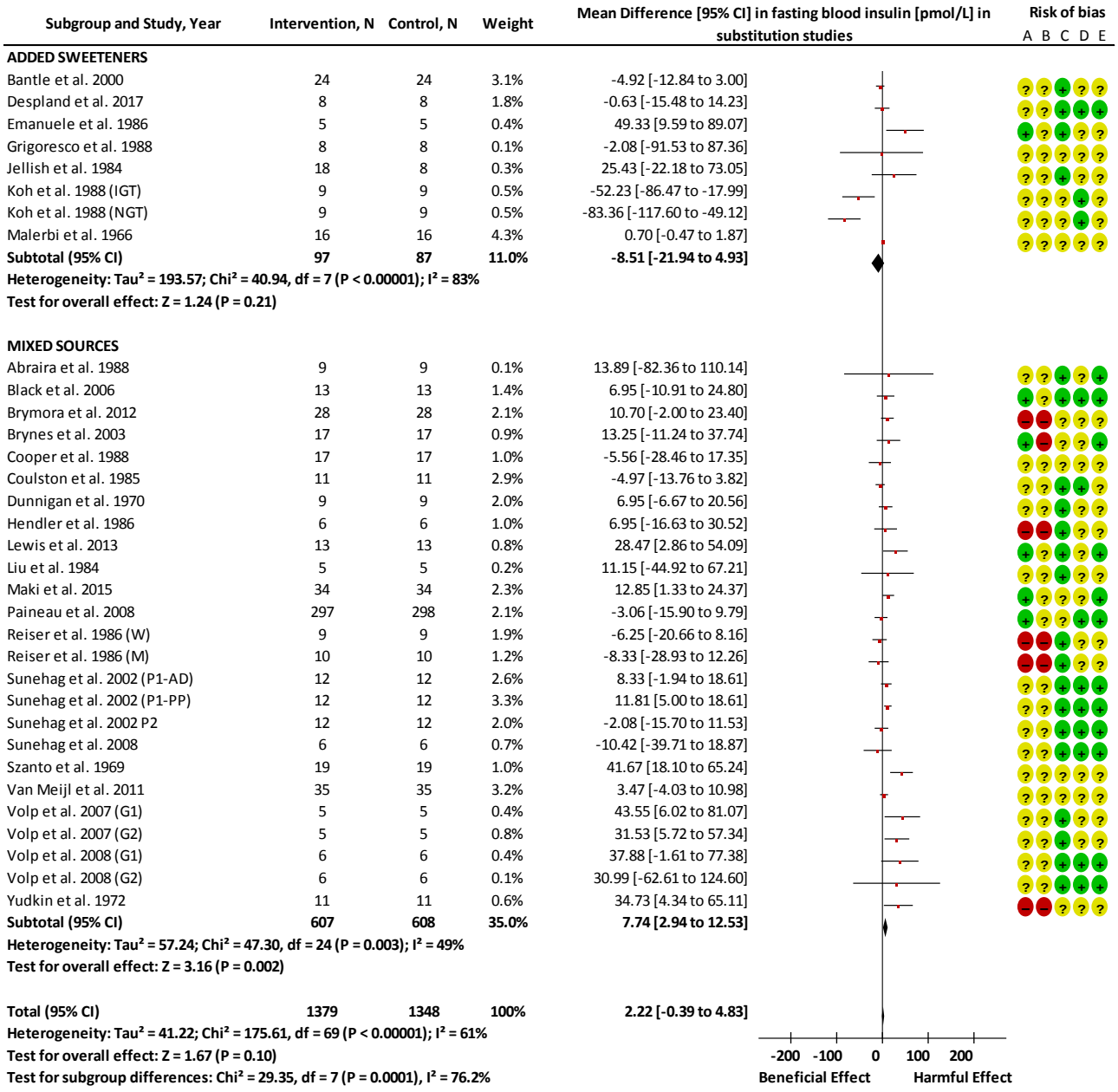


Supplementary Figure 17. Risk of bias (using The Cochrane Collaboration Tool) subgroup analysis for addition studies investigating the effect of isocaloric exchange of food sources of fructose-containing sugars for other macronutrients on fasting blood glucose. Point estimates for each subgroup level are the pooled effect estimates and are represented by diamonds. The residual I^2 value represents unexplained heterogeneity for each subgroup. HRB=High Risk of Bias, LRB=Low Risk of Bias, URB= Unclear Risk of Bias. *Within and/or between subgroup analysis could not be performed since no values were available for respective HRB/URB/LRB subgroups. Statistically significant pairwise subgroup effect modification by meta-regression analysis ($P< 0.05$).

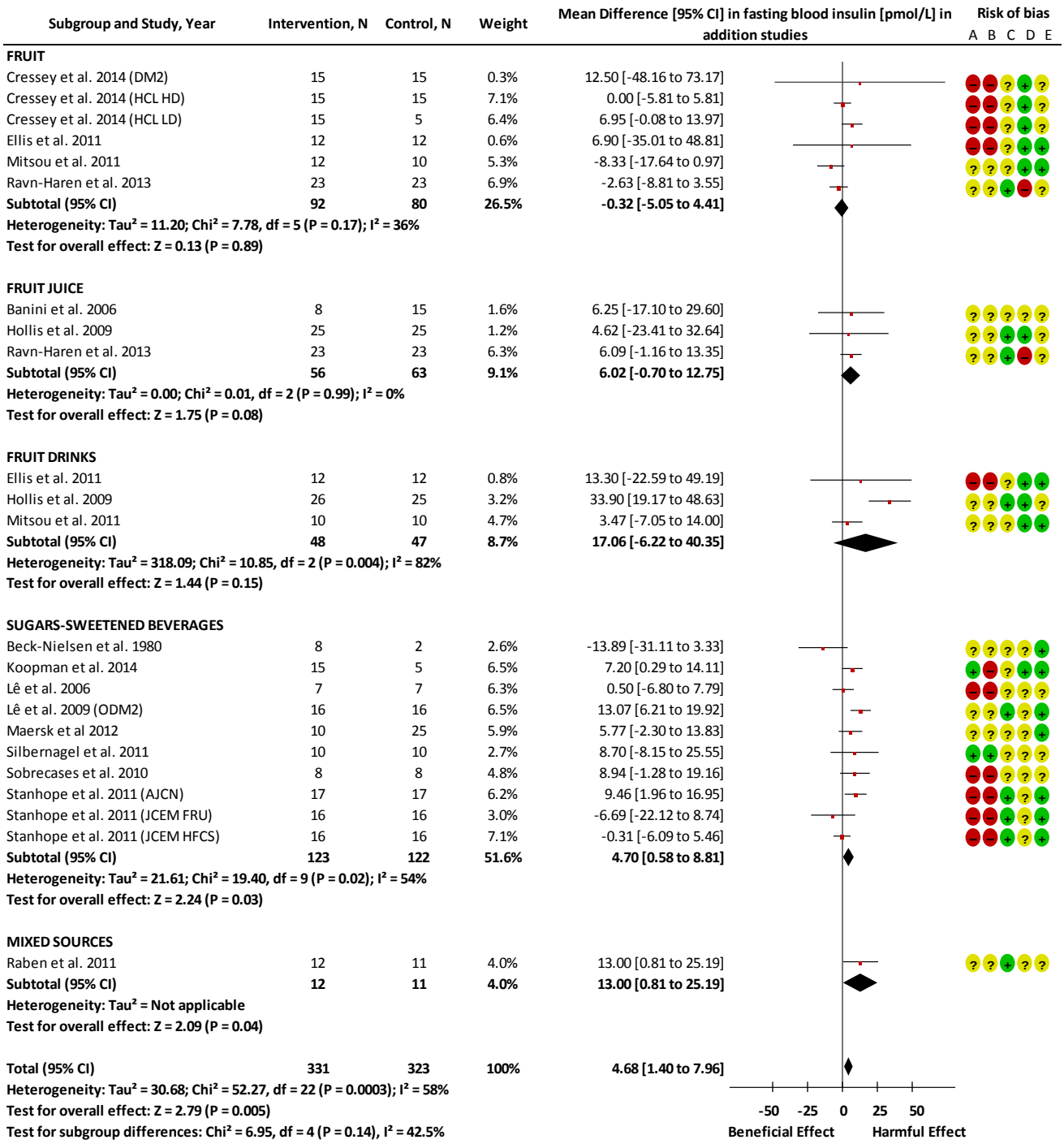
Subgroup and Study, Year	Intervention, N	Control, N	Weight	Mean Difference [95% CI] in fasting blood insulin [pmol/L] in substitution studies	Risk of bias A B C D E
FRUIT					
Agebratt et al. 2016	15	15	2.1%	-1.74 [-14.39 to 10.92]	+ ? ? + +
Conceição et al. 2003	26	9	0.3%	-15.28 [-60.28 to 29.72]	+ ? ? − +
Kolehmainen et al. 2012	15	12	0.7%	-14.58 [-44.04 to 14.87]	? ? ? − +
Lehtonen et al. 2010	28	22	4.1%	0.69 [-2.08 to 3.46]	? ? ? ? ?
Madero et al. 2011	65	66	1.6%	-16.19 [-32.98 to 0.60]	+ ? ? + +
Rodriguez et al. 2005	7	8	1.7%	-1.39 [-17.21 to 14.43]	? ? ? + +
Subtotal (95% CI)	**156**	**132**	**10.5%**	**-0.81 [-4.58 to 2.97]**	
Heterogeneity: Tau² = 2.70; Chi² = 5.30, df = 5 (P = 0.38); I² = 6%					
Test for overall effect: Z = 0.42 (P = 0.68)					
DRIED FRUIT					
Kaliora et al. 2016	21	23	0.9%	13.20 [-10.84 to 37.23]	+ + + + +
Subtotal (95% CI)	**21**	**23**	**0.9%**	**13.20 [-10.84 to 37.23]**	
Heterogeneity: Not applicable					
Test for overall effect: Z = 1.08 (P = 0.28)					
FRUIT JUICE					
Ribeiro et al. 2017	39	39	2.0%	-13.89 [-27.50 to -0.28]	+ ? ? + +
Subtotal (95% CI)	**39**	**39**	**2.0%**	**-13.89 [-27.50 to -0.28]**	
Heterogeneity: Not applicable					
Test for overall effect: Z = 2.00 (P = 0.05)					
SUGARS-SWEETENED BEVERAGES					
Aeberli et al. 2013	9	9	1.1%	4.05 [-17.75 to 25.85]	? + + + +
Beck-Nielsen et al. 1980	15	15	1.1%	-27.78 [-48.87 to -6.69]	? ? ? ? +
Heden et al. 2014 (AJCN-H)	20	20	1.8%	-4.15 [-19.30 to 11.00]	? ? ? − +
Heden et al. 2014 (AJCN-OW/OB)	20	20	0.9%	-5.90 [-31.17 to 19.37]	? ? ? − +
Heden et al. 2015	7	7	0.3%	7.00 [-40.57 to 54.57]	? ? ? ? ?
Jin et al. 2014	9	12	0.0%	149.32 [-250.31 to 548.95]	? ? + + +
Johnston et al. 2013 (T1)	15	17	1.5%	14.58 [-2.77 to 31.94]	+ + + + +
Johnston et al. 2013 (T2)	15	17	0.9%	-2.78 [-26.50 to 20.94]	+ + + + +
Koivisto and Yki-Järvinen 1993	10	10	0.5%	0.00 [-34.84 to 34.84]	? ? + ? ?
Maersk et al. 2012	10	12	2.5%	-21.04 [-31.97 to -10.11]	? ? ? ? +
Mark et al. 2014	35	38	2.1%	2.86 [-9.94 to 15.66]	? ? + ? +
Ngo Sock et al. 2010	11	11	3.3%	1.80 [-5.02 to 8.62]	? ? + ? ?
Schwarz et al. 2015	8	8	1.9%	1.39 [-12.48 to 15.26]	− − + + +
Silbernagel et al. 2011	10	10	1.1%	-4.90 [-26.05 to 16.25]	+ + ? ? ?
Stanhope et al. 2011 (AJCN)	17	15	2.5%	9.73 [-0.83 to 20.29]	− − + ? +
Stanhope et al. 2011 (JCEM)	32	16	3.1%	-4.04 [-11.79 to 3.70]	− − + ? +
Swarbrick et al. 2008	7	7	2.4%	3.57 [-7.42 to 14.57]	− − + + ?
Subtotal (95% CI)	**250**	**244**	**27.1%**	**-1.47 [-6.56 to 3.62]**	
Heterogeneity: Tau² = 43.71; Chi² = 29.86, df = 16 (P = 0.02); I² = 46%					
Test for overall effect: Z = 0.56 (P = 0.57)					
SWEETENED LOW-FAT MILK					
Lowndes et al. 2015-Fructose	30	65	2.6%	26.59 [9.51 to 43.68]	+ + + − +
Lowndes et al. 2015-Sucrose	61	31	1.5%	15.64 [5.18 to 26.10]	+ + + − +
Subtotal (95% CI)	**91**	**96**	**4.1%**	**18.95 [9.09 to 28.80]**	
Heterogeneity: Tau² = 7.74; Chi² = 1.15, df = 1 (P = 0.28); I² = 13%					
Test for overall effect: Z = 3.77 (P = 0.0002)					
BAKED GOODS, SWEETS AND DESSERTS					
Behall et al. 1980 (non-OC)	6	6	0.1%	-34.03 [-100.94 to 32.88]	? ? + ? ?
Behall et al. 1980 (OC)	6	6	0.4%	37.50 [0.05 to 74.95]	? ? + ? ?
Claesson et al. 2009	12	13	2.6%	9.00 [-1.29 to 19.29]	? ? ? + ?
Hallfrisch et al. 1983 (HI)	12	12	0.7%	26.39 [-3.26 to 56.04]	? ? + ? +
Hallfrisch et al. 1983 (H)	12	12	0.7%	1.39 [-28.26 to 31.04]	? ? + ? +
Jones et al. 2014	25	25	1.7%	0.91 [-14.69 to 16.50]	+ ? ? ? +
Kelsay et al. 1974	8	8	0.5%	0.00 [-36.01 to 36.01]	? ? + + ?
Malerbi et al. 1966	16	16	1.6%	-15.60 [-31.88 to 0.68]	? ? ? ? ?
Reiser et al. 1989 (HI)	10	10	0.6%	10.00 [-22.48 to 42.48]	− − + ? ?
Reiser et al. 1989 (H)	11	11	0.6%	2.00 [-28.97 to 32.97]	? ? + ? ?
Subtotal (95% CI)	**118**	**119**	**9.4%**	**3.97 [-5.26 to 13.20]**	
Heterogeneity: Tau² = 63.35; Chi² =13.35, df = 9 (P = 0.15); I² = 33%					
Test for overall effect: Z = 0.84 (P = 0.40)					



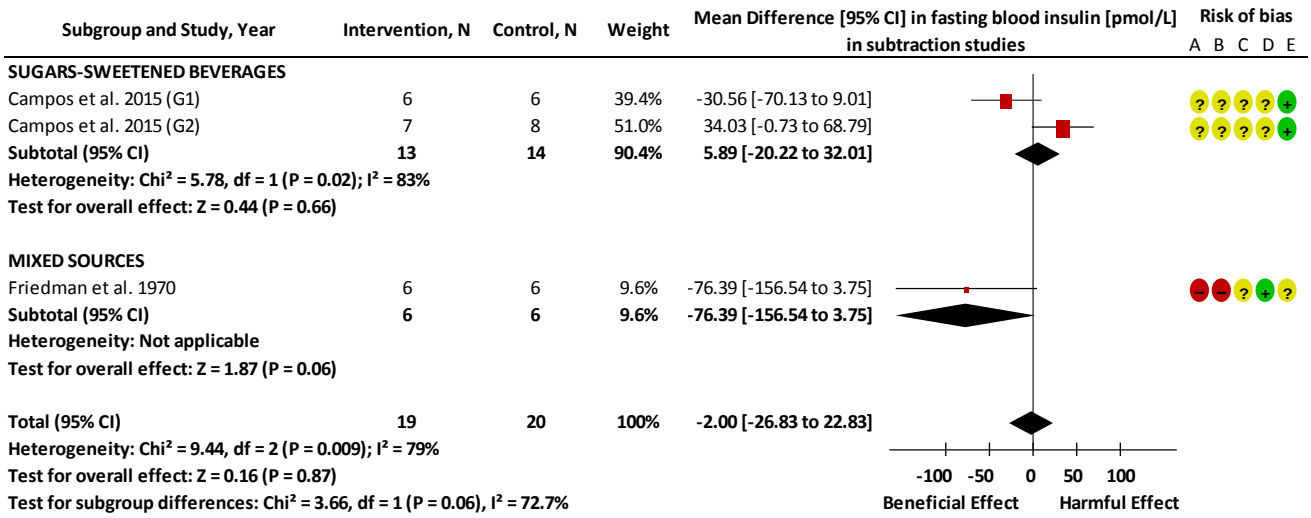
Supplementary Figure 18. Forest plot for substitution studies investigating the effect of isocaloric exchange of food sources of fructose-containing sugars for other macronutrients on fasting blood insulin (Continues next page).



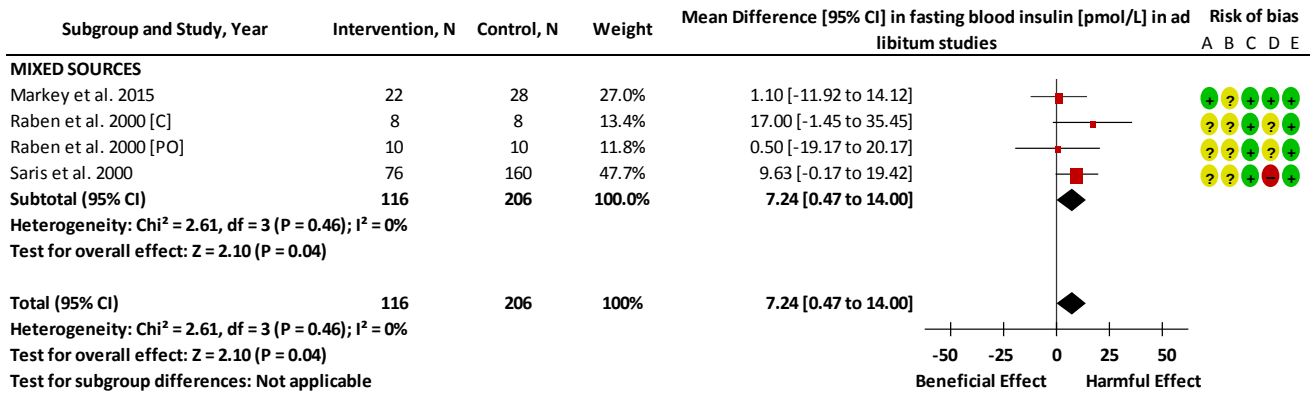
Supplementary Figure 18. (continued). Risk of bias: A=random sequence generation; B=allocation concealment; C=blinding of participants and personnel; D=incomplete outcome data; E=selective reporting.AD= adolescent; AJCN = American Journal of Clinical Nutrition; DM= diabetes mellitus; EXP1= experiment 1; EXP2= experiment 2; G1= group 1; G2= group 2; H=healthy; HC= high carbohydrate; HI=hyperinsulinemic; IGT= impaired glucose tolerance; JPAH= Journal of Physical Activity and Health; JCEM= Journal of Clinical Endocrinology and Metabolism; LC= low carbohydrate; M=men; N= number of participants; NGT= normal glucose tolerance; OC= oral contraceptive users; OW/OB= overweight/obese participants; PP=pre-pubertal; P1= protocol 1; P2= protocol 2; T1= trial 1; T2=Trial 2; W= women. Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals (CIs), using the generic inverse-variance method with random effects models. Paired analyses were applied to all crossover studies. Inter-study heterogeneity was tested by the Cochran Q-statistic at a significance level of $p < 0.10$ and quantified by I^2, level of ≥ 50 % represents substantial heterogeneity.



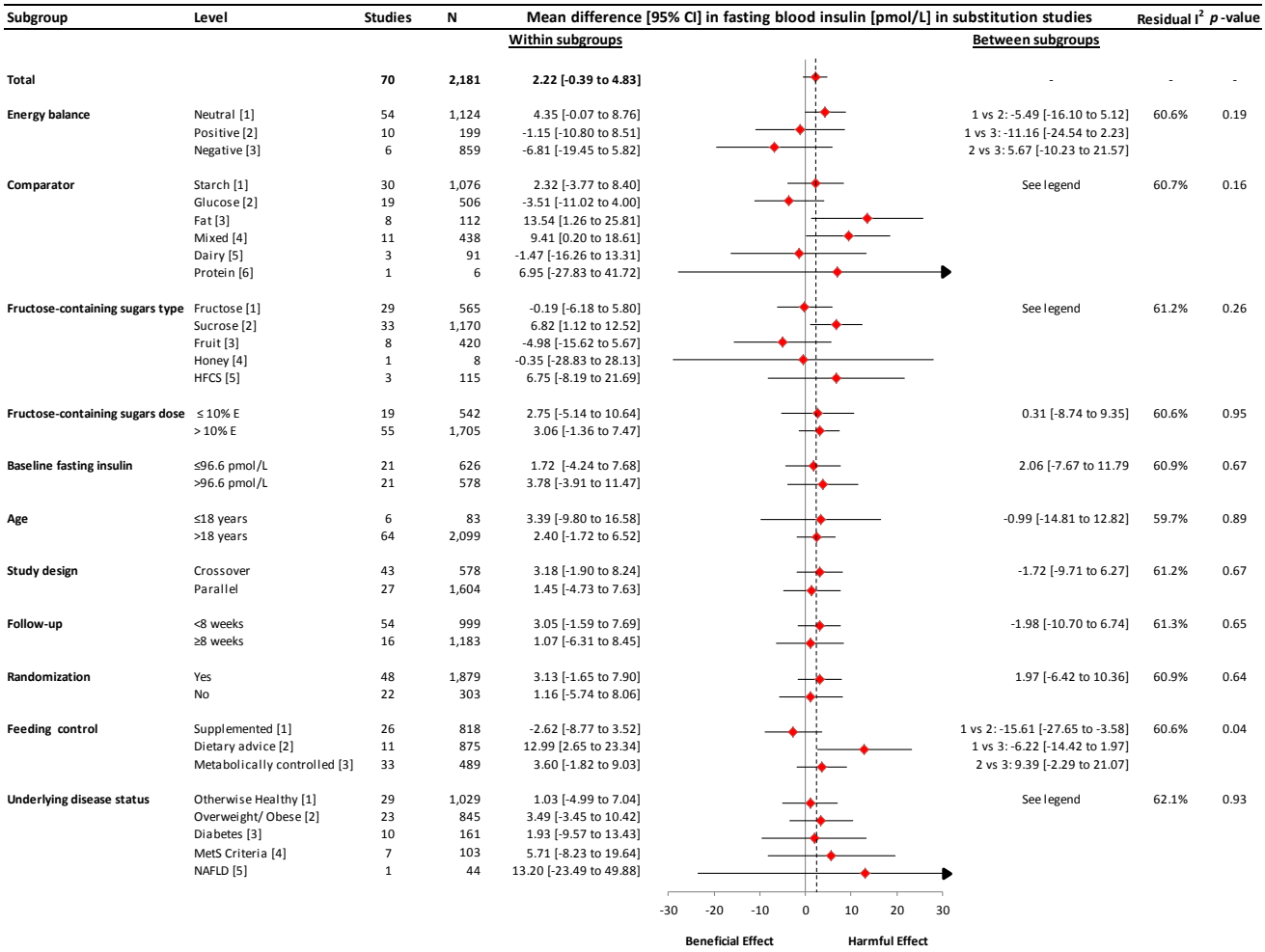
Supplementary Figure 19. Forest plot for addition studies investigating the effect of adding excess calories to the diet in the form of food sources of fructose-containing sugars on fasting blood insulin. Risk of bias: A=random sequence generation; B=allocation concealment; C=blinding of participants and personnel; D=incomplete outcome data; E=selective reporting. AJCN = American Journal of Clinical Nutrition; DM2= type 2 diabetes mellitus; EXP2= experiment 2; FRU=fructose; HCL= hypercholesterolemic; HD= high dose; HFCS= high fructose corn syrup; JCEM= Journal of Clinical Endocrinology and Metabolism; LD= low dose; N= number of participants; ODM2= offspring of people with type 2 diabetes. Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals (CIs), using the generic inverse-variance method with random effects models. Paired analyses were applied to all crossover studies. Inter-study heterogeneity was tested by the Cochran Q-statistic at a significance level of $p < 0.10$ and quantified by I^2, level of ≥ 50 % represents substantial heterogeneity.



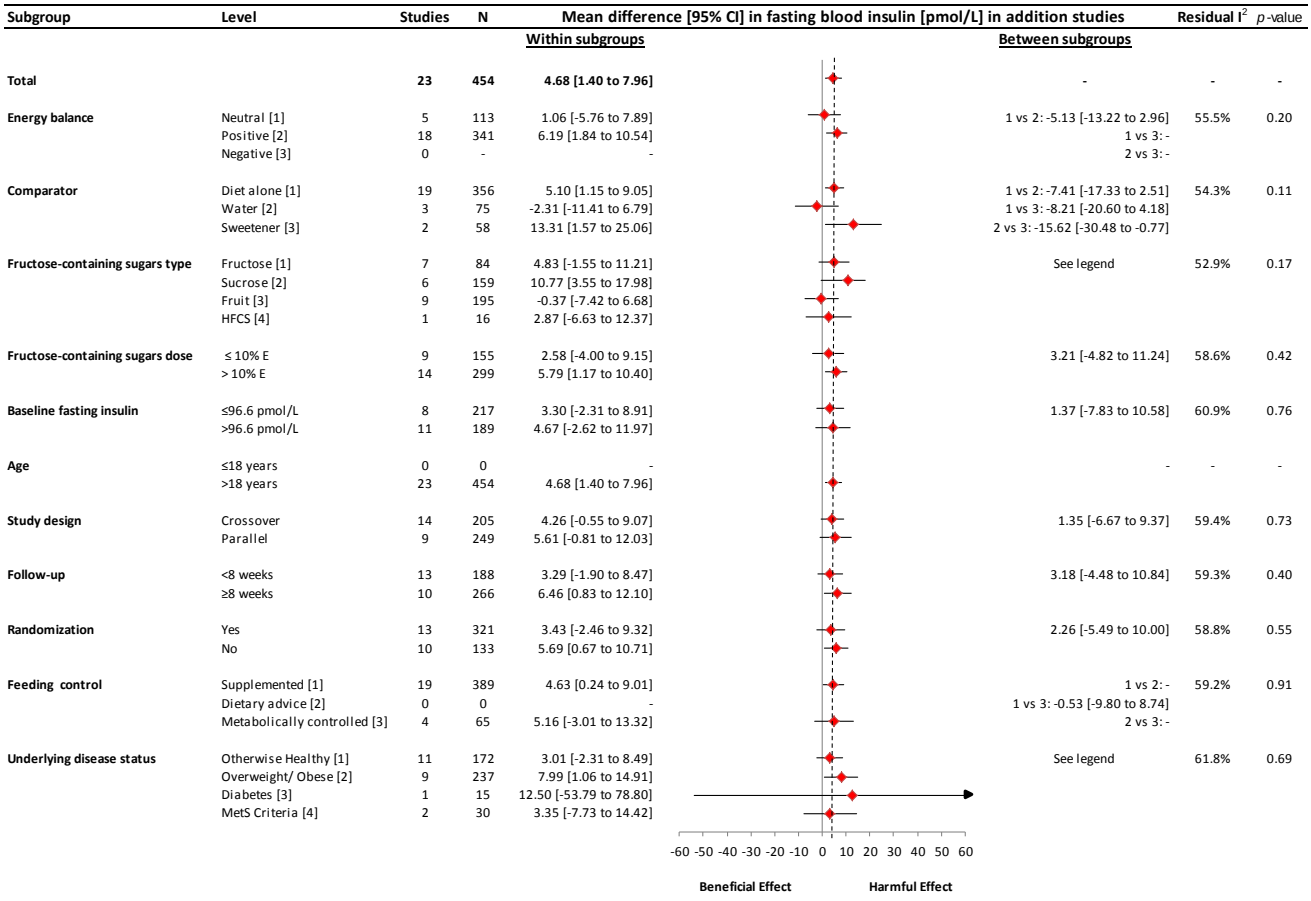
Supplementary Figure 20. Forest plot for subtraction studies investigating the effect of removing calories from the diet in the form of food sources of fructose-containing sugars on fasting blood insulin. Risk of bias: A=random sequence generation; B=allocation concealment; C=blinding of participants and personnel; D=incomplete outcome data; E=selective reporting. G1= group 1; G2= group 2; N= number of participants. Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals (CIs), using the generic inverse-variance method with fixed effects models. Paired analyses were applied to all crossover studies. Inter-study heterogeneity was tested by the Cochran Q-statistic at a significance level of $p < 0.10$ and quantified by I^2, level of ≥ 50 % represents substantial heterogeneity.



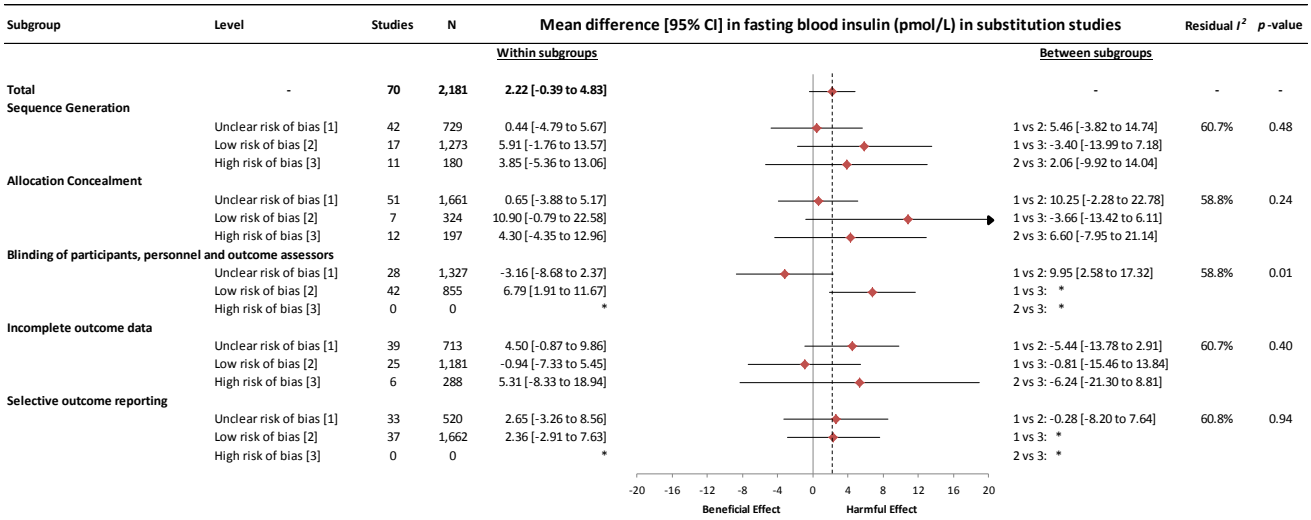
Supplementary Figure 21. Forest plot for ad libitum studies investigating the effect of freely replacing calories from food sources of fructose-containing sugars with other dietary sources on fasting blood insulin. Risk of bias: A=random sequence generation; B=allocation concealment; C=blinding of participants and personnel; D=incomplete outcome data; E=selective reporting. C=control; N= number of participants; PO= post-obese. Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals (CIs), using the generic inverse-variance method with fixed effects models. Paired analyses were applied to all crossover studies. Inter-study heterogeneity was tested by the Cochran Q-statistic at a significance level of $p < 0.10$ and quantified by I^2, level of ≥ 50 % represents substantial heterogeneity.



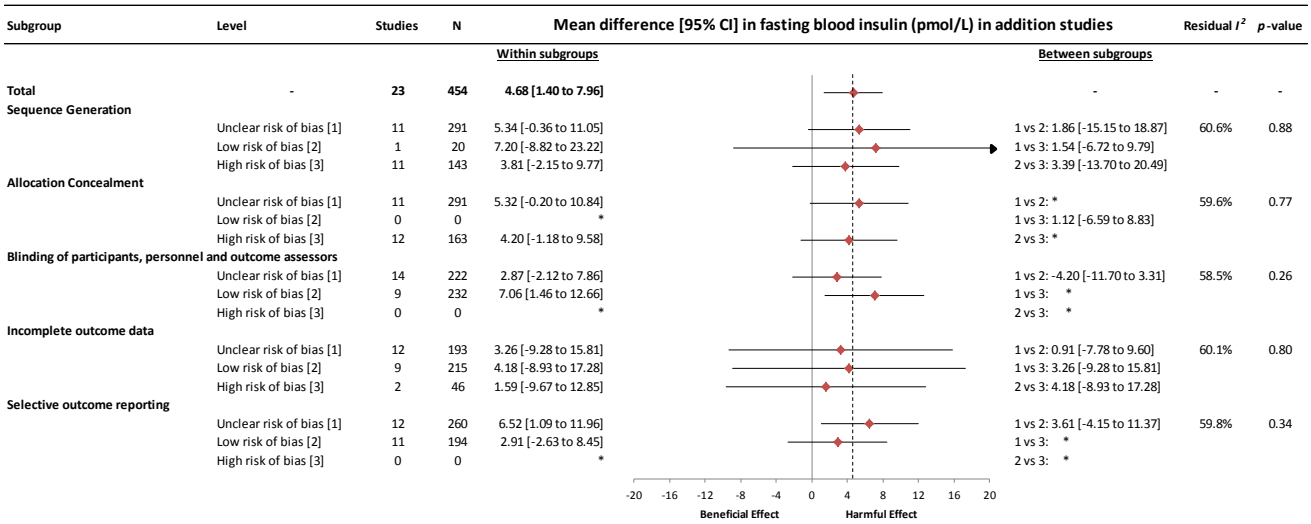
Supplementary Figure 22. Subgroup analyses for substitution studies investigating the effect of isocaloric exchange of food sources of fructose-containing sugars for other macronutrients on fasting blood insulin. E= energy; HFCS= high fructose corn syrup; MetS= metabolic syndrome; N= number of participants. Pooled effect estimates for each subgroup are represented by the diamonds. The dashed line represents the pooled effect estimate for the overall analysis. The residual I^2 value represents unexplained heterogeneity for each subgroup. Pairwise between-subgroup mean differences [95% CI] for comparator are as follows: 1 vs 2: -5.83 [-15.50 to 3.84]; 1 vs 3: 11.22 [-2.48 to 24.91]; 1 vs 4: 7.09 [-3.95 to 18.13]; 1 vs 5: -3.79 [-19.78 to 12.20]; 1 vs 6: 4.63 [-30.68 to 39.93]; 2 vs 3: -17.05 [-31.44 to -2.66]; 2 vs 4: -12.92 [-24.80 to -1.04]; 2 vs 5: -2.04 [-18.62 to 14.55]; 2 vs 6: -10.46 [-46.03 to 25.12]; 3 vs 4: 4.13 [-11.21 to 19.47]; 3 vs 5: 15.01 [-4.21 to 34.22]; 3 vs 6: 6.59 [-30.29 to 43.47]; 4 vs 5: 10.88 [-6.54 to 28.30]; 4 vs 6: 2.46 [-33.51 to 38.44]; 5 vs 6: -8.42 [-46.21 to 29.37]. Pairwise between-subgroup mean differences (95% CI) for fructose-containing sugars type are as follows: 1 vs 2: -7.01 [-15.28 to 1.26]; 1 vs 3: 4.79 [-7.42 to 17.00]; 1 vs 4: 0.16 [-28.94 to 29.26]; 1 vs 5: -6.94 [-23.03 to 9.16]; 2 vs 3: -11.80 [-23.87 to 0.28]; 2 vs 4: -7.17 [-36.21 to 21.88]; 2 vs 5: -0.07 [-16.06 to 15.92]; 3 vs 4: -4.63 [-35.03 to 25.77]; 3 vs 5: -11.73 [-30.06 to 6.61]; 4 vs 5: -7.10 [-39.25 to 25.06]. Pairwise between-subgroup mean differences [95% CI] for underlying disease status are as follows: 1 vs 2: 2.46 [-6.71 to 11.64]; 1 vs 3: 0.90 [-11.95 to 13.75]; 1 vs 4: 4.68 [-10.33 to 19.69]; 1 vs 5: 12.17 [-25.01 to 49.35]; 2 vs 3: 1.56 [-11.87 to 14.99]; 2 vs 4: -2.22 [-17.78 to 13.35]; 2 vs 5: -9.71 [-47.04 to 27.63]; 3 vs 4: -3.78 [-22.37 to 14.81]; 3 vs 5: -11.27 [-49.72 to 27.18]; 4 vs 5: -7.49 [-46.73 to 41.76].



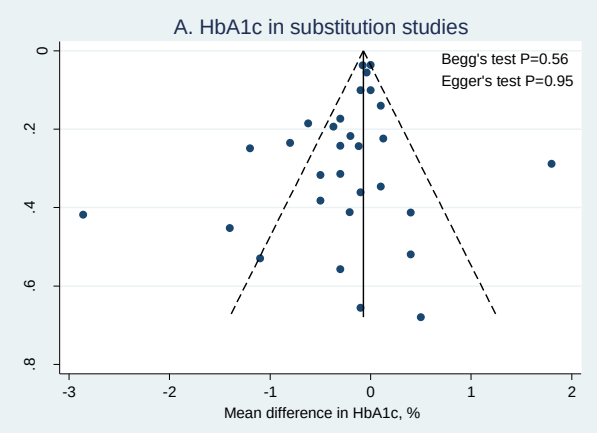
Supplementary Figure 23. Subgroup analyses for addition studies investigating the effect of adding excess calories to the diet in the form of food sources of fructose-containing sugars on fasting blood insulin. E= energy; HFCS= high fructose corn syrup; MetS= metabolic syndrome; N= number of participants. Pooled effect estimates for each subgroup are represented by the diamonds. The dashed line represents the pooled effect estimate for the overall analysis. The residual I^2 value represents unexplained heterogeneity for each subgroup. Pairwise between-subgroup mean differences (95% CI) for fructose-containing sugars type are as follows: 1 vs 2: -5.94 [-15.56 to 3.69]; 1 vs 3: 5.20 [-4.31 to 14.70]; 1 vs 4: 1.96 [-9.48 to 13.40]; 2 vs 3: 11.13 [1.05 to 21.22]; 2 vs 4: 7.90 [-4.03 to 19.82]; 3 vs 4: -3.24 [-15.06 to 8.59]. Pairwise between-subgroup mean differences (95% CI) for underlying disease status are as follows: 1 vs 2: 4.90 [-3.88 to 13.67]; 1 vs 3: 9.41 [-57.10 to 75.92]; 1 vs 4: 0.26 [-12.06 to 12.57]; 2 vs 3: -4.52 [-71.17 to 62.14]; 2 vs 4: 4.64 [-8.42 to 17.70]; 3 vs 4: 9.16 [-58.06 to 76.37].

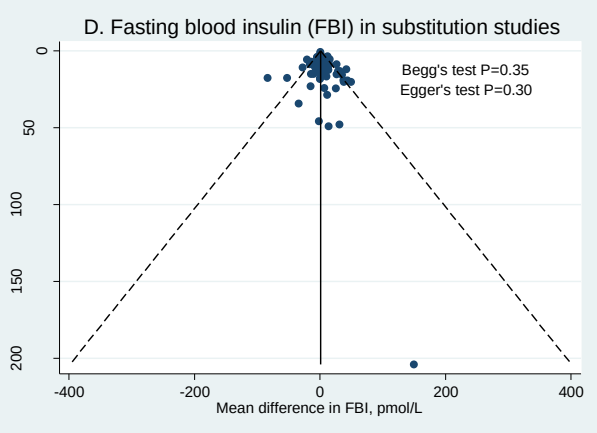


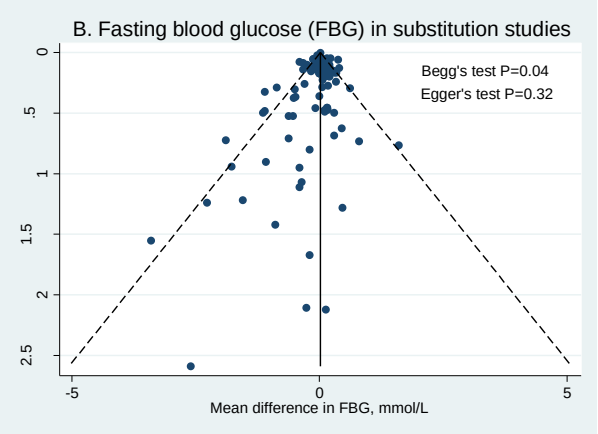
Supplementary Figure 24. Risk of bias (using The Cochrane Collaboration Tool) subgroup analysis for substitution studies investigating the effect of isocaloric exchange of food sources of fructose-containing sugars for other macronutrients on fasting blood insulin. Point estimates for each subgroup level are the pooled effect estimates and are represented by diamonds. The residual I^2 value represents unexplained heterogeneity for each subgroup. HRB=High Risk of Bias, LRB=Low Risk of Bias, URB= Unclear Risk of Bias. *Within and/or between subgroup analysis could not be performed since no values were available for respective HRB/URB/LRB subgroups. Statistically significant pairwise subgroup effect modification by meta-regression analysis ($P< 0.05$).

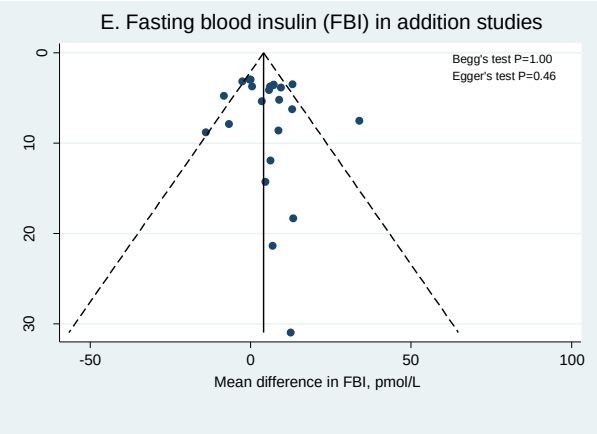


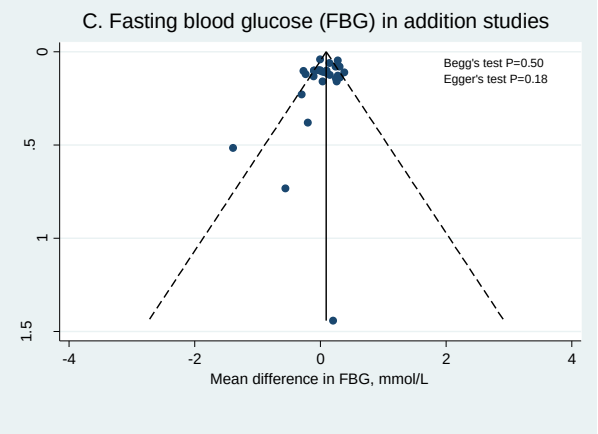
Supplementary Figure 25. Risk of bias (using The Cochrane Collaboration Tool) subgroup analysis for addition studies investigating the effect of adding excess calories to the diet in the form of food sources of fructose-containing sugars on fasting blood insulin. Point estimates for each subgroup level are the pooled effect estimates and are represented by diamonds. The residual I^2 value represents unexplained heterogeneity for each subgroup. HRB=High Risk of Bias, LRB=Low Risk of Bias, URB= Unclear Risk of Bias. *Within and/or between subgroup analysis could not be performed since no values were available for respective HRB/URB/LRB subgroups. Statistically significant pairwise subgroup effect modification by meta-regression analysis ($P< 0.05$).



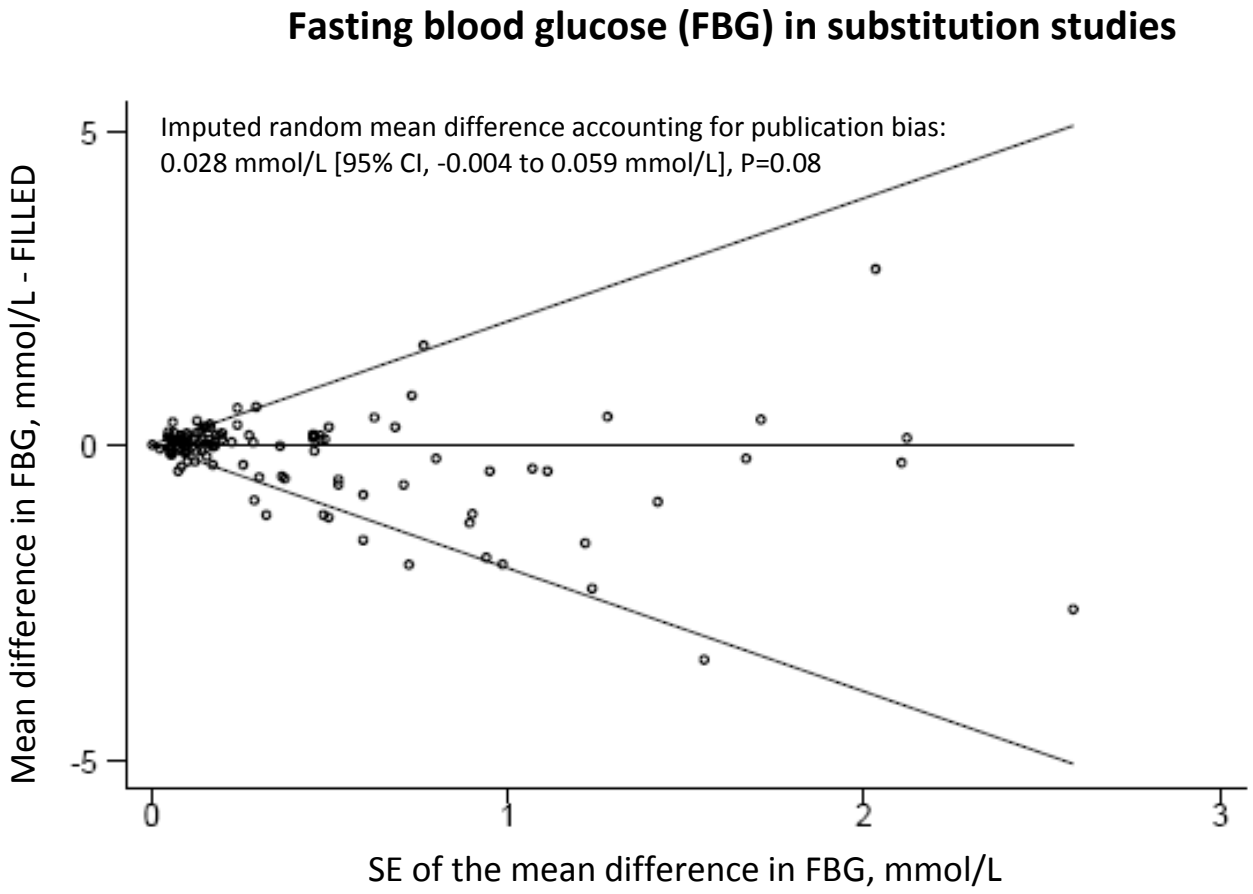








Supplementary Figure 26. Publication bias funnel plots for the effect of food sources of fructose-containing sugars on glycemic control in substitution and addition studies. The solid line represents the pooled effect estimate expressed as the weighted mean difference (MD). The dashed lines represent pseudo-95% confidence limits and the circles represent effect estimates for each included study. P-values were derived from quantitative assessment of publication bias by Egger's and Begg's tests set at a significance level of $p < 0.05$.



Supplementary Figure 27. Trim and Fill funnel plot for the effect of food sources of fructose-containing sugars on fasting blood glucose in substitution studies. The horizontal line represents the pooled effect estimate expressed as mean difference. The diagonal lines represent the pseudo-95% confidence limits, the circles represent the effect estimate for each included study, and squares represent the effect estimate for each imputed "missed" study. Imputed random mean difference is provided, $p<0.05$ is considered evidence of small-study effects.