Table 1. Summary of studies examining the relationship between added sugars and risk of cardiovascular disease

Author, Year Study Design; Location Risk of Bias*	Sample Size Age Gender	Added Sugars Intervention or Exposure Study Duration	Results	Summary of Findings
Intervention Studies				
Aeberli, 2011 **Randomized Controlled Trial (RCT) (crossover)** **Switzerland** **Risk of Bias: 4/28**	Initial N=29 Final N=29 Attrition=0% 26y (SD=7) 0% female	**Participants received 600ml beverages daily with either:** 1. *Medium fructose:* 40g/d fructose 2. *High fructose:* 80g/d fructose 3. *Medium glucose:* 40g/d glucose 4. *High glucose:* 80g/d glucose 5. *High sucrose:* 80g/d sucrose 6. *Control:* Received advice to decrease fructose **Study Duration:** 3-week interventions, 4-week washout	**Triglycerides, Total cholesterol, HDL, LDL, Blood pressure**: No differences between interventions (NS).	There were no differences in total cholesterol, LDL, HDL, triglycerides, or blood pressure after consuming 600ml/d sugar-sweetened beverages with either 40g/d (fructose or glucose) or 80g/d (fructose, glucose, or sucrose) for 3 weeks.
Aeberli, 2013 **RCT (crossover)** **Switzerland** **Risk of Bias: 2/28**	Initial N=9 Final N=9 Attrition=0% 23y (SD=2) 0% female	**Participants received 600ml beverages daily with either:** 1. *Medium fructose:* 40g/d fructose 2. *High fructose:* 80g/d fructose 3. *High glucose:* 80g/d glucose 4. *High sucrose:* 80g/d sucrose **Study Duration:** 3-week interventions, 4-week washout	**Total Cholesterol, LDL:** Total and LDL cholesterol were higher after the medium fructose compared to high glucose (P<0.05). **Triglycerides, HDL:** No differences between groups (NS).	Consuming SSBs (600ml/d) with medium fructose (40g/d), high fructose (80g/d), and high sucrose (80g/d) raised total cholesterol and LDL compared to high glucose. There were no differences in HDL or triglycerides.
Black, 2006 **RCT (crossover)** **UK**	Initial N=14 Final N=13 Attrition=7% 33y (SD=3)	**Participants received two isocaloric diets (55% energy from CHO, 30-35% energy from fat, 10-15% energy from protein, and 18g/d fiber), with either:** 1. *Low sucrose:* 10% sucrose	**Total cholesterol:** Total cholesterol was higher after the high vs. low sucrose diet (4.62±0.8 vs. 4.01±0.8; P<0.01). **LDL:** LDL cholesterol was higher after the high vs. low sucrose diet (2.25±0.25 vs. 2.78±0.3;	Consuming a high sucrose diet (25% sucrose) increased total and LDL cholesterol, but had no effect on HDL cholesterol or triglycerides.

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Risk of Bias: 7/28	0% female	2. *High sucrose:* 25% sucrose **Study Duration:** 6-week interventions, 4-week washout	P<0.01). **HDL, Triglycerides:** No differences between groups (NS).	
Faeh, 2005 **RCT (crossover)** **Switzerland** **Risk of Bias: 6/28**	Initial N=7 Final N=7 Attrition=0% 22-31y 0% female	**Participants received four diets:** 1. *Fish oil:* 7.2g/d for 28 days 2. *High fructose:* 3g/kg/d (~+25% energy requirement) 3. *Fish-oil + High fructose:* 7.2g/d fish oil + high fructose diet *4. Control* **Study Duration:** 28-day interventions, 12 week washout	**Triglycerides:** Triglycerides were lower after the fish oil+ high fructose diet compared to the high fructose diet alone (37%, P<0.05), but both were higher than the fish oil and control conditions (P<0.05).	Triglycerides were higher after consumption of a high fructose diet (3g/kg/d or ~25% extra kcal, with or without fish oil supplementation) compared to the fish oil supplement alone and the control condition.
Le, 2009 **RCT (crossover)** **Switzerland** **Risk of Bias: 6/28**	Initial N=24 Final N=24 Attrition=0% 25y (SD=1) 0% female	**Participants received two diets:** 1. *Isocaloric diet:* 55% carbohydrate, 30% fat, 15% protein 2. High fructose diet: Isocaloric diet +3.5g/kg fructose (+35% energy requirement) **Study Duration:** 1-week interventions, 4 to 5-week washout	**Triglycerides:** Triglycerides increased following the high fructose vs. the isocaloric diet (+35% in the control group, +73% in the group of participants who had a parent with diabetes).	A high fructose (and higher calorie) (3/5g/kg/d or +35% kcal) diet increased triglycerides compared to a control diet.
Lewis, 2013 **RCT (crossover)** **UK**	Initial N=17 Final N=13 Attrition=24% 46y (SD=2)	**Participants received two isocaloric diets (55% energy from CHO, 30-35% energy from fat, 10-15% energy from protein, and 18 g/d fiber), with either:**	**Total Cholesterol, LDL, HDL, Triglycerides, Blood pressure:** No differences between groups (NS).	There were no differences in blood pressure, total cholesterol, LDL, HDL, or triglycerides after consuming a high (15% sucrose) - vs. low-sucrose (5% sucrose) diet.

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Risk of Bias: 10/28	29% female	1. *Low sucrose:* 5% sucrose 2. *High sucrose:* 15% sucrose **Study Duration:** 6-week interventions, 4-week washout		
Lowndes, 2014a **RCT** **US** **Risk of Bias: 8/28**	Initial N=86 Final N=65 Attrition=25% 39y (SD=12) (25-60y) 52% female	**Participants received a 1% sweetened milk beverage daily with either:** 1. *HFCS 10%:* 10% of calories from high-fructose corn syrup (HFCS) 2. *HFCS 20%:* 20% of calories from HFCS 3. *Sucrose 10%:* 10% of calories from sucrose 4. *Sucrose 20%:* 20% of calories from sucrose **Study Duration:** 10 weeks	**HDL, Total Cholesterol:HDL ratio**: Sweetened milk consumption decreased HDL (P<0.01) and increased the TC:HDL ratio (P<0.01), but there were no differences between groups. **Total Cholesterol, LDL; Blood Pressure, Triglycerides**: No differences between groups (NS).	Drinking sweetened milk decreased HDL and increased the TC:HDL ratio. Drinking 20% sucrose milk significantly reduced total and LDL cholesterol compared to drinking 20% HFCS milk. However, no differences were seen in blood pressure or triglycerides.
Lowndes, 2014b **RCT** **US** **Risk of Bias: 6/28**	Initial N=465 Final N=355 Attrition=26% 40y (SD=12) (20-60y) 54% female	**Participants received a 1% sweetened milk beverage daily with either:** 1. *Low sucrose:* 8% of calories from sucrose 2. *Low HFCS:* 8% of calories from HFCS 3. *Moderate sucrose:* 18% of calories from sucrose 4. *Moderate HFCS:* 18% of calories from HFCS 5. *High sucrose:* 30% of calories from sucrose 6. *High HFCS:* 30% of calories from HFCS **Study Duration:** 10 weeks	**Systolic Blood Pressure:** There was a Time x Sugar Type x Sugar Level interaction, such that a decrease was observed in the 8% sucrose group (P<0.01). **Diastolic blood pressure, total Cholesterol, LDL, HDL, Triglycerides:** No differences between groups (NS). **Pooled Analyses:** In the entire cohort, drinking sugar-sweetened low-fat milk produced increased triglycerides (P<0.001) and decreased HDL (P<0.05).	Drinking sweetened milk increased triglycerides and decreased HDL, and the 8% sucrose drink decreased systolic blood pressure. However, no differences were seen in the other outcomes, or in the other intervention conditions.

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Maersk, 2012 **RCT** **Denmark** **Risk of Bias: 9/28**	Initial N=60 Final N=47 Attrition=21.7 % 38y (SD=9) 64% female	**Participants received a 1 liter/day of either:** 1. Regular cola 2. Aspartame-sweetened cola 3. Semi-skim milk 4. Still mineral water **Study Duration:** 6 months	**Total cholesterol**: Regular cola increased total cholesterol by 11.4% (SD 3.2) compared to milk 0.634% (SD 3.0, P<0.01), diet cola -5.89% (SD 3.0, P=0.05), and water -0.159% (SD 2.8, NS) (P for trend 0.004). **Triglycerides**: Regular cola increased triglycerides by 32.7% (SD 8.6) compared to milk -0.301% (SD 8.1, P=0.05), diet cola -14.1% (SD 8.1, P<0.01), water -14.2% (SD 7.7, P<0.01) (P for trend 0.001). **Systolic Blood Pressure**: Regular cola increased SBP by ~4% compared to milk (~-7%, P<0.05), diet cola (~-7%, P<0.05), and water (NS). **HDL, Diastolic Blood Pressure**: No significant differences between groups (NS; DBP: P<0.057).	Intake of 1 liter/d of sucrose-sweetened cola (compared to milk, diet soda, and water) increased total cholesterol, triglycerides, and systolic blood pressure, but had no effect on HDL cholesterol or diastolic blood pressure.
Raben, 2002 **RCT** **Denmark** **Risk of Bias: 5/28**	Initial N=42 Final N=41 Attrition=2.4% 35y (SD=2) 88% female	**Participants were instructed to consume their usual diet with either:** • Sucrose (~2g/kg body weight/d, or ~23% of calories) • Artificial sweeteners **Study Duration:** 10 weeks	**Blood pressure:** Systolic and diastolic blood pressure increased in the sucrose group and decreased in the artificial sweetener group (*Difference between groups: SBP:* 6.9 (95% CI 2-11.9), P<0.01; *DBP:* 5.3 (95% CI 1.1-9.6), P<0.05). Change in SBP was correlated with change in sucrose (r=0.43, P<0.01). Change in DBP was correlated with change in sucrose (r=0.39, P<0.05).	Consuming a diet higher in sucrose containing foods and drinks for 10 weeks increased blood pressure compared to consuming foods and drinks with artificial sweeteners. (~2g/kg/d or ~23% energy)

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Yu, 2013 **RCT** **US** **Risk of Bias: 6/28**	Initial N=465 Final N=138 Attrition=70% 38y (SD=11) (20-60y) 43% female	**Participants received a 1% sweetened milk beverage daily with either:** 1. *Low sucrose:* 8% of calories from sucrose 2. *Low HFCS:* 8% of calories from HFCS 3. *Moderate sucrose:* 18% of calories from sucrose 4. *Moderate HFCS:* 18% of calories from HFCS 5. *High sucrose:* 30% of calories from sucrose 6. *High HFCS:* 30% of calories from HFCS **Study Duration:** 10 weeks	**Triglycerides:** Triglycerides increased following all sweetened milk interventions (P<0.01), but there were no differences between groups.	Drinking sweetened milk increased triglycerides regardless of type of sweetener (sucrose vs. HFCS) or amount (8%, 18%, 30% of energy).
Observational Studies				
Barrio-Lopez, 2013 **PCS (Seguimiento University of Navarra (SUN) cohort)** **Spain** **Risk of Bias: 2/26**	N=8,157 ~36y 65% female	Sugar-sweetened carbonated colas and fruit-flavored carbonated sugar soft drinks (non-100% fruit juice excluded). **Study Duration:** 6 years	**Triglycerides:** Increasing sugar-sweetened beverage intake was associated with a higher risk of high triglycerides (Q5 vs. Q1; OR 1.7 (95% CI=1.1-2.6); P=0.015). **Blood pressure:** Increasing sugar-sweetened beverage intake was associated with a higher risk of high blood pressure (Q5 vs. Q1; OR 1.6 (95% CI=1.3-2.1); P=<0.001). **HDL cholesterol:** No significant association with change in sugar-sweetened beverage intake (NS).	Compared to those who did not change their sugar-sweetened beverage intake, those who increased intake of sugar-sweetened beverage (increase of >33ml/d) had an increased risk of having elevated triglycerides and blood pressure, but no difference in risk of reduced HDL cholesterol levels.

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Bernstein, 2012 **PCS (Nurses' Health Study; Health Professionals Follow-up Study)** **US** **Risk of Bias: 2/26**	N=127,456 ~58y females), ~62y (males) 66% female	Soda, including low-calorie with caffeine, other low-calorie carbonated beverages, sugar-sweetened cola caffeine, sugar-sweetened cola without caffeine). **Study Duration:** 28 years (women), 22 years (men)	**Total Stroke**: *Men:* No significant association with sugar-sweetened soda intake (NS) *Women:* Increased sugar-sweetened soda intake was associated with a higher risk of total stroke (P<0.02) (RR for 1 serving/day=1.14 (95% CI=1.02-1.27) *Total Sample:* Increased sugar-sweetened soda intake was associated with a higher risk of total stroke (P<0.02) (RR for 1 serving/day=1.12 (95% CI=1.02-1.24). **Ischemic Stroke, Hemorrhagic Stroke**: *Men, Women, Total Sample:* No significant associated with sugar-sweetened soda intake (NS).	Increased sugar-sweetened soda intake (1 serving/d) was associated with increased risk of total stroke in women, and in women and men combined, but not in men alone. There were no significant associations seen between sugar-sweetened soda intake and ischemic stroke and hemorrhagic stroke.

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Chen, 2010 **PCS (PREMIER)** **US** **Risk of Bias: 2/26**	N=801 50y (SD=9) 61.5% female	Sugar-sweetened beverages (SSB), including carbonated or non-carbonated drinks that were sweetened with sugars (sucrose or high-fructose corn syrup), such as regular soft drinks, fruit drinks, lemonade, fruit punch, and other sweetened beverages (diet drinks excluded). **Study Duration:** 18 months	**Systolic Blood Pressure**: Reducing SSB intake by 1 serving/d decreased SBP in: • *All participants:* (0.7 (95% CI=0.15-1.25), P=0.01) • *Whites:* (0.7 (95% CI=0.15-1.25), P=0.01) • *Men:* (0.78 (95% CI=0.09-1.47), P=0.03) • *Women:* (0.61 (95% CI=-0.27-1.48), P=0.01) *Non-hypertensives, Blacks:* No significant relationship between SSB intake and SBP (NS). **Diastolic Blood Pressure**: Reducing SSB intake by 1 serving/d decreased DBP in: • *All participants*: (0.38 (95% CI =0.02-0.75), P=0.04) • *Whites:* (0.38 (95% CI=0.02-0.75), P=0.04) • *Men:* (0.50 (95% CI=0.01-1.00), P=0.05) *Blacks, Women, Non-hypertensives:* No significant relationship between SSB intake and DBP (NS).	There were some modest associations between reduced consumption of sugar-sweetened beverages (by 1 serving/d) and decreased systolic and diastolic blood pressure.

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Cohen, 2012 **PCS (Nurses' Health Study; Health Professionals Follow-up Study)** **US** **Risk of Bias: 4/26**	N=223,891 ~45y (38-53y) 83% female	Sugar-sweetened beverages, including sugar-sweetened cola, sugar-sweetened caffeine-free cola, sugar-sweetened non-cola, and fruit punch or other sugar-sweetened fruit drinks. **Study Duration:** NHS I-38 years, NHS II-16 years, HPSF-22 years	**Incident Hypertension** *NHS I, NHS II:* Higher intake of SSB was associated with increased risk of hypertension (>1 SSB/month vs. ≥1 SSB/d), *NHS I:* HR=1.12 (95% CI 1.08-1.17) in NHS I; *NHS II:* HR=1.17 (95% CI 1.1-1.23). *HPFS:* NS *Cola vs. non-cola:* The association between SSB intake and hypertension incidence was stronger for cola vs. non-cola beverages in NHS I (P-interactions <0.001) and HPFS (P-interactions <0.04). *Carbonated vs. non-carbonated:* The association between SSB intake and hypertension incidence was stronger for carbonated vs. non-carbonated beverages in NHS I (P-interactions <0.001) and NHS II (P-interactions <0.03). *Fructose from SSB:* Fructose intake derived from SSBs is associated with increased risk of hypertension in NHS I (P=0.001) and NHS II (P=0.001).	Higher intake of sugar-sweetened beverages (>1 SSB/month vs. ≥1 SSB/d) was associated with increased risk of hypertension, particularly for colas and carbonated beverages.

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de Koning, 2012 **PCS (Health Professionals Follow-up Study)** **US** **Risk of Bias: 0/26**	N=42,883 40-75y 0% female	Sugar-sweetened beverages, including caffeinated colas, non-caffeinated colas, other carbonated sugar-sweetened beverages, non-carbonated sugar-sweetened beverages, and artificially sweetened beverages. **Study Duration:** 22 years	**Coronary Heart Disease:** Increased sugar-sweetened beverage intake was associated with higher risk of CHD (Never vs. 3.7/wk-9/d; HR: 1.18 (95% CI=1.06-1.31), P<0.01).	Consumption of sugar-sweetened beverages (Never vs. 3.7/wk to 9/d) was associated with a significantly increased risk of CHD.
Dhingra, 2007 **PCS (Framingham Heart Study)** **US** **Risk of Bias: 2/26**	N=6,039 53y (SD=10) 58% female	Soft drinks (regular and diet) **Study Duration:** 4 years	**Triglycerides**: Increasing soft drink intake was associated with a higher risk of high triglycerides (>1 serving/day; OR 1.25 (95% CI=1.04-1.51); P<0.05). **Blood pressure**: No significant association with soft drink intake (NS). **HDL cholesterol**: Increasing soft drink intake was associated with a higher risk of low HDL (>1 serving/day; OR 1.32 (95% CI=1.06-1.64); P<0.05)	Increased soft drink intake (>1 serving/day) was associated with increased risk of elevated triglycerides and reduced HDL cholesterol.
Duffey, 2010 **PCS (CARDIO Study)** **US** **Risk of Bias: 2/26**	N=2774 25y (SD=4) (18-30y) 54% female	Sugar-sweetened soda and fruit drinks **Study Duration:** 20 years	**Triglycerides:** Higher sugar-sweetened beverage intake (according to quartile average of years 0 and 7) was associated with increased risk of high triglycerides (RR=1.06 (95% CI=1.01-1.13), P<0.033). **LDL:** Higher sugar-sweetened beverage intake was associated with increased risk of high LDL (RR=1.18 (95% CI=1.02-1.36), P<0.018). **Hypertension:** Higher sugar-sweetened	Higher intake of sugar-sweetened beverages was associated with increased risk of high triglycerides, high LDL, and hypertension, but not with HDL levels.

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			beverage intake was associated with increased risk of hypertension (RR=1.06 (95% CI=1.01-1.12), P<0.023). **HDL:** No significant associations (NS).	
Eshak, 2012 **PCS** **Japan** **Risk of Bias: 2/26**	N=39,786 ~57y (SD=7) (40-59y) 53% female	Soft drinks that contained added caloric sweeteners, including cola-type beverages, flavored juices, and non-100% fruit juices. **Study Duration:** 18 years	**Stroke**: *Men:* No association between soft drink intake and risk of total stroke, hemorrhagic stroke, or ischemic stroke (NS) *Women:* Increased soft drink intake was associated with increased risk of total stroke (never/rarely vs. every day), (HR=1.21 (95% CI=0.88-1.68), P<0.02) and ischemic stroke (HR=1.83 (95% CI=1.22-2.75), P<0.001). There was no association between soft drink intake and hemorrhagic stroke (NS). **Ischemic Heart Disease**: *Men, Women:* No significant associations (NS).	Increased soft drink intake (never/rarely vs. every day) was associated with increased risk of total stroke and ischemic stroke in women.

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Fung, 2009 **PCS (Nurses' Health Study)** **US** **Risk of Bias: 0/26**	N=88,520 30-55y 100% female	Sugar-sweetened beverages, including caffeinated and non-caffeinated colas, other carbonated beverages with sugar, non-carbonated sweetened beverages. **Study Duration:** 24 years	**Coronary Heart Disease**: Increased sugar-sweetened beverage intake was associated with a greater risk of CHD (<1/mo vs. >2/d, HR=1.35 (95% CI=1.07-1.69), P<0.001). *Total SSBs:* A 2-serving increase in sugar-sweetened beverage intake was associated with a greater risk of CHD (HR=1.28 (95% CI=1.14-1.44), P<0.001) *Colas:* A 2-serving increase in cola intake was associated with a greater risk of CHD (HR=1.35 (95% CI=1.15-1.57), P<0.001) *Fruit drinks and punch:* A 2-serving increase in fruit drink/punch intake was associated with a greater risk of CHD (HR=1.33 (95% CI=1.03-1.71), P=0.03) *Carbonated noncola:* No significant association with CHD (NS).	Increased sugar-sweetened beverage intake (<1/mo vs. >2/d) was associated with a greater risk of CHD.
Larsson, 2014 **PCS (Swedish Mammography Cohort, Cohort of Swedish Men)** **Sweden** **Risk of Bias: 2/26**	N=68,459 ~60y (45-83y) 48% female	Soft drinks or sweetened juice drinks, including both sugar-sweetened and low-calorie drinks. **Study Duration:** 10 years	**Total Stroke**: Increased sugar-sweetened beverage intake was associated with a higher risk of total stroke (0 vs. >2 servings/day; OR 1.19 (95% CI=1.04-1.36); P<0.01). **Cerebral Infarction**: Increased sugar-sweetened beverage intake was associated with a higher risk of cerebral infarction (0 vs. >2 servings/day; OR 1.22 (95% CI=1.04-1.42); P<0.01). **Hemorrhagic Stroke:** No significant associations (NS).	Increased intake of sugar-sweetened beverages (0 vs. >2 servings/d) was associated with increased total stroke risk and increased risk of cerebral infarction, but not with hemorrhagic stroke.

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Tasevska, 2014 **PCS (NIH-AARP Diet and Health Study)** **Risk of Bias: 2/26**	N=353,751 ~61y (50-71y) 42% female	Added sugars included all mono- and disaccharides used as ingredients in processed and prepared foods, soft and alcoholic drinks, jams and jellies, candies, and ice cream, and sugars eaten separately. Added sucrose and fructose was the sum of sucrose and fructose from added sugars, plus sucrose and fructose from fruit juice, and half of sucrose and fructose from apple sauce and dried fruit (due to cellular disruption during processing). **Study Duration:** 13 years	**CVD Mortality**: Added sugars, added fructose, and added sucrose were not associated with CVD mortality in either women or men (NS).	Consumption of added sugars (total, as well as added sucrose and added fructose) was not associated with CVD mortality.
Yang, 2014 **PCS (National Health and Nutrition Examination Survey (NHANES) Linked Mortality Cohort)** **US** **Risk of Bias: 3/26**	N=11,733 20y and older Gender not reported	Added sugars included all sugars used in processed or prepared foods, such as sugar-sweetened beverages, grain-based desserts, fruit drinks, dairy desserts, candy, ready-to-eat cereals, and yeast breads (naturally occurring sugar excluded). **Study Duration:** 14.6 years	**CVD Mortality**: Increased added sugars intake was associated with higher risk of CVD mortality (0-10% vs. >25% calories from added sugars; HR: 2.75 (95% CI=1.40-5.42), P=0.004).	Increase intake of added sugars (0-10% vs. >25% energy) was associated with increased risk of CVD mortality.

*Risk of Bias as determined using the Nutrition Evidence Library Bias Assessment Tool