ARIC Manuscript Proposal #2067

PC Reviewed: 2/12/13               Status: A               Priority: 2
SC Reviewed: _______               Status: _____               Priority: ____

1. a. Full Title:
Sugar-sweetened beverage consumption and incident stroke in the Atherosclerosis Risk in Communities Study

b. Abbreviated Title (Length 32 characters):
Sugar-sweetened beverages and stroke

2. Writing Group (list individual with lead responsibility first):

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3. **Timeline:** One year
   - Approval of proposal ------------ 2 weeks
   - Literature review -------------- 4 weeks
   - Plan & outline paper ---------- 1 month
   - Data analysis------------------ 3 months
   - Manuscript preparation ------- 2 months
   - Revisions---------------------- 2 months
   - Peer-review & edits------------ 2 months

4. **Rationale:**
   Sugar-sweetened beverages (SSBs) are the largest source of added sugars in the American diet. They account for 33% of the average 22 teaspoons of sugar consumed per day.\(^1\) The typical 12-ounce soda contains roughly 140-150 calories and 35-37.5 grams of sugar.\(^2\) Because of growing concern over the effects of SSBs on obesity, diabetes, and cardiovascular health, the American Heart Association issued a scientific statement in 2009 recommending consumption of no more than ~100-150 kcal/d of sugar for most adults. Even modest SSB consumption would exceed these recommendations. SSBs modify several pathways related to cardio-metabolic risk.\(^2,3\) They are associated with increased adiposity and weight gain.\(^4-7\) The reduced satiety resulting from fluid calories is hypothesized to lead to increases in total caloric intake and subsequent weight gain. Furthermore, the high level of fructose in many sodas may lead to selective deposition of visceral fat.\(^8\) Fructose has also been linked to negative effects on lipid metabolism, blood pressure, and insulin sensitivity compared with glucose. SSBs contribute to high dietary glycemic load and cause large, rapid increases in glucose and insulin. Consistent with these findings, SSB intake has been associated with increased type II diabetes risk.\(^6,9,10\) Additional effects on cardiovascular risk include increases in chronic inflammation, serum uric acid, blood pressure, and cholesterol, which promote atherosclerosis, plaque instability, and thrombosis.\(^2,3\) Consumers of ≥1 sodas per day had a 22% higher risk each of hypertension, hypertriglyceridemia, and low HDL compared with those consuming no sodas.\(^2\) The PREMIER study, an 18-month RCT designed to assess the effect of dietary changes on blood pressure, reported an average reduction of 1.8/1.1 mm-Hg in systolic/diastolic blood pressure for a reduction of 1 12-oz SSB per day.\(^11\) Several other studies have reported positive relationships between SSB intake and blood pressure.\(^2,12-14\) Less is known about the effects of SSB on cardiovascular clinical endpoints, but associations have been reported for chronic kidney and coronary artery disease.\(^3,15\) In 2010, data from the ARIC study was published on the association of SSB consumption and kidney disease.\(^16\)

The body of evidence to date supports the plausibility of a positive association between SSBs and incident stroke. However, only two studies of which the author is
aware have assessed this relationship. One reported positive associations with total stroke in men and women from the Health Professionals Follow-Up and Nurses’ Health studies (RR=1.16, 95% CI 1.05-1.28 for ≥1 soda vs. none). The second study, a case-control study in Iran, reported no association between the highest vs. lowest tertile of SSB intake (OR=0.99; 95% CI 0.42-1.87). This estimate was imprecise and the study sample was subject to bias in the selection of cases and controls. Further investigation of the association between SSBs and incident stroke is warranted.

5. Main Study Questions and Aims:
   a. Characterize the consumption of SSB over time and according to participant characteristics (e.g. gender, race, dietary pattern, BMI).
   b. Estimate the dose response relationships between sugar-sweetened beverage consumption and incident ischemic and hemorrhagic stroke types using reduction models as well as isocaloric substitution models with substitution of SSB with other beverages (e.g. water, fruit juice, skim milk, and coffee).
   c. Estimate generalized impact fractions of population-level reductions in SSB consumption on stroke incidence.

6. Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodological limitations or challenges present).

   Study design: Prospective cohort of ARIC study participants from four U.S. communities, Forsyth County, North Carolina; Jackson, Mississippi; Suburban Minneapolis, Minnesota; and Washington County, Maryland. Study participants (N=15,792) were aged 45-64 years at initial recruitment in 1987-1989.

   Inclusion/exclusion criteria: Participants with a history of stroke at baseline (N=284) will be excluded as well as those with missing or invalid dietary data (energy intake <600 or >4,000 kcal/day for men; <500 or >3,600 kcal/day for women; N=293).

   Primary exposure: Sugar-sweetened beverage consumption. Usual dietary intake was assessed at Visit 1 (1987-1989) and Visit 3 (1993-1994) using a 66-item semi-quantitative food frequency questionnaire (FFQ), a modified version of the 61-item questionnaire developed and validated by Willet et al.17 The FFQ assessed average consumption over the past year of “Regular soft drinks, such as Coke, Pepsi, 7Up, ginger ale; 1 glass” and “Fruit-flavored punch or non-carbonated beverages, such as lemonade, Kool-Aid or Hawaiian Punch; not diet; 1 glass”. Response values were: 1) almost never; 2) 1-3 per month; 3) 1 per week; 4) 2-4 per week; 5) 5-6 per week; 6) 1 per day; 7) 2-3 per day; 8) 4-6 per day; and 9) >6 per day. FFQs have been validated against diet records in other populations and found to have high correlation (0.84) for soda consumption.3 We will examine sugar-sweetened sodas and sugared fruit drinks individually and combined.

   Outcome: Incident total (N=1115), ischemic (N=976) and hemorrhagic stroke (N=111). Stroke etiology was classified based on computer algorithm and medical record review.
**Covariates**: Age, sex, race, educational attainment, smoking history, physical activity level, alcohol intake, anti-hypertensive and statin medication use, and other dietary factors. Nutrient values for foods were obtained from the US Department of Agriculture. Additional covariates likely to be on the causal pathway but that will be considered in sensitivity/secondary analysis include BMI, cholesterol, diabetes, and blood pressure.

**Analysis Plan**: Cox proportional hazards regression will be used to estimate hazard ratios and 95% confidence intervals for the association between SSB consumption and incident stroke. Additional analyses will be performed to assess the dose-response relationship and analyses will be modified accordingly if linearity is violated. Options include category scores and categorization into fixed-width intervals or quantiles. SSB intake will be modeled as a time-dependent covariate, incorporating dietary intake measurements at visits 1 and 3. Generalized impact fractions will be estimated using effect estimates obtained from Cox regression models and population exposure estimates from NHANES survey 1999-2002.

7. **a. Will the data be used for non-CVD analysis in this manuscript?** No

   **b. If Yes, is the author aware that the file ICTDER01 must be used to exclude persons with a value RES_OTH = “CVD Research” for non-DNA analysis, and for DNA analysis RES_DNA = “CVD Research” would be used?** NA

8. **a. Will the DNA data be used in this manuscript?** No

   **b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER01 must be used to exclude those with value RES_DNA = “No use/storage DNA”?** NA

9. **The lead authors of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals wither published or still in active status.**

   Yes, we have reviewed the list of manuscript proposals. There was no significant overlap. A paper from ARIC was published with a similar exposure (SSB) and with chronic kidney disease as the outcome. There was some overlap with #750 and 1749 to the degree that sugar-sweetened beverage intake was considered as part of dietary pattern scores. The primary aims of these proposals, however, were to examine diet pattern and disease risk and not the effects of sugar-sweetened beverages in isolation.

10. **What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?**

    #1364: Sweetened beverage consumption and development of chronic kidney
disease, hyperuricemia, and albuminuria

#750: Influence of food intake patterns on incidence of CHD and stroke and all-cause mortality: ARIC

#1749: Adherence to the Dietary Approaches to Stop Hypertension (DASH) diet and risk of coronary heart disease and ischemic stroke among individuals with hypertension in the Atherosclerosis Risk In Communities (ARIC) study

#1322: Test of a Biomarker for Consumption of Sweets in the ARIC-MRI study

#1683 Ideal Cardiovascular Health Behaviors and Progression of Intima Media Thickness

References


