Presenter Disclosure

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Diet Soda Consumption and Risk of Incident End-Stage Renal Disease

FINANCIAL DISCLOSURE:
No relevant financial relationships exist.
Diet Soda Consumption and Risk of Incident End-Stage Renal Disease

Background

• Artificially-sweetened beverages (diet soda) are often consumed to limit the high caloric and sugar intake associated with sugar-sweetened beverage consumption.¹

• Recent studies have shown that diet soda and artificial sweeteners adversely impact glucose levels, and risk of metabolic syndrome and diabetes.²⁴

• Diet soda consumption may influence kidney disease risk due to its phosphorus content, by increasing dietary acid load, or as a proxy for poor diet quality.

³ Lutsey et al. Circulation 2008;117;754-761.  
Objective

• To investigate the relationship between diet soda consumption and the development of incident end-stage renal disease (ESRD) in a community-based population.

• To assess the independence of this association from ESRD risk factors and other dietary factors.
Atherosclerosis Risk in Communities Study

- 15,792 middle-aged (45-64 years of age) Caucasian and African-American men and women from 4 U.S. communities
- Excluded prevalent ESRD (n=423)
- Analytic N=15,369

Visit 1: 1987-89 (baseline)
Visit 2: 1990-92
Visit 3: 1993-95
Visit 4: 1996-98
Visit 5: 2011-13

Continuous surveillance & annual telephone follow-up
Assessment of Dietary Intake

• Semi-quantitative 66-item FFQ modified from the Willett questionnaire administered at baseline (study visit 1, 1987-89) and study visit 3 (1993-95)

  ![BEVERAGES]

  "In the past year, how often on average did you consume..."

  3. Low calorie soft drinks, such as any diet Coke, diet Pepsi, diet 7-Up; 1 glass .........

• Categorical frequency of consumption (<1, 1-4, 5-7, >7 glasses/week) using cumulative average diet to incorporate repeated assessment of dietary intake
Outcome Ascertainment

- Incident ESRD cases identified between baseline through the end of the observation period (December 31, 2012)

- Linkage to the U.S. Renal Data System registry (kidney transplant, dialysis)
Statistical Analysis

• Cox proportional hazards regression

• Base model (ESRD risk factors, Model 1):
  § demographics (age, sex, race-center)
  § socioeconomic status (education level)
  § health behaviors (smoking, physical activity)
  § total caloric intake
  § eGFR-Cr (linear spline terms with a knot at 90 mL/min/1.73 m$^2$)
  § comorbidities (BMI, diabetes, SBP)

• Base model + individual dietary factors
  § Model 2a: dietary acid load
  § Model 2b: diet quality*, sugar-sweetened beverages
  § Model 2c: dietary intake of phosphorus

* Diet quality defined using a modified AHEI-2010 index (includes: vegetables, fruits, whole grains, sugar-sweetened beverages and fruit juice, nuts and legumes, red and processed meat, trans fat, omega-3 fatty acids, polyunsaturated fatty acids, and sodium; excludes: alcohol); higher scores represent higher diet quality
## Baseline Characteristics

<table>
<thead>
<tr>
<th>Categories of Diet Soda Consumption (Glasses/Week)</th>
<th>&lt;1</th>
<th>1-4</th>
<th>5-7</th>
<th>&gt;7</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>6,678 (43.5%)</td>
<td>2,728 (17.8%)</td>
<td>3,885 (25.3%)</td>
<td>2,077 (13.5%)</td>
</tr>
<tr>
<td>Age</td>
<td>54</td>
<td>55</td>
<td>54</td>
<td>53</td>
</tr>
<tr>
<td>Female</td>
<td>52%</td>
<td>56%</td>
<td>58%</td>
<td>58%</td>
</tr>
<tr>
<td>Af-Am</td>
<td>35%</td>
<td>22%</td>
<td>24%</td>
<td>14%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>8%</td>
<td>9%</td>
<td>16%</td>
<td>21%</td>
</tr>
<tr>
<td>HTN</td>
<td>35%</td>
<td>33%</td>
<td>37%</td>
<td>35%</td>
</tr>
<tr>
<td>BMI category</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>40%</td>
<td>34%</td>
<td>27%</td>
<td>21%</td>
</tr>
<tr>
<td>Overweight</td>
<td>38%</td>
<td>40%</td>
<td>41%</td>
<td>40%</td>
</tr>
<tr>
<td>Obese</td>
<td>22%</td>
<td>26%</td>
<td>32%</td>
<td>39%</td>
</tr>
<tr>
<td>eGFR</td>
<td>103</td>
<td>102</td>
<td>102</td>
<td>102</td>
</tr>
</tbody>
</table>
## Diet Characteristics

<table>
<thead>
<tr>
<th>Category</th>
<th>&lt;1</th>
<th>1-4</th>
<th>5-7</th>
<th>&gt;7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dietary acid load, mEq/day</td>
<td>3.7</td>
<td>3.2</td>
<td>5.0</td>
<td>8.1</td>
</tr>
<tr>
<td>Dietary phosphorus, mg/day</td>
<td>1,021</td>
<td>1,070</td>
<td>1,088</td>
<td>1,214</td>
</tr>
<tr>
<td>Diet quality</td>
<td>42</td>
<td>45</td>
<td>46</td>
<td>45</td>
</tr>
<tr>
<td>SSB consumption, &lt;1 glass/week</td>
<td>26%</td>
<td>29%</td>
<td>43%</td>
<td>49%</td>
</tr>
<tr>
<td>Calories, kcal/day</td>
<td>1,645</td>
<td>1,584</td>
<td>1,565</td>
<td>1,680</td>
</tr>
</tbody>
</table>
Dose-Response Relationship Between Diet Soda and Incident ESRD

- **HR* for Incident ESRD**
  - 1 [Reference]
  - 1.06 (0.73, 1.52)
  - 1.32 (1.00, 1.73)
  - 1.80 (1.31, 2.48)

- **P-value for trend** <0.001

* Adjusted for age, sex, race-center, education level, smoking, physical activity, total caloric intake, eGFR-Cr, BMI, diabetes, SBP

**Diet Soda Consumption Frequency**
- <1 Glass/Week
- 1-4 Glasses/Week
- 5-7 Glasses/Week
- >7 Glasses/Week
## Risk of ESRD by Categories of Diet Soda Intake

<table>
<thead>
<tr>
<th>Categories of Diet Soda Consumption (Glasses/Week)</th>
<th>&lt;1</th>
<th>1-4</th>
<th>5-7</th>
<th>&gt;7</th>
<th>P for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1: ESRD risk factors*</td>
<td>1 [Ref]</td>
<td>1.06 (0.73, 1.52)</td>
<td>1.32 (1.00, 1.73)</td>
<td>1.80 (1.31, 2.48)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 2a: Model 1 + dietary acid load</td>
<td>1 [Ref]</td>
<td>1.02 (0.71, 1.47)</td>
<td>1.24 (0.93, 1.64)</td>
<td>1.73 (1.25, 2.40)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 2b: Model 1 + diet quality, SSB</td>
<td>1 [Ref]</td>
<td>1.02 (0.71, 1.47)</td>
<td>1.24 (0.93, 1.64)</td>
<td>1.73 (1.25, 2.39)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 2c: Model 1 + dietary phosphorus</td>
<td>1 [Ref]</td>
<td>1.01 (0.70, 1.45)</td>
<td>1.23 (0.93, 1.62)</td>
<td>1.62 (1.17, 2.26)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

* Adjusted for age, sex, race-center, education level, smoking, physical activity, total caloric intake, eGFR-Cr, BMI, diabetes, SBP
Risk of ESRD in Subgroups of the Study Population

P-value for interaction

- 0.54
  * HR for highest (>7 glasses/week) vs. lowest (<1 glass/week) frequency categories of diet soda consumption

- 0.43
  Adjusted for age, sex, race-center, education level, smoking, physical activity, total caloric intake, eGFR-Cr, BMI, diabetes, SBP

- 0.36
  Adjusted for age, sex, race-center, education level, smoking, physical activity, total caloric intake, eGFR-Cr, BMI, diabetes, SBP

- 0.78
  Adjusted for age, sex, race-center, education level, smoking, physical activity, total caloric intake, eGFR-Cr, BMI, diabetes, SBP
Summary of Findings

• In this community-based population of 15,369 African-American and Caucasian men and women, higher consumption of diet soda was associated with an elevated risk of incident ESRD over a median follow-up of 23 years.
  ▪ Dose-response
  ▪ Consistent across sub-groups
  ▪ Independent of ESRD risk factors and other dietary factors
Limitations & Strengths

• Limitations
  ▪ Measurement error with self-reported dietary intake (FFQ)
  ▪ Residual confounding

• Strengths
  ▪ Large (N=15,369), broadly generalizable (African-American and Caucasian men and women), prospective cohort study with long-term follow-up (median: 23 years)
  ▪ Clinically-relevant and validated outcome
Conclusions / Implications

• Our findings of the adverse health implications of diet soda consumption on kidney disease risk, in conjunction with other important clinical outcomes, should be considered when advising on healthy beverage consumption.

• Further research is necessary to validate these findings in other study populations and to examine potential mechanisms.
Acknowledgements

• The authors thank the staff and participants of the ARIC study for their important contributions.

• The ARIC study is carried out as a collaborative study supported by NHLBI contracts (HHSN268201100005C, HHSN268201100006C, HHSN268201100007C, HHSN268201100008C, HHSN268201100009C, HHSN268201100010C, HHSN268201100011C, and HHSN268201100012C).

• Some of the data reported here have been supplied by the U.S. Renal Data System (USRDS). The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as official policy or interpretation of the U.S. government.
Questions?

Thank You!
A CENTURY OF SAVING LIVES
MILLIONS AT A TIME

JOHNS HOPKINS
BLOOMBERG SCHOOL
OF PUBLIC HEALTH
Supplemental Slides
Potential Explanations

- Dietary intake of phosphorus
- Dietary acid load
- Diet quality
- Glucose intolerance
Public Health Implications

- Diet soda restriction for kidney disease prevention
- Alternatives to phosphorus additives
- Health promotion messages should not only warn against consuming specific beverage types but also recommend healthy beverage options

## Summary of ASB and Kidney Literature

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Study Population</th>
<th>Exposure</th>
<th>Outcome</th>
<th>Risk Estimate</th>
<th>Covariates</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHS (cohort)</td>
<td>3,318 Caucasian women</td>
<td>≥2 ASB/day vs. &lt;1/month</td>
<td>≥30% eGFR decline</td>
<td>OR: 2.02, 95% CI: 1.36, 3.01</td>
<td>Age, calories, HTN, BMI, DM, smoking, physical activity, CVD</td>
<td>Lin &amp; Curhan. CJASN 2011;6:160-166.</td>
</tr>
<tr>
<td>NC case-control study</td>
<td>214 CKD patients and 422 community-dwelling adults (self-respondents only)</td>
<td>≥2 ASB/day vs. &lt;1/week</td>
<td>CKD</td>
<td>OR: 4.21, 95% CI: 1.21, 14.61</td>
<td>Frequency matching: age, sex, race, proximity to study hospital</td>
<td>Saldana et al. Epidemiology 2007;18:501-506.</td>
</tr>
<tr>
<td>NHANES (cross-sectional)</td>
<td>9,358 US adults</td>
<td>Diet soda</td>
<td>albuminuria</td>
<td>OR: 0.94, 95% CI: 0.64, 1.39</td>
<td>SSB, age, race-ethnicity, gender, poverty status</td>
<td>Shoham et al. PLoS One 2008;3:e3431.</td>
</tr>
</tbody>
</table>
# Summary of ASB and Glucose Intolerance Literature

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Study Population</th>
<th>Exposure</th>
<th>Outcome</th>
<th>Risk Estimate</th>
<th>Covariates</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARIC</td>
<td>9,514</td>
<td>Diet soda (Q3 vs. Q1)</td>
<td>Incident metabolic syndrome</td>
<td>HR: 1.35, 95% CI: 1.24, 1.44</td>
<td>Age, sex, race, education, center, calories, smoking, physical activity + dietary intake of meat, dairy, fruits &amp; veg, grains</td>
<td>Lutsey et al. Circulation 2008;117:754-761.</td>
</tr>
<tr>
<td>MESA</td>
<td></td>
<td>Diet soda (≥1 glass/day vs. rare/never)</td>
<td>Incident metabolic syndrome, incident diabetes</td>
<td>Metabolic syndrome*: HR: 1.36, 95% CI: 1.11, 1.66; Diabetes: HR: 1.67, 95% CI: 1.27, 2.20</td>
<td>Age, sex, race/ethnicity, site, calories, education, physical activity, smoking, supplement use</td>
<td>Nettleton et al. Diabetes Care 2009;32:688-694.</td>
</tr>
</tbody>
</table>

* Individual components associated with diet soda: waist circumference and glucose
OGTT in mice fed saccharin (n=10) and glucose (n=9)

PCA of fecal microbiota composition for saccharin-consuming mice (blue triangles, n=5)

Functional characterization of saccharin-modulated microbiota.

Correlation Between ASB & SSB

Spearman rank correlation: 
\[ r = -0.2820 \]

Among those in the highest category for diet soda (ASB) consumption (>7 glasses/week), 49% are in the lowest category for SSB consumption (<1 glass/week).
## Risk of ESRD by Categories of SSB Intake

<table>
<thead>
<tr>
<th>Categories of SSB Consumption (Glasses/Week)</th>
<th>&lt;1</th>
<th>1-4</th>
<th>5-7</th>
<th>&gt;7</th>
<th>P for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ESRD, n (%)</strong></td>
<td>117 (2.3%)</td>
<td>92 (2.4%)</td>
<td>101 (2.6%)</td>
<td>46 (1.8%)</td>
<td>0.23</td>
</tr>
<tr>
<td>Model 1</td>
<td>1 [Ref]</td>
<td>0.90 (0.68, 1.19)</td>
<td>0.58 (0.43, 0.78)</td>
<td>0.32 (0.21, 0.47)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 2</td>
<td>1 [Ref]</td>
<td>1.10 (0.83, 1.46)</td>
<td>0.95 (0.71, 1.28)</td>
<td>0.59 (0.40, 0.87)</td>
<td>0.003</td>
</tr>
<tr>
<td>Model 3a</td>
<td>1 [Ref]</td>
<td>1.10 (0.83, 1.46)</td>
<td>0.95 (0.71, 1.28)</td>
<td>0.58 (0.39, 0.87)</td>
<td>0.003</td>
</tr>
<tr>
<td>Model 3b</td>
<td>1 [Ref]</td>
<td>1.17 (0.88, 1.56)</td>
<td>1.04 (0.77, 1.40)</td>
<td>0.64 (0.43, 0.96)</td>
<td>0.01</td>
</tr>
<tr>
<td>Model 3c</td>
<td>1 [Ref]</td>
<td>1.15 (0.86, 1.54)</td>
<td>1.04 (0.77, 1.41)</td>
<td>0.72 (0.47, 1.11)</td>
<td>0.07</td>
</tr>
</tbody>
</table>
## Risk of ESRD by Continuous SSB Intake

<table>
<thead>
<tr>
<th>Model</th>
<th>HR* (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td>0.63 (0.52, 0.77)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 2</td>
<td>0.82 (0.69, 0.98)</td>
<td>0.03</td>
</tr>
<tr>
<td>Model 3a</td>
<td>0.82 (0.69, 0.98)</td>
<td>0.03</td>
</tr>
<tr>
<td>Model 3b</td>
<td>0.75 (0.60, 0.93)</td>
<td>0.01</td>
</tr>
<tr>
<td>Model 3c</td>
<td>0.92 (0.76, 1.12)</td>
<td>0.43</td>
</tr>
</tbody>
</table>

* per 1 additional glass/day
Incident ESRD

• Validation study compared to physician-determined treated kidney failure based on medical chart review\textsuperscript{1}
  \begin{itemize}
    \item Sensitivity: 95\%
    \item Specificity: 100\%
  \end{itemize}