1. a. Full Title: Effect of Alcohol Consumption (and Type of Alcoholic Beverage Consumed) on Lipid Levels: The ARIC Study

b. Abbreviated Title (Length 26 characters): Alcohol Consumption & Lipids

2. Writing Group: Writing group members: Kelly Volcik
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I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal.

KV [please confirm with your initials electronically or in writing]

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3. Timeline: Statistical Analysis: October-December 06
   Manuscript Preparation: December 06-February 07
   Manuscript Revision: February-March 07
   Manuscript Submission: March 07

4. Rationale:
   The reduction in risk of CHD associated with moderate alcohol consumption is generally attributed to the beneficial effects of alcohol on lipids, namely an increase in HDL cholesterol.\textsuperscript{1,2} A decrease in LDL cholesterol with increased alcohol consumption has also been reported, but this effect is less consistent.\textsuperscript{6} In addition to HDL and LDL cholesterol, alcohol has been shown to effect levels of lipoprotein(a), apolipoprotein A-I, apolipoprotein A-II, apolipoprotein B and triglycerides.\textsuperscript{6-10}
The majority of studies evaluating the different effects of the type of alcoholic beverages consumed have focused on disease endpoints. The specific influence of different types of alcoholic beverages on lipids has been investigated to a lesser extent, and results do not show significant differences between the types of alcoholic beverages consumed and HDL cholesterol.\textsuperscript{11-15} To our knowledge, the majority of these studies have been conducted in European populations, with the few US studies being small (~1500 men and women) and not including African Americans.\textsuperscript{11-15} Additionally, the ARIC study has multiple manuscripts proposed/published with regards to alcohol consumption and specific cardiovascular diseases, sub-clinical atherosclerotic disease, and cognitive function, but the general effect of alcohol consumption and type of alcoholic beverage consumed on lipid levels has not been investigated. We believe our proposal would be beneficial and an important investigation in the large bi-ethnic population of the ARIC cohort.

5. Main Hypothesis/Study Questions:

Due to different drinking patterns between males and females and to variations in lipid measures between whites and African Americans, all analyses will be conducted separately by race-gender specific strata.

1. In a race- and gender-specific manner, evaluate the effect of total alcohol consumption (ethanol intake; ARIC variable ethanol03) on plasma lipid levels (i.e. HDL and LDL cholesterol, apolipoprotein A1 and B, triglycerides). These analyses will be carried out taking into account age, smoking status, cigarette years of smoking, BMI, education level, sport index and cholesterol medication use.

2. In a race- and gender-specific manner, evaluate the effect of specific types of alcohol consumption (wine, beer, shots of hard liquor; ARIC variables DTIA96, DTIA97, DTIA98) on plasma lipid levels (i.e. HDL and LDL cholesterol, apolipoprotein A1 and B, triglycerides). These analyses will be carried out taking into account age, smoking status, cigarette years of smoking, BMI, education level, sport index and cholesterol medication use.

6. Data (variables, time window, source, inclusions/exclusions):

The primary dependent variables will be lipid levels (evaluated individually). The usual ethnic group and missing data exclusion criteria will be used. Independent variables include but are not limited to age, BMI, smoking, education level, sport index and cholesterol medication use. With regards to cholesterol medication use, those taking cholesterol-lowering medication (cholmd01, n=448) will be excluded from the analysis. In analysis models, the derived variable indicating medications that secondarily lower cholesterol (cholmd02) will be included as a covariate.

Alcohol consumption will be considered as a categorical variable (never / low-moderate / heavy). Categories of low-moderate and heavy will be defined differently by gender using standard guidelines set forth by the U.S. Department of Health and Human Services / U.S. Department of Agriculture Dietary Guidelines 2005:

<table>
<thead>
<tr>
<th>Gender</th>
<th>Low-Moderate</th>
<th>Heavy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>≤ 2 drinks/day or ≤ 210 grams/week</td>
<td>&gt;2 drinks/day or &gt;210 grams/week</td>
</tr>
<tr>
<td>Women</td>
<td>≤ 1 drink/day or ≤ 105 grams/week</td>
<td>&gt;1 drink/day or &gt;105 grams/week</td>
</tr>
</tbody>
</table>

The reference group will only include never drinkers, thus avoiding the potential problem of including past drinkers which may include persons who have abstained from alcohol due to poor health (the “sick quitter effect”).
When considering the specific types of alcoholic beverages consumed, we understand that persons are not likely to consume only one type of alcoholic beverage, but rather consume different quantities of wine, beer and/or hard liquor. In order to best account for this situation, when evaluating intake of a specific alcoholic beverage among current drinkers, we will define a particular type of alcoholic beverage as predominant if consumption of that type of beverage (wine, beer, or liquor) accounts for two thirds or more of the total amount of ethanol consumed, with other drinkers classified as ‘no preference’ drinkers (the reference group will be never drinkers). This classification was utilized by Fuchs et al. in two previous ARIC manuscripts.\textsuperscript{16,17}

We note that these exclusions will lead to some groups with very small numbers, particularly those in the heavy drinking category, and in these cases we will not evaluate the heavy drinkers.

7.a. Will the data be used for non-CVD analysis in this manuscript? ___Yes ___X__No
7.b. If Yes, is the author aware that the file ICTDER02 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? ___Yes ___No

8.a. Will the DNA data be used in this manuscript? ___Yes ___X__No
8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER02 must be used to exclude those with value RES_DNA = “No use/storage DNA”? ___Yes ___No

9. The lead author 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 either published or still in active status. ___X__ Yes ___No

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)?

#004 Patsch ’89 (HDL, HDL2, HDL3 and Apo A-1 associations)
#1098 Volcik ’05 (Interaction effects of alcohol and HDL metabolism gene variation on risk of CHD)
#1138 Pankow ’06 (Influence ApoE and alcohol on HDL)

11. a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? ___Yes ___X__No
11.b. If yes, is the proposal
___ A. primarily the result of an ancillary study (list number*__________)
___ B. primarily based on ARIC data with ancillary data playing a minor role

12. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.

References: