**ARIC Manuscript Proposal #4289**

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| **PC Reviewed: 07/11/23** | **Status: _____** | **Priority: 2** |
| **SC Reviewed: _____** | **Status: _____** | **Priority: ____** |

**1.a. Full Title**: Potato consumption, healthy and unhealthy plant-based diet, and cardiometabolic health: a pooling analysis of US cohorts

**b. Abbreviated Title (Length 26 characters)**: Potatoes and cardiometabolic health

**2. Writing Group [please provide a middle name if available; EX: Adam Lee Williams]:**
Writing group members:

Luc Djousse, Lyn M. Steffen, So Yun Yi, Xia Zhou, Robyn McClelland, Howard Sesso, John Gaziano, I-Min Lee, Julie Buring, JoAnn Manson, Zhou Lan, Eunjung Kim, Jaewon Lim

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. __LD___ **[please confirm with your initials electronically or in writing]**

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**ARIC author** to be contacted if there are questions about the manuscript and the first author does not respond or cannot be located (this must be an ARIC investigator).
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**3. Timeline**: 1-2 years

**4. Rationale**:
Cardiovascular disease (CVD) remains one of the major causes of death and disability in the US[1]. About 1 in 20 Americans is affected by type 2 diabetes (T2D)[2] and the lifetime risk of developing hypertension is 90%[3]. Both T2D and hypertension are major determinants of CVD including myocardial infarction, stroke, and heart failure[1]. Data from previous clinical trials suggest that healthy diet can reduce the risk of CVD, T2D, and hypertension[4-6]. White potatoes are a good source for potassium, fiber, and plant polyphenols known to exert health benefits[7, 8], data in the literature remain sparse and inconsistent on the association of potato consumption with the risk of T2D[9, 10], hypertension[11], and CVD[12]. A recent meta-analysis reported no association of total potato consumption with risk of T2D, hypertension, or CVD but a higher risk of T2D and hypertension with fried potatoes[13]. Our preliminary analyses suggest a threshold relation of potato consumption with risk of coronary artery disease among US veterans and no association with stroke or heart failure.

Major gaps in existing data include (i) a lack of consideration of overall dietary patterns [i.e., adherence to plant-based diet index (PDI)[14]] when examining the association of potato consumption with cardiometabolic risk or mortality and (ii) the fact that most studies have focused on total potato consumption with little attention devoted to the association of types of potatoes consumed (French fries, mashed/baked/boiled potatoes, or potato chips) with cardiometabolic risk. These limitations could partially account for the inconsistencies of the data reported in the literature on the relation of total potato consumption with risk of CVD, T2D, hypertension, and mortality.

The current proposal will address above gaps by focusing on the role of PDI, healthy PDI (hPDI) and unhealthy PDI (uPDI) on the association of total, fried, boiled/mashed/bake, and other forms of potatoes with risk of CVD and CVD risk factors (T2D and hypertension) in large and diverse prospective US cohorts.

## 5. Main Hypothesis/Study Questions:

1. Total potato consumption is positively associated with incidence of CVD, hypertension, and T2D in people with unhealthy PDI (below median score) but not in people with healthy PDI (above median score).

2. Fried but not boiled/mashed/baked potato consumption is positively associated with incident CVD, T2D, and hypertension, especially in people who adhere to uPDI but not in those who adhere to hPDI.

## 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 methodologic limitations or challenges if present).

Population: The ARIC cohort will be one of the US cohorts included in this pooling project. Other cohorts include: Jackson Heart Study (JHS), Women's health Study (WHS), Physicians' Health Study (PHS), Women's Antioxidants Cardiovascular Study (WACS), COSMOS, Multi Ethnic Study of Atherosclerosis (MESA), and Atherosclerosis Risk in Communities (ARIC) study. All of these cohorts have used comparable food frequency questionnaires to assess diet and outcome variables including incident type 2 diabetes.

Design: Prospective cohort design with meta-analysis of harmonized individual-level results
Exposure: Consumption of total potatoes, French fries, boiled/mashed/baked potatoes, and potato chips will be evaluated separately.
PDI, hPDI, and uPDI: Seven healthy plant food groups: whole grains, fruits, vegetables, nuts, legumes, vegetable oils, and tea/coffee; four unhealthy plant food groups excluding potatoes: fruit juices, sugar-sweetened beverages, refined grains, and sweets/desserts; and six animal food groups: animal fats, dairy, eggs, fish/seafood, meat (poultry and red/processed meat), and miscellaneous animal-based foods (i.e., Pizza, chowder or cream soup). For the overall PDI, higher intakes of healthy and unhealthy plant food groups were given higher scores, whereas higher intakes of animal food groups were given lower scores. For the hPDI, we will give healthy plant food groups positive scores, and unhealthy plant food groups and animal food groups reverse scores as described previously[15]. For the uPDI, unhealthy plant food groups will receive positive scores, whereas healthy plant food groups and animal food groups will receive reverse scores. We will sum the quintile scores of each of the seventeen food groups to obtain hPDI and uPDI. A higher score on the hPDI will reflect a higher intake of healthy plant foods and/or a lower intake of unhealthy plant foods and animal foods; and a higher score on the uPDI will

reflect a higher intake of unhealthy plant foods and/or a lower intake of healthy plant foods and animal foods.

Outcomes: The main outcome will be incident CVD including fatal and non-fatal myocardial infarction, fatal and non-fatal stroke, coronary intervention, bypass surgery, and CVD deaths. Secondary outcomes will include incident T2D and hypertension. We will exclude prevalent events for each specific outcome.

Statistical analyses: Each cohort will use the same standardized analytical plan as previously described[16]. Initial analyses will be conducted stratified by healthy vs. unhealthy PDI using median as cut point of PDI score. We will use Cox regression model to estimate multivariable hazard ratios (95% confidence intervals). For multivariable adjustment in Cox models, we will use sequential model building based on a priori knowledge of confounding factors. Proportional hazards assumption will be evaluated using Schoenfeld residuals. We will assess the interaction between potato consumption and PDI by using an interaction term (potato x PDI, potato x hPDI, and potato x uPDI) in the multivariable adjusted Cox model. Hazard ratios obtained from each cohort will be used to complete pooled meta-analysis centrally using fixed effect (using inverse variance weighting). We will initially pool relative risks and their 95% CI from the highest versus lowest category of egg consumption in each study. We will assess the presence of influential studies using removal of one study at a time method. To assess dose-response relation and evaluate the shape of potato-outcome relation, we will use generalized least squares regression described by Greenland and Longnecker[17] and fit cubic splines with knots at 5, 35, 65, and 95 percentile of potato distribution. We will assess heterogeneity using Q statistic, I-squared. Statistical significance will be based on 2-sided p value <0.05.

**7.a. Will the data be used for non-ARIC analysis or by a for-profit organization in this manuscript? ____ Yes _X___ No**

**b. If Yes, is the author aware that the current derived consent file ICTDER05 must be used to exclude persons with a value RES_OTH and/or RES_DNA = "ARIC only" and/or "Not for Profit" ? ____ Yes ____ No**
(The file ICTDER has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

**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 current derived consent file ICTDER05 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.**
ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: http://www.cscc.unc.edu/aric/mantrack/maintain/search/dtSearch.html

__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)?**

**11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? __X__ Yes ____ No**

This manuscript proposal is based on Dr. Djousse's approved ARIC ancillary study of the same title; approval letter dated Mach 30, 2022. There wasn't an ancillary study number.

**11.b. If yes, is the proposal**

**_X__ A. primarily the result of an ancillary study** (ancillary study # 2022.06)
**_X__ B. primarily based on ARIC data with ancillary data playing a minor role (**the ancillary study uses only ARIC core data**)**

*ancillary studies are listed by number https://sites.cscc.unc.edu/aric/approved-ancillary-studies

**12a. 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.**

**12b. The NIH instituted a Public Access Policy in April, 2008** which ensures that the public has access to the published results of NIH funded research. It is **your responsibility to upload manuscripts to PubMed Central** whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted in http://www.cscc.unc.edu/aric/index.php, under Publications, Policies & Forms. http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.