NIH-AARP STaRs Proposal Details

Proposal Number: 201903-0001

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Project Information
Proposal Title: Dietary Cholesterol and Egg intakes in Relation to Total and Cause-specific Mortality in the NIH-AARP Cohort
Cancer Site /Outcome: MOR
Exposure: Intakes of cholesterol and eggs (g/day)
Geographic Identifiers: Don't know

Timeline
Data Tables: 4/15/2019
Abstract: 4/30/2019
Manuscript Draft: 5/31/2019
Anticipated Submission: 6/30/2019

Proposed Author List

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Proposal / Abstract

Background (including justification)
In the past, limiting dietary cholesterol intake to 300 mg/day has been widely recommended for prevention of cardiovascular disease (CVD) (1). However, accumulating evidence showed that ingestion of dietary cholesterol had only modest effects on LDL and HDL cholesterol and little influence on the ratio of LDL to HDL (2). Eggs are a major source of dietary cholesterol, whereas other beneficial nutrients such as unsaturated fats, lecithins and B-vitamins are also present, potentially offsetting any possible increased risk due to the cholesterol content (3). Therefore, due to the lack of effect of dietary cholesterol on blood cholesterol, the 2015 Dietary Guidelines Advisory Committee Report did not carry forward the upper limit for dietary cholesterol and recommended eggs as part of a healthy diet (4). Nonetheless, the effects of dietary cholesterol and eggs on cardiovascular health still remain unclear. A meta-analysis concluded that dietary cholesterol was not associated with the risk of cardiovascular death, coronary artery disease or stroke (5).
However, these reviewed studies had relatively smaller sample sizes or fewer cases, were too low-powered to obtain precise effect estimates, and were unable to examine the associations with mortality from various causes, such as cancer and diabetes. Several lines of evidence suggested positive relationships of dietary cholesterol with breast and pancreatic cancer (6, 7). Previous studies regarding egg consumption have also been inconsistent. Although a previous meta-analysis reported a doseresponse positive association of egg consumption with CVD risk (8), the latest meta-analysis revealed that egg consumption was not associated with increase in CVD or all-cause mortality whereas related to a small reduction in stroke (9). Notably, egg consumption has been associated with an increased risk of diabetes among the general population and CVD comorbidity among diabetic populations (2, 10). Overall, the scientific evidence for recommendations on dietary cholesterol and eggs is lacking. Therefore, a large-scale study is needed for assessing substantial associations of dietary cholesterol and egg intakes with various causes of death in American populations. Given the large number of participants and death cases in the AAPR cohort, findings from this study will provide the evidence base to inform dietary recommendations on dietary cholesterol and egg consumption for clinicians and policy makers.

Objectives
1. To investigate the associations of dietary cholesterol and egg intakes with total and cause-specific mortality in the NIH-AARP Cohort.
2. To evaluate whether the proposed associations differ among diabetic patients versus non-diabetic participants.

Study population
Participants from the NIH-AARP Cohort with complete dietary data at baseline.

Exclusions
Participants with implausible energy intake (4200 kcal/d for men and 3500 kcal/d for women).

Exposure
Intakes of cholesterol and eggs (g/day)

Outcome
All-cause mortality and cause-specific mortality from different causes

Statistical analysis (including statistical method, covariates, and sensitivity analysis)
Intakes of cholesterol and eggs will be expressed as functions of energy density (g · 2000 kcal-1 · d-1) by the nutrient density method. Cox proportional hazards regression models will be used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for mortality according to cholesterol and egg intakes with the lowest quintile (cholesterol) or non-consumers (egg) as the reference group. Established or suspected risk factors for death will be considered as covariates, including age, sex, race, marital status, education, household income, body mass index (BMI), alcohol, smoking, vigorous physical activity, usual activity at work, perceived health condition, history of cancer, heart disease, stroke, and diabetes at baseline, history of hypertension, history of hypercholesterolemia, family history of cancer, cholesterol-lowering medications use, aspirin use, hormones use (for women only), intake of total energy, and consumption of red and processed meats, vegetables, fruits, whole grains, legumes, dairy products, potatoes, and sugar sweetened beverages.

We will also assess the effects of substituting eggs for 1 serving of other common food groups (such as red meats, dairy products and legumes) on risk of death by including continuous variables for both eggs and the other food in the model along with other non-dietary confounders. In a secondary analysis, we will further analyze the associations for whole egg, egg whites and egg substitutes, respectively. Subgroup analyses will also be conducted according to important potential effect modifiers, such as diabetes, history of hypertension and hypercholesterolemia. P values for interactions will be tested by likelihood-ratio test.

Several sensitivity analyses will be performed: (i) further adjusting for a healthy eating-index-2015 to see whether findings materially change; (ii) excluding those with heart disease, stroke, cancer and diabetes at baseline; and (iii) excluding the initial 4 years of follow-up.

References
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Additional Comments

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Research Interests
- Investigation of dietary factors, using nutritional or molecular epidemiologic approaches, in the cause and prevention of cardiovascular disease, cancer, and other chronic diseases in cohort studies
- Investigation of nutrients, such as polyunsaturated fatty acids, in the prevention and control of cardiovascular diseases and other chronic diseases
- Molecular nutrition and nutrigenomic studies on the occurrence, intervention and control of cardiovascular diseases and other chronic diseases

Education Background and Work Experience
- 2015-: Associate professor, Department of Nutrition and Food Hygiene, School of Public Health, Zhejiang University, Hangzhou, Zhejiang, China
- 2012-2014: Lecturer, Department of Nutrition and Food Hygiene, School of Public Health, Zhejiang University, Hangzhou, Zhejiang, China
- 2009-2011: Postdoctoral research fellow, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA
- 2003-2008: Ph.D. in Food Science, Department of Food Science and Nutrition, College of Biosystems Engineering and Food Science, Zhejiang University, Hangzhou, Zhejiang, China
- 1999-2003: B.S. in Food Science, College of Food Science and Engineering, Shanxi Agriculture University, Jinzhong, Shanxi, China

Academic Committee Membership
2013-Now: Member, Chinese Nutrition Society
2013-Now: Member, Zhejiang Provincial Nutrition Society

Peer-reviewed Publications
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Funded Projects
1. Project title: Mechanism of action for effect of n-3 polyunsaturated fatty acids on promoting white-to-beige process of adipose and regulating glucose homeostasis imbalance via adipose-gut microbiota-liver axis
Duration: 2018-2021
Agency and Grant#: National Natural Science Foundation of China (81773419)
Role: PI
2. Project title: Mechanistic studies on amelioration effect of salmon unsaturated fatty acids on insulin resistance based on synergistic regulation of GLUT4 vesicular trafficking and adipose browning
Duration: 2015-2017
Agency and Grant#: National Natural Science Foundation of China (31401659)
Role: PI
3. Project title: Associations of plasma phospholipid fatty acids and body fat composition and metabolism syndrome
Duration: 2015-2016
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Agency and Grant#: National Fundamental Funds for the Central Universities of China (2015QNA7014)
Role: PI
4. Project title: Effect of marine n-3 polyunsaturated fatty acids on promotion of the browning of white adipose and regulation of nutrition-gene interaction
Duration: 2014-2016
Agency and Grant#: Zhejiang Natural Science Foundation (LY14C200008)
Role: PI
5. Project title: CMB Collaborating Program (CP) on modifiable chronic disease related risk factors control and health promotion
Duration: 2013-2015
Agency and Grant#: China Medical Board Foundation (12-108)
Role: Co-PI