ARIC Manuscript Proposal #2589

PC Reviewed: 8/11/15	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Trajectories of physical activity in mid-life and risk of functional decline and falls in later life

b. Abbreviated Title (Length 26 characters): Physical activity, physical function, and falls

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

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3. Timeline: 6 months

4. Rationale:
Since the seminal publication of the 1953 study of London Transport Workers by Morris et al.[1], substantial evidence has accumulated regarding the numerous benefits of being physically active. In the *2008 Physical Activity Guidelines for Americans*, the Advisory Committee determined that there is currently *strong evidence* to support that physical activity participation is a safe and beneficial primary prevention strategy among older

adults at increased risk for falls.[2] Similarly, the American Geriatric Society (AGS)[3,4] promotes physical activity as a fall prevention strategy. In a 2007 meta-regression of 12 RCTs[5] that examined the relationship between physical activity and falls, physical activity interventions effectively reduced risk of falls by 29%. Yet, several unanswered questions regarding the complex association between physical activity and falls remain largely unexplored in the literature.

The transition from mid- to late- life is a critical time during adulthood when risk of disability escalates. While the existing evidence base generally supports a beneficial effect of physical activity on risk of falls, these studies have primarily utilized an older adult population. Therefore, the importance of being physically active in midlife, and/or the cumulative exposure of physical activity from mid- to late-life and risk of falls in later life is largely unknown.

With nearly 30 years of longitudinal physical activity data that spans the mid- to late-life transition with falls data collected in late-life, the ARIC Study is uniquely positioned to address this research gap. We anticipate that these findings will support health promotion efforts that encourage mid-life adults to engage in habitual physical activity for the primary prevention of falls in later life. Targeting healthy lifestyle behaviors during mid-life, like engaging in regular physical activity, has been used successfully in the past for chronic disease prevention.[6,7]

5. Main Hypothesis/Study Questions:

The primary purpose of these analyses is to examine the association of trajectories of physical activity from mid- and late-life [Visit (V)1, V3 & V5; 1987-2013] with fall risk (2013-14 biannual follow-up) in later life.

Hypothesis 1: Four primary physical activity trajectory classes will emerge (decreasing activity over-time, consistently low active, consistently high active, and increasing activity over-time).

Hypothesis 2: When compared to those consistently low active, all other groups will have a lower risk of falls, with the consistently high activity class having the most favorable outcomes.

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).

Study Design: Longitudinal

Exclusions: Incomplete data at any time-point (V1, V3, V5 and/or 2013-14 biannual phone call).

Primary Exposure:
1. Reported physical activity (i.e., sports and recreation index score; V1, V3 & V5)
Note: We will also explore continuous physical activity estimates, expressed as $MET \cdot hr \cdot wk^{-1}$ that were recently developed by Evenson, Palta & Gabriel.
Outcomes:
1. Falls; Injurious and non-injurious (2013-14 biannual phone calls)

Other Variables:
age, sex, race, site, education, smoking status, alcohol status, comorbidity (hypertension, diabetes, coronary heart disease, heart failure, stroke), medication use (i.e., antihypertensive, psychotropic, sedatives), CES-D, SPPB, and grip strength

Data Analysis (summary):
As noted in the hypothesis, we expect that four trajectory classes will emerge over this 30 year time period as described above. Mid-to-late life physical activity trajectories will be constructed using Baecke physical activity scores (sports, exercise leisure, work index) from ARIC Visits 1, 3, and 5. Mid-life activity trajectories will be decomposed into baseline levels and changes for inclusion as predictors in the later-life GLMMs using a simplified generalized additive distributed lag-model (gaDLM) approach to quantify associations.[8] The bivariate mid-life baseline/change data will also be grouped to define and quantify proportions of participants falling into the four trajectory classes outlined above with category indicators included in GLMMs of later-life outcomes to quantify associations. Associations between mid-life activity trajectories and later-life outcomes will be estimated using log-Gamma, log-Negative-Binomial and logistic GLMMs for later-life physical activity, physical function and falls respectively.

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

b. If Yes, is the author aware that the file ICTDER03 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
(This 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 file ICTDER03 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/search.php

__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)?

MS #333B	Patterns of change in physical activity: six-year follow-up of the ARIC cohort	K. Evenson
MS #2310	Physical activity and cognitive decline	P. Palta
MS #2450	Physical Activity Patterns and Predictors of Change from Midlife to Older Adulthood: the Atherosclerosis Risk in Communities (ARIC) Study	P. Palta
MS #2548	Changes in Physical Activity and the Risk of Incident Heart Failure: The Atherosclerosis Risk in Communities (ARIC) Study	R. Florido
MS #2381	Falls Prevalence in Older Black and White ARIC Participants	L. Pompeii

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 (usually control variables; list number(s)* _____ _____ _____)

*ancillary studies are listed by number at http://www.cscc.unc.edu/aric/forms/

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.

References

1. Morris J, Heady JA, Raffle PAB, Roberts CG, Parks JW. Coronary heart disease and physical activity of work. *Lancet.* 1953;265:1053-1057, 1111-1120.
2. Physical Activity Guidelines Advisory Committee Report. 2008. http://www.health.gov/paguidelines/Report/pdf/CommitteeReport.pdf. Accessed March 19, 2011.
3. Summary of the Updated American Geriatrics Society/British Geriatrics Society clinical practice guideline for prevention of falls in older persons. *J Am Geriatr Soc.* Jan 2011;59(1):148-157.
4. Guideline for the prevention of falls in older persons. American Geriatrics Society, British Geriatrics Society, and American Academy of Orthopaedic Surgeons Panel on Falls Prevention. *J Am Geriatr Soc.* May 2001;49(5):664-672.
5. Campbell AJ, Robertson MC. Rethinking individual and community fall prevention strategies: a meta-regression comparing single and multifactorial interventions. *Age Ageing.* Nov 2007;36(6):656-662.
6. Eckel RH, Jakicic JM, Ard JD, et al. 2013 AHA/ACC Guideline on Lifestyle Management to Reduce Cardiovascular Risk: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation.* Nov 12 2013.
7. Opportunities for Cancer Prevention During Midlife. *American Journal of Preventive Medicine.* 2014;46(3 (Supplement 1)).
8. Zanobetti A, Wand MP, Schwartz J, Ryan LM. Generalized additive distributed lag models: quantifying mortality displacement. *Biostatistics.* Sep 2000;1(3):279-292.