ARIC Manuscript Proposal #1798

PC Reviewed: 5/10/11	**Status: <u>A</u>**	**Priority: <u>2</u>**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Trajectory of Self-Rated Health (SRH) and Functional Status Before and After Cancer Diagnosis

b. Abbreviated Title (Length 26 characters): SRH, Functional Status and Cancer

2. Writing Group:
Writing group members: Jessica Jensen, Debra Irwin, Anna Kucharska-Newton, Randi Foraker, Sally Stearns, Elizabeth Platz, Beverly Gwen Windham, Xuesong Han, Bryce Reeve, others welcome

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

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3. Timeline: Analysis will begin immediately after approval of manuscript proposal. Draft Manuscript anticipated late 2011.

4. Rationale:
Self-rated health (SRH) is one measure of general wellbeing and is obtained by asking individuals to objectively describe their health status on a four- to eight-point Likert scale (i.e., excellent, good, fair or poor) (Singh-Manoux 2007). SRH has been found to be associated with adverse health outcomes, such as repeated hospitalizations, and mortality. (Kennedy 2001; Wolinsky 2008). Thus, SRH has been utilized to predict adverse health outcomes.

Functional status is usually defined as the ability to perform self-care, self- maintenance and physical activities. Evaluation of functional status can identify risk of frailty and mobility disability that is independent of disease status, as well as the impact that a disease may have on a person's lifestyle, and provides a measure for a person's need for care. (Saltzman 2011, Lunney 2003, Haas 2008).

The long term impact of cancer is often assessed utilizing clinical endpoints such as remission and survival. However, these measures do not fully capture the impact of cancer on an individual's functional status and general wellbeing. Little information is available about the functional status and general wellbeing across the continuum of disease trajectories, including the time prior to a cancer diagnosis. Most studies that address these issues have limitations in their research design. Typically these studies consist of highly selected patient populations (e.g.: patients enrolled in clinical trials) or they measure these domains after the diagnosis has occurred and information prior to diagnosis is lacking. (Reeve 2009)

We propose to examine SRH and functional status trajectories prior to and after the diagnosis of cancer among the ARIC cohort participants.

5. Main Hypothesis/Study Questions:

1. Describe and compare the trajectory of functional status and SRH prior to and following an incident cancer diagnosis (lung, colorectal, prostate, breast cancer and all cancers).
   a. Compare SRH and functional status trajectory against that of a 'random' event occurring among a comparison group without a cancer diagnosis selected from the entire ARIC cohort.
   b. Evaluate the effect of age, gender, race, education, and marital status on the observed SRH and functional status trajectories.
   c. Determine whether the presence or absence of chronic diseases or conditions at baseline (e.g.: CHD, stroke, heart failure diabetes, obesity, diabetes or hypertension) modifies the observed SRH or functional status trajectories.
2. If average SRH or functional status declines post-cancer diagnosis, determine how much of this decline is due to deaths.

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
ARIC cohort data will be analyzed over the time period baseline-2006. Specifically, the SRH and functional status trajectories prior to (up to 5 years) and after the diagnosis of cancer (follow-up until death, loss to follow-up or last follow-up) will be analyzed. Six groups of ARIC cohort participants will be included:

1. cohort participants diagnosed with lung cancer
2. cohort participants diagnosed with breast cancer
3. cohort participants diagnosed with prostate cancer
4. cohort participants diagnosed with colon cancer
5. cohort participants diagnosed with any type of cancer
6. comparison group of a random sample (n=2000) of all cohort members without cancer and alive at a randomly-selected date

Utilizing a previously published method (Diehr 2001), a comparison group of 2,000 cohort participants will be formed by a random sample of all cohort members alive at a randomly-selected date without a cancer diagnosis, which represents a random "event" experienced by the comparison group. This comparison group will serve to help determine if the SRH or functional status trajectories differ from the trajectories that would be expected due to aging. This method was recently applied to SRH for ARIC heart failure cases (Foraker et.al. 2011 Age and Ageing in press). For the breast and prostate cancer groups, gender specific analyses will be performed in relation to the comparison group.

If sample size is sufficient, other cancer-specific groups will be considered for analysis. Upon initial review of the numbers of incident cases, bladder cancer and melanoma are the most likely groups to be considered. Functional status was assessed on annual follow-up phone interviews administered in the years 1993-2007. Hence, incident cancer cases diagnosed between 1993 – 2006 will be included for the functional status analysis for the groups 1-5 defined above.
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Primary Outcomes
SRH
SRH was measured at baseline and at each annual follow-up (AFU) phone interviews with the question, "Over the past year, compared to other people your age, would you say that your health has been *excellent*, *good*, *fair* or *poor*?" However, to get an accurate picture of SRH, it is important to take death into consideration in analyses. For example, if only live participants are considered during follow-up, SRH may be shown to improve after a sentinel health event, since the sickest patients (i.e. those with *fair* or *poor* SRH)

have died (Diehr 2003).

The response set is not precisely ordinal, and the responses will be transformed according to Diehr et al: 95 for *excellent*, 80 for *good*, 30 for *fair*, 15 for *poor*, and 0 for *death* (Diehr 2005) This transformation represents the estimated probability of persons being healthy two years later (Diehr 2003; Diehr 2001).

Functional Status
Information on functional status will be obtained from the annual follow-up questionnaires. Functional status was assessed in versions D through K of the AFU form, which were administered in the years 1993-2007.   Hence, incident cancer cases diagnosed between 1993 – 2006 will be utilized for this analysis for the groups 1-5 defined above.

The functional status questions assessed the ability to perform physical activities, including usual activities and the ability to go to work. The questions, most of which required a "Yes" or "No" answer, remained the same throughout the entire time that they were administered.   The outcome of interest for this study will be the percent of cohort members responding to individual questions (e.g. "Are you able to perform heavy housework?") in a way that indicates diminished functional ability.   Since the existing questions do not form a validated functional status instrument, we will evaluate them as separate entities.

Following are the functional status questions that are present in the ARIC study annual follow-up (AFU) forms D-K:

1.   Are you able to do heavy work around the house, like shoveling snow or washing windows, walls or floors without help? Y/N
2.   Are you able to walk up and down stairs to the second floor without help? Y/N
3.   Are you able to walk half a mile without help? That's about 8 ordinary blocks. Y/N
4.   Are you able to go to work? Y/N/NA
5.   During the past 4 weeks have you missed work for at least half a day because of your health? Y/N
6.   Are you able to do your usual activities, such as work around the house or recreation? Y/N
7.   During the past 4 weeks have you had to cut down on your usual activities (such as work around the house or recreation) for half a day or more because of your health? Y/N

Proposed Analyses
We are interested in evaluating trajectories of SRH and functional status over time prior to and following a cancer diagnosis. Factors influencing pre- and post-diagnosis trajectories are of interest, as well as covariates which play a role in the decline of SRH or functional status over the follow-up period will be assessed. These include: age, race, gender, ARIC study site, BMI, comorbid conditions (e.g.: CHD, stroke, heart failure diabetes, obesity, hypertension, heart failure, diabetes, chronic lung disease), alcohol use,

smoking status, and education. The feasibility of using other comorbid conditions likely to impact SRH or functional status (e.g.: arthritis, depressive symptoms) as covariates will be evaluated as well.

Disease-specific SRH at each time point of interest will be regressed on study covariates to generate estimated adjusted SRH values and standard errors. Similarily, functional status measured as the proportion of those with decreased functional abilities will be evaluated controlling for covariates.   To account for multiple statistical comparisons, the Bonferroni correction will be employed in analysis of variance testing.

Methodological Challenges
Sample size maybe limited for some of the less common cancer types.   Hence, exploratory analysis will be performed to determine if sample size is sufficient for other cancer-specific groups. In addition, an 'all cancer type' group will be analyzed.

Missing data for SRH and functional status will be assessed. The ARIC cohort has experienced little loss to follow-up, therefore, we anticipate being able to estimate (i.e. interpolate) missing data, with the exception of data missing due to death, from data collected before and after the missing assessment. Since missingness of SRH and functional status data may be due to impaired function, we will perform a sensitivity analysis to evaluate the trajectories under the assumption that SRH and functional status data may not be missing at random.

7.a. Will the data be used for non-CVD analysis in this manuscript?
__x__ Yes   ____ 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?   __x__ Yes ____ No
(This file ICTDER03 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# 1462: Foraker et al. "Socioeconomic Status (SES) and the Trajectory of Self-Rated Health (SRH): Before and After a Heart Failure Event" Dr. Foraker has been contacted and is a co-author of this proposal.

Ms# 1697: Kucharska-Newton et al. "Functional Status and Cardiovascular Disease". Dr. Kucharska-Newton has been contacted and is a co-author of this proposal.

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

11.b. If yes, is the proposal
_x__   A. primarily the result of an ancillary study (list number* ___1995.04_____)
___   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/

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.

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