

**ARIC Manuscript Proposal #3726**

**PC Reviewed:** 10/13/20  
**SC Reviewed:** \_\_\_\_\_

**Status:** \_\_\_\_\_  
**Status:** \_\_\_\_\_

**Priority:** 2  
**Priority:** \_\_\_\_\_

**1.a. Full Title:** Psychosocial impact of the social distancing imposed during the COVID-19 pandemic on cognitive and physical functioning among older adults

**b. Abbreviated Title (Length 26 characters):** Psychosocial wellbeing and dementia

**2. Writing Group:**

Writing group members: Priya Palta, Melissa Minotti, Kunihiro Matsushita, Jennifer Deal, Elizabeth Oelsner (invited), James Russell Pike (invited), Kim Ring, Lynne Wagenknecht (invited), Tim Hughes, Tom Mosley, Pam Lutsey, Finn O’Flaherty, Joe Coresh, Anna Kucharska-Newton

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

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**3. Timeline:** ASAP due to the time sensitive nature of pandemic related research.

Analyses to begin immediately following receipt of data for Washington County (November 2020) with the goal of writing a first paper (will include proxy information collected only in this center) within 2020. Completion of data collection in all centers take additional time and a separate paper will be written with all the data (if all centers finish within 2020 then the paper will be updated rapidly).

**4. Rationale:**

The current COVID-19 pandemic poses a significant challenge for older adults. Prior to the outbreak, approximately one-quarter of community-dwelling Americans aged 65 years and older were considered socially isolated<sup>1,2</sup> and nearly 1 in 3 older adults in the U.S. reported loneliness.<sup>3</sup> The pandemic is expected to amplify social isolation and loneliness as a result of sheltering in place, physical distancing, and fear of infection. This may disproportionately impact older individuals of lower socioeconomic status, who, as early data suggest, experience the greatest burden of COVID-19 infections, hospitalizations, and deaths.<sup>4</sup>

Social isolation, loneliness, and other indicators of social connection have negative associations with physical, cognitive, and psychological effects, health-related behaviors, and health-related quality of life. Among individuals 65 years and older, social isolation, defined as lack of engagement with others<sup>5</sup>, is associated with poorer global and domain-specific cognitive function, measured cross-sectionally and longitudinally.<sup>6,7</sup> Social isolation is considered a major source of mental and psychosocial stress, which contributes to the increased prevalence of cerebrovascular diseases and poor cognitive function.<sup>8</sup> Loneliness, defined as subjective perception of 'unfulfilled social needs'<sup>9</sup>, has also been found to be longitudinally associated with cognitive decline.<sup>10,11</sup> In contrast, a higher level of social support was observed to be associated with greater baseline global cognitive function in mid-life within the ARIC cohort, although not associated with cognitive decline from mid- to late-life.<sup>12</sup>

Social/physical distancing imposed during the COVID-19 pandemic, has also had a profound impact on the provision of formal and informal care to older adults. Family members, who often are the main source of support for older adults, are now less able to physically meet with their loved ones. Further, as recommendations to counter the loneliness and isolation of social distancing center around maintaining connections with family members and friends online, many older adults, who may not have access to the Internet<sup>13</sup> will be left out.

Our objective is to ascertain the immediate psychosocial impacts of the profound and abrupt physical isolation imposed by states and communities in response to the COVID-19 pandemic and estimate its associations with downstream cognitive outcomes.<sup>14,15</sup> A short 15-minute telephone-based questionnaire has been developed by this team of ARIC investigators to assess loneliness, social support, contact with family members friends, anxiety, depression, and barriers to social/physical distancing. Additionally, in the Washington County study center, a family member, designated by participants prior to the COVID-19 pandemic as their closest support person has been contacted to assess their wellbeing during the COVID-19 pandemic and to obtain their perspective on the ARIC participant's wellbeing. The administration of this questionnaire is almost complete. Data generated will provide the context for longer term evaluation of the rate of cognitive aging over the adult life course in the ARIC cohort.

This proposal builds on successful implementation of the Psychosocial wellbeing questionnaire and on the many strengths of ARIC-NCS, including, ready access to a population with in-depth prior characterization, ongoing monitoring by extant trained personnel, and repeat follow-up measures already in place to examine the wellbeing of older adults during the COVID-19

pandemic. This proposal will quantify factors (social isolation and support) that strongly influence the primary outcomes of the ARIC-NCS (converting from MCI to dementia, losing the ability to live independently, and cognitive and functional resilience). Participants with cognitive and physical deficits are more vulnerable to change, especially during the unprecedented societal changes resulting from COVID-19. Likewise, the proposal's focus on resilience and reserve is directly connected to the challenge posed by COVID-19 and will benefit from estimating the impact of a profound external stressor, such as the COVID-19 pandemic, on the cognitive health of older adults.

Across all aims, we will estimate if associations differ across subgroups of sex, race (blacks vs. whites), socioeconomic status (low vs. high SES), and coping skills (low vs. high coping skills).

## **5. Main Hypothesis/Study Questions:**

**Aim 1:** To examine how COVID-19 social/physical distancing impacted older adults' psychosocial wellbeing (loneliness, anxiety) as well as social support.

In a subset of participants who have repeat measures from previous visits and sAFU interviews, we will compare baseline measures pre-pandemic obtained from 2017-2019 to the interview administered during the 2020 pandemic outbreak.

Hypothesis (H1): Even a relatively short period of social/physical distancing (2-6 months at the time of questionnaire administration) will lead to reduced psychosocial wellbeing among older adults. This will be most pronounced among socially vulnerable groups, including persons of low socioeconomic status and those with cognitive impairment.

**Aim 2:** To quantify the impact of psychosocial wellbeing during the COVID-19 epidemic on older adults' cognitive status, with an emphasis on the transition from MCI to dementia.

In follow-up through Visit 9, we will also examine change in cognitive status between visit 7 (2018-2019) and assessments made during and after the pandemic (second half of 2020 by phone).

Hypothesis (H2): Compared to high psychosocial wellbeing, low psychosocial wellbeing will result in a faster rate of cognitive decline and accelerate the transition from MCI to dementia from 2018-19 to 2021.

**Aim 3:** To quantify the impact of impact of the COVID-19 pandemic and associated social distancing on physical function among older adults.

We will compare self-reported physical functioning during the pandemic to that reported pre-pandemic and to objective measures of physical functioning obtained at Visit 7 and self-reported measures from Visit 8.

Hypothesis (H3): Older adults physical physical activity levels will have decreased during the COVID-19 pandemic.

**Aim 4:** To explore the impact of the COVID-19 pandemic healthcare utilization among older adults in the ARIC cohort in Washington County, MD using the CRISP system real time reporting. We will explore trends in healthcare use of ARIC participants in Washington County over the period from March 2020 through September 2020 by age, gender, and metrics of psychosocial wellbeing obtained from the PSW questionnaire.

Hypothesis (H4): The prolonged social isolation imposed by the COVID-19 pandemic will lead to initially dramatically lower rate of hospitalization, in-person ambulatory visits, and Emergency Department visits. This will be combined with an increase in severity of hospitalized events.

**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).**

All ARIC cohort members who participated in Visit 7 were eligible for the administration of the Psychosocial wellbeing questionnaire (N~3,500). Data collection for ARIC is outlined in Table 1, with new data elements bolded. Although constructs, such as social support, have been assessed in ARIC prior to the COVID-19 pandemic, those were repeated here as those aspects of the participants' wellbeing may have changed as a result of social distancing restrictions imposed at the time of the pandemic.

**Table 1.** Design summary of existing and proposed data collected in ARIC and newly added (in bold) study measures, by ARIC study visit

Measure	ARIC STUDY VISIT											
	1	2	3	4	5	6	7	8	Proposed data collection	9	10	11
Years	1987-1989	1990-1992	1993-1994	1995-1996	2011-2013	2016-2017	2018-2019	2020	2020 PWP	2021	2022	2023
N (attending visits)	15,792	14,348	12,887	11,656	6,538	4,003	3,586	Suspended	~4232 (~80%)	~2,943	~2,693	~2,444
Age range, years	45-65	48-78	51-71	54-74	70-90	75-94	77-96	79-99		80-100	81-101	82-102
Cognitive testing		X		X	X	X	X	X (phone)		X	X	X
<b>Calls &amp; Surveillance</b>	<i>Telephone calls (semi-annually) ascertain health and identify all hospitalizations for abstraction of selected ICD codes</i>											
<b>Proposed data collection instruments and past collection of similar constructs</b>												
<b>Social support<sup>16</sup></b>		X				sAFU (2016-2020)			x			
<b>Living Alone Status</b>						sAFU (2012,2015-2020)			x			
<b>UCLA Loneliness Scale<sup>17</sup></b>								sAFU (2020)	x			
<b>Access to care</b>					X	sAFU (2014)			x			
<b>Coping/resilience<sup>18</sup></b>									x			
<b>Anxiety</b>							X	X	x			
<b>Closest support person interview</b>									x			

AFU – Annual Follow-up Interview; sAFU – Semi-annual Follow-up interview

**Population and data collection:**

Data collection instruments are listed in Table 2. As of September 30, 2020, 2662 Psychosocial Wellbeing Questionnaire (PWP) forms were completed among 5291

(adjusted) eligible participants. The response rate was 82.8% in Washington County where nearly all interviews are complete (1131 complete forms available now and completion anticipated before October 15, 2020); other centers anticipate completion of these questionnaires in November, 2020. Washington County also completed 717 PSI forms for approaching a closest contact of which 536 (76%) agreed to the interview and completed the PSQ form (other centers have not participated in this component). We will also examine the closest contact person data and include it as corroborating information in the Aim 1 paper.

Psychosocial Wellbeing Participant Interview	PWP
Psychosocial Wellbeing Proxy Interview	PWX
Psychosocial Wellbeing Closest Support Person Contact Information	PSQ
Psychosocial Wellbeing Closest Support Person Questionnaire	PSI

**Psychosocial Wellbeing – status and changes compared to pre-pandemic:**

The proposed questionnaire items will measure objective as well as subjective social isolation experienced during the time of the COVID-19 pandemic. Items will be examined independently and also combined into scales of loneliness, perceived isolation and anxiety.<sup>19</sup> The UCLA- 3 item loneliness scale will be used to classify participants' level of loneliness. The scores for each individual question of this questionnaire, ranging from 1-3, will be added to create a final score that will range from 3 to 9. The loneliness score will be dichotomized to classify participants as not lonely (3-5) and lonely (6-9). The UCLA- 3 item loneliness scale was administered to a subset of ARIC cohort participants during semi-annual follow up interviews (form GNG) that were completed prior to the COVID-19 pandemic (January 2020-mid-March 2020). For those participants, we will be able to compare their level of loneliness prior to and during the pandemic. We will examine the relative difference in the continuous scores as well as transition between the self-reported "not lonely" and "lonely" states. Anxiety will be constructed as a continuous score, based on responses to three questions regarding feelings of anxiety, fearfulness, and nervousness. Confirmatory factor analyses will be performed to assess validity of the constructed scales.

### **Outcome ascertainment:**

**Cognition/Cognitive Status.** In our examination of cognitive function, we will rely on prior cognitive assessments and those planned for Visits 8 and 9 as part of the parent ARIC-NCS. Outcomes will include (1) cognitive function assessed during Visit 8, which is concurrent with the administration of the Psychosocial Wellbeing questionnaire; (2) change in global and domain-specific cognitive function from Visit 7 to Visit 8 (eventually to Visit 9); and (3) cognitive status (cognitively normal, MCI, or dementia) ascertained at Visit 8 (and at a later date at Visit 9) by a classification committee.

### **Analytical approach**

**Change in Cognition.** We will need to take into account the change in the cognitive battery from in person to phone after March 2020. James Pike developed methods for looking at change using instrumental variables which will be employed to calibrate measures. Linear mixed models, which provide unbiased parameter estimates under the assumption that data are missing at random (MAR),<sup>20</sup> will be used to estimate a repeated measures model for change in cognition with the covariates as independent variables. We will specify either an unstructured or compound symmetry covariance matrix for the residuals based on the Bayes' Information Criterion. We will use multiple imputation by chained equations to handle missing data.<sup>21</sup>

**Risk of MCI/dementia.** Multivariable logistic regression models will be used to estimate the risk of dementia and MCI.

**Accounting for Attrition and Selection Bias.** MCI and dementia are associated with loss to follow-up and death, and therefore may result in selection biases in our analyses. We will quantify what percentage of participants died and the number of those who were alive but did not participate in the survey. We will examine the sociodemographic, clinical and social factors associated with non-attendance to identify common predictors for both death and dropout to incorporate in our models to adjust for attrition. Based on recommendations of the ARIC-NCS Working Group,<sup>22-24</sup> we will apply protocols that implement the use of joint modeling, multiple imputation, or inverse probability of attrition weights to account for cohort attrition. We will use these techniques on our main analytic results in this study to estimate the presence of, and adjustment for, potential bias introduced by attrition.

Another limitation that will need to be addressed is the difference in the measurement of cognition across study visits and the harmonization between the in-person (Visit 7) and telephone based cognitive assessment occurring during the COVID-19 pandemic (Visit 8 and

possibly also Visit 9). We will rely on the expertise within the ARIC Neurocognitive Study Working Group to apply the most appropriate modeling strategy.

**Medical utilization:** The CRISP Healthcare Information Exchange system in Maryland (also includes some other counties in the mid-Atlantic region) should allow us to look at healthcare utilization in near real time. We will explore the ability to analyze the association between the pandemic (by date) and pre-pandemic measures of healthcare utilization. Specifically, we will request from the CRISP database information regarding ARIC participants' (1) hospitalizations, (2) Emergency Department visits, (3) Ambulatory care visits, (4) Hospice care. Information regarding illness severity will be obtained from ICD-10 diagnostic codes. All data will be pulled by ARIC ID.

A sample data output table is provided below:

ARIC ppt. ID	Type of service	Start of service date	End of service date	Reason for admission	Diagnosis ICD-10 codes (discharge diagnosis codes if hospitalization)	Physician type if ambulatory care event
W1234	IP	04.24.2020	04.26.2020	[text]	All position ICD-10 codes	-
W1234	OP	04.12.2020	04.12.2020	[text]		PCP
W1234	ED	06.14.2020	06.14.2020	[text]		-
W1234	IP	06.14.2020	06.19.2020	[text]		-

**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.csc.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?  Yes  No**

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

- A. primarily the result of an ancillary study (list number\* 2020.19)**  
 **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 <https://sites.csc.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.csc.unc.edu/aric/index.php>, under Publications, Policies & Forms. [http://publicaccess.nih.gov/submit\\_process\\_journals.htm](http://publicaccess.nih.gov/submit_process_journals.htm) shows you which journals automatically upload articles to PubMed central.

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