ARIC Manuscript Proposal Form

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ARIC Manuscript Proposal Number: **# 4392**

1.a. Full Title: Head injury, depression, and cognitive decline and dementia in community-dwelling adults

b. Abbreviated Title: TBI, depression, dementia

2. Writing Group [please provide a middle initial if available; EX: Adam L Williams]:
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I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. **HCE**

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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 (The ARIC author should be involved enough in ARIC to be able to point the lead author to appropriate ancillary study PIs and to be able to search ARIC manuscript proposals if the lead author doesn't have the access needed to do such a search).

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3. Timeline:

[Data are currently available. We anticipate that analyses will be performed within 12 months of manuscript proposal approval with a goal to submit an abstract to a conference within this time period. We anticipate submitting the manuscript for publication within 2 years of manuscript proposal approval.]

4. Rationale:

[Traumatic brain injury (TBI) is a global public health problem associated with tremendous individual and societal cost.[1-4] The annual incidence of TBI approaches 69 million individuals globally.[5] In the United States (U.S.) an estimated 2.8 million individuals seek medical care for TBI in emergency departments, resulting in approximately 223,100 hospitalizations and 69,500 deaths anually.[6-8]

Individuals who sustain TBI experience cognitive symptoms,[9] and TBI is recognized as a modifiable risk factor for dementia in the most recent *Lancet* Commission.[10-23] Studies have previously demonstrated cognitive deficits within the first year of injury primarily in executive function,[24] attention and processing speed,[25,26] and working memory[27-30] among populations that include patients with moderate-to-severe TBI, military personnel, and athletes with repetitive TBIs. These prior studies were largely performed among specialized populations and therefore have limited generalizability. Indeed, moderate-to-severe TBI comprises the minority of injuries,[31] with up to 95% of individuals with TBI classified as having mild injury based on the duration and severity of their symptoms at presentation.[31-33] Prevalence estimates are also likely to systematically underestimate the true burden of mild TBI in populations, as many individuals do not seek medical attention.[34,35] Therefore, there is a need to investigate longer-term domain-specific cognitive trajectories among community-dwelling older adults who have largely sustained milder injuries.

Depressive symptoms are also highly prevalent among individuals with prior TBI[32,36] and have been associated with poor functional outcomes and diminished quality of life after injury.[37-39] Groups that may experience increased risk for depression following TBI that include older adults, individuals who are unemployed, and those with a pre-injury psychiatric history or comorbid substance use disorder.[32,40,41] Prevalence estimates from prior studies on depression after TBI vary substantially from 6 to 77%, reflecting essential differences in the population studied, time elapsed since injury, and methods used to ascertain depression.[14,42-44] Findings from many of these prior studies are also based on small samples of tertiary referral populations, thus limiting their generalizability.[45] The extant literature is further limited by the fact that few studies have longitudinally examined depression phenomenology beyond 1 year after TBI,[46,47] although recent research has suggested the risk of depression following TBI may increase over time.[11,14,42,43,48]

In summary, although prior research consistently demonstrates increased short-term risk of cognitive and mood symptoms following TBI, uncertainty persists regarding the expected long-term clinical course, particularly among older and community-dwelling adults. The proposed research will leverage data from the ARIC study to address these gaps in the extant literature by examining (1) the association between head injury and domain-specific cognitive performance, (2) the association between head injury and depressive symptoms, and (3) the joint implications of head injuries and depression for subsequent dementia diagnoses.

5. Main Hypothesis/Study Aims:

The proposed research is comprised of three related analyses with the specific research aim and study hypothesis for each analysis detailed below:

Aim 1: Examine the association between head injury and cognitive performance over time (Visit 5 to Visit 9 or 10, depending on the timing of data availability) across the domains of language, memory, and sustained attention and processing speed.
Hypothesis 1: As compared to individuals with no prior head injury, individuals with head injury will be more likely to exhibit cognitive impairment across all cognitive domains. We further hypothesize that individuals with head injury will exhibit chronic and progressive declines in cognitive function over the duration of follow-up.

Aim 2: Examine the association between head injury and depression over time (Visit 5 to Visit 9 or 10, depending on the timing of data availability).
Hypothesis 2: As compared to individuals with no prior head injury, individuals with head injury will be more likely to experience depressive symptoms at all timepoints.

Aim 3: Examine the joint implications of head injury and depression for incident dementia risk over time (Visit 5 to 12/31/2020, or most updated administrative censoring date at time of submission for publication).
Hypothesis 3: As compared to individuals with no prior history of head injury or depression, the risk of incident dementia will be increased among individuals with either head injury or

depression alone. The risk of incident dementia will be greatest among individuals with both depression and head injury as compared to individuals with neither.

6. Design and analysis - please address the following aspects:

a) inclusion/exclusion
b) study design
c) outcome and other variables of interest with specific reference to time of their collection
d) summary of data analysis
e) Any anticipated methodologic limitations or challenges if present

Study Design, Inclusion/Exclusion Criteria

In this prospective cohort study, we will examine (1) the association between head injury and domain-specific cognitive performance, (2) the association between head injury and depression, and (3) the joint implications of head injuries and depressive symptoms for subsequent dementia diagnoses. For the proposed analyses, follow-up will begin at Visit 5 (2011–2013), the first study visit at which robust measures of domain-specific cognitive performance and depression were evaluated. Follow-up for all individuals will extend through Visit 9 or 10 (depending on the timing of data availability) for Aims 1 and 2 and will extend until loss to follow-up, death, or administrative censoring at the end of the study period on December 31, 2020 (or most updated administrative censoring date at time of submission for publication) for Aim 3. We will exclude individuals of non-White and non-Black race and Black participants at the Minnesota and Maryland field centers (in accordance with ARIC study analysis recommendations due to race-center aliasing). We will further exclude participants missing head injury data, missing depression data, or missing data on statistical model covariates.

Head Injury

Head injury (either with or without loss of consciousness) is defined based on self-report, and data from emergency department visits and inpatient hospitalizations. Self-reported head injury was measured from Visit 3 onward based on questions about head injury requiring physician or hospital care, loss of consciousness, number of head injuries, and year of head injury (See **Table 1** for text of self-reported questions). Head injuries requiring hospital care were identified using codes from the *International Classification of Diseases, Ninth Revision* (ICD-9) and *Tenth Revision* (ICD-10) based on community surveillance of all hospitalizations occurring within ARIC study communities, medical records from hospitalizations occurring outside of ARIC study communities that were reported in telephone follow-up calls, and linked claims data from the Center for Medicare and Medicaid Services (CMS) according to the Centers for Disease Control and Prevention (CDC) case definition for traumatic brain injury[49-51] **(**See **Table 2** for relevant ICD codes**)**. Hospitalization records are currently available from ARIC Study surveillance of all community hospitals from January 1, 1987–December 31, 2020. Linked CMS data for hospitalizations and emergency department visits are currently available for participates aged 65 years and older enrolled in Medicare fee-for-service Part B from January 1, 1991–December 31, 2018.

We will create a time-varying indicator for head injury, allowing head injury to be updated at each study visit for Aims 1 and 2 and allowing person-time to be allocated to no head injury and head injury in Aim 3. We will create an alternative head injury variable that further classified

individuals into head injury groups based on the number of reported head injuries (none; one; two or more). Finally, among the subset of head injury cases identified by ICD code data, we will create a third classification based on the Department of Defense head injury severity classification (no head injury; mild head injury; moderate, severe, or penetrating head injury).[52]

Table 1. Self-reported head injury questions

ARIC Visit 3 (1993 – 1995)
1. Have you ever had a head injury which led you to see a physician or seek hospital care?
2. How many times has this happened?
3. How many of these head injuries resulted in your losing consciousness, no matter how briefly?
4. In what year was your head injury for which you sought medical care?
ARIC Visit 4 (1996 – 1998)
1. Have you ever had a major head injury? That is, one that resulted in your losing consciousness, no matter how briefly, or that led you to see a physician or seek hospital care?
2. How many times has this happened?
3. How many head injuries resulted in your losing consciousness, no matter how briefly?
4. In what year was your head injury for which you lost consciousness sought medical care?
ARIC Brain MRI Visit (2004 – 2006)[1]
1. Have you ever had a head injury that resulted in loss of consciousness (knocked out)?
2. How many times?
3. In what year or how old were you when this first occurred?
4. In what year or how old were you when this last occurred?
ARIC Visit 5 (2011 – 2013)[1]
1. Have you ever had a head injury that resulted in loss of consciousness?
2. Have you had a head injury with extended loss of consciousness (>5 minutes)?
3. Have you had a head injury that resulted in long-term problems or dysfunction?
ARIC Visit 6 (2016 – 2017)
1. Have you ever had a head injury that resulted in loss of consciousness?
2. Have you had a head injury with extended loss of consciousness (>5 minutes)?
3. Have you had a head injury that resulted in long-term problems or dysfunction?
ARIC Visit 7 (2018 – 2019)
1. Have you ever had a head injury that resulted in loss of consciousness?
2. Have you had a head injury with extended loss of consciousness (>5 minutes)?
3. Have you had a head injury that resulted in long-term problems or dysfunction?

1. Questions asked in a subgroup of ARIC participants selected for brain magnetic resonance imaging scans.

Table 2. ICD codes used to define head injury

ICD-9 Codes	
800.xx	Fracture of vault of skull
801.xx	Fracture of base of skull
803.xx	Other and unqualified skull fractures
804.xx	Multiple fractures involving skull or face with other bones
850.xx	Concussion
851.xx	Cerebral laceration and contusion
852.xx	Subarachnoid, subdural, and extradural hemorrhage following injury
853.xx	Other and unspecified intracranial hemorrhage following injury
854.xx	Intracranial injury of other and unspecified nature
959.01	Head injury, unspecified

ICD-10 Codes	
S02.0	Fracture of vault of skull
S02.1X	Fracture of base of skull
S02.8	Fractures of other unspecified skull and facial bones
S02.91	Unspecified fracture of skull
S04.02	Injury of optic chiasm
S04.03X	Injury of optic tract and pathways
S04.04X	Injury of visual cortex
S06.X	Intracranial injuries, concussion, traumatic cerebral edema, diffuse and focal traumatic brain injury, traumatic epidural, subdural, and subarachnoid hemorrhage
S07.1	Crushing injury of skull

Depressive Symptoms

Depressive symptoms were assessed starting at Visit 5 using the Center for Epidemiologic Studies Depression (CESD) scale 11-item version.[53,54] This version of the CES-D correlates highly with the original 20-item version of the CESD (Pearson's r=0.95).[53] The CES-D is a validated measure of frequency of depressive symptoms in the past week,[55] with responses scored as 0 (<1 day in the past week), 1 (1–2 days in the past week), or 2 (3–7 days in the past week) for each question. The scores are summed for a total scale score ranging from 0 to 22, with higher scores indicating greater depressive symptoms. The 11-item CES-D reflects four symptom domains: depressed affect, positive affect, somatic symptoms and interpersonal symptoms. On the 11-item CES-D scale, a score of ≥9 can identify individuals with clinically significant depressive symptoms.[53] For primary analyses, we will evaluate CES-D as a time-varying binary variable, with a score of ≥9 considered "positive" for depressive symptomology. In sensitivity analysis, CES-D score will be treated as a continuous variable.

Domain-Specific Cognitive Performance

Domain-specific cognitive performance will be evaluated using neuropsychological tests administered at Visits 5 – 9 or 10 (depending on the timing of data availability). The ARIC Neurocognitive Study (ARIC-NCS) battery includes 11 neuropsychological tests recommended for inclusion in the National Institute of Aging's National Alzheimer's Disease Coordinating Center (NACC) Uniform Data Set Battery.[56] Informed by prior research[57-59] and the presumed underlying neurological structures involved,[47] individual tests will be grouped into three previously validated domains: (1) Memory Domain (Delayed Word Recall Test, Logical Memory Test, Incidental Learning); (2) Language and Verbal Fluency Domain (Boston Naming Test, Word Fluency Test, Animal Naming); (3) Executive Function (Trail Making Test and Digit Symbol Substitution Test).

Dementia Diagnosis

Diagnosis of incident dementia has been previously described in detail for the ARIC Study.[60-62] Briefly, three levels of ascertainment are available. Level 1 includes only adjudicated dementia defined based on in-person evaluations conducted starting at ARIC visits 5. Level 2 incorporates telephone data from participants who were alive but did not attend ARIC visit (starting at ARIC visit 5) as well as data from informants of participants who died prior to attending these visits. Level three further incorporates dementia cases defined by ICD codes from inpatient hospitalizations or death certificates from study baseline through December 31, 2020 (or most updated administrative censoring date at time of submission for publication). The Level 3

outcome will serve as the primary outcome of interest in our analyses because dementia ascertainment is not dependent on visit attendance, and therefore potential biases due to attrition and competing risk of death are minimized. In sensitivity analyses, we will alternatively consider Level 1 and 2 outcomes.

Covariates

Covariates included in the analysis will be ascertained at Visit 5 (or the closest prior visit) and will include age (continuous), sex (male; female), race/center (Maryland White; Minnesota White; North Carolina White; North Carolina Black; Mississippi Black), education (<high school; high school/GED/vocational; any college/graduate/professional school), military veteran status (yes; no), physical activity (score ranging from 1–5, modified Baecke Physical Activity Questionnaire; continuous), cigarette smoking (current; former; never), hypertension (defined as systolic blood pressure ≥140mmHg, diastolic blood pressure ≥90mmHg, or use of medications), diabetes (defined as fasting glucose ≥126mg/dL, non-fasting glucose ≥200mg/dL, self-reported physician diagnosis of diabetes, or prescribed medication for diabetes) and APOE genotype. Additionally, the use of medications to treat antidepressants (including SSRI, SNRI, TCA, MAOI and atypical antidepressants) will be defined for each participant at each study visit.

Statistical Analysis

Below we describe three separate statistical analyses that examine (1) patterns of short- and long-term domain-specific cognitive impairment among individuals with prior head injury; (2) the short- and long-term burden of depressive symptoms among individuals with prior head injury; and (3) the joint implications of depressive symptoms and head injury for incident dementia in this population of community-dwelling adults.

Aim 1: Association between head injury and domain-specific cognitive performance

For Aim 1, we will examine patterns of domain-specific cognitive performance among ARIC participants with (N~1,847) and without head injury (N~4,511) who underwent neuropsychological testing during Visit 5. As a secondary analysis, among study participants with a history of head injury we will model cognitive performance as a function of time-since-head-injury using generalized linear models. Because neuropsychological assessments were administered across multiple visits, we will use generalized estimating equations (GEE) to estimate the marginal association between head injury status and cognitive impairment,[63] accounting for potential non-independence of repeated assessments.[64,65] We will model each cognitive domain as a function of time-since-head-injury using generalized linear models. Test performance for each cognitive domain will be specified as the dependent variable. To capture potential non-linearities, time-since-head-injury will be modeled using natural splines[66,67] with degrees of freedom selected based on model fit using the Akaike Information Criterion.[68] All analyses will consider continuous cognitive factor scores as the primary outcome.

As behavioral and health-related characteristics may confound the association between head injury and cognitive impairment, we will adjust for confounders in a step-wise fashion as follows: age, sex, race/field center, education (Model 1); Model 1 + smoking status, physical activity, military veteran status (Model 2); Model 2 + hypertension, diabetes, depression, and APOE genotype (Model 3). Loss-to-follow-up/death will be addressed using inverse probability of attrition weights using established methods[69] or alternatively with multiple imputation as a

method of handling data consistent with prior analysis of the ARIC study data.[70] In secondary analyses, we will examine the association of individual neuropsychological test scores with head injury status and time-since-head-injury. Additional analyses will explore the frequency (none, one, ≥two) and source (self-reported versus hospital-defined) of head injury in association with cognitive impairment.

Aim 2: Association between head injury and depression

For Aim 2, we will examine the prevalence of depression among ARIC participants with (N~1,847) and without head injury (N~4,511) who participated in Visit 5. As above, we will use GEE to estimate the marginal association between head injury status and depression,[63] accounting for potential non-independence of repeated assessments.[64,65] As a secondary analysis, among study participants with a history of head injury we will model depression risk as a function of time-since-head-injury using generalized linear models. To capture potential non-linearities, time-since-head-injury will be modeled using natural splines[66,67] with degrees of freedom selected based on model fit using the Akaike Information Criterion.[68] All analyses will consider depression (CES-D ≥9) as the primary outcome, with continuous CES-D score considered as a secondary outcome. As above, we will adjust for confounders in a step-wise fashion as follows: age, sex, race/field center, education (Model 1); Model 1 + smoking status, physical activity (Model 2); Model 2 + hypertension, diabetes, depression, and APOE genotype (Model 3). Loss-to-follow-up/death will be addressed using inverse probability of attrition weights using established methods[69] or alternatively with multiple imputation with chained equations.[70] Additional analyses will explore the frequency (none, one, ≥two) and source (self-reported versus hospital-defined) of head injury in association with depression.

Aim 3: Examine the joint implications of head injury and depression for incident dementia

In Aim 3, we will examine the risk of incident dementia as a function of both head injury and depression. Head injury will be treated as a time-varying covariate that equals zero in individuals with no prior head injury and equals one from the date of the first head injury onwards. Depression will be treated as a time-varying covariate that equals one for CES-D ≥ 9 and equals zero otherwise. Unlike head injuries, depression will not be treated as an absorbing state but rather will be modeled as a potentially episodic disease state wherein individuals whose CES-D score was consistent with depression at prior assessments could be depression-free in subsequent evaluations and vice-versa. Using these two time-varying variables, we will create a categorical exposure variable with the following levels: neither head injury or depression (the referent category), head injury only, depression only, both head injury and depression.

We will use Cox proportional regression analysis to estimate hazard ratios (HR) for the association of head injury and depression with incident dementia. As above, we will adjust for confounders in a stepwise fashion as follows: age, sex, race/field center, education (Model 1); Model 1 + smoking status, physical activity (Model 2); Model 2 + hypertension, diabetes, depression, and APOE genotype (Model 3). We will specifically consider the presence of multiplicative interaction between head injury and depression for incident dementia by including a product term in our statistical model. We will consider the presence of additive interaction between head injury and depression by calculating the relative excess risk of interaction (RERI).[71] Additional analyses will consider Level 1 and Level 2 outcome definitions for dementia and will explore the frequency (none, one, ≥two) and source (self-reported versus

hospital-defined) of head injury in association with dementia. In sensitivity analyses, we will use Fine Gray models accounting for the competing risk of death.

Limitations and Extensions

For aims which include depression (Aims 2 and 3), follow-up will begin at Visit 5, the first study visit during which depression was evaluated. We will explore an alternative analytic approach that uses a longer duration of follow-up with scores from the Vital Exhaustion Questionnaire used as a proxy for depressive symptoms.[72] Additionally for Aims 2 and 3 we may consider prescribed antidepressants as an effect modifier or as an alternative measure of depressive symtpoms. While our primary analysis for all aims will include individuals with prevalent head injury at Visit 5, as a sensitivity analysis for all study aims we will repeat our primary analysis considering only individuals with incident head injury.

A limitation relevant to all of the aims is that head injury was ascertained via hospital or emergency department diagnoses and self- reported head injuries. Definitions of TBI based on *ICD-9* or *ICD-10* codes are susceptible to misclassification, particularly for mild injuries, with validation studies reporting sensitivities of 55% to 72% and specificity of 80% to 85%, depending on the code definition used.[73,74] We used standard *ICD-9* and *ICD-10* codes to identify hospital and emergency department diagnoses of head injuries.[49,51] The language of questions used to assess self-reported head injury changed over time but focused on individuals who required medical attention or had an associated loss of conscious- ness. Therefore, mild head injuries may not have been captured, although the attenuation of the association with mortality observed when using self-report–defined head injury suggests that self-reported cases in the ARIC study are largely milder than the *ICD-9* and *ICD-10* code–defined ones.[75] However, prior research has suggested that self-report offers reliable assessment of head injury, even among individuals with cognitive impairment.

A limitation relevant to Aims 2 and 3 is that depression is only ascertained using the CES-D at study visits, leading to potential misclassification of the outcome (Aim 2) and exposure (Aim 3). However, we have no reason to suspect this misclassification will be differential with respect to exposure or outcome status. One of the main potential limitations for Aim 3 pertains to the methods of dementia ascertainment. Relying on hospital discharge and death certificate data to define incident cases of dementia may underestimate the true incidence of dementia in the study population. However, our definition of dementia is likely to be a highly specific case definition. As with any observational study, we will also not be able to rule out the possibility of residual confounding.

f) Will the author need Limited data to complete the proposed manuscript?

☒ **No, De-identified data will be sufficient.** Although this proposal notes that the head injury definition incorporates CMS data, direct access to CMS data will not be required for this work as Dr. Schneider has created a de-identified head injury dataset which will be shared with Dr. Elser.

*Please note, Limited dataset access is strict and rarely provided. Limited data includes identifiable information such as dates (birthdays, visit dates, etc.). CMS, Genomic, Geocoded,

Proteomics/Somalogic, and other -omic data all fall under the limited data category. De-identified data does not include dates. All dates are date adjusted to "Days since Visit 1".

7a. Will the data be used for non-ARIC analysis or by a for-profit organization in this manuscript? (Non-ARIC analysis means that the authors are not regarded as ARIC investigators and the "ARIC author" is essentially just a facilitator rather than an integral part of the writing group.) ☒ **No**

8a. Will the DNA data be used in this manuscript? ☒ **Yes** – APOE data

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**

9. The lead author or the "sponsoring" ARIC 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 website at: https://aric.cscc.unc.edu/aric9/proposalsearch ☒ **Yes**

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)?

4187: Timing of cognitive test score decline prior to dementia onset: The Atherosclerosis Risk in Communities (ARIC) Study

4179: Multisensory impairment and depression in the Atherosclerosis Risk in Communities Neurocognitive Study.

4051: Associations of Prior Head Injury and Hearing in ARIC-NCS

4041: Associations of Prior Head Injury with Physical Functioning, Frailty, and Falls in the Atherosclerosis Risk in Communities (ARIC) Study

3978: Associations between Head Injury and Mild Behavioral Impairment (MBI) Domains Across the Cognitive Spectrum

3958: Associations of Prior Head Injury with Olfactory Functioning

3965: Dynamics of Risk Factors for 32-Year Incident Dementia Across Mid And LateLife in ARIC: Implications for Dementia Prevention

3916: Associations of Head Injury with Neuropsychiatric Symptoms (NPS) and Mild Behavioral Impairment (MBI) Domains

3513: Timing of cognitive test score decline prior to dementia onset: The Atherosclerosis Risk in Communities (ARIC) Study

3204: Depression and mortality in the ARIC study.

3104: The association of systemic inflammation with late-life depression symptoms: The ARIC Study

2849: The SF-12 vs CES-D: A Comparison of Mental Health and Depression Scales in the ARIC Cohort Study

2769: The Association of Head Injury with Risk of Stroke, Cardiovascular Disease, and Mortality in the ARIC Study (Schneider)

2768: The Association of Head Injury and Cognition, Mild Cognitive Impairment, and Dementia in the ARIC Study (Schneider)

2327: Hearing impairment and cognitive performance in the Atherosclerosis Risk in Communities Neurocognitive Study (ARIC NCS): cross-sectional and longitudinal results

1700: Dynamics of Risk Factors for 32-Year Incident Dementia Across Mid And LateLife in ARIC: Implications for Dementia Prevention

879: Depression and mortality in the ARIC study.

876: Construction and validation of a depression measure in the ARIC study.

11a. Is this manuscript proposal associated with any ARIC ancillary studies or does it use current [or ongoing] ancillary study data (this includes ACHIEVE)? ☒ No

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 https://aric.cscc.unc.edu/aric9/publications/policies_forms_and_guidelines http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.

To view publications materials, click "Log in" at the top right of the ARIC website. Click "Forgot Password" if you are experiencing issues with logging in.

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