ARIC Manuscript Proposal #4041

PC Reviewed: 5/17/22 **Status: _____** **Priority: 2**
SC Reviewed: ___/___/___ **Status: _____** **Priority: ____**

1.a. Full Title: Associations of Prior Head Injury with Physical Functioning, Frailty, and Falls in the Atherosclerosis Risk in Communities (ARIC) Study

b. Abbreviated Title (Length 26 characters): Head Injury and Physical Function

2. Writing Group: Writing group members:

Katherine J. Hunzinger PhD (First Author)	University of Pennsylvania
Andrea L.C. Schneider MD PhD (Senior Author)	University of Pennsylvania
Douglas J. Wiebe PhD	University of Pennsylvania
Alexa E. Walter PhD	University of Pennsylvania
Rebecca F. Gottesman MD PhD	NIH/NINDS
B. Gwen Windham MD	University of Mississippi
Priya Palta PhD	Columbia University
Stephen P. Juraschek MD PhD	Harvard University/BIDMC
Caitlin Hicks MD MS	Johns Hopkins University

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

First author: Katherine J. Hunzinger PhD
Address: Department of Epidemiology, Biostatistics, and Informatics
University of Pennsylvania Perelman School of Medicine
423 Guardian Dr., Blockley Hall 937
Philadelphia, PA 19104

Phone: 630-621-5786
E-mail: Katherine.hunzinger@pennmedicine.upenn.edu

ARIC author to be contacted if there are questions about the manuscript and the first author does not respond or cannot be located (this must be an ARIC investigator).

Name: Andrea L.C. Schneider MD PhD
Address: Department of Neurology, Division of Neurocritical Care
Department of Epidemiology, Biostatistics, and Informatics
University of Pennsylvania Perelman School of Medicine
51 North 39th St., Andrew Mutch Building 416
Philadelphia, PA 19104

Phone: 443-827-2352 Fax: 215-662-9858
E-mail: andrea.schneider@pennmedicine.upenn.edu

3. Timeline:

Data are currently available. Analyses and manuscript preparation will be performed over the next 6-12 months.

4. Rationale:

Traumatic brain injury (TBI) is considered a chronic health condition due to its long-term sequalae and association with subsequent dysfunction and morbidity.[1,2] Older adults have the highest rates of TBI,[3] yet, a significant focus of the literature is on short-term outcomes, especially among college-aged individuals and athletes.[4–6] As such, a need exists to investigate the relationship between head injury and long-term objective outcomes in older populations.

Gait, mainly walking speed, is often considered to be the 6th vital sign since it correlates with balance, functional ability,[7] cognitive status,[8] postural control,[9] mental health status,[10,11] hospitalization,[12] and death.[13] Gait and postural control impairments are reported in collegiate athletes beyond clinical recovery from concussion (mild TBI; mTBI) and in individuals with a history of mTBI years post-injury.[14–19] Post-mTBI, individuals exhibit a conservative gait strategy that is characterized by a reduction in gait speed and stride length, and is theorized to be the result of lingering neuromuscular control and executive dysfunction.[20] These gait abnormalities have persisted in young athletes beyond clinical recovery and after return to sport, and are thought to be a mechanistic link between the observed 2-fold increased odds of subsequent lower-extremity musculoskeletal injury in athletes post-mTBI.[18,21,22] Despite evidence of lingering physical dysfunction post-mTBI and the potential additive effect of age and head injury on physical dysfunction among older individuals, the research on head injury and subsequent musculoskeletal injury and physical functioning is primarily limited to young athletes and young community dwelling adults (i.e., <35 years old).[21,23] Therefore, a gap in the literature exists to investigate the relationship between head injury and subsequent musculoskeletal functioning in older cohorts.

The ARIC study presents a unique opportunity for studying the relationship between head injury and musculoskeletal functioning in the form of physical function, frailty, and falls. Gait and physical function decrease with age while frailty increases with age; collectively, all of these factors increase risk for a fall in the ageing populations.[24] Based upon previous research, it is hypothesized that prior head injury is related to future risk of falls, potentially due to worse neuromuscular/musculoskeletal functioning observed after a head injury.[18,21] Moreover, this risk may be compounded by pre-existing factors (i.e., physical function and frailty). We acknowledge that the associations between head injury and physical functioning/frailty/fall risk are likely bi-directional. However, in this proposal we will examine the association between prior head injury and physical function and frailty at ARIC Visit 5 and the prospective relationship (ARIC Visit 5-7) between head injury, physical function, frailty, and falls (baseline ARIC Visit 5).

5. Main Hypothesis/Study Questions:

Aim 1: To examine associations between prior head injury and physical function and frailty assessed at Visit 5.

Hypothesis 1: Prior head injury will be associated with worse physical function and greater frailty at ARIC Visit 5 compared to no prior head injury. Further, individuals with multiple prior head injuries and more severe prior head injury will have greater physical dysfunction and frailty compared to individuals with no prior head injury and to individuals with a single prior head injury and to individuals with less severe prior head injury.

Aim 2: To examine the prospective (Visit 5-Visit 7) associations between prior head injury and physical function and frailty.

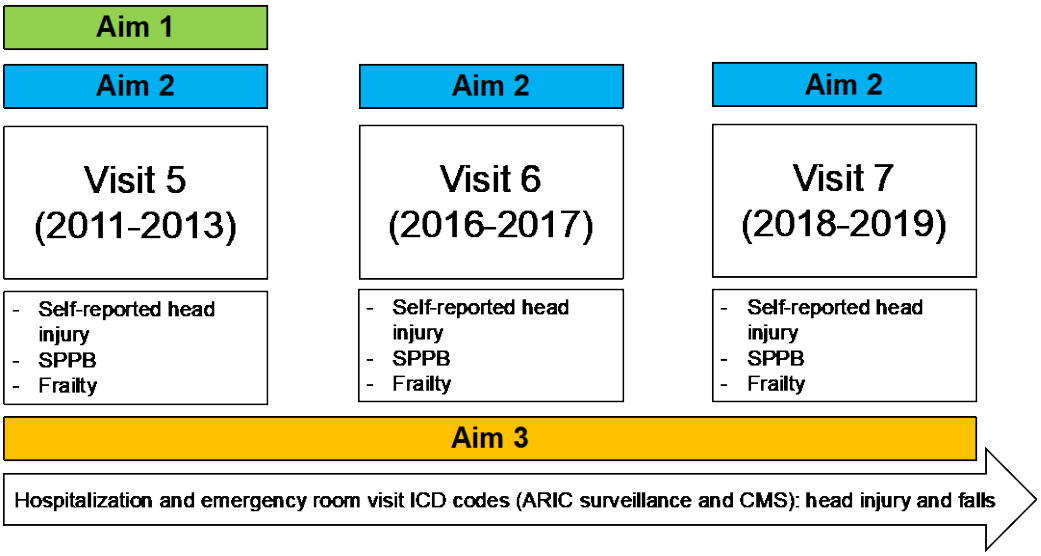
Hypothesis 2: Prior head injury will be associated with decreased physical function and increased frailty over time compared to no prior head injury. Individuals with multiple prior head injuries and more severe prior head injuries will have greater dysfunction (i.e., worse physical function and more frailty) over time compared to individuals with no prior head injury and to individuals with a single prior head injury and to individuals with less severe prior head injury.

Aim 3: To examine the prospective (baseline Visit 5) relationship between head injury and fall risk.

Hypothesis 3: Head injury will be associated with increased fall risk over time compared to no head injury. Individuals with multiple prior head injuries and more severe prior head injuries will have greater risk of falls over time compared to individuals with no prior head injury and to individuals with a single prior head injury and to individuals with less severe prior head injury.

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/Study Population:



Aim 1: Head injury occurring prior to Visit 5 and Visit 5 measures of physical function and frailty. All ARIC visit 5 participants with non-missing head injury, physical function, frailty, and covariate data will be included.

Aim 2: Prospective analysis using head injury occurring prior to Visit 5 and prospectively collected (Visit 5 to Visit 7) measures of physical function and frailty. We will also consider head injury as a time-varying exposure in order to include head injuries occurring after Visit 5. All ARIC visit 5 participants with non-missing head injury, Visit 5 physical function, Visit 5 frailty, and covariate data will be included. Included participants will also have non-missing Visit 6 and/or Visit 7 physical function and frailty data.

Aim 3: Prospective analysis using head injury occurring after Visit 5 with follow-up for incident falls through most updated CMS/hospitalization data. Head injury will be modeled as a time-varying exposure. All ARIC visit 5 participants without prior head injury and with complete covariate data will be included.

Exposure:

Consistent with previous work in ARIC,[25,26] prior head injury (yes; no) will be defined using a combination of self-reported data (from Visits 3, 4, 5, 6, 7, and the brain MRI visit) and ICD-9/10 code data from hospitalizations (ARIC hospitalization surveillance; Centers for Medicare and Medicaid Services [CMS] Fee-for-Service [FFS] data) and emergency department visits (CMS FFS data). As secondary exposures, we will use the number of previous head injuries (0; 1; 2+) and in the subset of head injuries identified using ICD-9/10 code data, we will separate by head injury severity (mild; moderate/severe). Below are self-reported questions and ICD-9/10 codes.

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. 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. 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 and 7 (2016-2017 and 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?

*Questions asked in a subgroup of ARIC participants selected for brain magnetic resonance imagining (MRI) scans.

ICD-9 and ICD-10 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

Outcomes:

We will investigate three primary outcomes of interest in this proposal: physical functioning, frailty, and falls.

Physical Function:

Physical function was assessed using the Short Physical Performance Battery (SPPB)[27,28] and grip strength[28] at ARIC Visit 5, 6, and 7. The SPPB is a measure of lower body performance.

The SPPB consists of 3 tasks: gait speed (time to walk 4 meters), chair stand (time to complete 5 unassisted chair stands without using their arms), and balance (timed side-by-side stance, semi-tandem stance, and tandem stand, held up to 10s each). Gait speed (m/s) with be calculated by dividing the 4m by the time to complete the 4m walk (sec). Each of the 3 tasks are scored 0 (worst) to 4 (best; the 3 components are summed for a total possible score ranging from 0 to 12. An SPPB composite score $\leq$6 will be considered poor physical function. Each SPPB task score $\leq$2 points will be considered poor physical function in that domain.[29] In addition to analyzing the composite SPPB as a dichotomous variable, we will also analyze as a continuous/count variable. Grip Strength[28] is a measure of upper body strength. Participants used their dominant hand and performed maximal hand squeeze using the Jamar Hydraulic Hand Dynamometer. The best of 2 trials will be used for analysis and is reported in kilograms of force.

Frailty:

Consistent with previous studies,[30] participants will be categorized into three groups: frailty (if $\geq$3 of the below listed components were present), pre-frailty (if 1-2 of the below listed components were present), and non-frailty (if none of the below listed components were present). The 5 components are listed below:

Weight loss	Unintentional weight loss of 10% between Visit 4 (1996-1999) and Visit 5 (2011-2013) or BMI <18.5 kg/m^2
Low physical activity	The 20th percentile in sex-specific Baeke leisure sport activity index
Slow walking speed	The 20th percentile in sex- and height-adjusted gait speed during a 4-m walk test using the cutoff values established from the Cardiovascular Health Study (CHS)[31]
Exhaustion	Responded “some of the time” or “most of the time” to 2 questions of the following the 11-item Center for Epidemiologic Studies-Depression scale (CES-D) questions: “I felt everything I did was an effort” or “I could not get going”
Weakness (low grip strength)	The 20th percentile in sex- and BMI-specific grip strength using the cutoff values established from CHS[31]

Falls:

Falls will be defined using ICD-9/E codes and ICD-10 codes from hospitalizations (ARIC hospitalization surveillance; CMS FFS data) and emergency department visits (CMS FFS data).

ICD-9/E Codes	
E804.xx	Fall in on or from railway train
E833.xx	Fall on stairs or ladders in water transport

E834.xx	Other fall from one level to another in water transport
E835.xx	Other and unspecified fall in water transport
E843.xx	Fall in on or from aircraft
E880.0	Accidental fall on or from escalator
E880.1	Accidental fall on or from sidewalk curb
E880.9	Accidental fall on or from other stairs or steps
E881.0	Accidental fall from ladder
E881.1	Accidental fall from scaffolding
E882	Accidental from or out of building or other structure
E883.1	Accidental fall into well
E883.2	Accidental fall into storm drain or manhole
E883.9	Accidental fall into other hole or other opening in surface
E884.xx	Accidental fall
E885.xx	Accidental fall
E886.xx	Accidental fall
E888.xx	Accidental fall
E913.3	Accidental mechanical suffocation by falling earth or other substance
E917.xx	Striking against or struck with or without subsequent fall
E929.3	Late effects of accidental fall
E987.xx	Falling from man-made structures
V15.88	History of fall
ICD-10 Codes	
v0011xx-v0089xx	Fall
w00xxxx-w19xxxx	Fall
y30xxxx	Falling from high place

Covariates:

Covariates included in statistical models were assessed at ARIC Visit 5, unless otherwise specified, and will include: age (continuous), sex (male/female), race/center (Minnesota whites; Maryland whites, North Carolina whites, North Carolina blacks, Mississippi blacks), education (assessed at ARIC Visit 1, <high school; high school, GED or vocational school; college, graduate, or professional school), cigarette smoking status (current; former; never), alcohol consumption (current; former; never), depression (defined by CES-D score ≥9), and cognitive status (normal; mild cognitive impairment; dementia). In models for physical functioning and fall outcomes, we will also include BMI, and physical activity (Baeke leisure sport activity index) (these measures are already included in the definition of frailty).

Statistical Analysis:

All analyses will be performed using Stata MP (Version 17, StataCorp, College Station, Texas). A two-sided p-value of <0.05 will be considered statistically significant.

Participant characteristics will be reported overall and stratified by head injury status (head injury occurring prior to Visit 5). Head injury (yes/no) groups will be compared using t-tests for continuous variables and chi-square tests for categorical variables.

For Aim 1, we will use logistic regression to estimate the ORs (95% CIs) for the associations between head injury exposure variables with low SPPB composite score (≤6) and with low scores for each SPPB task (≤2). We will use a linear regression to investigate the associations between prior head injury exposure variables and gait speed, time to complete chair stands, and grip strength. Multinomial logistic regression models will be used to investigate the associations between head injury exposure variables with the 3-level outcome variable consisting of frailty (≥ 3 components present), pre-frailty (1-2 components present), and non-frailty (none present).

For Aim 2, we will use a linear mixed effects model (with an unstructured covariance matrix and random effects for intercept and slopes) to estimate the mean rate of change in SPPB composite score and the mean rates of change in each SPPB task score over time (years from Visit 5 to Visit 7) by head injury status. We will consider the use of a 2-piece linear spline with a knot at Visit 6 to allow the rate of change in SPPB scores to vary between Visits 5 and 6 versus between Visits 6 and 7. In these analyses, we will also consider head injury as a time-varying exposure in order to account for head injuries occurring after Visit 5. Among individuals who were not classified as frail at Visit 5, we will use multinomial logistic regression models to investigate associations of head injury with pre-frailty and frailty at Visits 6 and 7.

For Aim 3, we will use Cox proportional hazard models to estimate the HRs (95% CIs) for fall risk to investigate the relationship between head injury and subsequent fall risk. In these analyses, we will model head injury as a time-varying exposure. We may consider expanding this analysis from the Visit 1 to Visit 7 time-period if there are not enough head injury/fall events which occur in the Visit 5 to Visit 7 time period.

In all analyses, we will perform 2 statistical models. Model 1 will be adjusted for age, sex, race/center, and education. Model 2 will be adjusted for variables included in Model 1 + cigarette smoking status, depression, and cognitive status (and in models for physical functioning and fall outcomes, BMI, and physical activity). For Aim 3 falls analysis, we will also include data on hypertension medication use, diuretic use, and psychotropic medications (antidepressants, antihypertensive, sedatives, hypnotics, antipsychotic medications, anti-epileptic medications, and anticholinergic medications) since these medications are associated with fall risk. We will perform a sensitivity analysis of these medications to determine whether to exclude these individuals taking these medications or to adjust for medication use.

Limitations:

One limitation is the utilization of self-reported and/or ICD-9 codes to define head injury. As such, we will not have specific details about the type of head injury, injury location, or treatment. Similarly, reliance on ICD codes for fall history may result in under-ascertainment. Additionally, we acknowledge that the associations between head injury and physical functioning/frailty/fall risk are likely bi-directional. In this MSP, we will primarily evaluate head injury as a risk factor for poor physical functioning, frailty, and fall risk, but in supplemental analyses, we will evaluate physical functioning and frailty as risk factors for subsequent head injury.

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.cscc.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)?

Head Injury-related MSPs:
- MSP #2767: The Association of Head Injury with Brain MR and Brain PET Amyloid Imaging in the ARIC Study (Andrea Schneider)
- MSP #2768: The Association of Head Injury and Cognition, Mild Cognitive Impairment, and Dementia in the ARIC Study (Andrea Schneider)
- MSP #2769: The Association of Head Injury with Risk of Stroke, Cardiovascular Disease, and Mortality in the ARIC Study (Andrea Schneider)
- MSP #2978: Associations between Head Injury and Mild Behavioral Impairment (MBI) Domains Across the Cognitive Spectrum (Nicholas Daneshvari)
- MSP #3668: The Risk of Post-traumatic Epilepsy in the ARIC Study (Andrea Schneider)
- MSP #3958: Associations of Prior Head Injury with Olfactory Functioning (Andrea Schneider)

Physical Function and Frailty-related MSPs:
- MSP #2700: Plasma phospholipids and physical function in ARIC (Danni Li)
- MSP #3238: Clinically recognized varicose veins and physical function in older individuals (Yejin Mok)
- MSP #3381: Physical Function in Older Adults – a genome-wide association study (ThuyVy Duong)

- MSP #3427: Identification of plasma sphingolipids as biomarkers of physical function decline in older adults (Danni Li)
- MSP #3438: Association of Mid- to Late-Life Physical Activity with Later Life Physical Function and Frailty: The Atherosclerosis Risk in Communities (ARIC) Study (Steven Nguyen)
- MSP #3553: The Association Between Hearing Impairment and Physical Function in the Atherosclerosis Risk in Communities (ARIC) Study (Pablo Martinez-Amezcua)
- MSP: #3944: Association Between Mid-life Diet Quality & Late-life Physical Function in the Atherosclerosis Risk in Communities (ARIC) Study (Xin Li)

Fall-related MSPs:

- MSP #2381: Falls Prevalence in Older Black and White ARIC Participants (Lisa Pompeii)
- MSP #2611: Orthostatic Hypotension and Risk of Falls in the Atherosclerosis Risk in Communities Study (ARIC) (Stephen Juraschek)
- MSP #3928: Association of Peripheral Neuropathy with Falls and Fractures in the ARIC Study (Caitlin Hicks)

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* _2008.06_)
___ 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.cscc.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.

Understood.

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.

Understood.

References

1. Masel BE, DeWitt DS. Traumatic brain injury: A disease process, not an event. *J Neurotrauma*. 2010;27(8):1529-1540. doi:10.1089/neu.2010.1358
2. Sandsmark DK, Bashir A, Wellington CL, Diaz-Arrastia R. Cerebral Microvascular Injury: A Potentially Treatable Endophenotype of Traumatic Brain Injury-Induced Neurodegeneration. *Neuron*. 2019;103(3):367-379. doi:10.1016/j.neuron.2019.06.002
3. Capizzi A, Woo J, Verduzco-Gutierrez M. Traumatic Brain Injury An Overview of Epidemiology, Pathophysiology, and Medical Management. *Med Clin NA*. 2020;104(2):213-238. doi:10.1016/j.mcna.2019.11.001
4. Iverson GL, Büttner F, Caccese JB. Age of First Exposure to Contact and Collision Sports and Later in Life Brain Health: A Narrative Review. *Front Neurol*. 2021;12:1-16. doi:10.3389/fneur.2021.727089
5. Martini DN, Broglio SP. Long-term effects of sport concussion on cognitive and motor performance: A review. *Int J Psychophysiol*. 2018;132(September):25-30. doi:10.1016/j.ijpsycho.2017.09.019
6. Broglio SP, McAllister T, Katz B, LaPradd M, Zhou W, McCrea M. The natural history of sport-related concussion in collegiate athletes Findings from the NCAA-DoD CARE Consortium. *Sport Med*. 2021;(In Press).
7. Fritz S, Lusardi M. White paper: "walking speed: The sixth vital sign." *J Geriatr Phys Ther*. 2009;32(2):2-5. doi:10.1519/00139143-200932020-00002
8. Yogev G, Hausdorff JM, Giladi N. The Role of Executive Function and Attention in Gait. *Mov Disord*. 2009;23(3):329-472. doi:10.1002/mds.21720
9. Woollacott M, Shumway-Cook A. Attention and the control of posture and gait: a review of an emerging area of research. *Gait Posture*. 2002;16(1):1-14. doi:10.1016/S0966-6362(01)00156-4
10. Lemke M, Wendorff T, Mieth B, Buhl K, Linnemann M. Spatiotemporal gait patterns during overground locomotion in major depression compared with healthy controls. *J Psychiatr Res*. 2000;34:277-283.
11. Middleton A, Fritz SL, Lusardi M. Walking Speed: The Functional Vital Sign. *J Aging Phys Act*. 2016;23(2):314-322. doi:10.1123/japa.2013-0236.Walking
12. Montero-Odasso M, Schapira M, Soriano ER, et al. Gait velocity as a single predictor of adverse events in healthy seniors aged 75 years and older. *Journals Gerontol - Ser A Biol Sci Med Sci*. 2005;60(10):1304-1309. doi:10.1093/gerona/60.10.1304
13. Hardy SE, Perera S, Roumani YF, Chandler JM, Studenski SA. Improvement in Usual Gait Speed Predicts Better Survival in Older Adults. *J Am Geriatr Soc*. 2007;55:1727-1734. doi:10.1111/j.1532-5415.2007.01413.x
14. Buckley TA, Vallabhajosula S, Oldham JR, et al. Evidence of a conservative gait strategy in athletes with a history of concussions. *J Sport Heal Sci*. 2016;5(4):417-423. doi:10.1016/j.jshs.2015.03.010
15. Lynall RC, Campbell KR, Mauntel TC, Blackburn JT, Mihalik JP. Single-Legged Hop and Single-Legged Squat Balance Performance in Recreational Athletes With a History of Concussion. *J Athl Train*. 2020;55(5):000-000. doi:10.4085/1062-6050-48.6.03
16. Martini DN, Sabin MJ, Depesa SA, et al. The chronic effects of concussion on gait. *Arch Phys Med Rehabil*. 2011;92(4):585-589. doi:10.1016/j.apmr.2010.11.029
17. Howell DR, Kirkwood MW, Provance A, Iverson GL, Meehan WP. Using concurrent gait

and cognitive assessments to identify impairments after concussion: a narrative review. *Concussion*. 2018;3(1). doi:10.2217/cnc-2017-0014
18. Howell DR, Lynall RC, Buckley TA, Herman DC. Neuromuscular Control Deficits and the Risk of Subsequent Injury after a Concussion: A Scoping Review. *Sport Med*. 2018;48(5):1097-1115. doi:10.1007/s40279-018-0871-y
19. Oldham JR, Howell DR, Knight CA, Crenshaw JR, Buckley TA. Single and dual-task tandem gait performance across clinical concussion milestones in collegiate student-athletes. *Clin J Sport Med*. 2020;In Press(00).
20. Fino PC, Parrington L, Pitt W, et al. Detecting gait abnormalities after concussion or mild traumatic brain injury: A systematic review of single-task, dual-task, and complex gait. *Gait Posture*. 2018;62:157-166. doi:10.1016/j.gaitpost.2018.03.021
21. McPherson AL, Nagai T, Webster KE, Hewett TE. Musculoskeletal Injury Risk After Sport-Related Concussion A Systematic Review and Meta-analysis. *Am J Sports Med*. Published online 2018:1-8. doi:10.1177/0363546518785901
22. Eagle SR, Kontos AP, Pepping G-J, et al. Increased Risk of Musculoskeletal Injury Following Sport-Related Concussion: A Perception–Action Coupling Approach. *Sport Med*. 2019;50:15-23. doi:10.1007/s40279-019-01144-3
23. Mcpherson AL, Shirley MB, Schilaty ND, Larson DR, Hewett TE. Effect of a Concussion on Anterior Cruciate Ligament Injury Risk in a General Population. *Sport Med*. 2020;50(6):1203-1210. doi:10.1007/s40279-020-01262-3
24. Dionyssiotis Y. Analyzing the problem of falls among older people. *Int J Gen Med*. Published online 2012:805-813. http://www.dovepress.com/getfile.php?fileID=14102%5Cnhttp://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed14&NEWS=N&AN=368854622
25. Schneider ALC, Selvin E, Liang M, et al. Association of Head Injury with Brain Amyloid Deposition: The ARIC-PET Study. *J Neurotrauma*. 2019;36(17):2549-2557. doi:10.1089/neu.2018.6213
26. Schneider ALC, Selvin E, Latour L, et al. Head injury and 25-year risk of dementia. *Alzheimer's Dement*. 2021;(August 2020):1-10. doi:10.1002/alz.12315
27. Windham BG, Harrison KL, Lirette S, et al. The Relationship of Midlife Cardiovascular Health with Late Life Physical Performance: the ARIC Study. *J Am Geriatr Soc*. 2017;65(5):1012-1018. doi:10.1111/jgs.14732.The
28. Matsushita K, Ballew SH, Sang Y, et al. Ankle-brachial index and physical function in older individuals: The Atherosclerosis Risk in Communities (ARIC) Study. *Atherosclerosis*. 2017;257:208-215. doi:10.1016/j.atherosclerosis.2016.11.023.Ankle-brachial
29. Martinez-Amezcua P, Powell D, Kuo PL, et al. Association of Age-Related Hearing Impairment with Physical Functioning among Community-Dwelling Older Adults in the US. *JAMA Netw Open*. 2021;4(6):1-13. doi:10.1001/jamanetworkopen.2021.13742
30. Kucharska-Newton AM, Palta P, Burgard S, et al. Operationalizing frailty in the atherosclerosis risk in communities study cohort. *Journals Gerontol - Ser A Biol Sci Med Sci*. 2017;72(3):382-388. doi:10.1093/gerona/glw144
31. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: Evidence for a phenotype. *Journals Gerontol - Ser A Biol Sci Med Sci*. 2001;56(3):146-157. doi:10.1093/gerona/56.3.m146