ARIC Manuscript Proposal #4164

PC Reviewed: 12/13/22 **Status: _____** **Priority: 2**
SC Reviewed: _____ **Status: _____** **Priority: ____**

1.a. Full Title: Validation of International Classification of Diseases Tenth Revision (ICD-10) Codes to Identify Incident Stroke- analysis of CMD Medicare claims

b. Abbreviated Title (Length 26 characters): ICD-10 Validation for Stroke

2. Writing Group:

Writing group members: Caitlin Hicks, Jesse Columbo, Natalie Data, Michelle Johansen, Andrea Schneider, Elizabeth Selvin; others welcome

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

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3. Timeline: Data to be used in this proposal are available. Analyses and manuscript preparation will be performed over the next 12 months.

4. Rationale:

Stroke is the fifth leading cause of death in the United States (1). The prevention of stroke has been the focus of many high-quality randomized trials and observational studies (2,3). This work has been complemented by comparative-effectiveness studies of interventions to prevent and treat stroke, which serve as the foundation for societal guidelines aimed at decreasing the incidence of stroke and its sequelae (4-11). Therefore, stroke remains an important cardiovascular outcome for a variety of stakeholders including patients, clinicians, payors, and administrators.

The accurate measurement of stroke can be difficult. Prospective studies with clinician-adjudicated events are expensive and time consuming. Accordingly, many contemporary investigators studying stroke have utilized less costly administrative claims data, but this approach introduces substantial methodologic challenges (5,12,13). Importantly, strokes that occur can be difficult to correctly ascertain using administrative data, because the accuracy of detection is predicated on which billing codes are used to define the outcome (14,15). Furthermore, the transition from the International Classification of Diseases Ninth Revision (ICD-9) to the Tenth Revision (ICD-10) in October 2015 has made the majority of prior studies on this topic irrelevant to contemporary work (16). The optimal algorithm for accurate stroke detection in ICD-10 Medicare claims data is currently unknown.

5. Main Hypothesis/Study Questions:

The overarching goal of this study is to create and optimize the sensitivity and specificity of a set of ICD-10 codes to identify patients experiencing an incident stroke using adjudicated stroke outcomes and Medicare-linked data from the Atherosclerosis Risk in Communities (ARIC) Study. We will address the following specific aims:

1. To create and optimize the sensitivity and specificity of ICD-10 codes for defining incident stroke in the ARIC study in participants without prevalent stroke
2. To create and optimize the sensitivity and specificity of ICD-10 codes for defining incident stroke in the ARIC study in participants with prevalent stroke

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).

Inclusion criteria:

- All ARIC participants with linked CMS Medicare data for the duration of the study period (2016-2019)
    - CMS transitioned from ICD-9 to ICD-10 in October 2015. Therefore, we will only include participants who have claims information from 2016 onward.

Exclusion criteria:

- Participants with self-reported history of stroke at visit 1
- Participants without a documented social security number

- Participants who died prior to reaching CMS eligibility age of 65 years
- Participants who are not Medicare-eligible at any point during follow-up

Primary Outcomes:

a. Incident stroke, as adjudicated by ARIC-NCS (considered gold standard in analysis)
    - Participants with no history of stroke prior to Jan 1, 2016
b. Second stroke, defined as an incident stroke that occurs after a previously adjudicated stroke
    - Participants with a previously adjudicated stroke by ARIC (previous stroke may have occurred before 2016 as long as it was adjudicated by ARIC)

Event Ascertainment:

- Incident stroke events will be ascertained in the CMS Medicare Provider Analysis and Review (MedPAR) file and from the linked ARIC medical records using a prespecified list of ICD-10 claims codes previously defined for identifying acute ischemic stroke (**Table 1**) (1), which have reported positive predictive values greater than 95% and sensitivity of 87% for in-hospital strokes (2,3).
- Incident events will be evaluated in 1) any position and 2) as a principle diagnosis code
- We will also evaluate the sensitivity and specificity of a stroke claims code + procedure code for either head computed tomography (CT scan) or magnetic resonance imaging (MRI) scan billed during the same hospitalization (**Table 2**)
- The following claims codes will be evaluated:
    - Any stroke claim in any diagnostic position
    - Any stroke claim in the principle diagnosis code position only
    - Any stroke claim in any diagnostic position + CT(A) or MR(A) imaging of the head in the same hospitalization
    - Any stroke claim in the principle diagnostic position + CT(A) or MR(A) imaging of the head in the same hospitalization

Table 1. Diagnosis codes for strokes

	ICD9-CM	**Rubric**	**ICD10-CM**	**Rubric**
Ischemic Strokes	362.30	Retinal vascular occlusion, unspecified	G46.3	Brain stem stroke syndrome
	362.31	Central retinal artery occlusion	G.46.4	Cerebellar stroke syndrome
	362.32	Retinal vascular occlusion, arterial branch	G46.5	Pure motor lacunar syndrome
	362.33	Retinal vascular occlusion, partial arterial occlusion	G46.6	Pure sensory lacunar syndrome
	433.*1	Occlusion and stenosis of precerebral artery with cerebral infarction	G46.7	Other lacunar syndromes
	434.*1	Occlusion and stenosis of cerebral artery with cerebral infarction	H34.1*	Central retinal artery occlusion

	436	Acute, but ill-defined, cerebrovascular disease	H34.21* H34.23* H34.9 I63.****	Partial retinal artery occlusion Retinal artery branch occlusion Unspecified retinal vascular occlusion Cerebral infarction, includes occlusion and stenosis of cerebral and precerebral arteries, resulting in vascular infarction
Hemorrhagic Strokes	430 431	Subarachnoid hemorrhage Intracerebral hemorrhage	I60.** I61.*	Nontraumatic subarachnoid hemorrhage Nontraumatic intracerebral hemorrhage
Systemic Embolism	444.**	Arterial embolism and thrombosis	174.**	Arterial embolism and thrombosis

Table 2. Claims codes used to identify computed tomography (CT) scan or magnetic resonance imaging (MRI) of the head

Modality	CPT	Rubric	ICD-10-PCS
CT	70450	CT Brain without contrast	B020
	70460	CT Brain with contrast	
	70470	CT Brain with and without contrast	
	70496	CT Angiography (CTA), Head	
MRI	70551	MRI Brain without contrast	B030
	70552	MRI Brain with contrast	
	70553	MRI Brain with and without contrast	
	70544	MR Angiography (MRA) Head without contrast	
	70545	MR Angiography (MRA) Head with contrast	
	70546	MR Angiography (MRA) Head with and without contrast	

Analysis Plan:

I. The incidence of A) incident strokes and B) second strokes (both as adjudicated by ARIC) will be described using cumulative incidence curves and incident rates
II. The estimated incidence of A) incident strokes and B) second strokes (as defined by the 4 claims code variations) will be described using cumulative incidence curves and incident rates
III. Incidence rate ratios (IRR) will be calculated for claims code vs. adjudicated outcomes
IV. The sensitivity, specificity, positive and negative predictive values, and Cohen's Kappa of the 4 claims code variations for new stroke will be evaluated (used ARIC adjudication as gold standard)

The analysis (I-IV) will be repeated for 1) incident stroke and 2) second stroke

V. We will then examine the individual claims codes to determine which codes, or code combinations, are being detected to identify incident stroke events (i.e. frequency)
VI. We will then examine if any stroke events are missed, and what codes are billed for those encounters.
VII. Using information from V and VI, we will revise our claims coding list to maximize the sensitivity, specificity, positive and negative predictive values to arrive at a final list of ICD-10 codes to use to define stroke in Medicare data.

Criteria for Success

- A predefined threshold of sensitivity and specificity of >85% for new stroke will be considered acceptable
- The most accurate claims code combination for A) incident strokes and B) second strokes will be chosen as the optimal diagnostic model

Possible Pitfalls and Solutions

The main pitfall of this study is that diagnostic accuracy may not meet the predefined threshold for success. If this occurs, we will evaluate the sensitivity and specificity to better understand whether the codes need to be broadened or more specific and adjust accordingly. If the specificity is poor, we will consider removing the systemic embolism codes, and/or limiting the analysis to ischemic strokes (i.e. removing hemorrhagic stroke codes). If the sensitivity poor, we will consider adding transient ischemic attack (TIA) codes to the analysis (**Table 3**).

We will also need to validate our diagnostic algorithm using an external cohort. We will work with investigators in the RESPECT study to test our final algorithm, and plan to report the same diagnostic performance criteria in this cohort as we used for the main analysis (above).

Table 3. Diagnosis codes for transient ischemic attacks (TIA)

	ICD-9 CM	Rubric	ICD-10 CM	Rubric
TIA	362.34	Transient retinal artery	G45.8	Other transient cerebral ischemic attacks and related syndromes
	435.8	Other unspecified transient cerebral ischemia occlusion	G45.9	Transient cerebral ischemic attack, unspecified
	435.9	Unspecified transient cerebral ischemia	H34.0	Transient retinal artery occlusion
			H34.0x	Transient retinal artery occlusion

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

b. If Yes, is the author aware that the file ICTDER03 must be used to exclude persons with a value RES_OTH = "CVD Research" for non-DNA analysis, and for DNA analysis RES_DNA = "CVD Research" would be used? ____ Yes ____ No
(This file ICTDER has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript? ____ Yes __X__ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER03 must be used to exclude those with value RES_DNA = "No use/storage DNA"? ____ Yes ____ No

9. The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status.
ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: http://www.cscc.unc.edu/ARIC/search.php

___X___ Yes _____ No

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?

There are currently no manuscript proposals in ARIC that evaluate the diagnostic validity of stroke using ICD-10 claims codes. Manuscript proposal #3845 evaluates the performance of phenotyping algorithms in a cohort data set of validated events within ARIC, but that proposal focuses on acute myocardial infarction and heart failure. Dr. Michele Johansen currently overseas the adjudication in stroke events in ARIC, and is included as a co-author on this proposal.

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

11.b. If yes, is the proposal

___ A. primarily the result of an ancillary study (list number)

___ B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* _____ _____ _____)

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

12a. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.

12b. The NIH instituted a Public Access Policy in April, 2008 which ensures that the public has access to the published results of NIH funded research. It is **your responsibility to upload manuscripts to PubMed Central** whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted in http://www.cscc.unc.edu/aric/index.php, under Publications, Policies & Forms. http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.

13. Per Data Use Agreement Addendum, approved manuscripts using CMS data shall be submitted by the Coordinating Center to CMS for informational purposes prior to publication. Approved manuscripts should be sent to Pingping Wu at CC, at pingping_wu@unc.edu. I will be using CMS data in my manuscript _X___ Yes ____ No.

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