MINI-SENTINEL SYSTEMATIC EVALUATION OF HEALTH OUTCOME OF INTEREST DEFINITIONS FOR STUDIES USING ADMINISTRATIVE DATA

CEREBROVASCULAR ACCIDENT/TRANSIENT ISCHEMIC ATTACK REPORT

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Mini-Sentinel is a pilot project sponsored by the U.S. Food and Drug Administration (FDA) to inform and facilitate development of a fully operational active surveillance system, the Sentinel System, for monitoring the safety of FDA-regulated medical products. Mini-Sentinel is one piece of the Sentinel Initiative, a multi-faceted effort by the FDA to develop a national electronic system that will complement existing methods of safety surveillance. Mini-Sentinel Collaborators include Data and Academic Partners that provide access to health care data and ongoing scientific, technical, methodological, and organizational expertise. The Mini-Sentinel Coordinating Center is funded by the FDA through the Department of Health and Human Services (HHS) Contract number HHSF223200910006I.

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Cerebrovascular Accident/Transient Ischemic Attack Report

I. EXECUTIVE SUMMARY 4

A. Overview of Project 4
B. Summary of Findings 4
C. Recommendation for algorithms and suggestion for future research 4

II. PROJECT OBJECTIVES 5

III. BACKGROUND 5

IV. METHODS 6

A. Search Strategy 6
B. Abstract Review 6
1. Abstract Review Methods 6
2. Abstract Exclusion Criteria 7
C. Full-Text Review 7
1. Full-Text Review Methods 7
2. Full-Text Exclusion Criteria 7
D. Mini-Sentinel Investigator Survey 7
E. Evidence Table Creation 7
F. Clinician or Topic-Expert Consultation 7

V. RESULTS 8

A. Search Strategy and Results 8
B. Abstract Reviews 13
C. Full-Text Reviews 13
D. Mini-Sentinel Investigator Survey 14
E. Evidence Included in Table 14
F. Summary and Discussion of Algorithms and Validation 14
1. Composite Endpoints, Stroke/TIA, or Cerebrovascular Disease 14
2. Stroke (Ischemic, Hemorrhagic, and Unspecified) 16
3. Transient Ischemic Attack (TIA) 19
4. Intracranial Bleeds (Intracerebral Hemorrhage and Subarachnoid Hemorrhage) 21
G. Summary of Excluded Populations and Diagnoses 22
H. Evidence Tables 23
I. Clinician or Topic-Expert Consultation 46

VI. SUMMARY AND CONCLUSIONS 47

A. Recommendations for Algorithms 47
B. Suggestions for Future Research Based on Evidence Gaps 48

VII. REFERENCES 49

VIII. APPENDICES 53

A. Appendix A: Abstracts of Studies Included in Evidence Table 53

B. Appendix B: List of Citations Selected for Full-Text Review but Not Included, By Reasons for Exclusion 68
1. Studies Excluded Because They Did Not Study the HOI 68
2. Studies Excluded Because They Did Not Use an Administrative Database 68
3. Studies Excluded Because They Were Not From the United States or Canada 73
4. Studies Excluded Due to Poorly Defined Algorithms 76
5. Studies Excluded Due to a Lack of Validation or Reporting of Validation Statistics 92
C. Appendix C: List and Definitions of ICD or Procedural Codes Included in Algorithms 112

I. EXECUTIVE SUMMARY

A. OVERVIEW OF PROJECT

The Food and Drug Administration (FDA) Mini-Sentinel contract is a pilot program that aims to conduct active surveillance to detect and refine safety signals that emerge for marketed medical products. To perform this active surveillance, it is necessary to develop and understand the validity of algorithms for identifying health outcomes of interest in administrative data. Thus, the goal of this project was to identify algorithms used to detect selected health outcomes of interest using administrative data sources and describe the performance characteristics of these algorithms as reported by the studies in which they were used. This report summarizes the process and findings of the cerebrovascular accident/transient ischemic attack (CVA/TIA) algorithm review.

B. SUMMARY OF FINDINGS

We found a total of 34 validation studies for CVA and/or TIA to include in this report. The studies fell into a number of subgroups, including those that evaluated composite endpoints (stroke/TIA or cerebrovascular disease), stroke exclusively, TIA exclusively, and intracranial bleeds (intracerebral hemorrhage and subarachnoid hemorrhage). While intracranial bleeds are included in a separate category for this report, many studies identifying stroke and cerebrovascular disease evaluated algorithms that included codes for bleeds (i.e., ICD-9 code 430 for subarachnoid hemorrhage; ICD-9 code 431 for intracerebral hemorrhage).

Studies reported on inpatient and outpatient events, incident and prevalent outcomes, and investigations of hospitalized patients, including the evaluation of algorithms based upon primary, secondary, and all position discharge diagnoses of possible CVA/TIA. Positive predictive values (PPVs) varied greatly depending on the specific outcomes and algorithms evaluated. Specific algorithms to evaluate the presence of stroke and intracranial bleeds were found to have high PPVs (80% or greater). Algorithms to evaluate TIA were generally found to have PPVs of 70% or greater. The criteria for validation of outcomes varied greatly among the studies reviewed. Validation of the presence of CVA/TIA was almost exclusively conducted via medical chart review.

C. RECOMMENDATION FOR ALGORITHMS AND SUGGESTION FOR FUTURE RESEARCH

Rather than using algorithms to identify composite endpoints, we recommend that investigators select algorithms that identify a condition as specifically as possible based on its pathogenesis and are aligned with the postulated mechanism for the health outcome as it best relates to the medication or device under study.

For stroke exclusively, studies reported the highest PPVs for inpatient ICD-9 codes 430.x, 431.x, 434.x, and 436.x. To evaluate acute ischemic stroke, algorithms that included ICD-9 codes 433.x1, 434 (excluding 434.x0), and 436, performed well (85% or higher). Use of codes in the principal position generally increased the PPVs slightly.

For TIA exclusively, ICD-9 codes 435.x in hospitalization or emergency encounter data generally demonstrated an adequate PPV (70% or higher).

While few studies evaluated intracranial bleeds exclusively, algorithms including hospitalization or emergency department visit codes 430.x and 431.x performed well for identification of subarachnoid hemorrhage (SAH) and intracerebral hemorrhage (ICH), with PPVs ranging from 80% to 98%. While only one study evaluated an algorithm using inpatient ICD-9 codes 430.x to 432.x for the identification of intracranial bleeds, the reported PPV was high (94%).

Gaps in the current literature include a lack of information on potential differences in the validity of algorithms according to patient age and sex. In addition, the validity of algorithms to further differentiate ischemic strokes due to thrombosis versus emboli has not been evaluated. Overall, comparison of the different algorithms using standard criteria would be most useful, as would the validation of incident versus incident/recurrent events. Lastly, very few validation studies have been conducted on ICD-10 codes or in men and women of different race/ethnicities. Evaluation of predictors of valid algorithms (those with a high PPV) could potentially allow for correction of estimates of association in studies evaluating drug and medical device safety.

II. PROJECT OBJECTIVES

The primary objective of this project was to identify studies that have validated algorithms used to identify various health outcomes of interest (HOIs) using administrative data from the United States or Canada, and to summarize the results of those validation studies. If fewer than five validation studies were identified, a secondary objective was to identify non-validated algorithms that have been used to identify the HOIs using administrative data.

III. BACKGROUND

The Food and Drug Administration (FDA) Mini-Sentinel contract is a pilot program that aims to conduct active surveillance to detect and refine safety signals that emerge for marketed medical products. In order to perform this work, the program needed to identify algorithms used to detect various health outcomes of interest using administrative data sources and identify the performance characteristics of these algorithms as measured in the studies in which they were used. The data sources of interest were limited to those from the United States or Canada to increase their relevance to the Mini-Sentinel data sources, which are all from the United States. The Mini-Sentinel Protocol Core developed a preliminary list of approximately 140 potential health outcomes of interest, based on several criteria. These criteria included: 1) previous validation studies had been identified in a textbook chapter reviewing the validity of drug and diagnosis data used in pharmacoepidemiologic studies;[1] 2) a list of designated medical events had been created from a proposed FDA rule on the safety reporting requirements for human drug and biological products;[2] 3) the Observational Medical Outcomes Partnership (OMOP)[i] had commissioned reports on algorithms used to identify the health outcome using administrative data.[3]

From the original list of 140 HOIs, the Protocol Core worked with FDA to select 20 for which reviews of algorithms would be completed. HOIs for which OMOP had already commissioned reports were purposefully excluded in order to avoid duplication of effort.

[i] For more information, visit the OMOP website.

CVA/TIA was one of the 20 HOIs selected for review. This report describes the review process and findings for the CVA/TIA definition algorithms.

IV. METHODS

A. SEARCH STRATEGY

The methods and search strategy for Mini-Sentinel systematic reviews are described in detail in a manuscript by Carnahan.[4] The general search strategy was developed based on prior work by OMOP and its contractors, and modified slightly for these reports. Originally, OMOP contracted with two organizations to perform reviews of 10 HOIs. Because the search strategies used by each organization resulted in very different sets of articles, OMOP investigators reviewed the PubMed indexing of the articles deemed useful in final reports and developed a strategy that would identify the majority of these citations while maintaining efficiency in the number of abstracts that would need to be reviewed. Mini-Sentinel investigators made minor changes to this strategy that would result in the identification of more citations, and confirmed empirically that the majority of relevant articles from one set of OMOP reports (angioedema) would be identified using this approach.[5, 6] The base search strategy was then combined with PubMed terms representing the HOIs. Medical subject heading (MeSH) terms were generally preferred as HOI search terms due to their likely specificity. Text word searches were sometimes used, particularly when the MeSH search resulted in a small number of citations for review. The workgroup also searched the database of the Iowa Drug Information Service (IDIS) using a similar search strategy to identify other relevant articles that were not found in the PubMed search. For a limited number of outcomes where very few citations were identified from PubMed and IDIS searches, Embase searches were conducted. Search results were restricted to articles published on or after January 1, 1990.

University of Iowa investigators compiled the search results from different databases and eliminated duplicate results using a citation manager program. The results were then output into two sets of files, one containing the abstracts for review and the other for documenting abstract review results.

The search strategy and results for CVA/TIA are detailed in the Results section. The PubMed search was conducted on May 7, 2010, and the IDIS searches on June 10, 2010.

B. ABSTRACT REVIEW

1. Abstract Review Methods

Each abstract was reviewed independently by two investigators to determine whether the full-text article should be reviewed. Exclusion criteria were documented sequentially (i.e., if exclusion criterion 1 was met then the other criteria were not documented). If the reviewers disagreed on whether the full-text should be reviewed, then it was selected for review. Inter-rater agreement on whether to include or exclude an abstract was calculated using a Cohen's kappa statistic. The goal was to review any administrative database study that used data from the United States or Canada and studied the HOI, as validation components of studies are not necessarily included in the abstract and other relevant citations might be identified from the references of such studies.

2. Abstract Exclusion Criteria

1. Did not study the HOI.
2. Not an administrative database study. Eligible sources included insurance claims databases as well as other secondary databases that identify health outcomes using billing codes.
3. Data source not from the United States or Canada.

C. FULL-TEXT REVIEW

1. Full-Text Review Methods

Full-text articles were reviewed independently by two investigators, with a goal of identifying validation studies described in the article itself or from the reference section of the article. Citations from the article's references were selected for full-text review if they were cited as a source for the HOI algorithm, or were otherwise deemed likely to be relevant. Full-text review exclusion criteria were applied sequentially, since if fewer than 5 validation studies were identified, up to 10 of the articles excluded based on the second criterion would need to be incorporated into the final report. If there was disagreement on whether a study should be included, the two reviewers attempted to reach consensus on inclusion by discussion. If the reviewers could not agree, a third investigator would be consulted to make the final decision.

2. Full-Text Exclusion Criteria

1. Poorly described HOI identification algorithm that would be difficult to operationalize.
2. No validation of outcome definition or reporting of validity statistics.

D. MINI-SENTINEL INVESTIGATOR SURVEY

Mini-Sentinel investigators were surveyed to request information on any published or unpublished studies that validated an algorithm to identify an HOI in administrative data. Studies that would not be excluded by one of the aforementioned criteria were included in the final report.

E. EVIDENCE TABLE CREATION

A single investigator abstracted each study for the final evidence table. The data included in the table were confirmed by a second investigator for accuracy.

F. CLINICIAN OR TOPIC-EXPERT CONSULTATION

A clinician or topic-expert was consulted to review the results of the evidence table and discuss how they compare to diagnostic methods currently used in clinical practice. This included whether certain diagnostic codes used in clinical practice were missing from the algorithms, and the appropriateness of the validation definitions compared to diagnostic criteria currently used in clinical practice. A summary of this consultation was included in the results.

V. RESULTS

A. SEARCH STRATEGY AND RESULTS

The following summarizes the search results obtained from PubMed and IDIS searches. The PubMed search identified 1405 citations (Table 1), and the two IDIS searches identified 78 unique citations (Table 2). The total number of unique citations from the combined searches was 1451. An additional PubMed search was conducted at a later date to amend the original search strategy with names of relevant databases that were not included in the original search. This search identified 29 citations (Table 3). A total of 1480 unique citations were identified.

Table 1. PubMed Search Strategy and Results (1405): Performed on 05/07/10

Search	Query	Results
#1	("Pharmaceutical preparations/adverse effects"[Mesh] OR "Pharmaceutical preparations/contraindications"[Mesh] OR "Pharmaceutical preparations/poisoning"[Mesh] OR "Pharmaceutical preparations/therapeutic use"[Mesh] OR "Pharmaceutical preparations/toxicity"[Mesh] OR "Pharmaceutical preparations/therapy"[Mesh] OR "Pharmaceutical preparations/analysis"[Mesh] OR "Chemical actions and uses/adverse effects"[Mesh] OR "Chemical actions and uses/contraindications"[Mesh] OR "Chemical actions and uses/poisoning"[Mesh] OR "Chemical actions and uses/therapeutic use"[Mesh] OR "Chemical actions and uses/toxicity"[Mesh] OR "Chemical actions and uses/therapy"[Mesh] OR "Chemical actions and uses/analysis"[Mesh] OR "Chemical actions and uses/epidemiology"[Mesh] OR "Drug toxicity"[Mesh] OR "Diseases Category/chemically induced"[Mesh] OR "Diseases Category/drug therapy"[Mesh] OR "Diseases Category/epidemiology"[Mesh] OR "Validation Studies"[pt] OR "Validation Studies as Topic"[Mesh] OR "Sensitivity and Specificity"[Mesh] OR "Predictive Value of Tests"[Mesh] OR "Reproducibility of Results"[Mesh] OR "Predictive Value"[tw]) Limits: Humans, English, Publication Date from 1980/01/01 to 2011/01/01	2133008
#2	("Premier"[All] OR "Solucient"[All] OR "Cerner"[All] OR "Ingenix"[All] OR "LabRx"[All] OR "IHCIS"[All] OR "marketscan"[All] OR "market scan"[All] OR "Medstat"[All] OR "Thomson"[All] OR "pharmetrics"[All] OR "healthcore"[All] OR "united healthcare"[All] OR "UnitedHealthcare"[All] OR "UHC"[All] OR "GPRD"[All] OR "general practice research database"[All] OR "Research Database"[All] OR "Group Health"[All] OR "HCUP"[All] OR ("Healthcare Cost"[All] AND "Utilization Project"[All]) OR ("Health Care Cost"[All] AND "Utilization Project"[All]) OR "MEPS"[All] OR "Medical Expenditure Panel Survey"[All] OR "NAMCS"[All] OR "National Hospital Ambulatory Medical Care Survey"[All] OR "National Ambulatory Medical Care Survey"[All] OR "NHIS"[All] OR "National Health Interview Survey"[All] OR "Kaiser"[All] OR "HMO Research"[All] OR "Health Maintenance Organization"[All] OR "HMO"[All] OR "Cleveland Clinic"[All] OR "Lovelace"[All] OR "Department of Defense"[All] OR "Henry Ford"[All] OR ("Denmark"[All] AND "Epidemiology"[All]) OR "i3 Drug Safety"[All] OR "i3"[All] OR "Aetna"[All] OR "Humana"[All] OR "Wellpoint"[All] OR "IMS"[All] OR "Intercontinental Marketing Services"[All] OR "IMS Health"[All] OR "Geisinger"[All] OR "GE Healthcare"[All] OR "MQIC"[All] OR "PHARMO"[All] OR "Institute for Drug Outcome Research"[All] OR "Pilgrim"[All] OR "Puget Sound"[All] OR "Regenstrief"[All] OR "Saskatchewan"[All] OR "Tayside"[All] OR "MEMO"[All] OR "Medicines Monitoring Unit"[All] OR "Veterans Affairs"[All] OR "Partners Healthcare"[All] OR "Mayo Clinic"[All] OR "Rochester Epidemiology"[All] OR "Indiana Health Information Exchange"[All] OR "Indiana Health"[All] OR "Intermountain"[All] OR "THIN"[All] OR "The health improvement network"[All] OR "blue cross"[All] OR "health partners"[All] OR "health plan"[All] OR "health services"[All] OR "Nationwide Inpatient Sample"[All] OR "National Inpatient Sample"[All] OR "medicaid"[All] OR "medicare"[All] OR "MediPlus"[All] OR	437272

	"Outcome Assessment"[All] OR "insurance database"[All] OR "insurance databases"[All] OR "Data Warehouse"[All] OR "ICD-9"[All] OR “international statistical classification"[All] OR “international classification of diseases"[All] OR "ICD-10"[All] OR "Database Management Systems"[Mesh] OR "Medical Records Systems, Computerized"[Mesh] OR "CPT"[All] OR "Current procedural terminology"[All] OR "drug surveillance"[All] OR (“claims”[tw] AND “administrative”[tw]) OR (“data”[tw] AND “administrative”[tw]) OR "Databases, Factual"[Mesh] OR "Databases as topic"[Mesh] OR "Medical Record Linkage"[Mesh] OR "ICD-9-CM"[All Fields] OR "ICD-10-CM"[All Fields] Limits: Humans, English, Publication Date from 1980/01/01 to 2011/01/01	
#3	("Clinical Trial"[pt] OR "Editorial"[pt] OR "Letter"[pt] OR "Meta-Analysis"[pt] OR "Randomized Controlled Trial"[pt] OR "Clinical Trial, Phase I"[pt] OR "Clinical Trial, Phase II"[pt] OR "Clinical Trial, Phase III"[pt] OR "Clinical Trial, Phase IV"[pt] OR "Comment"[pt] OR "Controlled Clinical Trial"[pt] OR "case reports"[pt] OR "Clinical Trials as Topic"[Mesh] OR "double-blind"[All] OR "placebo-controlled"[All] OR "pilot study"[All] OR "pilot projects"[Mesh] OR "Review"[pt] OR "Prospective Studies"[Mesh]) Limits: Humans, English, Publication Date from 1980/01/01 to 2011/01/01	3207185
#4	Search #1 and #2 Limits: Humans, English, Publication Date from 1980/01/01 to 2011/01/01	123566
#5	Search #4 not #3 Limits: Humans, English, Publication Date from 1980/01/01 to 2011/01/01	75587
#6	(((((("Brain Ischemia"[Mesh] OR "Basal Ganglia Cerebrovascular Disease"[Mesh]) OR "Carotid Artery Thrombosis"[Mesh]) OR "Intracranial Embolism and Thrombosis"[Mesh]) OR "Intracranial Hemorrhages"[Mesh]) OR "Stroke"[Mesh]) OR "Vasospasm, Intracranial"[Mesh] Limits: Humans, English, Publication Date from 1990/01/01 to 2011/01/01	71357
#7	Search #5 and #6 Limits: Humans, English, Publication Date from 1990/01/01 to 2011/01/01	1405

Table 2. IDIS Search Strategy and Results (78 unique citations): Performed on 06/10/10

Search 1: 40 Results

ADVANCED SEARCH

All Fields:

"Premier" OR "Solucient" OR "Cerner" OR "Ingenix" OR "LabRx" OR "IHCIS" OR "marketscan" OR "market scan" OR "Medstat" OR "Thomson" OR "pharmetrics" OR "healthcore" OR "united healthcare" OR "UnitedHealthcare" OR "UHC" OR "GPRD" OR "general practice research database" OR "Research Database" OR "Group Health" OR "HCUP" OR ("Healthcare Cost" AND "Utilization Project") OR ("Health Care Cost" AND "Utilization Project") OR "MEPS" OR "Medical Expenditure Panel Survey" OR "NAMCS" OR "National Hospital Ambulatory Medical Care Survey" OR "National Ambulatory Medical Care Survey" OR "NHIS" OR "National Health Interview Survey" OR "Kaiser" OR "HMO Research" OR "Health Maintenance Organization" OR "HMO" OR "Cleveland Clinic" OR "Lovelace" OR "Department of Defense" OR "Henry Ford" OR ("Denmark" AND "Epidemiology") OR "i3 Drug Safety" OR "i3" OR "Aetna" OR "Humana" OR "Wellpoint" OR "IMS" OR "Intercontinental Marketing Services" OR "IMS Health" OR "Geisinger" OR "GE Healthcare" OR "MQIC" OR "PHARMO" OR "Institute for Drug Outcome Research" OR "Pilgrim" OR "Puget Sound" OR "Regenstrief" OR "Saskatchewan" OR "Tayside" OR "MEMO" OR "Medicines Monitoring Unit" OR "Veterans Affairs" OR "Partners Healthcare" OR "Mayo Clinic" OR "Rochester Epidemiology" OR "Indiana Health Information Exchange" OR "Indiana Health" OR "Intermountain" OR "THIN" OR “The health improvement network" OR "blue cross" OR "health partners" OR "health plan" OR "health services" OR "Nationwide Inpatient Sample" OR "National Inpatient Sample" OR "medicaid" OR "medicare" OR "MediPlus" OR "Outcome Assessment" OR "insurance database" OR "insurance databases" OR "Data Warehouse" OR "ICD-9" OR “international statistical classification" OR “international classification of diseases" OR "ICD-10" OR "Database Management Systems" OR "Medical Records Systems, Computerized" OR "CPT" OR "Current procedural terminology" OR "drug surveillance" OR (“claims” AND “administrative”) OR (“data” AND “administrative”) OR "Databases, Factual" OR "Databases" OR "Medical Record Linkage" OR "ICD-9-CM" OR "ICD-10-CM"

AND **Disease**:

435. or 432. or 433.1 or 434. or 436. (NOTE: 435. ISCHEMIA, CEREBRAL, TRANSNT, 432. HEMORRHAGE, INTRACRANIAL NEC, 433.1 EMBOLISM/THROMBOSIS, CAROTID, 434. EMBOLISM/THROMBOSIS, CEREB, 436. DISEASE, CEREBROVASCULAR NEC)

AND NOT **Descriptor**:

"CASE REPORT ADULT 0" or “FDA APPROVAL PACKAGE 155” OR “FDA BLACK BOX WARNING 165” OR “PIVOTAL STUDY 162” OR "FDA ADVISORY COMMITTEE 164" or "CASE REPORT PEDIATRIC 1" or "CASE REPORT GERIATRIC 2" or "REVIEW ADULT 6" or "STUDY NON-CLINICAL 8" or "REVIEW PEDIATRIC 21" or "REVIEW GERIATRIC 23" or "STUDY RANDOMIZE ADULT 135" or "STUDY RANDOMIZE PEDIATRIC 136" or "STUDY RANDOMIZE GERIATRIC 137" or "CROSS-OVER 144" or "META-ANALYSIS 145" or "N-OF-ONE TRIAL 146" or "PRACTICE GUIDELINE 156" or "SYSTEMATIC REVIEW 161" or "ANNOTATED BIBLIOGRAPHY 167" or "PRIORITY CLIN PRACT GUIDE 168"

Years: 1990-2010

Records = 40

Search 2: 46 Results

ADVANCED SEARCH

All Fields:

"Premier" OR "Solucient" OR "Cerner" OR "Ingenix" OR "LabRx" OR "IHCIS" OR "marketscan" OR "market scan" OR "Medstat" OR "Thomson" OR "pharmetrics" OR "healthcore" OR "united healthcare" OR "UnitedHealthcare" OR "UHC" OR "GPRD" OR "general practice research database" OR "Research Database" OR "Group Health" OR "HCUP" OR ("Healthcare Cost" AND "Utilization Project") OR ("Health Care Cost" AND "Utilization Project") OR "MEPS" OR "Medical Expenditure Panel Survey" OR "NAMCS" OR "National Hospital Ambulatory Medical Care Survey" OR "National Ambulatory Medical Care Survey" OR "NHIS" OR "National Health Interview Survey" OR "Kaiser" OR "HMO Research" OR "Health Maintenance Organization" OR "HMO" OR "Cleveland Clinic" OR "Lovelace" OR "Department of Defense" OR "Henry Ford" OR ("Denmark" AND "Epidemiology") OR "i3 Drug Safety" OR "i3" OR "Aetna" OR "Humana" OR "Wellpoint" OR "IMS" OR "Intercontinental Marketing Services" OR "IMS Health" OR "Geisinger" OR "GE Healthcare" OR "MQIC" OR "PHARMO" OR "Institute for Drug Outcome Research" OR "Pilgrim" OR "Puget Sound" OR "Regenstrief" OR "Saskatchewan" OR "Tayside" OR "MEMO" OR

"Medicines Monitoring Unit" OR "Veterans Affairs" OR "Partners Healthcare" OR "Mayo Clinic" OR "Rochester Epidemiology" OR "Indiana Health Information Exchange" OR "Indiana Health" OR "Intermountain" OR "THIN" OR "The health improvement network" OR "blue cross" OR "health partners" OR "health plan" OR "health services" OR "Nationwide Inpatient Sample" OR "National Inpatient Sample" OR "medicaid" OR "medicare" OR "MediPlus" OR "Outcome Assessment" OR "insurance database" OR "insurance databases" OR "Data Warehouse" OR "ICD-9" OR "international statistical classification" OR "international classification of diseases" OR "ICD-10" OR "Database Management Systems" OR "Medical Records Systems, Computerized" OR "CPT" OR "Current procedural terminology" OR "drug surveillance" OR ("claims" AND "administrative") OR ("data" AND "administrative") OR "Databases, Factual" OR "Databases" OR "Medical Record Linkage" OR "ICD-9-CM" OR "ICD-10-CM"

AND **Descriptor**:

("82" or "84") Not ("CASE REPORT ADULT 0" or "FDA APPROVAL PACKAGE 155" OR "FDA BLACK BOX WARNING 165" OR "PIVOTAL STUDY 162" OR "FDA ADVISORY COMMITTEE 164" or "CASE REPORT PEDIATRIC 1" or "CASE REPORT GERIATRIC 2" or "REVIEW ADULT 6" or "STUDY NON-CLINICAL 8" or "REVIEW PEDIATRIC 21" or "REVIEW GERIATRIC 23" or "STUDY RANDOMIZE ADULT 135" or "STUDY RANDOMIZE PEDIATRIC 136" or "STUDY RANDOMIZE GERIATRIC 137" or "CROSS-OVER 144" or "META-ANALYSIS 145" or "N-OF-ONE TRIAL 146" or "PRACTICE GUIDELINE 156" or "SYSTEMATIC REVIEW 161" or "ANNOTATED BIBLIOGRAPHY 167" or "PRIORITY CLIN PRACT GUIDE 168")

(NOTE: SIDE EF CARDIOVASCULAR 82, SIDE EF NERVOUS 84)

AND **Abstract**:

"ischemi*" or "intracranial" or "stroke"

Years: 1990-2010

Records = 46

Table 3. Search to Update the Original PubMed Search with Additional Database Names (29): Performed on 07/06/10

Search	Query	Results
#1	("Pharmaceutical preparations/adverse effects"[Mesh] OR "Pharmaceutical preparations/contraindications"[Mesh] OR "Pharmaceutical preparations/poisoning"[Mesh] OR "Pharmaceutical preparations/therapeutic use"[Mesh] OR "Pharmaceutical preparations/toxicity"[Mesh] OR "Pharmaceutical preparations/therapy"[Mesh] OR "Pharmaceutical preparations/analysis"[Mesh] OR "Chemical actions and uses/adverse effects"[Mesh] OR "Chemical actions and uses/contraindications"[Mesh] OR "Chemical actions and uses/poisoning"[Mesh] OR "Chemical actions and uses/therapeutic use"[Mesh] OR "Chemical actions and uses/toxicity"[Mesh] OR "Chemical actions and uses/therapy"[Mesh] OR "Chemical actions and uses/analysis"[Mesh] OR "Chemical actions and uses/epidemiology"[Mesh] OR "Drug toxicity"[Mesh] OR "Diseases Category/chemically induced"[Mesh] OR "Diseases Category/drug therapy"[Mesh] OR "Diseases Category/epidemiology"[Mesh] OR "Validation Studies"[pt] OR "Validation Studies as Topic"[Mesh] OR "Sensitivity and Specificity"[Mesh] OR "Predictive Value of Tests"[Mesh] OR "Reproducibility of Results"[Mesh] OR "Predictive Value"[tw]) Limits: Humans, English, Publication Date from 1990/01/01 to 2011/01/01	1867752
#2	("Premier"[All] OR "Solucient"[All] OR "Cerner"[All] OR "Ingenix"[All] OR "LabRx"[All] OR "IHCIS"[All] OR "marketscan"[All] OR "market scan"[All] OR "Medstat"[All] OR "Thomson"[All] OR "pharmetrics"[All] OR "healthcore"[All] OR "united healthcare"[All] OR "UnitedHealthcare"[All] OR "UHC"[All] OR "GPRD"[All] OR "general practice research database"[All] OR "Research Database"[All] OR "Group Health"[All] OR "HCUP"[All] OR ("Healthcare Cost"[All] AND "Utilization Project"[All]) OR ("Health Care Cost"[All] AND "Utilization Project"[All]) OR "MEPS"[All] OR "Medical Expenditure Panel Survey"[All] OR "NAMCS"[All] OR "National Hospital Ambulatory Medical Care Survey"[All] OR "National Ambulatory Medical Care Survey"[All] OR "NHIS"[All] OR "National Health Interview Survey"[All] OR "Kaiser"[All] OR "HMO Research"[All] OR "Health Maintenance Organization"[All] OR "HMO"[All] OR "Cleveland Clinic"[All] OR "Lovelace"[All] OR "Department of Defense"[All] OR "Henry Ford"[All] OR ("Denmark"[All] AND "Epidemiology"[All]) OR "i3 Drug Safety"[All] OR "i3"[All] OR "Aetna"[All] OR "Humana"[All] OR "Wellpoint"[All] OR "IMS"[All] OR "Intercontinental Marketing Services"[All] OR "IMS Health"[All] OR "Geisinger"[All] OR "GE Healthcare"[All] OR "MQIC"[All] OR "PHARMO"[All] OR "Institute for Drug Outcome Research"[All] OR "Pilgrim"[All] OR "Puget Sound"[All] OR "Regenstrief"[All] OR "Saskatchewan"[All] OR "Tayside"[All] OR "MEMO"[All] OR "Medicines Monitoring Unit"[All] OR "Veterans Affairs"[All] OR "Partners Healthcare"[All] OR "Mayo Clinic"[All] OR "Rochester Epidemiology"[All] OR "Indiana Health Information Exchange"[All] OR "Indiana Health"[All] OR "Intermountain"[All] OR "THIN"[All] OR "The health improvement network"[All] OR "blue cross"[All] OR "health partners"[All] OR "health plan"[All] OR "health services"[All] OR "Nationwide Inpatient Sample"[All] OR "National Inpatient Sample"[All] OR "medicaid"[All] OR "medicare"[All] OR "MediPlus"[All] OR "Outcome Assessment"[All] OR "insurance database"[All] OR "insurance databases"[All] OR "Data Warehouse"[All] OR "ICD-9"[All] OR "international statistical classification"[All] OR "international classification of diseases"[All] OR "ICD-10"[All] OR "Database Management Systems"[Mesh] OR "Medical Records Systems, Computerized"[Mesh] OR "CPT"[All] OR "Current procedural terminology"[All] OR "drug surveillance"[All] OR ("claims"[tw] AND "administrative"[tw]) OR ("data"[tw] AND "administrative"[tw]) OR "Databases, Factual"[Mesh] OR "Databases as topic"[Mesh] OR "Medical Record Linkage"[Mesh] OR "ICD-9-CM"[All Fields] OR "ICD-10-CM"[All Fields] Limits: Humans, English, Publication Date from 1990/01/01 to 2011/01/01	399576

#3	("Clinical Trial"[pt] OR "Editorial"[pt] OR "Letter"[pt] OR "Meta-Analysis"[pt] OR "Randomized Controlled Trial"[pt] OR "Clinical Trial, Phase I"[pt] OR "Clinical Trial, Phase II"[pt] OR "Clinical Trial, Phase III"[pt] OR "Clinical Trial, Phase IV"[pt] OR "Comment"[pt] OR "Controlled Clinical Trial"[pt] OR "case reports"[pt] OR "Clinical Trials as Topic"[Mesh] OR "double-blind"[All] OR "placebo-controlled"[All] OR "pilot study"[All] OR "pilot projects"[Mesh] OR "Review"[pt] OR "Prospective Studies"[Mesh]) Limits: Humans, English, Publication Date from 1990/01/01 to 2011/01/01	2729582
#4	#1 NOT #2 Limits: Humans, English, Publication Date from 1990/01/01 to 2011/01/01	1748136
#5	#4 NOT #3 Limits: Humans, English, Publication Date from 1990/01/01 to 2011/01/01	819148
#6	(TennCare [tiab]) OR (RAMQ [tiab]) OR (Cigna [tiab]) OR ((british columbia[tiab]) AND ((health[tiab]) OR (data[tiab]) OR (database[tiab]) OR (population[tiab]))) OR (CIHI [All Fields]) OR ((manitoba[tiab]) AND ((center for health policy[all fields]) OR (population[tiab]) OR (health insurance[tiab]))) OR ((ontario[tiab]) AND ((population[tiab]) OR (OHIP[tiab]) OR (registered persons database[tiab]) OR (health insurance [tiab]) OR (ICES[All Fields]) OR (Institute for Clinical Evaluative Sciences[All Fields]))) OR ((Alberta[tiab]) AND ((health[tiab]) OR (data[tiab]) OR (database[tiab]) OR (population[tiab]) OR (Alberta Health and Wellness[All Fields]))) Limits: Humans, English, Publication Date from 1990/01/01 to 2011/01/01	5128
#7	#5 AND #6 Limits: Humans, English, Publication Date from 1990/01/01 to 2011/01/01	1579
#8	Search #7 AND ((((((("Brain Ischemia"[Mesh] OR "Basal Ganglia Cerebrovascular Disease"[Mesh]) OR "Carotid Artery Thrombosis"[Mesh]) OR "Intracranial Embolism and Thrombosis"[Mesh]) OR "Intracranial Hemorrhages"[Mesh]) OR "Stroke"[Mesh]) OR "Vasospasm, Intracranial"[Mesh]) Limits: Humans, English, Publication Date from 1990/01/01 to 2011/01/01	29

B. ABSTRACT REVIEWS

Of the 1480 abstracts reviewed, 587 were selected for full-text review; 229 were excluded because they did not study CVA or TIA, 440 were excluded because they were not administrative database studies, and 224 were excluded because the data source was not from the United States or Canada. Cohen's kappa for agreement between reviewers on the inclusion vs exclusion of abstracts was 0.68.

C. FULL-TEXT REVIEWS

Of the 587 full-text articles reviewed, 17 were included in the final evidence tables; 6 were excluded because they did not study CVA/TIA, 66 were excluded because they were not administrative database studies, 37 were excluded because the data source was not from the United States or Canada, 210 were excluded because the HOI identification algorithm was poorly defined, and 251 were excluded because they included no validation of the outcome definition or reporting of validity statistics. Reviewers identified 24 citations for review from full-text article references. Of these, 12 were included in the final report; 1 was excluded because it was not an administrative database study, 1 was excluded because the data source was not from the United States or Canada, 4 were excluded because the HOI algorithm was poorly defined, and 6 were excluded because they included no validation of the outcome definition or reporting of validity statistics. Cohen's kappa for agreement between reviewers on inclusion vs exclusion of the full-text articles reviewed was 0.88.

D. MINI-SENTINEL INVESTIGATOR SURVEY

Mini-Sentinel investigators provided 2 published and no unpublished reports of validation studies that had been completed by their teams. Of the 2 published reports, 1 had been identified from the full-text article reference reviews and the other had not been identified from the initial searches, full-text article reference reviews, or other methods.

They provided 4 published reports that they were familiar with but not directly involved in. Of the 4 published reports, none had been identified from the initial searches, full-text article reference reviews, or other methods.

E. EVIDENCE INCLUDED IN TABLE

Of the 34 studies included in the evidence tables, 17 were identified from the initial search strategy, 12 were identified through references of articles that underwent full-text review, and 5 were provided by Mini-Sentinel Investigators. Of these studies, 10 studies provided data to evaluate the validity of algorithms to identify the composite endpoints stroke/TIA or cerebrovascular disease, 25 reported data to evaluate the validity of stroke, 6 reported data to evaluate the validity of TIA, and 4 reported data to evaluate the validity of intracranial bleeds (intracerebral hemorrhage and subarachnoid hemorrhage).[7-40] The algorithms for each of these outcomes are reported separately.

A complete list of studies with clear HOI definitions that were eligible to be selected for inclusion is available in Appendix B.

F. SUMMARY AND DISCUSSION OF ALGORITHMS AND VALIDATION

The validity of the composite endpoints (stroke/TIA or cerebrovascular disease), stroke exclusively, TIA exclusively, and intracranial bleeds are summarized below.

1. Composite Endpoints, Stroke/TIA, or Cerebrovascular Disease

Codes Used in Algorithms. All 10 publications listed in evidence table 4A used ICD-9 or ICD-10 codes to identify patients with the composite endpoints of stroke/TIA or cerebrovascular disease. All studies evaluated algorithms that used ICD-9 codes to identify patients with outpatient encounters or hospitalizations for stroke/TIA or cerebrovascular disease. Most studies included codes 433.x to 436.x alone or in combination with other ICD-9 codes. Four studies excluded ICD-9 codes with the fifth digit specification of 0 (xxx.x0) for codes 433 and 434;[8,23,26,31] the fifth digit specification of 0 indicates that the diagnosis occurred without mention of cerebral infarction. Other common ICD-9 codes used in the algorithms of the included studies were: 430.x, 431.x, 432.x, 437.x, 438.x. See Appendix C for definitions of these stroke/TIA-related codes.

Only 2 studies validated a diagnosis of stroke/TIA using ICD-10 codes.[23,35] ICD-10 codes G45.x and I60.x to I64.x were always included in the algorithms. Other codes included in the algorithms were G46.x, H34.0, H34.1, and I65 to I69.x.

A majority of the studies (n=8) evaluated algorithms based exclusively on hospitalizations for stroke/TIA. A majority of the studies (n=6) identified both incident and prevalent cases of cerebrovascular disease (history or evidence of stroke/TIA or cerebrovascular disease).

Validation Criteria and Method. Nearly all studies (n=8) included in the report validated administrative coding data through the abstraction of information from medical charts. Criteria for confirmation of stroke/TIA varied greatly. Documentation of a written diagnosis was adequate to confirm the outcome in at least 3 studies.[8,9,19]

Two studies used clinical databases developed for specific patient populations (patients undergoing cardiac catheterization and kidney transplantation) to validate administrative codes.[21,26] Neither study reported PPVs; however, the reported estimates for sensitivity varied greatly with the different algorithms assessed in these studies (ranging from 14% to 88%).

Validation Algorithms. The PPVs reported varied greatly, ranging from 33% to 96%. In general, the algorithms that were more inclusive had lower PPVs. For example, the lowest PPVs were found for algorithms based upon codes 430.x to 438.x. Using this algorithm, So, et al.[35] reported a PPV of 33%, Humphries, et al.[19] reported a PPV of 71%, and Broderick, et al.[10] reported a PPV of 46%. Broderick, et al. reported higher PPVs using codes 430 to 436 (PPV=72% using either the primary or secondary diagnosis or PPV=83% using primary discharge codes only). The highest PPV (96%) reported to identify patients with a history or current stroke/TIA included codes 433.x1, 434.x1, 435.x, 436, 437.1x, 437.9x, and 438.x.[8] Kokotailo, et al. reported the highest PPVs to identify acute cerebrovascular events using ICD-9 codes 430.x, 431.x, 433.x1, 434.x1, 435.x, 436, and 362.3 (PPV=90%) and using ICD-10 codes I60.x to I64.x, H34.1, and G45.x (PPV=92%).[23]

Since few studies reported validation of ICD-10 codes, it is difficult to comment on the validation statistics between ICD-9 and 10 coding algorithms. Two studies directly compared the validation of ICD-9 and ICD-10 codes for evidence of cerebrovascular disease in the medical charts.[23,35] Kokotailo, et al. reported similar PPVs for ICD-9 coding and ICD-10 coding (90% and 92%) for identifying acute cerebrovascular events.[23] So, et al. reported a slightly higher PPV for ICD-10 coding (43%) compared to ICD-9 coding (33%) for identifying cerebrovascular disease.[35]

Select Patient Populations. A number of the studies restricted the study sample to patients with specific diseases (e.g., atrial fibrillation, acute myocardial infarction, kidney transplantation) and examined cerebrovascular disease as a comorbidity or outcome.[8,9,19,21,26,35] For example, Birman-Deych, et al. examined current/history of stroke or TIA in Medicare beneficiaries who were hospitalized for atrial fibrillation.[8] So, et al. examined cerebrovascular disease in patients hospitalized for acute myocardial infarction.[35] The validation statistics for these select study samples included the highest and lowest PPVs reported. The different algorithms evaluated in these studies may have impacted the observed PPVs (see above).

Age of Study Population. No information was provided on the proportion of validated cases according to various age strata.

Patient Sex. No studies provided information on the proportion of validated cases by patient sex.

Time Period of Data Collection. This report includes publications that evaluated algorithms to identify stroke/TIA and cerebrovascular disease using data collected between 1985 and 2003. The reported validation statistics did not vary substantially in earlier study periods (i.e., prior to 2000) compared to later study periods (e.g., 2000 and later).

Incident vs Prevalent Outcome Validation. A majority of the studies (n=6) identified both incident and prevalent cases (history or evidence of current stroke/TIA or cerebrovascular disease). The reported validation statistics did not appear to vary according to whether acute events or a history or evidence of current disease were being evaluated. For studies evaluating only acute events, the PPVs ranged from 57 to 92%. For studies evaluating either a history or evidence of current disease, the PPVs ranged from 33 to 96%.

Principal vs Secondary Discharge Diagnosis. The 2 studies that reported PPVs based upon the principal or most responsible (primary position) diagnosis reported high PPVs for stroke/TIA.[10,23] Kokotailo, et al. reported PPVs of 90% and 92% using algorithms that identified hospitalizations and emergency department visits with a most responsible diagnosis for stroke/TIA, using ICD-9 and ICD-10 codes.[23] Broderick, et al. reported a PPV of 83% using primary discharge codes 430 to 436 compared to a PPV of 72% using primary or secondary diagnoses.[10]

Hospitalization Diagnosis vs Outpatient Encounter. Seven studies included in this report used hospitalization diagnoses exclusively, one study used both hospitalizations and emergency department visit diagnoses, and two investigations used both hospitalization and outpatient visits to identify stroke/TIA. The study using both hospitalizations and emergency department visits reported PPVs higher than most studies using hospitalizations only.[23] The two studies that used both hospitalization and outpatient visits did not report PPVs.[9,26] The estimates of sensitivity from algorithms that used both inpatient and outpatient visits were 64%[9] and 88%.[26] The study by Lentine, et al. reported a sensitivity of 75% using only hospitalization claims compared to a sensitivity of 88% using both hospitalization and outpatient visit claims.[26]

2. Stroke (Ischemic, Hemorrhagic, and Unspecified)

Codes Used in Algorithms. All 25 publications listed in evidence Table 4B used ICD-8, ICD-9, or ICD-10 codes to identify patients with a stroke/cerebrovascular accident. All studies evaluated algorithms that used ICD-9 codes to identify patients with outpatient encounters or hospitalizations for stroke. The vast majority of studies evaluated ICD-9 codes 434 and 436, with many studies evaluating codes in the range 430 to 438 separately, as well as in combination. Other common ICD-9 codes used in the algorithms of the included studies were 325, 342.x, 362.8, 369.9, 671.5, 767,780.0, 780.4, 997.00, 997.01, 997.02, 997.09, and V57.x; however, these latter codes were generally only evaluated in one or two studies. See Appendix C for definitions of these stroke-related codes.

Only 1 study validated a diagnosis of stroke using ICD-10 codes.[23] ICD-10 codes H34.1, I63.x, and I64.x were included in the algorithm.

Validation Criteria and Method. All studies included in the report validated administrative coding data through abstraction of medical charts. Criteria for confirmation of stroke varied widely. Few studies stated that a specific standard criteria was used to confirm cases (e.g., World Health Organization [WHO] definitions).[41,42] However, the stated definitions/criteria for stroke often included elements of

such standard criteria. For example, the WHO criteria define stroke as a new neurologic deficit of presumed vascular origin lasting at least 24 hours or until death if death occurred within 24 hours.[24,41] This definition excludes TIA, which is defined as focal neurologic symptoms lasting less than 24 hours; the definition also excludes cases of obvious nonstroke cause such as symptoms caused by trauma and tumors. While only the studies by Benesch, et al.[7] and Lakshminarayan, et al.[24] specifically stated that the WHO definitions were used, other studies[33,34] listed the basic elements of the WHO criteria as necessary to confirm a case of acute stroke.

Validation Algorithms. In general, studies that evaluated 3-, 4-, or 5- digit ICD-9 codes in the range 430.x to 438.x separately reported the highest PPVs for codes 430.x, 431.x, 434.x, and 436.x. For most studies evaluating codes 430.x, 431.x, or 434.x separately, the reported PPVs were 80% or higher. For most studies evaluating code 436.x, the PPVs were 70% or higher. While most studies reported low PPVs for code 433.x, one study that evaluated hospital discharge codes 433.x1 separately from 433.x0 reported a much higher PPV for codes 433.x1 (71% compared with 13%).[32]

The majority of studies also reported PPVs for algorithms using a combination of codes, with PPVs of 85% and higher reported for several studies. Iribarren, et al. evaluated an algorithm including inpatient ICD-8 code 431 and ICD-9 codes 431 and 432 to identify intracerebral hemorrhagic stroke and reported a PPV of 91%.[20] Using an algorithm including codes 430, 431, 432, 434, and 436 in the discharge abstract, Ives, et al.[39] reported a PPV of 90% for incident stroke. Williams, et al. evaluated an algorithm that included primary position ICD-9 codes 434 and 436 to identify acute ischemic stroke and reported a PPV of 98%.[38] Using all hospital discharge codes (principal and secondary) 433.x1, 434 (excluding 434.x0) and 436, Tirschwell, et al. reported a PPV of 90% for ischemic stroke.[37] Kokotailo, et al. evaluated an algorithm using hospitalization and emergency department most responsible diagnosis ICD-9 codes 433.x1, 434.x1, 436, and 362.8 and reported a PPV of 85% for ischemic stroke.[23] To identify acute ischemic stroke, ICH, and SAH, Roumie, et al. used ICD-9 codes 430, 431, 433.x1, 434 (excluding 434.x0) and 436, and reported a PPV of 97% using primary discharge diagnosis codes.[34]

Since only one study reported validation of ICD-10 codes, it is difficult to comment on the validation statistics between ICD-9 and 10 coding algorithms. Kokotailo, et al. directly compared the validation of ICD-9 and ICD-10 codes for evidence of acute ischemic stroke in medical charts.[23] This study found the PPV of the ICD-10 codes H34.1, I63.x, and I64.x to be the same as the PPV of the ICD-9 codes 433.x1, 434.x1, 436, and 362.8 (85%).

Select Patient Populations. A majority of the studies did not restrict the study sample to patients with specific diseases. For example, most studies included the entire health plan membership or all patients admitted to specific hospitals without other restrictions. However, several studies included only patients with a certain condition (e.g., atrial fibrillation or diabetes) and examined stroke as a comorbidity or outcome. For example, Newton, et al. included only patients diagnosed with diabetes and reported a much lower PPV (45%) than most other studies; however, this study included both inpatient and outpatient encounters.[30] The study by Holick, et al. included patients receiving a medication for attention deficit hyperactivity disorder (ADHD) and a comparison group, and also reported a low PPV of 32% using ICD-9 codes 430.xx to 432.xx, 434.xx, and 436.xx.[18] Thompson, et al. evaluated the development of perioperative stroke among patients who underwent a modified or radical neck dissection using ICD-9 codes 433.x, 434.x, 436, 438.x, 997.00, 997.01, 997.02, 997.09, and reported a PPV of 14%; however, the charts of only 7 potential cases of perioperative stroke were reviewed.[36] Morgenstern, et al. also evaluated in-hospital stroke among patients hospitalized with AMI, CABG, or

percutaneous cardiac intervention using ICD-9 codes 430 to 437 and reported a PPV of 44% for stroke complications following cardiac symptoms.[29] Thus, most studies evaluating stroke among special populations reported low PPVs; however, the specific algorithms used (e.g., both inpatient and outpatient encounters), as well as the specific outcome assessed (e.g., in-hospital stroke) may account for these findings.

Age of Study Population. Many studies included only adult populations; no information was provided on the proportion of validated cases by age group. Two studies evaluated stroke among children.[15,16] Golomb, et al. evaluated inpatient and outpatient ICD-9 codes 342, 433, 434, 435, 436, 437, 438, and 767, and reported higher PPVs than those reported in studies among adult populations for a number of codes; for example, the PPV=79% for code 433 and PPV=84% for code 438, are much higher than those values reported for adult populations.[15] In another study, Golomb, et al. evaluated ICD-9 codes 325 to identify the presence of cerebral sinovenous thrombosis in children and reported a PPV of 93%.[16]

Patient Sex. No studies provided information on the proportion of validated cases of stroke in men as compared with women. One study reported the validity of ICD-9-codes 430, 431, 432.0 to 432.1, 432.9, 434, and 436 among women enrolled in the Women's Health Initiative.[17] The overall PPV of 81% and PPVs for specific codes were within the range of other studies using similar codes.

Time Period of Data Collection. This report includes publications that evaluated algorithms to identify potential acute strokes using data collected between 1978 and 2006. The reported validation statistics did not vary significantly in earlier study periods (i.e., prior to 2000) compared to later study periods (e.g., 2000 and later). One study evaluated the PPVs of hospital discharge codes 431, 432, 434, 436, and 437 to identify acute stroke during 5 calendar years: 1980, 1985, 1990, 1995, and 2000.[24] Using WHO criteria, the overall PPV was lowest in 1980 (55%). However, there was no consistent trend over time, and the PPV reported for the most recent year evaluated (2000) was the second lowest found (PPV=60%).

Incident vs Prevalent Outcome Validation. The majority of studies evaluated hospitalizations for acute strokes (incident or recurrent). Two studies evaluated incident strokes (cases without a history of prior stroke), as well as recurrent strokes.[25,34] To identify acute ischemic stroke, ICH, and SAH, Roumie, et al. evaluated primary discharge ICD-9 codes 430, 431, 433.x1, 434 (excluding 434.x0) and 436.[34] Excluding patients with a *prior hospitalization for stroke*, the investigators reported a PPV of 97% for acute stroke and 74% for incident stroke (no history of remote stroke). Excluding patients with a *prior hospitalization or outpatient visit diagnosis* of stroke, the PPV was 80% for incident stroke. Leibson, et al. evaluated primary discharge codes 430 to 438, and reported a PPV of 60% for any stroke and 47% for incident stroke events.[25] Evaluating codes 430, 431, 433, 434, 436 and 437 and using up to 3 discharge codes, the investigators reported a PPV of 79% for all strokes and 64% for incident strokes. Codes were also evaluated individually. The largest differences in the PPVs between incident as compared to all stroke (incident or recurrent) were for codes 431, 434, and 437; for each of these codes, the PPVs were greater than 10 percentage points higher for identification of all strokes compared to incident events only.

Principal vs Secondary Discharge Diagnosis. The majority of studies (n=20) evaluated both the principal and secondary diagnoses in an algorithm for identification of cases of acute stroke. A number of these studies also evaluated the principal diagnosis only; thus, approximately one half (n=13) of the studies evaluated the principal or most responsible discharge diagnosis only in an algorithm for identification of cases.[7,15,16,25,27,34,37] Studies that compared algorithms using the primary discharge diagnosis to those

using diagnoses in any position found slightly higher PPVs for algorithms using the primary discharge diagnosis only (generally < 10% higher). One exception was the study by Liu, et al.[27] who reported a PPV of 68% for an algorithm using primary diagnosis codes 430 to 438 compared to a PPV of 56% for an algorithm using primary, secondary or tertiary diagnoses at tertiary care hospitals; these investigators reported a similar difference at community hospitals that were evaluated (PPV of 61% compared to 47%).

Roumie, et al. compared an algorithm using a primary discharge diagnosis for stroke with another algorithm using the discharge diagnosis in any other position.[34] The PPV for the primary discharge diagnosis of stroke was 97% compared to 32% for a secondary diagnosis. The overall PPV for the algorithm using both primary and secondary diagnoses was 89% compared to 97% using only the primary discharge diagnosis.

Hospitalization Diagnosis vs Outpatient Encounter. Few studies evaluated algorithms using both hospitalization and outpatient encounter data to identify cases of acute stroke.[11,15,30,23] Given the different algorithms and study populations used in the various studies, it is difficult to adequately assess the impact of including outpatient encounter data. Brophy, et al. evaluated an algorithm using inpatient or outpatient ICD-9 codes 434, 435.0, 435.1, 435.3, 435.8, 435.9, 436, 437.1, 437.9, and 438 to identify cerebrovascular accident in patients with atrial fibrillation using a Veterans Affairs database and reported a PPV of 79%; however, the criteria for confirmation of cases was unspecified.[11] The study by Newton, et al. included only patients diagnosed with diabetes and reported a much lower PPV (45%) than most other studies, using an algorithm that included both inpatient and outpatient encounters.[30] Golomb, et al. evaluated inpatient and outpatient ICD-9 codes 342, 433, 434, 435, 436, 437, 438, and 767 to evaluate stroke in a pediatric population, and reported higher PPVs than those reported in studies among adult populations for a number of codes (see above section 'Age of study population').[15]

Using hospitalization and emergency department visits, Kokotailo, et al. evaluated ICD-9 codes in the most responsible (primary) position for evidence of acute ischemic stroke in the medical charts. This study reported that the PPV of ICD-9 codes 433.x1, 434.x1, 436, and 362.8 was 85%.[23]

Thus, the few studies that included outpatient data had PPVs at both the higher and lower range of values observed in studies evaluating the validity of algorithms to identify stroke.

3. Transient Ischemic Attack (TIA)

Codes Used in Algorithms. All 6 publications listed in evidence table 4C used ICD-9 or ICD-10 codes to identify patients with a TIA. All 6 studies evaluated ICD-9 codes to identify patients with outpatient encounters or hospitalizations for TIA. Four studies evaluated ICD-9 codes 435.x, one study evaluated ICD-9 code 435.9, and the other study evaluated ICD-9 codes 433 through 436. See Appendix C for definitions of these codes.

Only 1 study validated a diagnosis of TIA using ICD-10 codes.[23] ICD-10 code G45.x was included in the algorithm.

Four studies evaluated algorithms based exclusively on hospitalizations for TIA.[7,17,18,39]

Validation Criteria and Method. All 6 studies included in the report validated administrative coding data through the abstraction of data from medical charts. Criteria for confirmation of a TIA varied greatly. Documentation of a written diagnosis was adequate to confirm a TIA in some studies.[18,30] One study used the WHO definition for TIA.[7]

Validation Algorithms. In 3 of the 6 studies evaluating ICD-9 codes 435.x in hospitalizations or hospitalizations/emergency department encounters, the PPVs were 70% or higher.[7,17,23] Ives, et al. reported a much lower PPV of 28%; events were confirmed by an events committee rather than by standardized clinical criteria which may be a potential explanation for the lower percentage of cases validated.[39] Newton, et al. also reported a low PPV of 33%; however, this study included both inpatient and outpatient encounters and only evaluated 33 potential cases of TIA among a select population (patients diagnosed with diabetes).[30] One study also assessed the validity of other codes (ICD-9 codes 433, 434, and 436) and found much lower PPVs than those reported for ICD-9 code 435.x (PPVs of 9% or lower for both primary and secondary diagnoses and 14% or lower for primary diagnoses).[7] The PPV for ICD-9 code 435.9 reported by Holick, et al. (28%) was also low.[18]

Only 1 study reported validation of ICD-10 codes. This study directly compared the validation of ICD-9 and ICD-10 codes for evidence of TIA in medical charts.[23] The PPV of the ICD-10 codes (G45.x) was found to be higher than the PPV of the ICD-9 codes 435.x (97% vs 70%).

Selected Patient Populations. The 3 studies with the highest PPVs did not restrict the study sample to patients with specific conditions.[7,17,23] Ives, et al. also did not restrict the study sample to patients with specific conditions, but reported a much lower PPV of 28%.[39] Newton, et al. included only patients diagnosed with diabetes and reported a much lower PPV of 33%; however, this study included both inpatient and outpatient encounters and only evaluated 33 potential cases.[30] The study by Holick, et al. included patients receiving a medication for attention deficit hyperactivity disorder (ADHD) and a comparison group, and also reported a low PPV of 28%; however, this study evaluated ICD-9 code 435.9 only.[18]

Age of Study Population. Studies included only adult populations. No information was provided on the proportion of validated cases of TIA by age group.

Patient Sex. No studies provided information on the proportion of validated cases of TIA according to patient sex. One study reported the validity of ICD-9-code 435.x among women enrolled in the Women's Health Initiative.[17] The PPV of 72% was similar to those reported in 2 other studies that did not restrict the population to patients with specific conditions or sex.[7,23]

Time Period of Data Collection. This report includes publications that evaluated algorithms to identify TIA using data collected between 1989 and 2006. The reported validation statistics did not vary significantly in earlier study periods (i.e., prior to 2000) compared to more recent periods (i.e., 2000 and later).

Incident vs Prevalent Outcome Validation. Studies in the report evaluated acute events. The study by Newton, et al. also evaluated whether TIA was confirmed at any time during the observation period (PPV=42%), as well as whether TIA was confirmed within 60 days of the inpatient or outpatient encounter date with an ICD-9 code of 435.x (PPV=33%).[30]

Principal vs Secondary Discharge Diagnosis. Four studies evaluated algorithms based exclusively on hospitalizations for TIA.[7,17,18,39] Benesch, et al. reported a PPV of 89% for patients with a primary discharge diagnosis of ICD-9 435.x and a PPV of 77% for patients with this code as a primary or secondary discharge diagnosis.[7] Heckbert, et al. evaluated ICD-9 code 435.x using discharge diagnoses in any position and reported a PPV of 72%.[17] Ives, et al. evaluated ICD-9 code 435 in the discharge abstract, and reported a much lower PPV of 28%.[39] Thus, the limited data suggest that the PPV may be higher for algorithms using a principal discharge diagnosis only.

Kokotailo, et al. reported a PPV of 70% for patients with a most responsible (primary position) diagnosis of ICD-9 435.x recorded in a hospitalization or emergency department visit. [23]

Hospitalization Diagnosis vs Outpatient Encounter. The studies included in this report examined either hospitalizations or outpatient encounters to identify TIA. The study by Newton, et al. used both inpatient and outpatient encounters to identify patients with TIA, and reported a much lower PPV than most other studies (PPV=33%); however, this study only evaluated 33 potential cases of TIA.[30]

4. Intracranial Bleeds (Intracerebral Hemorrhage and Subarachnoid Hemorrhage)

Codes Used in Algorithms. All 4 publications listed in evidence table 4D used ICD-9 or ICD-10 codes to identify patients with intracranial bleeds. All 4 studies evaluated ICD-9 codes to identify patients with hospitalizations or emergency department visits for intracranial bleeds. All of the studies included codes 430.x and 431.x, potentially in combination with other codes such as 432.x. One study also included a number of codes related to fracture of the skull with hemorrhage (e.g., codes 800.2, 800.3, 800.7). See Appendix C for definitions of these codes.

Only 1 study validated a diagnosis of intracranial bleed using ICD-10 codes.[23] ICD-10 codes I61.x and I60.x were included in the algorithm.

Three studies evaluated algorithms based exclusively on hospitalizations for intracranial bleeds;[8,37,40] the other study evaluated both hospitalizations and emergency department visits.[23]

Validation Criteria and Method. All 4 studies included in the report validated administrative coding data through abstraction of medical charts. Criteria for confirmation of intracranial bleeds varied. Only one study specifically stated that the criteria included documentation of direct visualization of blood by a physician or imaging consistent with bleeding.[40]

Validation Algorithms. The PPVs reported were 77% or higher. The lowest PPV was reported by Birman-Deych, et al.;[7] this study evaluated the algorithm that used the largest number of codes (codes 430 to 432 plus a number of codes related to fracture of the skull with hemorrhage (e.g., codes 800.2, 800.3, 800.7, etc).[8] For studies that evaluated codes for SAH (ICD-9 codes 430.x) and ICH (ICD-9 codes 431.x) separately, the PPVs were similar for the two conditions, ranging from 86% to 98% for SAH and from 80% to 97% for ICH.

One study directly compared the validation of ICD-9 and ICD-10 codes for evidence of intracranial bleeds in the medical charts.[23] This study found the PPVs of the ICD-10 codes to be similar to those for ICD-9 codes (98% and 97% for ICH, and 91% and 98% for SAH, using ICD-10 and ICD-9 codes, respectively).

Select Patient Populations. Only 1 study restricted the patient population to patients with a specific condition (i.e., patients hospitalized with atrial fibrillation).[8] This study reported the lowest PPV (77%); however, the investigators evaluated an algorithm that included the largest number of ICD-9 codes, including codes related to fracture of the skull with hemorrhage.

Age of Study Population. No information was provided on the proportion of validated cases of intracranial bleeds by age group.

Patient Sex. No studies provided information on the proportion of validated cases of intracranial bleeds by patient sex.

Time Period of Data Collection. This report includes publications that evaluated algorithms to identify intracranial bleeds using data collected between 1990 and 2003. The reported validation statistics did not vary significantly in earlier study periods (i.e., prior to 2000) compared to later study periods (i.e., 2000 and later).

Incident vs Prevalent Outcome Validation. Studies in the report evaluated acute events.

Principal vs Secondary Diagnosis. The 2 studies that evaluated algorithms based upon the principal or most responsible diagnosis reported high PPVs for ICH and SAH (89% or higher).[23,37] Tirschwell, et al. reported a PPV of 89% for patients with a primary discharge code for ICH and a PPV of 80% for patients with a primary or secondary discharge diagnosis; similarly, the investigators reported a PPV of 94% for patients with a primary discharge code for SAH and a PPV of 86% for patients with a primary or secondary discharge diagnosis.[37] Kokotailo, et al. reported PPVs that ranged from 91% to 98% using algorithms that identified hospitalizations and emergency department visits with a most responsible diagnosis for ICH or SAH, using ICD-9 and ICD-10 codes.[23] However, in a study that used inpatient codes in any position, Arnason, et al. also reported a high PPV for intracranial bleeds (PPV=94%).[40]

Hospitalization Diagnosis vs Outpatient Encounters. Three studies[8,37,40] included in this report used hospitalization diagnoses exclusively and the other study[23] used both hospitalizations and emergency department visit diagnoses to identify intracranial bleeds. The study using both hospitalizations and emergency department visits reported comparable PPVs to those studies using hospitalizations only.

G. SUMMARY OF EXCLUDED POPULATIONS AND DIAGNOSES

As described in section F above, many studies evaluated stroke, TIA, and cerebrovascular disease in adult patients. In addition, several studies included only patients with a certain medical condition (e.g., atrial fibrillation, diabetes) that may have affected the PPVs observed. However, the specific algorithms used (e.g., use of either inpatient and outpatient encounters or specific codes used), as well as the specific outcome assessed (e.g., in-hospital stroke) may account for these findings. Few studies excluded patients with specific comorbid conditions. Exceptions included the study by Holick, et al. that excluded patients with a history of arrhythmia or heart failure in the 6 month baseline period.[18] Another study by Iribarren, et al. excluded patients with prior cerebrovascular disease, brain tumor, encephalitis, AIDS encephalopathy, toxoplasmosis, multiple sclerosis, diabetic coma, hepatic coma, or uremic coma.[20] Roumie, et al. excluded patients with a prior stroke hospitalization, any cancer except nonmelanoma skin cancer, liver failure, end stage renal disease, HIV infection, or organ transplant in the year prior to

cohort entry.[34] Finally, Tirschwell, et al. excluded cases if any codes for traumatic brain injury or rehabilitation were present.[37]

H. EVIDENCE TABLES

Table 4A. Positive Predictive Values by Algorithms to Identify Composite Endpoints (Stroke/Transient Ischemic Attack and Cerebrovascular Disease)

Citation	Study Population and Time Period	Description of Outcome Studied	Algorithm	Validation/Adjudication Procedure, Operational Definition, and Validation Statistics
Stroke/TIA				
Arnason, et al. (2006)[40]	patients discharged from a university-associated teaching hospital in Ottawa, Canada, 1999 to 2000	hospitalizations (stroke/TIA)	inpatient ICD-9-CM codes 433 to 436	Medical record review was conducted (N=179 cases of potential stroke/TIA). Confirmation of 'acute thromboembolism' required documentation of at least one of the following: direct visualization or imaging of a new thromboembolism or new clinical signs of a stroke/TIA combined with physician confirmation of newly completed stroke/TIA in the chart or a CT report showing acute or sub-acute cerebral infarct. PPV=57%
Birman-Deych, et al. (2005)[8]	Medicare beneficiaries who were hospitalized with atrial fibrillation identified using the National Registry of Atrial Fibrillation II dataset, including anonymous patient records gathered by the Quality Improvement/Peer Review Organization for the National Stroke Project, 1998 to 1999	hospitalizations (stroke/TIA, prevalent and incident)	inpatient ICD-9-CM codes 433.x1, 434.x1, 435.x, 436, 437.1x, 437.9x, 438.x	Medical record review was conducted. Outcome was confirmed if there was documentation of a history and/or current stroke/TIA. Current or past stroke/TIA: sensitivity=35% specificity=99% PPV=96% NPV=79%

Broderick, et al. (1998)[10]	Black residents of the Greater Cincinnati/Northern Kentucky region, identified by hospitalization discharges from 19 acute-care hospitals, 1993 to 1994	hospitalizations (stroke/TIA including intracerebral hemorrhage and subarachnoid hemorrhage)	inpatient ICD-9-CM codes 430 to 438, 747.81, 674.0, 325	Medical record review was conducted (N=733). The criteria that determined the various diagnostic categories of stroke were adapted from the Classification of Cerebrovascular Diseases III and from epidemiological studies of stroke in Rochester, Minnesota. code 430: PPV=64% code 431: PPV=83% code 432: PPV=0% code 433: PPV=35% code 434: PPV=80% code 435: PPV=83% code 436: PPV=64% code 437: PPV=12% code 438: PPV=2% codes 430-438: PPV=46% codes 430-436: PPV=72% (and would detect 97% of all strokes and TIAs) primary discharge codes 430-436: PPV=83% (would detect 84% of all strokes and TIAs)
Humphries, et al. (2000)[19]	adults identified by the British Columbia Cardiac Registries as having undergone a percutaneous coronary intervention at St. Paul's Hospital and whose data were linked to the British Columbia Patient Hospitalization Database, 1994 to 1995	hospitalizations (cerebrovascular disease: stroke, TIA, or carotid endarterectomy, prevalent or incident)	inpatient ICD-9 codes 430 to 438	Medical record review was conducted (N=817). The outcome was confirmed based upon documentation of a previous history of stroke, TIA, or carotid endarterectomy. sensitivity=42.9% specificity=99.2% PPV=71.4% NPV=97.5%
Kokotailo, et al. (2005)[23]	patients with inpatient visits or seen at the emergency department identified from hospital discharge abstracts database	hospitalizations and emergency department visits (stroke/TIA including intracerebral hemorrhage and subarachnoid	most responsible (primary position) diagnosis ICD-9 codes 430.x, 431.x, 433.x1, 434.x1, 435.x,	Medical record review was conducted on a sample of charts (N=461 identified with ICD-9 codes and N=256 identified with ICD-10 codes). Outcome was confirmed based upon trained research assistant determination, and neurologist determination in ambiguous cases, considering physical

	from 3 acute care hospitals in the Calgary health region, 2000 to 2003	hemorrhage)	436, 362.3; ICD-10 codes I60.x, I61.x, I63.x, I64.x, H34.1, G45.x	examination notes, physician progress notes, CT and MRI reports (if available), and discharge summaries. Cases were coded as TIA if they resolved within 24 hours of onset, and if imaging was performed, no detectable changes were evident. Assessment of correct coding was based on clinical data alone in 24% of charts and on clinical data and neurovascular imaging reports in 76% of charts. ICD-9 coding: overall: PPV=90% ICD-10 coding: overall: PPV=92%

Lentine, et al. (2009)[26]	kidney transplant patients at Washington University ages ≥18 years with Medicare as primary insurer, 1991 to 2002	incident or prevalent (stroke/TIA)	ICD-9-CM codes: 430, 431, 432, 433.x1, 434.x1, 435.x, 997.02; identified with Medicare Part A (institutional) claims and/or Medicare Part B (physician/suppliers) claims	Transplant center's clinical database was used to confirm stroke or TIA. Definition of stroke included new focal neurologic deficit lasting ≥ 24 hours, confirmed by brain imaging. Definition of TIA included new focal deficit that resolves within 24 hours and was attributed to a central cause by the examining provider.
				Claims within 30 days from event date recorded in the database:
				Medicare Part A
				sensitivity = 75.0% (95% CI 53.8 - 96.2%);
				Part B
				sensitivity = 81.3% (95% CI 62.1% - 100.0%);
				Part A or B
				sensitivity = 87.5% (95%CI 71.3% - 100.0%);
				1 Part A claim or 2 Part B claims submitted at least 1 day but no more than 365 days apart:
				sensitivity = 87.5%

Cerebrovascular Disease				
Borzecki, et al. (2004)[9]	Veterans Affairs patients with at least 1 hypertension diagnosis (ICD-9-CM code 401, 402, or 405) and additional sample without a hypertension diagnosis identified using the Out-Patient Clinic (OPC) and Patient	incident or prevalent (cerebrovascular disease)	inpatient or outpatient ICD-9-CM codes: 430.x to 438.x	Medical record review was conducted (981 patients with a hypertension diagnosis and 195 without a hypertension diagnosis). Outcome was confirmed based upon documentation of cerebrovascular disease in medical notes. sensitivity=64% specificity=95%

	Treatment (PTF) file, Department of Veterans Affairs (VA) databases, 1998 to 1999			
Jollis, et al. (1993)[21]	discharges containing a procedure code for coronary arteriography identified using administrative or insurance claims of Duke University Medical Center, 1985 to 1990	hospitalizations (cerebrovascular disease, incident and prevalent)	discharges with an ICD-9-CM code of 435, 436, 438, 437.1, 434, 38.12, 38.42	Clinical database was compared to coding by medical record technicians (N=12937). Cerebrovascular disease was confirmed based upon documentation in the clinical data. sensitivity= 14% specificity= 99%
Piriyawat, et al. (2002)[31]	residents of Nueces County Texas ≥ 45 years of age, 2000	hospitalizations (acute cerebrovascular events)	primary and secondary ICD-9 discharge codes for 430 to 438, except those with a fifth digit specification of 0 (xxx.x0); also excluded codes 437.0, 437.2, 437.3, 437.4, 437.5, 437.7, 437.8, and 438	Medical record review was conducted (N=815). Acute cerebrovascular events were confirmed based upon criteria specified by Morgenstern, et al. Cerebrovascular events resulting from trauma were excluded. sensitivity=89% PPV=72.8%
So, et al. (2006)[35]	patients ≥ 20 years of age hospitalized with acute myocardial infarction at 4 teaching hospitals in Alberta, Canada, 2003	hospitalizations (cerebrovascular disease, incident and prevalent)	inpatient ICD-9-CM codes: 430.x to 438.x; ICD-10 codes: G45.x, G46.x, H34.0, I60.x – I69.x	Medical record review was conducted (N=193) and outcome was confirmed based upon evidence of cerebrovascular disease in chart. ICD-9-CM codes: sensitivity = 100.0% (95% CI 54.1 - 100.0) specificity = 93.6% (89.1 – 96.6) PPV = 33.3% (13.3 – 59.0) NPV = 100.0% (97.9 – 100.0) ICD-10 codes: sensitivity = 100.0% (54.1 - 100.0) specificity = 95.7% (91.7 – 98.1) PPV = 42.9% (17.7 – 71.1) NPV = 100.0% (98.0 – 100.0)

Table 4B. Positive Predictive Values by Algorithms to Identify Cerebrovascular Accident (CVA)/Stroke

Citation	Study Population and Time Period	Description of Outcome Studied	Algorithm	Validation/Adjudication Procedure and Operational Definition
Benesch, et al. (1997)[7]	hospitalizations at 5 academic medical centers identified using the Academic Medical Center Consortium database, 1992	hospitalizations (stroke)	inpatient ICD-9 codes 433 to 436	Medical record review was conducted (N=649). Stroke was confirmed based upon the World Health Organization (WHO) definitions. primary and secondary diagnoses: code 433: PPV=6.1% code 434: PPV=85.0% code 435: PPV=9.1% code 436: PPV=82.6% primary diagnosis: code 433: PPV=9.1% code 434: PPV=90.3% code 435: PPV=6.3% code 436: PPV=88.9%
Brophy, et al. (2004)[11]	patients diagnosed with atrial fibrillation identified using the Veterans Affairs Boston Healthcare System database, 1998 to 2001	stroke	inpatient or outpatient ICD-9-CM codes 434, 435.0, 435.1, 435.3, 435.8, 435.9, 436, 437.1, 437.9, 438	Medical record review was conducted. Criteria for confirmation of cases (cerebrovascular accident) were unspecified. sensitivity=56% specificity=92% PPV=79%
Derby, et al. (2001)[12]	residents aged 35 to 74 years in Rhode Island and Massachusetts identified by hospital discharges from 7 hospitals, 1980 to 1992	hospitalizations (stroke)	primary ICD-9 discharge diagnosis codes 431, 432, 434, 436, 437	Medical record review was conducted (N=2124). Outcomes were confirmed as determined by a study physician based on whether: 1) the clinical description was consistent with a new, localized neurological defect involving the hemispheres, brain stem, and/or the cerebellum, and 2) whether there was evidence for intracerebral hemorrhage with or without intraventricular extension and with or without subarachnoid extension. Definite or probable stroke excluded cases that were: exclusively subarachnoid hemorrhage; cerebral infarction related to rheumatic mitral stenosis or infective endocarditis, or stroke in the presence of prosthetic cardiac valves; exclusively TIA; and evidence from the medical history that the hospitalization

				was for a previous stroke PPV=80%
Derby, et al. (2000)[13]	residents aged 35 to 74 years, in Rhode Island and Massachusetts identified by hospital discharges from 7 hospitals, 1980 to 1992	hospitalizations (stroke)	primary or secondary ICD-9 discharge diagnosis code 431, 432, 434, 435, 436, 437	Medical record review was conducted (N=3975). Outcomes were confirmed by a study physician based on whether: 1) the clinical description was consistent with a new, localized neurological defect involving the hemispheres, brain stem, and/or the cerebellum, and 2) whether there was evidence for intracerebral hemorrhage with or without intraventricular extension and with or without subarachnoid extension. Definite or probable stroke excluded cases that were: exclusively subarachnoid hemorrhage; cerebral infarction related to rheumatic mitral stenosis or infective endocarditis, or stroke in the presence of prosthetic cardiac valves; exclusively TIA; and evidence from the medical history that the hospitalization was for a previous stroke overall: PPV=59.5% codes 431-432: PPV=70.3% code 434: PPV=84.0% code 435: PPV=26.7% codes 436-437: PPV=55.2%
Goldstein, et al. (1998)[14]	hospitalizations from the Durham Veterans Affairs Medical Center, 1995 to 1997	hospitalizations (acute ischemic stroke)	primary discharge diagnosis of ICD-9-CM codes 433, 434, and 436	Medical record review was conducted (N=175). Outcome was confirmed based upon evidence in discharge summary. overall PPV=61% code 433: PPV=4% code 434: PPV=82% code 434.11: PPV=85% code 434.91: PPV=82% code 436: PPV=79% codes 434.11, 434.91, or 436: sensitivity=81% specificity=90%
Golomb, et al. (2006)[15]	children with an inpatient or outpatient visit to Riley Hospital for Children in	stroke	inpatient or outpatient ICD-9 codes 342, 433, 434, 435, 436, 437, 438,	Medical record review was conducted (N=663). Outcome was confirmed by a pediatric neurologist, based upon radiographic

	Indianapolis, IN, 1999 to 2004		767	evidence of infarction. stroke of any type **code in any position**: code 433: PPV=79% code 434: PPV=62% code 435: PPV=50% code 436: PPV=88% code 437: PPV=59% code 438: PPV=84% code 767: PPV=71% code 342: PPV=41% codes 433 and 436: PPV=86% codes 436 and 438: PPV=84% codes 433 and 438: PPV=83% codes 438 and 767: PPV=81% codes 436 and 767: PPV=81% codes 435 and 436: PPV=81% codes 435 and 438: PPV=80% codes 342 and 434: PPV=48% codes 342 and 438: PPV=48% codes 342 and 436: PPV=45% codes 342 and 767: PPV=43% codes 342 and 437: PPV=43% codes 342 and 433: PPV=42% codes 342 and 435: PPV=41% code 436 in **primary position**: PPV=92% arterial ischemic stroke **code in any position**: code 433: PPV=79% code 434: PPV=52% code 435: PPV=42% code 436: PPV=83% code 437: PPV=46% code 438: PPV=75% code 767: PPV=53% code 342: PPV=37% codes 433 and 436: PPV=81%

				codes 436 and 438: PPV=76% codes 433 and 438: PPV=75% codes 438 and 767: PPV=70% codes 436 and 767: PPV=70% codes 435 and 436: PPV=74% codes 435 and 438: PPV=71% codes 342 and 434: PPV=42% codes 342 and 438: PPV=43% codes 342 and 436: PPV=41% codes 342 and 767: PPV=38% codes 342 and 437: PPV=37% codes 342 and 433: PPV=38% codes 342 and 435: PPV=36% code 436 in the **primary position**: PPV=87% code 342 in the **primary position**: PPV=53% In general, codes with lower accuracy identified larger numbers of strokes.
Golomb, et al. (2007)[16]	children with an inpatient visit to Riley Hospital for Children in Indianapolis, IN, 1999 to 2005	hospitalizations (cerebral sinovenous thrombosis)	inpatient ICD-9 codes 325, 437.6, 671.5	Medical record review was conducted (N=56 patients for code 325, 1 patient for code 437.6, and 0 patients for code 671.5). Cerebral sinovenous thrombosis was determined by pediatric neurologist, based upon evidence in the chart, including radiographic evidence and evaluations of attending physicians; probable sinovenous thrombosis was defined as cases in which the radiographic imaging was highly suggestive of the diagnosis and the clinical picture usually supported the diagnosis; definite sinovenous thrombosis was defined as cases in which the radiographic imaging was clearly diagnostic and there was absolutely no doubt about the diagnosis code 325, any position (possible, probable, or definite case): PPV=92.9% code 325, primary position (N=7): PPV=100%
Heckbert, et al. (2004)[17]	hospitalizations among women enrolled in the Women's Health Initiative (WHI),	hospitalizations (stroke)	ICD-9 codes 430, 431, 432.0 to 432.1, 432.9, 434, 436	Medical record review was conducted. Outcomes were confirmed based upon WHI criteria for cardiovascular endpoints. Overall:

	1994 to 2000			PPV= 81% sensitivity=82% code 430: PPV=74% code 431: PPV=93% codes 432.0 to 432.1: PPV=24% code 432.9: PPV=60% code 434: PPV=85% code 436 : PPV=70%
Holick, et al. (2009)[18]	adults aged 18 years or older who received a first dispensing of atomoxetine or stimulant ADHD medication and comparison group identified using the Ingenix ResearchDataMart; excluded members with claims of history of arrhythmia or heart failure in 6 month baseline period), 2003 to 2006	hospitalizations (stroke)	inpatient ICD-9 codes: 430.xx to 432.xx, 434.xx, 436.xx;	Medical record review was conducted (N=132 potential CVAs). Criteria for confirming a CVA event included a stated diagnosis of CVA from a neurologist or in the hospital discharge summary, patient receiving a thrombolytic agent or stent placement, a positive imaging result, or a description of the event that is consistent with a CVA diagnosis (i.e., sudden onset longer than 1 hour and with persistent neurologic or cognitive deficits). CVA: PPV=31.8%
Iribarren, et al. (1996)[20]	Kaiser Permanente of Northern California members aged 40 to 89 years who had a cholesterol determination; excluded individuals with self-reported cerebrovascular disease or subdural hematoma of traumatic origin, brain tumor, encephalitis, AIDS encephalopathy, toxoplasmosis, multiple sclerosis, diabetic coma, hepatic coma, or uremic coma	hospitalizations (intracerebral hemorrhagic stroke)	inpatient ICD-8 code 431 and ICD-9 codes 431 and 432	Medical record review was conducted for 50 randomly selected patients. Intracerebral hemorrhagic stroke confirmed by CT of the head. PPV=91%

	identified in the computerized hospital discharge abstracts, 1978 to 1993			
Ives, et al. (1995)[39]	Cardiovascular health Study: residents ≥ 65 years in Sacramento County, CA; Washington County, MD; Forsyth County, NC; Pittsburgh, PA , 1989 to 1992	hospitalizations (incident)	ICD-9-CM 430, 431, 432, 434, 436 in the discharge abstract	Medical record review was conducted (N=79). Outcome was confirmed based upon decision by an Events Committee (stroke subcommittee), considering documentation of medical history, symptoms, course, and outcome of each event. PPV=90%
Klatsky, et al. (2005)[22]	members of Northern California Kaiser Permanente who supplied data on voluntary health examinations from 1978 to 1985 and followed up through 1996	hospitalizations	primary discharge diagnosis ICD-9 codes 430 to 438	Medical record review was conducted (N=3441). A physician reviewed and confirmed all final diagnoses. Confirmation of subarachnoid hemorrhage required documentation of rapid onset of headache, nuchal rigidity, nausea/ vomiting, with or without loss of consciousness or focal neurological deficit, plus one or more of: blood cerebrospinal fluid by nontraumatic lumbar puncture, either normal computerized tomography/magnetic resonance imaging or studies showing blood only in the subarachnoid space/ventricles, or surgery or autopsy showing blood only in the subarachnoid space/ventricles. Confirmation of ICH required rapid onset of focal neurological deficit, plus one or more of: only intraparenchymal hemorrhage on imaging study or surgery/autopsy showing only intraparenchymal hemorrhage. When historical data were incomplete, imaging tests and other clinical information were used to make a judgment about the diagnosis. PPV=77% for acute, classifiable events PPV=82% for chronic cerebrovascular disease or acute events Estimates calculated using data presented in the report.
Kokotailo, et al. (2005)[23]	patients with inpatient visits or seen at the emergency department identified from	hospitalizations and emergency department visits (acute ischemic stroke)	most responsible (primary position) diagnosis ICD-9 codes 433.x1,	Medical record review was conducted on a sample of charts (N=133 identified with ICD-9 codes and N=75 identified with ICD-10 codes). Outcome was confirmed based upon

	hospital discharge abstracts database from 3 acute care hospitals in the Calgary health region, 2000 to 2003		434.x1, 436, 362.8; ICD-10 codes I63.x, I64.x, H34.1	trained research assistant determination, and neurologist determination in ambiguous cases, considering physical examination notes, physician progress notes, CT and MRI reports (if available), and discharge summaries. Assessment of correct coding was based on clinical data alone in 24% of charts and on clinical data and neurovascular imaging reports in 76% of charts. ICD-9 coding: PPV=85% ICD-10 coding: PPV=85%
Lakshminarayan, et al. (2009)[24]	hospitalizations at all acute care hospitals serving the Minneapolis-St. Paul 7-county metropolitan area, 1980, 1985, 1990, 1995, 2000	hospitalizations (acute stroke)	inpatient discharge diagnoses ICD-9 codes 431, 432, 434, 436, 437	Medical record review was conducted (50% sample in 1980 to 1995 and 100% in 2000). Acute stroke was confirmed based upon 3 definitions: 1) WHO criteria, 2) Minnesota Stroke Survey (MSS) criteria (WHO criteria plus the presence of at least 1 major neurologic deficit or 2 minor neurologic deficits. Major deficits include aphasia, coma, visual field cut, and motor or sensory deficits in 1 or 3 (face, arm, leg) body parts. Minor deficits include dysarthria (slurred speech), motor or sensory deficits in 1 or 3 body parts, apraxia, and abnormal plantar reflex); 3) neuroimaging. 1980: WHO stroke definition, PPV=55%; MSS definition, PPV=36% 1985: WHO stroke definition, PPV=67%; MSS definition, PPV=47% 1990: WHO stroke definition, PPV=70%; MSS definition, PPV=41%; neuroimaging definition, PPV=49% 1995: WHO stroke definition, PPV=65%; MSS definition, PPV=45%; neuroimaging definition, PPV=45%

				2000: WHO stroke definition, PPV=60%; MSS definition, PPV=44%; neuroimaging definition, PPV=59%
Leibson, et al. (1994)[25]	hospital discharges among Olmstead County residents, 1970, 1980, 1989	hospitalizations (incident or recurrent stroke)	inpatient ICD-9-CM codes 430 to 438	Linkage to the Rochester Stroke Registry and medical record review was conducted. Outcome was confirmed by the registry or neurologist review, using the same criteria used in the Rochester Stroke Registry (Rochester Epidemiology Project). **primary discharge code**: codes 430-438: PPV=47% (incident stroke) PPV=60% (incident or recurrent stroke) **up to 3 discharge codes**: codes 430-438: PPV=43% (incident stroke) PPV=54% (incident or recurrent stroke) codes 430, 431, 433, 434, 436, 437: PPV=64% (incident stroke) PPV=79% (incident or recurrent stroke) **up to 5 discharge codes**: code 430: PPV=100% (incident stroke) code 431: PPV=74% (incident stroke) PPV=87% (incident or recurrent) code 432: PPV=0% (incident or recurrent) code 433: PPV=15% (incident stroke) PPV=15% (incident or recurrent) code 434: PPV=69% (incident stroke) PPV=85% (incident or recurrent) code 435: PPV=12% (incident stroke) PPV=15% (incident or recurrent) code 436: PPV=67% (incident stroke) PPV=86% (incident or recurrent) code 437: PPV=11% (incident stroke) PPV=22% (incident or recurrent) code 438: PPV=0% (incident or recurrent)
Liu, et al.	hospitalizations	hospitalizations	inpatient ICD-9	Medical record review was conducted

(1999)[27]	identified using the Saskatchewan Health Hospital Services Branch, 1990 to 1991	(acute stroke)	codes 430 to 438, 780.4, 780.0, 369.0 to 369.9, 342.0 to 342.9	(N=1494). Outcomes were confirmed based upon the criteria of the 1980 USA National Survey of Stroke (NSS), with an acute stroke considered for diagnostic certainty 'definite' or 'highly probable'. tertiary care hospitals, primary diagnosis: code 430: PPV=93% code 431: PPV=92% code 432: PPV=14% code 433: PPV=17% code 434.0: PPV=86% code 434.1 PPV=92% code 435: PPV=22% code 436: PPV=90% code 437: PPV=45% code 438: PPV= 17% codes 430-438: PPV=68% code 342: PPV=50% code 369: PPV=0% code 780: PPV=25% code 780.4: PPV=29% tertiary care hospitals, primary, secondary, or tertiary diagnosis: code 430: PPV=88% code 431: PPV=89% code 432: PPV=24% code 433: PPV=16% code 434.0: PPV=83% code 434.1 PPV=69% code 435: PPV=20% code 436: PPV=86% code 437: PPV=30% code 438: PPV= 7% codes 430-438: PPV=56% code 342: PPV=22% code 369: PPV=3% code 780: PPV=14%

				code 780.4: PPV=22% <u>community hospitals, primary diagnosis</u>:(fewer cases identified in community hospitals) code 430: PPV=0% code 431: PPV=33% code 432: PPV=67% code 433: no cases code 434.0: PPV=57% code 434.1 PPV=0% code 435: PPV=42% code 436: PPV=78% code 437: PPV=44% code 438: PPV= 0% codes 430-438: PPV=61% code 342: no cases code 369: no cases code 780: PPV=0% code 780.4: PPV=33% <u>community hospitals, primary, secondary, or tertiary diagnosis</u>: code 430: PPV=0% code 431: PPV=33% code 432: PPV=57% code 433: PPV=0% code 434.0: PPV=57% code 434.1 PPV=0% code 435: PPV=34% code 436: PPV=74% code 437: PPV=36% code 438: PPV= 7% codes 430-438: PPV=47% code 342: PPV=6% code 369: PPV=8% code 780: PPV=0% code 780.4: PPV=36%
Mayo, et al. (1993)[28]	hospitalizations identified from 5	hospitalizations (stroke)	inpatient discharge ICD-9	Medical record review was conducted (N=96 total charts: 87 charts by one

	acute-care hospitals in metropolitan Montreal, using MedEcho, Quebec's computerized listing of hospital discharges		codes 430 to 434, 436, 437	neurologist and 64 charts by another neurologist). Outcome was confirmed based upon documentation of neurological evidence, neuro-imaging, and other diagnoses ruled out. Neurologist 1: overall PPV= 80% code 430 PPV=100% code 431 PPV=100% codes 432 PPV=33% code 433 PPV=44% code 434 PPV=90% code 436 PPV=83% code 437 PPV=75% Neurologist 2: overall PPV= 72% code 430 PPV=100% code 431 PPV=100% codes 432 PPV=0% code 433 PPV=50% code 434 PPV=95% code 436 PPV=62% code 437 PPV=60%
Morgenstern, et al. (1999)[29]	residents of Nueces County, Texas, age 25 to 74 years hospitalized with AMI, CABG, or PTCA (Corpus Christi Health Project), 1988 to 1993	hospitalizations (stroke complication)	inpatient ICD-9 codes 430 to 437 during same hospital admission for AMI, PTCA, or CABG	Medical record review was conducted (N=161). A stroke complication following cardiac symptoms was confirmed based upon the National Institute of Neurological Disorders and Stroke Classification criteria. past/current stroke: PPV=53% current stroke after AMI, PTCA, or CABG all codes: PPV=44% code 430 to 432: PPV=50% code 433: PPV=10% code 434: PPV=67% code 435: PPV=73% code 436: PPV=76%

				code 437: PPV=18%
Newton, et al. (1999)[30]	Group Health Cooperative of Puget Sound members aged 18 and older with type 1 or type 2 diabetes, 1993 to 1995	incident or prevalent (stroke)	inpatient or outpatient ICD-9-CM codes 430, 431, 432.0, 432.1, 432.9, 434, 436; incident cases considered as those with code not present in 1992 (year before the observation period)	Medical record review was conducted among patients with multiple complications of diabetes (total N=471 and potential stroke N=118). Outcome was confirmed based upon the presence of a written diagnosis in the medical record. first confirmed date within 60 days of the automated record date: sensitivity=91.2% specificity=83.6% PPV=45.2% confirmed at any time during the observation period: sensitivity=92.3% specificity=85.4% PPV=52.2% selectively including patients with multiple complications for chart review may have influenced estimates
Reker, et al. (2001)[32]	patients receiving care at 11 Veterans Affairs medical centers, identified using the Patient Treatment File, 1998 to 1999	hospitalizations (new stroke)	admission or discharge primary diagnosis ICD-9 430.xx, 431.xx, 432.xx, 434.xx or 436.xx; admission or discharge primary diagnosis is V57.xx (Rehabilitation) and any secondary diagnosis ICD-9 342.xx (Hemiparesis), 430.xx, 431.xx, 432.xx, 433.xx, 434.xx, 435.xx, 436.xx, 437.xx or 438.xx; or admission or discharge primary diagnosis ICD-9 433.xx or 435.xx	Medical record review was conducted (N=671). Outcome was confirmed based upon documentation of a diagnosis of stroke. admission diagnosis: code 430.x: PPV=36% code 431.x: PPV=78% code 432.x: PPV=17% code 433.x0: PPV=7% code 433.x1: PPV=78% code 434.x0: PPV=43% code 434.x1: PPV=75% code 435.x: PPV=3% code 436.x: PPV=53% code 437.x: PPV=50% code 438.x: PPV=33% any codes: PPV=42% discharge diagnosis: code 430.x: PPV=33%

			and any secondary diagnosis code 342.xx, 430.xx, 431.xx, 432.xx, 434.xx, or 436.xx	code 431.x: PPV=80% code 432.x: PPV=21% code 433.x0: PPV=13% code 433.x1: PPV=71% code 434.x0: PPV=33% code 434.x1: PPV=72% code 435.x: PPV=3% code 436.x: PPV=48% code 437.x: PPV=100% code 438.x: PPV=33% any codes: PPV=42% broad, high sensitivity algorithm 1 (admission diagnosis, all codes/criteria specified in algorithm column): sensitivity=91% specificity=40% PPV=52% NPV=86% narrow, high-specificity algorithm 1 (admission diagnosis codes 431.x, 433.x1, 434.x1): sensitivity=54% specificity=87% PPV=75% NPV=73% broad, high sensitivity algorithm 2 (admission, discharge, and all secondary diagnosis fields, codes 430.x, 431.x, 432.x, 434.xx, and 436.x): sensitivity=89% specificity=57% PPV=60% NPV=88% narrow, high-specificity algorithm 2 (admission, discharge, and all secondary diagnosis fields, codes 431.x, 433.x1, 434.xx): sensitivity=59% specificity=84% PPV=72%

				NPV=74% codes 431, 434, and 436 were 'high-yielding' codes
Rosamond, et al. (1999)[33]	Atherosclerosis Risk in Communities (ARIC) Study participants, aged 45 to 64 years at baseline, 1987 to 1995	hospitalizations (stroke)	inpatient ICD-9-CM codes 430 to 438	Medical record review was conducted (N=1185). Minimum criteria for definite or probable stroke were evidence of sudden or rapid onset of neurological symptoms lasting for > 24 hours or leading to death, in the absence of evidence for a nonstroke cause. (excluded major brain trauma, neoplasm, coma due to metabolic disorders or disorders of fluid or electrolyte balance, vasculitis involving the brain, peripheral neuropathy, hematologic abnormalities, or central nervous system infections) Additional criteria were used to subtype definite or probable cases. code 430: PPV=86% code 431: PPV=83% code 432: PPV=9% code 433: PPV=14% code 434: PPV=77% code 435: PPV=12% code 436: PPV=70% code 437: PPV=2% code 438: PPV < 1% codes 430 to 434: PPV=44%
Roumie, et al. (2008)[34]	Tennessee Medicaid enrollees aged 50 to 84 years, 1999 to 2003. Patients with a stroke hospitalization, any cancer except non-melanoma skin cancer, liver failure, end stage renal disease, HIV infection, or organ transplant in the year prior to cohort entry were excluded from study.	hospitalizations (acute stroke)	discharge diagnosis of ischemic stroke (ICD-9-CM 433.x1, 434 [excluding 434.x0], or 436); intracerebral hemorrhage (431); and SAH (430). Hospitalizations with multiple stroke diagnoses were classified in the following priority: SAH > ICH > ischemic	Medical record review was conducted (200 NSAID users and 50 non-users of NSAIDs). Abstraction tool combined elements of the Reasons for Geographic and Racial Differences in Stroke Study (REGARDS)[43] endpoint morbidity review form and the Rochester, Minnesota Stroke study form. A physician investigator determined the presence of a stroke, defined as rapid onset of a persistent neurologic deficit attributed to an obstruction or rupture of the arterial system; the deficit was required to last > 24 hours unless death supervened, or demonstrable lesion on CT or MRI scan. In-hospital strokes were excluded, as were persons with a discharge diagnosis of traumatic brain injury, or brain tumor or infection. acute stroke:

			stroke	overall PPV=89% primary discharge diagnosis: PPV=97% secondary discharge diagnosis: PPV=32% true incident stroke (no history remote stroke): primary discharge diagnosis: PPV=74% excluding patients with a prior inpatient or outpatient diagnosis of stroke: primary discharge diagnosis: PPV=80%
Thompson, et al. (2004)[36]	patients who underwent a modified or radical neck dissection at any 3 of the adult hospital sites in Calgary identified using Calgary Health Region's centralized administrative hospital discharge database, 1994 to 2002. Patients who had undergone resection of the carotid artery were excluded.	hospitalizations, perioperative stroke (incident)	inpatient ICD-9-CM codes: 433.x, 434.x, 436, 438.x, 997.02, 997.00, 997.01, 997.09	Medical record review was conducted (N=7). Perioperative stroke was confirmed through documentation in chart. PPV=14%
Tirschwell, et al. (2002)[37]	hospitalizations for patients ≥ 20 years of age in Seattle, Washington, hospitals, identified using the Comprehensive Hospital Abstract Reporting System, 1990 to 1996.	hospitalizations (ischemic stroke)	inpatient ICD-9-CM codes 433.x1, 434, [excluding 434.x0], and 436; excluded cases if any codes for traumatic brain injury (ICD-9-CM 800-804, 850-854) or rehabilitation care (primary ICD-9-CM code V57) was present. Hospitalizations with multiple stroke diagnoses were classified in the	Medical record review was conducted (total N=147 and potential ischemic stroke N=50). Outcome was confirmed and classified by a stroke neurologist. Using all discharge codes: sensitivity=86% specificity=95% PPV=90% Using primary discharge code: sensitivity=74% specificity=95% PPV=88% sampling scheme for chart reviews may have influenced estimates of sensitivity and specificity

			following priority: SAH > ICH > ischemic stroke > TIA.	
Williams, et al. (2002)[38]	hospitalizations at Wishard Hospital, Indianapolis, IN, identified using the Regenstrief Medical Record System, 1993 to 1998.	hospitalizations (acute ischemic stroke)	primary position discharge diagnosis ICD-9 codes for acute ischemic stroke (434 and 436)	Medical record review was conducted (N=671). Criteria for confirmation of outcome was unspecified. PPV=98%

Table 4C. Positive Predictive Values by Algorithms to Identify Transient Ischemic Attack (TIA)

Citation	Study Population and Time Period	Description of Outcome Studied	Algorithm	Validation/Adjudication Procedure, Operational Definition, and Validation Statistics
Benesch, et al. (1997)[7]	hospitalizations at 5 academic medical centers identified using the Academic Medical Center Consortium database, 1992	hospitalizations (TIA)	inpatient ICD-9 codes 433 to 436	Medical record review was conducted (N=649). TIA was confirmed based upon the World Health Organization (WHO) definition. primary and secondary diagnoses: code 433: PPV=8.5%; code 434: PPV=5.3%; code 435: PPV=76.8%; code 436: PPV=3.4%; primary diagnosis: code 433: PPV=14.2%; code 434: PPV=5.9%; code 435: PPV=88.9%; code 436: PPV=5.6%;
Heckbert, et al. (2004)[17]	hospitalizations among women enrolled in the Women's Health Initiative (WHI), 1994 to 2000	hospitalizations (TIA)	TIA: ICD-9 code 435	Medical record review was conducted. Outcome was confirmed based upon WHI criteria for cardiovascular endpoints. PPV=72% sensitivity=73%
Holick, et al. (2009)[18]	adults aged 18 years or older who received a first dispensing of atomoxetine or stimulant ADHD	hospitalizations (TIA)	inpatient ICD-9 codes for TIA: 435.9x	Medical record review was conducted (N=83). Criteria for confirming a TIA event included a stated diagnosis of TIA from a neurologist or in the hospital discharge

	medication and comparison group identified using the Ingenix Research DataMart; excluded members with claims of history of arrhythmia or heart failure in 6 month baseline period), 2003 to 2006			summary or a description of the event that is consistent with a TIA diagnosis (i.e., sudden onset of rapid and complete resolution, relatively simultaneous involvement of all affected areas, and involvement of focal loss of neurologic function. PPV=28%
Ives, et al. (1995)[39]	Cardiovascular health Study: residents ≥ 65 years in Sacramento County, CA; Washington County, MD; Forsyth County, NC; Pittsburgh, PA , 1989 to 1992	hospitalizations (incident)	ICD-9-CM 435 in the discharge abstract	Medical record review was conducted (N=46). Outcome was confirmed based upon decision by an Events Committee (stroke subcommittee), considering documentation of medical history, symptoms, course, and outcome of each event. PPV=28% Estimate calculated using data presented in the report.
Kokotailo, et al. (2005)[23]	patients with inpatient visits or seen at the emergency department identified from hospital discharge abstracts database from 3 acute care hospitals in the Calgary health region, 2000 to 2003	hospitalizations and emergency department visits (TIA)	most responsible (primary position) diagnosis ICD-9 codes 435.x, ICD-10 G45.x	Medical record review was conducted on a sample of charts (N=37 identified with ICD-9 codes and N=60 identified with ICD-10 codes). Outcome was confirmed based upon trained research assistant determination, and neurologist determination in ambiguous cases, considering physical examination notes, physician progress notes, CT and MRI reports (if available), and discharge summaries. Cases were coded as TIA if they resolved within 24 hours of onset, and if imaging was performed, no detectable changes were evident. Assessment of correct coding was based on clinical data alone in 24% of charts and on clinical data and neurovascular imaging reports in 76% of charts. ICD-9 coding: PPV=70% ICD-10 coding: PPV=97%
Newton, et al. (1999)[30]	Group Health Cooperative of Puget Sound members aged 18 and older with type 1 or type 2 diabetes, 1993 to	incident or prevalent (TIA)	TIA: ICD-9-CM codes 435; incident cases considered as those with code not present in 1992 (year before the observation	Medical record review was conducted among patients with multiple complications of diabetes (N=471 total, N=33 potential TIAs). Outcome was confirmed based upon the presence of a written diagnosis in the medical record.

	1995		period)	first confirmed date within 60 days of the automated record date: sensitivity=61.1%; specificity=94.9%; PPV=33.3%; confirmed at any time during the observation period: sensitivity=66.7%; specificity=95.6%; PPV=42.2%; selectively including patients with multiple complications for chart review may have influenced estimates

Table 4D. Positive Predictive Values by Algorithms to Identify Intracranial Bleed (ICH) and Subarachnoid Hemorrhage (SAH)

Citation	Study Population and Time Period	Description of Outcome Studied	Algorithm	Validation/Adjudication Procedure, Operational Definition, and Validation Statistics
Arnason, et al. (2006)[40]	patients discharged from a university-associated teaching hospital in Ottawa, Canada, 1999 to 2000	hospitalizations (intracranial bleeds)	inpatient ICD-9-CM codes 430 to 432	Medical record review was conducted (N=78). Confirmation of 'definite bleeding' required at least one of the following: documentation of a direct visualization of blood by a physician; imaging consistent with bleeding; imaging of a bleeding source accompanied by signs of bleeding. PPV=94%
Birman-Deych, et al. (2005)[8]	Medicare beneficiaries who were hospitalized with atrial fibrillation identified using the National Registry of Atrial Fibrillation II dataset, including anonymous patient records gathered by the Quality Improvement/Peer Review Organization for the National Stroke Project, 1998	hospitalizations (intracranial hemorrhage)	inpatient ICD-9-CM codes: 430, 431, 432.x, 800.2, 800.3, 800.7, 800.8, 801.2, 801.3, 801.7, 801.8, 803.2, 803.3, 803.7, 803.8, 804.2, 804.3, 804.7, 804.8, 852.x, 853.x	Medical record review was conducted. Outcome was confirmed if there was documentation of a current intracranial hemorrhage. sensitivity=60% specificity > 99% PPV=77% NPV > 99%

	to 1999			
Kokotailo, et al. (2005)[23]	patients with inpatient visits or seen at the emergency department identified from hospital discharge abstracts database from 3 acute care hospitals in the Calgary health region, 2000 to 2003	hospitalizations and emergency department visits (SAH and ICH)	most responsible (primary position) diagnosis ICD-9 codes 430.x (SAH) and 431.x (ICH), ICD-10 codes I60.x (SAH), I61.x (ICH)	Medical record review was conducted on a sample of charts (N=76 ICH and 51 SAH identified with ICD-9 codes and N=67 ICH and 32 SAH identified with ICD-10 codes). Outcome was confirmed based upon trained research assistant determination, and neurologist determination in ambiguous cases, considering physical examination notes, physician progress notes, CT and MRI reports (if available), and discharge summaries. ICD-9 coding: ICH: PPV=97% SAH: PPV=98% ICD-10 coding: ICH: PPV=98% SAH: PPV=91%
Tirschwell, et al. (2002)[37]	hospitalizations for patients ≥ 20 years of age in Seattle, Washington, hospitals, identified using the Comprehensive Hospital Abstract Reporting System, 1990 to 1996.	hospitalizations (SAH and ICH)	inpatient ICD-9-CM codes for ICH (431) or SAH (430); excluded cases if any codes for traumatic brain injury (ICD-9-CM 800-804, 850-854) or rehabilitation care (primary ICD-9-CM code V57) was present. Hospitalizations with multiple stroke diagnoses were classified in the following priority: SAH > ICH > ischemic stroke > TIA.	Medical record review was conducted N=147 total, including N=39 potential ICH and N=51 potential SAH). Outcome was confirmed and classified by a stroke neurologist. Using all discharge codes: **ICH**: sensitivity=82% specificity=93% PPV=80% **SAH**: sensitivity=98% specificity=92% PPV=86% Using primary discharge code: **ICH**: sensitivity=85% specificity=96% PPV=89% **SAH**: sensitivity=90%

				specificity=97% PPV=94% sampling scheme for chart reviews may have influenced estimates of sensitivity and specificity

I. CLINICIAN OR TOPIC-EXPERT CONSULTATION

Cerebrovascular diseases encompass a diverse set of conditions related to the blood vessels supplying the brain. A stroke is defined specifically by the WHO as "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin." A TIA is defined as a sudden, focal neurologic deficit with symptoms lasting less than 24 hours, and patients with symptoms caused by subdural hemorrhage, tumors, poisoning, or trauma are excluded.[41]

Our classifications (stroke, TIA, stroke/TIA and cerebrovascular disease) were based on how the study authors identified their outcomes of interest. The authors of these papers used a variety of approaches. For example, some authors set out to identify patients with all types of cerebrovascular events including intracranial bleeds, while others chose to focus on ischemic strokes excluding bleeds. These varying approaches likely influenced PPVs and will impact on how useful these algorithms will be in future investigations. Included in the tables are algorithms that focused solely on ischemic strokes as well as those focused on bleeds (intracranial hemorrhage and subarachnoid hemorrhage). This level of detail may be helpful in categorizing subtypes of stroke based on pathophysiology, although there are still some limitations. For instance, no investigators to date have tried to differentiate ischemic strokes due to thrombosis versus emboli. Some authors chose to focus solely on TIAs. Given the "transient" nature of TIAs in that there are no lasting physical deficits or radiographic findings, it is not surprising that the PPVs were lower than those studies focused on stroke. Lastly, several authors used composite measures whereby a patient could have more than one condition. Some algorithms identified patients with either stroke or TIA or more broadly with cerebrovascular disease. In some studies it was unclear what specific conditions were included in the definition of the outcome of interest and this may substantially limit the usefulness of these algorithms.

The clinical usefulness of the algorithms presented in this report are best understood in light of the definitions of each of the various clinical entities, their pathological basis, and the health outcome of interest relevant to a specific post-marketing surveillance study. For example, the pathological basis for a stroke may relate to either ischemic or hemorrhagic disturbances of the cerebral circulation.[41,42] While ischemic strokes can be either thrombotic or embolic due to atherosclerosis or blood clots, hemorrhagic strokes are mainly due to hypertensive disease, coagulation disorders, or vascular malformations. Lacunar cerebral infarctions are small deep infarcts in the territory of small penetrating arteries, due to a local disease of these vessels, mainly related to chronic hypertension. Subarachnoid hemorrhages are mainly due to the rupture of aneurysms.

Since it is sometimes unclear exactly which subtype of stroke was included in studies included in the composite outcomes table, we recommend that investigators select algorithms that identify a condition as specifically as possible based on its pathogenesis, and are aligned with the postulated mechanism for the health outcome as it best relates to the medication or device under study.

Several studies included only patients with a certain medical condition (e.g., atrial fibrillation, diabetes) that may have affected the PPVs observed. However, the specific algorithms used (e.g., use of either inpatient and outpatient encounters or specific codes used), as well as the specific outcome assessed (e.g., in-hospital stroke) may account for these findings. In addition, PPVs may have been affected if different stroke subtypes were more prevalent in these populations. For example, patients diagnosed with atrial fibrillation might represent a population where the patients are at increased risk for embolic CVA (if inadequately anticoagulated) and at increased risk for intracranial bleed or hemorrhagic transformation of an embolic or thrombotic CVA (if supratherapeutic).

Other considerations to help refine existing algorithms include potential differences in the mortality rate for the various stroke subtypes before arrival to the hospital, differences in diagnostic work-ups between referral and community hospitals, and the expected follow-up and management of patients diagnosed with specific stroke subtypes.

VI. SUMMARY AND CONCLUSIONS

A. RECOMMENDATIONS FOR ALGORITHMS

Studies could be grouped into evaluations of composite endpoints (stroke/TIA or cerebrovascular disease), stroke exclusively, TIA exclusively, or intracerebral bleeds. While intracranial bleeds are included in a separate category, many studies identifying stroke and cerebrovascular disease evaluated algorithms that included codes for bleeds (i.e., ICD-9 code 430 for subarachnoid hemorrhage; ICD-9 code 431 for intracerebral hemorrhage).

For the composite endpoints, the highest PPV (96%) reported to identify patients with a history or current stroke/TIA included codes 433.x1, 434.x1, 435.x, 436, 437.1x, 437.9x, and 438.x.[8] The highest PPVs to identify acute cerebrovascular events included ICD-9 codes 430.x, 431.x, 433.x1, 434.x1, 435.x, 436, and 362.3 (PPV=90%) or ICD-10 codes I60.x to I64.x, H34.1, and G45.x (PPV=92%).[23] However, it may be more appropriate to evaluate the endpoints (stroke, TIA, and intracerebral bleeds) separately, as described below, in order to adequately assess the validity of specific algorithms and codes.

For stroke exclusively, studies reported the highest PPVs for inpatient ICD-9 codes 430.x, 431.x, 434.x, and 436.x. To identify acute ischemic stroke, algorithms that included ICD-9 codes 433.x1, 434 (excluding 434.x0) and 436, performed well (85% or higher). Use of codes in the principal position generally increased the PPVs slightly.

For TIA exclusively, ICD-9 codes 435.x in hospitalization or emergency encounter data generally demonstrated an adequate PPV (70% or higher).

While few studies evaluated intracranial bleeds exclusively, algorithms including hospitalization or emergency department visit codes 430.x and 431.x performed well for identification of SAH and ICH (PPVs ranging from 80% to 98%). While only one study evaluated an algorithm using inpatient ICD-9 codes 430.x to 432.x for identification of intracranial bleeds, the reported PPV was high (94%).

Studies evaluating stroke, TIA, or intracranial bleeds generally evaluated the validity of algorithms to identify acute events, rather than prevalent cerebrovascular disease. Since most acute events would be managed on an inpatient basis, use of algorithms incorporating hospitalization data only (excluding

outpatient data) would appear appropriate. There were a limited number of studies that evaluated prevalent cerebrovascular disease and these studies evaluated various different algorithms, making the assessment of the appropriateness of any specific algorithm difficult.

B. SUGGESTIONS FOR FUTURE RESEARCH BASED ON EVIDENCE GAPS

Gaps in the current literature include a lack of information on potential differences in the validity of algorithms according to patient age and sex. In addition, the validity of algorithms to further differentiate ischemic strokes due to thrombosis versus emboli has not been evaluated. Overall, comparison of the different algorithms using standard criteria would be most useful, as would the validation of incident versus incident/recurrent events. Lastly, very few validation studies have been conducted on ICD-10 codes or in men and women of different race/ethnicities. Evaluation of predictors of the validity of specific algorithms would potentially allow for correction of estimates of association in studies evaluating drug and device safety.

Large population-based administrative databases that include diagnosis data provide efficient sources of information to identify cases of acute CVAs and TIAs. A number of different algorithms for various stroke subtypes have been reported in the literature. The appropriateness and choice of the specific algorithm for drug and device safety research should not be made arbitrarily, but should have a sound biological rationale and take into account the study aims, population being studied, clinical practice related to the outcome of interest, and coding scheme in the specific health care system.

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VIII. APPENDICES

A. APPENDIX A: ABSTRACTS OF STUDIES INCLUDED IN EVIDENCE TABLE

Arnason T, Wells PS, van Walraven C, Forster AJ. Accuracy of coding for possible warfarin complications in hospital discharge abstracts. *Thromb Res*. 2006; 118(2): 253-62.

BACKGROUND: Hospital discharge abstracts could be used to identify complications of warfarin if coding for bleeding and thromboembolic events are accurate. OBJECTIVES: To measure the accuracy of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9CM) codes for bleeding and thromboembolic diagnoses. SETTING: University affiliated, tertiary care hospital in Ottawa, Canada. PATIENTS: A random sample of patients discharged between September 1999 and September 2000 with an ICD-9-CM code indicating a bleeding or thromboembolic diagnosis. METHODS: Gold-standard coding was determined by a trained chart abstractor using explicit standard diagnostic criteria for bleeding, major bleeding, and acute thromboembolism. The abstractor was blinded to the original coding. We calculated the sensitivity, specificity, positive, and negative predictive values of the original ICD-9CM codes for bleeding or thromboembolism diagnoses. RESULTS: We reviewed 616 medical records. 361 patients (59%) had a code indicating a bleeding diagnosis, 291 patients (47%) had a code indicating a thromboembolic diagnosis and 36 patients (6%) had a code indicating both. According to the gold standard criteria, 352 patients experienced bleeding, 333 experienced major bleeding, and 188 experienced an acute thromboembolism. For bleeding, the ICD-9CM codes had the following sensitivity, specificity, positive and negative predictive values [95% CI]: 93% [90-96], 88% [83-91], 91% [88-94], and 91% [87-94], respectively. For major bleeding, the ICD-9CM codes had the following sensitivity, specificity, positive and negative predictive values: 94% [91-96], 83% [78-87], 87% [83-90], and 92% [88-95], respectively. For thromboembolism, the ICD-9CM codes had the following sensitivity, specificity, positive and negative predictive values: 97% [94-99], 74% [70-79], 62% [57-68], and 98% [96-99], respectively. By selecting a sub-group of ICD-9CM codes for thromboembolism, the positive predictive value increased to 87%. CONCLUSION: In our centre, the discharge abstract could be used to identify and exclude patients hospitalized with a major bleed or thromboembolism. If coding quality for bleeding is similar in other hospitals, these ICD-9-CM diagnostic codes could be used to study population-based warfarin-associated hemorrhagic complications using administrative databases.

Benesch C, Witter DM Jr, Wilder AL, Duncan PW, Samsa GP, Matchar DB. Inaccuracy of the International Classification of Diseases (ICD-9-CM) in identifying the diagnosis of ischemic cerebrovascular disease. *Neurology*. 1997; 49(3): 660-4.

In administrative databases the International Classification of Diseases, Version 9, Clinical Modification (ICD-9-CM) is often used to identify patients with specific diagnoses. However, certain conditions may not be accurately reflected by the ICD-9 codes. We assessed the accuracy of ICD-9 coding for cerebrovascular disease by comparing ICD-9 codes in an administrative database with clinical findings ascertained from medical record abstractions. We selected patients with ICD-9 diagnostic codes of 433 through 436 (in either the primary or secondary positions) from an administrative database of patients hospitalized in five academic medical centers in 1992. Medical records of the selected patients were reviewed by trained medical abstractors, and the patients' clinical conditions during the admission (stroke, TIA, asymptomatic) were recorded, as well as any history of cerebrovascular symptoms. Results of the medical record review were compared with the ICD-9 codes from the administrative database. More than 85% of those patients with the ICD-9 code

433 were asymptomatic for the index admission. More than one-third of these asymptomatic patients did not undergo either cerebral angiography or carotid endarterectomy. For ICD-9 code 434, 85% of patients were classified as having a stroke and for ICD-9 code 435, 77% had TIAs. For code 436, 77% of patients were classified as having strokes. Limiting the identifying ICD-9 code to the primary position increased the likelihood of agreement with the medical record review. The ICD-9 coding scheme may be inaccurate in the classification of patients with ischemic cerebrovascular disease. Its limitations must be recognized in the analyses of administrative databases selected by using ICD-9 codes 433 through 436.

Birman-Deych E, Radford MJ, Nilasena DS, Gage BF. Use and effectiveness of warfarin in Medicare beneficiaries with atrial fibrillation. *Stroke*. 2006; 37: 1070-1074.

BACKGROUND AND PURPOSE: More than 2 million Americans have atrial fibrillation, and without antithrombotic therapy, their stroke rate is increased 5-fold. In randomized controlled trials, warfarin prevented 65% of ischemic strokes (hazard ratio [HR], 0.35; 95% CI, 0.26 to 0.48) compared with no antithrombotic therapy. However, the effectiveness of warfarin therapy outside of clinical trials is unknown, especially in black and Hispanic populations. Our goal was to quantify use of warfarin therapy, frequency of International Normalized Ratio monitoring, and effectiveness for stroke prophylaxis in Medicare beneficiaries with atrial fibrillation. METHODS: This was a cohort study of Medicare beneficiaries with atrial fibrillation who were hospitalized between March 1998 and April 1999 in all 50 US states. The primary outcome was incident hospitalizations for ischemic stroke based on validated International Classification of Diseases, 9th Revision, Clinical Modification codes. RESULTS: Two thirds of ideal anticoagulation candidates were prescribed warfarin on hospital discharge. In unadjusted analyses, the stroke rates per 100 patient years of warfarin therapy were 5.2 in (non-Hispanic) white Medicare beneficiaries, 10.6 in black beneficiaries, and 12.2 in Hispanic beneficiaries. After adjusting for comorbid conditions, warfarin prescription was more frequent and monitoring more regular in white Medicare beneficiaries than in black or Hispanic beneficiaries ($P<0.0001$). Warfarin use was associated with 35% fewer ischemic strokes (HR, 0.65; 95% CI, 0.55 to 0.76) compared with no antithrombotic therapy but was less effective in black and Hispanic beneficiaries (P for interaction=0.048). CONCLUSIONS: The use, monitoring, and effectiveness of warfarin therapy are suboptimal in Medicare beneficiaries, especially in black and Hispanic beneficiaries.

Borzecki AM, Wong AT, Hickey EC, Ash AS, Berlowitz DR. Identifying hypertension-related comorbidities from administrative data: what's the optimal approach? *Am J Med Qual*. 2004; 19(5): 201-6.

The objective was to determine the best strategy for identifying outpatients with hypertension-related diagnoses using Veterans Affairs (VA) administrative databases. We reviewed 1176 outpatient charts from 10 VA sites in 1999, taking the presence of 11 diagnoses relevant to hypertension management as the "gold standard" for identifying the comorbidity. We calculated agreement, sensitivity, and specificity for the chart versus several administrative data-based algorithms. Using 1999 data and requiring 1 administrative diagnosis, observed agreement ranged from 0.98 (atrial fibrillation) to 0.85 (hyperlipidemia), and kappas were generally high. Sensitivity varied from 38% (tobacco use) to 97% (diabetes); specificity exceeded 91% for 10 of 11 diagnoses. Requiring 2 years of data and 2 diagnoses improved most measures, with minimal sensitivity decrease. Agreement between the database and charts was good. Administrative data varied in its ability to identify all patients with a given diagnosis but identified accurately those without. The best strategy for case-finding required 2 diagnoses in a 2-year period.

Broderick J, Brott T, Kothari R, Miller R, Khoury J, Pancioli A, Gebel J, Mills D, Minneci L, Shukla R. The Greater Cincinnati/Northern Kentucky Stroke Study: preliminary first-ever and total incidence rates of stroke among blacks. *Stroke.* 1998; 29(2): 415-21.

BACKGROUND AND PURPOSE: The Greater Cincinnati/Northern Kentucky Stroke Study was designed to be the first large, population-based metropolitan study of temporal trends in stroke incidence rates and outcome within a biracial population. METHODS: We are identifying all hospitalized and autopsied cases of stroke and transient ischemic attack (TIA) among the 1.3 million inhabitants of a five-county region of Greater Cincinnati/Northern Kentucky for the period 7/1/93-6/30/94. We have already prospectively monitored for out-of-hospital stroke and TIAs for this same time period at 128 screening sites, including a random sample of all primary care physicians and nursing homes in the region. We have already identified all hospitalized and autopsied cases of stroke and TIA among blacks for 1/1/93-6/30/93 and report preliminary incidence rates for this 6-month period. RESULTS: The overall incidence rate for all first-ever hospitalized or autopsied stroke (excluding TIAs) among blacks in the Greater Cincinnati region was 288 per 100000 (95% CI, 250 to 325, age- and sex-adjusted to 1990 US population). The overall incidence rate for first-ever and recurrent stroke (excluding TIAs) was 411 per 100000 (95% CI, 366 to 456). By comparison, the overall incidence rate of first-ever stroke among whites in Rochester, Minn, during the period 1985-1989 was 179 per 100000 (95% CI, 164 to 194, age- and-sex adjusted to 1990 US population). The incidence rates among blacks in Greater Cincinnati were substantially greater than the rates among whites in Rochester, Minn, for all age categories except ages 75 and older, for which the rates were similar. CONCLUSIONS: We conservatively estimate that 731100 first-ever or recurrent strokes occurred in the United States during 1996. Studies of first-ever as well as total stroke among biracial and representative populations are critical for understanding temporal trends in the incidence rate and the burden of stroke in the US population.

Brophy MT, Snyder KE, Gaehde S, Ives C, Gagnon D, Fiore LD. Anticoagulant use for atrial fibrillation in the elderly. *J Am Geriatr Soc*. 2004; 52(7): 1151-6.

OBJECTIVES: To determine the influence of advanced age on anticoagulant use in subjects with atrial fibrillation and to explore the extent to which risk factors for stroke and contraindications to anticoagulant therapy predict subsequent use. DESIGN: Retrospective cohort study. SETTING: The Veterans Affairs Boston Healthcare System. PARTICIPANTS: A total of 2,217 subjects with nonvalvular atrial fibrillation. MEASUREMENTS: Administrative databases were use to identify subject's age, anticoagulant use, and the presence of a diagnosis of atrial fibrillation, cerebrovascular accident, hypertension, diabetes mellitus, congestive heart failure, or gastrointestinal or cerebral hemorrhage. RESULTS: Unadjusted analysis showed no difference in warfarin use between those aged 75 and older and younger subjects regardless of the presence (33.9% vs 35.7%, P=.37) or absence (33.4% vs 34.7%, P=.58) of contraindications to anticoagulant therapy. Multivariate modeling demonstrated a 14% reduction (95% confidence interval (CI)=4-22%) in anticoagulant use with each advancing decade of life. Intracranial hemorrhage was a significant deterrent (odds ratio (OR)=0.27 95% CI=0.06-0.85). History of hypertension (OR=2.90, 95% CI=2.15-3.89), congestive heart failure (OR=1.70, 95% CI=1.41-2.04), and cerebrovascular accident (OR=1.54, 95% CI=1.25-1.89) were significant independent predictors for anticoagulant use. CONCLUSION: Despite consensus guidelines to treat all atrial fibrillation patients aged 75 and older with anticoagulants, advancing age was found to be a deterrent to warfarin use. Better estimates of the risk:benefit ratio for oral anticoagulant therapy in older patients with atrial fibrillation are needed to optimize decision-making.

Derby CA, Lapane KL, Feldman HA, Carleton RA. Possible effect of DRGs on the classification of stroke: Implications for epidemiological surveillance. *Stroke*. 2001; 32: 1487-1491.

BACKGROUND AND PURPOSE: Accurate data on the distribution of stroke subtypes are essential for understanding the forces driving recent morbidity and mortality trends. The introduction of diagnosis-related groups (DRGs) in the 1980s may have affected the distribution of stroke subtypes as defined by International Classification of Diseases, Ninth Revision (ICD-9), discharge diagnosis codes. METHODS: The Pawtucket Heart Health Program cardiovascular surveillance data were used to examine trends in stroke classification for 1980 to 1991 in relation to the introduction of DRGs in 2 communities in Massachusetts and Rhode Island, where DRGs were implemented 2 years apart. Included were all hospital discharges for residents aged 35 to 74 with a primary ICD-9 diagnosis of 431 to 432, 434, or 436 to 437 (N=1386 in Rhode Island, N=1839 in Massachusetts). RESULTS: In each state, concurrently with the introduction of DRGs, the proportion of strokes classified as cerebral occlusion (ICD-9 434.0 to 434.9) increased, and the proportion classified as acute but ill-defined (ICD-9 436.0 to 436.9) decreased. Before DRGs, 30.0% of strokes in Rhode Island and 26.6% in Massachusetts were classified as cerebral occlusion, whereas 51.8% in Rhode Island and 51.7% in Massachusetts were classified as acute ill defined. After DRGs were instituted, the proportions of cerebral occlusion and acute, ill-defined stroke, respectively, were 70.9% and 8.5% in Rhode Island and 74.1% and 7.7% in Massachusetts (chi(2), all P<0.001). The proportions of strokes classified as intracerebral hemorrhage or transient cerebral ischemia remained constant. CONCLUSIONS: The implementation of DRGs may have influenced coding of strokes to the ICD-9. Findings highlight the limitations of hospital discharge data for evaluating stroke subtypes and demonstrate the need for community-based surveillance for monitoring specific trends in stroke.

Derby CA, Lapane KL, Feldman HA, Carleton RA. Trends in validated cases of fatal and nonfatal stroke, stroke classification, and risk factors in southeastern New England, 1980 to 1991: Data from the Pawtucket Heart Health Program. *Stroke*. 2000; 31: 875-881.

BACKGROUND AND PURPOSE: Recent US data suggest there is a slowing of the decline in stroke mortality rates, accompanied by a constant morbidity rate. Hospital discharge rates for patients with stroke are influenced by numerous factors, and community-based surveillance data for validated cases are rare. Thus, reasons for the observed trends remain unclear. In the present study, we examined trends in validated cases of stroke for 1980 to 1991 in the combined populations of the Pawtucket Heart Health Program study communities and examined concomitant trends in classification, use of diagnostic procedures, and levels of risk factors. METHODS: Discharges for residents aged 35 to 74 years with International Classification of Diseases, Ninth Revision codes 431, 432, and 434 to 437 were identified through retrospective surveillance. A physician reviewed the medical records to validate case status. RESULTS: Between 1980 and 1991, 2269 discharges were confirmed as representing definite or probable strokes (59.5% of 3811 cases reviewed). The fatal stroke rate declined (P<0.005) and the nonfatal stroke rate remained constant in both sexes. Case-fatality rates declined significantly (P=0.003), and among strokes, the relative odds of death in 1990 versus 1980 was 0.50 (95% CI 0.34 to 0.72). The proportion of stroke discharges in which the patient received a CT scan or MRI increased 120%, and fewer strokes were classified as ill defined. Hypertension prevalence, treatment, and control rates remained constant in these populations. CONCLUSIONS: Although causes for the observed trends remain unclear, results suggest that the decline in mortality rates is due to improved survival rates for patients with stroke. However, constant morbidity rates combined with constant rates of hypertension highlight the need for improved prevention to reduce the impact of stroke.

Goldstein LB. Accuracy of ICD-9-CM coding for the identification of patients with acute ischemic stroke: Effect of modifier codes. *Stroke*. 1998; 29: 1602-1604.

BACKGROUND AND PURPOSE: Discharge ICD-9-CM (International Classification of Diseases, 9th Revision, Clinical Modification) codes have been used to identify patients with acute stroke for epidemiological, quality of care, and cost studies. The aim of this study was to determine if the accuracy of the primary ICD-9-CM codes for ischemic stroke is improved by modifier codes and how specific codes reflect stroke subtype diagnoses. METHODS: Available hospital charts for all patients discharged from a single hospital between May 1995 and June 1997 with ICD-9-CM codes 433 (occlusion and stenosis of precerebral arteries), 434 (occlusion of cerebral arteries), or 436 (acute but ill-defined cerebrovascular disease) listed in the first position were reviewed. The primary discharge diagnosis was verified, and a presumed stroke subtype was assigned on the basis of information provided in the medical record. RESULTS: Charts were available for 175 of the 198 identified patients (88%). Of these, 61% had an acute ischemic stroke (code 433, 4%; 434, 82%; 436, 79%) with the remaining patients having other conditions. Of the 130 patients with a modifier code indicating cerebral infarction, 79% had an acute stroke; of the 45 patients with a modifier code indicating an absence of cerebral infarction, 7% had acute stroke (sensitivity, 0.97; specificity, 0.60). The codes with the highest proportions of ischemic stroke cases were 434.11 (embolic occlusion of cerebral arteries with infarction, 85%), 434.91 (unspecified occlusion of precerebral arteries with infarction, 82%), and 436 (79%), with a combined sensitivity of 0.81 and specificity of 0.90. On review, 73% of patients with code 434.11 had embolic strokes, and 47% of those with code 436 had an identified stroke cause. Of patients with code 434.91, 39% had stroke of uncertain cause, 25% "lacunar," 17% atherothrombosis, and 15% embolism. CONCLUSIONS: Despite the use of modifier codes, 15% to 20% of patients with the indicated primary ICD-9-CM codes have conditions other than acute ischemic stroke. Although the proportion of patients with acute stroke increased from 61% to 79% with the use of modifier codes, the inclusion of modifier codes did not have an appreciable effect on the accuracy of the coding if patients with code 433 are excluded. Assignment of presumed ischemic stroke subtype is particularly inaccurate.

Golomb MR, Garg BP, Saha C, Williams LS. Accuracy and yield of ICD-9 codes for identifying children with ischemic stroke. *Neurology*. 2006; 67: 2053-2055.

The medical records of all children at our hospital with International Classification of Diseases 9th revision (ICD-9) codes 342, 433 to 438, or 767 from May 1999 to May 2004 were reviewed to assess whether they had stroke (any type) or, specifically, arterial ischemic stroke (AIS). Code accuracy ranged from 37 to 88%; each code missed more than half of AIS identified by the combined code search. Studies are needed to determine whether other local and national ICD-9 databases have similar limitations.

Golomb MR, Garg BP, Williams LS. Accuracy of ICD-9 codes for identifying children with cerebral sinovenous thrombosis. *J Child Neurol*. 2007; 22: 45-48.

Childhood sinovenous thrombosis is rare, making it difficult to study; International Classification of Diseases, ninth revision (ICD-9), code searches across multiple hospitals would permit the identification of large numbers of children with sinovenous thrombosis. However, the accuracy of these codes for identifying childhood sinovenous thrombosis has not been established. We performed a retrospective search of admissions records for Riley Hospital for Children in Indianapolis, Indiana, from January 1999 to June 2005 using ICD-9 codes 325 (cerebral sinovenous thrombosis, excluding nonpyogenic cases and cases associated with pregnancy and the puerperium), 437.6 (cerebral venous thrombosis of nonpyogenic origin), and 671.5 (cerebral venous

thrombosis in pregnancy or the puerperium) in any position. During this period, there were 47042 admissions. ICD-9 code 325 identified 61 admissions on 56 children. Only 13% were of pyogenic origin. Fifty-two (92.9%) had "possible, probable, or definite" sinovenous thrombosis, but only 76.9% of those had "probable or definite" sinovenous thrombosis. Uncertainty in diagnoses stemmed from limitations in imaging and disagreement over interpretation of imaging studies. ICD-9 code 325 in the primary position identified 7 children; all had possible (n = 1), probable (n = 1), or definite (n = 5) sinovenous thrombosis. ICD-9 code 437.6 identified a single admission on a single case of probable cerebral venous thrombosis; it was unclear whether this case was "nonpyogenic." ICD-9 code 671.5 did not identify any children. ICD-9 code 325 is useful for identifying children likely to have sinovenous thrombosis, but it is not useful for differentiating pyogenic and nonpyogenic cases, and uncertainty in clinical diagnosis makes it difficult to gauge the true accuracy. Furthermore, it is important to search for the code in any position as limiting searches to the primary position misses most cases.

Heckbert SR, Kooperberg C, Safford MM, Psaty BM, Hsia J, McTiernan A, Gaziano JM, Frishman WH, Curb JD. Comparison of self-report, hospital discharge codes, and adjudication of cardiovascular events in the Women's Health Initiative. *Am J Epidemiol*. 2004; 160(12): 1152-8.

Limited information is available from large clinical investigations about the agreement among sources of diagnoses for endpoints. The authors used data from the Women's Health Initiative clinical trials and observational study from January 1994 to November 2000 to evaluate the agreement among self-report, hospital discharge codes, and two different levels of physician review of medical records for cardiovascular endpoints. For myocardial infarction, stroke, pulmonary embolism, and venous thrombosis, the agreement of hospital discharge codes or self-report with review by study physicians at clinical centers was substantial (kappa = 0.64-0.84). For coronary revascularization, agreement among these sources of information was substantial to almost perfect (kappa = 0.79-0.92), but for angina, congestive heart failure, and peripheral vascular disease, concordance was only fair to moderate (kappa = 0.37-0.56), indicating that these endpoints remain difficult to classify reliably. Agreement between physician adjudicators at clinical centers and central physician adjudicators was substantial to almost perfect (kappa = 0.67-0.94). The findings also suggest that, for the endpoint of myocardial infarction, physician review of events with hospital discharge codes for angina and congestive heart failure is an important source of validated events, and for stroke, review of all events with cerebrovascular codes is important.

Holick CN, Turnbull BR, Jones ME, Chaudhry S, Bangs ME, Seeger JD. Atomoxetine and cerebrovascular outcomes in adults. *J Clin Psychopharmacol*. 2009; 29: 453-460.

OBJECTIVE: The aim of this study was to estimate the association between atomoxetine and cerebrovascular accident (CVA) and transient ischemic attack (TIA) in adults. METHODS: This cohort study conducted within a health insurance database included 21,606 atomoxetine initiators matched to 21,606 stimulant attention-deficit/hyperactivity disorder (ADHD) medication initiators on the basis of propensity scores and a sample from the source population (N = 42,993). Outcomes were confirmed through a medical record review or a National Death Index search. Poisson regression was used to estimate the rate ratio and 95% confidence interval (CI) of CVA or TIA according to the treatment. Cox regression was used to estimate the hazards ratio (HR) and 95% CI for comparisons across cohorts. RESULTS: Forty-four CVAs and 21 TIAs occurred during a mean follow-up of 1.5 years. The rate ratio of the current atomoxetine compared with the current stimulant ADHD medication was 1.38 for CVA (95% CI, 0.42-4.54) and 0.31 for TIA (95% CI, 0.04-2.63). Results for atomoxetine compared with the stimulant ADHD medication according to initial

cohort assignment were consistent, with no increased risk for CVA or TIA. An increased risk of TIA was observed between initiation of an ADHD medication compared with the general population (HR, 3.44; 95% CI, 1.13-10.60); however, a similar pattern was not observed for CVA (HR, 0.71; 95% CI, 0.34-1.47). CONCLUSIONS: These results do not support an increased risk of CV events with atomoxetine compared with the stimulant ADHD medication. Users of ADHD medications may be at an increased risk of TIA compared with the general population.

Humphries KH, Rankin JM, Carere RG, Buller CE, Kiely FM, Spinelli JJ. Co-morbidity data in outcomes research: are clinical data derived from administrative databases a reliable alternative to chart review? *J Clin Epidemiol*. 2000; 53(4): 343-9.

Evaluation of co-morbidity data is essential in health outcomes research. Co-morbidity data derived from administrative databases has been criticized for lacking the accuracy required for clinical research. We compared co-morbidity data derived from a Canadian provincial hospitalization database with chart review in 817 adults treated with a percutaneous coronary intervention at a single tertiary care hospital between 1994 and 1995. While the administrative database tended to under-estimate the prevalence of some co-morbid conditions, the agreement between chart review and administrative data was good to very good for most conditions. Asymptomatic conditions were noted to have lower levels of agreement. Multivariate risk models for all-cause mortality constructed from both data sources were almost identical, suggesting minimal misclassification. The results indicate that clinical data abstracted from most Canadian hospitalization databases can provide reliable information regarding baseline co-morbid conditions believed to influence survival in a population undergoing percutaneous coronary interventions.

Iribarren C, Jacobs DR, Sadler M, Claxton AJ, Sidney S. Low total serum cholesterol and intracerebral hemorrhagic stroke: Is the association confined to elderly men? The Kaiser Permanente Medical Care Program. *Stroke*. 1996; 27: 1993-1998.

BACKGROUND AND PURPOSE: Epidemiological studies indicate a higher incidence of intracerebral (but not subarachnoid) hemorrhagic stroke among persons with low total serum cholesterol levels. This report further examines the prospective relationship of total serum cholesterol with subsequent intracerebral hemorrhage in a large, well-defined population. METHODS: The cohort included 61756 enrollees in a health plan from the San Francisco-Oakland metropolitan area (46% men, 63% white), aged 40 to 89 years and free of cardiovascular disease at baseline. Sixteen-year incidence of combined nonfatal and fatal intracerebral hemorrhagic stroke (International Classification of Diseases [ICD], 8th revision, code 431, or ICD, 9th revision, codes 431 and 432) was investigated in relation to serum cholesterol measured in multiphasic health checkups made in 1977 through 1985. Intracerebral hemorrhagic events were ascertained using hospital discharge records and as underlying cause of death by the California Mortality Linkage Information System. RESULTS: From 1978 through 1993 (average of 10.7 years), there were 386 events (201 in men, 29% fatal; 185 in women, 42% fatal). By multivariate proportional hazards life-table regression analysis, serum cholesterol level below the sex-specific 10th percentile (< 4.62 mmol/L [178 mg/dL] in men), compared with higher cholesterol level, was associated with a significantly increased risk of intracerebral hemorrhage in men aged 65 years or older (relative risk, 2.7; 95% confidence interval, 1.4 to 5.0). An excess risk was also observed among elderly women at the lowest cholesterol range, but a chance finding could not be ruled out. No relationship was seen among men or women aged 40 to 64, and no statistical interaction of low serum cholesterol with hypertension was found in either sex. CONCLUSIONS: In these data, the association between low serum cholesterol level and intracerebral hemorrhage was confined to elderly men.

Ives DG, Fitzpatrick AL, Bild DE, Psaty BM, Kuller LH, Crowley PM, Cruise RG, Theroux S. Surveillance and ascertainment of cardiovascular events. The Cardiovascular Health Study. *Ann Epidemiol*. 1995; 5: 278-85.

While previous prospective multicenter studies have conducted cardiovascular disease surveillance, few have detailed the techniques relating to the ascertainment of and data collection for events. The Cardiovascular Health Study (CHS) is a population-based study of coronary heart disease and stroke in older adults. This article summarizes the CHS events protocol and describes the methods of surveillance and ascertainment of hospitalized and nonhospitalized events, the use of medical records and other support documents, organizational issues at the field center level, and the classification of events through an adjudication process. We present data on incidence and mortality, the classification of adjudicated events, and the agreement between classification by the Events Subcommittee and the medical records diagnostic codes. The CHS techniques are a successful model for complete ascertainment, investigation, and documentation of events in an older cohort.

Jollis JG, Ancukiewicz M, DeLong ER, Pryor DB, Muhlbaier LH, Mark DB. Discordance of databases designed for claims payment versus clinical information systems. Implications for outcomes research. *Ann Intern Med*. 1993; 119(8): 844-50.

OBJECTIVE: To determine the suitability of insurance claims information for use in clinical outcomes research in ischemic heart disease. DESIGN: Concordance study of two databases. SETTING: Tertiary care referral center. PATIENTS: A total of 12,937 consecutive patients hospitalized for cardiac catheterization for suspected ischemic heart disease between July 1985 and May 1990. INTERVENTIONS: Two-by-two tables were used to compute overall and kappa measures of agreement comparing clinical versus claims data for 12 important predictors of prognosis in patients with ischemic heart disease. MEASUREMENTS: Kappa statistics (agreement adjusted for chance agreement) were used to quantify agreement rates. RESULTS: Agreement rates between the clinical and claims databases ranged from 0.83 for the diagnosis of diabetes to 0.09 for the diagnosis of unstable angina (kappa values). Claims data failed to identify more than one half of the patients with prognostically important conditions, including mitral insufficiency, congestive heart failure, peripheral vascular disease, old myocardial infarction, hyperlipidemia, cerebrovascular disease, tobacco use, angina, and unstable angina, when compared with the clinical information system. CONCLUSIONS: Our results suggest that insurance claims data lack important diagnostic and prognostic information when compared with concurrently collected clinical data in the study of ischemic heart disease. Thus, insurance claims data are not as useful as clinical data for identifying clinically relevant patient groups and for adjusting for risk in outcome studies, such as analyses of hospital mortality.

Klatsky AL, Friedman GD, Sidney S, Kipp H, Kubo A, Armstrong MA. Risk of hemorrhagic stroke in Asian American ethnic groups. *Neuroepidemiology*. 2005; 25: 26-31.

The sparseness of prospective data about hemorrhagic stroke (HS) risk among Asian American ethnic groups led to the investigation of 128,934 persons with self-classified ethnicity at health examinations in 1978-1985. Subsequently, 431 persons were hospitalized for HS; 31% for subarachnoid hemorrhage (SAH) and 69% for intracerebral hemorrhage (ICH). Ethnic predictors of HS were studied by Cox proportional hazard models with 7 covariates. With whites as reference, the adjusted relative risk (95% CI) of all Asians for HS was 1.6 (1.1-2.3, p = 0.01), due substantially to increased risks of SAH in Japanese people and ICH in Filipinos. These data mandate emphasis upon preventive measures in these groups.

Kokotailo RA, Hill MD. Coding of stroke and stroke risk factors using international classification of diseases, revisions 9 and 10. *Stroke*. 2005; 36: 1776-1781.

BACKGROUND AND PURPOSE: Surveillance is necessary to understand and meet the future demands stroke will place on health care. Administrative data are the most accessible data source for stroke surveillance in Canada. The International Classification of Diseases, 10th revision (ICD-10) coding system has potential improvements over ICD-9 for stroke classification. Our purpose was to compare hospital discharge abstract coding using ICD-9 and ICD-10 for stroke and its risk factors. METHODS: We took advantage of a switch in coding systems from ICD-9 to ICD-10 to independently review stroke patient charts. From time periods April 2000 to March 2001, 717 charts, and from April 2002 to March 2003, 249 charts were randomly selected for review. Using a before-and-after time period design, the accuracy of hospital coding of stroke (part I) and stroke risk factors (part II) using ICD-9 and ICD-10 was compared. We used careful definitions of stroke and its types based on ICD-9 using the fourth and fifth digit modifier codes. RESULTS: Stroke coding was equally good with ICD-9 (90% [CI95 86 to 93] correct) and ICD-10 [92% (CI95 88 to 95 correct) with ICD-10. There were some differences in coding by stroke type, notably with transient ischemic attack, but these differences were not statistically significant. Atrial fibrillation, coronary artery disease/ischemic heart disease, diabetes mellitus, and hypertension were coded with high sensitivity (81% to 91%) and specificity (83% to 100%). ICD-10 was as good as ICD-9 for stroke risk factor coding. CONCLUSIONS: Passive surveillance using administrative data are a useful tool for identifying stroke and its risk factors using both ICD-9 and ICD-10.

Lakshminarayan K, Anderson DC, Jacobs DR Jr, Barber CA, Luepker RV. Stroke rates: 1980-2000: The Minnesota Stroke Survey. *Am J Epidemiol*. 2009; 169: 1070-1078.

In this paper, the authors report trends in hospitalized stroke rates among Minneapolis-St. Paul, Minnesota (population 2.6 million) metropolitan area residents aged 30-74 years from 1980 to 2000. Cases were identified from lists of discharge diagnoses provided by hospitals serving the target population. Age-adjusted, sex-specific stroke attack rates were computed for each survey year by using 5 different diagnostic definitions: 2 based purely on International Classification of Diseases, Ninth Revision (ICD-9) codes and 3 including clinical and neuroimaging criteria. Stroke rates, as measured by a highly specific clinical definition, remained stable from 1980 to 2000 for women. For men, these rates declined modestly from 1980 to 1990 and leveled off during 1990-2000. In contrast, use of stroke-related ICD-9 discharge codes declined significantly from 1980 to 2000: 35% among men and 16% among women. Neuroimaging use increased significantly from 75% of cases in 1980 to 98% in 2000. Short-term (28-day) stroke survival improved significantly, by 16% for women and 12% for men, from 1980 to 2000. The decline in stroke ICD-9 code usage reflects the influence of increased neuroimaging on discharge coding. The improved short-term survival in the face of stable, clinically defined stroke rates may imply treatment advances or ascertainment of less severe strokes, possibly masking a true decline in stroke rates.

Leibson CL, Naessens JM, Brown RD, Whisnant JP. Accuracy of hospital discharge abstracts for identifying stroke. *Stroke*. 1994; 25(12): 2348-55.

BACKGROUND AND PURPOSE: Much of the available data on stroke occurrence, service use, and cost of care originated with hospital discharge abstracts. This article uses the unique resources of the Rochester Epidemiology Project to estimate the sensitivity and positive predictive value of hospital discharge abstracts for incident stroke. METHODS: The Rochester Stroke Registry was used to identify all confirmed first strokes (hospitalized and nonhospitalized) among Rochester residents

for 1970, 1980, 1984, and 1989 (n = 364). The sensitivity of discharge abstracts was estimated by following these individuals for 12 months after stroke to determine the proportion assigned a discharge diagnosis of cerebrovascular disease (International Classification of Diseases [ICD] codes 430 through 438.9). The positive predictive value of discharge abstracts was assessed by identifying all hospitalizations of Rochester residents with an ICD code of 430-438.9 in 1970, 1980, and 1989 (n = 377). Events were categorized as incident stroke, recurrent stroke, stroke sequelae, or nonstroke after review of the complete community-based medical record by a neurologist. RESULTS: Only 86% (n = 313) of all first-stroke patients in 1970, 1980, 1984, and 1989 were hospitalized. Of hospitalized patients, only 76% were assigned a principal discharge diagnosis code of 430-438.9. Fatal strokes and those occurring during a hospitalization were less likely to be identified. Among all hospitalizations of Rochester residents in 1970, 1980, and 1989, there were 377 with a principal diagnosis code of 430-438.9. Less than half (n = 177) were determined by the neurologist to be incident stroke; only 60% (n = 225) were either incident or recurrent stroke. Comparison of alternative approaches showed the validity of discharge abstracts was enhanced by increasing the number of diagnoses and excluding codes with poor positive predictive value. CONCLUSIONS: This study provides previously unavailable estimates of the sensitivity of stroke-coded hospitalizations for a US community. A model for improving the sensitivity and positive predictive value of discharge abstracts is presented.

Lentine KL, Schnitzler MA, Abbott KC, Bramesfeld K, Buchanan PM, Brennan DC. Sensitivity of billing claims for cardiovascular disease events among kidney transplant recipients. *Clin J Am Soc Nephrol*. 2009 Jul; 4(7): 1213-21.

BACKGROUND AND OBJECTIVES: Billing claims are increasingly examined beyond administrative functions as outcomes measures in observational research. Few studies have described the performance of billing claims as surrogate measures of clinical events among kidney transplant recipients. DESIGN, SETTING, PARTICIPANTS, & MEASUREMENTS: We investigated the sensitivity of Medicare billing claims for clinically verified cardiovascular diagnoses (five categories) and procedures (four categories) in a novel database linking Medicare claims to electronic medical records of one transplant program. Cardiovascular events identified in medical records for 571 Medicare-insured transplant recipients in 1991 through 2002 served as reference measures. RESULTS: Within a claims-ascertainment period spanning +/-30 d of clinically recorded dates, aggregate sensitivity of single claims was higher for case definitions incorporating Medicare Parts A and B for diagnoses and procedures (90.9%) compared with either Part A (82.3%) or Part B (84.6%) alone. Perfect capture of the four procedures was possible within +/-30 d or with short claims window expansion, but sensitivity for the diagnoses trended lower with all study algorithms (91.2% with window up to +/-90 d). Requirement for additional confirmatory diagnosis claims did not appreciably reduce sensitivity. Sensitivity patterns were similar in the early compared with late periods of the study. CONCLUSIONS: Combined use of Medicare Parts A and B billing claims composes a sensitive measure of cardiovascular events after kidney transplant. Further research is needed to define algorithms that maximize specificity as well as sensitivity of claims from Medicare and other insurers as research measures in this population.

Liu L, Reeder B, Shuaib A, Mazagri R. Validity of stroke diagnosis on hospital discharge records in Saskatchewan, Canada: implications for stroke surveillance. *Cerebrovasc Dis*. 1999; 9(4): 224-30.

This study examines the validity of the diagnosis of stroke on hospital discharge records in Saskatchewan, Canada. In total, 1,494 records with a discharge diagnosis of 'stroke' or a 'stroke-related condition' were reviewed. The clinical algorithm of the 1980 USA National Survey of Stroke

was considered the 'gold standard'. The positive predictive value of a primary diagnosis of stroke in the tertiary-care hospitals was about 90%. In community hospitals the majority of stroke cases were coded as ICD9 436 in which the positive predictive value was 78%. The variation between regions would limit the use of hospital discharge data for stroke surveillance.

Mayo NE, Danys I, Carlton J, Scott SC. Accuracy of hospital discharge coding for stroke. *Can J Cardiol*. 1993; 9(supplement D): 121D-124D.

[no abstract]

Morgenstern LB, Pandey DK, Smith MA, Ramsey D, Labarthe DR, Nichaman MZ. Greater stroke rate during hospitalization for acute heart disease among Mexican Americans than non-Hispanic whites. *Neuroepidemiology*. 1999; 18: 241-247.

BACKGROUND AND PURPOSE: This study compared the risk for stroke during acute myocardial infarction (AMI), percutaneous transluminal coronary angioplasty (PTCA) and coronary artery bypass grafting (CABG) between Mexican Americans (MAs) and non-Hispanic whites. METHODS: We examined the age-specific rate ratios (RR) of acute stroke during hospitalization for AMI, CABG and PTCA in a population-based study in Corpus Christi, Tex. by searching the cardiac surveillance data for ICD-9 codes for stroke (430-437). ICD-9 stroke codes were validated by comparing medical chart abstraction with ICD-9 discharge diagnoses. RESULTS: Stroke codes were found in 220 of the 5,697 admissions for AMI, CABG and PTCA. In the 45- to 59-year age-group MAs had a RR of 2.66 (95% CI 1.36-5.23) relative to non-Hispanic whites. In the 60- to 74-year age-group the RR was 1.52 (95% CI 1.11-2.08). There were no significant differences in the 25- to 44-year age-group. These ethnic relationships were found in nondiabetics but not in diabetics. Women in the 45- to 59-year age-group had a RR of 1.88 (95% CI 1.09-3.25) compared with men, but there were no significant sex differences in the 25- to 44- or 59- to 74-year age-groups. Stroke ICD-9 codes have a poor positive predictive value for acute stroke ranging from 10 to 76%. The stroke misclassifications were nondifferential with respect to ethnicity or sex. CONCLUSIONS: MAs have a higher stroke rate complicating acute heart disease in Corpus Christi. A rigorous stroke surveillance project is needed to study the burden of stroke in MAs, the United States' largest Hispanic population.

Newton KM, Wagner EH, Ramsey SD, McCulloch D, Evans R, Sandhu N, Davis C. The use of automated data to identify complications and comorbidities of diabetes: a validation study. *J Clin Epidemiol*. 1999; 52(3): 199-207.

We evaluated the accuracy of administrative data for identifying complications and comorbidities of diabetes using International Classification of Diseases, 9th edition, Clinical Modification and Current Procedural Terminology codes. The records of 471 randomly selected diabetic patients were reviewed for complications from January 1, 1993 to December 31, 1995; chart data served to validate automated data. The complications with the highest sensitivity determined by a diagnosis in the medical records identified within +/-60 days of the database date were myocardial infarction (95.2%); amputation (94.4%); ischemic heart disease (90.3%); stroke (91.2%); osteomyelitis (79.2%); and retinal detachment, vitreous hemorrhage, and vitrectomy (73.5%). With the exception of amputation (82.9%), positive predictive value was low when based on a diagnosis identified within +/-60 days of the database date but increased with relaxation of the time constraints to include confirmation of the condition at any time during 1993-1995: ulcers (88.5%); amputation (85.4%); and retinal detachment, vitreous hemorrhage and vitrectomy (79.8%). Automated data are useful for ascertaining potential cases of some diabetic complications but require confirmatory evidence when they are to be used for research purposes.

Piriyawat P, Smajsová M, Smith MA, Pallegar S, Al-Wabil A, Garcia NM, Risser JM, Moyé LA, Morgenstern LB. Comparison of active and passive surveillance for cerebrovascular disease: The Brain Attack Surveillance in Corpus Christi (BASIC) Project. *Am J Epidemiol*. 2002; 156(11): 1062-9.

To provide a scientific rationale for choosing an optimal stroke surveillance method, the authors compared active surveillance with passive surveillance. The methods involved ascertaining cerebrovascular events that occurred in Nueces County, Texas, during calendar year 2000. Active methods utilized screening of hospital and emergency department logs and routine visiting of hospital wards and out-of-hospital sources. Passive means relied on International Classification of Diseases, Ninth Revision (ICD-9), discharge codes for case ascertainment. Cases were validated by fellowship-trained stroke neurologists on the basis of published criteria. The results showed that, of the 6,236 events identified through both active and passive surveillance, 802 were validated to be cerebrovascular events. When passive surveillance alone was used, 209 (26.1%) cases were missed, including 73 (9.1%) cases involving hospital admission and 136 (17.0%) out-of-hospital strokes. Through active surveillance alone, 57 (7.1%)cases were missed. The positive predictive value of active surveillance was 12.2%. Among the 2,099 patients admitted to a hospital, passive surveillance using ICD-9 codes missed 73 cases of cerebrovascular disease and mistakenly included 222 noncases. There were 57 admitted hospital cases missed by active surveillance, including 13 not recognized because of human error. This study provided a quantitative means of assessing the utility of active and passive surveillance for cerebrovascular disease. More uniform surveillance methods would allow comparisons across studies and communities.

Reker DM, Hamilton BB, Duncan PW, Yeh SC, Rosen A. Stroke: Who's counting what? *J Rehabil Res Dev*. 2001; 38: 281-289.

INTRODUCTION: Patients with stroke are often selected for epidemiological reporting and research using ICD-9-CM (ICD-9) diagnostic codes. This study addresses the accuracy of these codes in identifying patients with stroke. METHODS: A sample of 279 patients with new stroke and 392 non-stroke (no evidence of new stroke) patients were identified by medical record review from 11 Veterans Affairs Medical Centers. Administrative records containing ICD-9-CM diagnoses were matched with this sample. Coding sensitivity and specificity were determined using individual ICD-9 codes and two coding algorithms. RESULTS: Significant variation was found in the accuracy of cerebrovascular ICD-9-CM codes in identifying patients diagnosed with stroke. Two coding algorithms were identified with the following performance statistics based on the sampled populations: 1) 91-percent sensitivity, 40-percent specificity; and 2) 54-percent sensitivity, 87-percent specificity. DISCUSSION/CONCLUSIONS: Variability in identifying patients with stroke using ICD-9 codes has been reported in the literature and confirmed. Two coding algorithms for maximizing sensitivity or specificity are proposed. Caution is urged when using ICD-9-coded administrative data to identify patients with stroke.

Rosamond WD, Folsom AR, Chambless LE, Wang CH, McGovern PG, Howard G, Copper LS, Shahar E. Stroke incidence and survival among middle-aged adults: 9-year follow-up of the Atherosclerosis Risk in Communities (ARIC) cohort. *Stroke*. 1999; 30(4): 736-43.

BACKGROUND AND PURPOSE: Although stroke mortality rates in the United States are well documented, assessment of incidence rates and case fatality are less well studied. METHODS: A cohort of 15 792 men and women aged 45 to 64 years from a population sample of households in 4 US communities was followed from 1987 to 1995, an average of 7. 2 years. Incident strokes were identified through annual phone contacts and hospital record searching and were then validated.

RESULTS: Of the 267 incident definite or probable strokes, 83% (n=221) were categorized as ischemic strokes, 10% (n=27) were intracerebral hemorrhages, and 7% (n=19) were subarachnoid hemorrhages. The age-adjusted incidence rate (per 1000 person-years)of total strokes was highest among black men (4.44), followed by black women(3.10), white men (1.78), and white women (1.24). The black versus white age-adjusted rate ratio (RR) for ischemic stroke was 2.41 (95% CI, 1.85 to 3.15), which was attenuated to 1.38 (95% CI, 1.01 to 1.89) after adjustment for baseline hypertension, diabetes, education level, smoking status, and prevalent coronary heart disease. There was a tendency for the adjusted case fatality rates to be higher among blacks and men, although none of the case fatality comparisons across sex or race was statistically significant. CONCLUSIONS: After accounting for established baseline risk factors, blacks still had a 38% greater risk of incident ischemic stroke compared with whites. Identification of new individual and community-level risk factors accounting for the elevated incidence of stroke requires further investigation and incorporation into intervention planning.

Roumie CL, Mitchel E, Gideon PS, Varas-Lorenzo C, Castellsague J, Griffin MR. Validation of ICD-9 codes with a high positive predictive value for incident strokes resulting in hospitalization using Medicaid health data. *Pharmacoepidemiol Drug Saf*. 2008; 17: 20-26.

PURPOSE: To validate ICD 9 codes with a high positive predictive value (PPV) for incident strokes. The study population consisted of Tennessee Medicaid enrollees aged from 50 to 84 years. METHODS: We identified all patients who were hospitalized with a discharge diagnosis of stroke between 1999 and 2003 using highly specific codes (ischemic stroke ICD 9-CM codes 433.x1, 434 [excluding 434.x0], or 436; intracerebral hemorrhage [431]; and subarachnoid hemorrhage [430]). We reviewed medical records of a systematic sample of 250 cohort members. We randomly selected 10-30 eligible records for review from hospitals with at least 10 stroke hospitalizations. RESULTS: We reviewed 231 charts (93% of total sampled), and 205 (89%) met study criteria for new outpatient stroke. Of the 205 confirmed new outpatient strokes, 196 had stroke listed as the primary discharge diagnosis (PPV = 96%). However, 46 (23%) of the 196 patients identified by the primary diagnosis also had a remote stroke history (recurrent stroke not incident). Thus the PPV of the primary discharge diagnosis for identifying incident stroke decreased to 74%. When we applied an algorithm that restricted our population to those with stroke as the primary diagnosis and excluded patients with any prior outpatient diagnosis of stroke, we identified incident stroke events with more precision (PPV = 80%). CONCLUSION: The PPV of incident strokes was 80% using our strategy of primary discharge diagnosis and excluding prior outpatient diagnoses of stroke. Although an unknown percentage of incident strokes are missed, this group of proven incident stroke patients can be used for etiologic studies of medication exposures.

So L, Evans D, Quan H. ICD-10 coding algorithms for defining comorbidities of acute myocardial infarction. *BMC Health Serv Res*. 2006; 6: 161.

BACKGROUND: With the introduction of ICD-10 throughout Canada, it is important to ensure that Acute Myocardial Infarction (AMI) comorbidities employed in risk adjustment methods remain valid and robust. Therefore, we developed ICD-10 coding algorithms for nine AMI comorbidities, examined the validity of the ICD-10 and ICD-9 coding algorithms in detection of these comorbidities, and assessed their performance in predicting mortality. The nine comorbidities that we examined were shock, diabetes with complications, congestive heart failure, cancer, cerebrovascular disease, pulmonary edema, acute renal failure, chronic renal failure, and cardiac dysrhythmias. METHODS: Coders generated a comprehensive list of ICD-10 codes corresponding to each AMI comorbidity. Physicians independently reviewed and determined the clinical relevance of each item on the list. To

ensure that the newly developed ICD-10 coding algorithms were valid in recording comorbidities, medical charts were reviewed. After assessing ICD-10 algorithms' validity, both ICD-10 and ICD-9 algorithms were applied to a Canadian provincial hospital discharge database to predict in-hospital, 30-day, and 1-year mortality. RESULTS: Compared to chart review data as a 'criterion standard', ICD-9 and ICD-10 data had similar sensitivities (ranging from 7.1-100%), and specificities (above 93.6%) for each of the nine AMI comorbidities studied. The frequencies for the comorbidities were similar between ICD-9 and ICD-10 coding algorithms for 49,861 AMI patients in a Canadian province during 1994-2004. The C-statistics for predicting 30-day and 1 year mortality were the same for ICD-9 (0.82) and for ICD-10 data (0.81). CONCLUSION: The ICD-10 coding algorithms developed in this study to define AMI comorbidities performed similarly as past ICD-9 coding algorithms in detecting conditions and risk-adjustment in our sample. However, the ICD-10 coding algorithms should be further validated in external databases.

Thompson SK, Southern DA, et al. Incidence of perioperative stroke after neck dissection for head and neck cancer: a regional outcome analysis. *Ann Surg*. 2004; 239(3): 428-31.

OBJECTIVE: To determine the incidence of perioperative stroke in patients undergoing a neck dissection. SUMMARY BACKGROUND DATA: The incidence of perioperative stroke in non-head and neck surgery is between 0.08 and 0.2%. In contrast, a critical review of the literature identified 2 studies stating the incidence of perioperative stroke in head and neck surgery to be 3.2% and 4.8%. The implications of these results are significant because they suggest a potential need for preoperative screening and/or intervention for carotid artery pathology. METHODS: This historical cohort study was conducted using discharge data for all neck dissections performed in a geographically-defined health region in Alberta, Canada, from 1994 to 2002. Subjects were selected for study if they had an assigned ICD-9CM procedure code for a neck dissection at one of the region's 3 adult-care hospitals. Our main outcome measure was perioperative stroke. RESULTS: Patients (n = 499) were identified as having had a neck dissection (mean age 56.5 +/- 15.3 SD, 65.3% male). Seven patients had ICD-9CM codes for postoperative central nervous system complications (incidence of 1.4%). However, on chart review, only one had had a true perioperative stroke corresponding to an incidence of 0.2% (95% confidence interval 0.01, 1.12). No missed strokes were found in a confirmatory random review of 10% of charts. CONCLUSIONS: The incidence of perioperative stroke in this study is significantly lower than that previously stated in the literature. This suggests that preoperative screening and/or intervention for carotid artery disease may not be necessary in this patient population.

Tirschwell DL, Longstreth WT Jr. Validating administrative data in stroke research. *Stroke*. 2002; 33: 2465-2470.

BACKGROUND AND PURPOSE: Research based on administrative data has advantages, including large numbers, consistent data, and low cost. This study was designed to compare different methods of stroke classification using administrative data. METHODS: Administrative hospital discharge data and medical record review of 206 patients were used to evaluate 3 algorithms for classifying stroke patients. These algorithms were based on all (algorithm 1), the first 2 (algorithm 2), or the primary (algorithm 3) administrative discharge diagnosis code(s). The diagnoses after review of medical record data were considered the gold standard. Then, using a large administrative data set, we compared patients with a primary discharge diagnosis of stroke with patients with their stroke discharge diagnosis code in a nonprimary position. RESULTS: Compared with the gold standard, algorithm 1 had the highest kappa for classifying ischemic stroke, with a sensitivity of 86%, specificity of 95%, positive predictive value of 90%, and kappa=0.82. Algorithm 3 had the highest

kappa values for intracerebral hemorrhage and subarachnoid hemorrhage. For intracerebral hemorrhage, the sensitivity was 85%, specificity was 96%, positive predictive value was 89%, and kappa=0.82. For subarachnoid hemorrhage, those values were 90%, 97%, 94%, and 0.88, respectively. Nonprimary position ischemic stroke patients had significantly greater comorbidity and 30-day mortality (odds ratio, 3.2) than primary position ischemic stroke patients. CONCLUSIONS: Stroke classification in these administrative data were optimal using all discharge diagnoses for ischemic stroke and primary discharge diagnosis only for intracerebral and subarachnoid hemorrhage. Selecting ischemic stroke patients on the basis of primary discharge diagnosis may bias administrative samples toward more benign, unrepresentative outcomes and should be avoided.

Williams LS, Rotich J, Qi R, et al. Effects of admission hyperglycemia on mortality and costs in acute ischemic stroke. *Neurology*. 2002; 59: 67-71.

BACKGROUND: Hyperglycemia at the time of acute ischemic stroke has been linked to worse outcome in both human and animal studies. OBJECTIVE: To describe the prevalence and severity of hyperglycemia on hospital admission among acute ischemic stroke patients, to examine the independent relationship of admission hyperglycemia to all-cause mortality, and to document the inpatient management of hyperglycemia. METHODS: Patients hospitalized with acute ischemic stroke at one hospital from July 1993 to June 1998 (n = 656) were identified. Demographic data, diagnoses, and blood glucose (BG) values were retrieved from the electronic medical record system. Admission stroke severity, fingerstick BG results, and new diabetes diagnoses were obtained by chart review. Hyperglycemia was defined as admitting random serum BG > or = 130 mg/dL. Hazard ratios (HR) for 30-day, 1-year, and 6-year mortality were calculated using multivariable Cox regression models. RESULTS: Hyperglycemia at admission to hospital was present in 40% of patients with acute stroke. Patients with hyperglycemia were more often women and more likely to have prior diagnoses of diabetes and heart failure. Almost all of these patients remained hyperglycemic during their hospital stay (mean BG = 206 mg/dL), and 43% received no inpatient hypoglycemic drugs. Hyperglycemic patients had longer hospital stay (7 vs 6 days, p = 0.015) and higher inpatient hospital charges ($6,611 vs $5,262, p < 0.001). Hyperglycemia independently increased the risk for death at 30 days (HR 1.87, p < or = 0.01), 1 year (HR 1.75, p < or = 0.01), and 6 years after stroke (HR 1.41, p </= 0.01). CONCLUSIONS: Admitting hyperglycemia was common among patients with acute ischemic stroke and was associated with increased short- and long-term mortality and with increased inpatient charges. Inpatient blood glucose management was suboptimal in this hospital. A trial of intensive treatment of hyperglycemia should be considered.

B. APPENDIX B: LIST OF CITATIONS SELECTED FOR FULL-TEXT REVIEW BUT NOT INCLUDED, BY REASONS FOR EXCLUSION

1. Studies Excluded Because They Did Not Study the HOI

Choma NN, Griffin MR, Huang RL, Mitchel EF, et al. An algorithm to identify incident myocardial infarction using Medicaid data. *Pharmacoepidemiology and Drug Safety.* 2009; 18(11): 1064-1071.

Engels JM, Diehr P. Imputation of missing longitudinal data: a comparison of methods. *Journal of Clinical Epidemiology.* Oct 2003; 56(10): 968-976.

Evans-Molina C, Regan S, Henault LE, Hylek EM, Schwartz GR. The new Medicare Part D prescription drug benefit: an estimation of its effect on prescription drug costs in a Medicare population with atrial fibrillation. *Journal of the American Geriatrics Society.* Jul 2007; 55(7): 1038-1043.

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2. Studies Excluded Because They Did Not Use an Administrative Database

Ballotta E, Da Giau G, Ermani M, et al. Early and long-term outcomes of carotid endarterectomy in the very elderly: an 18-year single-center study. *Journal of Vascular Surgery: Official Publication, the Society for Vascular Surgery [and] International Society for Cardiovascular Surgery, North American Chapter.* Sep 2009; 50(3): 518-525.

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C. APPENDIX C: LIST AND DEFINITIONS OF ICD OR PROCEDURAL CODES INCLUDED IN ALGORITHMS

Type of Code	Code	Description
ICD-9	325	PHLEBITIS INTRCRAN SINUS
ICD-9	342	HEMIPLEGIA*
ICD-9	342.0	FLACCID HEMIPLEGIA*
ICD-9	342.00	FLCCD HMIPLGA UNSPF SIDE
ICD-9	342.01	FLCCD HMIPLGA DOMNT SIDE
ICD-9	342.02	FLCCD HMIPLG NONDMNT SDE
ICD-9	342.1	SPASTIC HEMIPLEGIA*
ICD-9	342.10	SPSTC HMIPLGA UNSPF SIDE
ICD-9	342.11	SPSTC HMIPLGA DOMNT SIDE
ICD-9	342.12	SPSTC HMIPLG NONDMNT SDE
ICD-9	342.80	OT SP HMIPLGA UNSPF SIDE
ICD-9	342.81	OT SP HMIPLGA DOMNT SIDE
ICD-9	342.82	OT SP HMIPLG NONDMNT SDE
ICD-9	342.9	HEMIPLEGIA NOS*
ICD-9	342.90	UNSP HEMIPLGA UNSPF SIDE
ICD-9	342.91	UNSP HEMIPLGA DOMNT SIDE
ICD-9	342.92	UNSP HMIPLGA NONDMNT SDE
ICD-9	362.3	RETINAL VASC OCCLUSION*
ICD-9	369.0	PROFOUND BLIND BOTH EYES*
ICD-9	369.00	BOTH EYES BLIND-WHO DEF
ICD-9	369.01	TOT IMPAIRMENT-BOTH EYES
ICD-9	369.02	ONE EYE-NEAR TOT/OTH-NOS
ICD-9	369.03	ONE EYE-NEAR TOT/OTH-TOT
ICD-9	369.04	NEAR-TOT IMPAIR-BOTH EYE
ICD-9	369.05	ONE EYE-PROFOUND/OTH-NOS
ICD-9	369.07	ONE EYE-PRFND/OTH-NR TOT

ICD-9	369.08	PROFOUND IMPAIR BOTH EYE
ICD-9	369.1	MOD/SEV W PROFND IMPAIR*
ICD-9	369.10	BLINDNESS/LOW VISION
ICD-9	369.11	1 EYE-SEV/OTH-BLIND NOS
ICD-9	369.12	ONE EYE-SEVERE/OTH-TOTAL
ICD-9	369.13	ONE EYE-SEV/OTH-NEAR TOT
ICD-9	369.14	ONE EYE-SEV/OTH-PRFND
ICD-9	369.15	ONE EYE-MOD/OTH-BLIND
ICD-9	369.16	ONE EYE-MODERATE/OTH-TOT
ICD-9	369.17	ONE EYE-MOD/OTH-NEAR TOT
ICD-9	369.18	ONE EYE-MOD/OTH-PROFOUND
ICD-9	369.2	MOD/SEV IMPAIR-BOTH EYES*
ICD-9	369.20	LOW VISION, 2 EYES NOS
ICD-9	369.21	ONE EYE-SEVERE/OTH-NOS
ICD-9	369.22	SEVERE IMPAIR-BOTH EYES
ICD-9	369.23	ONE EYE-MODERATE/OTH-NOS
ICD-9	369.24	ONE EYE-MODERATE/OTH-SEV
ICD-9	369.25	MODERATE IMPAIR-BOTH EYE
ICD-9	369.3	BLINDNESS NOS, BOTH EYES
ICD-9	369.4	LEGAL BLINDNESS-USA DEF
ICD-9	369.6	PROFOUND IMPAIR-ONE EYE*
ICD-9	369.60	BLINDNESS, ONE EYE
ICD-9	369.61	ONE EYE-TOTAL/OTH-UNKNWN
ICD-9	369.62	ONE EYE-TOT/OTH-NEAR NOR
ICD-9	369.63	ONE EYE-TOTAL/OTH-NORMAL
ICD-9	369.64	ONE EYE-NEAR TOT/OTH-NOS
ICD-9	369.65	NEAR-TOT IMP/NEAR-NORMAL
ICD-9	369.66	NEAR-TOTAL IMPAIR/NORMAL
ICD-9	369.67	ONE EYE-PRFOUND/OTH-UNKN

ICD-9	369.68	PROFND IMPAIR/NEAR NORM
ICD-9	369.69	PROFOUND IMPAIR/NORMAL
ICD-9	369.7	MOD/SEVERE IMPAIR, 1 EYE*
ICD-9	369.70	LOW VISION, ONE EYE
ICD-9	369.71	ONE EYE-SEVERE/OTH-UNKNW
ICD-9	369.72	ONE EYE-SEV/OTH-NR NORM
ICD-9	369.74	ONE EYE-MOD/OTHER-UNKNWN
ICD-9	369.75	ONE EYE-MOD/OTH-NR NORM
ICD-9	369.76	ONE EYE-MOD/OTH NORMAL
ICD-9	369.8	VISUAL LOSS, ONE EYE NOS
ICD-9	369.9	VISUAL LOSS NOS
ICD-9	430	SUBARACHNOID HEMORRHAGE
ICD-9	431	INTRACEREBRAL HEMORRHAGE
ICD-9	432	INTRACRANIAL HEM NEC/NOS*
ICD-9	432.0	NONTRAUM EXTRADURAL HEM
ICD-9	432.1	SUBDURAL HEMORRHAGE
ICD-9	432.9	INTRACRANIAL HEMORR NOS
ICD-9	433	PRECEREBRAL OCCLUSION*
ICD-9	433.0	BASILAR ARTERY OCCLUSION*
ICD-9	433.00	OCL BSLR ART WO INFRCT
ICD-9	433.01	OCL BSLR ART W INFRCT
ICD-9	433.1	CAROTID ARTERY OCCLUSION*
ICD-9	433.10	OCL CRTD ART WO INFRCT
ICD-9	433.11	OCL CRTD ART W INFRCT
ICD-9	433.2	VERTEBRAL ART OCCLUSION*
ICD-9	433.20	OCL VRTB ART WO INFRCT
ICD-9	433.21	OCL VRTB ART W INFRCT
ICD-9	433.3	MULT PRECEREB OCCLUSION*
ICD-9	433.30	OCL MLT BI ART WO INFRCT

ICD-9	433.31	OCL MLT BI ART W INFRCT
ICD-9	433.8	PRECEREB OCCLUSION NEC*
ICD-9	433.80	OCL SPCF ART WO INFRCT
ICD-9	433.81	OCL SPCF ART W INFRCT
ICD-9	433.9	PRECEREB OCCLUSION NOS*
ICD-9	433.90	OCL ART NOS WO INFRCT
ICD-9	433.91	OCL ART NOS W INFRCT
ICD-9	434	CEREBRAL ARTERY OCCLUS*
ICD-9	434.0	CEREBRAL THROMBOSIS*
ICD-9	434.00	CRBL THRMBS WO INFRCT
ICD-9	434.01	CRBL THRMBS W INFRCT
ICD-9	434.1	CEREBRAL EMBOLISM*
ICD-9	434.10	CRBL EMBLSM WO INFRCT
ICD-9	434.11	CRBL EMBLSM W INFRCT
ICD-9	434.9	CEREBR ARTERY OCCLUS NOS*
ICD-9	434.90	CRBL ART OC NOS WO INFRC
ICD-9	434.91	CRBL ART OCL NOS W INFRC
ICD-9	435	TRANSIENT CEREB ISCHEMIA*
ICD-9	435.0	BASILAR ARTERY SYNDROME
ICD-9	435.1	VERTEBRAL ARTERY SYNDROM
ICD-9	435.2	SUBCLAVIAN STEAL SYNDROM
ICD-9	435.3	VERTBROBASLR ARTERY SYND
ICD-9	435.8	TRANS CEREB ISCHEMIA NEC
ICD-9	435.9	TRANS CEREB ISCHEMIA NOS
ICD-9	436	CVA
ICD-9	437	OTH CEREBROVASC DISEASE*
ICD-9	437.0	CEREBRAL ATHEROSCLEROSIS
ICD-9	437.1	AC CEREBROVASC INSUF NOS
ICD-9	437.2	HYPERTENS ENCEPHALOPATHY

ICD-9	437.3	NONRUPT CEREBRAL ANEURYM
ICD-9	437.4	CEREBRAL ARTERITIS
ICD-9	437.5	MOYAMOYA DISEASE
ICD-9	437.6	NONPYOGEN THROMBOS SINUS
ICD-9	437.7	TRANSIENT GLOBAL AMNESIA
ICD-9	437.8	CEREBROVASC DISEASE NEC
ICD-9	437.9	CEREBROVASC DISEASE NOS
ICD-9	438	LATE EFF CEREBROVASC DIS*
ICD-9	438.0	LATE EF CV DIS-COGNF DEF
ICD-9	438.10	LATE EF-SPCH/LNG DEF NOS
ICD-9	438.11	LATE EFF CV DIS-APHASIA
ICD-9	438.12	LATE EFF CV DIS-DYSPHSIA
ICD-9	438.19	LATE EF-SPCH/LANG DF NEC
ICD-9	438.20	LATE EF-HEMPLGA SIDE NOS
ICD-9	438.21	LATE EF-HEMPLGA DOM SIDE
ICD-9	438.22	LATE EF-HEMIPLGA NON-DOM
ICD-9	438.30	LATE EF-MPLGA UP LMB NOS
ICD-9	438.31	LATE EF-MPLGA UP LMB DOM
ICD-9	438.32	LT EF-MPLGA UPLMB NONDOM
ICD-9	438.40	LTE EF-MPLGA LOW LMB NOS
ICD-9	438.41	LTE EF-MPLGA LOW LMB DOM
ICD-9	438.42	LT EF-MPLGA LOWLMB NONDM
ICD-9	438.50	LT EF OTH PARAL SIDE NOS
ICD-9	438.51	LT EF OTH PARAL DOM SIDE
ICD-9	438.52	LT EF OTH PARALS NON-DOM
ICD-9	438.53	LT EF OTH PARALS-BILAT
ICD-9	438.81	LATE EFF CV DIS-APRAXIA
ICD-9	438.82	LATE EF CV DIS DYSPHAGIA
ICD-9	438.89	LATE EFFECT CV DIS NEC

ICD-9	438.9	LATE EFFECT CV DIS NOS
ICD-9	671.5	OTH THROMBOS COMPL PREG*
ICD-9	674.0	PUERP CEREBVASC DIS
ICD-9	747.81	CEREBROVASCULAR ANOMALY
ICD-9	767	BIRTH TRAUMA*
ICD-9	767.0	CEREBRAL HEM AT BIRTH
ICD-9	780.0	COMA AND STUPOR*
ICD-9	780.4	DIZZINESS AND GIDDINESS
ICD-9	800.2	CL SKL VLT FX/MENING HEM*
ICD-9	800.3	CL SKULL VLT FX/HEM NEC*
ICD-9	800.7	OPN SKL VLT FX/ HEM
ICD-9	800.8	OPN SKULL VLT FX/HEM NEC*
ICD-9	801.2	CL SKL BASE FX/ HEM
ICD-9	801.3	CL SKULL BASE FX/HEM NEC
ICD-9	801.7	OPN SKL BASE FX / HEM
ICD-9	801.8	OP SKL BASE FX-/ HEM
ICD-9	803.2	CL SKL FX NEC/MENING HEM*
ICD-9	803.3	CL SKULL FX NEC/HEM NEC
ICD-9	803.7	OPN SKL FX NEC/ HEM
ICD-9	803.8	OPN SKULL FX NEC/HEM NEC*
ICD-9	804.2	CL SKL/OTH FX/MENING HEM*
ICD-9	804.3	CL SKUL W OTH FX/HEM NEC*
ICD-9	804.7	OPN SKL/OTH FX-HEM
ICD-9	804.8	OPN SKL W OTH FX/HEM NEC*
ICD-9	852	MENINGEAL HEM FOLLOW INJ*
ICD-9	852.0	TRAUM SUBARACHNOID HEM*
ICD-9	852.00	TRAUM SUBARACHNOID HEM
ICD-9	852.01	SUBARACHNOID HEM-NO COMA
ICD-9	852.02	SUBARACH HEM-BRIEF COMA

ICD-9	852.03	SUBARACH HEM-MOD COMA
ICD-9	852.04	SUBARACH HEM-PROLNG COMA
ICD-9	852.05	SUBARACH HEM-DEEP COMA
ICD-9	852.06	SUBARACH HEM-COMA NOS
ICD-9	852.09	SUBARACH HEM-CONCUSSION
ICD-9	852.1	SUBARACH HEM W OPN WOUND*
ICD-9	852.10	SUBARACH HEM W OPN WOUND
ICD-9	852.11	OPN SUBARACH HEM-NO COMA
ICD-9	852.16	OP SUBARACH HEM-COMA NOS
ICD-9	852.2	TRAUMATIC SUBDURAL HEM*
ICD-9	852.20	TRAUMATIC SUBDURAL HEM
ICD-9	852.21	SUBDURAL HEM W/O COMA
ICD-9	852.22	SUBDURAL HEM-BRIEF COMA
ICD-9	852.23	SUBDURAL HEMORR-MOD COMA
ICD-9	852.24	SUBDURAL HEM-PROLNG COMA
ICD-9	852.25	SUBDURAL HEM-DEEP COMA
ICD-9	852.26	SUBDURAL HEMORR-COMA NOS
ICD-9	852.29	SUBDURAL HEM-CONCUSSION
ICD-9	852.3	SUBDURAL HEM W OPN WOUND*
ICD-9	852.30	SUBDURAL HEM W OPN WOUND
ICD-9	852.31	OPEN SUBDUR HEM W/O COMA
ICD-9	852.4	TRAUMATIC EXTRADURAL HEM*
ICD-9	852.40	TRAUMATIC EXTRADURAL HEM
ICD-9	852.41	EXTRADURAL HEM W/O COMA
ICD-9	852.42	EXTRADUR HEM-BRIEF COMA
ICD-9	852.43	EXTRADURAL HEM-MOD COMA
ICD-9	852.44	EXTRADUR HEM-PROLN COMA
ICD-9	852.45	EXTRADURAL HEM-DEEP COMA
ICD-9	852.46	EXTRADURAL HEM-COMA NOS

ICD-9	852.50	EXTRADURAL HEM W OPN WND
ICD-9	852.52	EXTRADUR HEM-BRIEF COMA
ICD-9	852.56	EXTRADURAL HEM-COMA NOS
ICD-9	852.59	EXTRADURAL HEM-CONCUSS
ICD-9	853	OTH TRAUMATIC BRAIN HEM*
ICD-9	853.0	TRAUMATIC BRAIN HEM NEC*
ICD-9	853.00	TRAUMATIC BRAIN HEM NEC
ICD-9	853.01	BRAIN HEM NEC W/O COMA
ICD-9	853.02	BRAIN HEM NEC-BRIEF COMA
ICD-9	853.03	BRAIN HEM NEC-MOD COMA
ICD-9	853.04	BRAIN HEM NEC-PROLN COMA
ICD-9	853.05	BRAIN HEM NEC-DEEP COMA
ICD-9	853.06	BRAIN HEM NEC-COMA NOS
ICD-9	853.09	BRAIN HEM NEC-CONCUSSION
ICD-9	853.1	BRAIN HEM NEC W OPN WND*
ICD-9	853.10	BRAIN HEM NEC W OPN WND
ICD-9	853.11	BRAIN HEM OPN W/O COMA
ICD-9	853.12	BRAIN HEM OPN-BRF COMA
ICD-9	853.14	BRAIN HEM OPN-PROLN COMA
ICD-9	853.15	BRAIN HEM OPEN-DEEP COMA
ICD-9	853.19	BRAIN HEM OPN-CONCUSSION
ICD-9	997.00	NERVOUS SYST COMPLC NOS
ICD-9	997.01	SURG COMPLICATION - CNS
ICD-9	997.02	IATROGEN CV INFARC/HMRHG
ICD-9	997.09	SURG COMP NERV SYSTM NEC
ICD-9	V57	REHABILITATION PROCEDURE*
ICD-9	V57.0	BREATHING EXERCISES
ICD-9	V57.1	PHYSICAL THERAPY NEC
ICD-9	V57.2	OCCUPAT/VOCATION THERAPY*

ICD-9	V57.21	ENCNTR OCCUPATNAL THRPY
ICD-9	V57.22	ENCNTR VOCATIONAL THRPY
ICD-9	V57.3	SPEECH THERAPY
ICD-9	V57.4	ORTHOPTIC TRAINING
ICD-9	V57.8	OTH REHABILITATION PROC*
ICD-9	V57.81	ORTHOTIC TRAINING
ICD-9	V57.89	REHABILITATION PROC NEC
ICD-9	V57.9	REHABILITATION PROC NOS
ICD-9 procedure	38.12	ENDARTERECTOMY
ICD-9 procedure	38.42	RESECTION VESSEL W/REPLACE-HEAD AND NECK
ICD-10	G45	TIA/RELATED SYNDROMES
ICD-10	G45.0	VERTEBRO-BASILAR ARTERY SYNDROME
ICD-10	G45.1	CAROTID ARTERY SYNDROME (HEMISPHERIC)
ICD-10	G45.2	MULTIPLE/ BILATERAL PRECEREBRAL ARTERY SYNDROME
ICD-10	G45.3	AMAUROSIS FUGAX
ICD-10	G45.4	TRANSIENT GLOBAL AMNESIA
ICD-10	G45.8	OTHER TIA/RELATED SYNDROMES
ICD-10	G45.9	TRANSIENT CEREBRAL ISCHAEMIC ATTACK, UNSPECIFIED
ICD-10	G46	VASCULAR SYND BRAIN IN CEREBROVASCULAR DISEASES
ICD-10	G46.0	MIDDLE CEREBRAL ARTERY SYNDROME
ICD-10	G46.1	ANTERIOR CEREBRAL ARTERY SYNDROME
ICD-10	G46.2	POSTERIOR CEREBRAL ARTERY SYNDROME
ICD-10	G46.3	BRAIN STEM STROKE SYNDROME
ICD-10	G46.4	CEREBELLAR STROKE SYNDROME
ICD-10	G46.5	PURE MOTOR LACUNAR SYNDROME
ICD-10	G46.6	PURE SENSORY LACUNAR SYNDROME
ICD-10	G46.7	OTHER LACUNAR SYNDROMES
ICD-10	G46.8	OTH VASCULAR SYND BRAIN IN CEREBROVASCULAR DISEASES
ICD-10	H34.0	TRANSIENT RETINAL ARTERY OCCLUSION

ICD-10	H34.1	CENTRAL RETINAL ARTERY OCCLUSION
ICD-10	I60	SUBARACHNOID HEMORRHAGE
ICD-10	I60.0	SUBARACHNOID HEMORRHAGE CAROTID SIPHON AND B
ICD-10	I60.1	SUBARACHNOID HEMORRHAGE MIDDLE CEREBRAL ARTE
ICD-10	I60.2	SUBARACHNOID HEMORRHAGE ANTERIOR COMMUNICATI
ICD-10	I60.3	SUBARACHNOID HEMORRHAGE POSTERIOR COMMUNICAT
ICD-10	I60.4	SUBARACHNOID HEMORRHAGE FROM BASILAR ARTERY
ICD-10	I60.5	SUBARACHNOID HEMORRHAGE FROM VERTEBRAL ARTERY
ICD-10	I60.6	SUBARACHNOID HEMORRHAGE FROM OTHER INTRACRANIAL A
ICD-10	I60.7	SUBARACHNOID HEMORRHAGE FROM INTRACRANIAL ARTERY
ICD-10	I60.8	OTHER SUBARACHNOID HEMORRHAGE
ICD-10	I60.9	SUBARACHNOID HEMORRHAGE, UNSPECIFIED
ICD-10	I61	INTRACEREBRAL HEMORRHAGE
ICD-10	I61.0	INTRACEREBRAL HEMORRHAGE IN HEMISPHERE, SUBCORTIC
ICD-10	I61.1	INTRACEREBRAL HEMORRHAGE IN HEMISPHERE, CORTICAL
ICD-10	I61.2	INTRACEREBRAL HEMORRHAGE IN HEMISPHERE, UNSPECIFI
ICD-10	I61.3	INTRACEREBRAL HEMORRHAGE IN BRAIN STEM
ICD-10	I61.4	INTRACEREBRAL HEMORRHAGE IN CEREBELLUM
ICD-10	I61.5	INTRACEREBRAL HEMORRHAGE, INTRAVENTRICULAR
ICD-10	I61.6	INTRACEREBRAL HEMORRHAGE, MULTIPLE LOCALISED
ICD-10	I61.8	OTHER INTRACEREBRAL HEMORRHAGE
ICD-10	I61.9	INTRACEREBRAL HEMORRHAGE, UNSPECIFIED
ICD-10	I62	OTHER NONTRAUMATIC INTRACRANIAL HEMORRHAGE
ICD-10	I62.0	SUBDURAL HEMORRHAGE (ACUTE) (NONTRAUMATIC)
ICD-10	I62.1	NONTRAUMATIC EXTRADURAL HEMORRHAGE
ICD-10	I62.9	INTRACRANIAL HEMORRHAGE (NONTRAUMATIC), UNSPECIFI
ICD-10	I63	CEREBRAL INFARCTION
ICD-10	I63.0	CEREBRAL INFARCTION DUE TO THROMBOSIS OF PRECEREBR
ICD-10	I63.1	CEREBRAL INFARCTION DUE TO EMBOLISM OF PRECEREBRAL

ICD-10	I63.2	CEREBRAL INFARCTION DUE TO UNSPECIFIED OCCLUSION O
ICD-10	I63.3	CEREBRAL INFARCTION DUE TO THROMBOSIS OF CEREBRAL
ICD-10	I63.4	CEREBRAL INFARCTION DUE TO EMBOLISM OF CEREBRAL AR
ICD-10	I63.5	CEREBRAL INFARCTION DUE TO UNSPECIFIED OCCLUSION O
ICD-10	I63.6	CEREBRAL INFARCTION DUE TO CEREBRAL VENOUS THROMBO
ICD-10	I63.8	OTHER CEREBRAL INFARCTION
ICD-10	I63.9	CEREBRAL INFARCTION, UNSPECIFIED
ICD-10	I64	STROKE, NOT SPECIFIED AS HEMORRHAGE OR INFARCTION
ICD-10	I65	OCCLUSION/ STENOSIS PRECEREBRAL ARTERIES, NOT RESU
ICD-10	I65.0	OCCLUSION AND STENOSIS OF VERTEBRAL ARTERY
ICD-10	I65.1	OCCLUSION AND STENOSIS OF BASILAR ARTERY
ICD-10	I65.2	OCCLUSION AND STENOSIS OF CAROTID ARTERY
ICD-10	I65.3	OCCLUSION AND STENOSIS OF MULTIPLE AND BILATERAL P
ICD-10	I65.8	OCCLUSION AND STENOSIS OF OTHER PRECEREBRAL ARTERY
ICD-10	I65.9	OCCLUSION AND STENOSIS OF UNSPECIFIED PRECEREBRAL
ICD-10	I66	OCCLUSION/ STENOSIS OF CEREBRAL ARTERIES, NOT RESULTI
ICD-10	I66.0	OCCLUSION AND STENOSIS OF MIDDLE CEREBRAL ARTERY
ICD-10	I66.1	OCCLUSION AND STENOSIS OF ANTERIOR CEREBRAL ARTERY
ICD-10	I66.2	OCCLUSION AND STENOSIS OF POSTERIOR CEREBRAL ARTER
ICD-10	I66.3	OCCLUSION AND STENOSIS OF CEREBELLAR ARTERIES
ICD-10	I66.4	OCCLUSION AND STENOSIS OF MULTIPLE AND BILATERAL C
ICD-10	I66.8	OCCLUSION AND STENOSIS OF OTHER CEREBRAL ARTERY
ICD-10	I66.9	OCCLUSION AND STENOSIS OF UNSPECIFIED CEREBRAL ART
ICD-10	I67	OTHER CEREBROVASCULAR DISEASES
ICD-10	I67.0	DISSECTION OF CEREBRAL ARTERIES, NONRUPTURED
ICD-10	I67.1	CEREBRAL ANEURYSM, NONRUPTURED
ICD-10	I67.2	CEREBRAL ATHEROSCLEROSIS
ICD-10	I67.3	PROGRESSIVE VASCULAR LEUKOENCEPHALOPATHY
ICD-10	I67.4	HYPERTENSIVE ENCEPHALOPATHY

ICD-10	I67.5	MOYAMOYA DISEASE
ICD-10	I67.6	NONPYOGENIC THROMBOSIS OF INTRACRANIAL VENOUS SYST
ICD-10	I67.7	CEREBRAL ARTERITIS, NOT ELSEWHERE CLASSIFIED
ICD-10	I67.8	OTHER SPECIFIED CEREBROVASCULAR DISEASES
ICD-10	I67.9	CEREBROVASCULAR DISEASE, UNSPECIFIED
ICD-10	I68	CEREBROVASCULAR DIS IN DISEASES CLASSIFIED ELSEWHE
ICD-10	I68.0	CEREBRAL AMYLOID ANGIOPATHY
ICD-10	I68.1	CEREBRAL ARTERITIS IN INFECTIOUS AND PARASITIC DIS
ICD-10	I68.2	CEREBRAL ARTERITIS IN OTHER DISEASES CLASSIFIED EL
ICD-10	I68.8	OTHER CEREBROVASCULAR DISORDERS IN DISEASES CLASSI
ICD-10	I69	SEQUELAE OF CEREBROVASCULAR DISEASE
ICD-10	I69.0	SEQUELAE OF SUBARACHNOID HEMORRHAGE
ICD-10	I69.1	SEQUELAE OF INTRACEREBRAL HEMORRHAGE
ICD-10	I69.2	SEQUELAE OF OTH NONTRAUMATIC INTRACRANIAL HEMOR
ICD-10	I69.3	SEQUELAE OF CEREBRAL INFARCTION
ICD-10	I69.4	SEQUELAE OF STROKE, NOT SPECIFIED AS HEMORRHAGE O
ICD-10	I69.8	SEQUELAE OF OTHER AND UNSPECIFIED CEREBROVASCULAR