**eAppendix**

**eFigure 1. Number of inpatient diagnosis codes by month**



**eFigure 2. Number of outpatient diagnosis codes by month**



**eTable 1. Covariates defined using inpatient diagnosis codes only**

| **Outcome** | **Hospital Discharge Code(s)** | **Comments** |
| --- | --- | --- |
| Ischemic stroke | ICD-9 Dx 433.x1 Occlusion and stenosis of precerebral arteries with cerebral infarctionICD-9 Dx 434.x1 Occlusion and stenosis of cerebral arteries with cerebral infarction | PPV 95.5% in commercially-insured population[Wahl PM](https://www.ncbi.nlm.nih.gov/pubmed/?term=Wahl%20PM%5BAuthor%5D&cauthor=true&cauthor_uid=20140892), [Rodgers K](https://www.ncbi.nlm.nih.gov/pubmed/?term=Rodgers%20K%5BAuthor%5D&cauthor=true&cauthor_uid=20140892), [Schneeweiss S](https://www.ncbi.nlm.nih.gov/pubmed/?term=Schneeweiss%20S%5BAuthor%5D&cauthor=true&cauthor_uid=20140892), [Gage BF](https://www.ncbi.nlm.nih.gov/pubmed/?term=Gage%20BF%5BAuthor%5D&cauthor=true&cauthor_uid=20140892), [Butler J](https://www.ncbi.nlm.nih.gov/pubmed/?term=Butler%20J%5BAuthor%5D&cauthor=true&cauthor_uid=20140892), [Wilmer C](https://www.ncbi.nlm.nih.gov/pubmed/?term=Wilmer%20C%5BAuthor%5D&cauthor=true&cauthor_uid=20140892), [Nash M](https://www.ncbi.nlm.nih.gov/pubmed/?term=Nash%20M%5BAuthor%5D&cauthor=true&cauthor_uid=20140892), [Esper G](https://www.ncbi.nlm.nih.gov/pubmed/?term=Esper%20G%5BAuthor%5D&cauthor=true&cauthor_uid=20140892), [Gitlin N](https://www.ncbi.nlm.nih.gov/pubmed/?term=Gitlin%20N%5BAuthor%5D&cauthor=true&cauthor_uid=20140892), [Osborn N](https://www.ncbi.nlm.nih.gov/pubmed/?term=Osborn%20N%5BAuthor%5D&cauthor=true&cauthor_uid=20140892), [Short LJ](https://www.ncbi.nlm.nih.gov/pubmed/?term=Short%20LJ%5BAuthor%5D&cauthor=true&cauthor_uid=20140892), [Bohn RL](https://www.ncbi.nlm.nih.gov/pubmed/?term=Bohn%20RL%5BAuthor%5D&cauthor=true&cauthor_uid=20140892). Validation of claims-based diagnostic and procedure codes for cardiovascular and gastrointestinal serious adverse events in a commercially insured population. *Pharmcoepidemiol Drug Saf*. 2010;19(6): 596-603. |
| Hemorrhagic stroke | As primary ICD-9 discharge diagnosis (Dx):430.x Subarachnoid hemorrhage (SAH)431.x Intracerebral hemorrhage (ICH) | Median PPV 96% (86% if all discharge diagnoses) for ICH based on 2 validation studies;PPV 93% (80% if all discharge diagnoses) for SAH based on 2 validation studies[Andrade SE](https://www.ncbi.nlm.nih.gov/pubmed/?term=Andrade%20SE%5BAuthor%5D&cauthor=true&cauthor_uid=22262598), [Harrold LR](https://www.ncbi.nlm.nih.gov/pubmed/?term=Harrold%20LR%5BAuthor%5D&cauthor=true&cauthor_uid=22262598), [Tjia J](https://www.ncbi.nlm.nih.gov/pubmed/?term=Tjia%20J%5BAuthor%5D&cauthor=true&cauthor_uid=22262598), [Cutrona SL](https://www.ncbi.nlm.nih.gov/pubmed/?term=Cutrona%20SL%5BAuthor%5D&cauthor=true&cauthor_uid=22262598), [Saczynski JS](https://www.ncbi.nlm.nih.gov/pubmed/?term=Saczynski%20JS%5BAuthor%5D&cauthor=true&cauthor_uid=22262598), [Dodd KS](https://www.ncbi.nlm.nih.gov/pubmed/?term=Dodd%20KS%5BAuthor%5D&cauthor=true&cauthor_uid=22262598), [Goldberg RJ](https://www.ncbi.nlm.nih.gov/pubmed/?term=Goldberg%20RJ%5BAuthor%5D&cauthor=true&cauthor_uid=22262598), [Gurwitz JH](https://www.ncbi.nlm.nih.gov/pubmed/?term=Gurwitz%20JH%5BAuthor%5D&cauthor=true&cauthor_uid=22262598). A systematic review of validated methods for identifying cerebrovascular accident or transient ischemic attack using administrative data. *Pharmcoepidemiol Drug Saf*. 2012;21: 100-128.  |
| Myocardial infarction (MI) | ICD-9 Dx 410.X (acute myocardial infarction) excluding 410.x2 (subsequent episode of care), as the principal (primary) or the next (secondary) diagnosisAND a length of stay (LOS) between 3-180 days, or death if LOS is < 3 days | PPV 94% in Medicare claims data[Kiyota Y](https://www.ncbi.nlm.nih.gov/pubmed/?term=Kiyota%20Y%5BAuthor%5D&cauthor=true&cauthor_uid=15215798), [Schneeweiss S](https://www.ncbi.nlm.nih.gov/pubmed/?term=Schneeweiss%20S%5BAuthor%5D&cauthor=true&cauthor_uid=15215798), [Glynn RJ](https://www.ncbi.nlm.nih.gov/pubmed/?term=Glynn%20RJ%5BAuthor%5D&cauthor=true&cauthor_uid=15215798), [Cannuscio CC](https://www.ncbi.nlm.nih.gov/pubmed/?term=Cannuscio%20CC%5BAuthor%5D&cauthor=true&cauthor_uid=15215798), [Avorn J](https://www.ncbi.nlm.nih.gov/pubmed/?term=Avorn%20J%5BAuthor%5D&cauthor=true&cauthor_uid=15215798), [Solomon DH](https://www.ncbi.nlm.nih.gov/pubmed/?term=Solomon%20DH%5BAuthor%5D&cauthor=true&cauthor_uid=15215798). Accuracy of Medicare claims-based diagnosis of acute myocardial infarction: estimating positive predictive value on the basis of review of hospital records. *Am J Heart*. 2004;148(1):99-104. |
| Deep vein thrombosis (DVT) | Validated algorithm:ICD-9 451.1x (Phlebitis and thrombophlebitis of deep vessels of lower extremities)ICD-9 451.2x (of lower extremities, unspecified)ICD-9 451.81 (of Iliac vein)ICD-9 451.9x (of unspecified site)ICD-9 453.1x (thrombophlebitis migrans)ICD-9 453.2x ( venous embolism and thrombosis of vena cava)ICD-9 453.8x (venous embolism and thrombosis of other specified veins)ICD-9 453.9x (venous embolism and thrombosis of unspecified site)Not in the validated algorithm but will be included following Mini-Sentinel recommendation for VTE outcome:ICD-9 453.40 (Venous embolism and thrombosis of unspecified deep vessels of lower extremity (includes DVT)ICD-9 453.41 (Venous embolism and thrombosis of deep vessels of proximal lower extremity (includes femoral, iliac, popliteal, thigh, and upper leg)ICD-9 453.42 (Venous embolism and thrombosis of deep vessels of distal lower extremity (includes calf, lower leg, peroneal, and tibia)ICD-9 453.0 (Hepatic vein thrombosis) | Algorithm for Deep vein thrombosis (DVT): ICD-9 codes of 451.1, 451.2, 451.81, 451.9, 453.1, 453.2, 453.8, 453.9 [hospital discharge, any position] had PPV of 0.72 and specificity > 0.99 in Medicare population[Birman-Deych E](https://www.ncbi.nlm.nih.gov/pubmed/?term=Birman-Deych%20E%5BAuthor%5D&cauthor=true&cauthor_uid=15838413), [Waterman AD](https://www.ncbi.nlm.nih.gov/pubmed/?term=Waterman%20AD%5BAuthor%5D&cauthor=true&cauthor_uid=15838413), [Yan Y](https://www.ncbi.nlm.nih.gov/pubmed/?term=Yan%20Y%5BAuthor%5D&cauthor=true&cauthor_uid=15838413), [Nilasena DS](https://www.ncbi.nlm.nih.gov/pubmed/?term=Nilasena%20DS%5BAuthor%5D&cauthor=true&cauthor_uid=15838413), [Radford MJ](https://www.ncbi.nlm.nih.gov/pubmed/?term=Radford%20MJ%5BAuthor%5D&cauthor=true&cauthor_uid=15838413), [Gage BF](https://www.ncbi.nlm.nih.gov/pubmed/?term=Gage%20BF%5BAuthor%5D&cauthor=true&cauthor_uid=15838413). Accuracy of ICD-9-CM diagnosis codes for identifying cardiovascular and stroke risk factors. *Med Care*. 2005;43(5):480-485. |
| Pulmonary Embolism (PE) | ICD-9 415.1x (pulmonary embolism and infarction) | PPV of 72% in a community sample (45 YO and older) [Cushman M](https://www.ncbi.nlm.nih.gov/pubmed/?term=Cushman%20M%5BAuthor%5D&cauthor=true&cauthor_uid=15210384), [Tsai AW](https://www.ncbi.nlm.nih.gov/pubmed/?term=Tsai%20AW%5BAuthor%5D&cauthor=true&cauthor_uid=15210384), [White RH](https://www.ncbi.nlm.nih.gov/pubmed/?term=White%20RH%5BAuthor%5D&cauthor=true&cauthor_uid=15210384), [Heckbert SR](https://www.ncbi.nlm.nih.gov/pubmed/?term=Heckbert%20SR%5BAuthor%5D&cauthor=true&cauthor_uid=15210384), [Rosamond WD](https://www.ncbi.nlm.nih.gov/pubmed/?term=Rosamond%20WD%5BAuthor%5D&cauthor=true&cauthor_uid=15210384), [Enright P](https://www.ncbi.nlm.nih.gov/pubmed/?term=Enright%20P%5BAuthor%5D&cauthor=true&cauthor_uid=15210384), [Folsom AR](https://www.ncbi.nlm.nih.gov/pubmed/?term=Folsom%20AR%5BAuthor%5D&cauthor=true&cauthor_uid=15210384). Deep vein thrombosis and pulmonary embolism in two cohorts: the longitudinal investigation of thromboembolism etiology. *Am J Med*. 2004;117(1): 19-25. |
| Major upper GI bleed | ICD-9 diagnoses: 531.0x (acute gastric ulcer with hemorrhage with/without obstruction)531.2x (with hemorrhage and perforation with/without obstruction)531.4x (chronic or unspecified gastric ulcer with hemorrhage with/without obstruction)531.6x (with hemorrhage and perforation with/without obstruction)532.0x (acute duodenal ulcer with hemorrhage with/without obstruction)532.2x (with hemorrhage and perforation with/without obstruction)532.4x (chronic or unspecified duodenal ulcer with hemorrhage with/without obstruction)532.6x (with hemorrhage and perforation with/without obstruction)533.0x (acute peptic ulcer of unspecified site with hemorrhage with/without obstruction)533.2x (with hemorrhage and perforation with/without obstruction)533.4x (chronic or unspecified peptic ulcer of unspecified site with hemorrhage with/without obstruction)533.6x (with hemorrhage and perforation with/without obstruction), 534.0x (acute gastrojejunal ulcer with hemorrhage with/without obstruction)534.2x (with hemorrhage and perforation with/without obstruction)534.4x (chronic or unspecified gastrojejunal ulcer with hemorrhage with/without obstruction)534.6x (with hemorrhage and perforation with/without obstruction)578.0 (hematemesis) ORICD-9 procedure code 44.43 (endoscopic control of gastric or duodenal bleeding) ORCPT code 43255 (upper gastrointestinal endoscopy including esophagus, stomach, and either the duodenum and/or jejunum as appropriate with control of bleeding, any method) | PPV of 87.8% in commercially-insured population[Wahl PM](https://www.ncbi.nlm.nih.gov/pubmed/?term=Wahl%20PM%5BAuthor%5D&cauthor=true&cauthor_uid=20140892), [Rodgers K](https://www.ncbi.nlm.nih.gov/pubmed/?term=Rodgers%20K%5BAuthor%5D&cauthor=true&cauthor_uid=20140892), [Schneeweiss S](https://www.ncbi.nlm.nih.gov/pubmed/?term=Schneeweiss%20S%5BAuthor%5D&cauthor=true&cauthor_uid=20140892), [Gage BF](https://www.ncbi.nlm.nih.gov/pubmed/?term=Gage%20BF%5BAuthor%5D&cauthor=true&cauthor_uid=20140892), [Butler J](https://www.ncbi.nlm.nih.gov/pubmed/?term=Butler%20J%5BAuthor%5D&cauthor=true&cauthor_uid=20140892), [Wilmer C](https://www.ncbi.nlm.nih.gov/pubmed/?term=Wilmer%20C%5BAuthor%5D&cauthor=true&cauthor_uid=20140892), [Nash M](https://www.ncbi.nlm.nih.gov/pubmed/?term=Nash%20M%5BAuthor%5D&cauthor=true&cauthor_uid=20140892), [Esper G](https://www.ncbi.nlm.nih.gov/pubmed/?term=Esper%20G%5BAuthor%5D&cauthor=true&cauthor_uid=20140892), [Gitlin N](https://www.ncbi.nlm.nih.gov/pubmed/?term=Gitlin%20N%5BAuthor%5D&cauthor=true&cauthor_uid=20140892), [Osborn N](https://www.ncbi.nlm.nih.gov/pubmed/?term=Osborn%20N%5BAuthor%5D&cauthor=true&cauthor_uid=20140892), [Short LJ](https://www.ncbi.nlm.nih.gov/pubmed/?term=Short%20LJ%5BAuthor%5D&cauthor=true&cauthor_uid=20140892), [Bohn RL](https://www.ncbi.nlm.nih.gov/pubmed/?term=Bohn%20RL%5BAuthor%5D&cauthor=true&cauthor_uid=20140892). Validation of claims-based diagnostic and procedure codes for cardiovascular and gastrointestinal serious adverse events in a commercially insured population. *Pharmcoepidemiol Drug Saf*. 2010;19(6): 596-603. |

|  |  |  |
| --- | --- | --- |
| Hepatotoxicity | Inpatient ICD-9 diagnoses:570.xx acute and subacute necrosis of liver573.3x hepatitis unspecified (toxic)572.2x hepatic coma (hepatic encephalopathy) | PPV of 83% (95% CI 72-91%) in patients hospitalized for acetaminophen overdose and who developed hepatotoxicity (ALT>1000 U/L)[Myers RP](https://www.ncbi.nlm.nih.gov/pubmed/?term=Myers%20RP%5BAuthor%5D&cauthor=true&cauthor_uid=17910762), [Leung Y](https://www.ncbi.nlm.nih.gov/pubmed/?term=Leung%20Y%5BAuthor%5D&cauthor=true&cauthor_uid=17910762), [Shaheen AA](https://www.ncbi.nlm.nih.gov/pubmed/?term=Shaheen%20AA%5BAuthor%5D&cauthor=true&cauthor_uid=17910762), [Li B](https://www.ncbi.nlm.nih.gov/pubmed/?term=Li%20B%5BAuthor%5D&cauthor=true&cauthor_uid=17910762). Validation of ICD-9-CM/ICD-10 coding algorithms for the identification of patients with acetaminophen overdose and hepatotoxicity using administrative data. *BMC Health Serv Res.* 2007;7:159.  |
| Hip Fracture | Hip fracture diagnosis during hospitalization (ICD-9: 820.xx, 733.14) + procedure code during hospitalization (ICD: 78.55, 79.05, 79.15, 79.25, 79.35, 79.65, CPT-4: 27230-27248) | Solomon DH, Rassen JA, Glynn RJ, Lee J, Levin R, Schneeweiss S. The Comparative Safety of Analgesics in Older Adults With Arthritis. *Arch Intern Med.* 2010;170(22):1968–1978.  |
| **Acute kidney injury based on claims**[[1]](#endnote-1) | The following two ARF and ARF-D **individually and then as a composite** |  |
| ARF | Identify patients with inpatient codes for ARF by the presence of ICD-9CM codes 584.5x, 584.6x, 584.7x, 584.8x, or 584.9x in any of the listed diagnoses | Waikar SS, Wald R, Chertow GM, Curhan GC, Winkelmayer WC, Liangos O, Sosa MA, Jaber BL: Validity of ICD-9-CM Codes for Acute Renal Failure. *J Am Soc Nephrol.* 2006;17:1688-1694. |
| ARF-D | ARF-D can be identified by the additional presence of any of the following ICD-9CM codes for hemodialysis: procedure code 39.95 (hemodialysis) or diagnosis codes V45.1x (renal dialysis status), V56.0x (extracorporeal dialysis), or V56.1x (fitting and adjustment of dialysis catheter).  |

**eTable 2. Covariates defined using inpatient or outpatient diagnosis codes**

| **Covariate** | **Definition** | **Comments** |
| --- | --- | --- |
| Coronary Artery Disease (CAD) | ICD-9 Dx: 410.x-414.x, 429.2 V45.81  |  |
| DVT | * + 1. ICD-9 : 451.xx, 453.xx
 |  |
| PE | ICD-9: 415.11, 415.12, 415.19 |  |
| Atrial fibrillation/flutter | one ICD-9 diagnosis code of 427.3 (Atrial fibrillation/flutter), 427.31 (atrial fibrillation), 427.32 (Atrial flutter) |  |
| Hypertension | At least 1 Dx of ICD-9 codes 401.x – 405.x ORAt least 1 dispensing of a CCB, ACEI, ARB, BB, a thiazide diuretic or a direct antihypertensive agent |  |
| Diabetes | At least 2 outpatient diagnoses of DM (ICD-9 250.X (diabetes)) OR 1 hospital discharge Dx of DM OR 1 diagnosis of DM plus an insulin or oral antidiabetic dispensing |  |
| Hyperlipidemia | ICD-9 272.0, 272.2, 272.4 |  |
| Heart failure (CHF) | 1 inpatient or 2 outpatient claims with any of ICD-9 codes : 428.x, 398.91, 402.01, 402.11, 402.91, 404.01, 404.11, 404.91, 404.03, 404.13, 404.93 | Validated in Medicare algorithm:Hospital discharge ICD-9 codes: 428.x, 398.91, 402.01, 402.11, 402.91, 404.01, 404.11, 404.91, 404.03, 404.13, 404.93PPV 0.97, Spec. 0.97, Sens. 0.76[1](#_ENREF_1) |
| Hemorrhagic stroke | 1 inpatient or 2 outpatient claims with any of 430.x – 432.x, |  |
| Ischemic stroke |  1 inpatient or 2 outpatient claims with any of ICD-9 codes: 433.x, 434.x, 436.x, 437.1 | Differs from the outcome definition as higher sensitivity is preferred for covariates definition |
|  COPD | 491.xx, 492.xx, or 496.xx |  |
| Pneumonia | 480.xx – 486.xx, 487.0x, 507.xx |  |
|  Cancer | 140.x-195.x, 196.x-198.x, 199.x, 200.x-208.x, 230.x-234.x, 235.x-238.x, 239.x, excluding non-melanoma skin cancer ( = 173.xx), v10.xx  |  |
|  Acute MI | ICD-9 410 |  |
|  Peptic Ulcer Disease | Diseases of esophagus: 530.1x – 530.4x, 530.8x, 530.9xGastric ulcer: 531.xDuodenal ulcer: 532.xPeptic ulcer: 533.xAcute gastritis: 535.0xOther specified gastritis: 535.4xUnspecified gastritis and gastroduodenitis: 535.5xDuodenitis: 535.6x |  |
| Upper GI bleed | ICD-9 diagnosis: 531.0x, 531.2x, 531.4x, 531.6x532.0x, 532.2x, 532.4x, 532.6x, 533.0x, 533.2x, 533.4x, 533.6x, 534.0x, 534.2x, 534.4x, 534.6x, 578.0 ORICD-9 procedure code 44.43 ORCPT code 43255 |  |
| Prior liver disease | ICD-9 diagnosis:070.x viral hepatitis571.x chronic liver disease and cirrhosis572.x liver abscess and sequalae of chronic liver disease573.x other disorders of liver456.0 – 456.2x esophageal varices155.0 primary cancer of liver155.1 cancer of intrahepatic bile ducts155.2 cancer of liver not specified as primary or secondary576.8 cholestasisICD-9 procedure codes:39.1 intra-abdominal venous shunt42.91 ligation of esophageal varices |  |
| Chronic Kidney Disease | Acute renal disease (see below)Chronic renal disease (see below)Diabetic nephropathy (see below)Hypertensive nephropathy (see below)Miscellaneous Renal Insufficiency (see below)Or ESRD (see below) | This definition of renal dysfunction is based on prior work[3](#_ENREF_3),[4](#_ENREF_4) and will be used for covariate adjustment. It is a combination of several diagnoses that are not well distinguished in claims databases. |
| *Acute Renal Disease* | 580.0, 580.4, 580.8, 580.9, 581.0, 581.1, 581.2, 581.2, 581.3, 581.8, 581.9, 584.6, 584.7, 584.8, 584.9 |  |
| *Chronic Renal Insufficiency* | 582.x, 583.x, 585.x, 586.x, 587.x |  |
| *Diabetic Nephropathy* | 250.4, 250.40, 250.41,250.42, 250.43 |  |
| *Hypertensive Nephropathy* | 403.xx, 404.xx |  |
| *Miscellaneous Renal Insufficiency* | 274.10, 440.1, 442.1, 453.3,581.xx, 593.xx, 753.0,753.3, 866.00 866.01,866.1 |  |
| *ESRD (with and without dialysis)* | DIALYSISICD-9 procedure:39.95 hemodialysis54.98 peritoneal dialysis38.95 Venous catheterization for renal dialysis39.27 Arteriovenostomy for renal dialysis39.42 Revision of arteriovenous shunt for renal dialysis39.43 Removal of arteriovenous shunt for renal dialysisICD-9 diagnoses:V45.1 renal dialysis statusV56.0 extracorporeal dialysisV56.8 peritoneal dialysisCPT4:90935      HEMODIALYSIS PROC W/SINGLE PHYSICIAN EVALUATION90937      HEMODIALYSIS, REPEATED EVAL, W/WO REVISION DIALYSIS PRESCRIPTION90940      HEMODIALYSIS ACCESS FLOW STUDY, BY INDICATOR DILUTION METHOD, HOOK UP;  MEASUREMENT & DISCONNECTION90945      DIALYSIS, OTHER THAN HEMODIALYSIS, SINGLE PHYSICIAN EVAL90947      DIALYSIS PROCEDURE, OTHER THAN HEMODIALYSIS, REPEATED PHYSICIAN EVAL90989      DIALYSIS TRAINING, PATIENT, W/HELPER WHERE APPLICABLE, ANY MODE, COMPLETED COURSE90993      DIALYSIS TRAINING, PATIENT, W/HELPER WHERE APPLICABLE, ANY MODE, COURSE INCOMPLETE, PER SESSION99512      HOME VISIT, HEMODIALYSIS99559      HOME INFUSION, PERITONEAL DIALYSIS, PER VISITORRENAL TRANSPLANTV42.0    Kidney transplant55.6x     Kidney transplant996.81  Complication of transplanted kidneyCPT4:50360       RENAL ALLOTRANSPLANTATION, IMPLANTATION, GRAFT; W/O DONOR & RECIPIENT NEPHRECTOMY50365      RENAL ALLOTRANSPLANTATION, IMPLANTATION, GRAFT; W/RECIPIENT NEPHRECTOMY50380      RENAL AUTOTRANSPLANTATION, REIMPLANTATION, KIDNEYORRENAL ICD9-defined ESRD585.5 ESKD with no mention of dialysis585.6 ESKD on dialysis |  |

1. Waikar SS, Wald R, Chertow GM, Curhan GC, Winkelmayer WC, Liangos O, Sosa MA, Jaber BL: Validity of ICD-9-CM Codes for Acute Renal Failure. J Am Soc Nephrol 2006; 17:1688-1694. [↑](#endnote-ref-1)