MINI-SENTINEL METHODS

ANALYTIC METHODS FOR USING LABORATORY TEST RESULTS IN ACTIVE DATABASE SURVEILLANCE: FINAL REPORT APPENDICES

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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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Mini-Sentinel Methods

Analytic Methods for Using Laboratory Test Results In Active Database Surveillance: Final Report Appendices

Table of Contents

A. APPENDIX A: LITERATURE REVIEW SEARCH TERMS AND NUMBERS OF ARTICLES IDENTIFIED IN EACH SEARCH APPROACH

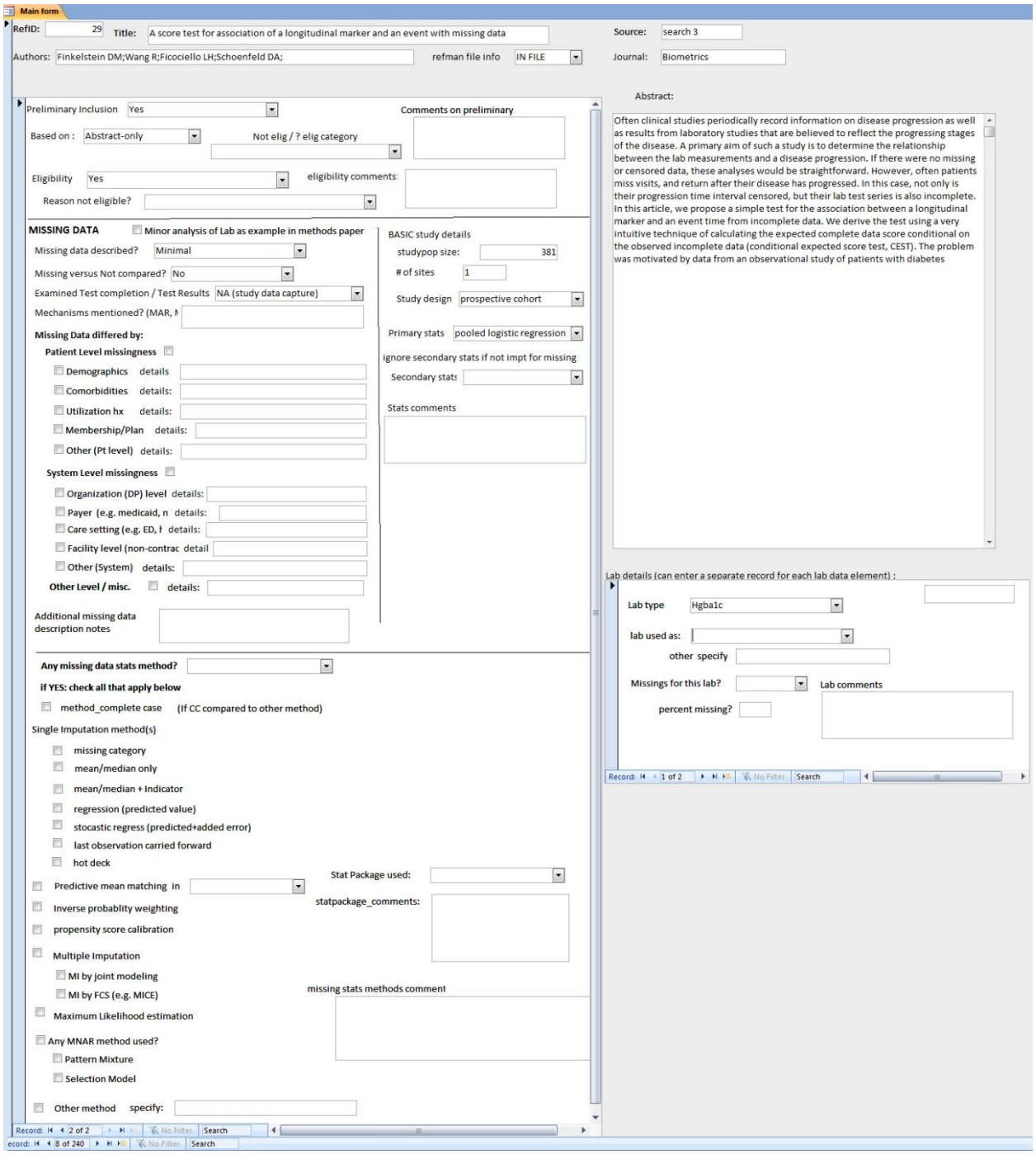
	Search descriptions [a]	Initial outcome	Final select
Preliminary searches	Electronic health record (subject heading) + Missing data (key word)	Thousands each only 12 in overlap	5- eligible 1-review article (Lin et al. 2013[a]) 6 not eligible
	"electronic medical record research laboratory data missing data"	10 articles located, 8 reviewed in more detail	3 not eligible 3 methods only 1 –other nonlab analyses only 1 – review article (Lin et al. 2013[a])
	((((missing or missingness[Text Word])) AND laboratory[Text Word]) OR diagnostic test, routine[MeSH Terms])	2864 hits 32 after title review 30 after second reviewer title review	8 eligible 4 describe missing data 7 methods only 11 not eligible
Focused methods based searches	(laboratory[Text Word] OR diagnostic test, routine[MeSH Terms]) or any of primary 11 specific labs (glucose, HGB, HgBA1c, platelets, ALP, ALT,bilirubin,creatinine, CK, lipase, INR) AND multiple imputation[text word]	49 total hits 23 retained after initial abstract review	16 eligible after article review 6 not eligible 1 methods only
	((laboratory[Text Word] OR diagnostic test, routine[MeSH Terms]) or any of primary 11 specific labs (glucose, HGB, HgBA1c, platelets, ALP, ALT,bilirubin,creatinine, CK, lipase, INR) AND (pattern mixture or selection model)	(> 800,000 in lab selections, 118 with 'pattern mixture', 532 with 'selection model') 12 articles with pattern mixture or selection model AND lab capture	1 potential eligible (pattern mixture) 11- not eligible Most selection model articles related to genetics, none with potential lab data
	((laboratory[Text Word] OR diagnostic test, routine[MeSH Terms]) or any of primary 11 specific labs (glucose, HGB, HgBA1c, platelets, ALP, ALT,bilirubin,creatinine, CK, lipase, INR) AND 'Longitudinal studies' , 2010-2014	resulted in 55 articles, 6 already captured in prior searches, 16 saved to review further.	Of 16- 3- unclear by abstract, missing data analyses unlikely and full article not accessible Of remaining 13: 3- not eligible 1-describes missing data only 9 – eligible (6 of 9 were complete case analyses)
	((laboratory[Text Word] OR diagnostic test, routine[MeSH Terms]) or any of primary 11 specific labs (glucose, HGB, HgBA1c, platelets, ALP, ALT,bilirubin,creatinine, CK,	>800,000 lab records captured. Only 13 articles showed up with the 'Predictive mean matching' text word and none overlapped with lab records captured. Six of	1-Eligible (methods article but with lab data in example, had also been sent by workgroup member) 5- methods only

	Search descriptions [a]	Initial outcome	Final select
	lipase, INR) AND 'Predictive mean matching' as text word.	the 13 articles captured were reviewed in more detail for potential lab data in methods examples.	
Search of references from key review article	References searched from review article (Lin et al. 2013[b])	96 primary articles references in review, text mentioned 41 had some lab data, 17 articles potentially eligible after title/abstract reviews	Of 17 articles: 8 – eligible 9 – not eligible
Search of articles with lab data in single journal (PDA)	General lab and primary 11 specific labs (glucose, HGB, HgBA1c, platelets, ALP, ALT,bilirubin,creatinine, CK, lipase, INR) done as 1st capture and crossed with Pharmepi D&S journal	>800,000 records from lab results of which 112 captured in Pharmepi D&S journal	22 – eligible 3 – describe missing lab data only 1 – used lab data for cohort entry 86 – not eligible

[a] Search descriptions simplified to retain only the most pertinent elements. All searches retained English Language articles only.

[b] Lin J, Jiao T, Biskupiak JE, McAdam-Marx C. Application of electronic medical record data for health outcomes research: a review of recent literature. *Expert Rev. Pharmacoecon. Outcomes Res* 2013;13(2):191-200.

B. APPENDIX B. SCREENSHOT OF RELATIONAL DATABASE ENTRY FORM



C. APPENDIX C. COPY OF PROJECT-SPECIFIC CONTENTS OF RELATIONAL DATABASE

A copy of the project-specific contents of the relational database is available upon request. Please contact the Sentinel Operations Center (info@sentinelsystem.org) for assistance.

D. APPENDIX D. SPECIFICATION DOCUMENTS FOR TEST CASES

1. MS Lab Methods Workgroup - Baseline Confounder Test Case #1

Test Case
Test Case Purpose: Confounding Adjustment ***Exposure***: Second generation antipsychotic (SGA) newly-started in adults without diabetes diagnosis ***Baseline***: Baseline is defined as within 183 days before through t0 where t0 = cohort entry date/date of initial SGA dispensing ***Outcome***: Diabetes diagnosis
Inclusion Criteria
Exposure Initiation of SGA, with no prior SGA in 183 consecutive days prior to T0. MSOC has updated the NDC code list to include drugs through 2013. Second generation Antipsychotics: ARIPIPRAZOLE ASENAPINE MALEATE ILOPERIDONE LURASIDONE HCL OLANZAPINE OLANZAPINE PAMOATE OLANZAPINE/FLUOXETINE HCL PALIPERIDONE PALIPERIDONE PALMITATE QUETIAPINE FUMARATE RISPERIDONE RISPERIDONE MICROSPHERES ZIPRASIDONE HCL ZIPRASIDONE MESYLATE
Enrollment Timeframe Medical AND drug coverage for >=183 days prior to T_0 through up to 365 days after T_0. Bridge up to 45 day gaps. (For compatibility with Outcome Test Case: +365 days of coverage is not a requirement. Capture all events, date of enrollment end if prior to +365, or date of death if prior to +365) (will be applied when this test case is later used for outcomes identification)
Enrollment Hierarchy 1st enrollment with all of the following: medical coverage, drug coverage, and initiation of SGA
Age 21 + at time of T_0

Inclusion, with flags	
• Prior/Current diabetes diagnosis within 183 days prior to T0 • Patients with zero medical encounters in the 183 days prior to T_0. • Switch of SGA • Addition of a 2nd SGA	
Censoring Criteria – which ever happens first	
• Death • Discontinuation of medical OR drug coverage • Discontinuation of SGA- no refills for either 30 or 60 days after run-out date- determination after review of data - Initial analyses planned as intent to treat ---capture future SGA prescriptions to allow for analyses examining discontinuation of SGA?	
Exclusion Criteria	
Pregnancy	The presence of any of the codes indicating a diagnosis associated with pregnancy.
Polycystic Ovarian Syndrome	An ICD-9 code of 2564
Pre-existing Diabetes	The presence of any of the codes indicating a diagnosis associated with diabetes.
Outcome	
Diagnoses of diabetes or hyperglycemia by • ICD-9 codes of • Elevated HgA1C • Blood glucose	
Covariates to capture	
Age	
Sex	
Site	
Pharmacy	Anti anxiety agents ANTICONVULSANTS ANTIDEPRESSANTS ANTIPSYCHOTIC-1ST GEN ANTI_DIABETICS BENZODIAZEPINES GLUCOCORTICOIDS HYPNOTIC-OTHER INJECTABLE ANTIPSYCHOTIC LITHIUM STATINS STIMULANTS
Utilization - in 180 days prior to T_0	Counts of medical encounters- ED ,IP, IS and AV visits

Comorbidities
Cardiac arrhythmias
Hypertension
Diabetes (distinguishes complicated vs uncomplicated)
Liver disease
Hemorragic stroke
Ischemic stroke
Metastatic cancer
CHF
Depression
Dementia
Peripheral Vascular disease
Psychoses
Alcohol abuse
Hemiplegia
Weight loss
Obesity
Chronic pulmonary disease
Pulmonary circulation disorders
Renal failure
Rheumatoid arthritis
Oseoarthritis
Myocardial Infarction
Anemia
HIV
Electrolytic Disorders

2. MS Lab Methods Workgroup – Baseline Confounder Test Case # 2

Test Case

Test case purpose: confounding adjustment

Exposure: ACE inhibitor (ACEi) initiation in patients with existing diabetes diagnosis

Baseline confounder laboratory test result value: serum creatinine.

Baseline is defined as within 183 days before drug initiation through 0 or 3 days after drug initiation. Hyperkalemia can occur within the first few days after ACE initiation. Therefore, we will not include anything beyond 3 days after drug initiation in our consideration of baseline. Inclusion of days 1 through 3 after drug initiation will be considered primarily to determine whether the baseline proportion with serum creatinine results available increases substantially when those days are included.

Outcome: Coded hyperkalemia diagnosis (K+ laboratory result values not in MSDD) in any care setting

Inclusion Criteria

Initiation is defined as no use of ACEi in the prior 183 days
ACEi dispensing in Jan 1, 2008 through Oct 31, 2012
ACE Inhibitor Generic Name List:

BENAZEPRIL & HYDROCHLOROT BENAZEPRIL HCL CAPTOPRIL CAPTOPRIL & HYDROCHLOROTH ENALAPRIL MALEATE	ENALAPRIL MALEATE & HCTZ ENALAPRIL MALEATE & HYDRO ENALAPRIL MALEATE-FELODIP ENALAPRILAT FOSINOPRIL SODIUM FOSINOPRIL SODIUM & HYDRO	LISINOPRIL LISINOPRIL & HYDROCHLOROT MOEXIPRIL HCL MOEXIPRIL-HYDROCHLOROTHIA PERINDOPRIL ERBUMINE	QUINAPRIL HCL QUINAPRIL-HYDROCHLOROTHIA RAMIPRIL TRANDOLAPRIL TRANDOLAPRIL-VERAPAMIL HC

Age 21 or older on date of initial ACEi dispensing

At least one diabetes diagnosis before ACEi dispensing
- ICD9 in
250* = Diabetes mellitus

Medical and drug coverage for at least 183 days before ACEi dispensing. Bridge up to 45 day gaps.

Exclusion Criteria
ESRD or acute kidney failure with dialysis at any time before ACEi dispensing. The rationale for excluding these patients is as follows: Patients with acute kidney failure have rapidly changing clinical status and can have rapid fluctuations in potassium values. Patients with ESRD will have potassium values that rise/fall depending (in part) on proximity to dialysis procedures. Because neither of these scenarios is the intent of this lab results missingness analysis work, nor is it our intent to determine rates of hyperkalemia in various patient groups, and we will have sufficient sample size without including these subsets of patients, we are not including them. Patients with lesser degrees of chronic kidney disease are included (see Baseline Covariates below). - (Any code below in IP or ED setting) OR (>=2 codes below in outpatient setting on different days) ICD9 diagnoses 403.*1 = Hypertensive chronic kidney disease, CKD Stage V or ESRD 404.*2 = Hypertensive heart and chronic kidney disease, without heart failure and with CKD stage V or ESRD 404.*3 = Hypertensive heart and chronic kidney disease, with heart failure and with CKD stage V or ESRD 584* = Acute kidney failure 585.6 = End stage renal disease 586 = Renal failure, unspecified 996.56 = Mechanical complication of other specified prosthetic device, implant, and graft due to peritoneal dialysis catheter 996.68 = Infection and inflammatory reaction due to internal prosthetic device, implant, and graft due to peritoneal dialysis catheter 996.73 = Other complications of internal (biological) (synthetic) prosthetic device, implant, and graft due to renal dialysis device, implant, and graft V45.1* = Renal dialysis status V56* = Encounter for dialysis and dialysis catheter care ICD9 procedures 39.95 = Hemodialysis 54.98 = Peritoneal dialysis CPT procedures 90921 = Dialysis, deprecated code 90925 = Dialysis, deprecated code 90935-90999 = Dialysis
Exposure
ACEi initiation: select 1st ACEi dispensing / enrollment period that satisfies all inclusion and exclusion criteria
Baseline Covariates (collection of baseline covariates occurs from 183 days prior to initiation of ACEi to 3 days after initiation of ACEi, inclusive
Age in years at initiation of ACEi
Sex
Race/Ethnicity (some Data Partners have this data element available and we will determine whether its inclusion changes findings and interpretation))
Data Partner Site
All diagnoses of hyperpotassemia during the baseline period
All serum creatinine result value measurements and serum creatinine procedure codes during the baseline period

Any dispensings of drugs that affect potassium during the baseline period
Generic Name List:

ALISKIREN FUMARATE	HEPARIN (PORCINE) IN SODI	BROMFENAC SODIUM	PHENYLBUTAZONE
ALISKIREN-HYDROCHLOROTHIA	HEPARIN SOD (PORCINE) IN	CELECOXIB	PIROXICAM
ALISKIREN-VALSARTAN	HEPARIN SODIUM	DICLOFENAC POTASSIUM	ROFECOXIB
	HEPARIN SODIUM (BOVINE)	DICLOFENAC SODIUM	SALSALATE
FLUCONAZOLE	HEPARIN SODIUM (PORCINE)	DICLOFENAC W/ MISOPROSTOL	SODIUM THIOSALICYLATE
FLUCONAZOLE IN NACL		DIFLUNISAL	SULINDAC
ITRACONAZOLE		ETODOLAC	TOLMETIN SODIUM
KETOCONAZOLE	AMILORIDE & HYDROCHLOROTH	FENOPROFEN CALCIUM	VALDECOXIB
POSACONAZOLE	AMILORIDE HCL	FLURBIPROFEN	
VORICONAZOLE	EPLERENONE	IBUPROFEN	PENTAMIDINE ISETHIONATE
	SPIRONOLACTONE	INDOMETHACIN	
ACEBUTOLOL HCL	SPIRONOLACTONE/HCTZ	INDOMETHACIN SODIUM	CYCLOSPORINE
ATENOLOL	SPIRONOLACTONE & HCTZ	KETOPROFEN	CYCLOSPORINE MODIFIED (FO
BETAXOLOL HCL	SPIRONOLACTONE & HYDROCHL	KETOROLAC	EVEROLIMUS
BISOPROLOL FUMARATE	TRIAMTERENE	TROMETHAMINE	EVEROLIMUS (IMMUNOSUPPRES
CARTEOLOL HCL	TRIAMTERENE & HCTZ	MAGNESIUM SALICYLATE	PIMECROLIMUS
CARVEDILOL	TRIAMTERENE & HYDROCHLORO	MECLOFENAMATE SODIUM	SIROLIMUS
CARVEDILOL PHOSPHATE		MEFENAMIC ACID	TACROLIMUS
LABETALOL HCL	POTASSIUM	MELOXICAM	TACROLIMUS (TOPICAL)
METOPROLOL SUCCINATE	POTASSIUM ACET, BICARB &	MEPROBAMATE-ASPIRIN	TEMSIROLIMUS
METOPROLOL TARTRATE	POTASSIUM ACETATE	NABUMETONE	POLYMYXIN B-TRIMETHOPRIM
NADOLOL	POTASSIUM BICARB & CHLORI	NAPROXEN	TRIMETHOPRIM
NEBIVOLOL HCL	POTASSIUM BICARBONATE	NAPROXEN SODIUM	TRIMETHOPRIM HCL
PENBUTOLOL SULFATE	POTASSIUM BICARBONATE-CIT	OXAPROZIN	TRIMETHOPRIM/SULFAMETHOXA
PINDOLOL	POTASSIUM CHLORIDE		SULFAMETHOXAZOLE-TRIMETHO
PROPRANOLOL HCL	POTASSIUM CHLORIDE MICROE		SULFAMETHOXAZOLE/TRIMETHOPRIM
PROPRANOLOL HCL SUSTAINED	POTASSIUM GLUCONATE		
PROPRANOLOL HYDROCHLORIDE			
TIMOLOL MALEATE	SODIUM POLYSTYRENE SULFON		
DIGOXIN			

All diagnoses of chronic kidney disease, except as indicated in Exclusion Criteria, during the baseline period
- ICD9 in
403* = Hypertensive chronic kidney disease, except 403.*1 (see Exclusion Criteria)
404* = Hypertensive heart and chronic kidney disease, except 404.*2 and 404.*3 (see Exclusion Criteria)
585* = Chronic kidney disease, except 585.6 (see Exclusion Criteria)

All diagnoses of comorbidities included in the comorbidity score developed by Gagne et al (J Clin Epidemiology, 2011 July; 64(7): 749-759). This score is implemented in the CIDA tool from the Mini-Sentinel Operations Center. We will keep separate disease indicators as well as the overall score. These comorbidities must remain in the baseline covariates list because they are part of the CIDA tool and the CIDA tool will be used to facilitate/expedite cohort identification. We do not expect many of these to contribute in important ways to confounding, but we will include this standard set of comorbidities for all test cases for consistency and robustness. - ICD9 in AIDS/HIV Congestive Heart Failure Cardiac arrhythmias Hypertension Dementia Complicated diabetes Liver disease Any tumor Metastatic cancer Peripheral vascular disease Chronic pulmonary disease Pulmonary circulation disorders Renal failure: This disease indicator is part of the typical Gagne score elements and is listed here for that reason. For this study, severe renal disease is excluded and specific renal disease of interest is coded above and we don't anticipate using this additional renal indicator. Anemia Fluid and electrolyte disorders Psychoses Alcohol abuse Weight loss Hemiplegia Coagulopathy
All diagnoses of the following comorbidities in addition to the ones captured in the Gagne comorbidity score, during the baseline period: - ICD9 in 410* = Acute myocardial infarction 412* = Old myocardial infarction 430* = Subarachnoid hemorrhage 431* = Intracerebral hemorrhage 432* = Other and unspecified intracranial hemorrhage 433* = Occlusion and stenosis of precerebral arteries 434* = Occlusion of cerebral arteries 436* = Acute, but ill-defined cerebrovascular disease
Counts of encounters during the baseline period grouped by - Outpatient visits - ED visits - Hospitalizations - Non-acute institutional stays
Indicator of zero encounters during the baseline period
Count of unique drug classes among dispensings during the baseline period

Outcome of interest

Hyperkalemia
- ICD9 in
276.7 = hyperpotassemia

Censoring Events (collection of censoring events begins at initiation of ACEi)

- End of either medical or drug coverage
- Discontinuation of ACEi: no refills for 60 days after run-out date (with discontinuation date defined as date of run-out of dispensed days' supply)
- New occurrence of ESRD or Dialysis as defined in Exclusion Criteria:
  (1st occurrence of any code below in IP or ED setting) OR (2nd occurrence on a different day than the 1st occurrence of any code below in an outpatient setting. The 1st occurrence may have occurred during the baseline period.)

  ICD9 diagnoses
  403.*1 = Hypertensive chronic kidney disease, CKD Stage V or ESRD
  404.*2 = Hypertensive heart and chronic kidney disease, without heart failure and with CKD stage V or ESRD
  404.*3 = Hypertensive heart and chronic kidney disease, with heart failure and with CKD stage V or ESRD
  584* = Acute kidney failure
  585.6 = End stage renal disease
  586 = Renal failure, unspecified
  996.56 = Mechanical complication of other specified prosthetic device, implant, and graft due to peritoneal dialysis catheter
  996.68 = Infection and inflammatory reaction due to internal prosthetic device, implant, and graft due to peritoneal dialysis catheter
  996.73 = Other complications of internal (biological) (synthetic) prosthetic device, implant, and graft due to renal dialysis device, implant, and graft
  V45.1* = Renal dialysis status
  V56* = Encounter for dialysis and dialysis catheter care

  ICD9 procedures
  39.95 = Hemodialysis
  54.98 = Peritoneal dialysis

  CPT procedures
  90921 = Dialysis, deprecated code
  90925 = Dialysis, deprecated code
  90935-90999 = Dialysis

- Death
- 31OCT2013
- Initiation of ACEi + 365 days
- First occurrence of hyperkalemia/hyperpotassemia

Follow-up

Start = Initiation of ACEi
End = Earliest censoring event defined above
For each patient, we will collect exposure (ACEi dispensings) and an indicator (y/n) of outcome (hyperkalemia diagnoses) during the follow-up period, and control for baseline serum creatinine testing value as a confounder.

3. MS Lab Methods Workgroup – Baseline Confounder Test Case # 3

Test Case
Test Case Purpose: Confounding adjustment ***Exposure:*** Initiation of selected antimicrobials in patients undergoing chronic warfarin (W) therapy. Chronic warfarin therapy is defined as having at least two dispensings of warfarin prior to the dispensing date of the antimicrobial of interest (i.e., warfarin therapy started prior to the antimicrobial). The cohort entry date (T_0) is the dispensing date of the antimicrobial. The days' supply dispensed of the last dispensing of warfarin prior to T_0 must span T_0. ***Baseline confounder laboratory test result value***: INR. For this test case, baseline INR monitoring is defined as any INR result value up to 30 days before and including T_0 (i.e., determined from lab results [procedure codes also pulled]. If more than one INR monitoring within days – 30 and T_0, keep the relative date closest to T_0 that INR monitoring occurs. ***Outcom***e: Coded bleeding/hemorrhage diagnosis within 30 days after T_0.
Inclusion Criteria
1) Antimicrobials: Dispensing of any of the antimicrobial agents listed below from Jan 1, 2008 through Nov 30, 2013. These antimicrobials reflect agents considered to potentially interact with warfarin to increase bleeding risk with moderate or major bleeding risk. KPCO has identified the relevant NDCs for these antimicrobials.
Include all oral formulations for all the antimicrobials listed (e., for erythromycin this includes the base, stearate, ethylsuccinate, etc.). Also, include single agent as well as combination products (e.g., for sulfamethoxazole, also include it in combination with trimethoprim). NDC and days supply for index antimicrobial will be retained in the data. Potentially interacting antimicrobial generic names: Fluconazole Itraconazole Ketoconazole Miconazole Ciprofloxacin Levofloxacin Moxifloxacin Norfloxacin Ofloxacin Azithromycin Erythromycin Sulfamethoxazole Sulfisoxazole Tetracycline Doxycycline Demeclocycline Chloramphenicol Isoniazid Metronidazole Neomycin Comparator antimicrobial generic names: Cephalexin Clindamycin Trimethoprim (only products **NOT** in combination with sulfamethoxazole)
2) Age 21 or older on T_0.
3) Medical and drug coverage for >= 183 days before antimicrobial dispensing. Bridge up to 45 day gaps.

Exclusion Criteria
1) Only one dispensing of warfarin. 2) Diagnosis codes for bleeding/hemorrhagic associated with traumatic injury: 801.21, Closed fracture of base of skull with subarachnoid, subdural, and extradural hemorrhage 852.16, Subarachnoid hemorrhage following injury 852.20, Subarachnoid hemorrhage following injury 852.21, Subarachnoid hemorrhage following injury 852.25, Subarachnoid hemorrhage following injury
Exposure
- Antimicrobial prescription - Select 1st Antimicrobial dispensing / enrollment period that satisfies all inclusion and exclusion criteria - Date of exposure = t0
Baseline Covariates (Baseline covariates are defined as occurring from 183 days prior to T_0 through T_0, unless otherwise specified.
Age at cohort entry date
Sex
Race
Ethnicity
Data Partner Site
Counts of encounters grouped by - Outpatient visits - ED visits - Hospitalizations - Non-acute institutional stays
Indicator of zero encounters in the 183 days before index date
Count of unique drug classes among dispensings in the 183 days prior to T0
Drug Covariates: Dispensings of selected other drugs with potential to affect INR. KPCO has identified relevant NDCs for these drugs. The included drug covariates are shown in Tables 1 and 2. Table 1. Drugs Other than Antimicrobials that should be avoided when Possible in Warfarin Users due to potential for *Increased* Anticoagulant Effect or that otherwise increase Bleeding Risk aminosalicylic acid, amiodarone, apixaban, argatroban, aspirin, bosentan, celecoxib, cimetidine, clofibrate, clopidogrel, dabigatran, dipyridamole, diflunisal, disulfiram, esomeprazole, fenofibrate, fenoprofen calcium, fluoxetine, fluvastatin, fluvoxamine, gemfibrozil, indomethacin, ketoprofen, lansoprazole, lovastatin, meclofenamate, mefenamic acid, omeprazole, pantoprazole, pentoxifylline, phenylbutazone, piroxicam, pravastatin, propafenone, propoxyphene, quinidine, rabeprazole, rivaroxaban, sulfinpyrazone, sulindac, zafirlukast, zileuton

Table 2. Drugs Other than Antimicrobials that should be avoided when Possible in Warfarin Users due to potential for Decreased Anticoagulant Effect

amobarbital	phenobarbital	secobarbital
butabarbital	phenytoin	sucralfate
carbamazepine	primidone	vitamin K
cholestyramine		

All diagnoses of comorbidities included in the comorbidity score developed by Gagne et al (J Clin Epidemiology, 2011 July; 64(7): 749-759). This score is implemented in the CIDA tool from the Mini-Sentinel Operations Center. We will keep separate disease indicators as well as the overall score. These comorbidities must remain in the baseline covariates list because they are part of the CIDA tool and the CIDA tool will be used to facilitate/expedite cohort identification. We do not expect many of these to contribute in important ways to confounding, but we will include this standard set of comorbidities for all test cases for consistency and robustness. These comorbidities include:
AIDS/HIV
Congestive Heart Failure
Cardiac arrhythmias
Hypertension
Dementia
Complicated diabetes
Liver disease
Any tumor
Metastatic cancer
Peripheral vascular disease
Chronic pulmonary disease
Pulmonary circulation disorders
Renal failure
Anemia
Fluid and electrolyte disorders
Psychoses
Alcohol abuse
Weight loss
Hemiplegia
Coagulopathy

INR lab capture

All INR result value measurements and INR procedure codes in 60 days and post t0

Outcome of interest

Any of the following coded bleeding diagnoses from an inpatient care setting within 60 days after t0 (outcomes within 30 days will be primary focus, 60 days captured for sensitivity analyses).
The code list below was developed after review of the following documents:
1) Witt DM, Delate T, Clark NP et al. Nonadherence with INR Monitoring and Anticoagulant Complications. Thrombosis Research 2013;e124-e130.
2) Tsai TT, Ho M, Xu S, et al. Increased Risk of Bleeding in Patients on Clopidogrel Therapy After Drug-Eluting Stents Implantation: Insights From the HMO Research Network-Stent Registry (HMORN-Stent). Circ Cardiovasc Interv 2010;3:230-235.
Bleeding:
DX,type
285.1,Acute posthemorrhagic anemia
285.9 ,Anemia, unspecified (must be in combination with another bleeding code from this list)
286.5, Hemorrhagic disorder due to circulating anticoagulants

286.6, Defibrination syndrome
286.9, Other and unspecified coagulation defects
287.8,other bleeding
287.9,other bleeding
360.43, Hemophthalmos
372.72, Conjunctival hemorrhage
379.23, Vitreous hemorrhage
423.0,Hemipericardium
430,Intracranial hemorrhage
431,Intracranial hemorrhage
432,Intracranial hemorrhage
432.0,Intracranial hemorrhage
432.1,Intracranial hemorrhage
432.9,Intracranial hemorrhage
455.2,GI Hemorrhage
455.5,GI Hemorrhage
455.8,GI Hemorrhage
456.0,GI Hemorrhage
456.20,GI Hemorrhage
459.0,"Hemorrhage,unspecified"
530.7,GI Hemorrhage
530.82,GI Hemorrhage
531.00,GI Hemorrhage
531.01,GI Hemorrhage
531.20,GI Hemorrhage
531.21,GI Hemorrhage
531.40,GI Hemorrhage
531.41,GI Hemorrhage
531.60,GI Hemorrhage
531.61,GI Hemorrhage
532.00,GI Hemorrhage
532.01,GI Hemorrhage
532.20,GI Hemorrhage
532.21,GI Hemorrhage
532.40,GI Hemorrhage
532.41,GI Hemorrhage
532.60,GI Hemorrhage
532.61,GI Hemorrhage
533.00,GI Hemorrhage
533.01,GI Hemorrhage
533.20,GI Hemorrhage
533.21,GI Hemorrhage
533.40,GI Hemorrhage
533.41,GI Hemorrhage
533.60,GI Hemorrhage
533.61,GI Hemorrhage
534.00,GI Hemorrhage
534.01,GI Hemorrhage
534.20,GI Hemorrhage
534.21,GI Hemorrhage
534.40,GI Hemorrhage

534.41,GI Hemorrhage
534.60,GI Hemorrhage
534.61,GI Hemorrhage
535.01,GI Hemorrhage
535.11,GI Hemorrhage
535.21,GI Hemorrhage
535.31,GI Hemorrhage
535.41,GI Hemorrhage
535.51,GI Hemorrhage
535.61,GI Hemorrhage
537.83,GI Hemorrhage
562.02,GI Hemorrhage
562.03,GI Hemorrhage
562.12,GI Hemorrhage
562.13,GI Hemorrhage
568.81,GI Hemorrhage
569.3,GI Hemorrhage
569.85,GI Hemorrhage
578.0,GI Hemorrhage
578.1,GI Hemorrhage
578.9,GI Hemorrhage
599.7,Hematuria
626.2,Vaginal bleeding
627.0,Vaginal bleeding
627.1,Vaginal bleeding
719.10,Hemarthrosis
719.11,Hemarthrosis
719.12,Hemarthrosis
719.13,Hemarthrosis
719.14,Hemarthrosis
719.15,Hemarthrosis
719.16,Hemarthrosis
719.17,Hemarthrosis
719.18,Hemarthrosis
719.19,Hemarthrosis
782.7, Spontaneous ecchymosis
784.7,Epistaxis
784.8,Hemorrhage from throat
786.3,Hemoptysis
790.92, Abnormal coagulation profile
852.00,Intracranial hemorrhage
852.01,Intracranial hemorrhage
852.02,Intracranial hemorrhage
852.03,Intracranial hemorrhage
852.04,Intracranial hemorrhage
852.05,Intracranial hemorrhage
852.06,Intracranial hemorrhage
852.09,Intracranial hemorrhage
852.20,Intracranial hemorrhage
852.21,Intracranial hemorrhage
852.22,Intracranial hemorrhage

852.23,Intracranial hemorrhage
852.24,Intracranial hemorrhage
852.25,Intracranial hemorrhage
852.26,Intracranial hemorrhage
852.29,Intracranial hemorrhage
852.40,Intracranial hemorrhage
852.41,Intracranial hemorrhage
852.42,Intracranial hemorrhage
852.43,Intracranial hemorrhage
852.44,Intracranial hemorrhage
852.45,Intracranial hemorrhage
852.46,Intracranial hemorrhage
852.49,Intracranial hemorrhage
853.00,Intracranial hemorrhage
853.01,Intracranial hemorrhage
853.02,Intracranial hemorrhage
853.03,Intracranial hemorrhage
853.04,Intracranial hemorrhage
853.05,Intracranial hemorrhage
853.06,Intracranial hemorrhage
853.09,Intracranial hemorrhage
922.31, Contusion of back
923.11, Contusion of elbow
924.00, Contusion of thigh,
924.01, Contusion of hip
924.11, Contusion of knee
964.2, Poisoning by anticoagulant
998.11,other bleeding

Censoring Events (collection of censoring events begins at initiation of antimicrobial)

- End of either medical or drug coverage
- Death
- Dec 31 2013 (Initiation of antimicrobial + 30 days)
- First occurrence of bleeding outcome

Follow-up

Start = Index date
End = earliest of any censoring event:
For each patient, we will collect exposure (antimicrobial dispensing) and an indicator (y/n) of outcome (bleeding diagnoses) during the 30 day follow-up period, and control for baseline INR as a confounder.

4. MS Lab Methods Workgroup – Cohort Identification Test Case #1: Pregnancy Cohort

Test Case

Test Case Purpose: Enhancement of Cohort Identification.

1) The value in lab results data is to enhance cohort ID (e.g., including women who may not have delivered a live born infant).
2) The estimated gestational length is potentially more accurate with lab results included compared to methods that do not use lab results (such as those discussed in the following paper: Margulis AV, Palmsten K, Andrade SE, et a. Beginning and duration of pregnancy in automated health care databases: review of estimation methods and validation results. Pharmacoepidemiol Drug Saf 2015; 24: 335–342).

Questions to be Addressed:

1) How many pregnancies do we gain by not relying solely on claims (i.e., by including pregnancies identified using laboratory test results that include women with pregnancy loss/no live born delivery)?
    a. Find first pregnancy per person with diagnosis/procedure codes only
    b. Find first pregnancy per person with diagnosis/procedure codes and lab test results (qualitative and/or quantitative)
    c. Find first pregnancy per person with lab test results (qualitative and/or quantitative) only
    d. Determine numbers and proportions of pregnancies detected
        i. by labs only
        ii. by diagnosis/procedure codes only
        iii. by both methods
    e. For women with first pregnancy that includes a lab test result, describe (mean, median, range) of the number of QL and/or QN lab test results per woman
    f. Determine the numbers and proportions of pregnancies detected by each of the method in 1) d. above that meets one of the outcomes categories of interest (see Outcomes Section below).
2) For women with live born deliveries whose pregnancies were determined as having both diagnosis/procedure codes and lab test results, how does the presence of the first (positive qualitative or quantitative) lab test result change the timing of when a pregnancy is first identified in electronic data? What is the difference in how early a pregnancy is identified when lab results are incorporated?
    a. What proportion of these women have the pregnancy identified earlier using the lab test result? Summarize the "lead time" (e.g., days or weeks earlier that the pregnancy is identified) gained by having the lab test result.
    b. What proportion of these women have a pregnancy identified earlier using the diagnosis/procedure code? Summarize the "lead time" gained by having the diagnosis/procedure code.
    c. Does this differ by DP?
    d. Using the 270 day metric that has been applied in previous observation studies based only on delivery outcomes codes (delivery code date minus 270 days = estimated length of gestation)
        i. Among the women who have a pregnancy first identified from the lab test result (with or without a diagnosis/procedure code), for what proportion does the date of the first positive pregnancy lab test result fall within the date range of the 270 day metric?
        ii. Use the 270 day metric to identify the first trimester as the initial 90 days among women who have a pregnancy identified using a lab test result (with or without a diagnosis/procedure code and the lab test result can be prior to or after the code; this group includes more women that d.i.). Describe how many women have a lab only in the first trimester period vs. diagnosis/procedure codes vs. both labs and diagnosis/procedure codes.

Drug Exposure: None.

Exposure: Positive pregnancy lab test result, prenatal care visits/procedures, and/or prenatal pregnancy diagnosis code/procedure

***Outcome*:** Not required for cohort identification but will be used to assess estimated gestational length. Outcomes to be captured include:

1) Live born Delivery
    a. Term
    b. Preterm (using categories available from diagnosis codes)
2) Pregnancy Loss
    a. Ectopic and other extra-uterine
    b. Fetal death
    c. Stillborn
    d. Miscarriage and therapeutic/elective abortion
3) Disenrollment, death, end of study timeframe
4) Uncertain: It's possible to have a woman who is alive, enrolled, had an exposure event but no outcome. These women will be included and described, but will not be included in analysis for questions of interest.

Inclusion Criteria

4) Age 14 - 50 on t0 or t0L. T0 or T0L is the first indication of pregnancy based on earliest date, whether that date is associated with a lab test result, a diagnosis code, or a procedure code ("exposure"). Will capture t0 date for diagnosis/procedure or t0L for lab result date for women who have only diagnosis/procedure code or lab test result. For women with both t0 and t0L, we will capture both. We expect women with t0 and women with t0L to account for the majority of identified pregnancies.
5) Flag but don't filter: Medical and drug coverage for >= 183 days before t0, bridging gaps up to 45 days and <= 270 days after t0. This will NOT be required for inclusion because we want to quantify (i.e., describe) those women who enter cohort after pregnancy starts. However, these medical and drug coverage criteria for inclusion will be applied for the primary analysis.
6) Flag but don't filter: QN and QL pregnancy laboratory test results
7) Female
8) Date range inclusive of January 1, 2008 – December 31, 2013

Exclusion Criteria

None

Exposure

Positive pregnancy lab result, or prenatal care visits/procedures, or prenatal pregnancy diagnosis code/procedure: see Exposures.xls for diagnosis codes and procedure codes.

Lab Test Name and Definition of 'Positive'
PG_QL = POSITIVE
PG_QL_U = POSITIVE
PG_B_QN > 25 mIU/mL
PG_QN > 25 mIU/mL

Baseline Covariates (Baseline covariates are defined as occurring from 183 days prior to T0 [or T0L] through T0 [or T0L], unless otherwise specified.)

All enrollment periods

Age at cohort entry date

Race

Ethnicity

Data Partner Site

Counts of encounters grouped by
- Outpatient visits

- ED visits
- Hospitalizations
- Non-acute institutional stays

Indicator of zero encounters in the 183 days before index date

Pregnancy lab results capture

For both QN and QL lab test results, we will capture all QN lab results within the woman's included enrollment periods date ranges. For analysis, we will then limit to the first qualifying pregnancy identified for each woman. All positive qualitative and all quantitative pregnancy result value measurements and procedure/diagnoses codes in the 90 days prior to and 300 days post t0 or t0L will be identified.

Other Covariates (Other covariates are defined as occurring from 183 days prior to T0 [or T0L] 270 days post T0 [or T0L])

1) Women with any of the following tumor codes

157.4	Malignant neoplasm of pancreas - Islets of Langerhans
181*	Malignant neoplasm of placenta
183*	Malignant neoplasm of ovary and other uterine adnexa
209*	Neuroendocrine tumors
211.7	Benign neoplasm of pancreas - Islets of Langerhans
220*	Benign neoplasm of ovary
630*	Hydatidiform mole
631*	Other abnormal product of conception

2) Women with injections or ingestion of hCG (see hCG code list on covariate Excel spreadsheet)

Outcome of interest

1) Live born delivery (term and preterm): see list of codes in Outcomes.xls
2) Pregnancy Loss (ectopic and other extra-uterine pregnancies, fetal death, stillbirth, miscarriage, therapeutic/elective abortion): see list of codes in Outcomes.xls
3) Disenrollment, death, end of study timeframe
4) Uncertain: It's possible to have a woman who is alive, enrolled, had an exposure event but no outcome.

Censoring Events (collection of censoring events begins t0)

- End of medical or drug coverage
- Death
- Dec 31 2013
- Delivery, pregnancy loss or any other outcome as defined above (i.e., we will include only the first pregnancy in the date range of the study)

Follow-up

Start = t0 and/or t0L
End = earliest of any censoring event (see above)

Other notes

We will also capture all outcomes in such a way that we can also describe women who are only identified as 'pregnant' at the time of their delivery or other outcome. (Most will be due to recent enrollments but there will likely be a few 'unusual' cases with longer enrollments (women without pre-natal care, pregnancy loss).

Margulis paper looked at timing (beginning and duration) of pregnancy
normal pregnancy might not have a lab on record
most women have 1st indication at about 8 weeks
encounter codes indicate ultrasound but no details of ultrasound
women often present with home pregnancy lab test (urine qualitative)
ob/gyn rarely administers pregnancy lab tests to women with normal pregnancies
do serum bhcg if some questions unanswered (potential trouble, risk of poor outcome, question about age of fetus, track pregnancy [rising or falling bhcg], borderline test at home, borderline serum bhcg, spotting/miscarriage [if falling confirms fetal death], confirm ectopic pregnancy, trophoblastic results in very high bhcg)

5. MS Lab Methods Workgroup – Cohort Identification Test Case #2: Chronic Kidney Disease Cohort

Test Case
Test Case Purpose: Augmenting Identification of a Cohort of Patients with Chronic Kidney Disease by including laboratory test results. Use laboratory data from outpatient encounters (serum creatinine) to Employ the CKD-EPI equation[1] (to estimate patient's glomerular filtration rate; eGFR)[1] to expand identifying a cohort of adults aged >=21 through <=89 years with CKD. We will also assess the percent agreement between using laboratory test results and diagnosis codes in the cohort of CKD patients. This test case will identify a cohort of patients with a mix of prevalent and incident CKD since we will only require 183 days minimum enrollment time prior to first indicator of CKD. This design will provide a higher proportion of patients with later stage CKD versus a focus on incident cases only. This is important for drug safety research because later stage patients are more often candidates for medication dosage/frequency of dosing adjustment and at higher risk of adverse outcome if medications are not appropriately adjusted for level of renal dysfunction. ***Questions to be Addressed with Test Case:*** 3) What is the percent agreement between CKD identified using **at least 2 eGFR values** <60ml/min/1.73m^2 (with no intervening values >=60) measured at least 90 days apart compared to identifying CKD using **at least 1 coded diagnosis** of CKD. 4) What is the percent agreement between CKD identified using **at least 2 eGFR values** <60ml/min/1.73m^2 (with no intervening values >=60) measured at least 90 days apart compared to identifying CKD using **at least 2 coded diagnoses** of CKD. 5) What is the percent agreement between CKD identified using **at least 1 eGFR value** <60ml/min/1.73m^2 compared to identifying CKD using **at least 1 coded diagnosis** of CKD. 6) Describe the CKD cohort by age (e.g. < 65, >= 65 - < 75, and >=75 – 89). 7) Describe the CKD cohort by CKD stage (e.g. stage 3, Stages 4, Stage 5/ESRD, and unstaged). 8) Describe cohort augmentation by calendar year. Note: The "primary" cohort for questions will be the 2012 CKD cohort. Two other cohorts, 2010, and 2008 will also be identified. These other two cohorts will be employed to answer this question. 9) Each analysis will be repeated by Data Partner These analyses not only answer the question of how many additional patients we gain in a CKD cohort by including lab test results, but also assist in understanding whether differences in how lab result values are available to identify patients for inclusion in a CKD cohort leads to variation in cohort characteristics ***Drug Exposure:*** None ***Exposure:*** Serum creatinine result value (to be used to estimate GFR using CKD-EPI equation) ***Outcome*:** Not required. However, will capture all coded diagnoses of CKD Stages 3, 4, 5/ESRD, and unstaged across the project date range for all patients in the cohort.

[1] We will quantify the n and % of patients with and without race data in this cohort. For patients without race data, we will assume non-African American when employing the CKD-EPI equation to estimate GFR.

Inclusion Criteria
9) Age >=21 and <=89 years at time of first serum creatinine result value in study timeframe
10) Medical and drug coverage for >=183 (and >=365) days prior to index date (t0 or t0L) in 2008, 2010, or 2012. The index date T0 is defined as the first of CKD diagnosis code in the project date range. The index date t0L is defined as the first eGFR (based on serum creatinine result value) < 60 ml/min when that serum creatinine result date precedes the date of the first CKD diagnosis code or when there is no CKD diagnosis code for a patient. The earliest of t0 or t0L will be used for the 365 day baseline medical and drug coverage determination. 11) Project date range inclusive of January 1, 2007 – December 31, 2013 (cohort identification occurs in 2008, 2010, and 2012 with baseline data up to one year prior).
Exclusion Criteria
Exclude patients with coded diagnosis of kidney transplant or dialysis codes at baseline (within 365 days prior to t0 or t0L): hemodialysis 39.95 venous catheterization for renal dialysis 38.95 peritoneal dialysis 54.98 hypotension of dialysis 458.21 Mechanical complication of other device due to peritoneal dialysis catheter 996.56 renal dialysis status V45.1 encounter for dialysis V56 extracorporeal dialysis V56.0 fitting and adjustment of extracorporeal catheter V56.1 fitting and adjustment of peritoneal catheter V56.2 encounter for adequacy testing for dialysis V56.3 encounter for adequacy testing for hemodialysis V56.31 other dialysis V56.8 Dialysis other than hemodialysis 90945 Dialysis other than hemodialysis 90947 Hemodialysis procedure with single physician evaluation 90935 Hemodialysis procedure requiring repeated evaluation(s) with or without substantial revision of dialysis prescription 90937 COMPLICATIONS OF TRANSPLANTED KIDNEY 996.81 KIDNEY REPLACED BY TRANSPLANT V42.0 Transplant of kidney 55.6 Renal autotransplantation 55.61 Other kidney transplantation 55.69 Renal allotransplantation 50360 Renal allotransplantation 50365 Removal of transplanted renal allograft 50370 Renal autotransplantation 50380 End stage renal disease 585.6
Exposure
Serum creatinine result values

Baseline Covariates (Baseline covariates are defined as occurring from 183 (and 365) days prior to T0 or T0L through T0 or T0L, unless otherwise specified.
Age at cohort entry date
Sex
Race
Ethnicity
Data Partner Site
Counts of encounters grouped by - Outpatient visits - ED visits - Hospitalizations - Non-acute institutional stays
Indicator of zero encounters in the 183 (365) days before index date
All diagnoses of comorbidities included in the comorbidity score developed by Gagne et al (J Clin Epidemiology, 2011 July; 64(7): 749-759). This score is implemented in the CIDA tool from the Mini-Sentinel Operations Center. We will keep separate disease indicators as well as the overall score. We do not expect many of these to contribute in important ways to confounding, but we will include this standard set of comorbidities for use in describing the cohort. Hypertension and diabetes are likely to be of particular importance in a CKD cohort. The Gagne et al. comorbidity score includes an indicator for renal failure which will not be included in the score for this project to avoid clouding the primary results here that focus on CKD. The remaining comorbidities include: AIDS/HIV Congestive Heart Failure Cardiac arrhythmias Hypertension Dementia Complicated diabetes Liver disease Any tumor Metastatic cancer Peripheral vascular disease Chronic pulmonary disease Pulmonary circulation disorders ~~Renal failure~~ (removed from comorbidity score for this test case) Anemia Fluid and electrolyte disorders Psychoses Alcohol abuse Weight loss Hemiplegia Coagulopathy
All diagnoses of the following comorbidities in addition to the ones captured in the Gagne comorbidity score, during the baseline period: Any Diabetes (since Gagne et al. indicator only captures complicated diabetes) AMI Ischemic/hemorrhagic stroke CKD Stage 3, 4, or 5 Diagnosis Code in 2007 (for 2008 cohort), 2009 (for 2010 cohort) and 2011 (for 2012 cohort). Note: All other covariates are assessed for the 183 (and 365) days prior to T0 or T0L. The following CKD codes were included (REF)

ICD-9 CM Code	Description
250.4	Diabetes with renal manifestations
274.1	Gouty nephropathy
283.11	Hemolytic-uremic syndrome
403	Hypertensive chronic kidney disease, malignant, with chronic kidney disease stage I through stage IV, or unspecified
403.01	Hypertensive chronic kidney disease, malignant, with chronic kidney disease stage V or end stage renal disease
403.11	Hypertensive chronic kidney disease, benign, with chronic kidney disease stage V or end stage renal disease
403.9	Hypertensive chronic kidney disease, unspecified, with chronic kidney disease stage I through stage IV, or unspecified
403.91	Hypertensive chronic kidney disease, unspecified, with chronic kidney disease stage V or end stage renal disease
404	Hypertensive heart and chronic kidney disease, malignant, without heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.01	Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.1	Hypertensive heart and chronic kidney disease, benign, without heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.11	Hypertensive heart and chronic kidney disease, benign, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.12	Hypertensive heart and chronic kidney disease, benign, without heart failure and with chronic kidney disease stage V or end stage renal disease
404.13	Hypertensive heart and chronic kidney disease, benign, with heart failure and chronic kidney disease stage V or end stage renal disease
404.9	Hypertensive heart and chronic kidney disease, unspecified, without heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.91	Hypertensive heart and chronic kidney disease, unspecified, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.92	Hypertensive heart and chronic kidney disease, unspecified, without heart failure and with chronic kidney disease stage V or end stage renal disease
404.93	Hypertensive heart and chronic kidney disease, unspecified, with heart failure and chronic kidney disease stage V or end stage renal disease
572.4	Hepatorenal syndrome
581	Nephrotic syndrome

581.9	Nephrotic syndrome, unspecified.
582	Chronic glomerulonephritis
582.9	Glomerulonephritis, chronic, unspecified
585	Chronic renal failure
585.3	Chronic kidney disease, Stage III (moderate)
585.4	Chronic kidney disease, Stage IV (severe)
585.5	Chronic kidney disease, Stage V
585.9	Chronic kidney disease, unspecified
586	Renal failure, unspecified
587	Renal sclerosis, unspecified
753.12	Polycystic kidney, unspecified type
753.13	Polycystic kidney, autosomal dominant
753.14	Polycystic kidney, autosomal recessive
753.16	Medullary cystic kidney
753.17	Medullary sponge kidney
753.19	Other specified cystic kidney disease
794.4	Nonspecific abnormal results of function study of kidney

Serum Creatinine Result Values lab capture

All serum creatinine result value measurements within each patient's unique project timeframe. In circumstances where patients have two or more eGFRs on the same date that differ in result value, a standard decision rule (e.g., take highest versus average result) will be applied to all.

Outcome of interest

Presence or absence of any CKD Stage 3, 4, 5/ESRD, unstaged diagnosis code

Censoring Events

- End of either medical or drug coverage
- Death
- Dec 31 2013
- First occurrence of dialysis (e.g., hemo-, peritoneal) or kidney transplant code
- 365 days post t0

Follow-up

Start = See definition of t0 and t0L above
End = Earliest of any censoring event

1. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604-12.

6. MS Lab Methods Workgroup -- Outcomes Detection Test Case #1: Diabetes among Adults Initiating a Second Generation Antipsychotic

Test Case

Test Case Purpose: Outcomes Identification

Questions to be Addressed with Test Case:

1) Does inclusion of follow-up GLU (e.g., random/fasting glucose and HbA1c) laboratory test result value(s) after SGA initiation identify additional preliminary indications of diabetes?
    a. How many additional outcomes are identified?
    b. How many cases of diabetes are identifier earlier using lab results versus diagnoses codes only?
2) Regarding the timing after SGA initiation until the observed elevated GLU laboratory test result value:
    a. What is the distribution of time until observed GLU result values after T_0?
    b. Does the time until the GLU result value after T_0 vary by SGA?
3) When is the appropriate time to censor patients from the cohort if no GLU result value is observed?
4) What are the considerations around imputing GLU outcomes?

Clinical Question to be Addressed with Test Case:

Does risk of diabetes differ by specific SGA? (Look at both glucose and HbA1c patterns after initiation of SGA).

Exposure: Second generation antipsychotic (SGA) newly-started in adults without diabetes diagnosis

Baseline: Baseline is defined as within 183 days before through t0 where t0 = cohort entry date/date of initial SGA dispensing

Outcome: Any single diabetes diagnosis, GLU, or antihyperglycemic medication dispensing compatible with impaired fasting glucose or random glucose compatible with diabetes or HbA1c $\geq$ 6.5 within 365 days after T_0. This outcome will be considered a "Preliminary Indication of Diabetes."
Specifically, the outcome of preliminary indication of diabetes is defined as the any one of the following within +365 days after starting the SGA:

1) Inpatient diagnosis code (ICD-9-CM 250.x);
2) Hemoglobin $A_{1c} \geq$ 6.5%;
3) Fasting plasma glucose $\geq$ 126mg/dl;
4) Random plasma glucose $\geq$ 200mg/dl;
5) Outpatient diagnosis code (same codes as for inpatient);
6) Any anti-hyperglycemic medication (ANTI_DIABETICS) dispensing

Inclusion Criteria

1) Initiation of SGA, with no prior SGA in 183 consecutive days prior to T_0. MSOC has updated the NDC code list to include drugs through 2013.

The following Second Generation Antipsychotics were included in the original data pulled for this cohort of individuals newly-initiating an SGA:

ARIPIPRAZOLE
ASENAPINE MALEATE
ILOPERIDONE
LURASIDONE HCL
OLANZAPINE; OLANZAPINE PAMOATE; OLANZAPINE/FLUOXETINE HCL
PALIPERIDONE; PALIPERIDONE PALMITATE
QUETIAPINE FUMARATE
RISPERIDONE; RISPERIDONE MICROSPHERES
ZIPRASIDONE HCL; ZIPRASIDONE MESYLATE

Because use of ASENAPINE MALEATE, ILOPERIDONE, LURASIDONE HCL, PALIPERIDONE, PALIPERIDONE PALMITATE,
ZIPRASIDONE HCL, and ZIPRASIDONE MESYLATE was very low, the outcomes test case cohort will include only patients exposed to one of the following four SGAS:
ARIPIPRAZOLE
OLANZAPINE; OLANZAPINE PAMOATE; OLANZAPINE/FLUOXETINE HCL
QUETIAPINE FUMARATE
RISPERIDONE; RISPERIDONE MICROSPHERES

2) Medical AND drug coverage for >=183 days prior to T_0. Bridge up to 45 day gaps. 1st enrollment with all of the following: medical coverage, drug coverage, and initiation of SGA

3) Project date range: January 1, 2008 – December 31, 2013

4) 21 + at time of T_0, where T_0 is date of first SGA dispensing.

Inclusion, with flags

- Patients with zero medical encounters in the 183 days prior to T_0.
- Switch of SGA
- Addition of a 2nd SGA

Censoring Criteria – which ever happens first

- Death
- Discontinuation of medical OR drug coverage
- Discontinuation of SGA- no refills for either 60 days after run-out date- determination after review of data - Initial analyses planned as intent to treat ---capture future SGA prescriptions to allow for analyses examining discontinuation of SGA?
- Diabetes outcome (diagnosis, lab, and/or med)
- End of study period (December 31, 2013)

Exclusion Criteria	
Prior/Current diabetes diagnosis within 183 days prior to T_0	
Diabetes medication within 183 days prior to T_0	(ANTI_DIABETICS)
Elevated GLU laboratory test within 183 days prior to T_0	hemoglobin $A_{1c} \geq 6.5\%$; fasting plasma glucose $\geq$ 126mg/dl; or random plasma glucose $\geq$ 200mg/dl
Pregnancy	The presence of any of the codes indicating a diagnosis associated with pregnancy.
Polycystic Ovarian Syndrome	An ICD-9 code of 256.4
Pre-existing Diabetes	The presence of any of the codes indicating a diagnosis associated with diabetes (see diabetes codes below).

Outcome

Preliminary Diabetes Indicator: Defined as the any one of one of the following:

1) Inpatient diagnosis code (ICD-9-CM 250.x);
2) Hemoglobin $A_{1c} \geq 6.5\%$;
3) Fasting plasma glucose $\geq$ 126mg/dl;
4) Random plasma glucose $\geq$ 200mg/dl;
5) Outpatient diagnosis code (same codes as for inpatient);
6) Any anti-hyperglycemic medication (ANTI_DIABETICS) dispensing

This set of outcomes definitions provides a very sensitive (less specific) definition/indication of diabetes that we consider as preliminary indication of diabetes rather than a clear, stringent definition of diabetes. A more stringent set of criteria for diabetes would be defined as the earlier of one inpatient diagnosis (ICD-9-CM 250.x) or any combination of two of the following events, using the date of the first event in the pair as the identification date: 1) hemoglobin $A_{1c} \geq 6.5\%$; 2) fasting plasma glucose $\geq$ 126mg/dl; 3) random plasma glucose $\geq$ 200mg/dl; 4) an outpatient diagnosis code (same codes as for inpatient); 5) any anti-hyperglycemic medication (ANTI_DIABETICS) dispense. For the purposes of this methods test case work, a preliminary indication of a diabetes outcome is applicable.

- ICD-9 codes

250.xx	Diabetes Mellitus
250.x1, 250.x3	Type 1 Diabetes Mellitus
250.x0, 250.x2	Type 2 Diabetes Mellitus
250.10, 250.12	Diabetes ketoacidosis, type 2 or unspecified type. NOTE: These codes are NOT to be included as Type 2 Diabetes codes for the purposes of the eMERGE Type 2 Diabetes algorithms (#8 and #9)

- Elevated HbA1C (HbA1c $\geq$= 6.5%)
- Blood glucose (random glucose $\geq$ 200 mg/dl, and/or fasting glucose $\geq$ 126 mg/dl)
- December 31, 2013
- ANTI_DIABETICS

Covariates to capture	
Age at t0	
Sex	
Race/Ethnicity	
Site	
Pharmacy – baseline (in 183 days prior to t0) and throughout cohort inclusion period	Anti-anxiety agents ANTICONVULSANTS ANTIDEPRESSANTS ANTIPSYCHOTIC-1ST GEN BENZODIAZEPINES GLUCOCORTICOIDS HYPNOTIC-OTHER INJECTABLE ANTIPSYCHOTIC LITHIUM STATINS STIMULANTS
SGA dosage	
Utilization - in 183 days prior to T_0 AND 365 days after T_0	Counts of medical encounters- ED ,IP, IS and AV visits
Comorbidities Cardiac arrhythmias Hypertension Diabetes (distinguishes complicated vs uncomplicated) Liver disease Metastatic cancer CHF Dementia Peripheral Vascular disease Psychoses Alcohol abuse Hemiplegia Weight loss Chronic pulmonary disease Pulmonary circulation disorders Renal failure Anemia HIV/AIDS Fluid/Electrolytic Disorders Coagulation disorder Tumor, any Additional comorbidities specific to test case Ischemic stroke Depression Osteoarthritis Hemorrhagic stroke Myocardial Infarction Obesity Rheumatoid arthritis	
Other Notes and Questions	

7. MS Lab Methods Workgroup -- Outcomes Detection Test Case #2, Gastrointestinal Bleeding among Adults Initiating a Non-steroidal Anti-inflammatory Drug (NSAID)

Test Case

Test Case Purpose: Outcomes identification

Questions to be Addressed with Test Case:

1. What numbers (%) of patients have Hgb results available? Specifically, within a cohort newly-starting an NSAID stratified by data partner type, describe the numbers and proportions of patients with Hgb laboratory test results available before, after, and both before and after exposure to an NSAID from different care settings. For example, some % will have "before" Hgb results from the ambulatory setting and "after" Hgb results from the inpatient setting, and those permutations need to be included as categories. That is, 4 settings need to be considered along with transitions. These include ambulatory only, ambulatory to inpatient, inpatient only, emergency department to inpatient, and emergency department only. (Note: The emergency department setting lab results data are only from one participating site).
2. In the ambulatory, ambulatory to inpatient, inpatient, and emergency department to inpatient care locations, does use of available Hgb laboratory test results identify additional cases of GI bleeding beyond the use of diagnosis codes alone? Specifically, among patients with at least two Hgb laboratory result values when one Hgb is an outcome result value and one or more Hgb are baseline result value(s) (defined as prior to outcome, not necessary baseline relative to NSAID exposure), define GI bleeding as a decrease of >=3 g/dL between the two Hgb results.
3. Independent of the care location, does use of available Hgb laboratory test results, either alone or in combination with outpatient diagnosis codes, identify additional cases of GI bleeding beyond the use of inpatient diagnosis codes alone (i.e., standard claims-based definition)?
4. For questions 1 through 3 above, compare GI bleeding occurrence between individuals exposed to COX-2 selection vs. non-selective NSAIDs. NOTE: Data partner sites 1 and 2 may have too low COX-2 use to analyze using this approach. If so, only non-selective NSAIDs will be grouped for use in analyses.
5. What is the confirmation rate of the diagnosis code (e.g., % of times change in Hgb "confirms" the diagnosis code)?

Drug Exposure: Any NSAID, with comparison between COX-2 selective and non-selective; data partner sites 1 and 2 may have too low COX-2 use to analyze using this approach. If so, only non-selective NSAIDs will be grouped for use in analyses.

Exposure: Newly prescribed (not used in prior 183 days) NSAIDS in individuals aged >=18 years of age

***Outcome*s:**

1. Acute GI bleeding or gastric ulcer based on inpatient codes alone within 30 days and within 6 months after NSAID initiation (i.e., standard claims-based definition).
2. Among those who do not meet criterion #1, acute GI bleeding or gastric ulcer based on non-inpatient codes PLUS a decrease of >=3 g/dL between two Hgb results.
3. Among those who do not meet criteria #1 or #2, identify patients with a drop in HGB only of >= 3 g/dL (i.e., no coded bleeding diagnosis).
4. Among those who do not meet criteria #1, #2, or #3, identify patients with a GI bleeding or gastric ulcer event based on a coded non-inpatient diagnosis who do not have a drop in HGB (i.e., HGB results available but decrease of < 3 mg/dL between two HGB results.

Inclusion Criteria

1) Age 18 on date of NSAID initiation
2) Medical and drug coverage for >= 183 days before t0, bridging gaps up to 45 days NOTE: Will look back up to 365 days for baseline Hgb.
3) Date range for NSAID initiation inclusive of January 1, 2008 – April 30, 2013

Exclusion Criteria
1) Hematologic cancers (ICD9-CM codes 200-208 including all 3, 4, and 5 digit codes, V10.6, V10.7) 2) Pregnancy 3) Diagnosed bleeding of any type during baseline period Include (in this exclusion) all GI bleeding codes that are our outcome of interest CODES: 430, 431, 432.0, 432.1, 432.9, 852.0x, 852.2x, 852.4x, 853.0 -- stroke codes 423.0x, 599.7x, 719.11, 784.7x, 784.8x, and 786.3x Lower GI Site: 455.2, 455.5, 455.8, 562.02, 562.03, 562.12, 562.13, 568.81, 569.3x
Exposure
Newly prescribed (not used in prior 183 days) NSAIDS started in adults Drugs included: Non-Selective NSAIDS: DICLOFENAC ORAL DICLOFENAC SODIUM INJECTION ETODOLAC FENOPROFEN FLURBIPROFEN IBUPROFEN IBUPROFEN INJECTION IBUPROFEN ORAL INDOMETHACIN INDOMETHACIN ORAL INDOMETHACIN RECTAL KETOPROFEN KETOROLAC TROMETHAMINE (Systemic) KETOROLAC TROMETHAMINE INJECTION KETOROLAC TROMETHAMINE INTRANASAL KETOROLAC TROMETHAMINE ORAL MECLOFENAMATE SODIUM MEFENAMIC ACID MELOXICAM NABUMETONE NAPROXEN OXAPROZIN PIROXICAM SULINDAC TOLMETIN Selective COX-2 Inhibitors: CELECOXIB NOTE: While it is our intent to compare selective vs. non-selective NSAIDS, we anticipate that use of celecoxib may be very low at two of the three participating sites. We will examine the frequency distribution of use of all NSAIDS across the three sites and then make a final determination whether it is feasible to make the planned comparison. If not, we will then decide what drugs should be included in the revised comparison (e.g., ibuprofen + celecoxib vs. naproxyn, or other).

Baseline Covariates (Baseline covariates are defined as occurring from 183 days prior to T0 through T0, unless otherwise specified.)
Age at NSAID initiation; results be stratified by age Race Ethnicity Data Partner Site Counts of encounters grouped by - Outpatient visits - ED visits - Hospitalizations Non-acute institutional stays Indicator of zero encounters in the 183 days before index date Count of unique drug classes among dispensings in the 183 days prior to T0 Discuss: All diagnoses of comorbidities included in the comorbidity score developed by Gagne et al (J Clin Epidemiology, 2011 July; 64(7): 749-759). This score is implemented in the CIDA tool from the Mini-Sentinel Operations Center. We will keep separate disease indicators as well as the overall score. These comorbidities include: AIDS/HIV Congestive Heart Failure Cardiac arrhythmias Hypertension Dementia Complicated diabetes Liver disease Any tumor Metastatic cancer Peripheral vascular disease Chronic pulmonary disease Pulmonary circulation disorders Renal failure Anemia Fluid and electrolyte disorders Psychoses Alcohol abuse Weight loss Hemiplegia Coagulopathy

Additional covariates

Flag these diagnoses (during baseline period):

1) Diagnosis of peptic ulcer disease prior to NSAID initiation
2) Osteoarthritis
3) Rheumatoid arthritis
4) GERD
5) Diagnosis of any cancer (use metastatic and tumor variables of Gagne comorbidity score)
6) CKD
7) Drugs that affect coagulation (dispensing during baseline or concurrent with NSAID): Warfarin

Heparin
Aspirin
Argatroban
Bivalirudin
Dabigatran
Desirudin
Apixaban
Edoxaban
Fondaparinux
Rivaroxaban
Heparin
Dalteparin
Enoxaparin

8) Misoprostol (dispensing during baseline or concurrent with NSAID)
9) H2 blockers (dispensing during baseline or concurrent with NSAID): CIMETIDINE

FAMOTIDINE INJECTION
FAMOTIDINE ORAL
FAMOTIDINE/CALCIUM CARBONATE/MAGNESIUM HYDROXIDE
NIZATIDINE
RANITIDINE

10) Proton Pump Inhibitors (dispensing during baseline or concurrent with NSAID): DEXLANSOPRAZOLE

ESOMEPRAZOLE ORAL, ESOMEPRAZOLE
SODIUM INJECTION LANSOPRAZOLE
OMEPRAZOLE
PANTOPRAZOLE SODIUM INJECTION, PANTOPRAZOLE SODIUM ORAL
OMEPRAZOLE/SODIUM BICARBONATE
RABEPRAZOLE SODIUM

11) Other medications

CLOPIDOGREL
ANTIPLATELETS
GLUCOCORTICOIDS
SSRIs

12) CPT/procedure code

Transfusion (packed cells or whole blood)
CPT/procedure codes EPOETIN 82668

Outcome of interest
***Outcome*s:** 1. Acute GI bleeding or gastric ulcer based on inpatient codes alone within 30 days and within 6 months after NSAID initiation (i.e., standard claims-based definition). 2. Either acute GI bleeding or gastric ulcer based on inpatient codes alone OR a decrease of >=3 g/dL between two Hgb results (i.e., standard claims-based definition enriched with additional outcomes identified with Hgb) 3. Either acute GI bleeding or gastric ulcer based on inpatient codes alone OR a decrease of >= 3 g/dL between two Hgb results PLUS an outpatient acute GI bleeding or gastric ulcer code within ± 15 days of the 2nd Hgb result (i.e., this is a subset of #2 that requires some evidence of gastrotoxicity in addition to the change in Hgb to increase the likelihood that "minor" bleeds or bleeds that do not require hospitalization are GI-related) Codes (used in prior Mini-sentinel methods project): ICD-9 discharge Diagnoses for hospitalization for GI, Peptic ulcer disease or esophageal bleeding (530.82, 531.x, 532.x, 533.x, 534.x, 535.x, 578.x)
Gastroduodenal site: 530.21, 531.0x, 531.1x, 531.2x, 531.4x, 531.6x, 532.0x, 532.1x, 532.2x, 532.4x, 532.6x, 533.1x, 533.2x, 533.4x, 533.6x, 534.0x, 534.1x, 534.2x, 534.4x, 534.6x, 535.01, 535.11, 535.21, 535.31, 535.41, 535.51, 535.61, 537.83, 537.84, 562.02, 562.03, 562.12, 562.13, 569.86 Esophageal site: 456.0, 456.20, 530.21, 530.7, 530.82 Upper GI Unspecified: 534.0x, 534.1x, 534.2x, 534.4x, 534.6x, 562.02, 562.03, 578.0 Unspecified GI Site: 533.0x,533.1x, 533.2x, 533.4x, 533.6x, 568.81, 578.x, 569.85, 569.86
Censoring Events (collection of censoring events begins t0)
• End of medical or drug coverage • Death • October 31, 2013 • Bring back days' supply and dispensing relative dates to be able to determine whether intention-to-treat approach vs. as-treated approach (i.e., discontinuation of NSAID) Whichever occurs first
Follow-up
Start = t0 End = earliest of any censoring event

Other notes
y = include as baseline exclusion and outcome x = include as baseline exclusion y530.7 y530.82 x569.3 y537.83 y562.02 y562.03 x562.12 x562.13 x568.81 y569.85 y578.0 x578.1 y578.9 x599.7 x719.11 x784.7 y784.8 x786.3 y456.0 y456.20 x459.0 x459.0 6 months before exposure to 6 months after exposure: collect exposure, outcome dx, outcome lab result, outcome lab px, encounter type

E. APPENDIX E. BASELINE CONFOUNDER TEST CASE 3, BASELINE INR IN WARFARIN USERS STARTING AN ANTIMICROBIAL MEDICATION, STANDARDIZED DIFFERENCES SUPPLEMENTARY TABLES

1. Supplementary Table 1. Baseline Confounder Test Case 3, Warfarin Users Starting an Interacting versus Non-Interacting Antimicrobial Agent: Standardized Difference on Matched Data, Excluding INR

Variable [a]	All Sites Combined N=41,156	SITE 1 N=2874	SITE 2 N=15,562	SITE 3 N=22,604
	SD (95%CI)	SD (95%CI)	SD (95%CI)	SD (95%CI)
Age	0.002 (-0.017, 0.021)	0.015 (-0.058, 0.088)	-0.001 (-0.032, 0.031)	-0.001 (-0.027, 0.025)
Number of unique medication classes dispensed	0.008 (-0.012, 0.027)	0.015 (-0.058, 0.088)	0.009 (-0.023, 0.040)	-0.001 (-0.027, 0.025)
Number of ambulatory medical visits during baseline	0.003 (-0.017, 0.022)	0.021 (-0.052, 0.094)	0.002 (-0.030, 0.033)	0.007 (-0.020, 0.033)
Gender	0.011 (-0.009, 0.030)	-0.006 (-0.079, 0.068)	0.002 (-0.030, 0.033)	-0.004 (-0.030, 0.022)
Race	0.002 (-0.017, 0.022)	0.032 (-0.041, 0.105)	0.014 (-0.018, 0.045)	0.011 (-0.015, 0.037)
Hispanic ethnicity	-0.002 (-0.021, 0.017)	0.026 (-0.047, 0.099)	0.007 (-0.025, 0.038)	0.000 (-0.026, 0.026)
Year of cohort entry	0.012 (-0.008, 0.031)	0.040 (-0.034, 0.113)	0.016 (-0.016, 0.047)	0.017 (-0.009, 0.043)
Site	0.008 (-0.012, 0.027)	NA	NA	NA
Additional antimicrobial dispensing within 30 days	0.001 (-0.018, 0.020)	0.000 (-0.073, 0.073)	0.000 (-0.031, 0.031)	0.000 (-0.026, 0.026)
Emergency department visit during baseline	0.004 (-0.016, 0.023)	0.009 (-0.064, 0.082)	0.008 (-0.024, 0.039)	-0.009 (-0.035, 0.017)
Hospitalization during baseline	-0.002 (-0.022, 0.017)	0.030 (-0.043, 0.103)	0.008 (-0.024, 0.039)	0.007 (-0.019, 0.033)
Institutional stay during baseline	0.006 (-0.013, 0.026)	0.025 (-0.048, 0.098)	0.006 (-0.026, 0.037)	-0.001 (-0.027, 0.026)
Alcohol abuse	-0.008 (-0.027, 0.011)	0.010 (-0.063, 0.084)	-0.007 (-0.039, 0.024)	-0.010 (-0.036, 0.016)
Anemia	0.008 (-0.012, 0.027)	0.009 (-0.064, 0.082)	0.012 (-0.020, 0.043)	-0.002 (-0.028, 0.025)
Arrhythmia	0.004 (-0.015, 0.024)	0.004 (-0.069, 0.077)	0.002 (-0.030, 0.033)	0.003 (-0.023, 0.029)
Congestive heart failure	-0.001 (-0.021, 0.018)	-0.003 (-0.076, 0.070)	-0.006 (-0.038, 0.025)	-0.004 (-0.030, 0.022)
Coagulation disorder	0.003 (-0.017, 0.022)	0.012 (-0.061, 0.085)	0.003 (-0.028, 0.034)	-0.002 (-0.028, 0.024)
Dementia	0.001 (-0.019, 0.020)	0.008 (-0.065, 0.081)	-0.004 (-0.036, 0.027)	-0.005 (-0.031, 0.021)
HIV/AIDS	0.007 (-0.012, 0.026)	0.000 (-0.073, 0.073)	0.015 (-0.016, 0.047)	0.015 (-0.011, 0.041)
Hypertension	0.004 (-0.015, 0.024)	0.004 (-0.069, 0.077)	0.007 (-0.025, 0.038)	-0.002 (-0.028, 0.024)
Liver disease	0.004 (-0.016, 0.023)	0.010 (-0.063, 0.083)	0.005 (-0.026, 0.037)	0.007 (-0.019, 0.033)

Variable [a]	All Sites Combined N=41,156	SITE 1 N=2874	SITE 2 N=15,562	SITE 3 N=22,604
	SD (95%CI)	SD (95%CI)	SD (95%CI)	SD (95%CI)
Pulmonary disease, chronic	-0.004 (-0.023, 0.015)	0.014 (-0.059, 0.088)	-0.003 (-0.035, 0.028)	-0.006 (-0.032, 0.020)
Peripheral vascular disease	0.008 (-0.011, 0.027)	0.008 (-0.065, 0.081)	-0.002 (-0.033, 0.030)	0.010 (-0.016, 0.036)
Renal failure	0.008 (-0.011, 0.028)	-0.012 (-0.085, 0.061)	0.012 (-0.019, 0.044)	0.004 (-0.022, 0.030)
Tumor, any	-0.003 (-0.022, 0.017)	0.033 (-0.040, 0.106)	0.003 (-0.028, 0.035)	-0.004 (-0.030, 0.022)
Weight loss	0.000 (-0.019, 0.019)	0.000 (-0.073, 0.073)	0.012 (-0.020, 0.043)	0.000 (-0.026, 0.026)
Prior history of any bleed	-0.006 (-0.025, 0.014)	0.027 (-0.046, 0.100)	-0.005 (-0.036, 0.027)	-0.008 (-0.034, 0.018)
Any dispensing of non-antimicrobial drug that can increase anticoagulant effect/bleeding risk of warfarin	0.006 (-0.014, 0.025)	0.002 (-0.072, 0.075)	-0.005 (-0.036, 0.027)	0.000 (-0.026, 0.026)
Any dispensing of non-antimicrobial drug that can decrease anticoagulant effect/bleeding risk of warfarin	0.001 (-0.018, 0.021)	-0.020 (-0.093, 0.053)	-0.009 (-0.040, 0.022)	-0.002 (-0.028, 0.024)

[a] Due to low cell sizes, complicated diabetes, hemiplegia, metastatic cancer, psychosis, and pulmonary circulation disorder are not shown

2. Supplementary Table 2. Baseline Confounder Test Case 3, Warfarin Users Starting an Interacting versus Non-Interacting Antimicrobial Agent: Standardized Difference on Matched Data, Continuous and Indicator INR Variables are Included in Matching

Variable [a]	All Sites Combined N=41,158	SITE 1 N=2868	SITE 2 N=15,566	SITE 3 N=22,604
	SD (95%CI)	SD (95%CI)	SD (95%CI)	SD (95%CI)
Age	-0.009 (-0.028, 0.011)	0.001 (-0.072, 0.075)	-0.000 (-0.032, 0.031)	0.004 (-0.022, 0.030)
Unique medication classes dispensed	0.000 (-0.019, 0.020)	-0.002 (-0.075, 0.071)	0.008 (-0.024, 0.039)	0.008 (-0.018, 0.034)
Ambulatory medical visits during baseline	0.003 (-0.017, 0.022)	-0.004 (-0.077, 0.069)	-0.007 (-0.038, 0.025)	-0.003 (-0.029, 0.024)
Gender	0.012 (-0.008, 0.031)	-0.014 (-0.087, 0.059)	0.006 (-0.025, 0.038)	0.007 (-0.019, 0.033)
Race	0.009 (-0.010, 0.029)	0.013 (-0.060, 0.086)	0.014 (-0.017, 0.046)	0.014 (-0.012, 0.040)
Hispanic ethnicity	0.005 (-0.014, 0.024)	0.026 (-0.048, 0.099)	-0.007 (-0.038, 0.025)	-0.004 (-0.030, 0.022)
Year of cohort entry	0.015 (-0.005, 0.034)	0.059 (-0.014, 0.132)	0.010 (-0.021, 0.042)	0.013 (-0.013, 0.039)
Site	0.009 (-0.011, 0.028)	NA	NA	NA
Additional antimicrobial dispensing within 30 days	0.001 (-0.018, 0.020)	0.000 (-0.073, 0.073)	0.000 (-0.031, 0.031)	0.000 (-0.026, 0.026)
Emergency department visit during baseline	0.002 (-0.018, 0.021)	-0.004 (-0.077, 0.069)	-0.004 (-0.036, 0.027)	0.001 (-0.025, 0.027)
Hospitalization during baseline	0.005 (-0.014, 0.025)	0.010 (-0.063, 0.083)	0.003 (-0.029, 0.034)	-0.003 (-0.029, 0.023)
Institutional stay during baseline	0.007 (-0.012, 0.026)	0.000 (-0.073, 0.073)	0.006 (-0.025, 0.038)	0.003 (-0.023, 0.029)
Alcohol abuse	0.001 (-0.018, 0.021)	-0.022 (-0.095, 0.051)	0.001 (-0.030, 0.032)	0.010 (-0.016, 0.036)
Anemia	0.004 (-0.015, 0.024)	0.005 (-0.069, 0.078)	0.005 (-0.026, 0.037)	0.003 (-0.024, 0.029)
Arrhythmia	0.006 (-0.013, 0.025)	-0.004 (-0.077, 0.069)	-0.007 (-0.038, 0.025)	0.004 (-0.023, 0.030)
Congestive heart failure	0.008 (-0.012, 0.027)	0.000 (-0.073, 0.073)	-0.006 (-0.038, 0.025)	-0.002 (-0.028, 0.025)
Coagulation disorder	0.005 (-0.015, 0.024)	-0.013 (-0.086, 0.060)	0.003 (-0.028, 0.034)	-0.003 (-0.029, 0.023)
Dementia	-0.001 (-0.020, 0.019)	0.017 (-0.056, 0.090)	-0.009 (-0.040, 0.023)	-0.009 (-0.035, 0.017)
HIV/AIDS	0.007 (-0.012, 0.026)	0.000 (-0.073, 0.073)	0.012 (-0.020, 0.043)	0.010 (-0.016, 0.036)
Hypertension	0.004 (-0.015, 0.024)	-0.008 (-0.082, 0.065)	-0.004 (-0.035, 0.028)	0.015 (-0.011, 0.041)
Liver disease	0.016 (-0.004, 0.035)	-0.031 (-0.105, 0.042)	-0.003 (-0.035, 0.028)	0.009 (-0.017, 0.035)
Pulmonary disease, chronic	0.002 (-0.018, 0.021)	-0.007 (-0.080, 0.066)	0.001 (-0.030, 0.032)	0.002 (-0.025, 0.028)
Peripheral vascular disease	0.004 (-0.015 , 0.024)	0.027 (-0.046, 0.100)	-0.002 (-0.033, 0.030)	-0.006 (-0.032, 0.021)
Renal failure	-0.005 (-0.025, 0.014)	0.028 (-0.045, 0.101)	0.002 (-0.029, 0.034)	0.014 (-0.012, 0.040)

Variable [a]	All Sites Combined N=41,158	SITE 1 N=2868	SITE 2 N=15,566	SITE 3 N=22,604
	SD (95%CI)	SD (95%CI)	SD (95%CI)	SD (95%CI)
Tumor, any	-0.001 (-0.020, 0.019)	-0.009 (-0.082, 0.064)	0.003 (-0.029, 0.034)	0.004 (-0.023, 0.030)
Weight loss	0.013 (-0.007, 0.032)	0.000 (-0.073, 0.073)	0.008 (-0.023, 0.039)	-0.006 (-0.032, 0.020)
Prior history of any bleed	-0.005 (-0.025, 0.014)	-0.002 (-0.075, 0.071)	0.003 (-0.029, 0.034)	0.013 (-0.013, 0.039)
Dispensing of non-antimicrobial drug that can increase anticoagulant effect/bleeding risk of warfarin	0.001 (-0.018, 0.021)	-0.030 (-0.103, 0.043)	-0.004 (-0.035, 0.028)	-0.009 (-0.035, 0.017)
Dispensing of non-antimicrobial drug that can decrease anticoagulant effect/bleeding risk of warfarin	0.006 (-0.014, 0.025)	0.006 (-0.067, 0.080)	0.000 (-0.031, 0.031)	-0.001 (-0.027, 0.025)

[a] Due to low cell sizes, complicated diabetes, hemiplegia, metastatic cancer, psychosis, and pulmonary circulation disorder are not shown

3. Supplementary Table 3. Baseline Confounder Test Case 3, Warfarin Users Starting an Interacting versus Non-Interacting Antimicrobial Agent: Standardized Difference on Matched Data, Imputed INR is Included in the Matching

Confounder [a]	All Sites Combined			SITE 1			SITE 2			SITE 3		
	Min	Max	std	Min	Max	std	Min	Max	std	Min	Max	std
Age	-0.0044	0.0116	0.0051	-0.0181	0.0215	0.0125	-0.0087	0.0059	0.0046	-0.0068	0.0237	0.0089
Unique medication classes dispensed	-0.0041	0.0096	0.0048	-0.0231	0.0059	0.0100	-0.0037	0.0074	0.0033	-0.0135	0.0056	0.0070
Ambulatory medical visits during baseline	-0.0088	0.0123	0.0061	-0.0265	0.0244	0.0159	-0.0027	0.0126	0.0041	-0.0068	0.0144	0.0079
Gender	0.0042	0.0181	0.0041	-0.0293	0.0167	0.0140	-0.0077	0.0124	0.0065	-0.0056	0.0099	0.0055
Race	0.0028	0.0125	0.0035	0.0084	0.0392	0.0093	0.0069	0.0192	0.0039	0.008	0.0277	0.0061
Hispanic ethnicity	-0.0059	0.0078	0.0043	-0.0099	0.0161	0.0072	-0.0028	0.0199	0.0066	-0.018	0.0208	0.0109
Year of cohort entry	0.0075	0.0187	0.0034	0.0222	0.0584	0.0124	0.0112	0.0217	0.0035	0.0074	0.0239	0.0047
Site	0.0002	0.0119	0.0040	NA	NA	NA	NA	NA	NA	NA	NA	NA
Additional antimicrobial dispensing within 30 days	0	0.0011	0.0005	0	0	0.0000	0	0	0.0000	0	0	0.0000
Emergency department visit during baseline	-0.0012	0.0139	0.0043	-0.0094	0.0477	0.0172	-0.0087	0.0155	0.0080	-0.0124	0.0088	0.0061
Hospitalization during baseline	-0.005	0.0085	0.0039	-0.0103	0.0271	0.0112	-0.0078	0.0109	0.0057	-0.0172	0.0066	0.0075
Institutional stay during baseline	-0.0081	0.0054	0.0043	-0.0189	0.0181	0.0122	-0.0036	0.0098	0.0036	-0.0007	0.0161	0.0056
Alcohol abuse	-0.0057	0.0059	0.0041	-0.0222	0.0053	0.0086	-0.0139	0.0092	0.0062	-0.017	0.0059	0.0078
Anemia	-0.0083	0.0034	0.0041	-0.0428	0.0261	0.0227	-0.0032	0.0116	0.0046	-0.012	0.0092	0.0078
Arrhythmia	-0.0092	0.0057	0.0043	-0.0211	0.007	0.0093	-0.0028	0.0077	0.0033	-0.0101	0.0094	0.0068
Congestive heart failure	-0.0066	0.0122	0.0058	-0.0288	0.0302	0.0161	-0.0053	0.0069	0.0040	-0.0129	0.0121	0.0098
Coagulation disorder	0.001	0.0133	0.0040	-0.026	0.0123	0.0113	-0.001	0.0069	0.0030	-0.0121	0.0059	0.0063
Dementia	-0.015	0.0032	0.0055	0	0.0245	0.0082	-0.0162	0.0056	0.0073	-0.0128	0.0208	0.0099
HIV/AIDS	-0.0103	0.0101	0.0068	0	0	0.0000	0.0041	0.0184	0.0051	-0.0077	0.0067	0.0056
Hypertension	-0.009	0.0038	0.0039	-0.0377	0.0265	0.0194	-0.0013	0.014	0.0048	-0.0146	0.0116	0.0081
Liver disease	-0.0065	0.0094	0.0048	-0.0259	0.0192	0.0132	-0.0031	0.015	0.0053	-0.0078	0.0105	0.0058
Pulmonary disease, chronic	-0.003	0.0111	0.0044	-0.0097	0.0215	0.0099	-0.0097	0.017	0.0067	-0.0148	0.0044	0.0061
Peripheral vascular disease	-0.0054	0.0099	0.0050	-0.0112	0.0271	0.0127	-0.0049	0.0077	0.0034	-0.0111	0.0118	0.0089
Renal failure	-0.007	0.0109	0.0052	-0.0607	0.0172	0.0258	-0.0023	0.0155	0.0051	-0.0146	0.0026	0.0054
Tumor, any	-0.0007	0.0133	0.0055	-0.0131	0.0248	0.0120	-0.002	0.0097	0.0039	-0.0115	0.0065	0.0062
Weight loss	-0.0065	0.0127	0.0054	0	0	0.0000	-0.0093	0.0117	0.0069	-0.0064	0.0133	0.0067
Prior history of any bleed	-0.0116	0.0063	0.0054	-0.0173	0.0374	0.0160	-0.0035	0.0067	0.0037	-0.0119	0.0073	0.0060
Dispensing of non-antimicrobial drug that can increase anticoagulant effect/bleeding risk of warfarin	-0.0025	0.0126	0.0049	-0.033	0.0193	0.0159	-0.0124	0.0121	0.0075	-0.0108	0.0113	0.0076
Dispensing of non-antimicrobial drug that can decrease anticoagulant effect/ bleeding risk of warfarin	-0.0068	0.0127	0.0052	-0.0425	0.0301	0.0212	-0.009	0.005	0.0048	-0.0132	0.0112	0.0065

[a] Due to low cell sizes, complicated diabetes, hemiplegia, metastatic cancer, psychosis, and pulmonary circulation disorder are not shown

F. APPENDIX F. ADDITIONAL RESULTS FROM 5 AND FROM 20 IMPUTED DATASETS FOR BASELINE CONFOUNDER TEST CASE 2

The table below shows estimated relative efficiency with varying numbers of imputation datasets for Baseline Confounder Test Case 2 (ACEi and hyperkalemia outcomes ; serum creatinine is lab confounder of interest). Imputations for this test case were all run site specific. Serum creatinine was the only variable imputed and so the missing data pattern was monotone. We implemented the multiple imputations using the regression method of the SAS Proc MI procedure.

The sites had divergent sample sizes and missing data percentages but the relative efficiency estimates were generally consistent and supported using the same number of imputation datasets at all the sites. The test case in this report used ten imputed datasets and had this been doubled to 20 only a minor gain in relative efficiency would have been likely.

Example of varying relative efficiency estimates with increasing number of imputations: Baseline Confounder Test case 2

	Site 1 N=8,497	Site 2 N=56,266	Site 3 N=133,502
# and % with serum creatinine results available	6716 (79.0)	42,920 (76.3)	59,417 (44.5)

Relative efficiency estimate for the Multiple imputation runs by site and number of imputation runs

# of imputation datasets	Site 1	Site 2	Site 3
5	0.852	0.849	0.855
10	0.925	0.916	0.920
20	0.961	0.958	0.964

G. APPENDIX G.PPREGNANCY-RELATED DIAGNOSIS AND PROCEDURE CODES USED TO IDENTIFY PREGNANCIES

Code	Code Type	Description
36460	CPT	TRANSFUSION, INTRAUTERINE, FETAL
59000	CPT	AMNIOCENTESIS
59001	CPT	AMNIOCENTESIS; THERAPEUTIC AMNIOTIC FLUID REDUCTIO
59012	CPT	CORDOCENTESIS
59015	CPT	CHORIONIC VILLUS SAMPLING
59020	CPT	FETAL CONTRACTION STRESS TEST
59025	CPT	FETAL CONTRACTION NON-STRESS TEST
59030	CPT	FETAL SCALP BLOOD SAMPLING
59050	CPT	FETAL MONITORING DURING LABOR BY CONSULTING PHYSIC
59051	CPT	FETAL MONITORING DURING LABOR BY CONSULTING PHYSIC
59070	CPT	TRANSABDOMINAL AMNIOINFUSION, INCLUDING ULTRASOUND
59072	CPT	FETAL UMBILICAL CORD OCCLUSION, INCLUDING ULTRASOU
59074	CPT	FETAL FLUID DRAINAGE (E.G., VESICOCENTESIS, THORAC
59076	CPT	FETAL SHUNT PLACEMENT, INCLUDING ULTRASOUND GUIDAN
59320	CPT	CERCLAGE OF CERVIX, DURING PREGNANCY; VAGINAL
59325	CPT	CERCLAGE OF CERVIX, DURING PREGNANCY; ABDOMINAL
59412	CPT	EXTERNAL CEPHALIC VERSION, W OR WO TOCOLYSIS
59425	CPT	ANTEPARTUM CARE ONLY; 4-6 VISITS
59426	CPT	ANTEPARTUM CARE ONLY; 7 OR MORE VISITS
59866	CPT	MULTIFETAL PREGNANCY REDUCTIONS(S) (MPR)
59897	CPT	UNLISTED FETAL INVASIVE PROCEDURE, INCLUDING ULTRS
76801	CPT	ULTRASOUND, PREGNANT UTERUS, FIRST TRIMESTER, TRAN
76802	CPT	ULTRASOUND, PREGNANT UTERUS, FIRST TRIMESTER, TRAN
76805	CPT	ULTRASOUND, PREGNANT UTERUS, AFTER FIRST TRIMESTER
76810	CPT	ULTRASOUND, PREGNANT UTERUS, AFTER THE FIRST TRIME
76811	CPT	ULTRASOUND, PREGNANT UTERUS, PLUS DETAILED FETAL A
76812	CPT	ULTRASOUND, PREGNANT UTERUS, AFTER THE FIRST TRIME
76813	CPT	ULTRASOUND, PREGNANT UTERUS, FIRST TRIMESTER, FETA
76814	CPT	ULTRASOUND, PREGNANT UTERUS, FIRST TRIMESTER, FETA
76815	CPT	ULTRASOUND, PREGNANT UTERUS, LIMITED
76816	CPT	ULTRASOUND, PREGNANT UTERUS, FOLLOW-UP OR REPEAT
76817	CPT	ULTRASOUND, PREGNANT UTERUS, TRANSVAGINAL
76818	CPT	FETAL BIOPHYSICAL PROFILE
76819	CPT	FETAL BIOPHYSICAL PROFILE; WITHOUT NON-STRESS TES
76820	CPT	DOPPLER VELOCIMETRY, FETAL; UMBILICAL ARTERY
76821	CPT	DOPPLER VELOCIMETRY, FETAL; MIDDLE CEREBRAL ARTER
76825	CPT	ECHOCARDIOGRAPHY, FETAL
76826	CPT	ECHOCARDIOGRAPHY, FETAL, FOLLOW-UP OR REPEAT
76827	CPT	DOPPLER ECHOCARDIOGRAPHY, FETAL

Code	Code Type	Description
76828	CPT	DOPPLER ECHOCARDIOGRAPHY, FETAL, FOLLOW UP OR REPE
76946	CPT	ULTRASONIC GUIDANCE FOR AMNIOCENTESIS
84163	CPT	Pregnancy-associated plasma protein-A (PAPP-A)
99500	CPT	HOME VISIT PRENATAL
0500F	CPT	INITIAL PRENATAL CARE VI
0501F	CPT	PRENATAL FLOW SHEET
0502F	CPT	SUBSEQUENT PRENATAL CARE
S2400	HCPCS	REPAIR, CONGENITAL DIAPHRAGMATIC HERNIA IN THE FET
S2401	HCPCS	REPAIR, URINARY TRACT OBSTRUCTION IN THE FETUS, PR
S2402	HCPCS	REPAIR, CONGENITAL CYSTIC ADENOMATOID MALFORMATION
S2403	HCPCS	REPAIR, EXTRALOBAR PULMONARY SEQUESTRATION IN THE
S2404	HCPCS	REPAIR, MYELOMENINGOCELE IN THE FETUS, PROCEDURE P
S2405	HCPCS	REPAIR OF SACROCOCCYGEAL TERATOMA IN THE FETUS, PR
S2409	HCPCS	REPAIR, CONGENITAL MALFORMATION OF FETUS, PROCEDUR
S2411	HCPCS	FETOSCOPIC LASER THERAPY FOR TREATMENT OF TWIN-TO-
S3625	HCPCS	Maternal serum triple marker screen including alph
S3626	HCPCS	Maternal serum quadruple marker screen
S9214	HCPCS	Home management of gestation diabetes
75.1	ICD-9	Diagnostic amniocentesis
75.2	ICD-9	Intrauterine transfusion
75.3	ICD-9	Other intrauterine operations on fetus and amnion
75.31	ICD-9	AMNIOSCOPY
75.32	ICD-9	FETAL EKG
75.33	ICD-9	FETAL BLOOD SAMPLING AND BIOPSY
75.34	ICD-9	FETAL MONITORING, NOS
75.35	ICD-9	OTHER DIAGNOSTIC PROCEDURES ON FETUS AND AMNION
75.36	ICD-9	CORRECTION OF FETAL DEFECT
87.71	ICD-9	X-ray of gravid uterus
88.78	ICD-9	Diagnostic ultrasound of gravid uterus
638.0	ICD-9	ATTEM ABORT W PELVIC INF
638.1	ICD-9	ATTEM ABORT W HEMORRHAGE
638.2	ICD-9	ATTEM ABORT W PELV DAMAG
638.3	ICD-9	ATTEM ABORT W RENAL FAIL
638.4	ICD-9	ATTEM ABOR W METABOL DIS
638.7	ICD-9	ATTEMP ABORT W COMPL NEC
638.8	ICD-9	ATTEMP ABORT W COMPL NOS
638.9	ICD-9	ATTEMPTED ABORT UNCOMPL
640	ICD-9	HEMORRHAGE IN EARLY PREG*
640.0	ICD-9	THREATENED ABORTION*
640.00	ICD-9	THREATENED ABORT-UNSPEC
640.03	ICD-9	THREATEN ABORT-ANTEPART
640.8	ICD-9	HEMORR IN EARLY PREG NEC*

Code	Code Type	Description
640.80	ICD-9	HEM EARLY PREG NEC-UNSP
640.83	ICD-9	HEM EARLY PG NEC-ANTEPAR
640.9	ICD-9	HEMORR IN EARLY PREG NOS*
640.90	ICD-9	HEMORR EARLY PREG-UNSPEC
640.93	ICD-9	HEM EARLY PREG-ANTEPART
641	ICD-9	ANTEPART HEM & PLAC PREV*
641.0	ICD-9	PLACENTA PREVIA W/O HEM*
641.00	ICD-9	PLACENTA PREVIA-UNSPEC
641.03	ICD-9	PLACENTA PREVIA-ANTEPART
641.1	ICD-9	HEMORR FROM PLACENT PREV*
641.10	ICD-9	PLACENTA PREV HEM-UNSPEC
641.13	ICD-9	PLACEN PREV HEM-ANTEPART
641.2	ICD-9	PREM SEPARATION PLACENTA*
641.20	ICD-9	PREM SEPAR PLACEN-UNSPEC
641.23	ICD-9	PREM SEPAR PLAC-ANTEPART
641.30	ICD-9	COAG DEF HEMORR-UNSPEC
641.33	ICD-9	COAG DEF HEMORR-ANTEPART
641.8	ICD-9	ANTEPARTUM HEMORR NEC*
641.80	ICD-9	ANTEPART HEM NEC-UNSPEC
641.83	ICD-9	ANTEPART HEM NEC-ANTEPAR
641.9	ICD-9	ANTEPARTUM HEMORR NOS*
641.90	ICD-9	ANTEPART HEM NOS-UNSPEC
641.93	ICD-9	ANTEPART HEM NOS-ANTEPAR
642	ICD-9	HYPERTENSION COMPL PREG*
642.0	ICD-9	ESSEN HYPERTEN COMP PREG*
642.00	ICD-9	ESSEN HYPERTEN PREG-UNSP
642.03	ICD-9	ESSEN HYPERTEN-ANTEPART
642.1	ICD-9	RENAL HYPERTEN OF PREG*
642.10	ICD-9	RENAL HYPERTEN PREG-UNSP
642.13	ICD-9	RENAL HYPERTEN-ANTEPART
642.2	ICD-9	OLD HYPERTEN PREG NEC*
642.20	ICD-9	OLD HYPERTEN PREG-UNSPEC
642.23	ICD-9	OLD HYPERTEN NEC-ANTEPAR
642.3	ICD-9	TRANS HYPERTENSION PREG*
642.30	ICD-9	TRANS HYPERTEN PREG-UNSP
642.33	ICD-9	TRANS HYPERTEN-ANTEPART
642.4	ICD-9	MILD/NOS PRE-ECLAMPSIA*
642.40	ICD-9	MILD/NOS PREECLAMP-UNSP
642.43	ICD-9	MILD/NOS PREECLAMP-ANTEP
642.5	ICD-9	SEVERE PRE-ECLAMPSIA*
642.50	ICD-9	SEVERE PREECLAMP-UNSPEC
642.53	ICD-9	SEV PREECLAMP-ANTEPARTUM

Code	Code Type	Description
642.6	ICD-9	ECLAMPSIA*
642.60	ICD-9	ECLAMPSIA-UNSPECIFIED
642.63	ICD-9	ECLAMPSIA-ANTEPARTUM
642.7	ICD-9	TOXEMIA W OLD HYPERTEN*
642.70	ICD-9	TOX W OLD HYPERTEN-UNSP
642.73	ICD-9	TOX W OLD HYPER-ANTEPART
642.9	ICD-9	HYPERTENS COMPL PREG NOS*
642.90	ICD-9	HYPERTEN PREG NOS-UNSPEC
642.93	ICD-9	HYPERTENS NOS-ANTEPARTUM
643	ICD-9	EXCESS VOMITING IN PREG*
643.0	ICD-9	MILD HYPEREMESIS GRAVID*
643.00	ICD-9	MILD HYPEREM GRAV-UNSPEC
643.03	ICD-9	MILD HYPEREMESIS-ANTEPAR
643.1	ICD-9	HYPEREM GRAV W METAB DIS*
643.10	ICD-9	HYPEREM W METAB DIS-UNSP
643.13	ICD-9	HYPEREM W METAB-ANTEPART
643.20	ICD-9	LATE VOMIT OF PREG-UNSP
643.23	ICD-9	LATE VOMIT PREG-ANTEPART
643.8	ICD-9	VOMITING COMPL PREG NEC*
643.80	ICD-9	VOMIT COMPL PREG-UNSPEC
643.83	ICD-9	VOMIT COMPL PREG-ANTEPAR
643.9	ICD-9	VOMITING PREGNANCY NOS*
643.90	ICD-9	VOMIT OF PREG NOS-UNSPEC
643.93	ICD-9	VOMIT OF PG NOS-ANTEPART
644	ICD-9	EARLY/THREATENED LABOR*
644.0	ICD-9	THREATEN PREMATURE LABOR*
644.00	ICD-9	THREAT PREM LABOR-UNSPEC
644.03	ICD-9	THRT PREM LABOR-ANTEPART
644.1	ICD-9	THREATENED LABOR NEC*
644.10	ICD-9	THREAT LABOR NEC-UNSPEC
644.13	ICD-9	THREAT LABOR NEC-ANTEPAR
644.2	ICD-9	EARLY ONSET OF DELIVERY*
644.20	ICD-9	EARLY ONSET DELIV-UNSPEC
645	ICD-9	PROLONGED PREGNANCY*
645.10	ICD-9	POST TERM PREG-UNSP
645.13	ICD-9	POST TERM PREG-ANTEPAR
645.20	ICD-9	PROLONGED PREG-UNSP
645.23	ICD-9	PROLONGED PREG-ANTEPAR
646	ICD-9	OTHER COMPL OF PREGNANCY*
646.0	ICD-9	PAPYRACEOUS FETUS*
646.00	ICD-9	PAPYRACEOUS FETUS-UNSPEC
646.03	ICD-9	PAPYRACEOUS FET-ANTEPAR

Code	Code Type	Description
646.1	ICD-9	EDEMA IN PREGNANCY*
646.10	ICD-9	EDEMA IN PREG-UNSPEC
646.13	ICD-9	EDEMA IN PREG-ANTEPARTUM
646.2	ICD-9	RENAL DIS IN PREG NOS*
646.20	ICD-9	RENAL DIS PREG NOS-UNSP
646.23	ICD-9	RENAL DIS NOS-ANTEPARTUM
646.3	ICD-9	HABITUAL ABORTER*
646.30	ICD-9	HABITUAL ABORTER-UNSPEC
646.33	ICD-9	HABITUAL ABORT-ANTEPART
646.4	ICD-9	PERIPHERAL NEURITIS PREG*
646.40	ICD-9	NEURITIS OF PREG-UNSPEC
646.43	ICD-9	NEURITIS OF PREG-ANTEPAR
646.5	ICD-9	ASYMPT BACTERIURIA PREG*
646.50	ICD-9	BACTERIURIA PREG-UNSPEC
646.53	ICD-9	ASY BACTERIURIA-ANTEPART
646.6	ICD-9	GU TRACT INFECT IN PREG*
646.60	ICD-9	GU INFECT IN PREG-UNSPEC
646.63	ICD-9	GU INFECTION-ANTEPARTUM
646.7	ICD-9	LIVER DISORDER IN PREG*
646.70	ICD-9	LIVER DIS IN PREG-UNSPEC
646.73	ICD-9	LIVER DISORDER-ANTEPART
646.8	ICD-9	PREGNANCY COMPL NEC*
646.80	ICD-9	PREG COMPL NEC-UNSPEC
646.83	ICD-9	PREG COMPL NEC-ANTEPART
646.9	ICD-9	PREGNANCY COMPL NOS*
646.90	ICD-9	PREG COMPL NOS-UNSPEC
646.93	ICD-9	PREG COMPL NOS-ANTEPART
647	ICD-9	INFECTIVE DIS IN PREG*
647.0	ICD-9	SYPHILIS IN PREGNANCY*
647.00	ICD-9	SYPHILIS IN PREG-UNSPEC
647.03	ICD-9	SYPHILIS-ANTEPARTUM
647.1	ICD-9	GONORRHEA IN PREGNANCY*
647.13	ICD-9	GONORRHEA-ANTEPARTUM
647.2	ICD-9	OTH VENEREAL DIS IN PREG*
647.20	ICD-9	OTHER VD IN PREG-UNSPEC
647.23	ICD-9	OTHER VD-ANTEPARTUM
647.3	ICD-9	TUBERCULOSIS IN PREG*
647.30	ICD-9	TB IN PREG-UNSPECIFIED
647.33	ICD-9	TUBERCULOSIS-ANTEPARTUM
647.40	ICD-9	MALARIA IN PREG-UNSPEC
647.50	ICD-9	RUBELLA IN PREG-UNSPEC
647.6	ICD-9	OTHER VIRAL DIS IN PREG*

Code	Code Type	Description
647.60	ICD-9	OTH VIRUS IN PREG-UNSPEC
647.63	ICD-9	OTH VIRAL DIS-ANTEPARTUM
647.80	ICD-9	INF DIS IN PREG NEC-UNSP
647.83	ICD-9	INFECT DIS NEC-ANTEPART
647.9	ICD-9	INFECTION IN PREG NOS*
647.90	ICD-9	INFECT IN PREG NOS-UNSP
647.93	ICD-9	INFECT NOS-ANTEPARTUM
648	ICD-9	OTH CURRENT COND IN PREG*
648.0	ICD-9	DIABETES MELLIT IN PREG*
648.00	ICD-9	DIABETES IN PREG-UNSPEC
648.03	ICD-9	DIABETES-ANTEPARTUM
648.1	ICD-9	THYROID DYSFUNC IN PREG*
648.10	ICD-9	THYROID DYSFUN PREG-UNSP
648.13	ICD-9	THYROID DYSFUNC-ANTEPART
648.2	ICD-9	ANEMIA IN PREGNANCY*
648.20	ICD-9	ANEMIA IN PREG-UNSPEC
648.23	ICD-9	ANEMIA-ANTEPARTUM
648.3	ICD-9	DRUG DEPENDENCE IN PREG*
648.30	ICD-9	DRUG DEPEND PREG-UNSPEC
648.33	ICD-9	DRUG DEPENDENCE-ANTEPART
648.4	ICD-9	MENTAL DISORDERS IN PREG*
648.40	ICD-9	MENTAL DIS PREG-UNSPEC
648.43	ICD-9	MENTAL DISORDER-ANTEPART
648.5	ICD-9	CONG CARDIOVAS DIS IN PG*
648.50	ICD-9	CONGEN CV DIS PREG-UNSP
648.53	ICD-9	CONGEN CV DIS-ANTEPARTUM
648.6	ICD-9	CARDIOVAS DIS NEC IN PG*
648.60	ICD-9	CV DIS NEC PREG-UNSPEC
648.63	ICD-9	CV DIS NEC-ANTEPARTUM
648.7	ICD-9	BONE DISORDER IN PREG*
648.70	ICD-9	BONE DISORD IN PREG-UNSP
648.73	ICD-9	BONE DISORDER-ANTEPARTUM
648.8	ICD-9	ABN GLUC TOLERAN IN PREG*
648.80	ICD-9	ABN GLUCOSE IN PREG-UNSP
648.83	ICD-9	ABN GLUCOSE-ANTEPARTUM
648.9	ICD-9	OTH CURRENT COND OF PREG*
648.90	ICD-9	OTH CURR COND PREG-UNSP
648.93	ICD-9	OTH CURR COND-ANTEPARTUM
649	ICD-9	COMPL REL PREG
649.0	ICD-9	TOBACCO USE COMP PREG
649.00	ICD-9	TOBACCO USE COMP PREG-UNSPEC
649.03	ICD-9	TOBACCO USE COMP-ANTEPARTUM

Code	Code Type	Description
649.1	ICD-9	OBESITY COMPL PREG*
649.10	ICD-9	OBESITY COMP PREG-UNSP
649.13	ICD-9	OBESITY COMP PREG-ANTEPART
649.2	ICD-9	BARIATR SURG COMP PREGNANCY*
649.20	ICD-9	BARIATR SURG COMP PREG-UNSPEC
649.23	ICD-9	BARIATR SURG COMP-ANTEPARTUM
649.3	ICD-9	COAG DEF COMPL PREG*
649.30	ICD-9	COAG DEF COMP PREG-UNSPEC
649.33	ICD-9	COAG DEF COMP PREG-ANTEPART
649.4	ICD-9	EPILEPSY COMP PREG
649.40	ICD-9	EPILEPSY COMP PREG-UNSPEC
649.43	ICD-9	EPILEPSY COMP-ANTEPARTUM
649.5	ICD-9	SPOTTING COMPL PREG*
649.50	ICD-9	SPOTTING COMP PREG-UNSP
649.53	ICD-9	SPOTTING COMP PREG-ANTEPART
649.6	ICD-9	UTERINE SIZE DATE DISCREP*
649.60	ICD-9	UTERINE SIZE DATE DISCREP-UNSPEC
649.63	ICD-9	UTERINE SIZE DATE DISCREP-ANTEPARTUM
649.7	ICD-9	CERIVCAL SHORTEN PREG*
649.70	ICD-9	CERVICAL SHORTEN-UNSPEC
649.73	ICD-9	CERVICAL SHORTEN-ANTEPART
651	ICD-9	MULTIPLE GESTATION*
651.0	ICD-9	TWIN PREGNANCY*
651.00	ICD-9	TWIN PREGNANCY-UNSPEC
651.03	ICD-9	TWIN PREGNANCY-ANTEPART
651.1	ICD-9	TRIPLET PREGNANCY*
651.10	ICD-9	TRIPLET PREGNANCY-UNSPEC
651.13	ICD-9	TRIPLET PREG-ANTEPARTUM
651.20	ICD-9	QUADRUPLET PREG-UNSPEC
651.23	ICD-9	QUADRUPLET PREG-ANTEPART
651.3	ICD-9	TWINS W FETAL LOSS*
651.30	ICD-9	TWINS W FETAL LOSS-UNSP
651.33	ICD-9	TWINS W FETAL LOSS-ANTE
651.43	ICD-9	TRIPLETS W FET LOSS-ANTE
651.50	ICD-9	QUADS W FETAL LOSS-UNSP
651.53	ICD-9	QUADS W FETAL LOSS-ANTE
651.63	ICD-9	MULT GES W FET LOSS-ANTE
651.80	ICD-9	MULTI GESTAT NEC-UNSPEC
651.83	ICD-9	MULTI GEST NEC-ANTEPART
651.9	ICD-9	MULTIPLE GESTATION NOS*
651.90	ICD-9	MULTI GESTAT NOS-UNSPEC
651.93	ICD-9	MULTI GEST NOS-ANTEPART

Code	Code Type	Description
652	ICD-9	MALPOSITION OF FETUS*
652.0	ICD-9	UNSTABLE LIE*
652.00	ICD-9	UNSTABLE LIE-UNSPECIFIED
652.03	ICD-9	UNSTABLE LIE-ANTEPARTUM
652.1	ICD-9	CEPHALIC VERSION NOS*
652.10	ICD-9	CEPHALIC VERS NOS-UNSPEC
652.13	ICD-9	CEPHAL VERS NOS-ANTEPART
652.2	ICD-9	BREECH PRESENTATION*
652.20	ICD-9	BREECH PRESENTAT-UNSPEC
652.23	ICD-9	BREECH PRESENT-ANTEPART
652.3	ICD-9	TRANSVERSE/OBLIQUE LIE*
652.30	ICD-9	TRANSV/OBLIQ LIE-UNSPEC
652.33	ICD-9	TRANSV/OBLIQ LIE-ANTEPAR
652.40	ICD-9	FACE/BROW PRESENT-UNSPEC
652.43	ICD-9	FACE/BROW PRES-ANTEPART
652.5	ICD-9	HIGH HEAD AT TERM*
652.50	ICD-9	HIGH HEAD AT TERM-UNSPEC
652.53	ICD-9	HIGH HEAD TERM-ANTEPART
652.6	ICD-9	MULT GEST W MALPRESENTAT*
652.60	ICD-9	MULT GEST MALPRESEN-UNSP
652.63	ICD-9	MULT GES MALPRES-ANTEPAR
652.7	ICD-9	PROLAPSED ARM*
652.70	ICD-9	PROLAPSED ARM-UNSPEC
652.8	ICD-9	MALPOSITION NEC*
652.80	ICD-9	MALPOSITION NEC-UNSPEC
652.83	ICD-9	MALPOSITION NEC-ANTEPART
652.9	ICD-9	MALPOSITION NOS*
652.90	ICD-9	MALPOSITION NOS-UNSPEC
652.93	ICD-9	MALPOSITION NOS-ANTEPART
653	ICD-9	DISPROPORTION*
653.00	ICD-9	PELVIC DEFORM NOS-UNSPEC
653.03	ICD-9	PELV DEFORM NOS-ANTEPART
653.10	ICD-9	CONTRACT PELV NOS-UNSPEC
653.13	ICD-9	CONTRAC PELV NOS-ANTEPAR
653.20	ICD-9	INLET CONTRACTION-UNSPEC
653.23	ICD-9	INLET CONTRACT-ANTEPART
653.3	ICD-9	OUTLET CONTRACT PELVIS*
653.30	ICD-9	OUTLET CONTRACTION-UNSP
653.33	ICD-9	OUTLET CONTRACT-ANTEPART
653.4	ICD-9	FETOPELVIC DISPROPORTION*
653.40	ICD-9	FETOPELV DISPROP-UNSPEC
653.43	ICD-9	FETOPEL DISPROP-ANTEPART

Code	Code Type	Description
653.5	ICD-9	FETAL DISPROPORTION NOS*
653.50	ICD-9	FETAL DISPROP NOS-UNSPEC
653.53	ICD-9	FETAL DISPRO NOS-ANTEPAR
653.60	ICD-9	HYDROCEPHAL FETUS-UNSPEC
653.63	ICD-9	HYDROCEPH FETUS-ANTEPART
653.7	ICD-9	OTH FETAL ABN W DISPROP*
653.70	ICD-9	OTH ABN FET DISPROP-UNSP
653.73	ICD-9	OTH ABN FET DISPRO-ANTEP
653.80	ICD-9	DISPROPORTION NEC-UNSPEC
653.83	ICD-9	DISPROPOR NEC-ANTEPARTUM
653.90	ICD-9	DISPROPORTION NOS-UNSPEC
653.93	ICD-9	DISPROPOR NOS-ANTEPARTUM
654	ICD-9	ABN PELVIC ORGAN IN PREG*
654.0	ICD-9	CONG ABN UTERUS IN PREG*
654.00	ICD-9	CONG ABN UTER PREG-UNSP
654.03	ICD-9	CONGEN ABN UTER-ANTEPART
654.1	ICD-9	UTERINE TUMOR IN PREG*
654.10	ICD-9	UTER TUMOR IN PREG-UNSP
654.13	ICD-9	UTERINE TUMOR-ANTEPARTUM
654.2	ICD-9	PREVIOUS C-SECTION NOS*
654.20	ICD-9	PREV C-DELIVERY UNSPEC
654.23	ICD-9	PREV C-DELIVERY-ANTEPART
654.3	ICD-9	RETROVERT GRAVID UTERUS*
654.30	ICD-9	RETROVERT UTERUS-UNSPEC
654.33	ICD-9	RETROVERT UTER-ANTEPART
654.4	ICD-9	ABN SHAPE GRAVID UTERUS*
654.40	ICD-9	ABN GRAV UTERUS NEC-UNSP
654.43	ICD-9	ABN UTERUS NEC-ANTEPART
654.5	ICD-9	CERVIX INCOMPET IN PREG*
654.50	ICD-9	CERV INCOMPET PREG-UNSP
654.53	ICD-9	CERV INCOMPET-ANTEPARTUM
654.6	ICD-9	ABN CERVIX NEC IN PREG*
654.60	ICD-9	ABN CERVIX NEC PREG-UNSP
654.63	ICD-9	ABN CERVIX NEC-ANTEPART
654.7	ICD-9	ABNORMAL VAGINA IN PREG*
654.70	ICD-9	ABN VAGINA IN PREG-UNSP
654.73	ICD-9	ABNORM VAGINA-ANTEPARTUM
654.8	ICD-9	ABNORMAL VULVA IN PREG*
654.80	ICD-9	ABN VULVA IN PREG-UNSPEC
654.83	ICD-9	ABNORMAL VULVA-ANTEPART
654.9	ICD-9	ABN PELV ORG NOS IN PREG*
654.90	ICD-9	ABN PEL NEC IN PREG-UNSP

Code	Code Type	Description
654.93	ICD-9	ABN PELV ORG NEC-ANTEPAR
655	ICD-9	FETAL ABN AFFECT MOTHER*
655.0	ICD-9	FETAL CNS MALFORMATION*
655.00	ICD-9	FETAL CNS MALFORM-UNSPEC
655.03	ICD-9	FETAL CNS MALFOR-ANTEPAR
655.1	ICD-9	FETAL CHROMOSOMAL ABN*
655.10	ICD-9	FETAL CHROMOS ABN-UNSPEC
655.13	ICD-9	FET CHROMO ABN-ANTEPART
655.2	ICD-9	FAM HERED DIS AFF FETUS*
655.20	ICD-9	FAMIL HEREDIT DIS-UNSPEC
655.23	ICD-9	FAMIL HERED DIS-ANTEPART
655.3	ICD-9	FETAL DAMAGE D/T VIRUS*
655.30	ICD-9	FET DAMG D/T VIRUS-UNSP
655.33	ICD-9	FET DAMG D/T VIRUS-ANTEP
655.4	ICD-9	FETAL DAMAGE D/T OTH DIS*
655.40	ICD-9	FET DAMG D/T DIS-UNSPEC
655.43	ICD-9	FET DAMG D/T DIS-ANTEPAR
655.5	ICD-9	FETAL DAMAGE D/T DRUG*
655.50	ICD-9	FETAL DAMG D/T DRUG-UNSP
655.53	ICD-9	FET DAMG D/T DRUG-ANTEPA
655.6	ICD-9	RADIATION FETAL DAMAGE*
655.60	ICD-9	RADIAT FETAL DAMAG-UNSP
655.63	ICD-9	RADIAT FET DAMAG-ANTEPAR
655.70	ICD-9	DECREASE FETL MOVMT UNSP
655.73	ICD-9	DEC FETAL MOVMT ANTEPART
655.8	ICD-9	FETAL ABNORMALITY NEC*
655.80	ICD-9	FETAL ABNORM NEC-UNSPEC
655.83	ICD-9	FETAL ABNORM NEC-ANTEPAR
655.9	ICD-9	FETAL ABNORMALITY NOS*
655.90	ICD-9	FETAL ABNORM NOS-UNSPEC
655.93	ICD-9	FETAL ABNORM NOS-ANTEPAR
656	ICD-9	OTH FETAL PROB AFF MOTH*
656.0	ICD-9	FETAL-MATERNAL HEMORR*
656.00	ICD-9	FETAL-MATERNAL HEM-UNSP
656.03	ICD-9	FETAL-MATERN HEM-ANTEPAR
656.1	ICD-9	RHESUS ISOIMMUNIZATION*
656.10	ICD-9	RH ISOIMMUNIZATION-UNSP
656.13	ICD-9	RH ISOIMMUNIZAT-ANTEPART
656.2	ICD-9	ABO ISOIMMUNIZATION*
656.20	ICD-9	ABO ISOIMMUNIZATION-UNSP
656.23	ICD-9	ABO ISOIMMUNIZAT-ANTEPAR
656.3	ICD-9	FETAL DISTRESS*

Code	Code Type	Description
656.30	ICD-9	FETAL DISTRESS-UNSPEC
656.33	ICD-9	FETAL DISTRESS-ANTEPART
656.5	ICD-9	POOR FETAL GROWTH*
656.50	ICD-9	POOR FETAL GROWTH-UNSPEC
656.53	ICD-9	POOR FETAL GRTH-ANTEPART
656.6	ICD-9	EXCESSIVE FETAL GROWTH*
656.60	ICD-9	EXCESS FETAL GRTH-UNSPEC
656.63	ICD-9	EXCESS FET GRTH-ANTEPART
656.7	ICD-9	OTH PLACENTAL CONDITIONS*
656.70	ICD-9	OTH PLACENT COND-UNSPEC
656.73	ICD-9	OTH PLACENT COND-ANTEPAR
656.8	ICD-9	FETAL/PLACENTAL PROB NEC*
656.80	ICD-9	FET/PLAC PROB NEC-UNSPEC
656.83	ICD-9	FET/PLAC PROB NEC-ANTEPA
656.9	ICD-9	FETAL/PLACENTAL PROB NOS*
656.90	ICD-9	FET/PLAC PROB NOS-UNSPEC
656.93	ICD-9	FET/PLAC PROB NOS-ANTEPA
657	ICD-9	POLYHYDRAMNIOS*
657.00	ICD-9	POLYHYDRAMNIOS-UNSPEC
657.03	ICD-9	POLYHYDRAMNIOS-ANTEPART
658	ICD-9	OTH AMNIOTIC CAVITY PROB*
658.0	ICD-9	OLIGOHYDRAMNIOS*
658.00	ICD-9	OLIGOHYDRAMNIOS-UNSPEC
658.03	ICD-9	OLIGOHYDRAMNIOS-ANTEPAR
658.1	ICD-9	PREMAT RUPTURE MEMBRANES*
658.10	ICD-9	PREM RUPT MEMBRAN-UNSPEC
658.13	ICD-9	PREM RUPT MEMB-ANTEPART
658.2	ICD-9	PROLONG RUPT MEMBRAN NOS*
658.20	ICD-9	PROLONG RUPT MEMB-UNSPEC
658.23	ICD-9	PROLONG RUP MEMB-ANTEPAR
658.3	ICD-9	DELAY DEL POSTARTIF RUPT*
658.30	ICD-9	ARTIFIC RUPT MEMBR-UNSP
658.33	ICD-9	ARTIF RUPT MEMB-ANTEPART
658.4	ICD-9	INFECT AMNIOTIC CAVITY*
658.40	ICD-9	AMNIOTIC INFECTION-UNSP
658.43	ICD-9	AMNIOTIC INFECT-ANTEPART
658.8	ICD-9	AMNIOTIC CAVITY PROB NEC*
658.80	ICD-9	AMNIOTIC PROB NEC-UNSPEC
658.83	ICD-9	AMNION PROB NEC-ANTEPART
658.9	ICD-9	AMNIOTIC CAVITY PROB NOS*
658.90	ICD-9	AMNIOTIC PROB NOS-UNSPEC
658.93	ICD-9	AMNION PROB NOS-ANTEPART

Code	Code Type	Description
659	ICD-9	OTH INDICAT CARE DELIVER*
659.0	ICD-9	FAIL MECHAN INDUCT LABOR*
659.00	ICD-9	FAIL MECHAN INDUCT-UNSP
659.03	ICD-9	FAIL MECH INDUCT-ANTEPAR
659.1	ICD-9	FAIL INDUCTION LABOR NOS*
659.10	ICD-9	FAIL INDUCTION NOS-UNSP
659.13	ICD-9	FAIL INDUCT NOS-ANTEPART
659.20	ICD-9	PYREXIA IN LABOR-UNSPEC
659.23	ICD-9	PYREXIA IN LABOR-ANTEPAR
659.3	ICD-9	SEPTICEMIA DURING LABOR*
659.30	ICD-9	SEPTICEMIA IN LABOR-UNSP
659.33	ICD-9	SEPTICEM IN LABOR-ANTEPA
659.4	ICD-9	GRAND MULTIPARITY*
659.40	ICD-9	GRAND MULTIPARITY-UNSPEC
659.43	ICD-9	GRAND MULTIPARITY-ANTEPA
659.5	ICD-9	ELDERLY PRIMIGRAVIDA*
659.50	ICD-9	ELDERLY PRIMIGRAVID-UNSP
659.53	ICD-9	ELDER PRIMIGRAVID-ANTEPA
659.60	ICD-9	ELDERLY MULTIGRAVIDA-UNS
659.63	ICD-9	ELDERLY MULTIGRAVD-ANTEP
659.7	ICD-9	ABN FTL HRT RATE*
659.70	ICD-9	ABN FTL HRT RATE/RHY-UNS
659.73	ICD-9	ABN FTL HRT RATE/RHY-ANT
659.8	ICD-9	INDICAT CARE LAB/DEL NEC*
659.80	ICD-9	COMPLIC LABOR NEC-UNSP
659.83	ICD-9	COMPL LABOR NEC-ANTEPART
659.9	ICD-9	INDICAT CARE LAB/DEL NOS*
659.90	ICD-9	COMPLIC LABOR NOS-UNSP
659.93	ICD-9	COMPL LABOR NOS-ANTEPART
760	ICD-9	MATERN COND AFF FETUS/NB*
760.0	ICD-9	MATERN HYPERTEN AFF NB
760.1	ICD-9	MATERN URINE DIS AFF NB
760.2	ICD-9	MATERNAL INFEC AFF NB
760.3	ICD-9	MATERN CARDIORESP AFF NB
760.4	ICD-9	MATERN NUTRIT DIS AFF NB
760.5	ICD-9	MATERNAL INJURY AFF NB
760.6	ICD-9	SURG OP ON MOTHER AFF NB
760.7	ICD-9	NOXIOUS SUBSTANCE AFF NB*
760.70	ICD-9	NOXIOUS SUBST NOS AFF NB
760.71	ICD-9	MATERNAL ALCOHOL AFF NB
760.72	ICD-9	MATERNAL NARCOTIC AFF NB
760.73	ICD-9	MATERNAL HALLUCIN AFF NB

Code	Code Type	Description
760.74	ICD-9	MATERNAL ANTI-INF AFF NB
760.75	ICD-9	COCAINE - NXS INFL FETUS
760.76	ICD-9	FTS/NB AFCTD MTRNL DES
760.79	ICD-9	NOXIOUS SUBST NEC AFF NB
760.8	ICD-9	MATERNAL COND NEC AFF NB
760.9	ICD-9	MATERNAL COND NOS AFF NB
761	ICD-9	MATERNAL COMPL AFF NB*
761.0	ICD-9	INCOMPETNT CERVIX AFF NB
761.1	ICD-9	PREMAT RUPT MEMB AFF NB
761.2	ICD-9	OLIGOHYDRAMNIOS AFF NB
761.3	ICD-9	POLYHYDRAMNIOS AFF NB
761.4	ICD-9	ECTOPIC PREGNANCY AFF NB
761.5	ICD-9	MULT PREGNANCY AFF NB
761.6	ICD-9	MATERNAL DEATH AFF NB
761.7	ICD-9	ANTEPART MALPRES AFF NB
761.8	ICD-9	MATERN COMPL NEC AFF NB
761.9	ICD-9	MATERN COMPL NOS AFF NB
762	ICD-9	COMPL PLACEN/CORD AFF NB*
762.0	ICD-9	PLACENTA PREVIA AFF NB
762.1	ICD-9	PLACENTA HEM NEC AFF NB
762.2	ICD-9	ABN PLAC NEC/NOS AFF NB
762.3	ICD-9	PLACENT TRANSFUSION SYN
762.4	ICD-9	PROLAPSED CORD AFF NB
762.5	ICD-9	OTH UMBIL CORD COMPRESS
762.6	ICD-9	UMBIL COND NEC AFF NB
762.7	ICD-9	CHORIOAMNIONITIS AFF NB
762.8	ICD-9	ABN AMNION NEC AFF NB
762.9	ICD-9	ABN AMNION NOS AFF NB
V22	ICD-9	NORMAL PREGNANCY*
V22.0	ICD-9	SUPERVIS NORMAL 1ST PREG
V22.1	ICD-9	SUPERVIS OTH NORMAL PREG
V22.2	ICD-9	PREG STATE, INCIDENTAL
V23	ICD-9	SUPERVIS HIGH-RISK PREG*
V23.0	ICD-9	PREG W HX OF INFERTILITY
V23.1	ICD-9	PREG W HX-TROPHOBLAS DIS
V23.2	ICD-9	PREG W HX OF ABORTION
V23.3	ICD-9	GRAND MULTIPARITY
V23.4	ICD-9	PREG W POOR OBSTETRIC HX
V23.41	ICD-9	PREG W HX PRETERM LABOR
V23.49	ICD-9	PREG W OTH POOR OBSTETRIC HX
V23.5	ICD-9	PREG W POOR REPRODUCT HX
V23.7	ICD-9	INSUFFICNT PRENATAL CARE

Code	Code Type	Description
V23.8	ICD-9	SUPRV HIGH-RISK PREG NEC*
V23.81	ICD-9	SUPRV ELDERLY PRIMIGRAV
V23.82	ICD-9	SUPRV ELDERLY MULTIGRAV
V23.83	ICD-9	SUPRV YOUNG PRIMIGRAVIDA
V23.84	ICD-9	SUPRV YOUNG MULTIGRAVIDA
V23.89	ICD-9	SUPRV HIGH-RISK PREG NEC
V23.9	ICD-9	SUPRV HIGH-RISK PREG NOS
V28	ICD-9	ANTENATAL SCREENING*
V28.0	ICD-9	SCREENING-CHROMOSOM ANOM
V28.1	ICD-9	SCREEN-ALPHAFETOPROTEIN
V28.2	ICD-9	SCREEN BY AMNIOCENT NEC
V28.3	ICD-9	SCREEN-FETAL MALFORM
V28.4	ICD-9	SCREEN-FETAL RETARDATION
V28.5	ICD-9	SCREEN-ISOIMMUNIZATION
V28.6	ICD-9	ANTENATAL SCREEN STREP B
V28.8	ICD-9	ANTENATAL SCREENING NEC
V28.9	ICD-9	ANTENATAL SCREENING NOS
V72.42	ICD-9	Pregnancy examination or test, positive result

H. APPENDIX H. AUGMENTATION OF A CKD COHORT IDENTIFIED USING LABORATORY TEST RESULTS CRITERIA

1. Supplementary Table 30, SITE 1: Characteristics of Individuals in the 2012 Chronic Kidney Disease Overall Cohort Identification Test Case 2 Population

Characteristics [a]	CKD Identified by ≥ 1 Diagnosis Code, by ≥ 1 eGFR values <60ml/min/1.73m² (Calculated from Serum Creatinine Result Values), or by Both Methods					
	≥ 2 CKD Diagnosis Codes [b] N = 17,593 (37.5%)	1 CKD Diagnosis Code and ≥ 1 low eGFR N = 3,982 (8.5%)	≥ 2 Low eGFRs (no diagnosis) N = 5,985 (12.8%)	1 CKD Diagnosis only N = 1,105 (2.4%)	1 low eGFR only N = 18,221 (38.9%)	Total N = 46,886
Estimated stage from diagnosis code, N [c]	n=17,593	n=3,982	N/A	n=1,105	N/A	n=22,680
Stage 3	13,687 (77.8)	1,790 (45.0)		592 (53.6)		16,069 (70.9)
Stage 4	1,097 (6.2)	81 (2.0)		5 (0.5)		1,183 (5.2)
Stage 5	37 (0.2)	1 (0.0)		1 (0.1)		39 (0.2)
Stage unspecified/other	2,772 (15.8)	2,110 (53.0)		507 (45.9)		5,389 (23.8)
Estimated stage from eGFR, N	n=15,472	n=3,982	n=5,985	N/A	n=18,221	n=43,660
Stage 3 (30-59)	13,676 (88.4)	3,802 (95.5)	5,949 (99.4)		18,110 (99.4)	41,537 (95.1)
Stage 4 (15-29)	1,608 (10.4)	151 (3.8)	36 (0.6)		95 (0.5)	1,890 (4.3)
Stage 5 (<15)	188 (1.2)	29 (0.7)	0 (0.0)		16 (0.1)	233 (0.5)
Combined diagnosis and eGFR stage estimate[d]	n=17,593	n=3,982	n=5,985	n=1,105	n=18,221	n=46,886
Stage 3	14,710 (83.6)	3,738 (93.9)	5,949 (99.4)	592 (53.6)	18,110 (99.4)	43,099 (91.9)
Stage 4	2,086 (11.9)	215 (5.4)	36 (0.6)	5 (0.5)	95 (0.5)	2,437 (5.2)
Stage 5	205 (1.2)	29 (0.7)	0 (0.0)	1 (0.1)	16 (0.1)	251 (0.5)
Stage unspecified/other	592 (3.4)	0 (0.0)	0 (0.0)	507 (45.9)	0 (0.0)	1,099 (2.3)
Age in years, mean (SD)	73.2 ± 10.7	71.3 ± 12.1	72.5 ± 9.6	64.9 ± 14.3	66.9 ± 11.5	70.3 ± 11.5
Age < 65 years 65-74 years 75-89 years	3,268 (18.6) 5,170 (29.4) 9,155 (52.0)	1,005 (25.2) 1,150 (28.9) 1,827 (45.9)	1,211 (20.2) 2,111 (35.3) 2,663 (44.5)	503 (45.5) 285 (25.8) 317 (28.7)	7,184 (39.4) 6,054 (33.2) 4,983 (27.3)	13,171 (28.1) 14,770 (31.5) 18,945 (40.4)
Female sex	8,994 (51.1)	2,225 (55.9)	4,129 (69.0)	520 (47.1)	11,724 (64.3)	27,592 (58.8)
Any serum creatinine value available in 2012	16,999 (96.6)	3,948 (99.1)[e]	5,985 (100.0)	767 (69.4)	18,221 (100.0)	45,920 (97.9)
Serum creatinine procedure code in 2012	17,143 (97.5)	3,952 (99.2)	5,983 (100.0)	861 (78.8)	18,206 (99.9)	46,145 (98.5)

Characteristics [a]	CKD Identified by ≥ 1 Diagnosis Code, by ≥ 1 eGFR values <60ml/min/1.73m² (Calculated from Serum Creatinine Result Values), or by Both Methods					
	≥ 2 CKD Diagnosis Codes [b] N = 17,593 (37.5%)	1 CKD Diagnosis Code and ≥ 1 low eGFR N = 3,982 (8.5%)	≥ 2 Low eGFRs (no diagnosis) N = 5,985 (12.8%)	1 CKD Diagnosis only N = 1,105 (2.4%)	1 low eGFR only N = 18,221 (38.9%)	Total N = 46,886
Race						
White	13,235 (75.2)	3,058 (76.8)	4,652 (77.7)	704 (63.7)	13,776 (75.6)	35,425 (75.6)
Black	936 (5.3)	173 (4.3)	99 (1.7)	76 (6.9)	462 (2.5)	1,746 (3.7)
Other	504 (2.9)	92 (2.3)	133 (2.2)	23 (2.1)	411 (2.3)	1,163 (2.5)
Unknown	2,918 (16.6)	659 (16.5)	1,101 (18.4)	302 (27.3)	3,572 (19.6)	8,552 (18.2)
No encounters in prior 183 days	440 (2.5)	106 (2.7)	138 (2.3)	42 (3.8)	782 (4.3)	1,508 (3.2)
Number of ambulatory medical visits during baseline, mean (SD)	4.2 ± 4.7	4.3 ± 5.1	3.8 ± 4.2	3.9 ± 5.9	3.8 ± 4.5	4.0 ± 4.6
Emergency department visit during baseline, N (%) yes	1,578 (9.0)	408 (10.2)	415 (6.9)	105 (9.5)	1,469 (8.1)	3,975 (8.5)
Hospitalization during baseline, N (%) yes	1,032 (5.9)	240 (6.0)	212 (3.5)	51 (4.6)	1,054 (5.8)	2,589 (5.5)
Institutional stay during baseline, N (%) yes	295 (1.7)	59 (1.5)	56 (0.9)	8 (0.7)	149 (0.8)	567 (1.2)
Comorbidity score, [69] mean (SD) [e]	1.4 ± 2.3	1.4 ± 2.4	0.7 ± 1.8	1.0 ± 2.1	0.7 ± 1.8	1.1 ± 2.1
Selected individual comorbidities						
Congestive heart failure	2,966 (16.9)	549 (13.8)	500 (8.4)	103 (9.3)	1,195 (6.6)	5,313 (11.3)
HIV/AIDS	24 (0.1)	7 (0.2)	8 (0.1)	1 (0.1)	23 (0.1)	63 (0.1)
Hypertension	12,700 (72.2)	2,645 (66.4)	3,822 (63.9)	649 (58.7)	9,463 (51.9)	29,279 (62.4)
Pulmonary disease, chronic	3,599 (20.5)	812 (20.4)	903 (15.1)	170 (15.4)	2,826 (15.5)	8,310 (17.7)
Peripheral vascular disease	2,356 (13.4)	457 (11.5)	440 (7.4)	87 (7.9)	1,090 (6.0)	4,430 (9.4)
Tumor, any	1,894 (10.8)	508 (12.8)	585 (9.8)	108 (9.8)	1,678 (9.2)	4,773 (10.2)
Diabetes, any	7,022 (39.9)	1,098 (27.6)	1,351 (22.6)	344 (31.1)	2,862 (15.7)	12,677 (27.0)
Myocardial infarction or stroke	1,285 (7.3)	263 (6.6)	265 (4.4)	67 (6.1)	782 (4.3)	2,662 (5.7)
Previous CKD diagnosis in 2011	13,039 (74.1)	1,004 (25.2)	438 (7.3)	513 (46.4)	854 (4.7)	15,848 (33.8)
Mean follow-up time (SD) [g]	349.0 ± 59.1	340.6 ± 76.4	361.9 ± 21.7	318.5 ± 106.0	344.5 ± 70.7	347.5 ± 64.3
Death within one year	927 (5.3)	268 (6.7)	64 (1.1)	70 (6.3)	412 (2.3)	1,741 (3.7)

[a] Covariates assessed for the 183 days prior to cohort entry date (T0 or T0L) except as noted

Characteristics [a]	CKD Identified by ≥ 1 Diagnosis Code, by ≥ 1 eGFR values <60ml/min/1.73m² (Calculated from Serum Creatinine Result Values), or by Both Methods					
	≥ 2 CKD Diagnosis Codes [b] N = 17,593 (37.5%)	1 CKD Diagnosis Code and ≥ 1 low eGFR N = 3,982 (8.5%)	≥ 2 Low eGFRs (no diagnosis) N = 5,985 (12.8%)	1 CKD Diagnosis only N = 1,105 (2.4%)	1 low eGFR only N = 18,221 (38.9%)	Total N = 46,886

[b] Patients with ≥ 2 CKD diagnosis codes within 365 days were assigned to this group whether or not they also had low eGFRs available
[c] Based on second diagnosis code for those with 2 coded diagnoses
[d] Combined stage reflects worst stage from diagnosis or lab measures
[e] Determined over the 183 days prior to the cohort entry date
[f] Serum creatinine to calculate low eGFR not available in 2012 for entire 100% because 365 day follow-up could extend into 2013
[g] Maximum follow-up time assessed was 365 days

2. Supplementary Table 30, SITE 2. Characteristics of Individuals in the 2012 Chronic Kidney Disease Overall Cohort Identification Test Case 2 Population

Characteristics [a]	CKD Identified by ≥ 1 Diagnosis Code, by ≥ 1 eGFR values <60ml/min/1.73m² (Calculated from Serum Creatinine Result Values), or by Both Methods					
	≥ 2 CKD Diagnosis Codes [b] N =93,350 (50.3%)	1 CKD Diagnosis Code and ≥ 1 low eGFR N =17,976 (9.7%)	≥ 2 Low eGFRs (no diagnosis) N = 19,574 (10.6%)	1 CKD Diagnosis only N =5,180 (2.8%)	1 low eGFR only N =49,484 (26.7%)	Total N = 185,564
Estimated stage from diagnosis code, N [c]	n=93,350	n=17,976	N/A	n=5,180	N/A	n=116,506
Stage 3	70,441 (75.5)	10,189 (56.7)		2,671 (51.6)		83,301 (71.5)
Stage 4	4,428 (4.7)	151 (0.8)		50 (1.0)		4,629 (4.0)
Stage 5	376 (0.4)	13 (0.1)		15 (0.3)		404 (0.3)
Stage unspecified/other	18,105 (19.4)	7,623 (42.4)		2,444 (47.2)		28,172 (24.2)
Estimated stage from eGFR, N	n=81,002	n=17,976	n=19,574	N/A	n=49,484	n=168,036
Stage 3 (30-59)	70,010 (86.4)	16,703 (92.9)	19,370 (99.0)		48,748 (98.5)	154,831 (92.1)
Stage 4 (15-29)	9,321 (11.5)	1,005 (5.6)	201 (1.0)		613 (1.2)	11,140 (6.6)
Stage 5 (<15)	1,671 (2.1)	268 (1.5)	3 (0.0)		123 (0.2)	2,065 (1.2)
Combined diagnosis and eGFR stage estimate[d]	n=93,350	n=17,976	n=19,574	n=5,180	n=49,484	n=185,564
Stage 3	75,880 (81.3)	16,638 (92.6)	19,370 (99.0)	2,671 (51.6)	48,748 (98.5)	163,307 (88.0)
Stage 4	10,310 (11.0)	1,065 (5.9)	201 (1.0)	50 (1.0)	613 (1.2)	12,239 (6.6)

Characteristics [a]	CKD Identified by ≥ 1 Diagnosis Code, by ≥ 1 eGFR values <60ml/min/1.73m^2 (Calculated from Serum Creatinine Result Values), or by Both Methods					
	≥ 2 CKD Diagnosis Codes [b] N =93,350 (50.3%)	1 CKD Diagnosis Code and ≥ 1 low eGFR N =17,976 (9.7%)	≥ 2 Low eGFRs (no diagnosis) N = 19,574 (10.6%)	1 CKD Diagnosis only N =5,180 (2.8%)	1 low eGFR only N =49,484 (26.7%)	Total N = 185,564
Stage 5	1,776 (1.9)	273 (1.5)	3 (0.0)	15 (0.3)	123 (0.2)	2,190 (1.2)
Stage unspecified/other	5,384 (5.8)	0 (0.0)	0 (0.0)	2,444 (47.2)	0 (0.0)	7,828 (4.2)
Age in years, mean (SD)	72.7 ± 10.6	72.0 ± 11.5	73.4 ± 10.1	65.7 ± 13.3	69.7 ± 11.6	71.7 ± 11.1
Age < 65 years	17,284 (18.5)	4,263 (23.7)	4,044 (20.7)	2,107 (40.7)	15,776 (31.9)	43,474 (23.4)
65-74 years	30,696 (32.9)	5,384 (30.0)	5,670 (29.0)	1,656 (32.0)	14,847 (30.0)	58,253 (31.4)
75-89 years	45,370 (48.6)	8,329 (46.3)	9,860 (50.4)	1,417 (27.4)	18,861 (38.1)	83,837 (45.2)
Female sex	50,241 (53.8)	9,964 (55.4)	11,313 (57.8)	2,544 (49.1)	27,834 (56.2)	101,896 (54.9)
Any serum creatinine value available in 2012	91,548 (98.1)	17,903 (99.6)[f]	19,574 (100.0)	4,111 (79.4)	49,483 (100.0)	182,619 (98.4)
Serum creatinine procedure code in 2012	91,599 (98.1)	17,904 (99.6)	19,565 (100.0)	4,159 (81.0)	49,406 (99.8)	182,633 (98.5)
Race	n=93,350	n=17,976	n=19,574	n=5,180	n=49,484	n=185,564
White	65,227 (69.9)	13,351 (74.3)	14,972 (76.5)	3,275 (63.2)	37,532 (75.8)	134,357 (72.4)
Black	9,249 (9.9)	1,491 (8.3)	993 (5.1)	676 (13.1)	3,044 (6.2)	15,453 (8.3)
Other	14,176 (15.2)	2,248 (12.5)	2,594 (13.3)	840 (16.2)	6,110 (12.3)	25,968 (14.0)
Unknown	4,698 (5.0)	886 (4.9)	1,015 (5.2)	389 (7.5)	2,798 (5.7)	9,786 (5.3)
No encounters in prior 183 days	9,138 (9.8)	1,821 (10.1)	1,638 (8.4)	519 (10.0)	4,107 (8.3)	17,223 (9.3)
Number of ambulatory medical visits during baseline, mean (SD)	4.7 ± 6.0	4.6 ± 6.1	4.2 ± 4.9	3.8 ± 5.5	4.9 ± 6.2	4.7 ± 6.0
Emergency department visit during baseline, N (%) yes	10,656 (11.4)	2,262 (12.6)	1,924 (9.8)	600 (11.6)	6,755 (13.7)	22,197 (12.0)
Hospitalization during baseline, N (%) yes	5,182 (5.6)	1,193 (6.6)	654 (3.3)	237 (4.6)	3,601 (7.3)	10,867 (5.9)
Institutional stay during baseline, N (%) yes	1,359 (1.5)	277 (1.5)	127 (0.6)	93 (1.8)	719 (1.5)	2,575 (1.4)
Comorbidity score, [69] mean (SD) [e]	1.3 ± 2.2	1.2 ± 2.4	0.6 ± 1.7	1.0 ± 2.0	1.0 ± 2.2	1.1 ± 2.2

Characteristics [a]	CKD Identified by ≥ 1 Diagnosis Code, by ≥ 1 eGFR values <60ml/min/1.73m^2 (Calculated from Serum Creatinine Result Values), or by Both Methods					
	≥ 2 CKD Diagnosis Codes [b] N =93,350 (50.3%)	1 CKD Diagnosis Code and ≥ 1 low eGFR N =17,976 (9.7%)	≥ 2 Low eGFRs (no diagnosis) N = 19,574 (10.6%)	1 CKD Diagnosis only N =5,180 (2.8%)	1 low eGFR only N =49,484 (26.7%)	Total N = 185,564
Selected individual comorbidities						
Congestive heart failure	15,232 (16.3)	2,388 (13.3)	1,865 (9.5)	477 (9.2)	4,777 (9.7)	24,739 (13.3)
HIV/AIDS	304 (0.3)	65 (0.4)	85 (0.4)	12 (0.2)	208 (0.4)	674 (0.4)
Hypertension	79,146 (84.8)	14,403 (80.1)	15,121 (77.3)	3,896 (75.2)	34,321 (69.4)	146,887 (79.2)
Pulmonary disease, chronic	20,526 (22.0)	3,820 (21.3)	3,428 (17.5)	1,021 (19.7)	9,758 (19.7)	38,553 (20.8)
Peripheral vascular disease	17,095 (18.3)	3,224 (17.9)	2,512 (12.8)	692 (13.4)	6,939 (14.0)	30,462 (16.4)
Tumor, any	9,541 (10.2)	2,055 (11.4)	1,853 (9.5)	427 (8.2)	5,607 (11.3)	19,483 (10.5)
Diabetes, any	42,705 (45.7)	5,641 (31.4)	5,944 (30.4)	2,498 (48.2)	11,742 (23.7)	68,530 (36.9)
Myocardial infarction or stroke	6,688 (7.2)	1,128 (6.3)	913 (4.7)	251 (4.8)	2,877 (5.8)	11,857 (6.4)
Previous CKD diagnosis in 2011	68,536 (73.4)	5,670 (31.5)	1,495 (7.6)	2,567 (49.6)	2,266 (4.6)	80,534 (43.4)
Mean follow-up time (SD) [g]	348.8 ± 60.4	337.5 ± 83.1	362.0 ± 21.4	328.7 ± 95.2	339.2 ± 81.8	346.0 ± 68.2
Death within one year	4,915 (5.3)	1,398 (7.8)	279 (1.4)	298 (5.8)	2,505 (5.1)	9,395 (5.1)

[a] Covariates assessed for the 183 days prior to cohort entry date (T0 or T0L) except as noted
[b] Patients with ≥ 2 CKD diagnosis codes within 365 days were assigned to this group whether or not they also had low eGFRs available
[c] Based on second diagnosis code for those with 2 coded diagnoses
[d] Combined stage reflects worst stage from diagnosis or lab measures
[e] Determined over the 183 days prior to the cohort entry date
[f] Serum creatinine to calculate low eGFR not available in 2012 for entire 100% because 365 day follow-up could extend into 2013
[g] Maximum follow-up time assessed was 365 days

3. Supplementary Table 30, SITE 3. Characteristics of Individuals in the 2012 Chronic Kidney Disease Overall Cohort Identification Test Case 2 Population

Characteristics [a]	CKD Identified by ≥ 1 Diagnosis Code, by ≥ 1 eGFR values <60ml/min/1.73m^2 (Calculated from Serum Creatinine Result Values), or by Both Methods					
	≥ 2 CKD Diagnosis Codes [b] N =188,808 (50.0%)	1 CKD Diagnosis Code and ≥ 1 low eGFR N = 28,582 (7.6%)	≥ 2 Low eGFRs (no diagnosis) N = 52,296 (13.8%)	1 CKD Diagnosis only N = 25,663 (6.8%)	1 low eGFR only N = 82,453 (21.8%)	Total N = 377,802
Estimated stage from diagnosis code, N [c]	n=188,808	n=28,582	N/A	n=25,663	N/A	n=243,053
Stage 3	114,417 (60.6)	9,295 (32.5)		9,269 (36.1)		132,981 (54.7)
Stage 4	10,965 (5.8)	367 (1.3)		376 (1.5)		11,708 (4.8)
Stage 5	859 (0.5)	35 (0.1)		109 (0.4)		1,003 (0.4)
Stage unspecified/other	62,567 (33.1)	18,885 (66.1)		15,909 (62.0)		97,361 (40.1)
Estimated stage from eGFR, N	n=123,639	n=28,582	n=52,296	N/A	n=82,453	n=286,970
Stage 3 (30-59)	106,090 (85.8)	26,929 (94.2)	51,227 (98.0)		81,360 (98.7)	265,606 (92.6)
Stage 4 (15-29)	15,446 (12.5)	1,480 (5.2)	1,037 (2.0)		914 (1.1)	18,877 (6.6)
Stage 5 (<15)	2,103 (1.7)	173 (0.6)	32 (0.1)		179 (0.2)	2,487 (0.9)
Combined diagnosis and eGFR stage estimate[d]	n=188,808	n=28,582	n=52,296	n=25,663	n=82,453	n=377,802
Stage 3	137,554 (72.9)	26,672 (93.3)	51,227 (98.0)	9,269 (36.1)	81,360 (98.7)	306,082 (81.0)
Stage 4	21,341 (11.3)	1,710 (6.0)	1,037 (2.0)	376 (1.5)	914 (1.1)	25,378 (6.7)
Stage 5	2,711 (1.4)	200 (0.7)	32 (0.1)	109 (0.4)	179 (0.2)	3,231 (0.9)
Stage unspecified/other	27,202 (14.4)	0 (0.0)	0 (0.0)	15,909 (62.0)	0 (0.0)	43,111 (11.4)
Age in years, mean (SD)	74.6 ± 8.9	74.3 ± 8.8	75.0 ± 7.8	71.6 ± 10.5	72.9 ± 8.8	74.0 ± 8.9
Age < 65 years	19,757 (10.5)	3,115 (10.9)	3,830 (7.3)	4,722 (18.4)	10,730 (13.0)	42,154 (11.2)
65-74 years	68,506 (36.3)	10,807 (37.8)	20,985 (40.1)	10,413 (40.6)	35,894 (43.5)	146,605 (38.8)
75-89 years	100,545 (53.3)	14,660 (51.3)	27,481 (52.5)	10,528 (41.0)	35,829 (43.5)	189,043 (50.0)

Characteristics [a]	CKD Identified by ≥ 1 Diagnosis Code, by ≥ 1 eGFR values <60ml/min/1.73m² (Calculated from Serum Creatinine Result Values), or by Both Methods					
	≥ 2 CKD Diagnosis Codes [b] N =188,808 (50.0%)	1 CKD Diagnosis Code and ≥ 1 low eGFR N = 28,582 (7.6%)	≥ 2 Low eGFRs (no diagnosis) N = 52,296 (13.8%)	1 CKD Diagnosis only N = 25,663 (6.8%)	1 low eGFR only N = 82,453 (21.8%)	Total N = 377,802
Female sex	98,243 (52.0)	15,775 (55.2)	34,227 (65.4)	12,637 (49.2)	50,899 (61.7)	211,781 (56.1)
Any serum creatinine value available in 2012	142,380 (75.4)	28,045 (98.1)[f]	52,296 (100.0)	11,356 (44.3)	82,453 (100.0)	316,530 (83.8)
Serum creatinine procedure code in 2012	182,615 (97.1)	28,044 (98.3)	51,692 (99.0)	23,427 (92.7)	81,081 (98.7)	366,859 (97.5)
Race						
White	143,953 (76.2)	22,882 (80.1)	44,710 (85.5)	19,143 (74.6)	67,529 (81.9)	298,217 (78.9)
Black	30,690 (16.3)	3,466 (12.1)	4,166 (8.0)	3,762 (14.7)	6,870 (8.3)	48,954 (13.0)
Other	4,650 (2.5)	646 (2.3)	1,046 (2.0)	583 (2.3)	1,749 (2.1)	8,674 (2.3)
Unknown	9,515 (5.0)	1,588 (5.6)	2,374 (4.5)	2,175 (8.5)	6,305 (7.6)	21,957 (5.8)
No encounters in prior 183 days	4,471 (2.4)	1,056 (3.7)	2,014 (3.9)	897 (3.5)	4,320 (5.2)	12,758 (3.4)
Number of ambulatory medical visits during baseline, mean (SD)	9.8 ± 9.2	9.0 ± 8.7	7.2 ± 6.9	9.1 ± 9.0	7.6 ± 7.8	8.8 ± 8.6
Emergency department visit during baseline, N (%) yes	21,990 (11.6)	3,417 (12.0)	4,724 (9.0)	3,240 (12.6)	8,294 (10.1)	41,665 (11.0)
Hospitalization during baseline, N (%) yes	19,625 (10.4)	2,978 (10.4)	3,244 (6.2)	2,830 (11.0)	6,482 (7.9)	35,159 (9.3)
Institutional stay during baseline, N (%) yes	13,061 (6.9)	2,012 (7.0)	2,545 (4.9)	1,925 (7.5)	4,659 (5.7)	24,202 (6.4)
Comorbidity score, [69] mean (SD) [e]	2.2 ± 2.5	1.8 ± 2.5	0.9 ± 2.0	1.9 ± 2.5	1.0 ± 2.1	1.7 ± 2.4
Selected individual comorbidities						
Congestive heart failure	57,219 (30.3)	7,134 (25.0)	8,285 (15.8)	6,085 (23.7)	12,847 (15.6)	91,570 (24.2)
HIV/AIDS	399 (0.2)	67 (0.2)	64 (0.1)	52 (0.2)	160 (0.2)	742 (0.2)
Hypertension	168,833 (89.4)	25,442 (89.0)	46,481 (88.9)	21,546 (84.0)	68,034 (82.5)	330,336 (87.4)
Pulmonary disease, chronic	55,810 (29.6)	7,904 (27.7)	10,289 (19.7)	7,422 (28.9)	17,414 (21.1)	98,839 (26.2)
Peripheral vascular disease	65,771 (34.8)	7,827 (27.4)	8,468 (16.2)	6,882 (26.8)	13,716 (16.6)	102,664 (27.2)

Characteristics [a]	CKD Identified by ≥ 1 Diagnosis Code, by ≥ 1 eGFR values <60ml/min/1.73m^2 (Calculated from Serum Creatinine Result Values), or by Both Methods					
	≥ 2 CKD Diagnosis Codes [b] N =188,808 (50.0%)	1 CKD Diagnosis Code and ≥ 1 low eGFR N = 28,582 (7.6%)	≥ 2 Low eGFRs (no diagnosis) N = 52,296 (13.8%)	1 CKD Diagnosis only N = 25,663 (6.8%)	1 low eGFR only N = 82,453 (21.8%)	Total N = 377,802
Tumor, any	29,863 (15.8)	4,687 (16.4)	6,661 (12.7)	3,800 (14.8)	11,302 (13.7)	56,313 (14.9)
Diabetes, any	99,222 (52.6)	13,124 (45.9)	21,659 (41.4)	11,695 (45.6)	28,608 (34.7)	174,308 (46.1)
Myocardial infarction or stroke	34,163 (18.1)	5,098 (17.8)	6,774 (13.0)	4,135 (16.1)	10,663 (12.9)	60,833 (16.1)
Previous CKD diagnosis in 2011	128,232 (67.9)	8,511 (29.8)	6,700 (12.8)	8,873 (34.6)	7,248 (8.8)	159,564 (42.2)
Mean follow-up time (SD) [g]	335.5 ± 80.1	336.0 ± 80.1	358.5 ± 29.8	308.3 ± 114.0	327.8 ± 91.2	335.2 ± 81.5
Death within one year	12,005 (6.4)	2,208 (7.7)	535 (1.0)	1,892 (7.4)	3,051 (3.7)	19,691 (5.2)

[a] Covariates assessed for the 183 days prior to cohort entry date (T0 or T0L) except as noted
[b] Patients with ≥ 2 CKD diagnosis codes within 365 days were assigned to this group whether or not they also had low eGFRs available
[c] Based on second diagnosis code for those with 2 coded diagnoses
[d] Combined stage reflects worst stage from diagnosis or lab measures
[e] Determined over the 183 days prior to the cohort entry date
[f] Serum creatinine to calculate low eGFR not available in 2012 for entire 100% because 365 day follow-up could extend into 2013
[g] Maximum follow-up time assessed was 365 days

4. **Supplementary Table 31 by SITE. Identification of a Cohort of Patients with Chronic Kidney Disease using an Electronic Data Definition that requires at Least Two Coded Diagnoses: Cohort Augmentation Using Laboratory Test Results Criteria**

SITE 1	Patients Identified Using Coded Diagnosis Definition Requiring >=2 Diagnoses (with or without eGFR < 60 ml/min/1.73m^2)	Additional Patients Identified Using Laboratory Test Results (No or 1 Diagnosis with eGFR < 60 ml/min/1.73m^2)		Total Patients in CKD Cohort
		Patients with 1 Coded Diagnosis and >=1 eGFR < 60 ml/min/1.73m^2	Patients with >=2 eGFR < 60 ml/min/1.73m^2 (No Coded Diagnosis)	
N (%) in Subgroup	17,593 (63.8) [a]	3,982 (14.5)	5,985 (21.7)	27,560
Subtotal		9,967 (36.2)		
[a] Comprised of 2,421 (8.8%) with coded diagnoses only and 15,172 (55.1%) with codes diagnoses and >=1 eGFR < 60 ml/min/1.73m^2				

SITE 2	Patients Identified Using Coded Diagnosis Definition Requiring >=2 Diagnoses (with or without eGFR < 60 ml/min/1.73m^2)	Additional Patients Identified Using Laboratory Test Results (No or 1 Diagnosis with eGFR < 60 ml/min/1.73m^2)		Total Patients in CKD Cohort
		Patients with 1 Coded Diagnosis and >=1 eGFR < 60 ml/min/1.73m^2	Patients with >=2 eGFR < 60 ml/min/1.73m^2 (No Coded Diagnosis)	
N (%) in Subgroup	93,350 (71.3) [a]	17,976 (13.7)	19,574 (15.0)	130,900
Subtotal		37,550 (28.7)		
[a] Comprised of 13,857 (10.6%) with coded diagnoses only and 79,493 (60.7%) with codes diagnoses and >=1 eGFR < 60 ml/min/1.73m^2				

SITE 3	Patients Identified Using Coded Diagnosis Definition Requiring >=2 Diagnoses (with or without eGFR < 60 ml/min/1.73m^2)	Additional Patients Identified Using Laboratory Test Results (No or 1 Diagnosis with eGFR < 60 ml/min/1.73m^2)		Total Patients in CKD Cohort
		Patients with 1 Coded Diagnosis and >=1 eGFR < 60 ml/min/1.73m^2	Patients with >=2 eGFR < 60 ml/min/1.73m^2 (No Coded Diagnosis)	
N (%) in Subgroup	188,808 (70.0) [a]	28,582 (10.6)	52,296 (19.4)	269,686
Subtotal		80,878 (30.0)		
[a] Comprised of 69,158 (25.6%) with coded diagnoses only and 119,650 (44.4%) with codes diagnoses and >=1 eGFR < 60 ml/min/1.73m^2				

5. Supplementary Table 33 by SITE. Identification of a Cohort of Patients with Chronic Kidney Disease using an Electronic Data Definition that requires at Least One Coded Diagnoses: Cohort Augmentation Using Laboratory Test Results Criteria

SITE 1	Patients Identified Using Coded Diagnosis Definition Requiring >=1 Diagnoses (with or without eGFR < 60 ml/min/1.73m^2)	Lab Results >=2 eGFR < 60 ml/min/1.73m^2	Total Patients in CKD Cohort
N (%) in Subgroup	22,680 (79.1) [a]	5,985 (20.9)	28,665
[a] Comprised of 1,105 (3.9%) with 1 coded diagnosis only, 3,982 (13.9%) with 1 coded diagnosis and >=1 eGFR < 60 ml/min/1.73m^2, 2,421 (8.5%) with >=2 coded diagnoses only, and 15,172 (52.9%) with >=2 coded diagnoses and >=1 eGFR < 60 ml/min/1.73m^2			

SITE 2	Patients Identified Using Coded Diagnosis Definition Requiring >=1 Diagnoses (with or without eGFR < 60 ml/min/1.73m^2)	Lab Results >=2 eGFR < 60 ml/min/1.73m^2	Total Patients in CKD Cohort
N (%) in Subgroup	116,506 (85.6) [a]	19,574 (14.4)	136,080
[a] Comprised of 5,180 (3.8%) with 1 coded diagnosis only, 17,976 (13.2%) with 1 coded diagnosis and >=1 eGFR < 60 ml/min/1.73m^2, 13,857 (10.2%) with >=2 coded diagnoses only, and 79,493 (58.4%) with >=2 coded diagnoses and >=1 eGFR < 60 ml/min/1.73m^2			

SITE 3	Patients Identified Using Coded Diagnosis Definition Requiring >=1 Diagnoses (with or without eGFR < 60 ml/min/1.73m^2)	Lab Results >=2 eGFR < 60 ml/min/1.73m^2	Total Patients in CKD Cohort
N (%) in Subgroup	243,053 (82.3) [a]	52,296 (17.7)	295,349
[a] Comprised of 25,663 (8.7%) with 1 coded diagnosis only, 28,582 (9.7%) with 1 coded diagnosis and >=1 eGFR < 60 ml/min/1.73m^2, 69,158 (23.4%) with >=2 coded diagnoses only, and 119,650 (40.5%) with >=2 coded diagnoses and >=1 eGFR < 60 ml/min/1.73m^2			

I. APPENDIX I. CODED DIAGNOSES IN PATIENTS WITH BLEEDING OUTCOMES WITHIN 30 DAYS AFTER NSAID EXPOSURE

1. Table 1. Upper Gastrointestinal Bleeding Diagnoses Coded in the Inpatient Care Setting (with or without an observed drop in HGB ≥ 3 g/dL) among 1657 Patients

Diagnosis	Number of Patients (Total N = 1657)	Percentage with Diagnosis Code [a]
UPPER GI HEMORRHAGE	1199	72.4
ANTRAL ULCER	349	21.1
DUODENAL ULCER	229	13.8
HEMATEMESIS	208	12.6
CHRONIC DUODENAL ULCER W HEMORRHAGE	195	11.8
PEPTIC ULCER	171	10.3
H PYLORI GASTRITIS W HEMORRHAGE	70	4.2
ACUTE GASTRIC ULCER	68	4.1
EROSIVE GASTRITIS W HEMORRHAGE	49	3
MALLORY WEISS SYNDROME	47	2.8
CHRONIC GASTRIC ULCER W PERFORATION	36	2.2
ESOPHAGEAL HEMORRHAGE	35	2.1
ANGIODYSPLASIA OF STOMACH W HEMORRHAGE	34	2.1
CHRONIC PERFORATED DUODENAL ULCER.	30	1.8
ULCER OF ESOPHAGUS WITH BLEEDING	30	1.8
SECONDARY ESOPHAGEAL VARICES W BLEEDING	29	1.8
INTESTINAL ANGIODYSPLASIA W HEMORRHAGE	28	1.7
ACUTE GASTRITIS WITH HEMORRHAGE	27	1.6
EROSIVE DUODENITIS W HEMORRHAGE	23	1.4
ACUTE DUODENAL ULCER W/PERFORATION	21	1.3
BLEEDING ESOPHAGEAL VARICES	18	1.1
CHRONIC DUODENAL ULCER	14	0.8
GASTROJEJUNAL ULCER	12	0.7
ACUTE PEPTIC ULCER W/HEMORRHAGE	11	0.7
DIEULAFOY LESION OF STOMACH AND DUODENUM	11	0.7
CHRONIC ATROPHIC GASTRITIS W HEMORRHAGE	9	0.5
ACUTE PEPTIC ULCER	8	0.5
CHRONIC PEPTIC ULCER W PERFORATION	8	0.5
ANASTOMOTIC ULCER W HEMORRHAGE	8	0.5
ACUTE DUODENAL ULCER W/HEMORRHAGE&OBSTRUCTION	8	0.5
CHRONIC/UNSPEC DUODEN ULCER W/HEMORR&OBSTRUCTION	8	0.5
ACUTE PEPTIC ULCER W PERFORATION	6	0.4
ALCOHOLIC GASTRITIS W/HEMORRHAGE	5	0.3
THROAT HEMORRHAGE	3	0.2
ACUTE GASTRIC ULCER W/HEMORRHAGE AND OBSTRUCTION	3	0.2
DUODENAL ULCER W OBSTRUCTION.	3	0.2
ACUTE DUODENAL ULCER W/PERFOR+OBSTR	3	0.2
GASTROJEJUNAL ULCER W HEMORRHAGE, W PERFORATION	3	0.2

Diagnosis	Number of Patients (Total N = 1657)	Percentage with Diagnosis Code [a]
ACUTE MARGINAL ULCER W/PERFORATION	3	0.2
DIVERTICULOSIS OF SMALL INTESTINE W HEMORRHAGE	2	0.1
ACUTE MARGINAL ULCER NOS	2	0.1
PEPTIC ULCER W OBSTRUCTION	2	0.1
PEPTIC ULCER W HEMORRHAGE, W OBSTRUCTION, W PERFORATION	1	0.1
CHRONIC PEPTIC ULCER W HEMORRHAGE, W PERFORATION	1	0.1
ACUTE PEPTIC ULCER W OBSTRUCTION.	1	0.1
GASTRIC MUCOSAL HYPERTROPHY WITH HEMORRHAGE	1	0.1
CHRONIC DUODENAL ULCER NOS W/OBSTR	1	0.1
PEPTIC ULCER W OBSTRUCTION, W PERFORATION	1	0.1
CHRON MARGINAL ULCER W/PERFORATION	1	0.1
CHRONIC DUODENAL ULCER W HEMORRHAGE, W OBSTRUCTION, W PERFORATION	1	0.1
GASTRIC ULCER W OBSTRUCTION, W PERFORATION	1	0.1
ACUTE DUODENAL ULCER W OBSTRUCTION	1	0.1
DUODENAL ULCER W OBSTRUCTION, W PERFORATION	1	0.1
DIEULAFOY LESION OF INTESTINE	1	0.1
ACUTE MARGINAL ULCER W/HEMORR+OBSTR	1	0.1
CHRONIC PEPTIC ULCER NOS W/OBSTRUCT	1	0.1
[a] Total exceeds 100% because some patients had more than one type of UGI bleeding diagnosis coded		

2. Table 2. Upper Gastrointestinal Bleeding Diagnoses Coded in Non-Inpatient Care Settings with an Observed Drop in HGB ≥ 3 g/dL among 58 Patients

Diagnosis	Number of Patients (Total N = 58)	Percentage with Diagnosis Code [a]
UPPER GI HEMORRHAGE	48	82.8
ANTRAL ULCER	8	13.8
DUODENAL ULCER	7	12.1
PEPTIC ULCER	3	5.2
CHRONIC DUODENAL ULCER W HEMORRHAGE	3	5.2
EROSIVE GASTRITIS W HEMORRHAGE	2	3.4
H PYLORI GASTRITIS W HEMORRHAGE	1	1.7
ACUTE GASTRITIS WITH HEMORRHAGE	1	1.7
ACUTE PEPTIC ULCER	1	1.7
HEMATEMESIS	1	1.7
EROSIVE DUODENITIS W HEMORRHAGE	1	1.7
[a] Total exceeds 100% because some patients had more than one type of UGI bleeding diagnosis coded		

3. **Table 3. Upper Gastrointestinal Bleeding Diagnoses Coded in Non-Inpatient Care Settings without an Observed Drop in HGB (i.e., HGB results not available) or with an Observed Drop in HGB < 3 g/dL among 3303 Patients**

Diagnosis	Number of Patients (Total N = 3303)	Percentage with Diagnosis Code [a]
UPPER GI HEMORRHAGE	1536	46.5
PEPTIC ULCER	717	21.7
ANTRAL ULCER	438	13.3
HEMATEMESIS	196	5.9
DUODENAL ULCER	166	5
EROSIVE GASTRITIS W HEMORRHAGE	56	1.7
ACUTE GASTRIC ULCER	55	1.7
ACUTE PEPTIC ULCER	35	1.1
ACUTE GASTRITIS WITH HEMORRHAGE	33	1
MALLORY WEISS SYNDROME	29	0.9
H PYLORI GASTRITIS W HEMORRHAGE	20	0.6
ACUTE PEPTIC ULCER W/HEMORRHAGE	20	0.6
THROAT HEMORRHAGE	19	0.6
ESOPHAGEAL HEMORRHAGE	19	0.6
GASTROJEJUNAL ULCER	18	0.5
ACUTE DUODENAL ULCER W/PERFORATION	17	0.5
ULCER OF ESOPHAGUS WITH BLEEDING	13	0.4
BLEEDING ESOPHAGEAL VARICES	13	0.4
INTESTINAL ANGIODYSPLASIA W HEMORRHAGE	12	0.4
CHRONIC ATROPHIC GASTRITIS W HEMORRHAGE	12	0.4
CHRONIC DUODENAL ULCER W HEMORRHAGE	11	0.3
CHRONIC DUODENAL ULCER	10	0.3
PEPTIC ULCER W OBSTRUCTION.	6	0.2
ANGIODYSPLASIA OF STOMACH W HEMORRHAGE	5	0.2
EROSIVE DUODENITIS W HEMORRHAGE	5	0.2
DIVERTICULOSIS OF SMALL INTESTINE W HEMORRHAGE	4	0.1
ACUTE PEPTIC ULCER W OBSTRUCTION, W PERFORATION	4	0.1
CHRONIC PERFORATED DUODENAL ULCER.	4	0.1
DIVERTICULITIS OF SMALL INTESTINE W HEMORRHAGE, W PERFORATION	3	0.1
GASTROJEJUNAL ULCER NOS W/OBSTRUCT	3	0.1
CHRONIC PEPTIC ULCER W PERFORATION	3	0.1
ACUTE PEPTIC ULCER W PERFORATION	3	0.1
ACUTE PEPTIC ULCER, SITE UNSPECIFIED, WITH PERFORATION.	3	0.1
DIEULAFOY LESION OF STOMACH AND DUODENUM	2	0.1
ACUTE MARGINAL ULCER NOS	2	0.1
ACUTE PEPTIC ULCER W OBSTRUCTION.	2	0.1
ACUTE DUODENAL ULCER W/HEMORRHAGE&OBSTRUCTION	2	0.1
CHRONIC GASTRIC ULCER W PERFORATION	2	0.1
SECONDARY ESOPHAGEAL VARICES W BLEEDING	2	0.1

Diagnosis	Number of Patients (Total N = 3303)	Percentage with Diagnosis Code [a]
ALCOHOLIC GASTRITIS W/HEMORRHAGE	1	0
CHRONIC MARGINAL ULCER NOS	1	0
GASTROJEJUNAL ULCER W HEMORRHAGE, W PERFORATION	1	0
ANASTOMOTIC ULCER W HEMORRHAGE	1	0
ACUTE GASTROJEJUNAL ULCER WITH HEMORRHAGE	1	0
PEPTIC ULCER, SITE UNSPECIFIED, UNSPECIFIED AS ACUTE OR CHRON	1	0
ACUT PEPTIC ULCER UNSPEC SITE W/HEMORR PERF&OBST	1	0
CHRONIC DUODENAL ULCER NOS W/OBSTR	1	0
ACUTE DUODENAL ULCER W/PERFOR+OBSTR	1	0
GASTRIC ULCER W HEMORRHAGE, W OBSTRUCTION	1	0
ACUTE GASTRIC ULCER W HEMORRHAGE, W OBSTRUCTION, W PERFORATION	1	0
ACUTE GASTRIC ULCER W/PERFORATION&OBSTRUCTION	1	0
ACUTE GASTRIC ULCER WITH HEMORRHAGE	1	0
[a] Total exceeds 100% because some patients had more than one type of UGI bleeding diagnosis coded		

4. Table 4. Coded Bleeding Diagnoses Associated with Observed Drop in HGB > 3 g/dL among 2619 Patients with no Coded Upper Gastrointestinal Bleeding Diagnosis

Diagnosis	Number of Patients (Total N = 2619)	Percentage with Diagnosis Code
No other coded bleeding diagnosis	2369	90.5
Pulmonary hemorrhage following pulmonary procedure	77	2.9
Postmenopausal bleeding	24	0.9
Dysphagia, late effect of non-traumatic subarachnoid hemorrhage	23	0.9
Hemorrhage of blood vessel	18	0.7
Hemorrhage of rectum and anus	17	0.6
Vitreous hemorrhage	10	0.4
Non-traumatic subdural hemorrhage	8	0.3
Intracerebral hemorrhage	8	0.3
Abnormal perimenopausal bleeding	8	0.3
Aphasia, late effect of non-traumatic subarachnoid hemorrhage	8	0.3
Abnormal bleeding of female genital tract	7	0.3
Hemorrhage, secondary or recurrent	6	0.2
Diverticulosis of cecum with hemorrhage	4	0.2
Non-traumatic subarachnoid hemorrhage, vertebral artery	4	0.2
Traumatic cerebellar hemorrhage	4	0.2
Third trimester antepartum hemorrhage	4	0.2
Right facial weakness, late effect of non-traumatic Intracerebral hemorrhage	3	0.1
Dysphasia, late effect of non-traumatic Intracerebral hemorrhage	3	0.1
Unspecific intracranial hemorrhage	2	0.1
Post-abortion hemorrhage	2	0.1
Diverticulitis of colon with hemorrhage	2	0.1
Cause of accidental cut or hemorrhage, heart catheterization	1	0
Left sub-retinal hemorrhage	1	0
Second and recurrent hemorrhage as an early complication of trauma	1	0
Subarachnoid hemorrhage, after injury, with coma	1	0
Closed fracture of base of skull, with intracranial hemorrhage	1	0
Legal abortion, incomplete, complicated by delayed or excessive hemorrhage	1	0
Prostate hemorrhage	1	0
Bladder wall hemorrhage	1	0