

Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Estimate of the frequency with which hospitalizations for severe acute liver injury (ALI) were possibly caused by a medication.

There is no accepted international gold standard for determining drug-induced causality of severe ALI.¹ Therefore, in a sample of patients with a hospitalization for severe ALI in the primary study, we estimated the frequency with which a medication caused or contributed to the severe ALI based on review of medical records by hepatologists.

Among the initiators of suspected hepatotoxic medications (defined by at least four published reports of hepatotoxicity based on assessment of the LiverTox website²) in the primary study, we selected a random sample of 75 patients electronically identified as having a hospitalization for severe ALI. Two hepatologists independently reviewed these patients' electronic medical records, including hospital admission notes, gastroenterology/hepatology notes, other specialist consultation notes, hospital progress notes, hospital laboratory results, and discharge summaries.

Each hepatologist adjudicator first separately assessed whether the patient had a condition that might exclude drug-induced ALI as a cause of the severe ALI, including: 1) ischemic events, 2) vascular abnormalities, 3) viral hepatitis, 4) pancreaticobiliary disease, 5) hepatic infiltrative disease, 6) non-viral hepatitis, and 7) metabolic/genetic disorders (detailed in **eMethods Table 1**).

eMethods Table 1. Non-drug-related categories and conditions of severe acute liver injury with methods of confirmation.

| Category of Non-Drug-Related ALI | Conditions | Methods of Confirmation |
|----------------------------------|--|--|
| Ischemic events | Cardiogenic, hypovolemic, septic shock | Acute elevations in liver aminotransferases in context of documented hypoperfusion event |
| Vascular abnormality | Congestive hepatopathy; hepatic vein thrombosis (Budd-Chiari syndrome) | History, abdominal imaging |
| Viral hepatitis | Hepatitis A, B, C, D, E; cytomegalovirus; Epstein-Barr virus; herpes simplex virus | Serologic or virologic tests |
| Pancreaticobiliary disease | Cholangitis, cholecystitis, choledocholithiasis, pancreaticobiliary cancer, primary sclerosing cholangitis | History, abdominal imaging, pathology |
| Hepatic infiltrative disease | Hepatocellular carcinoma, hepatic metastasis of cancer, leukemia/lymphoma | History, abdominal imaging, pathology |
| Non-viral hepatitis | Alcoholic hepatitis/liver disease, alpha-1-antitrypsin deficiency, autoimmune hepatitis | History, serology, pathology |
| Metabolic/genetic disorders | Celiac disease, hereditary hemochromatosis, rhabdomyolysis, thyrotoxicosis, Wilson's disease | Clinical history, serology, pathology |

Abbreviations: ALI, acute liver injury

Next, the hepatologists determined if a medication possibly caused or contributed to this patient's severe ALI based on clinical, biochemical, and/or histological evidence; time between the start of a medication and the onset of ALI; clinical signature; evidence of improvement of the ALI upon medication withdrawal (de-challenge; if applicable); and the effect of any rechallenge.^{1,3} Since drug-induced ALI is a challenging and subjective diagnosis to confirm,^{1,3} even for experts, we classified a severe ALI event as medication-related if *either* hepatologist indicated a possible drug-induced causality.

We estimated that a sample of 75 patients with a hospitalization for severe ALI would allow determination of the proportion that had a medication as the etiology with a maximum 95% confidence interval of $\pm 10\%$, assuming at least 80% had drug-induced severe ALI.⁴ Data were analyzed using SAS 9.4 (SAS Institute Inc., Cary, NC).

Among the 75 patients selected for medical record review, 57 (76.0%; 95% confidence interval, 64.7-85.1%) had a hospitalization for severe ALI that was deemed by a hepatologist to be medication-related. **eMethods Table 2** reports the causes of all non-drug-related severe ALI events as adjudicated by the hepatologist reviewers. Among the 18 patients classified as not having had severe ALI caused by a medication, the most common diagnoses identified by the hepatologists as likely causing their severe ALI were congestive hepatopathy (n=7; 38.9%), hypovolemic shock (n=4; 22.2%), alcoholic hepatitis (n=4; 22.2%) and sepsis (n=4; 22.2%).

eMethods Table 2. Etiologies of severe acute liver events that were adjudicated as non-drug-related by hepatologists.

| Patient | Non-Drug-Related Etiologies for Hospitalization for Severe Acute Liver Injury* |
|---------|--|
| 1 | Pancreaticobiliary cancer; sepsis |
| 2 | Hemolysis; sepsis |
| 3 | Sepsis; rhabdomyolysis |
| 4 | Cardiovascular shock; hypovolemic shock |
| 5 | Hypovolemic shock |
| 6 | Congestive hepatopathy; SIRS; alcoholic hepatitis |
| 7 | Congestive hepatopathy; alcoholic hepatitis |
| 8 | Lymphoma; cardiovascular shock |
| 9 | Congestive hepatopathy; rhabdomyolysis |
| 10 | Congestive hepatopathy |
| 11 | Choledocholithiasis; hypovolemic shock; SIRS |
| 12 | Small bowel obstruction; cardiovascular shock |
| 13 | Sepsis; congestive hepatopathy |
| 14 | Alcoholic hepatitis; congestive hepatopathy |
| 15 | Hemorrhagic shock; SIRS |
| 16 | Colonic perforation; cancer |
| 17 | Congestive hepatopathy; alcoholic hepatitis; hepatitis C |
| 18 | Hypovolemic shock |

Abbreviations: SIRS, systemic inflammatory response syndrome

*Adjudicators could indicate multiple possible etiologies for a non-drug-related severe acute liver injury event.

REFERENCES

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Table 1. Categories of medications classified as suspected hepatotoxic based on numbers of published cases of idiosyncratic drug-induced liver injury (category A, ≥50 cases; category B, 12-49 cases; category C, 4-11 cases). Italicized medications (n=26) were unable to be evaluated because they were not marketed in the United States,^a not dispensed within the VA during the study period;^b administered via injection/intravenous route;^c anticoagulants;^d or used for alcohol use disorder or liver disease treatment.^e

| # | Category A (n=48) | Category B (n=76) | Category C (n=96) |
|----|---|---------------------------------|----------------------------------|
| 1 | Allopurinol | Acarbose | Abacavir |
| 2 | Amiodarone | Amitriptyline | Acebutolol |
| 3 | Androgenic steroids ^f | <i>Amodiaquine</i> ^a | Acitretin |
| 4 | Atorvastatin | Amoxicillin | Adalimumab |
| 5 | Auranofin or gold products ^f | Asparaginase or pegaspargase | Albendazole |
| 6 | Azathioprine mercaptopurine | Azithromycin | Alfuzosin |
| 7 | Busulfan | Captopril | Amlodipine |
| 8 | Carbamazepine | <i>Cefazolin</i> ^c | Amphetamines ^g |
| 9 | Chlorpromazine | Ceftriaxone | <i>Amphotericin</i> ^c |
| 10 | Clavulanate with amoxicillin | Celecoxib | <i>Ampicillin</i> ^c |
| 11 | Dantrolene | Chlorpropamide | Anakinra |
| 12 | Diclofenac | Chlorzoxazone | Atomoxetine |
| 13 | Didanosine | Cimetidine | Bosentan |
| 14 | <i>Disulfiram</i> ^e | Ciprofloxacin | Bupropion |
| 15 | Efavirenz | Clarithromycin | Candesartan |
| 16 | Erythromycin | Clindamycin | Cephalexin |
| 17 | Estrogens or progestins ^f | Clopidogrel | Citalopram or escitalopram |
| 18 | <i>Floxuridine</i> ^c | Cloxacillin | Clomiphene |
| 19 | <i>Flucloxacillin</i> ^a | Clozapine | Cyproheptadine |
| 20 | Flutamide | Cyclophosphamide or ifosfamide | Cytarabine |
| 21 | <i>Halothane</i> ^b | <i>Cyproterone</i> ^a | <i>Dactinomycin</i> ^c |
| 22 | Hydralazine | <i>Dacarbazine</i> ^c | <i>Daptomycin</i> ^c |
| 23 | Ibuprofen | Dicloxacillin | <i>Desflurane</i> ^c |
| 24 | Infliximab | Doxorubicin | Diflunisal |
| 25 | <i>Interferon-α or peginterferon</i> ^e | Duloxetine | Diltiazem |
| 26 | Interferon-β | Enalapril | Disopyramide |
| 27 | Isoniazid | <i>Enflurane</i> ^c | Doxycycline |
| 28 | Ketoconazole | Etanercept | <i>Dronedarone</i> ^b |
| 29 | Methotrexate | Ethionamide | Erlotinib |
| 30 | Methyldopa | Felbamate | Etodolac |
| 31 | Minocycline | Fenofibrate | Etoposide |
| 32 | Nevirapine | Fluconazole | Ezetimibe |
| 33 | <i>Nimesulide</i> ^a | Fluvastatin | Famotidine |
| 34 | Nitrofurantoin | Glyburide (Glibenclamide) | Flavocoxid |
| 35 | Phenytoin or fosphenytoin | Haloperidol | Fluorouracil |
| 36 | Propylthiouracil | <i>Heparin</i> ^d | Fluoxetine |
| 37 | Pyrazinamide | Imatinib | Gabapentin |
| 38 | Quinidine | Imipramine | Gefitinib |
| 39 | Rifampin | Irinotecan | Gemcitabine |
| 40 | Simvastatin | <i>Isoflurane</i> ^c | Gemfibrozil |
| 41 | Sulfamethoxazole with trimethoprim | Itraconazole | Glimepiride |
| 42 | Sulfasalazine | <i>Ketamine</i> ^c | Glipizide |
| 43 | <i>Sulfonamides (unspecified)</i> ^{b,f} | Lamotrigine | Hydroxyurea |
| 44 | Sulindac | Leflunomide | Indomethacin |
| 45 | Telithromycin | Levofloxacin or ofloxacin | Irbesartan |
| 46 | Thioguanine | Lisinopril | Isotretinoin |

| # | Category A (n=48) | Category B (n=76) | Category C (n=96) |
|----|----------------------|---------------------------------|---------------------------------------|
| 47 | Ticlopidine | Lovastatin | Ketoprofen |
| 48 | Valproate | Melphalan | Labetalol |
| 49 | | Metformin | Lansoprazole or dexlansoprazole |
| 50 | | Methimazole (Thiamazole) | Lenalidomide or thalidomide |
| 51 | | Moxifloxacin | Levetiracetam |
| 52 | | Naproxen | Levocetirizine or cetirizine |
| 53 | | Nifedipine | Linezolid |
| 54 | | Olanzapine | Losartan |
| 55 | | Omeprazole or esomeprazole | Meloxicam |
| 56 | | Oxacillin | Mesalamines ^h |
| 57 | | Oxaliplatin | Methoxsalen |
| 58 | | Paroxetine | Methylphenidate or dexmethylphenidate |
| 59 | | Penicillamine | Metronidazole |
| 60 | | Phenobarbital | Mexiletine |
| 61 | | Piroxicam | Mirtazapine |
| 62 | | Propafenone | Mitomycin |
| 63 | | Quinine | Montelukast |
| 64 | | Ranitidine | <i>Nafcillin</i> ^c |
| 65 | | <i>Rivaroxaban</i> ^d | Natalizumab |
| 66 | | Rosuvastatin | Nefazodone |
| 67 | | Sertraline | Nilutamide |
| 68 | | <i>Sevoflurane</i> ^c | Norfloxacin |
| 69 | | Stavudine | Orlistat |
| 70 | | Tamoxifen | Oxaprozin |
| 71 | | Terbinafine | Pantoprazole |
| 72 | | Thiabendazole | Penicillin G |
| 73 | | Thioridazine | Phenelzine |
| 74 | | Venlafaxine or dexvenlafaxine | Pioglitazone |
| 75 | | Voriconazole | Pravastatin |
| 76 | | Zidovudine | Pregabalin |
| 77 | | | Procainamide |
| 78 | | | Prochlorperazine |
| 79 | | | Pyrimethamine |
| 80 | | | Quetiapine |
| 81 | | | Ramipril |
| 82 | | | Risperidone |
| 83 | | | Ritonavir |
| 84 | | | Rosiglitazone |
| 85 | | | Sorafenib |
| 86 | | | Temozolomide |
| 87 | | | Tolcapone |
| 88 | | | Topiramate |
| 89 | | | Trastuzumab |
| 90 | | | Trazodone |
| 91 | | | <i>Trimethoprim</i> ^b |
| 92 | | | Vancomycin |
| 93 | | | Verapamil |
| 94 | | | Vincristine |
| 95 | | | <i>Warfarin</i> ^d |
| 96 | | | Zafirlukast |

Original category as defined by Björnsson and Hoofnagle, *Hepatology* 2016;63:590-603. Medications listed in the National Institutes of Health LiverTox database were classified into categories of likelihood for causing acute liver injury based on the number of published reports of hepatotoxicity (category A, ≥50 cases; category B, 12-49 cases; category C, 4-11 cases).

^a Not evaluated because the medication was not marketed in the United States during the study period.

- ^b Not evaluated because the medication was not dispensed within the VA during the study period.
- ^c Not evaluated because the medication is administered via injection or intravenous route.
- ^d Not evaluated because the medication is an anticoagulant.
- ^e Not evaluated because the medication is used for alcohol use disorder or liver disease treatment.
- ^f Represents groups of medications.
- ^g Includes amphetamine, dextroamphetamine, lisdexamfetamine, and methamphetamine.
- ^h Includes mesalamine, balsalazide, and olsalazine.

eTable 2. List of International Classification of Diseases, Ninth Revision (ICD-9) and International Classification of Diseases, Tenth Revision (ICD-10) diagnostic codes used to identify liver/biliary disease for exclusion and censoring. Five diagnostic codes in the other unspecified hepatitis/liver disease category were not used for censoring because of the potential for clinicians to record drug-induced liver injury with these codes.

| Type of Liver/Biliary Disease | Code Type | Code | Description |
|--------------------------------|-----------|--------|--|
| Alcoholic liver disease | ICD-9 | 571.0 | Alcoholic fatty liver |
| Alcoholic liver disease | ICD-9 | 571.1 | Acute alcoholic hepatitis |
| Alcoholic liver disease | ICD-9 | 571.2 | Alcoholic cirrhosis of the liver |
| Alcoholic liver disease | ICD-9 | 571.3 | Alcoholic liver damage, unspecified |
| Alcoholic liver disease | ICD-10 | K70 | Alcoholic liver disease |
| Alcoholic liver disease | ICD-10 | K70.0 | Alcoholic fatty liver |
| Alcoholic liver disease | ICD-10 | K70.1 | Alcoholic hepatitis |
| Alcoholic liver disease | ICD-10 | K70.10 | Alcoholic hepatitis without ascites |
| Alcoholic liver disease | ICD-10 | K70.11 | Alcoholic hepatitis with ascites |
| Alcoholic liver disease | ICD-10 | K70.2 | Alcoholic fibrosis/sclerosis of the liver |
| Alcoholic liver disease | ICD-10 | K70.3 | Alcoholic cirrhosis of liver |
| Alcoholic liver disease | ICD-10 | K70.30 | Alcoholic cirrhosis of liver without ascites |
| Alcoholic liver disease | ICD-10 | K70.31 | Alcoholic cirrhosis of liver with ascites |
| Alcoholic liver disease | ICD-10 | K70.4 | Alcoholic hepatic failure |
| Alcoholic liver disease | ICD-10 | K70.40 | Alcoholic hepatic failure without coma |
| Alcoholic liver disease | ICD-10 | K70.41 | Alcoholic hepatic failure with coma |
| Alcoholic liver disease | ICD-10 | K70.9 | Alcoholic liver disease, unspecified |
| Alpha-1-antitrypsin deficiency | ICD-9 | 273.4 | Alpha-1-antitrypsin deficiency |
| Alpha-1-antitrypsin deficiency | ICD-10 | E88.01 | Alpha-1-antitrypsin deficiency |
| Autoimmune hepatitis | ICD-9 | 571.42 | Autoimmune hepatitis |
| Autoimmune hepatitis | ICD-10 | K75.4 | Autoimmune hepatitis |
| Biliary disease | ICD-9 | 574 | Cholelithiasis |
| Biliary disease | ICD-9 | 574.0 | Calculus of gallbladder with acute cholecystitis |
| Biliary disease | ICD-9 | 574.00 | Calculus of gallbladder with acute cholecystitis, without mention of obstruction |
| Biliary disease | ICD-9 | 574.01 | Calculus of gallbladder with acute cholecystitis, with obstruction |
| Biliary disease | ICD-9 | 574.1 | Calculus of gallbladder with other cholecystitis |
| Biliary disease | ICD-9 | 574.10 | Calculus of gallbladder with other cholecystitis, without mention of obstruction |
| Biliary disease | ICD-9 | 574.11 | Calculus of gallbladder with other cholecystitis, with obstruction |
| Biliary disease | ICD-9 | 574.2 | Calculus of gallbladder without mention of cholecystitis |

| Type of Liver/Biliary Disease | Code Type | Code | Description |
|-------------------------------|-----------|--------|--|
| Biliary disease | ICD-9 | 574.20 | Calculus of gallbladder without mention of cholecystitis, without mention of obstruction |
| Biliary disease | ICD-9 | 574.21 | Calculus of gallbladder without mention of cholecystitis, with obstruction |
| Biliary disease | ICD-9 | 574.3 | Calculus of bile duct with acute cholecystitis |
| Biliary disease | ICD-9 | 574.30 | Calculus of bile duct with acute cholecystitis, without mention of obstruction |
| Biliary disease | ICD-9 | 574.31 | Calculus of bile duct with acute cholecystitis, with obstruction |
| Biliary disease | ICD-9 | 574.4 | Calculus of bile duct with other cholecystitis |
| Biliary disease | ICD-9 | 574.40 | Calculus of bile duct with other cholecystitis, without mention of obstruction |
| Biliary disease | ICD-9 | 574.41 | Calculus of bile duct with other cholecystitis, with obstruction |
| Biliary disease | ICD-9 | 574.5 | Calculus of bile duct without mention of cholecystitis |
| Biliary disease | ICD-9 | 574.50 | Calculus of bile duct without mention of cholecystitis, without mention of obstruction |
| Biliary disease | ICD-9 | 574.51 | Calculus of bile duct without mention of cholecystitis, with obstruction |
| Biliary disease | ICD-9 | 574.6 | Calculus of gallbladder and bile duct with acute cholecystitis |
| Biliary disease | ICD-9 | 574.60 | Calculus of gallbladder and bile duct with acute cholecystitis, without mention of obstruction |
| Biliary disease | ICD-9 | 574.61 | Calculus of gallbladder and bile duct with acute cholecystitis, with obstruction |
| Biliary disease | ICD-9 | 574.7 | Calculus of gallbladder and bile duct with other cholecystitis |
| Biliary disease | ICD-9 | 574.70 | Calculus of gallbladder and bile duct with other cholecystitis, without mention of obstruction |
| Biliary disease | ICD-9 | 574.71 | Calculus of gallbladder and bile duct with other cholecystitis, with obstruction |
| Biliary disease | ICD-9 | 574.8 | Calculus of gallbladder and bile duct with acute and chronic cholecystitis |
| Biliary disease | ICD-9 | 574.80 | Calculus of gallbladder and bile duct with acute and chronic cholecystitis, without mention of obstruction |
| Biliary disease | ICD-9 | 574.81 | Calculus of gallbladder and bile duct with acute and chronic cholecystitis, with obstruction |
| Biliary disease | ICD-9 | 574.9 | Calculus of gallbladder and bile duct without cholecystitis |
| Biliary disease | ICD-9 | 574.90 | Calculus of gallbladder and bile duct without cholecystitis, without mention of obstruction |
| Biliary disease | ICD-9 | 574.91 | Calculus of gallbladder and bile duct without cholecystitis, with obstruction |
| Biliary disease | ICD-9 | 575 | Other disorders of gallbladder |
| Biliary disease | ICD-9 | 575.0 | Acute cholecystitis |
| Biliary disease | ICD-9 | 575.1 | Other cholecystitis |
| Biliary disease | ICD-9 | 575.10 | Cholecystitis, unspecified |
| Biliary disease | ICD-9 | 575.11 | Chronic cholecystitis |
| Biliary disease | ICD-9 | 575.12 | Acute and chronic cholecystitis |
| Biliary disease | ICD-9 | 575.2 | Obstruction of gallbladder |
| Biliary disease | ICD-9 | 575.3 | Hydrops of gallbladder |
| Biliary disease | ICD-9 | 575.4 | Perforation of gallbladder |
| Biliary disease | ICD-9 | 575.5 | Fistula of gallbladder |

| Type of Liver/Biliary Disease | Code Type | Code | Description |
|-------------------------------|-----------|--------|--|
| Biliary disease | ICD-9 | 575.9 | Unspecified disorder of gallbladder |
| Biliary disease | ICD-9 | 576.1 | Cholangitis |
| Biliary disease | ICD-9 | 576.2 | Obstruction of bile duct |
| Biliary disease | ICD-9 | 576.3 | Perforation of bile duct |
| Biliary disease | ICD-9 | 576.4 | Fistula of bile duct |
| Biliary disease | ICD-9 | 576.9 | Unspecified disorder of biliary tract |
| Biliary disease | ICD-9 | 575.8 | Other specified disorders of gallbladder |
| Biliary disease | ICD-9 | 576.8 | Other specified disorders of biliary tract |
| Biliary disease | ICD-10 | K80 | Cholelithiasis |
| Biliary disease | ICD-10 | K80.0 | Calculus of gallbladder with acute cholecystitis |
| Biliary disease | ICD-10 | K80.00 | Calculus of gallbladder with acute cholecystitis without obstruction |
| Biliary disease | ICD-10 | K80.01 | Calculus of gallbladder with acute cholecystitis with obstruction |
| Biliary disease | ICD-10 | K80.1 | Calculus of gallbladder with other cholecystitis |
| Biliary disease | ICD-10 | K80.10 | Calculus of gallbladder with chronic cholecystitis without obstruction |
| Biliary disease | ICD-10 | K80.11 | Calculus of gallbladder with chronic cholecystitis with obstruction |
| Biliary disease | ICD-10 | K80.12 | Calculus of gallbladder with acute and chronic cholecystitis without obstruction |
| Biliary disease | ICD-10 | K80.13 | Calculus of gallbladder with acute and chronic cholecystitis with obstruction |
| Biliary disease | ICD-10 | K80.18 | Calculus of gallbladder with other cholecystitis without obstruction |
| Biliary disease | ICD-10 | K80.19 | Calculus of gallbladder with other cholecystitis with obstruction |
| Biliary disease | ICD-10 | K80.2 | Calculus of gallbladder without cholecystitis |
| Biliary disease | ICD-10 | K80.20 | Calculus of gallbladder without cholecystitis without obstruction |
| Biliary disease | ICD-10 | K80.21 | Calculus of gallbladder without cholecystitis with obstruction |
| Biliary disease | ICD-10 | K80.3 | Calculus of bile duct with cholangitis |
| Biliary disease | ICD-10 | K80.30 | Calculus of bile duct with cholangitis unspecified, without obstruction |
| Biliary disease | ICD-10 | K80.31 | Calculus of bile duct with cholangitis unspecified, with obstruction |
| Biliary disease | ICD-10 | K80.32 | Calculus of bile duct with acute cholangitis without obstruction |
| Biliary disease | ICD-10 | K80.33 | Calculus of bile duct with acute cholangitis with obstruction |
| Biliary disease | ICD-10 | K80.34 | Calculus of bile duct with chronic cholangitis without obstruction |
| Biliary disease | ICD-10 | K80.35 | Calculus of bile duct with chronic cholangitis with obstruction |
| Biliary disease | ICD-10 | K80.36 | Calculus of bile duct with acute and chronic cholangitis without obstruction |
| Biliary disease | ICD-10 | K80.37 | Calculus of bile duct with acute and chronic cholangitis with obstruction |
| Biliary disease | ICD-10 | K80.4 | Calculus of bile duct with cholecystitis |
| Biliary disease | ICD-10 | K80.40 | Calculus of bile duct with cholecystitis unspecified, without obstruction |
| Biliary disease | ICD-10 | K80.41 | Calculus of bile duct with cholecystitis unspecified, with obstruction |

| Type of Liver/Biliary Disease | Code Type | Code | Description |
|-------------------------------|-----------|--------|--|
| Biliary disease | ICD-10 | K80.42 | Calculus of bile duct with acute cholecystitis without obstruction |
| Biliary disease | ICD-10 | K80.43 | Calculus of bile duct with acute cholecystitis with obstruction |
| Biliary disease | ICD-10 | K80.44 | Calculus of bile duct with chronic cholecystitis without obstruction |
| Biliary disease | ICD-10 | K80.45 | Calculus of bile duct with chronic cholecystitis with obstruction |
| Biliary disease | ICD-10 | K80.46 | Calculus of bile duct with acute and chronic cholecystitis without obstruction |
| Biliary disease | ICD-10 | K80.47 | Calculus of bile duct with acute and chronic cholecystitis with obstruction |
| Biliary disease | ICD-10 | K80.5 | Calculus of bile duct without cholangitis or cholecystitis |
| Biliary disease | ICD-10 | K80.50 | Calculus of bile duct without cholangitis or cholecystitis without obstruction |
| Biliary disease | ICD-10 | K80.51 | Calculus of bile duct without cholangitis or cholecystitis with obstruction |
| Biliary disease | ICD-10 | K80.6 | Calculus of gallbladder and bile duct with cholecystitis |
| Biliary disease | ICD-10 | K80.60 | Calculus of gallbladder and bile duct with cholecystitis unspecified, without obstruction |
| Biliary disease | ICD-10 | K80.61 | Calculus of gallbladder and bile duct with cholecystitis unspecified, with obstruction |
| Biliary disease | ICD-10 | K80.62 | Calculus of gallbladder and bile duct with acute cholecystitis without obstruction |
| Biliary disease | ICD-10 | K80.63 | Calculus of gallbladder and bile duct with acute cholecystitis with obstruction |
| Biliary disease | ICD-10 | K80.64 | Calculus of gallbladder and bile duct with chronic cholecystitis without obstruction |
| Biliary disease | ICD-10 | K80.65 | Calculus of gallbladder and bile duct with chronic cholecystitis with obstruction |
| Biliary disease | ICD-10 | K80.66 | Calculus of gallbladder and bile duct with acute and chronic cholecystitis without obstruction |
| Biliary disease | ICD-10 | K80.67 | Calculus of gallbladder and bile duct with acute and chronic cholecystitis with obstruction |
| Biliary disease | ICD-10 | K80.7 | Calculus of gallbladder and bile duct without cholecystitis |
| Biliary disease | ICD-10 | K80.70 | Calculus of gallbladder and bile duct without cholecystitis without obstruction |
| Biliary disease | ICD-10 | K80.71 | Calculus of gallbladder and bile duct without cholecystitis with obstruction |
| Biliary disease | ICD-10 | K80.8 | Other cholelithiasis |
| Biliary disease | ICD-10 | K80.80 | Other cholelithiasis without obstruction |
| Biliary disease | ICD-10 | K80.81 | Other cholelithiasis with obstruction |
| Biliary disease | ICD-10 | K81 | Cholecystitis |
| Biliary disease | ICD-10 | K81.0 | Acute cholecystitis |
| Biliary disease | ICD-10 | K81.1 | Chronic cholecystitis |
| Biliary disease | ICD-10 | K81.2 | Acute cholecystitis with chronic cholecystitis |
| Biliary disease | ICD-10 | K81.9 | Cholecystitis, unspecified |
| Biliary disease | ICD-10 | K82 | Other diseases of gallbladder |
| Biliary disease | ICD-10 | K82.0 | Obstruction of gallbladder |
| Biliary disease | ICD-10 | K82.1 | Hydrops of gallbladder |
| Biliary disease | ICD-10 | K82.2 | Perforation of gallbladder |

| Type of Liver/Biliary Disease | Code Type | Code | Description |
|-------------------------------------|-----------|--------|--|
| Biliary disease | ICD-10 | K82.3 | Fistula of gallbladder |
| Biliary disease | ICD-10 | K82.8 | Other specified diseases of gallbladder |
| Biliary disease | ICD-10 | K82.9 | Disease of gallbladder, unspecified |
| Biliary disease | ICD-10 | K82.A | Disorders of gallbladder in diseases classified elsewhere |
| Biliary disease | ICD-10 | K82.A1 | Gangrene of gallbladder in cholecystitis |
| Biliary disease | ICD-10 | K82.A2 | Perforation of gallbladder in cholecystitis |
| Biliary disease | ICD-10 | K83.0 | Cholangitis |
| Biliary disease | ICD-10 | K83.09 | Other cholangitis |
| Biliary disease | ICD-10 | K83.1 | Obstruction of bile duct |
| Biliary disease | ICD-10 | K83.2 | Perforation of bile duct |
| Biliary disease | ICD-10 | K83.3 | Fistula of bile duct |
| Biliary disease | ICD-10 | K83.5 | Biliary cyst |
| Biliary disease | ICD-10 | K83.8 | Other specified diseases of biliary tract |
| Biliary disease | ICD-10 | K83.9 | Disease of biliary tract, unspecified |
| Biliary disease | ICD-10 | K87 | Disorders of gallbladder, biliary tract and pancreas in diseases classified elsewhere |
| Cancer in the liver or biliary tree | ICD-9 | 155 | Malignant neoplasm of liver and intrahepatic bile ducts |
| Cancer in the liver or biliary tree | ICD-9 | 155.0 | Malignant neoplasm of liver, primary |
| Cancer in the liver or biliary tree | ICD-9 | 155.1 | Malignant neoplasm of intrahepatic bile ducts |
| Cancer in the liver or biliary tree | ICD-9 | 155.2 | Malignant neoplasm liver, not specified as primary or secondary |
| Cancer in the liver or biliary tree | ICD-9 | 156 | Malignant neoplasm of gallbladder and extrahepatic bile ducts |
| Cancer in the liver or biliary tree | ICD-9 | 156.0 | Malignant neoplasm of gallbladder |
| Cancer in the liver or biliary tree | ICD-9 | 156.1 | Malignant neoplasm of extrahepatic bile ducts |
| Cancer in the liver or biliary tree | ICD-9 | 156.2 | Malignant neoplasm of ampulla of Vater |
| Cancer in the liver or biliary tree | ICD-9 | 156.8 | Malignant neoplasm of other specified sites of gallbladder and extrahepatic bile ducts |
| Cancer in the liver or biliary tree | ICD-9 | 156.9 | Malignant neoplasm of biliary tract, part unspecified site |
| Cancer in the liver or biliary tree | ICD-9 | 197.7 | Malignant neoplasm of liver, secondary |
| Cancer in the liver or biliary tree | ICD-9 | 209.72 | Secondary neuroendocrine tumor of liver |
| Cancer in the liver or biliary tree | ICD-9 | 230.8 | Carcinoma in situ of liver and biliary system |
| Cancer in the liver or biliary tree | ICD-10 | C22 | Malignant neoplasm of liver and intrahepatic bile ducts |
| Cancer in the liver or biliary tree | ICD-10 | C22.0 | Liver cell carcinoma |
| Cancer in the liver or biliary tree | ICD-10 | C22.1 | Intrahepatic bile duct carcinoma |
| Cancer in the liver or biliary tree | ICD-10 | C22.2 | Hepatoblastoma |
| Cancer in the liver or biliary tree | ICD-10 | C22.3 | Angiosarcoma of liver |
| Cancer in the liver or biliary tree | ICD-10 | C22.4 | Other sarcomas of liver |

| Type of Liver/Biliary Disease | Code Type | Code | Description |
|--|-----------|--------|--|
| Cancer in the liver or biliary tree | ICD-10 | C22.7 | Other specified carcinomas of liver |
| Cancer in the liver or biliary tree | ICD-10 | C22.8 | Malignant neoplasm of liver, primary, unspecified as to type |
| Cancer in the liver or biliary tree | ICD-10 | C22.9 | Malignant neoplasm liver not specified as primary/secondary |
| Cancer in the liver or biliary tree | ICD-10 | C23 | Malignant neoplasm of gallbladder |
| Cancer in the liver or biliary tree | ICD-10 | C24 | Malignant neoplasm of other and unspecified parts of biliary tract |
| Cancer in the liver or biliary tree | ICD-10 | C24.0 | Malignant neoplasm of extrahepatic bile duct |
| Cancer in the liver or biliary tree | ICD-10 | C24.1 | Malignant neoplasm of ampulla of Vater |
| Cancer in the liver or biliary tree | ICD-10 | C24.8 | Malignant neoplasm of overlapping sites of biliary tract |
| Cancer in the liver or biliary tree | ICD-10 | C24.9 | Malignant neoplasm of biliary tract, unspecified |
| Cancer in the liver or biliary tree | ICD-10 | C78.7 | Secondary malignant neoplasm of liver and intrahepatic bile duct |
| Cancer in the liver or biliary tree | ICD-10 | C7B.02 | Secondary carcinoid tumors of liver |
| Cancer in the liver or biliary tree | ICD-10 | D01.5 | Carcinoma in situ of liver, gallbladder and bile ducts |
| Cirrhosis (compensated or decompensated) | ICD-9 | 456.0 | Esophageal varices with bleeding |
| Cirrhosis (compensated or decompensated) | ICD-9 | 456.1 | Esophageal varices without bleeding |
| Cirrhosis (compensated or decompensated) | ICD-9 | 456.2 | Esophageal varices in diseases classified elsewhere |
| Cirrhosis (compensated or decompensated) | ICD-9 | 456.20 | Esophageal varices in diseases classified elsewhere with bleeding |
| Cirrhosis (compensated or decompensated) | ICD-9 | 456.21 | Esophageal varices in diseases classified elsewhere without bleeding |
| Cirrhosis (compensated or decompensated) | ICD-9 | 567.23 | Spontaneous bacterial peritonitis |
| Cirrhosis (compensated or decompensated) | ICD-9 | 571.5 | Cirrhosis of liver without mention of alcohol |
| Cirrhosis (compensated or decompensated) | ICD-9 | 572.2 | Hepatic encephalopathy |
| Cirrhosis (compensated or decompensated) | ICD-9 | 572.3 | Portal hypertension |
| Cirrhosis (compensated or decompensated) | ICD-9 | 572.4 | Hepatorenal syndrome |
| Cirrhosis (compensated or decompensated) | ICD-9 | 789.5 | Ascites |
| Cirrhosis (compensated or decompensated) | ICD-9 | 789.59 | Other ascites |
| Cirrhosis (compensated or decompensated) | ICD-10 | I85 | Esophageal varices |
| Cirrhosis (compensated or decompensated) | ICD-10 | I85.0 | Esophageal varices |
| Cirrhosis (compensated or decompensated) | ICD-10 | I85.00 | Esophageal varices without bleeding |
| Cirrhosis (compensated or decompensated) | ICD-10 | I85.01 | Esophageal varices with bleeding |
| Cirrhosis (compensated or decompensated) | ICD-10 | I85.1 | Secondary esophageal varices |
| Cirrhosis (compensated or decompensated) | ICD-10 | I85.10 | Secondary esophageal varices without bleeding |
| Cirrhosis (compensated or decompensated) | ICD-10 | I85.11 | Secondary esophageal varices with bleeding |
| Cirrhosis (compensated or decompensated) | ICD-10 | K65.2 | Spontaneous bacterial peritonitis |
| Cirrhosis (compensated or decompensated) | ICD-10 | K71.51 | Toxic liver disease with chronic active hepatitis with ascites |
| Cirrhosis (compensated or decompensated) | ICD-10 | K72.1 | Chronic hepatic failure |

| Type of Liver/Biliary Disease | Code Type | Code | Description |
|--|-----------|---------|---|
| Cirrhosis (compensated or decompensated) | ICD-10 | K72.10 | Chronic hepatic failure without coma |
| Cirrhosis (compensated or decompensated) | ICD-10 | K72.11 | Chronic hepatic failure with coma |
| Cirrhosis (compensated or decompensated) | ICD-10 | K72.9 | Hepatic failure, unspecified |
| Cirrhosis (compensated or decompensated) | ICD-10 | K72.90 | Hepatic failure, unspecified without coma |
| Cirrhosis (compensated or decompensated) | ICD-10 | K72.91 | Hepatic failure, unspecified with coma |
| Cirrhosis (compensated or decompensated) | ICD-10 | K74.1 | Hepatic sclerosis |
| Cirrhosis (compensated or decompensated) | ICD-10 | K74.2 | Hepatic fibrosis with hepatic sclerosis |
| Cirrhosis (compensated or decompensated) | ICD-10 | K74.60 | Unspecified cirrhosis of liver |
| Cirrhosis (compensated or decompensated) | ICD-10 | K76.7 | Hepatorenal syndrome |
| Cirrhosis (compensated or decompensated) | ICD-10 | K76.81 | Hepatopulmonary syndrome |
| Cirrhosis (compensated or decompensated) | ICD-10 | R18.8 | Other ascites |
| Congestive hepatopathy | ICD-9 | 573.0 | Chronic passive congestion of the liver |
| Congestive hepatopathy | ICD-10 | K76.1 | Chronic passive congestion of the liver |
| Hemochromatosis | ICD-9 | 275.01 | Hereditary hemochromatosis |
| Hemochromatosis | ICD-9 | 275.02 | Hemochromatosis due to repeated red blood cell transfusions |
| Hemochromatosis | ICD-9 | 275.03 | Other hemochromatosis |
| Hemochromatosis | ICD-10 | E83.110 | Hereditary hemochromatosis |
| Hepatitis A | ICD-9 | 070.0 | Viral hepatitis A with hepatic coma |
| Hepatitis A | ICD-9 | 070.1 | Viral hepatitis A without mention of hepatic coma |
| Hepatitis A | ICD-10 | B15 | Acute hepatitis A |
| Hepatitis A | ICD-10 | B15.0 | Hepatitis A with hepatic coma |
| Hepatitis A | ICD-10 | B15.9 | Hepatitis A without hepatic coma |
| Hepatitis B | ICD-9 | 070.2 | Viral hepatitis B with hepatic coma |
| Hepatitis B | ICD-9 | 070.20 | Viral hepatitis B with hepatic coma, acute or unspecified, without mention of hepatitis delta |
| Hepatitis B | ICD-9 | 070.22 | Chronic viral hepatitis B with hepatic coma without mention of hepatitis delta |
| Hepatitis B | ICD-9 | 070.3 | Viral hepatitis B without mention of hepatic coma |
| Hepatitis B | ICD-9 | 070.30 | Viral hepatitis B without mention of hepatic coma, acute or unspecified, without mention of hepatitis delta |
| Hepatitis B | ICD-9 | 070.32 | Chronic viral hepatitis B without mention of hepatic coma without mention of hepatitis delta |
| Hepatitis B | ICD-9 | V02.61 | Hepatitis B Carrier |
| Hepatitis B | ICD-10 | B16 | Acute hepatitis B |
| Hepatitis B | ICD-10 | B16.2 | Acute hepatitis B without delta-agent with hepatic coma |
| Hepatitis B | ICD-10 | B16.9 | Acute hepatitis B without delta-agent and without hepatic coma |
| Hepatitis B | ICD-10 | B18.1 | Chronic viral hepatitis B without delta-agent |

| Type of Liver/Biliary Disease | Code Type | Code | Description |
|--|-----------|--------|---|
| Hepatitis B | ICD-10 | B19.1 | Unspecified viral hepatitis B |
| Hepatitis B | ICD-10 | B19.10 | Unspecified viral hepatitis B without hepatic coma |
| Hepatitis B | ICD-10 | B19.11 | Unspecified viral hepatitis B with hepatic coma |
| Hepatitis B and D | ICD-9 | 070.21 | Viral hepatitis B with hepatic coma, acute or unspecified, with hepatitis delta |
| Hepatitis B and D | ICD-9 | 070.23 | Chronic viral hepatitis B with hepatic coma with hepatitis delta |
| Hepatitis B and D | ICD-9 | 070.31 | Viral hepatitis B without mention of hepatic coma, acute or unspecified, with hepatitis delta |
| Hepatitis B and D | ICD-9 | 070.33 | Chronic viral hepatitis B without mention of hepatic coma with mention of hepatitis delta |
| Hepatitis B and D | ICD-9 | 070.42 | Hepatitis delta without mention of active hepatitis B disease with hepatic coma |
| Hepatitis B and D | ICD-9 | 070.52 | Hepatitis delta without mention of active hepatitis B disease or hepatic coma |
| Hepatitis B and D | ICD-10 | B16.0 | Acute hepatitis B with delta-agent with hepatic coma |
| Hepatitis B and D | ICD-10 | B16.1 | Acute hepatitis B with delta-agent without hepatic coma |
| Hepatitis B and D | ICD-10 | B17.0 | Acute delta-(super) infection of hepatitis B carrier |
| Hepatitis B and D | ICD-10 | B18.0 | Chronic viral hepatitis B with delta-agent |
| Hepatitis C | ICD-9 | 070.41 | Acute hepatitis C with hepatic coma |
| Hepatitis C | ICD-9 | 070.44 | Chronic hepatitis C with hepatic coma |
| Hepatitis C | ICD-9 | 070.51 | Acute hepatitis C without mention of hepatic coma |
| Hepatitis C | ICD-9 | 070.54 | Chronic hepatitis C without mention of hepatic coma |
| Hepatitis C | ICD-9 | 070.7 | Unspecified viral hepatitis C |
| Hepatitis C | ICD-9 | 070.70 | Unspecified viral hepatitis C without hepatic coma |
| Hepatitis C | ICD-9 | 070.71 | Unspecified viral hepatitis C with hepatic coma |
| Hepatitis C | ICD-9 | V02.62 | Hepatitis C carrier |
| Hepatitis C | ICD-10 | B17.1 | Acute hepatitis C |
| Hepatitis C | ICD-10 | B17.10 | Acute hepatitis C without hepatic coma |
| Hepatitis C | ICD-10 | B17.11 | Acute hepatitis C with hepatic coma |
| Hepatitis C | ICD-10 | B18.2 | Chronic viral hepatitis C |
| Hepatitis C | ICD-10 | B19.2 | Unspecified viral hepatitis C |
| Hepatitis C | ICD-10 | B19.20 | Unspecified viral hepatitis C without hepatic coma |
| Hepatitis C | ICD-10 | B19.21 | Unspecified viral hepatitis C with hepatic coma |
| Hepatitis E | ICD-9 | 070.43 | Hepatitis E with hepatic coma |
| Hepatitis E | ICD-9 | 070.53 | Hepatitis E without mention of hepatic coma |
| Hepatitis E | ICD-10 | B17.2 | Acute hepatitis E |
| Metabolic dysfunction-associated steatotic liver disease | ICD-9 | 571.8 | Other chronic non-alcoholic liver disease |

| Type of Liver/Biliary Disease | Code Type | Code | Description |
|--|-----------|---------|---|
| Metabolic dysfunction-associated steatotic liver disease | ICD-9 | 571.9 | Unspecified chronic liver disease without mention of alcohol |
| Metabolic dysfunction-associated steatotic liver disease | ICD-10 | K76.0 | Fatty change of liver, not elsewhere classified |
| Other acute or unspecified viral hepatitis | ICD-9 | 070 | Viral hepatitis |
| Other acute or unspecified viral hepatitis | ICD-9 | 070.4 | Other specified viral hepatitis with hepatic coma |
| Other acute or unspecified viral hepatitis | ICD-9 | 070.49 | Other specified viral hepatitis with hepatic coma |
| Other acute or unspecified viral hepatitis | ICD-9 | 070.5 | Other specified viral hepatitis without mention of hepatic coma |
| Other acute or unspecified viral hepatitis | ICD-9 | 070.59 | Other specified viral hepatitis without mention of hepatic coma |
| Other acute or unspecified viral hepatitis | ICD-9 | 070.6 | Unspecified viral hepatitis with hepatic coma |
| Other acute or unspecified viral hepatitis | ICD-9 | 070.9 | Unspecified viral hepatitis without mention of hepatic coma |
| Other acute or unspecified viral hepatitis | ICD-9 | 072.71 | Mumps hepatitis |
| Other acute or unspecified viral hepatitis | ICD-9 | 573.1 | Hepatitis in viral diseases classified elsewhere |
| Other acute or unspecified viral hepatitis | ICD-9 | V02.69 | Other viral hepatitis carrier |
| Other acute or unspecified viral hepatitis | ICD-10 | B00.81 | Herpesviral hepatitis |
| Other acute or unspecified viral hepatitis | ICD-10 | B17 | Other acute viral hepatitis |
| Other acute or unspecified viral hepatitis | ICD-10 | B17.8 | Other specified acute viral hepatitis |
| Other acute or unspecified viral hepatitis | ICD-10 | B17.9 | Acute viral hepatitis, unspecified |
| Other acute or unspecified viral hepatitis | ICD-10 | B18 | Chronic viral hepatitis |
| Other acute or unspecified viral hepatitis | ICD-10 | B18.8 | Other chronic viral hepatitis |
| Other acute or unspecified viral hepatitis | ICD-10 | B18.9 | Chronic viral hepatitis, unspecified |
| Other acute or unspecified viral hepatitis | ICD-10 | B19 | Unspecified viral hepatitis |
| Other acute or unspecified viral hepatitis | ICD-10 | B19.0 | Unspecified viral hepatitis with hepatic coma |
| Other acute or unspecified viral hepatitis | ICD-10 | B19.9 | Unspecified viral hepatitis without hepatic coma |
| Other acute or unspecified viral hepatitis | ICD-10 | B25.1 | Cytomegaloviral hepatitis |
| Other acute or unspecified viral hepatitis | ICD-10 | B26.81 | Mumps hepatitis |
| Other acute or unspecified viral hepatitis | ICD-10 | B94.2 | Sequelae of viral hepatitis |
| Other acute or unspecified viral hepatitis | ICD-10 | O98.4 | Viral hepatitis complicating pregnancy, childbirth and the puerperium |
| Other acute or unspecified viral hepatitis | ICD-10 | O98.41 | Viral hepatitis complicating pregnancy |
| Other acute or unspecified viral hepatitis | ICD-10 | O98.411 | Viral hepatitis complicating pregnancy, first trimester |
| Other acute or unspecified viral hepatitis | ICD-10 | O98.412 | Viral hepatitis complicating pregnancy, second trimester |
| Other acute or unspecified viral hepatitis | ICD-10 | O98.413 | Viral hepatitis complicating pregnancy, third trimester |
| Other acute or unspecified viral hepatitis | ICD-10 | O98.419 | Viral hepatitis complicating pregnancy, unspecified trimester |
| Other acute or unspecified viral hepatitis | ICD-10 | O98.42 | Viral hepatitis complicating childbirth |
| Other acute or unspecified viral hepatitis | ICD-10 | O98.43 | Viral hepatitis complicating the puerperium |

| Type of Liver/Biliary Disease | Code Type | Code | Description |
|--|-----------|---------------------|---|
| Other acute or unspecified viral hepatitis | ICD-10 | P35.3 | Congenital viral hepatitis |
| Other unspecified hepatitis/liver disease | ICD-9 | 091.62 | Secondary syphilitic hepatitis |
| Other unspecified hepatitis/liver disease | ICD-9 | 130.5 | Hepatitis due to toxoplasmosis |
| Other unspecified hepatitis/liver disease | ICD-9 | 571 | Chronic liver disease and cirrhosis |
| Other unspecified hepatitis/liver disease | ICD-9 | 571.4 | Chronic hepatitis |
| Other unspecified hepatitis/liver disease | ICD-9 | 571.40 | Chronic hepatitis, unspecified |
| Other unspecified hepatitis/liver disease | ICD-9 | 571.41 | Chronic persistent hepatitis |
| Other unspecified hepatitis/liver disease | ICD-9 | 571.49 | Other chronic hepatitis |
| Other unspecified hepatitis/liver disease | ICD-9 | 573.2 | Hepatitis in other infectious diseases classified elsewhere |
| Other unspecified hepatitis/liver disease | ICD-9 | 573.3 ^a | Hepatitis, unspecified |
| Other unspecified hepatitis/liver disease | ICD-9 | 573.4 | Hepatic infarction |
| Other unspecified hepatitis/liver disease | ICD-9 | 573.8 ^a | Other specified disorder of liver |
| Other unspecified hepatitis/liver disease | ICD-9 | 573.9 ^a | Unspecified disorder of liver |
| Other unspecified hepatitis/liver disease | ICD-10 | A51.45 | Secondary syphilitic hepatitis |
| Other unspecified hepatitis/liver disease | ICD-10 | B58.1 | Toxoplasma hepatitis |
| Other unspecified hepatitis/liver disease | ICD-10 | K73 | Chronic hepatitis, not elsewhere classified |
| Other unspecified hepatitis/liver disease | ICD-10 | K73.0 | Chronic persistent hepatitis, not elsewhere classified |
| Other unspecified hepatitis/liver disease | ICD-10 | K73.1 | Chronic lobular hepatitis, not elsewhere classified |
| Other unspecified hepatitis/liver disease | ICD-10 | K73.2 | Chronic active hepatitis, not elsewhere classified |
| Other unspecified hepatitis/liver disease | ICD-10 | K73.8 | Other chronic hepatitis, not elsewhere classified |
| Other unspecified hepatitis/liver disease | ICD-10 | K73.9 | Chronic hepatitis, unspecified |
| Other unspecified hepatitis/liver disease | ICD-10 | K76.89 ^a | Other specified diseases of liver |
| Other unspecified hepatitis/liver disease | ICD-10 | K76.9 ^a | Liver disease, unspecified |
| Primary sclerosing cholangitis | ICD-10 | K83.01 | Primary sclerosing cholangitis |
| Primary/secondary biliary cirrhosis | ICD-9 | 571.6 | Biliary cirrhosis |
| Primary/secondary biliary cirrhosis | ICD-10 | K74.3 | Primary biliary cirrhosis |
| Primary/secondary biliary cirrhosis | ICD-10 | K74.4 | Secondary biliary cirrhosis |
| Primary/secondary biliary cirrhosis | ICD-10 | K74.5 | Biliary cirrhosis, unspecified |
| Wilson's disease | ICD-9 | 275.1 | Disorders of copper metabolism |
| Wilson's disease | ICD-10 | E83.01 | Wilson's disease |

Abbreviations: ICD-9=International Classification of Diseases, Ninth Revision; ICD-10=International Classification of Diseases, Tenth Revision

^a Diagnostic code was not used for censoring because of the potential for clinicians to record drug-induced liver injury.

eTable 3. List of International Classification of Diseases, Ninth Revision (ICD-9) and International Classification of Diseases, Tenth Revision (ICD-10) diagnostic codes used to identify certain conditions that could precipitate findings consistent with severe acute liver injury for exclusion and censoring.

| Type of Non-Drug-Related Condition | Code Type | Code | Description |
|------------------------------------|-----------|--------|--|
| Acquired hemolytic anemia | ICD-9 | 283.1 | Non-autoimmune hemolytic anemia |
| Acquired hemolytic anemia | ICD-9 | 283.10 | Non-autoimmune hemolytic anemia, unspecified |
| Acquired hemolytic anemia | ICD-9 | 283.11 | Hemolytic uremic syndrome |
| Acquired hemolytic anemia | ICD-9 | 283.19 | Other non-autoimmune hemolytic anemias |
| Acquired hemolytic anemia | ICD-9 | 283.2 | Hemoglobinuria due to hemolysis from external causes |
| Acquired hemolytic anemia | ICD-9 | 283.9 | Acquired hemolytic anemia, unspecified |
| Acquired hemolytic anemia | ICD-10 | D59.1 | Other autoimmune hemolytic anemias |
| Acquired hemolytic anemia | ICD-10 | D59.10 | Autoimmune hemolytic anemia, unspecified |
| Acquired hemolytic anemia | ICD-10 | D59.11 | Warm autoimmune hemolytic anemia |
| Acquired hemolytic anemia | ICD-10 | D59.12 | Cold autoimmune hemolytic anemia |
| Acquired hemolytic anemia | ICD-10 | D59.13 | Mixed type autoimmune hemolytic anemia |
| Acquired hemolytic anemia | ICD-10 | D59.19 | Other autoimmune hemolytic anemia |
| Acquired hemolytic anemia | ICD-10 | D59.3 | Hemolytic-uremic syndrome |
| Acquired hemolytic anemia | ICD-10 | D59.30 | Hemolytic-uremic syndrome, unspecified |
| Acquired hemolytic anemia | ICD-10 | D59.31 | Infection-associated hemolytic-uremic syndrome |
| Acquired hemolytic anemia | ICD-10 | D59.32 | Hereditary hemolytic-uremic syndrome |
| Acquired hemolytic anemia | ICD-10 | D59.39 | Other hemolytic-uremic syndrome |
| Acquired hemolytic anemia | ICD-10 | D59.4 | Other nonautoimmune hemolytic anemias |
| Acquired hemolytic anemia | ICD-10 | D59.5 | Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli] |
| Acquired hemolytic anemia | ICD-10 | D59.6 | Hemoglobinuria due to hemolysis from other external causes |
| Acquired hemolytic anemia | ICD-10 | D59.8 | Other acquired hemolytic anemias |
| Acquired hemolytic anemia | ICD-10 | D59.9 | Acquired hemolytic anemia, unspecified |
| Alcohol dependence | ICD-9 | 291.1 | Alcohol-induced persisting amnesic disorder |
| Alcohol dependence | ICD-9 | 291.2 | Alcohol-induced persisting dementia |
| Alcohol dependence | ICD-9 | 291.3 | Alcohol-induced psychotic disorder with hallucinations |
| Alcohol dependence | ICD-9 | 291.5 | Alcohol-induced psychotic disorder with delusions |
| Alcohol dependence | ICD-9 | 291.82 | Alcohol induced sleep disorders |
| Alcohol dependence | ICD-9 | 291.89 | Other alcohol-induced mental disorders |
| Alcohol dependence | ICD-9 | 291.9 | Unspecified alcohol-induced mental disorders |
| Alcohol dependence | ICD-9 | 303.00 | Acute alcoholic intoxication in alcoholism, unspecified |
| Alcohol dependence | ICD-9 | 303.01 | Acute alcoholic intoxication in alcoholism, continuous |
| Alcohol dependence | ICD-9 | 303.02 | Acute alcoholic intoxication in alcoholism, episodic |

| Type of Non-Drug-Related Condition | Code Type | Code | Description |
|--|-----------|---------|--|
| Alcohol dependence | ICD-9 | 303.90 | Other and unspecified alcohol dependence, unspecified |
| Alcohol dependence | ICD-9 | 303.91 | Other and unspecified alcohol dependence, continuous |
| Alcohol dependence | ICD-9 | 303.92 | Other and unspecified alcohol dependence, episodic |
| Alcohol dependence | ICD-10 | F10.20 | Alcohol dependence, uncomplicated |
| Alcohol dependence | ICD-10 | F10.22 | Alcohol dependence with intoxication |
| Alcohol dependence | ICD-10 | F10.220 | Alcohol dependence with intoxication, uncomplicated |
| Alcohol dependence | ICD-10 | F10.221 | Alcohol dependence with intoxication delirium |
| Alcohol dependence | ICD-10 | F10.229 | Alcohol dependence with intoxication, unspecified |
| Alcohol dependence | ICD-10 | F10.24 | Alcohol dependence with alcohol-induced mood disorder |
| Alcohol dependence | ICD-10 | F10.25 | Alcohol dependence with alcohol-induced psychotic disorder |
| Alcohol dependence | ICD-10 | F10.250 | Alcohol dependence with alcohol-induced psychotic disorder with delusions |
| Alcohol dependence | ICD-10 | F10.251 | Alcohol dependence with alcohol-induced psychotic disorder with hallucinations |
| Alcohol dependence | ICD-10 | F10.259 | Alcohol dependence with alcohol-induced psychotic disorder, unspecified |
| Alcohol dependence | ICD-10 | F10.26 | Alcohol dependence with alcohol-induced persisting amnesic disorder |
| Alcohol dependence | ICD-10 | F10.27 | Alcohol dependence with alcohol-induced persisting dementia |
| Alcohol dependence | ICD-10 | F10.28 | Alcohol dependence with other alcohol-induced disorders |
| Alcohol dependence | ICD-10 | F10.280 | Alcohol dependence with alcohol-induced anxiety disorder |
| Alcohol dependence | ICD-10 | F10.281 | Alcohol dependence with alcohol-induced sexual dysfunction |
| Alcohol dependence | ICD-10 | F10.282 | Alcohol dependence with alcohol-induced sleep disorder |
| Alcohol dependence | ICD-10 | F10.288 | Alcohol dependence with other alcohol-induced disorder |
| Alcohol dependence | ICD-10 | F10.29 | Alcohol dependence with unspecified alcohol-induced disorder |
| Alcohol withdrawal with abuse/dependence | ICD-9 | 291.0 | Alcohol withdrawal delirium |
| Alcohol withdrawal with abuse/dependence | ICD-9 | 291.81 | Alcohol withdrawal |
| Alcohol withdrawal with abuse/dependence | ICD-10 | F10.13 | Alcohol abuse with withdrawal |
| Alcohol withdrawal with abuse/dependence | ICD-10 | F10.130 | Alcohol abuse with withdrawal, uncomplicated |
| Alcohol withdrawal with abuse/dependence | ICD-10 | F10.131 | Alcohol abuse with withdrawal delirium |
| Alcohol withdrawal with abuse/dependence | ICD-10 | F10.132 | Alcohol abuse with withdrawal with perceptual disturbance |
| Alcohol withdrawal with abuse/dependence | ICD-10 | F10.139 | Alcohol abuse with withdrawal, unspecified |
| Alcohol withdrawal with abuse/dependence | ICD-10 | F10.23 | Alcohol dependence with withdrawal |
| Alcohol withdrawal with abuse/dependence | ICD-10 | F10.230 | Alcohol dependence with withdrawal, uncomplicated |
| Alcohol withdrawal with abuse/dependence | ICD-10 | F10.231 | Alcohol dependence with withdrawal delirium |
| Alcohol withdrawal with abuse/dependence | ICD-10 | F10.232 | Alcohol dependence with withdrawal with perceptual disturbance |
| Alcohol withdrawal with abuse/dependence | ICD-10 | F10.239 | Alcohol dependence with withdrawal, unspecified |
| Alcohol withdrawal with abuse/dependence | ICD-10 | F10.93 | Alcohol use, unspecified with withdrawal |
| Alcohol withdrawal with abuse/dependence | ICD-10 | F10.930 | Alcohol use, unspecified with withdrawal, uncomplicated |
| Alcohol withdrawal with abuse/dependence | ICD-10 | F10.931 | Alcohol use, unspecified with withdrawal delirium |

| Type of Non-Drug-Related Condition | Code Type | Code | Description |
|--|-----------|---------|--|
| Alcohol withdrawal with abuse/dependence | ICD-10 | F10.932 | Alcohol use, unspecified with withdrawal with perceptual disturbance |
| Alcohol withdrawal with abuse/dependence | ICD-10 | F10.939 | Alcohol use, unspecified with withdrawal, unspecified |
| Anemia in chronic diseases | ICD-9 | 285.2 | Anemia of chronic illness |
| Anemia in chronic diseases | ICD-9 | 285.21 | Anemia in chronic kidney disease |
| Anemia in chronic diseases | ICD-9 | 285.22 | Anemia in neoplastic disease |
| Anemia in chronic diseases | ICD-9 | 285.29 | Anemia in other chronic disease |
| Anemia in chronic diseases | ICD-10 | D63 | Anemia in chronic diseases classified elsewhere |
| Anemia in chronic diseases | ICD-10 | D63.0 | Anemia in neoplastic disease |
| Anemia in chronic diseases | ICD-10 | D63.1 | Anemia in chronic kidney disease |
| Anemia in chronic diseases | ICD-10 | D63.8 | Anemia in other chronic diseases classified elsewhere |
| Anemia due to enzyme disorders | ICD-9 | 282.2 | Anemias due to disorders of glutathione metabolism |
| Anemia due to enzyme disorders | ICD-9 | 282.3 | Other hemolytic anemias due to enzyme deficiency |
| Anemia due to enzyme disorders | ICD-10 | D55 | Anemia due to enzyme disorders |
| Anemia due to enzyme disorders | ICD-10 | D55.0 | Anemia due to glucose-6-phosphate dehydrogenase [G6PD] deficiency |
| Anemia due to enzyme disorders | ICD-10 | D55.1 | Anemia due to other disorders of glutathione metabolism |
| Anemia due to enzyme disorders | ICD-10 | D55.2 | Anemia due to disorders of glycolytic enzymes |
| Anemia due to enzyme disorders | ICD-10 | D55.21 | Anemia due to pyruvate kinase deficiency |
| Anemia due to enzyme disorders | ICD-10 | D55.29 | Anemia due to other disorders of glycolytic enzymes |
| Anemia due to enzyme disorders | ICD-10 | D55.3 | Anemia due to disorders of nucleotide metabolism |
| Anemia due to enzyme disorders | ICD-10 | D55.8 | Other anemias due to enzyme disorders |
| Anemia due to enzyme disorders | ICD-10 | D55.9 | Anemia due to enzyme disorder, unspecified |
| Budd Chiari Syndrome | ICD-9 | 453.0 | Budd-Chiari syndrome |
| Budd Chiari Syndrome | ICD-10 | I82.0 | Budd Chiari syndrome |
| Cancer of the pancreas | ICD-9 | 157 | Malignant neoplasm of pancreas |
| Cancer of the pancreas | ICD-9 | 157.0 | Malignant neoplasm of head of pancreas |
| Cancer of the pancreas | ICD-9 | 157.1 | Malignant neoplasm of body of pancreas |
| Cancer of the pancreas | ICD-9 | 157.2 | Malignant neoplasm of tail of pancreas |
| Cancer of the pancreas | ICD-9 | 157.3 | Malignant neoplasm of pancreatic duct |
| Cancer of the pancreas | ICD-9 | 157.4 | Malignant neoplasm of islets of Langerhans |
| Cancer of the pancreas | ICD-9 | 157.8 | Malignant neoplasm of other specified sites of pancreas |
| Cancer of the pancreas | ICD-9 | 157.9 | Malignant neoplasm of pancreas, part unspecified |
| Cancer of the pancreas | ICD-10 | C25 | Malignant neoplasm of pancreas |
| Cancer of the pancreas | ICD-10 | C25.0 | Malignant neoplasm of head of pancreas |
| Cancer of the pancreas | ICD-10 | C25.1 | Malignant neoplasm of body of pancreas |
| Cancer of the pancreas | ICD-10 | C25.2 | Malignant neoplasm of tail of pancreas |

| Type of Non-Drug-Related Condition | Code Type | Code | Description |
|------------------------------------|-----------|--------|---|
| Cancer of the pancreas | ICD-10 | C25.3 | Malignant neoplasm of pancreatic duct |
| Cancer of the pancreas | ICD-10 | C25.4 | Malignant neoplasm of endocrine pancreas |
| Cancer of the pancreas | ICD-10 | C25.7 | Malignant neoplasm of other parts of pancreas |
| Cancer of the pancreas | ICD-10 | C25.8 | Malignant neoplasm of overlapping sites of pancreas |
| Cancer of the pancreas | ICD-10 | C25.9 | Malignant neoplasm of pancreas, unspecified |
| Celiac disease | ICD-9 | 579.0 | Celiac disease |
| Celiac disease | ICD-10 | K90.0 | Celiac disease |
| Hypotension | ICD-9 | 458 | Hypotension |
| Hypotension | ICD-9 | 458.0 | Orthostatic hypotension |
| Hypotension | ICD-9 | 458.1 | Chronic hypotension |
| Hypotension | ICD-9 | 458.2 | Iatrogenic hypotension |
| Hypotension | ICD-9 | 458.21 | Hypotension of hemodialysis |
| Hypotension | ICD-9 | 458.29 | Other iatrogenic hypotension |
| Hypotension | ICD-9 | 458.8 | Other specified hypotension |
| Hypotension | ICD-9 | 458.9 | Hypotension, unspecified |
| Hypotension | ICD-10 | I95 | Hypotension |
| Hypotension | ICD-10 | I95.0 | Idiopathic hypotension |
| Hypotension | ICD-10 | I95.1 | Orthostatic hypotension |
| Hypotension | ICD-10 | I95.2 | Hypotension due to drugs |
| Hypotension | ICD-10 | I95.3 | Hypotension of hemodialysis |
| Hypotension | ICD-10 | I95.8 | Other hypotension |
| Hypotension | ICD-10 | I95.81 | Postprocedural hypotension |
| Hypotension | ICD-10 | I95.89 | Other hypotension |
| Hypotension | ICD-10 | I95.9 | Hypotension, unspecified |
| Other hereditary hemolytic anemias | ICD-9 | 282 | Hereditary hemolytic anemias |
| Other hereditary hemolytic anemias | ICD-9 | 282.0 | Hereditary spherocytosis |
| Other hereditary hemolytic anemias | ICD-9 | 282.1 | Hereditary elliptocytosis |
| Other hereditary hemolytic anemias | ICD-9 | 282.7 | Other hemoglobinopathies |
| Other hereditary hemolytic anemias | ICD-9 | 282.8 | Other specified hereditary hemolytic anemias |
| Other hereditary hemolytic anemias | ICD-9 | 282.9 | Hereditary hemolytic anemia, unspecified |
| Other hereditary hemolytic anemias | ICD-10 | D58 | Other hereditary hemolytic anemias |
| Other hereditary hemolytic anemias | ICD-10 | D58.0 | Hereditary spherocytosis |
| Other hereditary hemolytic anemias | ICD-10 | D58.1 | Hereditary elliptocytosis |
| Other hereditary hemolytic anemias | ICD-10 | D58.2 | Other hemoglobinopathies |
| Other hereditary hemolytic anemias | ICD-10 | D58.8 | Other specified hereditary hemolytic anemias |

| Type of Non-Drug-Related Condition | Code Type | Code | Description |
|------------------------------------|-----------|--------|--|
| Other hereditary hemolytic anemias | ICD-10 | D58.9 | Hereditary hemolytic anemia, unspecified |
| Pancreatitis | ICD-9 | 577 | Diseases of pancreas |
| Pancreatitis | ICD-9 | 577.0 | Acute pancreatitis |
| Pancreatitis | ICD-9 | 577.1 | Chronic pancreatitis |
| Pancreatitis | ICD-9 | 577.2 | Cyst and pseudocyst of pancreas |
| Pancreatitis | ICD-9 | 577.9 | Unspecified disease of pancreas |
| Pancreatitis | ICD-9 | 577.8 | Other specified diseases of pancreas |
| Pancreatitis | ICD-10 | K85.0 | Idiopathic acute pancreatitis |
| Pancreatitis | ICD-10 | K85.00 | Idiopathic acute pancreatitis without necrosis or infection |
| Pancreatitis | ICD-10 | K85.01 | Idiopathic acute pancreatitis with uninfected necrosis |
| Pancreatitis | ICD-10 | K85.02 | Idiopathic acute pancreatitis with infected necrosis |
| Pancreatitis | ICD-10 | K85.1 | Biliary acute pancreatitis |
| Pancreatitis | ICD-10 | K85.10 | Biliary acute pancreatitis without necrosis or infection |
| Pancreatitis | ICD-10 | K85.11 | Biliary acute pancreatitis with uninfected necrosis |
| Pancreatitis | ICD-10 | K85.12 | Biliary acute pancreatitis with infected necrosis |
| Pancreatitis | ICD-10 | K85.2 | Alcohol induced acute pancreatitis |
| Pancreatitis | ICD-10 | K85.20 | Alcohol induced acute pancreatitis without necrosis or infection |
| Pancreatitis | ICD-10 | K85.21 | Alcohol induced acute pancreatitis with uninfected necrosis |
| Pancreatitis | ICD-10 | K85.22 | Alcohol induced acute pancreatitis with infected necrosis |
| Pancreatitis | ICD-10 | K85.8 | Other acute pancreatitis |
| Pancreatitis | ICD-10 | K85.80 | Other acute pancreatitis without necrosis or infection |
| Pancreatitis | ICD-10 | K85.81 | Other acute pancreatitis with uninfected necrosis |
| Pancreatitis | ICD-10 | K85.82 | Other acute pancreatitis with infected necrosis |
| Pancreatitis | ICD-10 | K85.9 | Acute pancreatitis, unspecified |
| Pancreatitis | ICD-10 | K85.90 | Acute pancreatitis without necrosis or infection, unspecified |
| Pancreatitis | ICD-10 | K85.91 | Acute pancreatitis with uninfected necrosis, unspecified |
| Pancreatitis | ICD-10 | K85.92 | Acute pancreatitis with infected necrosis, unspecified |
| Pancreatitis | ICD-10 | K86 | Other diseases of pancreas |
| Pancreatitis | ICD-10 | K86.0 | Alcohol-induced chronic pancreatitis |
| Pancreatitis | ICD-10 | K86.1 | Other chronic pancreatitis |
| Pancreatitis | ICD-10 | K86.2 | Cyst of pancreas |
| Pancreatitis | ICD-10 | K86.3 | Pseudocyst of pancreas |
| Pancreatitis | ICD-10 | K86.8 | Other specified diseases of pancreas |
| Pancreatitis | ICD-10 | K86.81 | Exocrine pancreatic insufficiency |
| Pancreatitis | ICD-10 | K86.89 | Other specified diseases of pancreas |
| Pancreatitis | ICD-10 | K86.9 | Disease of pancreas, unspecified |

| Type of Non-Drug-Related Condition | Code Type | Code | Description |
|------------------------------------|-----------|----------|---|
| Rhabdomyolysis | ICD-9 | 728.88 | Rhabdomyolysis |
| Rhabdomyolysis | ICD-10 | M62.82 | Rhabdomyolysis |
| Rhabdomyolysis | ICD-10 | T79.6 | Traumatic ischemia of the muscle |
| Rhabdomyolysis | ICD-10 | T79.6XXA | Traumatic ischemia of the muscle initial encounter |
| Rhabdomyolysis | ICD-10 | T79.6XXD | Traumatic ischemia of the muscle subsequent encounter |
| Rhabdomyolysis | ICD-10 | T79.6XXS | Traumatic ischemia of the muscle sequela |
| Sepsis without shock | ICD-9 | 003.1 | Salmonella septicemia |
| Sepsis without shock | ICD-9 | 020.2 | Septicemic plague |
| Sepsis without shock | ICD-9 | 022.3 | Anthrax septicemia |
| Sepsis without shock | ICD-9 | 038 | Septicemia |
| Sepsis without shock | ICD-9 | 038.0 | Streptococcal septicemia |
| Sepsis without shock | ICD-9 | 038.1 | Staphylococcal septicemia |
| Sepsis without shock | ICD-9 | 038.10 | Staphylococcal septicemia, unspecified |
| Sepsis without shock | ICD-9 | 038.11 | Methicillin susceptible Staphylococcus aureus septicemia |
| Sepsis without shock | ICD-9 | 038.12 | Methicillin resistant Staphylococcus aureus septicemia |
| Sepsis without shock | ICD-9 | 038.19 | Other staphylococcal septicemia |
| Sepsis without shock | ICD-9 | 038.2 | Pneumococcal septicemia [Streptococcus pneumoniae septicemia] |
| Sepsis without shock | ICD-9 | 038.3 | Septicemia due to anaerobes |
| Sepsis without shock | ICD-9 | 038.4 | Septicemia due to other gram-negative organisms |
| Sepsis without shock | ICD-9 | 038.40 | Septicemia due to gram-negative organism, unspecified |
| Sepsis without shock | ICD-9 | 038.41 | Septicemia due to hemophilus influenzae [H. influenzae] |
| Sepsis without shock | ICD-9 | 038.42 | Septicemia due to escherichia coli [E. coli] |
| Sepsis without shock | ICD-9 | 038.43 | Septicemia due to pseudomonas |
| Sepsis without shock | ICD-9 | 038.44 | Septicemia due to serratia |
| Sepsis without shock | ICD-9 | 038.49 | Other septicemia due to gram-negative organisms |
| Sepsis without shock | ICD-9 | 038.8 | Other specified septicemias |
| Sepsis without shock | ICD-9 | 038.9 | Unspecified septicemia |
| Sepsis without shock | ICD-9 | 670.2 | Puerperal sepsis |
| Sepsis without shock | ICD-9 | 670.20 | Puerperal sepsis, unspecified as to episode of care or not applicable |
| Sepsis without shock | ICD-9 | 670.22 | Puerperal sepsis, delivered, with mention of postpartum complication |
| Sepsis without shock | ICD-9 | 670.24 | Puerperal sepsis, postpartum condition or complication |
| Sepsis without shock | ICD-9 | 790.7 | Bacteremia |
| Sepsis without shock | ICD-9 | 995.9 | Systemic inflammatory response syndrome (SIRS) |
| Sepsis without shock | ICD-9 | 995.90 | Systemic inflammatory response syndrome, unspecified |
| Sepsis without shock | ICD-9 | 995.91 | Sepsis |
| Sepsis without shock | ICD-9 | 995.92 | Severe sepsis |

| Type of Non-Drug-Related Condition | Code Type | Code | Description |
|------------------------------------|-----------|--------|--|
| Sepsis without shock | ICD-9 | 995.93 | Systemic inflammatory response syndrome due to noninfectious process without acute organ dysfunction |
| Sepsis without shock | ICD-9 | 995.94 | Systemic inflammatory response syndrome due to noninfectious process with acute organ dysfunction |
| Sepsis without shock | ICD-10 | A02.1 | Salmonella sepsis |
| Sepsis without shock | ICD-10 | A20.7 | Septicemic plague |
| Sepsis without shock | ICD-10 | A22.7 | Anthrax sepsis |
| Sepsis without shock | ICD-10 | A26.7 | Erysipelothrix sepsis |
| Sepsis without shock | ICD-10 | A32.7 | Listerial sepsis |
| Sepsis without shock | ICD-10 | A40 | Streptococcal sepsis |
| Sepsis without shock | ICD-10 | A40.0 | Sepsis due to streptococcus, group A |
| Sepsis without shock | ICD-10 | A40.1 | Sepsis due to streptococcus, group B |
| Sepsis without shock | ICD-10 | A40.3 | Sepsis due to Streptococcus pneumoniae |
| Sepsis without shock | ICD-10 | A40.8 | Other streptococcal sepsis |
| Sepsis without shock | ICD-10 | A40.9 | Streptococcal sepsis, unspecified |
| Sepsis without shock | ICD-10 | A41 | Other sepsis |
| Sepsis without shock | ICD-10 | A41.0 | Sepsis due to Staphylococcus aureus |
| Sepsis without shock | ICD-10 | A41.01 | Sepsis due to Methicillin susceptible Staphylococcus aureus |
| Sepsis without shock | ICD-10 | A41.02 | Sepsis due to Methicillin resistant Staphylococcus aureus |
| Sepsis without shock | ICD-10 | A41.1 | Sepsis due to other specified staphylococcus |
| Sepsis without shock | ICD-10 | A41.2 | Sepsis due to unspecified staphylococcus |
| Sepsis without shock | ICD-10 | A41.3 | Sepsis due to Hemophilus influenzae |
| Sepsis without shock | ICD-10 | A41.4 | Sepsis due to anaerobes |
| Sepsis without shock | ICD-10 | A41.5 | Sepsis due to other Gram-negative organisms |
| Sepsis without shock | ICD-10 | A41.50 | Gram-negative sepsis, unspecified |
| Sepsis without shock | ICD-10 | A41.51 | Sepsis due to Escherichia coli [E. coli] |
| Sepsis without shock | ICD-10 | A41.52 | Sepsis due to Pseudomonas |
| Sepsis without shock | ICD-10 | A41.53 | Sepsis due to Serratia |
| Sepsis without shock | ICD-10 | A41.59 | Other Gram-negative sepsis |
| Sepsis without shock | ICD-10 | A41.8 | Other specified sepsis |
| Sepsis without shock | ICD-10 | A41.81 | Sepsis due to Enterococcus |
| Sepsis without shock | ICD-10 | A41.89 | Other specified sepsis |
| Sepsis without shock | ICD-10 | A41.9 | Sepsis, unspecified organism |
| Sepsis without shock | ICD-10 | A42.7 | Actinomycotic sepsis |
| Sepsis without shock | ICD-10 | A54.86 | Gonococcal sepsis |
| Sepsis without shock | ICD-10 | B37.7 | Candidal sepsis |

| Type of Non-Drug-Related Condition | Code Type | Code | Description |
|------------------------------------|-----------|----------|---|
| Sepsis without shock | ICD-10 | O03.37 | Sepsis following incomplete spontaneous abortion |
| Sepsis without shock | ICD-10 | O03.87 | Sepsis following complete or unspecified spontaneous abortion |
| Sepsis without shock | ICD-10 | O04.87 | Sepsis following (induced) termination of pregnancy |
| Sepsis without shock | ICD-10 | O07.37 | Sepsis following failed attempted termination of pregnancy |
| Sepsis without shock | ICD-10 | O08.82 | Sepsis following ectopic and molar pregnancy |
| Sepsis without shock | ICD-10 | O85 | Puerperal sepsis |
| Sepsis without shock | ICD-10 | R65 | Symptoms and signs specifically associated with systemic inflammation and infection |
| Sepsis without shock | ICD-10 | R65.1 | Systemic inflammatory response syndrome (SIRS) of non-infectious origin |
| Sepsis without shock | ICD-10 | R65.10 | Systemic inflammatory response syndrome (SIRS) of non-infectious origin without acute organ dysfunction |
| Sepsis without shock | ICD-10 | R65.11 | Systemic inflammatory response syndrome (SIRS) of non-infectious origin with acute organ dysfunction |
| Sepsis without shock | ICD-10 | R65.20 | Severe sepsis without septic shock |
| Sepsis without shock | ICD-10 | R78.81 | Bacteremia |
| Sepsis without shock | ICD-10 | T81.44 | Sepsis following a procedure |
| Sepsis without shock | ICD-10 | T81.44XA | Sepsis following a procedure initial encounter |
| Sepsis without shock | ICD-10 | T81.44XD | Sepsis following a procedure subsequent encounter |
| Sepsis without shock | ICD-10 | T81.44XS | Sepsis following a procedure sequela |
| Shock | ICD-9 | 785.5 | Shock without mention of trauma |
| Shock | ICD-9 | 785.50 | Shock, unspecified |
| Shock | ICD-9 | 785.51 | Cardiogenic shock |
| Shock | ICD-9 | 785.52 | Septic shock |
| Shock | ICD-9 | 785.59 | Other shock without mention of trauma |
| Shock | ICD-9 | 998.0 | Postoperative shock not elsewhere classified |
| Shock | ICD-9 | 998.00 | Postoperative shock, unspecified |
| Shock | ICD-9 | 998.01 | Postoperative shock, cardiogenic |
| Shock | ICD-9 | 998.02 | Postoperative shock, septic |
| Shock | ICD-9 | 998.09 | Postoperative shock, other |
| Shock | ICD-10 | R57 | Shock, not elsewhere classified |
| Shock | ICD-10 | R57.0 | Cardiogenic shock |
| Shock | ICD-10 | R57.1 | Hypovolemic shock |
| Shock | ICD-10 | R57.8 | Other shock |
| Shock | ICD-10 | R57.9 | Shock, unspecified |
| Shock | ICD-10 | R65.21 | Severe sepsis with septic shock |
| Shock | ICD-10 | T81.1 | Postprocedural shock |
| Shock | ICD-10 | T81.10 | Postprocedural shock unspecified |

| Type of Non-Drug-Related Condition | Code Type | Code | Description |
|------------------------------------|-----------|----------|---|
| Shock | ICD-10 | T81.10XA | Postprocedural shock, unspecified, initial encounter |
| Shock | ICD-10 | T81.10XD | Postprocedural shock, unspecified, subsequent encounter |
| Shock | ICD-10 | T81.10XS | Postprocedural shock, unspecified, sequela |
| Shock | ICD-10 | T81.11 | Postprocedural cardiogenic shock |
| Shock | ICD-10 | T81.11XA | Postprocedural cardiogenic shock, unspecified, initial encounter |
| Shock | ICD-10 | T81.11XD | Postprocedural cardiogenic shock, unspecified, subsequent encounter |
| Shock | ICD-10 | T81.11XS | Postprocedural cardiogenic shock, unspecified, sequela |
| Shock | ICD-10 | T81.12 | Postprocedural septic shock |
| Shock | ICD-10 | T81.12XA | Postprocedural septic shock, unspecified, initial encounter |
| Shock | ICD-10 | T81.12XD | Postprocedural septic shock, unspecified, subsequent encounter |
| Shock | ICD-10 | T81.12XS | Postprocedural septic shock, unspecified, sequela |
| Shock | ICD-10 | T81.19 | Other postprocedural shock |
| Shock | ICD-10 | T81.19XA | Other postprocedural shock, unspecified, initial encounter |
| Shock | ICD-10 | T81.19XD | Other postprocedural shock, unspecified, subsequent encounter |
| Shock | ICD-10 | T81.19XS | Other postprocedural shock, unspecified, sequela |
| Sickle cell | ICD-9 | 282.5 | Sickle cell trait |
| Sickle cell | ICD-9 | 282.6 | Sickle cell anemia, unspecified |
| Sickle cell | ICD-9 | 282.61 | Sickle cell anemia, without crisis |
| Sickle cell | ICD-9 | 282.62 | Sickle cell anemia, with crisis |
| Sickle cell | ICD-9 | 282.63 | Sickle cell/Hb-C disease without crisis |
| Sickle cell | ICD-9 | 282.64 | Sickle cell/Hb-C disease with crisis |
| Sickle cell | ICD-9 | 282.68 | Other sickle cell disease without crisis |
| Sickle cell | ICD-9 | 282.69 | Other sickle cell disease with crisis |
| Sickle cell | ICD-10 | D57.0 | Sickle-cell anemia with crisis |
| Sickle cell | ICD-10 | D57.00 | Hb-SS disease with crisis, unspecified |
| Sickle cell | ICD-10 | D57.01 | Hb-SS disease with acute chest syndrome |
| Sickle cell | ICD-10 | D57.02 | Hb-SS disease with splenic sequestration |
| Sickle cell | ICD-10 | D57.03 | Hb-SS disease with cerebral vascular involvement |
| Sickle cell | ICD-10 | D57.09 | Hb-SS disease with crisis with other specified complication |
| Sickle cell | ICD-10 | D57.1 | Sickle-cell anemia without crisis |
| Sickle cell | ICD-10 | D57.2 | Double heterozygous sickling disorders |
| Sickle cell | ICD-10 | D57.20 | Sickle-cell/Hb-C disease without crisis |
| Sickle cell | ICD-10 | D57.21 | Sickle-cell/Hb-C disease with crisis |
| Sickle cell | ICD-10 | D57.211 | Sickle-cell/Hb-C disease with acute chest syndrome |
| Sickle cell | ICD-10 | D57.212 | Sickle-cell/Hb-C disease with splenic sequestration |
| Sickle cell | ICD-10 | D57.213 | Sickle-cell/Hb-C disease with cerebral vascular involvement |

| Type of Non-Drug-Related Condition | Code Type | Code | Description |
|------------------------------------|-----------|---------|---|
| Sickle cell | ICD-10 | D57.218 | Sickle-cell/Hb-C disease with crisis with other specified complication |
| Sickle cell | ICD-10 | D57.219 | Sickle-cell/Hb-C disease with crisis, unspecified |
| Sickle cell | ICD-10 | D57.3 | Sickle-cell trait |
| Sickle cell | ICD-10 | D57.8 | Other sickle-cell disorders |
| Sickle cell | ICD-10 | D57.80 | Other sickle-cell disorders without crisis |
| Sickle cell | ICD-10 | D57.81 | Other sickle-cell disorders with crisis |
| Sickle cell | ICD-10 | D57.811 | Other sickle-cell disorders with acute chest syndrome |
| Sickle cell | ICD-10 | D57.812 | Other sickle-cell disorders with splenic sequestration |
| Sickle cell | ICD-10 | D57.813 | Other sickle-cell disorders with cerebral vascular involvement |
| Sickle cell | ICD-10 | D57.818 | Other sickle-cell disorders with crisis with other specified complication |
| Sickle cell | ICD-10 | D57.819 | Other sickle-cell disorders with crisis, unspecified |
| Thalassemia | ICD-9 | 282.4 | Thalassemias |
| Thalassemia | ICD-9 | 282.40 | Thalassemia, unspecified |
| Thalassemia | ICD-9 | 282.41 | Sickle-cell thalassemia without crisis |
| Thalassemia | ICD-9 | 282.42 | Sickle-cell thalassemia with crisis |
| Thalassemia | ICD-9 | 282.43 | Alpha thalassemia |
| Thalassemia | ICD-9 | 282.44 | Beta thalassemia |
| Thalassemia | ICD-9 | 282.45 | Delta-beta thalassemia |
| Thalassemia | ICD-9 | 282.46 | Thalassemia minor |
| Thalassemia | ICD-9 | 282.47 | Hemoglobin E-beta thalassemia |
| Thalassemia | ICD-9 | 282.49 | Other thalassemia |
| Thalassemia | ICD-10 | D56 | Thalassemia |
| Thalassemia | ICD-10 | D56.0 | Alpha thalassemia |
| Thalassemia | ICD-10 | D56.1 | Beta thalassemia |
| Thalassemia | ICD-10 | D56.2 | Delta-beta thalassemia |
| Thalassemia | ICD-10 | D56.3 | Thalassemia minor |
| Thalassemia | ICD-10 | D56.4 | Hereditary persistence of fetal hemoglobin [HPFH] |
| Thalassemia | ICD-10 | D56.5 | Hemoglobin E-beta thalassemia |
| Thalassemia | ICD-10 | D56.8 | Other thalassemias |
| Thalassemia | ICD-10 | D56.9 | Thalassemia, unspecified |
| Thyrotoxicosis | ICD-9 | 242 | Thyrotoxicosis with or without goiter |
| Thyrotoxicosis | ICD-9 | 242.0 | Toxic diffuse goiter |
| Thyrotoxicosis | ICD-9 | 242.00 | Toxic diffuse goiter without mention of thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-9 | 242.01 | Toxic diffuse goiter with mention of thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-9 | 242.1 | Toxic uninodular goiter |
| Thyrotoxicosis | ICD-9 | 242.10 | Toxic uninodular goiter without mention of thyrotoxic crisis or storm |

| Type of Non-Drug-Related Condition | Code Type | Code | Description |
|------------------------------------|-----------|--------|--|
| Thyrotoxicosis | ICD-9 | 242.11 | Toxic uninodular goiter with mention of thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-9 | 242.2 | Toxic multinodular goiter |
| Thyrotoxicosis | ICD-9 | 242.20 | Toxic multinodular goiter without mention of thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-9 | 242.21 | Toxic multinodular goiter with mention of thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-9 | 242.3 | Toxic nodular goiter, unspecified |
| Thyrotoxicosis | ICD-9 | 242.30 | Toxic nodular goiter, unspecified type, without mention of thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-9 | 242.31 | Toxic nodular goiter, unspecified type, with mention of thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-9 | 242.4 | Thyrotoxicosis from ectopic thyroid nodule |
| Thyrotoxicosis | ICD-9 | 242.40 | Thyrotoxicosis from ectopic thyroid nodule without mention of thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-9 | 242.41 | Thyrotoxicosis from ectopic thyroid nodule with mention of thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-9 | 242.8 | Thyrotoxicosis from other specified origin |
| Thyrotoxicosis | ICD-9 | 242.80 | Thyrotoxicosis of other specified origin without mention of thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-9 | 242.81 | Thyrotoxicosis of other specified origin with mention of thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-9 | 242.9 | Thyrotoxicosis without mention of goiter or other cause, and without mention of thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-9 | 242.90 | Thyrotoxicosis without mention of goiter or other cause, and without mention of thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-9 | 242.91 | Thyrotoxicosis without mention of goiter or other cause, with mention of thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-10 | E05 | Thyrotoxicosis [hyperthyroidism] |
| Thyrotoxicosis | ICD-10 | E05.0 | Thyrotoxicosis with diffuse goiter |
| Thyrotoxicosis | ICD-10 | E05.00 | Thyrotoxicosis with diffuse goiter without thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-10 | E05.01 | Thyrotoxicosis with diffuse goiter with thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-10 | E05.1 | Thyrotoxicosis with toxic single thyroid nodule |
| Thyrotoxicosis | ICD-10 | E05.10 | Thyrotoxicosis with toxic single thyroid nodule without thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-10 | E05.11 | Thyrotoxicosis with toxic single thyroid nodule with thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-10 | E05.2 | Thyrotoxicosis with toxic multinodular goiter |
| Thyrotoxicosis | ICD-10 | E05.20 | Thyrotoxicosis with toxic multinodular goiter without thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-10 | E05.21 | Thyrotoxicosis with toxic multinodular goiter with thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-10 | E05.3 | Thyrotoxicosis from ectopic thyroid tissue |
| Thyrotoxicosis | ICD-10 | E05.30 | Thyrotoxicosis from ectopic thyroid tissue without thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-10 | E05.31 | Thyrotoxicosis from ectopic thyroid tissue with thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-10 | E05.4 | Thyrotoxicosis factitia |
| Thyrotoxicosis | ICD-10 | E05.40 | Thyrotoxicosis factitia without thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-10 | E05.41 | Thyrotoxicosis factitia with thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-10 | E05.5 | Thyroid crisis or storm |

| Type of Non-Drug-Related Condition | Code Type | Code | Description |
|------------------------------------|-----------|--------|--|
| Thyrotoxicosis | ICD-10 | E05.8 | Other thyrotoxicosis |
| Thyrotoxicosis | ICD-10 | E05.80 | Other thyrotoxicosis without thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-10 | E05.81 | Other thyrotoxicosis with thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-10 | E05.9 | Thyrotoxicosis, unspecified |
| Thyrotoxicosis | ICD-10 | E05.90 | Thyrotoxicosis, unspecified without thyrotoxic crisis or storm |
| Thyrotoxicosis | ICD-10 | E05.91 | Thyrotoxicosis, unspecified with thyrotoxic crisis or storm |

Abbreviations: ICD-9=International Classification of Diseases, Ninth Revision; ICD-10=International Classification of Diseases, Tenth Revision

eTable 4. List of International Classification of Diseases, Ninth Revision (ICD-9) and International Classification of Diseases, Tenth Revision (ICD-10) diagnostic codes used to identify diabetes mellitus and hyperlipidemia.

| Condition | Code Type | Code | Description |
|-------------------|-----------|---------|--|
| Diabetes mellitus | ICD-9 | 250.0x | Diabetes mellitus without mention of complication |
| Diabetes mellitus | ICD-9 | 250.1x | Diabetes with ketoacidosis |
| Diabetes mellitus | ICD-9 | 250.2x | Diabetes with hyperosmolarity |
| Diabetes mellitus | ICD-9 | 250.3x | Diabetes with other coma |
| Diabetes mellitus | ICD-9 | 250.4x | Diabetes with renal manifestations |
| Diabetes mellitus | ICD-9 | 250.5x | Diabetes with ophthalmic manifestations |
| Diabetes mellitus | ICD-9 | 250.6x | Diabetes with neurological manifestations |
| Diabetes mellitus | ICD-9 | 250.7x | Diabetes with peripheral circulatory disorders |
| Diabetes mellitus | ICD-9 | 250.8x | Diabetes with other specified manifestations |
| Diabetes mellitus | ICD-9 | 250.9x | Diabetes with unspecified complication |
| Diabetes mellitus | ICD-10 | E10.1x | Type 1 diabetes mellitus with ketoacidosis |
| Diabetes mellitus | ICD-10 | E10.21 | Type 1 diabetes mellitus with diabetic nephropathy |
| Diabetes mellitus | ICD-10 | E10.22 | Type 1 diabetes mellitus with diabetic chronic kidney disease |
| Diabetes mellitus | ICD-10 | E10.29 | Type 1 diabetes mellitus with other diabetic kidney complication |
| Diabetes mellitus | ICD-10 | E10.3x | Type 1 diabetes mellitus with diabetic retinopathy |
| Diabetes mellitus | ICD-10 | E10.4x | Type 1 diabetes mellitus with diabetic neuropathy |
| Diabetes mellitus | ICD-10 | E10.5x | Type 1 diabetes mellitus with diabetic peripheral angiopathy |
| Diabetes mellitus | ICD-10 | E10.61x | Type 1 diabetes mellitus with diabetic arthropathy |
| Diabetes mellitus | ICD-10 | E10.62x | Type 1 diabetes mellitus with skin complications |
| Diabetes mellitus | ICD-10 | E10.63x | Type 1 diabetes mellitus with oral complications |
| Diabetes mellitus | ICD-10 | E10.64x | Type 1 diabetes mellitus with hypoglycemia |
| Diabetes mellitus | ICD-10 | E10.65 | Type 1 diabetes mellitus with hyperglycemia |
| Diabetes mellitus | ICD-10 | E10.69 | Type 1 diabetes mellitus with other specified complication |
| Diabetes mellitus | ICD-10 | E10.8 | Type 1 diabetes mellitus with unspecified complications |
| Diabetes mellitus | ICD-10 | E10.9 | Type 1 diabetes mellitus without complications |
| Diabetes mellitus | ICD-10 | E11.0x | Type 2 diabetes mellitus with hyperosmolarity |
| Diabetes mellitus | ICD-10 | E11.1x | Type 2 diabetes mellitus with ketoacidosis |
| Diabetes mellitus | ICD-10 | E11.21 | Type 2 diabetes mellitus with diabetic nephropathy |
| Diabetes mellitus | ICD-10 | E11.22 | Type 2 diabetes mellitus with diabetic chronic kidney disease |
| Diabetes mellitus | ICD-10 | E11.29 | Type 2 diabetes mellitus with other diabetic kidney complication |
| Diabetes mellitus | ICD-10 | E11.3x | Type 2 diabetes mellitus with diabetic retinopathy |
| Diabetes mellitus | ICD-10 | E11.4x | Type 2 diabetes mellitus with diabetic neuropathy |
| Diabetes mellitus | ICD-10 | E11.5x | Type 2 diabetes mellitus with diabetic peripheral angiopathy |

| Condition | Code Type | Code | Description |
|-------------------|-----------|---------|---|
| Diabetes mellitus | ICD-10 | E11.61x | Type 2 diabetes mellitus with diabetic arthropathy |
| Diabetes mellitus | ICD-10 | E11.62x | Type 2 diabetes mellitus with skin complications |
| Diabetes mellitus | ICD-10 | E11.63x | Type 2 diabetes mellitus with oral complications |
| Diabetes mellitus | ICD-10 | E11.64x | Type 2 diabetes mellitus with hypoglycemia |
| Diabetes mellitus | ICD-10 | E11.65 | Type 2 diabetes mellitus with hyperglycemia |
| Diabetes mellitus | ICD-10 | E11.69 | Type 2 diabetes mellitus with other specified complication |
| Diabetes mellitus | ICD-10 | E11.8 | Type 2 diabetes mellitus with unspecified complications |
| Diabetes mellitus | ICD-10 | E11.9 | Type 2 diabetes mellitus without complications |
| Diabetes mellitus | ICD-10 | E13.0x | Other specified diabetes mellitus with hyperosmolarity |
| Diabetes mellitus | ICD-10 | E13.1x | Other specified diabetes mellitus with ketoacidosis |
| Diabetes mellitus | ICD-10 | E13.21 | Other specified diabetes mellitus with diabetic nephropathy |
| Diabetes mellitus | ICD-10 | E13.22 | Other specified diabetes mellitus with diabetic chronic kidney disease |
| Diabetes mellitus | ICD-10 | E13.29 | Other specified diabetes mellitus with other diabetic kidney complication |
| Diabetes mellitus | ICD-10 | E13.3x | Other specified diabetes mellitus with diabetic retinopathy |
| Diabetes mellitus | ICD-10 | E13.4x | Other specified diabetes mellitus with diabetic neuropathy |
| Diabetes mellitus | ICD-10 | E13.5x | Other specified diabetes mellitus with diabetic peripheral angiopathy |
| Diabetes mellitus | ICD-10 | E13.61x | Other specified diabetes mellitus with diabetic arthropathy |
| Diabetes mellitus | ICD-10 | E13.62x | Other specified diabetes mellitus with skin complications |
| Diabetes mellitus | ICD-10 | E13.63x | Other specified diabetes mellitus with oral complications |
| Diabetes mellitus | ICD-10 | E13.64x | Other specified diabetes mellitus with hypoglycemia |
| Diabetes mellitus | ICD-10 | E13.65 | Other specified diabetes mellitus with hyperglycemia |
| Diabetes mellitus | ICD-10 | E13.69 | Other specified diabetes mellitus with other specified complication |
| Diabetes mellitus | ICD-10 | E13.8 | Other specified diabetes mellitus with unspecified complications |
| Diabetes mellitus | ICD-10 | E13.9 | Other specified diabetes mellitus without complications |
| Hyperlipidemia | ICD-9 | 272.0 | Pure hypercholesterolemia |
| Hyperlipidemia | ICD-9 | 272.1 | Hypertriglyceridemia |
| Hyperlipidemia | ICD-9 | 272.2 | Mixed hyperlipidemia |
| Hyperlipidemia | ICD-9 | 272.3 | Hyperchylomicronemia |
| Hyperlipidemia | ICD-9 | 272.4 | Other and unspecified hyperlipidemia |
| Hyperlipidemia | ICD-9 | 272.5 | Hyperlipidemia, unspecified |
| Hyperlipidemia | ICD-10 | E78.00 | Pure hypercholesterolemia, unspecified |
| Hyperlipidemia | ICD-10 | E78.01 | Familial hypercholesterolemia |
| Hyperlipidemia | ICD-10 | E78.1 | Pure hyperglyceridemia |
| Hyperlipidemia | ICD-10 | E78.2 | Mixed hyperlipidemia |
| Hyperlipidemia | ICD-10 | E78.3 | Hyperchylomicronemia |
| Hyperlipidemia | ICD-10 | E78.49 | Other hyperlipidemia |

| Condition | Code Type | Code | Description |
|----------------|-----------|-------|---|
| Hyperlipidemia | ICD-10 | E78.5 | Hyperlipidemia, unspecified |
| Hyperlipidemia | ICD-10 | E78.6 | Lipoprotein deficiency |
| Hyperlipidemia | ICD-10 | E78.9 | Disorder of lipoprotein metabolism, unspecified |

Abbreviations: ICD-9=International Classification of Diseases, Ninth Revision; ICD-10=International Classification of Diseases, Tenth Revision

eTable 5. List of International Classification of Diseases, Ninth Revision (ICD-9) and International Classification of Diseases, Tenth Revision (ICD-10) diagnostic codes and Current Procedural Terminology (CPT) procedure codes used to identify liver transplantation.

| Code Type | Code | Description |
|-----------|--------|---|
| ICD-9 | 996.82 | Complications of transplanted liver |
| ICD-9 | 50.5x | Liver transplant |
| ICD-9 | V42.7 | Liver replaced by transplant |
| ICD-10 | T86.40 | Unspecified complication of liver transplant |
| ICD-10 | T86.41 | Liver transplant rejection |
| ICD-10 | T86.42 | Liver transplant failure |
| ICD-10 | T86.43 | Liver transplant infection |
| ICD-10 | T86.49 | Other complications of liver transplant |
| ICD-10 | Z48.23 | Encounter for aftercare following liver transplant |
| ICD-10 | Z94.4 | Liver transplant status |
| CPT | 47133 | Donor hepatectomy, from cadaver donor |
| CPT | 47135 | Liver allotransplantation; orthotopic, partial or whole |
| CPT | 47136 | Liver allotransplantation; heterotopic, partial or whole, from cadaver or living donor, any age |
| CPT | 47143 | Preparation of cadaver donor whole liver graft prior to allotransplantation; without trisegment or lobe split |
| CPT | 47144 | Preparation of cadaver donor whole liver graft prior to allotransplantation; with trisegment split of whole liver graft into two partial liver grafts |
| CPT | 47145 | Preparation of cadaver donor whole liver graft prior to allotransplantation; with lobe split into two partial liver grafts |
| CPT | 47146 | Backbench reconstruction of cadaver or living donor liver graft prior to allotransplantation; venous anastomosis |
| CPT | 47147 | Backbench reconstruction of cadaver or living donor liver graft prior to allotransplantation; arterial anastomosis |

Abbreviations: CPT=Current Procedural Terminology; ICD-9=International Classification of Diseases, Ninth Revision; ICD-10=International Classification of Diseases, Tenth Revision

eTable 6. Reasons for exclusion of patients within each of the 194 medication initiator cohorts.

| Medication | Original Category ^a | No. Patients | <1 Year of Baseline | Baseline Anti-Coagulant Use | Baseline Severe Acute Liver Injury ^b | Pre-Existing Liver/Biliary Disease ^c | Other Baseline Evidence of Liver Injury ^d | Final Sample |
|---|--------------------------------|--------------|---------------------|-----------------------------|---|---|--|--------------|
| ALLOPURINOL | A | 612,366 | 152,146 (24.8%) | 49,693 (8.1%) | 918 (0.1%) | 62,759 (10.2%) | 21,906 (3.6%) | 324,944 |
| AMIODARONE | A | 267,031 | 48,421 (18.1%) | 93,500 (35.0%) | 671 (0.3%) | 22,330 (8.4%) | 5,301 (2.0%) | 96,808 |
| AMOXICILLIN WITH CLAVULANATE | A | 1,998,069 | 256,264 (12.8%) | 130,020 (6.5%) | 7,427 (0.4%) | 299,773 (15.0%) | 69,442 (3.5%) | 1,235,143 |
| ANDROGENIC STEROIDS ^e | A | 195,051 | 27,936 (14.3%) | 7,219 (3.7%) | 186 (0.1%) | 20,192 (10.4%) | 11,581 (5.9%) | 127,937 |
| ATORVASTATIN | A | 2,328,287 | 291,845 (12.5%) | 143,771 (6.2%) | 1,875 (0.1%) | 258,228 (11.1%) | 88,797 (3.8%) | 1,543,771 |
| AURANOFIN OR GOLD PRODUCTS ^e | A | 299 | 79 (26.4%) | 13 (4.3%) | 0 (0.0%) | 42 (14.0%) | 16 (5.4%) | 149 |
| AZATHIOPRINE OR MERCAPTOPYRINE | A | 31,240 | 7,067 (22.6%) | 1,827 (5.8%) | 241 (0.8%) | 4,433 (14.2%) | 1,639 (5.2%) | 16,033 |
| BUSULFAN | A | 144 | 26 (18.1%) | 21 (14.6%) | 0 (0.0%) | 28 (19.4%) | 9 (6.3%) | 60 |
| CARBAMAZEPINE | A | 120,184 | 22,278 (18.5%) | 3,695 (3.1%) | 196 (0.2%) | 21,106 (17.6%) | 4,409 (3.7%) | 68,500 |
| CHLORPROMAZINE | A | 36,637 | 4,547 (12.4%) | 1,991 (5.4%) | 390 (1.1%) | 10,691 (29.2%) | 1,569 (4.3%) | 17,449 |
| DANTROLENE | A | 3,361 | 687 (20.4%) | 285 (8.5%) | 3 (0.1%) | 512 (15.2%) | 130 (3.9%) | 1,744 |
| DICLOFENAC | A | 865,043 | 155,285 (18.0%) | 10,671 (1.2%) | 621 (0.1%) | 102,037 (11.8%) | 29,028 (3.4%) | 567,401 |
| DIDANOSINE | A | 2,594 | 704 (27.1%) | 35 (1.3%) | 14 (0.5%) | 755 (29.1%) | 196 (7.6%) | 890 |
| EFAVIRENZ | A | 13,762 | 3,948 (28.7%) | 213 (1.5%) | 53 (0.4%) | 3,870 (28.1%) | 718 (5.2%) | 4,960 |
| ERYTHROMYCIN | A | 128,569 | 22,192 (17.3%) | 5,246 (4.1%) | 389 (0.3%) | 19,101 (14.9%) | 4,543 (3.5%) | 77,098 |
| ESTROGENS OR PROGESTINS ^e | A | 354,603 | 88,487 (25.0%) | 18,187 (5.1%) | 2,038 (0.6%) | 55,282 (15.6%) | 10,928 (3.1%) | 179,681 |
| FLUTAMIDE | A | 16,207 | 3,793 (23.4%) | 1,022 (6.3%) | 12 (0.1%) | 1,155 (7.1%) | 992 (6.1%) | 9,233 |
| HYDRALAZINE OR ISOSORBIDE DINITRATE | A | 296,091 | 35,148 (11.9%) | 36,839 (12.4%) | 1,019 (0.3%) | 54,641 (18.5%) | 9,770 (3.3%) | 158,674 |
| IBUPROFEN | A | 2,601,823 | 747,227 (28.7%) | 35,300 (1.4%) | 3,198 (0.1%) | 271,319 (10.4%) | 64,959 (2.5%) | 1,479,820 |
| INFLIXIMAB | A | 1,837 | 233 (12.7%) | 71 (3.9%) | 4 (0.2%) | 254 (13.8%) | 161 (8.8%) | 1,114 |
| INTERFERON-β | A | 6,650 | 2,327 (35.0%) | 80 (1.2%) | 2 (0.0%) | 333 (5.0%) | 235 (3.5%) | 3,673 |
| ISONIAZID | A | 45,772 | 9,214 (20.1%) | 1,892 (4.1%) | 116 (0.3%) | 12,550 (27.4%) | 1,524 (3.3%) | 20,476 |
| KETOCONAZOLE | A | 47,909 | 8,808 (18.4%) | 1,549 (3.2%) | 57 (0.1%) | 4,956 (10.3%) | 2,563 (5.3%) | 29,976 |
| METHOTREXATE | A | 91,560 | 19,520 (21.3%) | 4,467 (4.9%) | 51 (0.1%) | 7,802 (8.5%) | 3,605 (3.9%) | 56,115 |
| METHYLDOPA | A | 5,009 | 1,570 (31.3%) | 169 (3.4%) | 2 (0.0%) | 341 (6.8%) | 84 (1.7%) | 2,843 |
| MINOCYCLINE | A | 156,877 | 17,305 (11.0%) | 11,427 (7.3%) | 368 (0.2%) | 24,735 (15.8%) | 5,516 (3.5%) | 97,526 |
| NEVIRAPINE | A | 2,829 | 849 (30.0%) | 39 (1.4%) | 5 (0.2%) | 751 (26.5%) | 182 (6.4%) | 1,003 |
| NITROFURANTOIN | A | 359,882 | 33,456 (9.3%) | 41,134 (11.4%) | 881 (0.2%) | 54,048 (15.0%) | 10,412 (2.9%) | 219,951 |
| PHENYTOIN OR FOSPHENYTOIN | A | 80,150 | 27,883 (34.8%) | 4,646 (5.8%) | 260 (0.3%) | 12,704 (15.9%) | 2,813 (3.5%) | 31,844 |
| PROPYLTHIOURACIL | A | 4,821 | 1,378 (28.6%) | 599 (12.4%) | 8 (0.2%) | 679 (14.1%) | 215 (4.5%) | 1,942 |
| PYRAZINAMIDE | A | 4,748 | 879 (18.5%) | 235 (4.9%) | 27 (0.6%) | 1,409 (29.7%) | 264 (5.6%) | 1,934 |
| QUINIDINE | A | 7,075 | 3,026 (42.8%) | 518 (7.3%) | 14 (0.2%) | 438 (6.2%) | 153 (2.2%) | 2,926 |
| RIFAMPIN | A | 51,221 | 5,930 (11.6%) | 4,293 (8.4%) | 277 (0.5%) | 13,255 (25.9%) | 2,139 (4.2%) | 25,327 |
| SIMVASTATIN | A | 3,248,110 | 1,322,419 (40.7%) | 92,170 (2.8%) | 1,392 (0.0%) | 186,302 (5.7%) | 78,158 (2.4%) | 1,567,669 |
| SULFAMETHOXAZOLE WITH TRIMETHOPRIM | A | 1,640,476 | 230,362 (14.0%) | 82,178 (5.0%) | 5,628 (0.3%) | 242,264 (14.8%) | 54,921 (3.3%) | 1,025,123 |
| SULFASALAZINE | A | 46,041 | 9,684 (21.0%) | 2,068 (4.5%) | 52 (0.1%) | 5,527 (12.0%) | 2,375 (5.2%) | 26,335 |
| SULINDAC | A | 238,832 | 42,148 (17.6%) | 3,211 (1.3%) | 214 (0.1%) | 29,708 (12.4%) | 8,032 (3.4%) | 155,519 |
| TELITHROMYCIN | A | 32 | 2 (6.3%) | 8 (25.0%) | 0 (0.0%) | 4 (12.5%) | 1 (3.1%) | 17 |
| THIOGUANINE | A | 123 | 35 (28.5%) | 7 (5.7%) | 2 (1.6%) | 32 (26.0%) | 9 (7.3%) | 38 |

| Medication | Original Category ^a | No. Patients | <1 Year of Baseline | Baseline Anti-Coagulant Use | Baseline Severe Acute Liver Injury ^b | Pre-Existing Liver/Biliary Disease ^c | Other Baseline Evidence of Liver Injury ^d | Final Sample |
|---------------------------------|--------------------------------|--------------|---------------------|-----------------------------|---|---|--|--------------|
| TICLOPIDINE | A | 4,077 | 1,466 (36.0%) | 161 (3.9%) | 5 (0.1%) | 204 (5.0%) | 104 (2.6%) | 2,137 |
| VALPROATE | A | 439,141 | 82,807 (18.9%) | 12,788 (2.9%) | 437 (0.1%) | 85,898 (19.6%) | 13,164 (3.0%) | 244,047 |
| ACARBOSE | B | 73,908 | 7,042 (9.5%) | 4,676 (6.3%) | 68 (0.1%) | 6,859 (9.3%) | 4,863 (6.6%) | 50,400 |
| AMITRIPTYLINE | B | 642,731 | 142,248 (22.1%) | 21,151 (3.3%) | 838 (0.1%) | 77,118 (12.0%) | 21,689 (3.4%) | 379,687 |
| AMOXICILLIN | B | 1,741,588 | 254,466 (14.6%) | 98,107 (5.6%) | 3,535 (0.2%) | 238,460 (13.7%) | 54,827 (3.1%) | 1,092,193 |
| ASPARAGINASE OR PEGASPARGASE | B | 17 | 0 (0.0%) | 2 (11.8%) | 0 (0.0%) | 4 (23.5%) | 2 (11.8%) | 9 |
| AZITHROMYCIN | B | 2,038,855 | 296,212 (14.5%) | 100,902 (4.9%) | 2,964 (0.1%) | 265,326 (13.0%) | 69,491 (3.4%) | 1,303,960 |
| CAPTOPRIL | B | 55,099 | 25,686 (46.6%) | 4,502 (8.2%) | 181 (0.3%) | 4,600 (8.3%) | 1,267 (2.3%) | 18,863 |
| CEFTRIAZONE | B | 36,092 | 6,005 (16.6%) | 987 (2.7%) | 63 (0.2%) | 5,925 (16.4%) | 831 (2.3%) | 22,281 |
| CELECOXIB | B | 218,437 | 33,972 (15.6%) | 13,464 (6.2%) | 172 (0.1%) | 23,207 (10.6%) | 7,114 (3.3%) | 140,508 |
| CHLORPROPAMIDE | B | 480 | 336 (70.0%) | 9 (1.9%) | 0 (0.0%) | 16 (3.3%) | 8 (1.7%) | 111 |
| CHLORZOXAZONE | B | 36,256 | 6,656 (18.4%) | 1,002 (2.8%) | 21 (0.1%) | 4,257 (11.7%) | 992 (2.7%) | 23,328 |
| CIMETIDINE | B | 43,074 | 14,385 (33.4%) | 898 (2.1%) | 65 (0.2%) | 4,451 (10.3%) | 1,160 (2.7%) | 22,115 |
| CIPROFLOXACIN | B | 1,816,459 | 221,701 (12.2%) | 110,508 (6.1%) | 12,945 (0.7%) | 282,180 (15.5%) | 63,665 (3.5%) | 1,125,460 |
| CLARITHROMYCIN | B | 341,383 | 47,787 (14.0%) | 13,291 (3.9%) | 1,026 (0.3%) | 57,180 (16.7%) | 11,743 (3.4%) | 210,356 |
| CLINDAMYCIN | B | 787,990 | 71,376 (9.1%) | 66,005 (8.4%) | 2,377 (0.3%) | 139,949 (17.8%) | 27,388 (3.5%) | 480,895 |
| CLOPIDOGREL | B | 1,066,528 | 229,886 (21.6%) | 70,450 (6.6%) | 1,176 (0.1%) | 101,255 (9.5%) | 27,528 (2.6%) | 636,233 |
| CLOXACILLIN | B | 75 | 21 (28.0%) | 5 (6.7%) | 0 (0.0%) | 11 (14.7%) | 2 (2.7%) | 36 |
| CLOZAPINE | B | 4,684 | 393 (8.4%) | 120 (2.6%) | 6 (0.1%) | 1,512 (32.3%) | 235 (5.0%) | 2,418 |
| CYCLOPHOSPHAMIDE OR IFOSPHAMIDE | B | 6,954 | 1,085 (15.6%) | 867 (12.5%) | 25 (0.4%) | 1,565 (22.5%) | 428 (6.2%) | 2,984 |
| DICLOXACILLIN | B | 135,905 | 18,326 (13.5%) | 10,250 (7.5%) | 504 (0.4%) | 22,998 (16.9%) | 5,056 (3.7%) | 78,771 |
| DOXORUBICIN | B | 371 | 71 (19.1%) | 25 (6.7%) | 4 (1.1%) | 108 (29.1%) | 11 (3.0%) | 152 |
| DULOXETINE | B | 558,051 | 49,749 (8.9%) | 30,744 (5.5%) | 598 (0.1%) | 85,794 (15.4%) | 19,302 (3.5%) | 371,864 |
| ENALAPRIL | B | 189,514 | 59,276 (31.3%) | 10,632 (5.6%) | 226 (0.1%) | 13,751 (7.3%) | 4,458 (2.4%) | 101,171 |
| ETANERCEPT | B | 30,487 | 4,334 (14.2%) | 1,284 (4.2%) | 29 (0.1%) | 4,185 (13.7%) | 2,432 (8.0%) | 18,223 |
| ETHIONAMIDE | B | 28 | 5 (17.9%) | 2 (7.1%) | 0 (0.0%) | 6 (21.4%) | 3 (10.7%) | 12 |
| FELBAMATE | B | 55 | 15 (27.3%) | 1 (1.8%) | 0 (0.0%) | 5 (9.1%) | 1 (1.8%) | 33 |
| FENOFIBRATE | B | 130,075 | 14,331 (11.0%) | 7,683 (5.9%) | 85 (0.1%) | 12,888 (9.9%) | 10,151 (7.8%) | 84,937 |
| FLUCONAZOLE | B | 475,801 | 70,384 (14.8%) | 24,317 (5.1%) | 2,321 (0.5%) | 74,979 (15.8%) | 16,154 (3.4%) | 287,646 |
| FLUVASTATIN | B | 122,739 | 17,177 (14.0%) | 6,718 (5.5%) | 73 (0.1%) | 8,185 (6.7%) | 6,911 (5.6%) | 83,675 |
| GLYBURIDE (GLIBENCLAMIDE) | B | 379,651 | 157,869 (41.6%) | 15,058 (4.0%) | 577 (0.2%) | 23,316 (6.1%) | 16,622 (4.4%) | 166,209 |
| HALOPERIDOL | B | 92,452 | 15,132 (16.4%) | 5,757 (6.2%) | 931 (1.0%) | 25,705 (27.8%) | 3,171 (3.4%) | 41,756 |
| IMATINIB | B | 6,848 | 1,462 (21.3%) | 496 (7.2%) | 23 (0.3%) | 1,202 (17.6%) | 299 (4.4%) | 3,366 |
| IMIPRAMINE | B | 35,014 | 6,728 (19.2%) | 1,383 (3.9%) | 28 (0.1%) | 4,365 (12.5%) | 959 (2.7%) | 21,551 |
| IRINOTECAN | B | 201 | 46 (22.9%) | 23 (11.4%) | 2 (1.0%) | 76 (37.8%) | 12 (6.0%) | 42 |
| ITRACONAZOLE | B | 24,490 | 4,290 (17.5%) | 887 (3.6%) | 48 (0.2%) | 2,954 (12.1%) | 934 (3.8%) | 15,377 |
| LAMOTRIGINE | B | 193,391 | 28,502 (14.7%) | 5,223 (2.7%) | 220 (0.1%) | 34,705 (17.9%) | 6,799 (3.5%) | 117,942 |
| LEFLUNOMIDE | B | 20,191 | 2,533 (12.5%) | 1,369 (6.8%) | 9 (0.0%) | 2,120 (10.5%) | 1,201 (5.9%) | 12,959 |
| LEVOFLOXACIN OR OFLOXACIN | B | 1,026,045 | 157,279 (15.3%) | 77,460 (7.5%) | 5,669 (0.6%) | 167,378 (16.3%) | 38,049 (3.7%) | 580,210 |
| LISINAPRIL | B | 3,136,396 | 1,142,174 (36.4%) | 111,659 (3.6%) | 2,736 (0.1%) | 228,030 (7.3%) | 86,788 (2.8%) | 1,565,009 |
| LOVASTATIN | B | 506,415 | 161,420 (31.9%) | 20,149 (4.0%) | 196 (0.0%) | 26,655 (5.3%) | 16,292 (3.2%) | 281,703 |
| MELPHALAN | B | 3,818 | 611 (16.0%) | 525 (13.8%) | 10 (0.3%) | 731 (19.1%) | 174 (4.6%) | 1,767 |

| Medication | Original Category ^a | No. Patients | <1 Year of Baseline | Baseline Anti-Coagulant Use | Baseline Severe Acute Liver Injury ^b | Pre-Existing Liver/Biliary Disease ^c | Other Baseline Evidence of Liver Injury ^d | Final Sample |
|-------------------------------|--------------------------------|--------------|---------------------|-----------------------------|---|---|--|--------------|
| METFORMIN | B | 1,505,207 | 450,240 (29.9%) | 59,320 (3.9%) | 1,234 (0.1%) | 114,232 (7.6%) | 81,263 (5.4%) | 798,918 |
| METHIMAZOLE (THIAMAZOLE) | B | 29,508 | 5,273 (17.9%) | 3,850 (13.0%) | 43 (0.1%) | 7,421 (25.1%) | 1,056 (3.6%) | 11,865 |
| MOXIFLOXACIN | B | 616,421 | 49,684 (8.1%) | 47,399 (7.7%) | 3,069 (0.5%) | 115,145 (18.7%) | 24,757 (4.0%) | 376,367 |
| NAPROXEN | B | 2,316,826 | 577,820 (24.9%) | 29,932 (1.3%) | 1,875 (0.1%) | 239,482 (10.3%) | 63,126 (2.7%) | 1,404,591 |
| NIFEDIPINE | B | 306,884 | 85,315 (27.8%) | 13,920 (4.5%) | 461 (0.2%) | 36,760 (12.0%) | 8,095 (2.6%) | 162,333 |
| OLANZAPINE | B | 199,009 | 40,365 (20.3%) | 7,716 (3.9%) | 653 (0.3%) | 46,631 (23.4%) | 5,319 (2.7%) | 98,325 |
| OMEPRAZOLE OR ESOMEPRAZOLE | B | 3,514,693 | 716,415 (20.4%) | 167,100 (4.8%) | 10,182 (0.3%) | 406,436 (11.6%) | 110,199 (3.1%) | 2,104,361 |
| OXACILLIN | B | 30 | 6 (20.0%) | 3 (10.0%) | 0 (0.0%) | 4 (13.3%) | 1 (3.3%) | 16 |
| OXALIPLATIN | B | 227 | 35 (15.4%) | 20 (8.8%) | 5 (2.2%) | 87 (38.3%) | 15 (6.6%) | 65 |
| PAROXETINE | B | 462,996 | 127,546 (27.5%) | 12,966 (2.8%) | 671 (0.1%) | 60,259 (13.0%) | 12,298 (2.7%) | 249,256 |
| PENICILLAMINE | B | 754 | 179 (23.7%) | 21 (2.8%) | 2 (0.3%) | 125 (16.6%) | 26 (3.4%) | 401 |
| PHENOBARBITAL | B | 10,693 | 3,892 (36.4%) | 354 (3.3%) | 79 (0.7%) | 2,119 (19.8%) | 320 (3.0%) | 3,929 |
| PIROXICAM | B | 218,154 | 50,727 (23.3%) | 2,649 (1.2%) | 142 (0.1%) | 23,061 (10.6%) | 6,636 (3.0%) | 134,939 |
| PROPAFENONE | B | 14,909 | 4,342 (29.1%) | 4,468 (30.0%) | 7 (0.0%) | 562 (3.8%) | 180 (1.2%) | 5,350 |
| QUININE | B | 83,432 | 19,499 (23.4%) | 4,677 (5.6%) | 228 (0.3%) | 6,995 (8.4%) | 2,795 (3.4%) | 49,238 |
| RANITIDINE | B | 1,658,068 | 434,338 (26.2%) | 66,015 (4.0%) | 3,646 (0.2%) | 189,216 (11.4%) | 52,829 (3.2%) | 912,024 |
| ROSUVASTATIN | B | 853,733 | 74,071 (8.7%) | 58,391 (6.8%) | 482 (0.1%) | 79,442 (9.3%) | 41,639 (4.9%) | 599,708 |
| SERTRALINE | B | 1,472,779 | 356,480 (24.2%) | 54,769 (3.7%) | 2,232 (0.2%) | 192,861 (13.1%) | 38,218 (2.6%) | 828,219 |
| STAVUDINE | B | 2,960 | 1,320 (44.6%) | 37 (1.3%) | 14 (0.5%) | 702 (23.7%) | 137 (4.6%) | 750 |
| TAMOXIFEN | B | 9,454 | 2,069 (21.9%) | 409 (4.3%) | 17 (0.2%) | 1,065 (11.3%) | 355 (3.8%) | 5,539 |
| TERBINAFINE | B | 404,848 | 54,941 (13.6%) | 16,270 (4.0%) | 197 (0.0%) | 36,835 (9.1%) | 13,418 (3.3%) | 283,187 |
| THIABENDAZOLE | B | 485 | 79 (16.3%) | 20 (4.1%) | 2 (0.4%) | 57 (11.8%) | 15 (3.1%) | 312 |
| THIORIDAZINE | B | 2,616 | 779 (29.8%) | 55 (2.1%) | 4 (0.2%) | 522 (20.0%) | 68 (2.6%) | 1,188 |
| VENLAFAXINE OR DEXVENLAFAXINE | B | 630,606 | 117,725 (18.7%) | 19,278 (3.1%) | 900 (0.1%) | 97,237 (15.4%) | 19,623 (3.1%) | 375,843 |
| VORICONAZOLE | B | 6,476 | 647 (10.0%) | 729 (11.3%) | 98 (1.5%) | 2,006 (31.0%) | 378 (5.8%) | 2,618 |
| ZIDOVUDINE | B | 12,800 | 7,542 (58.9%) | 92 (0.7%) | 37 (0.3%) | 1,961 (15.3%) | 385 (3.0%) | 2,783 |
| ABACAVIR | C | 11,239 | 2,162 (19.2%) | 296 (2.6%) | 59 (0.5%) | 3,670 (32.7%) | 705 (6.3%) | 4,347 |
| ACEBUTOLOL | C | 869 | 367 (42.2%) | 70 (8.1%) | 0 (0.0%) | 48 (5.5%) | 14 (1.6%) | 370 |
| ACITRETIN | C | 14,722 | 1,678 (11.4%) | 801 (5.4%) | 14 (0.1%) | 1,905 (12.9%) | 681 (4.6%) | 9,643 |
| ADALIMUMAB | C | 47,907 | 5,331 (11.1%) | 1,942 (4.1%) | 42 (0.1%) | 6,667 (13.9%) | 3,585 (7.5%) | 30,340 |
| ALBENDAZOLE | C | 4,990 | 441 (8.8%) | 207 (4.1%) | 7 (0.1%) | 730 (14.6%) | 162 (3.2%) | 3,443 |
| ALFUZOSIN | C | 137,641 | 7,463 (5.4%) | 11,041 (8.0%) | 198 (0.1%) | 18,716 (13.6%) | 3,707 (2.7%) | 96,516 |
| AMLODIPINE | C | 1,870,558 | 325,133 (17.4%) | 85,559 (4.6%) | 2,589 (0.1%) | 214,472 (11.5%) | 56,628 (3.0%) | 1,186,177 |
| AMPHETAMINE ^f | C | 111,061 | 28,032 (25.2%) | 999 (0.9%) | 45 (0.0%) | 9,673 (8.7%) | 2,931 (2.6%) | 69,381 |
| ANAKINRA | C | 939 | 60 (6.4%) | 151 (16.1%) | 1 (0.1%) | 220 (23.4%) | 83 (8.8%) | 424 |
| ATOMOXETINE | C | 30,506 | 4,307 (14.1%) | 360 (1.2%) | 25 (0.1%) | 6,269 (20.6%) | 856 (2.8%) | 18,689 |
| BOSENTAN | C | 475 | 44 (9.3%) | 162 (34.1%) | 1 (0.2%) | 52 (10.9%) | 17 (3.6%) | 199 |
| BUPROPION | C | 1,396,975 | 315,431 (22.6%) | 33,882 (2.4%) | 1,254 (0.1%) | 189,846 (13.6%) | 37,971 (2.7%) | 818,591 |
| CANDESARTAN | C | 37,949 | 14,182 (37.4%) | 2,549 (6.7%) | 24 (0.1%) | 1,758 (4.6%) | 1,170 (3.1%) | 18,266 |
| CEPHALEXIN | C | 1,849,301 | 233,375 (12.6%) | 140,475 (7.6%) | 4,467 (0.2%) | 261,521 (14.1%) | 62,085 (3.4%) | 1,147,378 |
| CITALOPRAM OR ESCITALOPRAM | C | 1,521,239 | 381,250 (25.1%) | 56,085 (3.7%) | 2,616 (0.2%) | 197,205 (13.0%) | 39,607 (2.6%) | 844,476 |
| CLOMIPHENE | C | 9,399 | 967 (10.3%) | 161 (1.7%) | 5 (0.1%) | 847 (9.0%) | 436 (4.6%) | 6,983 |

| Medication | Original Category ^a | No. Patients | <1 Year of Baseline | Baseline Anti-Coagulant Use | Baseline Severe Acute Liver Injury ^b | Pre-Existing Liver/Biliary Disease ^c | Other Baseline Evidence of Liver Injury ^d | Final Sample |
|---------------------------------------|--------------------------------|--------------|---------------------|-----------------------------|---|---|--|--------------|
| CYPROHEPTADINE | C | 113,968 | 15,139 (13.3%) | 4,963 (4.4%) | 392 (0.3%) | 24,235 (21.3%) | 4,000 (3.5%) | 65,239 |
| CYTARABINE | C | 90 | 15 (16.7%) | 7 (7.8%) | 1 (1.1%) | 28 (31.1%) | 10 (11.1%) | 29 |
| DIFLUNISAL | C | 7,148 | 1,462 (20.5%) | 110 (1.5%) | 10 (0.1%) | 1,091 (15.3%) | 238 (3.3%) | 4,237 |
| DILTIAZEM | C | 464,582 | 140,534 (30.2%) | 73,377 (15.8%) | 754 (0.2%) | 39,653 (8.5%) | 10,470 (2.3%) | 199,794 |
| DISOPYRAMIDE | C | 1,290 | 638 (49.5%) | 148 (11.5%) | 0 (0.0%) | 54 (4.2%) | 18 (1.4%) | 432 |
| DOXYCYCLINE | C | 1,600,292 | 169,947 (10.6%) | 111,376 (7.0%) | 3,075 (0.2%) | 238,256 (14.9%) | 53,738 (3.4%) | 1,023,900 |
| ERLOTINIB | C | 10,846 | 1,276 (11.8%) | 1,118 (10.3%) | 169 (1.6%) | 3,265 (30.1%) | 662 (6.1%) | 4,356 |
| ETODOLAC | C | 969,852 | 213,911 (22.1%) | 14,468 (1.5%) | 825 (0.1%) | 111,712 (11.5%) | 29,788 (3.1%) | 599,148 |
| ETOPOSIDE | C | 8,631 | 1,041 (12.1%) | 920 (10.7%) | 75 (0.9%) | 2,724 (31.6%) | 518 (6.0%) | 3,353 |
| EZETIMIBE | C | 235,425 | 17,380 (7.4%) | 19,307 (8.2%) | 155 (0.1%) | 20,429 (8.7%) | 13,552 (5.8%) | 164,602 |
| FAMOTIDINE | C | 419,185 | 25,977 (6.2%) | 34,578 (8.2%) | 934 (0.2%) | 68,191 (16.3%) | 13,156 (3.1%) | 276,349 |
| FLAVOCOXID | C | 7 | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 7 |
| FLUOROURACIL | C | 3,391 | 440 (13.0%) | 269 (7.9%) | 57 (1.7%) | 981 (28.9%) | 128 (3.8%) | 1,516 |
| FLUOXETINE | C | 739,640 | 176,154 (23.8%) | 19,878 (2.7%) | 979 (0.1%) | 101,688 (13.7%) | 20,344 (2.8%) | 420,597 |
| GABAPENTIN | C | 2,252,034 | 342,175 (15.2%) | 115,491 (5.1%) | 4,056 (0.2%) | 319,421 (14.2%) | 76,793 (3.4%) | 1,394,098 |
| GEFITINIB | C | 1,557 | 337 (21.6%) | 168 (10.8%) | 6 (0.4%) | 323 (20.7%) | 122 (7.8%) | 601 |
| GEMCITABINE | C | 494 | 50 (10.1%) | 55 (11.1%) | 24 (4.9%) | 121 (24.5%) | 26 (5.3%) | 218 |
| GEMFIBROZIL | C | 587,462 | 157,106 (26.7%) | 22,746 (3.9%) | 307 (0.1%) | 43,693 (7.4%) | 34,543 (5.9%) | 329,067 |
| GLIMEPIRIDE | C | 62,092 | 9,203 (14.8%) | 4,783 (7.7%) | 36 (0.1%) | 6,366 (10.3%) | 3,387 (5.5%) | 38,317 |
| GLIPIZIDE | C | 898,704 | 214,707 (23.9%) | 49,644 (5.5%) | 1,307 (0.1%) | 80,959 (9.0%) | 51,564 (5.7%) | 500,523 |
| HYDROXYUREA | C | 15,271 | 3,239 (21.2%) | 1,331 (8.7%) | 37 (0.2%) | 2,215 (14.5%) | 623 (4.1%) | 7,826 |
| INDOMETHACIN | C | 473,544 | 80,568 (17.0%) | 14,685 (3.1%) | 558 (0.1%) | 57,891 (12.2%) | 17,383 (3.7%) | 302,459 |
| IRBESARTAN | C | 160,548 | 60,609 (37.8%) | 8,741 (5.4%) | 75 (0.0%) | 7,484 (4.7%) | 4,300 (2.7%) | 79,339 |
| ISOTRETINOIN | C | 6,957 | 1,325 (19.0%) | 152 (2.2%) | 1 (0.0%) | 649 (9.3%) | 263 (3.8%) | 4,567 |
| KETOPROFEN | C | 3,071 | 575 (18.7%) | 39 (1.3%) | 5 (0.2%) | 482 (15.7%) | 103 (3.4%) | 1,867 |
| LABETALOL | C | 39,597 | 8,930 (22.6%) | 2,229 (5.6%) | 126 (0.3%) | 7,951 (20.1%) | 1,103 (2.8%) | 19,258 |
| LANSOPRAZOLE OR DEXLANSOPRAZOLE | C | 300,473 | 113,878 (37.9%) | 13,738 (4.6%) | 942 (0.3%) | 29,051 (9.7%) | 8,372 (2.8%) | 134,492 |
| LENALIDOMIDE OR THALIDOMIDE | C | 18,282 | 2,568 (14.0%) | 2,448 (13.4%) | 65 (0.4%) | 4,090 (22.4%) | 920 (5.0%) | 8,191 |
| LEVETIRACETAM | C | 122,058 | 15,834 (13.0%) | 12,152 (10.0%) | 677 (0.6%) | 25,650 (21.0%) | 4,477 (3.7%) | 63,268 |
| LEVOCETIRIZINE OR CETIRIZINE | C | 1,192,714 | 145,266 (12.2%) | 54,860 (4.6%) | 1,265 (0.1%) | 141,075 (11.8%) | 41,787 (3.5%) | 808,461 |
| LINEZOLID | C | 43,911 | 3,078 (7.0%) | 7,806 (17.8%) | 734 (1.7%) | 14,578 (33.2%) | 1,912 (4.4%) | 15,803 |
| LOSARTAN | C | 911,311 | 147,112 (16.1%) | 58,968 (6.5%) | 683 (0.1%) | 88,238 (9.7%) | 31,734 (3.5%) | 584,576 |
| MELOXICAM | C | 1,460,153 | 201,441 (13.8%) | 26,555 (1.8%) | 1,074 (0.1%) | 174,849 (12.0%) | 49,583 (3.4%) | 1,006,651 |
| MESALAMINE ^g | C | 51,216 | 14,544 (28.4%) | 2,073 (4.0%) | 59 (0.1%) | 5,146 (10.0%) | 1,453 (2.8%) | 27,941 |
| METHOXSALEN | C | 1,655 | 316 (19.1%) | 55 (3.3%) | 2 (0.1%) | 215 (13.0%) | 81 (4.9%) | 986 |
| METHYLPHENIDATE OR DEXMETHYLPHENIDATE | C | 133,323 | 27,643 (20.7%) | 3,298 (2.5%) | 234 (0.2%) | 16,056 (12.0%) | 4,506 (3.4%) | 81,586 |
| METRONIDAZOLE | C | 744,282 | 97,625 (13.1%) | 43,180 (5.8%) | 8,057 (1.1%) | 144,301 (19.4%) | 27,453 (3.7%) | 423,666 |
| MEXILETINE | C | 8,149 | 1,272 (15.6%) | 2,265 (27.8%) | 31 (0.4%) | 894 (11.0%) | 264 (3.2%) | 3,423 |
| MIRTAZAPINE | C | 923,157 | 144,052 (15.6%) | 45,156 (4.9%) | 2,856 (0.3%) | 193,171 (20.9%) | 25,519 (2.8%) | 512,403 |
| MITOMYCIN | C | 3,382 | 149 (4.4%) | 307 (9.1%) | 9 (0.3%) | 519 (15.3%) | 88 (2.6%) | 2,310 |
| MONTELUKAST | C | 370,563 | 60,782 (16.4%) | 18,331 (4.9%) | 155 (0.0%) | 31,936 (8.6%) | 11,584 (3.1%) | 247,775 |
| NATALIZUMAB | C | 85 | 3 (3.5%) | 3 (3.5%) | 0 (0.0%) | 4 (4.7%) | 8 (9.4%) | 67 |

| Medication | Original Category ^a | No. Patients | <1 Year of Baseline | Baseline Anti-Coagulant Use | Baseline Severe Acute Liver Injury ^b | Pre-Existing Liver/Biliary Disease ^c | Other Baseline Evidence of Liver Injury ^d | Final Sample |
|------------------|--------------------------------|--------------|---------------------|-----------------------------|---|---|--|--------------|
| NEFAZODONE | C | 33,492 | 11,519 (34.4%) | 511 (1.5%) | 49 (0.1%) | 5,585 (16.7%) | 762 (2.3%) | 15,066 |
| NILUTAMIDE | C | 5,249 | 754 (14.4%) | 339 (6.5%) | 6 (0.1%) | 540 (10.3%) | 373 (7.1%) | 3,237 |
| NORFLOXACIN | C | 1,472 | 296 (20.1%) | 93 (6.3%) | 158 (10.7%) | 306 (20.8%) | 22 (1.5%) | 597 |
| ORLISTAT | C | 29,945 | 2,335 (7.8%) | 1,340 (4.5%) | 13 (0.0%) | 3,193 (10.7%) | 1,872 (6.3%) | 21,192 |
| OXAPROZIN | C | 28,023 | 7,594 (27.1%) | 311 (1.1%) | 24 (0.1%) | 2,836 (10.1%) | 805 (2.9%) | 16,453 |
| PANTOPRAZOLE | C | 919,491 | 96,858 (10.5%) | 77,955 (8.5%) | 4,924 (0.5%) | 157,557 (17.1%) | 31,925 (3.5%) | 550,272 |
| PENICILLIN G | C | 403,922 | 54,329 (13.5%) | 16,449 (4.1%) | 761 (0.2%) | 71,602 (17.7%) | 12,322 (3.1%) | 248,459 |
| PHENELZINE | C | 849 | 190 (22.4%) | 18 (2.1%) | 0 (0.0%) | 147 (17.3%) | 24 (2.8%) | 470 |
| PIOGLITAZONE | C | 186,247 | 24,799 (13.3%) | 8,928 (4.8%) | 67 (0.0%) | 15,368 (8.3%) | 10,883 (5.8%) | 126,202 |
| PRAVASTATIN | C | 844,799 | 112,631 (13.3%) | 47,043 (5.6%) | 618 (0.1%) | 84,087 (10.0%) | 37,614 (4.5%) | 562,806 |
| PREGABALIN | C | 257,043 | 14,819 (5.8%) | 20,611 (8.0%) | 458 (0.2%) | 45,372 (17.7%) | 10,432 (4.1%) | 165,351 |
| PROCAINAMIDE | C | 2,625 | 1,089 (41.5%) | 484 (18.4%) | 5 (0.2%) | 118 (4.5%) | 50 (1.9%) | 879 |
| PROCHLORPERAZINE | C | 348,765 | 49,764 (14.3%) | 25,088 (7.2%) | 3,639 (1.0%) | 85,303 (24.5%) | 17,192 (4.9%) | 167,779 |
| PYRIMETHAMINE | C | 658 | 132 (20.1%) | 30 (4.6%) | 4 (0.6%) | 210 (31.9%) | 44 (6.7%) | 238 |
| QUETIAPINE | C | 608,240 | 104,880 (17.2%) | 21,821 (3.6%) | 1,439 (0.2%) | 129,971 (21.4%) | 16,944 (2.8%) | 333,185 |
| RAMIPRIL | C | 48,531 | 15,319 (31.6%) | 3,408 (7.0%) | 27 (0.1%) | 2,550 (5.3%) | 1,143 (2.4%) | 26,084 |
| RISPERIDONE | C | 372,844 | 69,691 (18.7%) | 13,362 (3.6%) | 943 (0.3%) | 78,623 (21.1%) | 10,844 (2.9%) | 199,381 |
| RITONAVIR | C | 22,023 | 4,219 (19.2%) | 362 (1.6%) | 88 (0.4%) | 12,116 (55.0%) | 714 (3.2%) | 4,524 |
| ROSIGLITAZONE | C | 218,052 | 53,118 (24.4%) | 11,085 (5.1%) | 101 (0.0%) | 10,790 (4.9%) | 9,819 (4.5%) | 133,139 |
| SORAFENIB | C | 9,781 | 730 (7.5%) | 633 (6.5%) | 439 (4.5%) | 6,995 (71.5%) | 134 (1.4%) | 850 |
| TEMOZOLOMIDE | C | 6,185 | 969 (15.7%) | 436 (7.0%) | 20 (0.3%) | 1,133 (18.3%) | 442 (7.1%) | 3,185 |
| TOLCAPONE | C | 179 | 62 (34.6%) | 6 (3.4%) | 0 (0.0%) | 7 (3.9%) | 1 (0.6%) | 103 |
| TOPIRAMATE | C | 348,245 | 50,140 (14.4%) | 10,868 (3.1%) | 407 (0.1%) | 55,179 (15.8%) | 13,187 (3.8%) | 218,464 |
| TRASTUZUMAB | C | 18 | 5 (27.8%) | 1 (5.6%) | 0 (0.0%) | 5 (27.8%) | 0 (0.0%) | 7 |
| TRAZODONE | C | 1,800,672 | 407,636 (22.6%) | 71,004 (3.9%) | 4,169 (0.2%) | 272,567 (15.1%) | 51,677 (2.9%) | 993,619 |
| VANCOMYCIN | C | 55,603 | 3,380 (6.1%) | 10,622 (19.1%) | 1,172 (2.1%) | 19,382 (34.9%) | 2,003 (3.6%) | 19,044 |
| VERAPAMIL | C | 165,822 | 67,832 (40.9%) | 7,196 (4.3%) | 95 (0.1%) | 11,564 (7.0%) | 3,715 (2.2%) | 75,420 |
| VINCRISTINE | C | 336 | 64 (19.0%) | 38 (11.3%) | 3 (0.9%) | 85 (25.3%) | 13 (3.9%) | 133 |
| ZAFIRLUKAST | C | 9,175 | 2,936 (32.0%) | 274 (3.0%) | 2 (0.0%) | 492 (5.4%) | 211 (2.3%) | 5,260 |

^a Original category as defined by Björnsson and Hoofnagle, *Hepatology* 2016;63:590-603. Medications listed in the National Institutes of Health LiverTox database were classified into categories of likelihood for causing acute liver injury based on the number of published reports of hepatotoxicity (category A, ≥50 cases; category B, 12-49 cases; category C, 4-11 cases).

^b Baseline severe acute liver injury defined as total bilirubin >2.0 mg/dL plus either alanine aminotransferase >120 U/L or international normalized ratio ≥1.5 prior to the index date.

^c Pre-existing liver/biliary disease defined as 1) a laboratory diagnosis of hepatitis B or hepatitis C viral infection, or 2) a liver/biliary diagnostic code (see Supplement Table 2) prior to the index date.

^d Other baseline evidence of liver injury defined as any of the following during the baseline period: 1) two alanine aminotransferases ≥40 U/L separated by at least six months, 2) one elevated alanine aminotransferase >100 U/L, or 3) one alkaline phosphatase >172 mg/dL.

^e Represents groups of medications.

^f Includes amphetamine, dextroamphetamine, lisdexamfetamine, and methamphetamine.

^g Includes mesalamine, balsalazide, and olsalazine.

eTable 7. Age-/sex-adjusted incidence rates of severe acute liver injury among initiators of 91 medications that were not included in the primary analysis because either the width of the 95% confidence interval for the severe acute liver injury incidence rate was ≥ 3 times the point estimate or there was $<10,000$ person-years of follow-up present.

| Medication | Original Category ^a | No. Initiators | Age (y), Median (IQR) | Male, n (%) | No. Person-Years | No. Events | Adjusted IR ^b (95% CI), Events/10,000 Person-Years |
|---|--------------------------------|----------------|-----------------------|-----------------|------------------|------------|---|
| DIDANOSINE | A | 890 | 47.6 (41.2-54.9) | 865 (97.2%) | 410 | 2 | 43.4 (10.8-174.4) |
| NEVIRAPINE | A | 1,003 | 49.3 (42.1-56.6) | 975 (97.2%) | 435 | 2 | 38.8 (9.6-156.0) |
| PYRAZINAMIDE | A | 1,934 | 64.1 (55.9-74.2) | 1,869 (96.6%) | 252 | 1 | 24.7 (3.5-176.1) |
| LINEZOLID | C | 15,803 | 65.9 (57.2-75.3) | 14,965 (94.7%) | 651 | 1 | 9.7 (1.4-69.2) |
| CYCLOPHOSPHAMIDE OR IFOSPHAMIDE | B | 2,984 | 69.9 (62.6-76.6) | 2,822 (94.6%) | 812 | 1 | 7.3 (1.0-52.0) |
| TICLOPIDINE | A | 2,137 | 71.8 (63.1-78.5) | 2,087 (97.7%) | 831 | 1 | 6.7 (0.9-47.9) |
| QUINIDINE | A | 2,926 | 70.2 (61.1-77.1) | 2,793 (95.5%) | 963 | 1 | 6.1 (0.9-43.4) |
| RITONAVIR | C | 4,524 | 50.3 (42.6-57.9) | 4,279 (94.6%) | 1,974 | 1 | 4.3 (0.6-30.5) |
| ERYTHROMYCIN | A | 77,098 | 61.1 (51.2-71.0) | 68,911 (89.4%) | 3,454 | 2 | 4.1 (1.0-16.6) |
| NEFAZODONE | C | 15,066 | 53.5 (46.4-59.3) | 13,550 (89.9%) | 4,354 | 2 | 3.7 (0.9-14.9) |
| ABACAVIR | C | 4,347 | 52.8 (43.7-60.7) | 4,191 (96.4%) | 2,206 | 1 | 3.6 (0.5-26.0) |
| TAMOXIFEN | B | 5,539 | 59.3 (48.7-70.8) | 2,412 (43.5%) | 2,543 | 1 | 3.6 (0.5-25.6) |
| RIFAMPIN | A | 25,327 | 61.6 (51.8-70.5) | 23,568 (93.1%) | 3,744 | 2 | 3.4 (0.9-13.8) |
| ITRACONAZOLE | B | 15,377 | 59.8 (48.5-69.3) | 14,220 (92.5%) | 2,169 | 1 | 3.2 (0.5-22.9) |
| CHLORZOXAZONE | B | 23,328 | 57.4 (47.6-69.2) | 21,242 (91.1%) | 2,425 | 1 | 3.1 (0.4-21.9) |
| DICLOXACILLIN | B | 78,771 | 61.2 (51.7-71.4) | 73,116 (92.8%) | 2,682 | 1 | 2.5 (0.4-18.1) |
| PENICILLIN G | C | 248,459 | 56.2 (45.5-65.2) | 222,982 (89.7%) | 7,447 | 2 | 2.0 (0.5-8.2) |
| HYDROXYUREA | C | 7,826 | 74.0 (66.5-81.0) | 7,555 (96.5%) | 3,286 | 1 | 1.6 (0.2-11.6) |
| HALOPERIDOL | B | 41,756 | 64.6 (50.4-79.6) | 38,154 (91.4%) | 8,415 | 2 | 1.6 (0.4-6.3) |
| SULFASALAZINE | A | 26,335 | 62.6 (52.9-70.7) | 23,409 (88.9%) | 8,732 | 2 | 1.6 (0.4-6.2) |
| CIMETIDINE | B | 22,115 | 61.7 (52.1-72.1) | 20,141 (91.1%) | 5,574 | 1 | 1.2 (0.2-8.4) |
| LABETALOL | C | 19,258 | 64.5 (54.3-74.2) | 16,926 (87.9%) | 7,620 | 1 | 0.8 (0.1-5.9) |
| ETANERCEPT | B | 18,223 | 60.6 (50.9-68.1) | 15,958 (87.6%) | 9,254 | 1 | 0.8 (0.1-5.6) |
| AURANOFIN OR GOLD PRODUCTS ^c | A | 149 | 63.6 (56.6-72.0) | 136 (91.3%) | 46 | 0 | .. ^d |
| BUSULFAN | A | 60 | 73.9 (68.4-80.4) | 57 (95.0%) | 17 | 0 | .. ^d |
| DANTROLENE | A | 1,744 | 57.1 (47.2-66.7) | 1,530 (87.7%) | 451 | 0 | .. ^d |
| EFAVIRENZ | A | 9,233 | 76.9 (70.3-82.0) | 9,216 (99.8%) | 2,453 | 0 | .. ^d |
| FLUTAMIDE | A | 1,114 | 55.4 (43.4-64.0) | 992 (89.0%) | 151 | 0 | .. ^d |
| INFLIXIMAB | A | 3,673 | 49.7 (40.8-57.9) | 2,790 (76.0%) | 1,858 | 0 | .. ^d |
| INTERFERON- β | A | 2,843 | 62.0 (38.5-74.6) | 1,772 (62.3%) | 1,065 | 0 | .. ^d |
| METHYLDOPA | A | 1,942 | 64.0 (51.4-75.1) | 1,581 (81.4%) | 607 | 0 | .. ^d |
| PROPYLTHIOURACIL | A | 17 | 61.8 (58.2-74.8) | 14 (82.4%) | 0 | 0 | .. ^d |
| TELITHROMYCIN | A | 38 | 67.8 (56.9-72.9) | 35 (92.1%) | 6 | 0 | .. ^d |

| Medication | Original Category ^a | No. Initiators | Age (y), Median (IQR) | Male, n (%) | No. Person-Years | No. Events | Adjusted IR ^b (95% CI), Events/10,000 Person-Years |
|------------------------------|--------------------------------|----------------|-----------------------|----------------|------------------|------------|---|
| THIOGUANINE | A | 9 | 62.2 (39.7-68.0) | 9 (100.0%) | 1 | 0 | .. ^d |
| ASPARAGINASE OR PEGASPARGASE | B | 22,281 | 43.0 (31.7-57.5) | 18,973 (85.2%) | 214 | 0 | .. ^d |
| CEFTRIAXONE | B | 111 | 70.3 (58.3-78.1) | 105 (94.6%) | 45 | 0 | .. ^d |
| CHLORPROPAMIDE | B | 36 | 56.8 (49.6-69.0) | 36 (100.0%) | 1 | 0 | .. ^d |
| CLOXACILLIN | B | 2,418 | 53.7 (44.3-61.1) | 2,143 (88.6%) | 1,061 | 0 | .. ^d |
| CLOZAPINE | B | 152 | 69.8 (59.2-76.2) | 133 (87.5%) | 18 | 0 | .. ^d |
| DOXORUBICIN | B | 12 | 66.8 (60.0-76.1) | 12 (100.0%) | 2 | 0 | .. ^d |
| ETHIONAMIDE | B | 33 | 53.4 (45.4-67.9) | 31 (93.9%) | 8 | 0 | .. ^d |
| FELBAMATE | B | 3,366 | 70.2 (62.6-77.9) | 3,242 (96.3%) | 1,770 | 0 | .. ^d |
| IMATINIB | B | 21,551 | 62.8 (51.0-73.7) | 18,559 (86.1%) | 6,669 | 0 | .. ^d |
| IMIPRAMINE | B | 42 | 69.8 (58.4-77.3) | 39 (92.9%) | 9 | 0 | .. ^d |
| IRINOTECAN | B | 12,959 | 64.8 (56.4-71.8) | 10,968 (84.6%) | 5,535 | 0 | .. ^d |
| LEFLUNOMIDE | B | 1,767 | 76.3 (70.7-81.3) | 1,741 (98.5%) | 214 | 0 | .. ^d |
| MELPHALAN | B | 16 | 68.6 (58.7-77.8) | 16 (100.0%) | 0 | 0 | .. ^d |
| OXACILLIN | B | 65 | 68.0 (60.9-75.0) | 64 (98.5%) | 11 | 0 | .. ^d |
| OXALIPLATIN | B | 401 | 57.5 (48.0-67.9) | 362 (90.3%) | 48 | 0 | .. ^d |
| PENICILLAMINE | B | 3,929 | 61.2 (51.0-72.5) | 3,554 (90.5%) | 1,095 | 0 | .. ^d |
| PHENOBARBITAL | B | 5,350 | 73.5 (66.2-80.0) | 5,185 (96.9%) | 2,302 | 0 | .. ^d |
| PROPAFENONE | B | 312 | 62.8 (54.0-71.3) | 296 (94.9%) | 8 | 0 | .. ^d |
| THIABENDAZOLE | B | 1,188 | 58.3 (51.4-71.0) | 1,100 (92.6%) | 312 | 0 | .. ^d |
| THIORIDAZINE | B | 2,618 | 67.2 (60.4-73.0) | 2,503 (95.6%) | 602 | 0 | .. ^d |
| VORICONAZOLE | B | 2,783 | 48.7 (40.7-55.8) | 2,409 (86.6%) | 765 | 0 | .. ^d |
| ZIDOVUDINE | B | 370 | 71.3 (62.9-78.2) | 336 (90.8%) | 183 | 0 | .. ^d |
| ACEBUTOLOL | C | 9,643 | 64.2 (55.0-71.6) | 9,047 (93.8%) | 2,935 | 0 | .. ^d |
| ACITRETIN | C | 3,443 | 54.6 (39.0-66.1) | 2,831 (82.2%) | 100 | 0 | .. ^d |
| ALBENDAZOLE | C | 424 | 61.7 (51.8-70.8) | 384 (90.6%) | 108 | 0 | .. ^d |
| ANAKINRA | C | 18,689 | 37.9 (31.6-48.9) | 14,851 (79.5%) | 4,876 | 0 | .. ^d |
| ATOMOXETINE | C | 199 | 69.9 (63.6-76.8) | 185 (93.0%) | 71 | 0 | .. ^d |
| BOSENTAN | C | 6,983 | 36.8 (31.6-45.8) | 3,795 (54.3%) | 1,817 | 0 | .. ^d |
| CLOMIPHENE | C | 29 | 71.2 (59.3-76.1) | 28 (96.6%) | 4 | 0 | .. ^d |
| CYTARABINE | C | 4,237 | 59.1 (51.1-69.9) | 3,912 (92.3%) | 880 | 0 | .. ^d |
| DIFLUNISAL | C | 432 | 69.6 (59.6-77.5) | 404 (93.5%) | 181 | 0 | .. ^d |
| DISOPYRAMIDE | C | 3,353 | 67.7 (62.1-73.7) | 3,228 (96.3%) | 376 | 0 | .. ^d |
| ETOPOSIDE | C | 7 | 69.2 (42.5-79.6) | 4 (57.1%) | 1 | 0 | .. ^d |
| FLAVOCOXID | C | 1,516 | 67.8 (61.2-75.1) | 1,464 (96.6%) | 156 | 0 | .. ^d |
| FLUOROURACIL | C | 601 | 70.8 (63.5-76.7) | 595 (99.0%) | 150 | 0 | .. ^d |
| GEFITINIB | C | 218 | 71.5 (64.2-76.9) | 218 (100.0%) | 18 | 0 | .. ^d |
| GEMCITABINE | C | 4,567 | 36.9 (29.8-51.7) | 3,267 (71.5%) | 1,445 | 0 | .. ^d |

| Medication | Original Category ^a | No. Initiators | Age (y), Median (IQR) | Male, n (%) | No. Person-Years | No. Events | Adjusted IR ^b (95% CI), Events/10,000 Person-Years |
|---------------|--------------------------------|----------------|-----------------------|----------------|------------------|------------|---|
| ISOTRETINOIN | C | 1,867 | 55.9 (46.6-65.5) | 1,647 (88.2%) | 324 | 0 | .. ^d |
| KETOPROFEN | C | 986 | 63.7 (54.7-73.0) | 926 (93.9%) | 203 | 0 | .. ^d |
| METHOXSALEN | C | 3,423 | 70.0 (61.2-77.0) | 3,314 (96.8%) | 1,265 | 0 | .. ^d |
| MEXILETINE | C | 2,310 | 71.9 (64.9-79.2) | 2,270 (98.3%) | 75 | 0 | .. ^d |
| MITOMYCIN | C | 67 | 45.9 (39.4-52.8) | 46 (68.7%) | 9 | 0 | .. ^d |
| NATALIZUMAB | C | 3,237 | 77.0 (70.1-82.6) | 3,237 (100.0%) | 1,039 | 0 | .. ^d |
| NILUTAMIDE | C | 597 | 68.3 (58.4-77.0) | 559 (93.6%) | 26 | 0 | .. ^d |
| NORFLOXACIN | C | 21,192 | 55.2 (46.2-62.4) | 15,529 (73.3%) | 5,373 | 0 | .. ^d |
| ORLISTAT | C | 16,453 | 57.2 (48.5-67.7) | 15,088 (91.7%) | 4,396 | 0 | .. ^d |
| OXAPROZIN | C | 470 | 55.5 (44.9-63.9) | 404 (86.0%) | 130 | 0 | .. ^d |
| PHENELZINE | C | 879 | 73.3 (66.7-78.1) | 873 (99.3%) | 251 | 0 | .. ^d |
| PROCAINAMIDE | C | 238 | 55.7 (44.9-65.0) | 217 (91.2%) | 40 | 0 | .. ^d |
| PYRIMETHAMINE | C | 850 | 68.1 (62.2-76.4) | 829 (97.5%) | 224 | 0 | .. ^d |
| SORAFENIB | C | 3,185 | 66.0 (58.3-73.0) | 3,070 (96.4%) | 549 | 0 | .. ^d |
| TEMOZOLOMIDE | C | 103 | 70.2 (64.8-75.8) | 102 (99.0%) | 44 | 0 | .. ^d |
| TOLCAPONE | C | 7 | 53.3 (49.2-61.5) | 1 (14.3%) | 1 | 0 | .. ^d |
| TRASTUZUMAB | C | 19,044 | 69.7 (60.0-78.6) | 17,122 (89.9%) | 1,166 | 0 | .. ^d |
| VANCOMYCIN | C | 133 | 69.9 (59.3-77.2) | 130 (97.7%) | 18 | 0 | .. ^d |
| VINCRISTINE | C | 5,260 | 66.3 (55.0-75.5) | 4,611 (87.7%) | 2,017 | 0 | .. ^d |
| ZAFIRLUKAST | C | 149 | 63.6 (56.6-72.0) | 136 (91.3%) | 46 | 0 | .. ^d |

Abbreviations: CI=confidence interval; IQR=interquartile range; IR=incidence rate

^a Original category as defined by Björnsson and Hoofnagle, *Hepatology* 2016;63:590-603. Medications listed in the National Institutes of Health LiverTox database were classified into categories of likelihood for causing acute liver injury based on the number of published reports of hepatotoxicity (category A, ≥50 cases; category B, 12-49 cases; category C, 4-11 cases).

^b Incidence rates adjusted for age and sex.

^c Represents groups of medications.

^d No events were observed among initiators of this medication. Thus, no unadjusted or adjusted incidence rates were calculated.

eTable 8. Incidence rates of severe acute liver injury for Group 3-5 medications with ≥4 published reports of hepatotoxicity (categories A, B, C).

| Medication | Original Category ^a | No. Initiators | Age (y), Median (IQR) | Male, n (%) | No. Person-Years | No. Events | Adjusted IR ^b (95% CI), Events/10,000 Person-Years |
|---|--------------------------------|----------------|-----------------------|-------------------|------------------|------------|---|
| GROUP 3 (3.0-4.9 events/10,000 person-years) | | | | | | | |
| CYPROHEPTADINE | C | 65,239 | 58.3 (44.9-70.6) | 57,982 (88.9%) | 14,625 | 10 | 4.96 (2.6-9.3) |
| ESTROGENS OR PROGESTINS ^c | A | 179,681 | 56.8 (37.7-75.7) | 91,232 (50.8%) | 48,270 | 24 | 4.9 (3.3-7.4) |
| METHIMAZOLE (THIAMAZOLE) | B | 11,865 | 64.4 (53.1-73.8) | 9,884 (83.3%) | 4,546 | 3 | 4.4 (1.4-13.6) |
| AMIODARONE | A | 96,808 | 73.9 (67.0-80.7) | 95,618 (98.8%) | 32,303 | 25 | 4.0 (2.6-6.0) |
| AZITHROMYCIN | B | 1,303,960 | 60.9 (48.9-70.3) | 1,163,672 (89.2%) | 24,105 | 14 | 4.0 (2.3-6.8) |
| HYDRALAZINE OR ISOSORBIDE DINITRATE | A | 158,674 | 70.6 (62.9-78.7) | 153,010 (96.4%) | 63,745 | 43 | 3.8 (2.7-5.2) |
| CEPHALEXIN | C | 1,147,378 | 62.5 (51.9-71.9) | 1,053,891 (91.9%) | 33,037 | 18 | 3.7 (2.3-5.9) |
| GROUP 4 (1.0-2.9 events/10,000 person-years) | | | | | | | |
| DOXYCYCLINE | C | 1,023,900 | 62.4 (50.5-71.3) | 922,978 (90.1%) | 58,035 | 23 | 2.7 (1.8-4.2) |
| CARBAMAZEPINE | A | 68,500 | 58.0 (46.8-68.9) | 60,661 (88.6%) | 19,733 | 7 | 2.6 (1.2-5.5) |
| LANSOPRAZOLE OR DEXLANSOPRAZOLE | C | 134,492 | 65.9 (54.4-74.9) | 125,021 (93.0%) | 44,590 | 18 | 2.6 (1.6-4.2) |
| CLINDAMYCIN | B | 480,895 | 60.6 (50.2-69.3) | 429,305 (89.3%) | 14,492 | 5 | 2.5 (1.0-5.9) |
| NITROFURANTOIN | A | 219,951 | 67.0 (54.8-76.0) | 152,562 (69.4%) | 10,896 | 4 | 2.3 (0.9-6.1) |
| PHENYTOIN OR FOSPHENYTOIN | A | 31,844 | 66.0 (55.6-76.3) | 30,452 (95.6%) | 11,500 | 4 | 2.1 (0.8-5.7) |
| QUININE | B | 49,238 | 70.4 (60.0-77.6) | 47,261 (96.0%) | 16,697 | 6 | 2.1 (0.9-4.7) |
| IRBESARTAN | C | 79,339 | 69.9 (60.0-76.8) | 76,544 (96.5%) | 45,193 | 16 | 2.1 (1.3-3.5) |
| RAMIPRIL | C | 26,084 | 70.5 (61.4-77.5) | 25,478 (97.7%) | 14,030 | 5 | 2.1 (0.8-5.0) |
| ADALIMUMAB | C | 30,340 | 59.1 (46.8-67.7) | 26,295 (86.7%) | 15,390 | 4 | 2.0 (0.7-5.3) |
| RANITIDINE | B | 912,024 | 61.7 (50.2-71.8) | 826,157 (90.6%) | 287,636 | 84 | 1.9 (1.5-2.5) |
| AMOXICILLIN | B | 1,092,193 | 60.4 (49.3-69.8) | 984,698 (90.2%) | 33,475 | 9 | 1.9 (1.0-3.7) |
| ENALAPRIL | B | 101,171 | 69.3 (60.1-77.5) | 98,353 (97.2%) | 53,213 | 17 | 1.9 (1.1-3.0) |
| ALLOPURINOL | A | 324,944 | 67.7 (59.4-75.6) | 319,514 (98.3%) | 158,458 | 49 | 1.8 (1.4-2.5) |
| PIROXICAM | B | 134,939 | 57.6 (48.2-67.0) | 121,920 (90.4%) | 40,917 | 9 | 1.6 (0.8-3.1) |
| RISPERIDONE | C | 199,381 | 56.6 (44.6-70.3) | 179,219 (89.9%) | 60,785 | 13 | 1.5 (0.9-2.7) |
| AMITRIPTYLINE | B | 379,687 | 56.2 (44.7-66.1) | 327,028 (86.1%) | 105,547 | 21 | 1.5 (1.0-2.4) |
| TRAZODONE | C | 993,619 | 56.9 (43.2-67.7) | 877,287 (88.3%) | 275,521 | 53 | 1.4 (1.1-1.9) |
| OMEPRAZOLE OR ESOMEPRAZOLE | B | 2,104,361 | 63.8 (52.8-73.9) | 1,941,156 (92.2%) | 892,075 | 198 | 1.4 (1.2-1.7) |
| FAMOTIDINE | C | 276,349 | 64.0 (50.5-72.7) | 238,542 (86.3%) | 81,739 | 17 | 1.3 (0.8-2.2) |
| LEVETIRACETAM | C | 63,268 | 66.2 (55.4-75.4) | 58,253 (92.1%) | 23,307 | 5 | 1.3 (0.6-3.2) |
| SULINDAC | A | 155,519 | 58.8 (48.6-68.8) | 141,261 (90.8%) | 33,910 | 6 | 1.3 (0.6-2.8) |
| MESALAMINE ^d | C | 27,941 | 64.0 (50.6-73.2) | 25,374 (90.8%) | 10,441 | 2 | 1.2 (0.3-5.0) |
| OLANZAPINE | B | 98,325 | 55.7 (43.8-69.4) | 87,821 (89.3%) | 29,886 | 5 | 1.2 (0.5-3.0) |
| INDOMETHACIN | C | 302,459 | 59.9 (49.6-68.7) | 282,558 (93.4%) | 29,322 | 5 | 1.2 (0.5-3.0) |
| GLYBURIDE (GLIBENCLAMIDE) | B | 166,209 | 65.1 (57.7-74.2) | 161,212 (97.0%) | 89,497 | 17 | 1.2 (0.7-1.9) |

| Medication | Original Category ^a | No. Initiators | Age (y), Median (IQR) | Male, n (%) | No. Person-Years | No. Events | Adjusted IR ^b (95% CI), Events/10,000 Person-Years |
|--|--------------------------------|----------------|-----------------------|-------------------|------------------|------------|---|
| CLOPIDOGREL | B | 636,233 | 71.4 (64.0-78.6) | 623,472 (98.0%) | 350,863 | 74 | 1.2 (0.9-1.5) |
| PREGABALIN | C | 165,351 | 62.0 (51.3-70.0) | 142,408 (86.1%) | 61,718 | 10 | 1.1 (0.6-2.1) |
| MIRTAZAPINE | C | 512,403 | 58.1 (44.0-69.7) | 461,055 (90.0%) | 155,849 | 25 | 1.1 (0.8-1.7) |
| NAPROXEN | B | 1,404,591 | 56.3 (43.8-66.4) | 1,254,033 (89.3%) | 245,252 | 37 | 1.1 (0.8-1.6) |
| PAROXETINE | B | 249,256 | 56.3 (43.0-67.7) | 218,123 (87.5%) | 88,672 | 13 | 1.1 (0.6-1.9) |
| METHYLPHENIDATE OR DEXMETHYLPHENIDATE | C | 81,586 | 43.9 (32.7-58.2) | 66,950 (82.1%) | 27,650 | 3 | 1.1 (0.3-3.3) |
| GLIPIZIDE | C | 500,523 | 66.5 (59.2-74.3) | 481,992 (96.3%) | 272,608 | 47 | 1.0 (0.8-1.4) |
| SERTRALINE | B | 828,219 | 56.9 (41.4-68.6) | 729,176 (88.0%) | 313,499 | 44 | 1.0 (0.8-1.4) |
| LAMOTRIGINE | B | 117,942 | 48.8 (36.5-60.2) | 90,808 (77.0%) | 45,088 | 5 | 1.0 (0.4-2.5) |
| CITALOPRAM OR ESCITALOPRAM | C | 844,476 | 57.5 (43.5-69.3) | 742,613 (87.9%) | 314,401 | 44 | 1.0 (0.7-1.4) |
| DILTIAZEM | C | 199,794 | 69.8 (60.7-78.0) | 190,111 (95.2%) | 98,831 | 17 | 1.0 (0.6-1.6) |
| GROUP 5 (<1.0 event/10,000 person-years) | | | | | | | |
| ATORVASTATIN | A | 1,543,771 | 65.8 (57.3-72.0) | 1,457,503 (94.4%) | 789,334 | 124 | 0.99 (0.8-1.2) |
| FLUVASTATIN | B | 83,675 | 65.7 (57.9-74.2) | 80,025 (95.6%) | 37,870 | 6 | 0.99 (0.4-2.2) |
| LISINAPRIL | B | 1,565,009 | 65.1 (56.5-74.1) | 1,492,448 (95.4%) | 829,033 | 128 | 0.97 (0.8-1.2) |
| LOVASTATIN | B | 281,703 | 65.6 (57.0-74.3) | 269,335 (95.6%) | 141,138 | 22 | 0.97 (0.6-1.5) |
| PANTOPRAZOLE | C | 550,272 | 65.1 (53.2-73.5) | 492,381 (89.5%) | 231,547 | 35 | 0.97 (0.7-1.4) |
| GLIMEPIRIDE | C | 38,317 | 68.9 (60.1-74.1) | 36,400 (95.0%) | 19,176 | 3 | 0.9 (0.3-3.0) |
| IBUPROFEN | A | 1,479,820 | 54.6 (41.1-65.1) | 1,302,237 (88.0%) | 191,047 | 21 | 0.9 (0.6-1.3) |
| SIMVASTATIN | A | 1,567,669 | 63.2 (54.9-72.8) | 1,488,844 (95.0%) | 834,140 | 111 | 0.9 (0.7-1.1) |
| VERAPAMIL | C | 75,420 | 59.2 (46.5-70.5) | 65,035 (86.2%) | 33,473 | 4 | 0.8 (0.3-2.2) |
| DICLOFENAC | A | 567,401 | 56.4 (44.7-65.8) | 500,659 (88.2%) | 122,557 | 13 | 0.8 (0.5-1.4) |
| ETODOLAC | C | 599,148 | 57.4 (47.0-67.0) | 543,326 (90.7%) | 127,177 | 14 | 0.8 (0.5-1.4) |
| GABAPENTIN | C | 1,394,098 | 61.9 (50.6-71.1) | 1,260,443 (90.4%) | 419,066 | 48 | 0.8 (0.6-1.0) |
| ROSIGLITAZONE | C | 133,139 | 66.6 (58.2-74.4) | 130,183 (97.8%) | 75,718 | 9 | 0.7 (0.4-1.4) |
| CELECOXIB | B | 140,508 | 60.6 (49.4-70.8) | 121,732 (86.6%) | 39,466 | 4 | 0.7 (0.3-1.9) |
| FLUOXETINE | C | 420,597 | 54.2 (39.6-65.1) | 354,870 (84.4%) | 159,871 | 14 | 0.7 (0.4-1.2) |
| LOSARTAN | C | 584,576 | 68.0 (60.0-75.3) | 551,935 (94.4%) | 334,509 | 39 | 0.7 (0.5-1.0) |
| LEVOCETIRIZINE OR CETIRIZINE | C | 808,461 | 60.2 (46.4-69.4) | 686,286 (84.9%) | 229,431 | 22 | 0.7 (0.5-1.1) |
| QUETIAPINE | C | 333,185 | 56.1 (43.0-68.2) | 297,253 (89.2%) | 105,147 | 10 | 0.7 (0.4-1.3) |
| MONTELUKAST | C | 247,775 | 62.3 (49.0-71.7) | 207,118 (83.6%) | 103,942 | 10 | 0.7 (0.4-1.2) |
| DULOXETINE | B | 371,864 | 57.5 (44.4-68.1) | 310,439 (83.5%) | 141,362 | 12 | 0.7 (0.4-1.2) |
| VENLAFAXINE OR DEXVENLAFAXINE | B | 375,843 | 53.5 (40.0-64.0) | 311,482 (82.9%) | 137,264 | 11 | 0.7 (0.4-1.2) |
| BUPROPION | C | 818,591 | 53.9 (40.8-62.8) | 714,446 (87.3%) | 237,022 | 18 | 0.6 (0.4-1.0) |
| ALFUZOSIN | C | 96,516 | 70.1 (64.9-77.5) | 96,200 (99.7%) | 43,850 | 5 | 0.6 (0.3-1.5) |
| VALPROATE | A | 230,237 | 52.1 (38.7-63.3) | 215,936 (88.5%) | 76,549 | 6 | 0.6 (0.3-1.4) |
| METFORMIN | B | 798,918 | 64.1 (56.1-71.4) | 750,342 (93.9%) | 415,935 | 40 | 0.6 (0.4-0.9) |
| ROSUVASTATIN | B | 599,708 | 65.5 (59.1-73.0) | 568,282 (94.8%) | 320,330 | 32 | 0.6 (0.4-0.9) |

| Medication | Original Category ^a | No. Initiators | Age (y), Median (IQR) | Male, n (%) | No. Person-Years | No. Events | Adjusted IR ^b (95% CI), Events/10,000 Person-Years |
|----------------------------------|--------------------------------|----------------|-----------------------|-------------------|------------------|------------|---|
| ANDROGENIC STEROIDS ^c | A | 127,937 | 59.9 (50.4-66.6) | 126,880 (99.2%) | 57,806 | 5 | 0.6 (0.3-1.5) |
| PRAVASTATIN | C | 562,806 | 65.5 (58.5-73.7) | 529,419 (94.1%) | 279,100 | 28 | 0.6 (0.4-0.9) |
| AMLODIPINE | C | 1,186,177 | 67.6 (59.5-76.3) | 1,128,097 (95.1%) | 662,083 | 68 | 0.6 (0.5-0.8) |
| METHOTREXATE | A | 56,115 | 63.4 (53.5-71.4) | 48,821 (87.0%) | 25,134 | 2 | 0.5 (0.1-2.2) |
| GEMFIBROZIL | C | 329,067 | 60.9 (53.0-69.5) | 317,133 (96.4%) | 150,507 | 11 | 0.5 (0.3-0.9) |
| NIFEDIPINE | B | 162,333 | 67.6 (58.3-75.9) | 153,224 (94.4%) | 80,493 | 6 | 0.4 (0.2-1.0) |
| FENOFIBRATE | B | 81,251 | 62.4 (55.3-69.2) | 82,031 (96.6%) | 45,060 | 3 | 0.4 (0.1-1.4) |
| MELOXICAM | C | 1,006,651 | 58.4 (45.8-67.5) | 886,004 (88.0%) | 266,967 | 16 | 0.4 (0.3-0.7) |
| EZETIMIBE | C | 164,602 | 67.3 (59.5-73.9) | 157,046 (95.4%) | 84,786 | 6 | 0.4 (0.2-1.0) |
| TOPIRAMATE | C | 218,464 | 48.5 (37.3-59.5) | 160,502 (73.5%) | 67,429 | 3 | 0.4 (0.1-1.3) |
| TERBINAFINE | B | 283,187 | 60.9 (50.5-69.5) | 262,266 (92.6%) | 54,510 | 3 | 0.4 (0.1-1.2) |
| AMPHETAMINE ^e | C | 69,381 | 37.1 (30.8-48.3) | 54,758 (78.9%) | 32,364 | 1 | 0.4 (0.0-2.5) |
| PIOGLITAZONE | C | 126,202 | 66.3 (59.6-73.2) | 121,842 (96.5%) | 69,919 | 4 | 0.4 (0.1-0.9) |
| ACARBOSE | B | 50,400 | 65.8 (59.5-73.1) | 48,778 (96.8%) | 20,253 | 1 | 0.3 (0.0-2.2) |
| MINOCYCLINE | A | 97,526 | 61.4 (47.4-69.9) | 84,792 (86.9%) | 14,161 | 0 | .. ^f |
| CANDESARTAN | C | 18,266 | 70.8 (61.4-77.3) | 17,433 (95.4%) | 11,037 | 0 | .. ^f |

Abbreviations: CI=confidence interval; IQR=interquartile range; IR=incidence rate

^a Original category as defined by Björnsson and Hoofnagle, *Hepatology* 2016;63:590-603. Medications listed in the National Institutes of Health LiverTox database were classified into categories of likelihood for causing acute liver injury based on the number of published reports of hepatotoxicity (category A, ≥50 cases; category B, 12-49 cases; category C, 4-11 cases).

^b Incidence rates adjusted for age and sex.

^c Represents a group of medications.

^d Includes mesalamine, balsalazide, and olsalazine.

^e Includes amphetamine, dextroamphetamine, lisdexamfetamine, and methamphetamine.

^f No events were observed among initiators of this medication. Thus, no unadjusted or adjusted incidence rates were calculated.

eTable 9. Incidence rates of severe acute liver injury, by sex, for medications with rates that could be estimated with sufficient precision.

| Medication | Group in Primary Analysis | Males | | | | | Females | | | | |
|--------------------------------------|---------------------------|----------------|------------------|------------|---|-------|----------------|------------------|------------|---|-------|
| | | No. Initiators | No. Person-Years | No. Events | Adjusted IR ^a (95% CI), Events/10,000 Person-Years | Group | No. Initiators | No. Person-Years | No. Events | Adjusted IR ^a (95% CI), Events/10,000 Person-Years | Group |
| ESTROGENS OR PROGESTINS ^b | 3 | 91,232 | 18,018 | 24 | 10.4 (6.9-15.5) | 1 | 88,449 | 30,252 | 0 | .. ^c | 5 |
| RANITIDINE | 4 | 826,157 | 265,716 | 83 | 2.9 (2.3-3.6) | 4 | 85,867 | 21,920 | 1 | 0.4 (0.1-2.9) | 5 |
| AMITRIPTYLINE | 4 | 327,028 | 91,956 | 20 | 2.2 (1.4-3.5) | 4 | 52,659 | 13,591 | 1 | 0.7 (0.1-5.2) | 5 |
| OMEPRAZOLE OR ESOMEPRAZOLE | 4 | 1,941,156 | 837,894 | 193 | 2.1 (1.8-2.4) | 4 | 163,205 | 54,181 | 5 | 0.8 (0.3-1.9) | 5 |
| TRAZODONE | 4 | 877,287 | 245,666 | 50 | 2.1 (1.6-2.7) | 4 | 116,332 | 29,855 | 3 | 0.98 (0.3-3.1) | 5 |
| PAROXETINE | 4 | 218,123 | 78,319 | 13 | 1.7 (1.0-2.9) | 4 | 31,133 | 10,352 | 0 | .. ^c | 5 |
| CLOPIDOGREL | 4 | 623,472 | 344,556 | 71 | 1.7 (1.3-2.1) | 4 | 12,761 | 6,307 | 3 | 2.8 (0.8-9.2) | 4 |
| NAPROXEN | 4 | 1,254,033 | 222,983 | 34 | 1.6 (1.1-2.2) | 4 | 150,558 | 22,269 | 3 | 1.3 (0.4-4.1) | 4 |
| MIRTAZAPINE | 4 | 461,055 | 141,992 | 22 | 1.5 (1.0-2.3) | 4 | 51,348 | 13,857 | 3 | 1.9 (0.6-6.1) | 4 |
| CITALOPRAM OR ESCITALOPRAM | 4 | 742,613 | 278,449 | 42 | 1.5 (1.1-2.0) | 4 | 101,863 | 35,952 | 2 | 0.5 (0.1-2.2) | 5 |
| SERTRALINE | 4 | 729,176 | 278,073 | 41 | 1.5 (1.1-2.0) | 4 | 99,043 | 35,426 | 3 | 0.8 (0.3-2.6) | 5 |
| ATORVASTATIN | 5 | 1,457,503 | 749,553 | 119 | 1.4 (1.2-1.7) | 4 | 86,268 | 39,781 | 5 | 0.9 (0.4-2.3) | 5 |
| LISINAPRIL | 5 | 1,492,448 | 794,836 | 125 | 1.4 (1.2-1.7) | 4 | 72,561 | 34,197 | 3 | 0.7 (0.2-2.1) | 5 |
| PANTOPRAZOLE | 5 | 492,381 | 210,433 | 32 | 1.4 (1.0-1.9) | 4 | 57,891 | 21,115 | 3 | 1.2 (0.4-3.7) | 4 |
| LAMOTRIGINE | 4 | 90,808 | 35,008 | 4 | 1.3 (0.5-3.6) | 4 | 27,134 | 10,080 | 1 | 1.1 (0.1-7.5) | 4 |
| SIMVASTATIN | 5 | 1,488,844 | 796,535 | 109 | 1.3 (1.0-1.5) | 4 | 78,825 | 37,605 | 2 | 0.4 (0.1-1.7) | 5 |
| IBUPROFEN | 5 | 1,302,237 | 170,620 | 19 | 1.2 (0.8-1.9) | 4 | 177,583 | 20,427 | 2 | 1.0 (0.3-4.0) | 4 |
| GABAPENTIN | 5 | 1,260,443 | 384,095 | 48 | 1.2 (0.9-1.6) | 4 | 133,655 | 34,971 | 0 | .. ^c | 5 |
| DICLOFENAC | 5 | 500,659 | 110,353 | 12 | 1.1 (0.6-2.0) | 4 | 66,742 | 12,204 | 1 | 0.8 (0.1-5.5) | 5 |
| LEVOCETIRIZINE OR CETIRIZINE | 5 | 686,286 | 195,897 | 22 | 1.1 (0.7-1.7) | 4 | 122,175 | 33,534 | 0 | .. ^c | 5 |
| LOSARTAN | 5 | 551,935 | 317,594 | 39 | 1.1 (0.8-1.4) | 4 | 32,641 | 16,915 | 0 | .. ^c | 5 |
| FLUOXETINE | 5 | 354,870 | 135,746 | 13 | 1.0 (0.6-1.8) | 4 | 65,727 | 24,125 | 1 | 0.4 (0.1-3.1) | 5 |
| QUETIAPINE | 5 | 297,253 | 94,321 | 9 | 0.96 (0.5-1.8) | 5 | 35,932 | 10,826 | 1 | 0.9 (0.1-6.4) | 5 |
| DULOXETINE | 5 | 310,439 | 117,976 | 11 | 0.96 (0.5-1.7) | 5 | 61,425 | 23,386 | 1 | 0.4 (0.1-2.8) | 5 |
| VENLAFAXINE OR DEXVENLAFAXINE | 5 | 311,482 | 114,536 | 10 | 0.9 (0.5-1.8) | 5 | 64,361 | 22,728 | 1 | 0.4 (0.1-3.1) | 5 |
| METFORMIN | 5 | 750,342 | 394,222 | 40 | 0.9 (0.7-1.3) | 5 | 48,576 | 21,713 | 0 | .. ^c | 5 |
| BUPROPION | 5 | 714,446 | 204,314 | 17 | 0.9 (0.6-1.5) | 5 | 104,145 | 32,708 | 1 | 0.3 (0.0-2.2) | 5 |
| PRAVASTATIN | 5 | 529,419 | 264,211 | 28 | 0.9 (0.6-1.4) | 5 | 33,387 | 14,889 | 0 | .. ^c | 5 |
| MONTELUKAST | 5 | 207,118 | 88,836 | 9 | 0.9 (0.5-1.8) | 5 | 40,657 | 15,105 | 1 | 0.6 (0.1-4.2) | 5 |
| ROSUVASTATIN | 5 | 568,282 | 305,723 | 32 | 0.9 (0.7-1.3) | 5 | 31,426 | 14,607 | 0 | .. ^c | 5 |
| AMLODIPINE | 5 | 1,128,097 | 633,967 | 66 | 0.9 (0.7-1.1) | 5 | 58,080 | 28,115 | 2 | 0.5 (0.1-2.0) | 5 |
| MELOXICAM | 5 | 886,004 | 238,328 | 15 | 0.6 (0.4-1.0) | 5 | 120,647 | 28,638 | 1 | 0.3 (0.0-2.2) | 5 |
| TOPIRAMATE | 5 | 160,502 | 49,193 | 2 | 0.5 (0.1-1.9) | 5 | 57,962 | 18,236 | 1 | 0.6 (0.1-4.2) | 5 |

Abbreviations: CI=confidence interval; IQR=interquartile range; IR=incidence rate

^a Incidence rates adjusted for age.

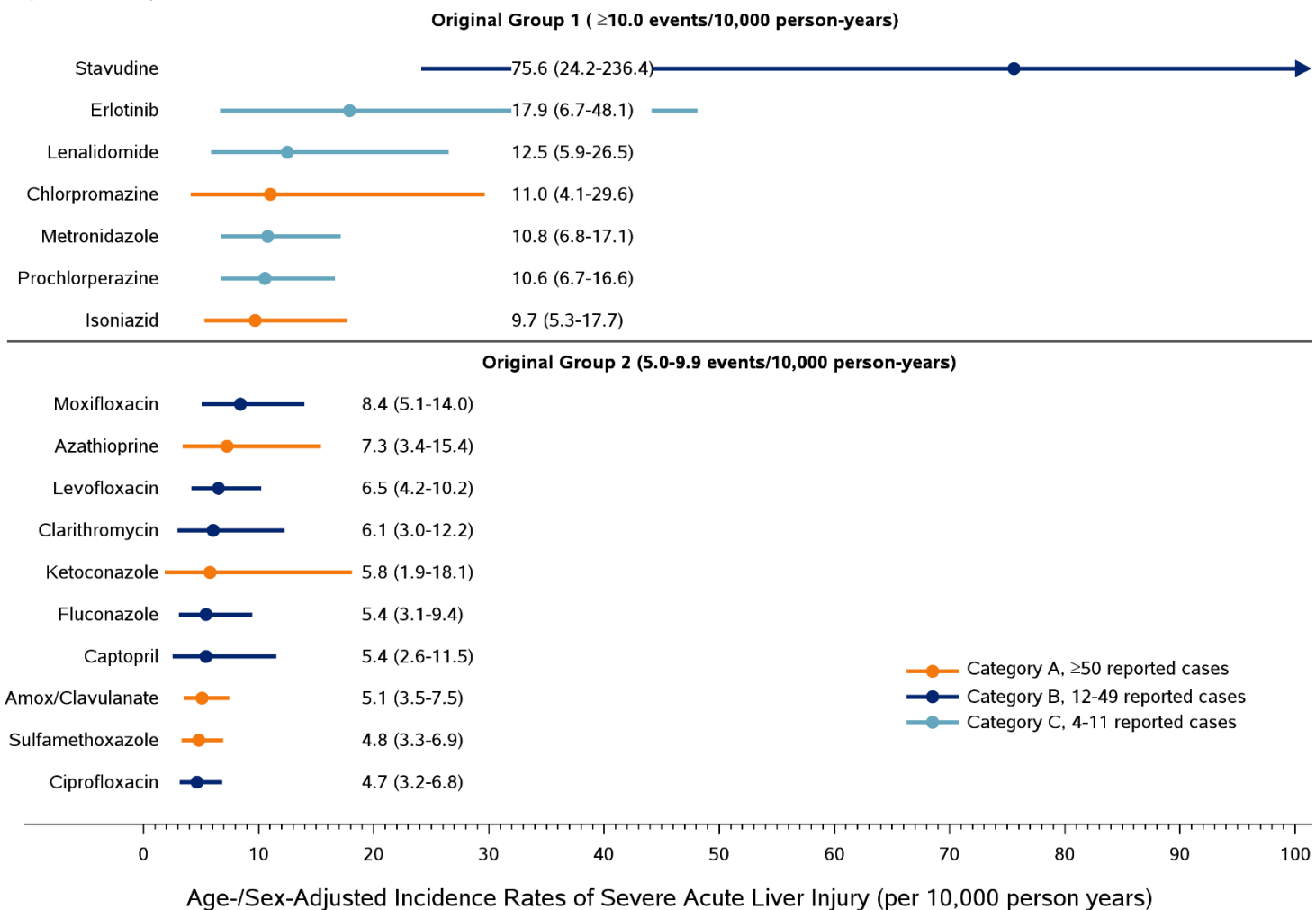
^b Represents a group of medications.

^c No events were observed among initiators of this medication. Thus, no unadjusted or adjusted incidence rates were calculated.

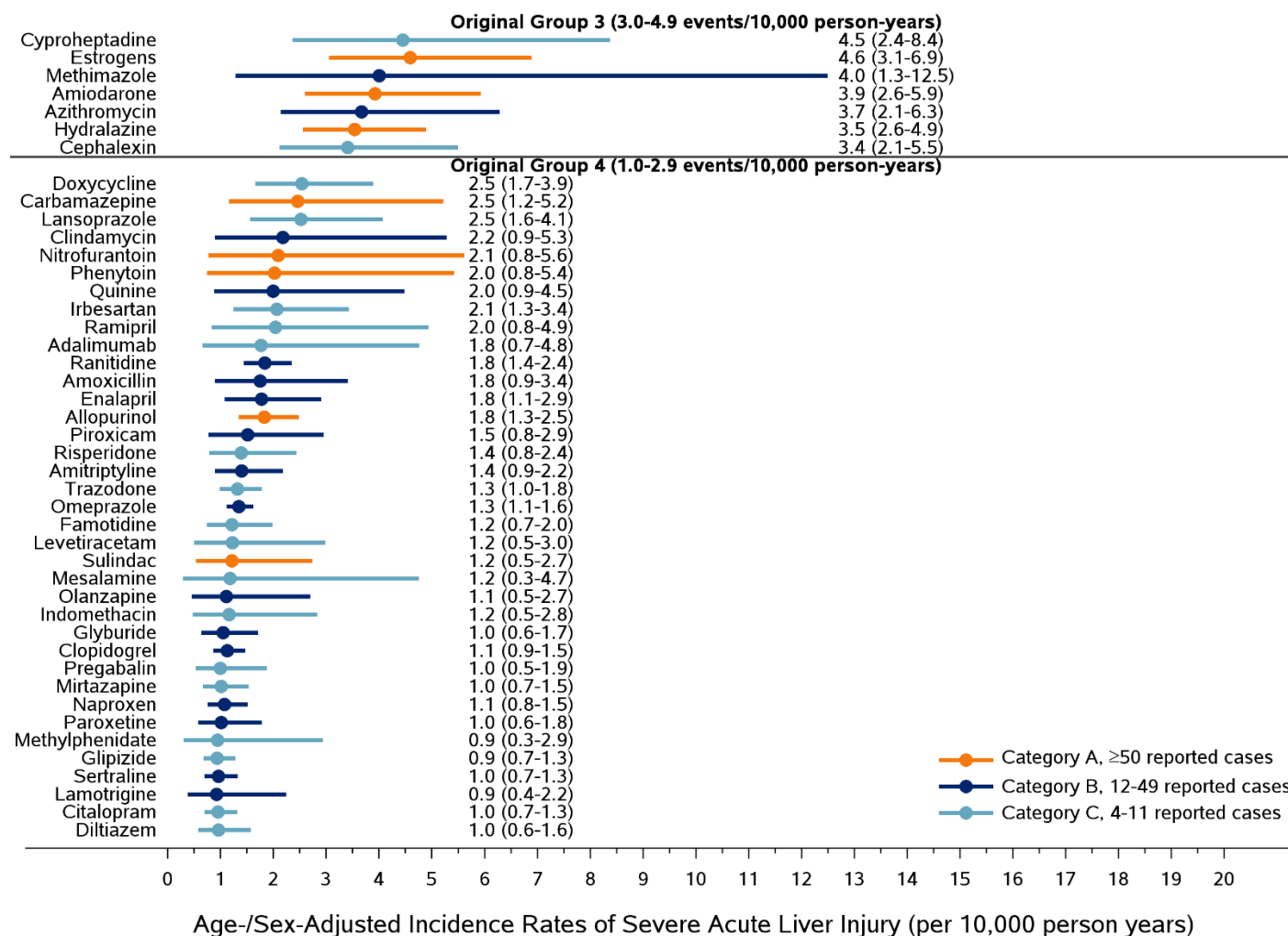
eTable 10. Most common Group 1 and Group 2 medications that were additionally dispensed within 90 days of initiation of each medication of interest.

| Medication | No. (%) with Additional Group 1-2 Medications | No. (%) with Top Co-Medication #1 | No. (%) with Top Co-Medication #2 | No. (%) with Top Co-Medication #3 |
|------------------|---|--|--|--|
| Stavudine | 350/750 (46.7%) | Sulfamethoxazole: 261/750 (34.8%) | Fluconazole: 115/750 (15.3%) | Levofloxacin: 31/750 (4.1%) |
| Erlotinib | 1,275/4,356 (29.3%) | Prochlorperazine: 648/4,356 (14.9%) | Moxifloxacin: 271/4,356 (6.2%) | Clavulanate: 190/4,356 (4.4%) |
| Lenalidomide | 1,724/8,191 (21.0%) | Prochlorperazine: 640/8,191 (7.8%) | Sulfamethoxazole: 527/8,191 (6.4%) | Clavulanate: 195/8,191 (2.4%) |
| Chlorpromazine | 3,021/17,449 (17.3%) | Prochlorperazine: 945/17,449 (5.4%) | Clavulanate: 568/17,449 (3.3%) | Ciprofloxacin: 543/17,449 (3.1%) |
| Metronidazole | 196,118/423,666 (46.3%) | Ciprofloxacin: 99,401/423,666 (23.5%) | Clarithromycin: 23,462/423,666 (5.5%) | Sulfamethoxazole: 21,775/423,666 (5.1%) |
| Prochlorperazine | 34,723/167,779 (20.7%) | Ciprofloxacin: 8,525/167,779 (5.1%) | Clavulanate: 7,723/167,779 (4.6%) | Sulfamethoxazole: 7,532/167,779 (4.5%) |
| Isoniazid | 2,716/20,476 (13.3%) | Ciprofloxacin: 586/20,476 (2.9%) | Sulfamethoxazole: 577/20,476 (2.8%) | Clavulanate: 559/20,476 (2.7%) |
| Moxifloxacin | 55,969/376,367 (14.9%) | Clavulanate: 19,892/376,367 (5.3%) | Sulfamethoxazole: 12,134/376,367 (3.2%) | Ciprofloxacin: 11,972/376,367 (3.2%) |
| Azathioprine | 2,612/16,033 (16.3%) | Sulfamethoxazole: 988/16,033 (6.2%) | Metronidazole: 719/16,033 (4.5%) | Ciprofloxacin: 538/16,033 (3.4%) |
| Levofloxacin | 96,843/580,210 (16.7%) | Clavulanate: 27,289/580,210 (4.7%) | Sulfamethoxazole: 25,671/580,210 (4.4%) | Ciprofloxacin: 17,291/580,210 (3.0%) |
| Clarithromycin | 44,076/210,356 (21.0%) | Metronidazole: 23,422/210,356 (11.1%) | Clavulanate: 6,696/210,356 (3.2%) | Ciprofloxacin: 4,327/210,356 (2.1%) |
| Ketoconazole | 3,701/29,976 (12.3%) | Sulfamethoxazole: 793/29,976 (2.6%) | Clavulanate: 785/29,976 (2.6%) | Ciprofloxacin: 753/29,976 (2.5%) |
| Fluconazole | 81,378/287,646 (28.3%) | Metronidazole: 19,932/287,646 (6.9%) | Sulfamethoxazole: 19,207/287,646 (6.7%) | Clavulanate: 19,187/287,646 (6.7%) |
| Captopril | 1,687/18,863 (8.9%) | Levofloxacin: 549/18,863 (2.9%) | Clavulanate: 318/18,863 (1.7%) | Sulfamethoxazole: 315/18,863 (1.7%) |
| Clavulanate | 117,457/1,235,143 (9.5%) | Sulfamethoxazole: 33,562/1,235,143 (2.7%) | Ciprofloxacin: 30,151/1,235,143 (2.4%) | Levofloxacin: 17,197/1,235,143 (1.4%) |
| Sulfamethoxazole | 148,344/1,025,123 (14.5%) | Ciprofloxacin: 52,528/1,025,123 (5.1%) | Clavulanate: 41,050/1,025,123 (4.0%) | Levofloxacin: 18,316/1,025,123 (1.8%) |
| Ciprofloxacin | 198,842/1,125,460 (17.7%) | Metronidazole: 79,864/1,125,460 (7.1%) | Sulfamethoxazole: 54,166/1,125,460 (4.8%) | Clavulanate: 36,391/1,125,460 (3.2%) |

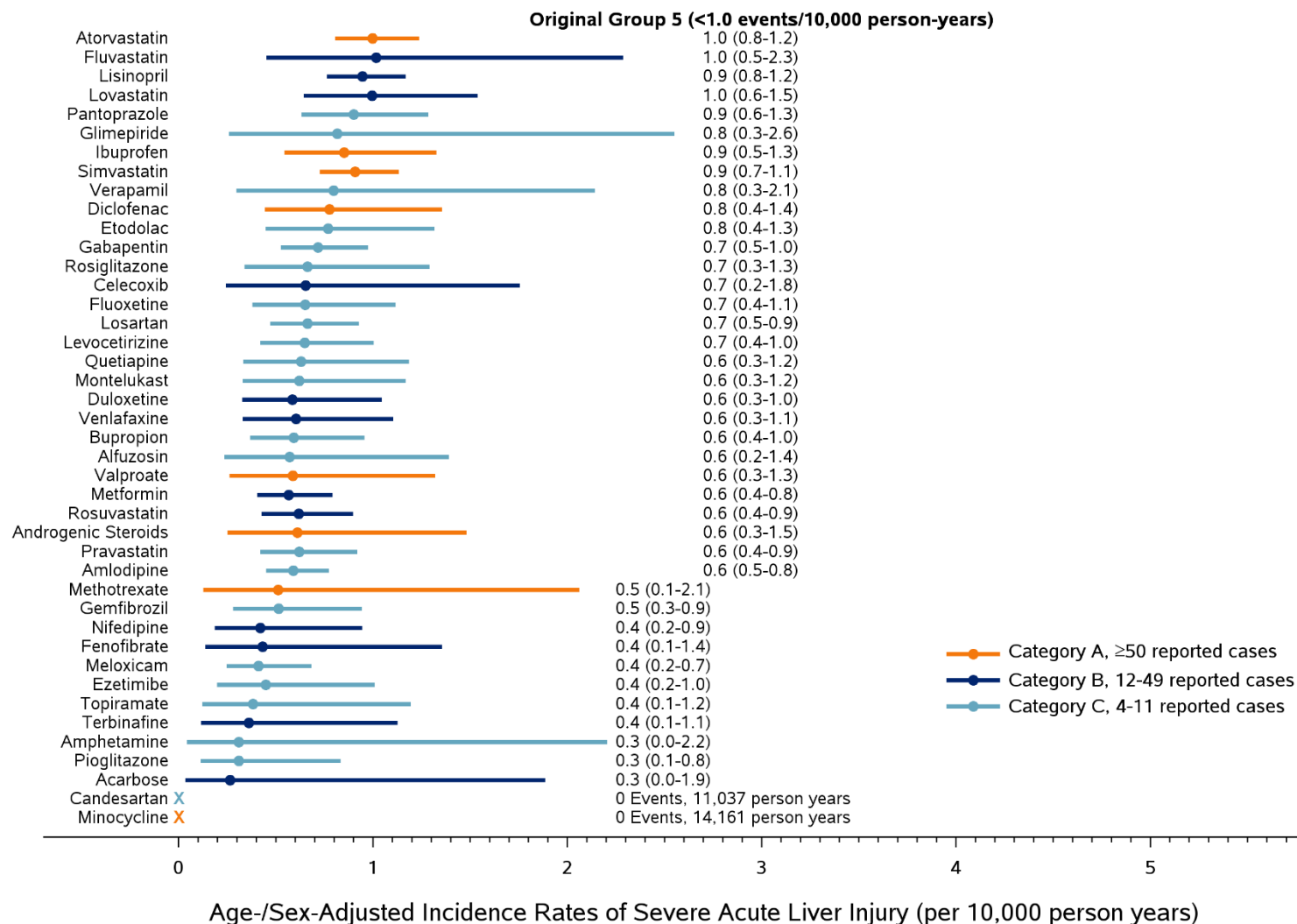
eFigure 1. Rates of severe acute liver injury for Group 1-2 initiators additionally adjusted for metabolic comorbidities. Age-/sex-adjusted incidence rates of severe acute liver injury (per 10,000 person years and with 95% confidence intervals) are reported for medications classified in Group 1 (≥ 10.0 events/10,000 person-years) and Group 2 (5.0-9.9 events/10,000 person-years) in the primary analysis after additionally adjusting for diabetes mellitus, hyperlipidemia, and obesity (body mass index >30 kg/m²). Colors represent the categories of likelihood to cause severe acute liver injury based on numbers of published case reports of hepatotoxicity.



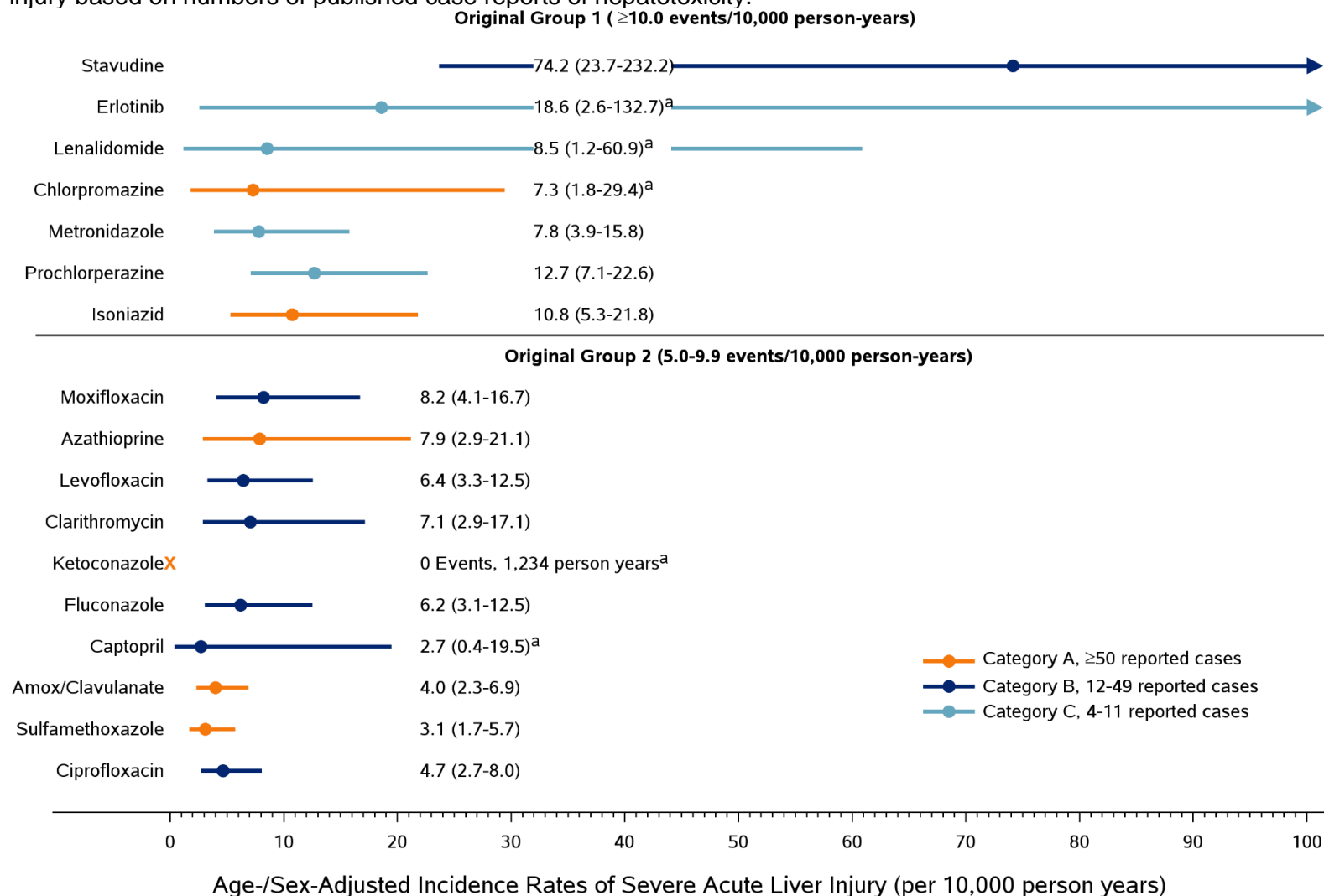
eFigure 2. Rates of severe acute liver injury for Group 3-4 initiators additionally adjusted for metabolic comorbidities. Age-/sex-adjusted incidence rates of severe acute liver injury (per 10,000 person years and with 95% confidence intervals) are reported for medications classified in Group 3 (3.0-4.9 events/10,000 person-years) and Group 4 (1.0-2.9 events/10,000 person-years) in the primary analysis after additionally adjusting for diabetes mellitus, hyperlipidemia, and obesity (body mass index >30 kg/m²). Colors represent the categories of likelihood to cause severe acute liver injury based on numbers of published case reports of hepatotoxicity.



eFigure 3. Rates of severe acute liver injury for Group 5 initiators additionally adjusted for metabolic comorbidities. Age-/sex-adjusted incidence rates of severe acute liver injury (per 10,000 person years and with 95% confidence intervals) are reported for medications classified in Group 5 (<1.0 events/10,000 person-years) in the primary analysis after additionally adjusting for diabetes mellitus, hyperlipidemia, and obesity (body mass index >30 kg/m²). Colors represent the categories of likelihood to cause severe acute liver injury based on numbers of published case reports of hepatotoxicity.

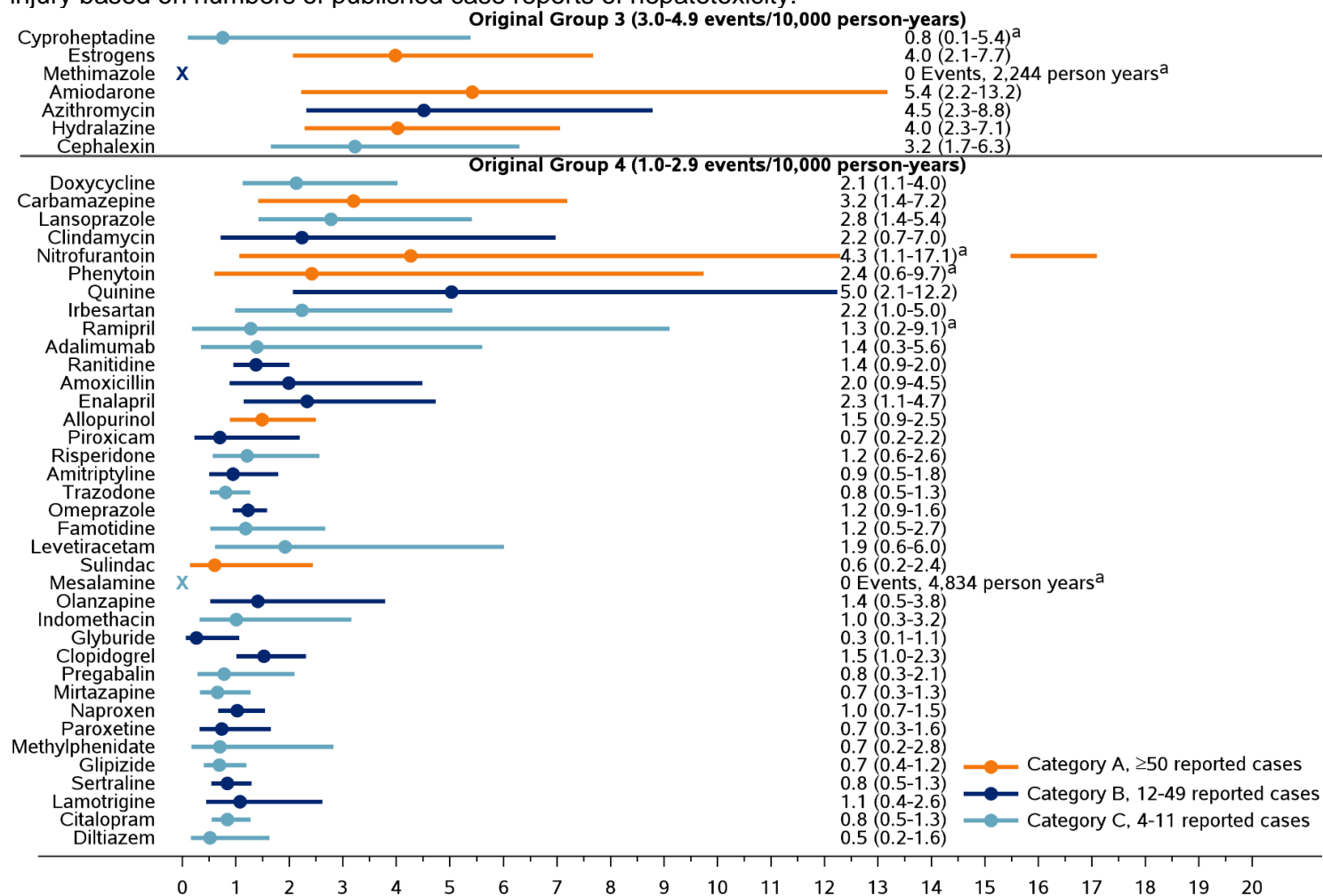


eFigure 4. Rates of severe acute liver injury for Group 1-2 initiators <65 years of age. Age-/sex-adjusted incidence rates of severe acute liver injury (per 10,000 person years and with 95% confidence intervals) are reported for medications classified in Group 1 (≥ 10.0 events/10,000 person-years) and Group 2 (5.0-9.9 events/10,000 person-years) in the primary analysis after limiting each medication initiator cohort to persons <65 years of age. Colors represent the categories of likelihood to cause severe acute liver injury based on numbers of published case reports of hepatotoxicity.



^a After exclusion of initiators on multiple hepatotoxic medications, the 95% confidence interval of the incidence rate was too wide to meet our initial criteria for classification into Groups 1-5.

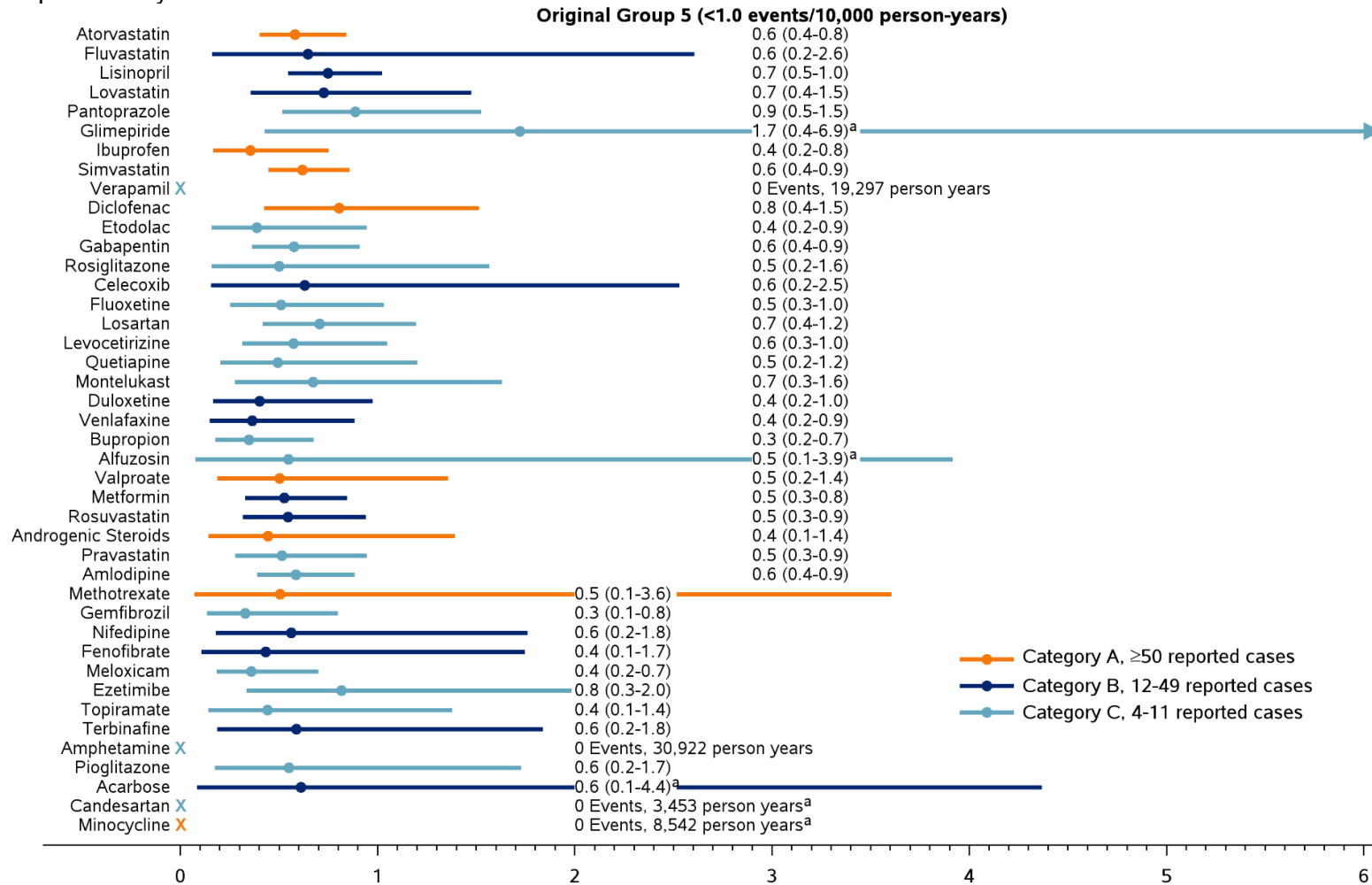
eFigure 5. Rates of severe acute liver injury for Group 3-4 initiators <65 years of age. Age-/sex-adjusted incidence rates of severe acute liver injury (per 10,000 person years and with 95% confidence intervals) are reported for medications classified in Group 3 (3.0-4.9 events/10,000 person-years) and Group 4 (1.0-2.9 events/10,000 person-years) in the primary analysis after limiting each medication initiator cohort to persons <65 years of age. Colors represent the categories of likelihood to cause severe acute liver injury based on numbers of published case reports of hepatotoxicity.



Age-/Sex-Adjusted Incidence Rates of Severe Acute Liver Injury (per 10,000 person years)

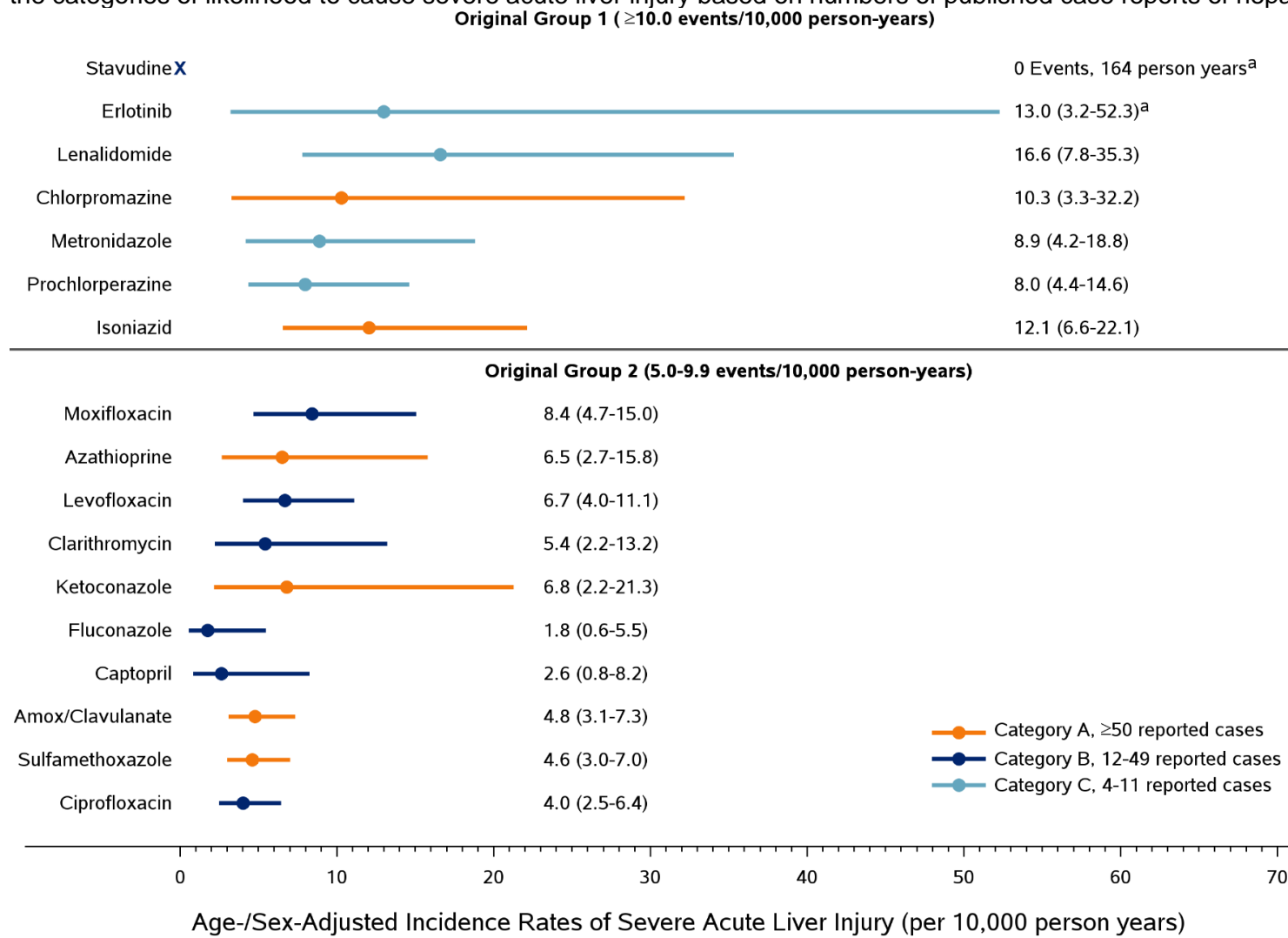
^a After exclusion of initiators on multiple hepatotoxic medications, the 95% confidence interval of the incidence rate was too wide to meet our initial criteria for classification into Groups 1-5.

eFigure 6. Rates of severe acute liver injury for Group 5 initiators <65 years of age. Age-/sex-adjusted incidence rates of severe acute liver injury (per 10,000 person years and with 95% confidence intervals) are reported for medications classified in Group 5 (<1.0 events/10,000 person-years) in the primary analysis after limiting each medication initiator cohort to persons <65 years of age. Colors represent the categories of likelihood to cause severe acute liver injury based on numbers of published case reports of hepatotoxicity.



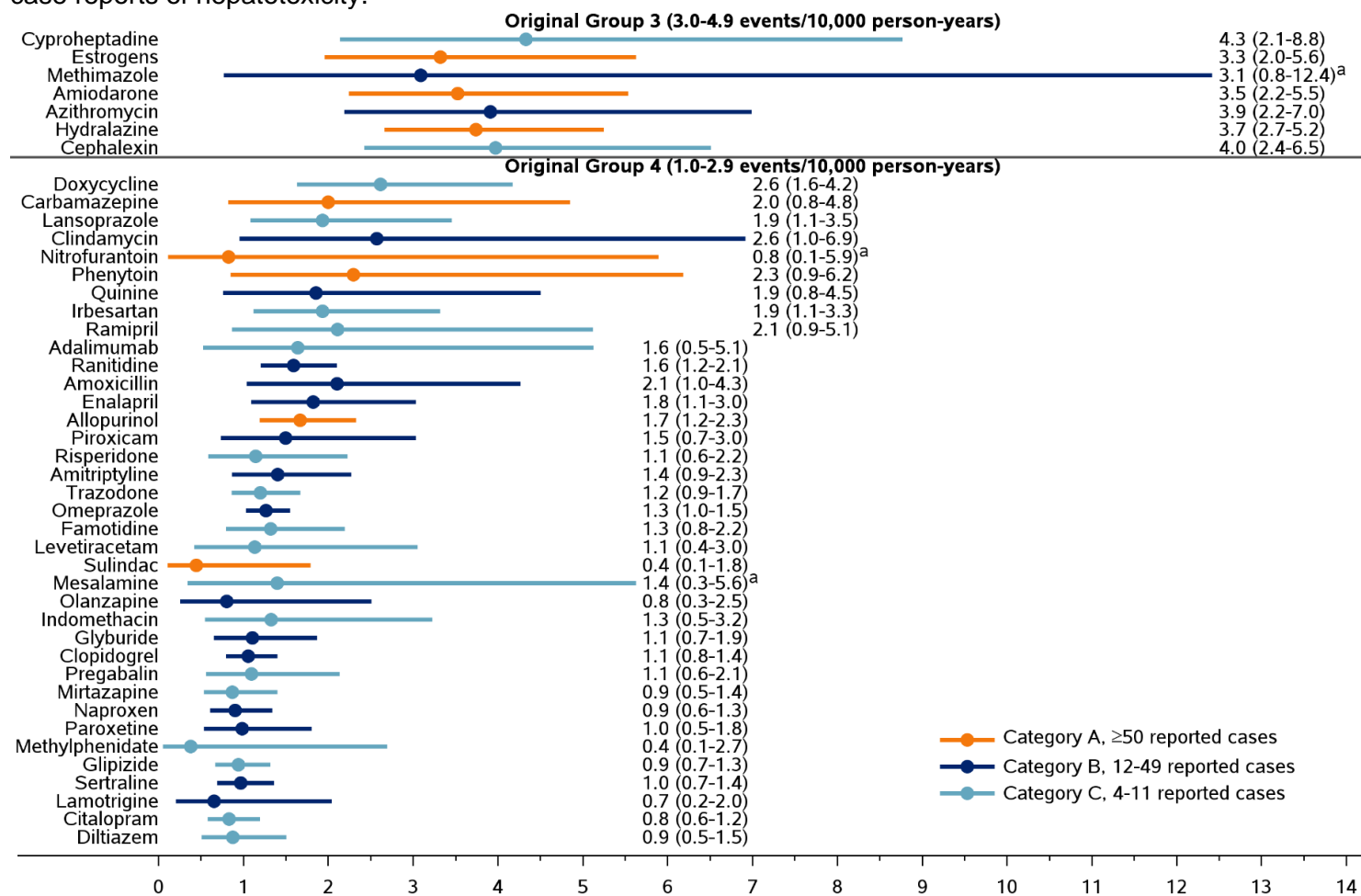
^a After exclusion of initiators on multiple hepatotoxic medications, the 95% confidence interval of the incidence rate was too wide to meet our initial criteria for classification into Groups 1-5.

eFigure 7. Rates of severe acute liver injury for Group 1-2 initiators additionally dispensed Group 1-2 medications. Age-/sex-adjusted incidence rates of severe acute liver injury (per 10,000 person years and with 95% confidence intervals) are reported for medications classified in Group 1 (≥ 10.0 events/10,000 person-years) and Group 2 (5.0-9.9 events/10,000 person-years) in the primary analysis after exclusion of initiators who were additionally dispensed any other Group 1 or 2 medications. Colors represent the categories of likelihood to cause severe acute liver injury based on numbers of published case reports of hepatotoxicity.



^a After exclusion of initiators on multiple hepatotoxic medications, the 95% confidence interval of the incidence rate was too wide to meet our initial criteria for classification into Groups 1-5.

eFigure 8. Rates of severe acute liver injury for Group 3-4 initiators additionally dispensed Group 1-2 medications. Age-/sex-adjusted incidence rates of severe acute liver injury (per 10,000 person years and with 95% confidence intervals) are reported for medications classified in Group 3 (3.0-4.9 events/10,000 person-years) and Group 4 (1.0-2.9 events/10,000 person-years) in the primary analysis after exclusion of initiators who were additionally dispensed any Group 1 or 2 medications (as identified in the primary analysis). Colors represent the categories of likelihood to cause severe acute liver injury based on numbers of published case reports of hepatotoxicity.



Age-/Sex-Adjusted Incidence Rates of Severe Acute Liver Injury (per 10,000 person years)

^a After exclusion of initiators on multiple hepatotoxic medications, the 95% confidence interval of the incidence rate was too wide to meet our initial criteria for classification into Groups 1-5.

eFigure 9. Rates of severe acute liver injury for Group 5 initiators additionally dispensed Group 1-2 medications. Age-/sex-adjusted incidence rates of severe acute liver injury (per 10,000 person years and with 95% confidence intervals) are reported for medications classified in Group 5 (<1.0 events/10,000 person-years) in the primary analysis after exclusion of initiators who were additionally dispensed any Group 1 or 2 medications (as identified in the primary analysis). Colors represent the categories of likelihood to cause severe acute liver injury based on numbers of published case reports of hepatotoxicity.

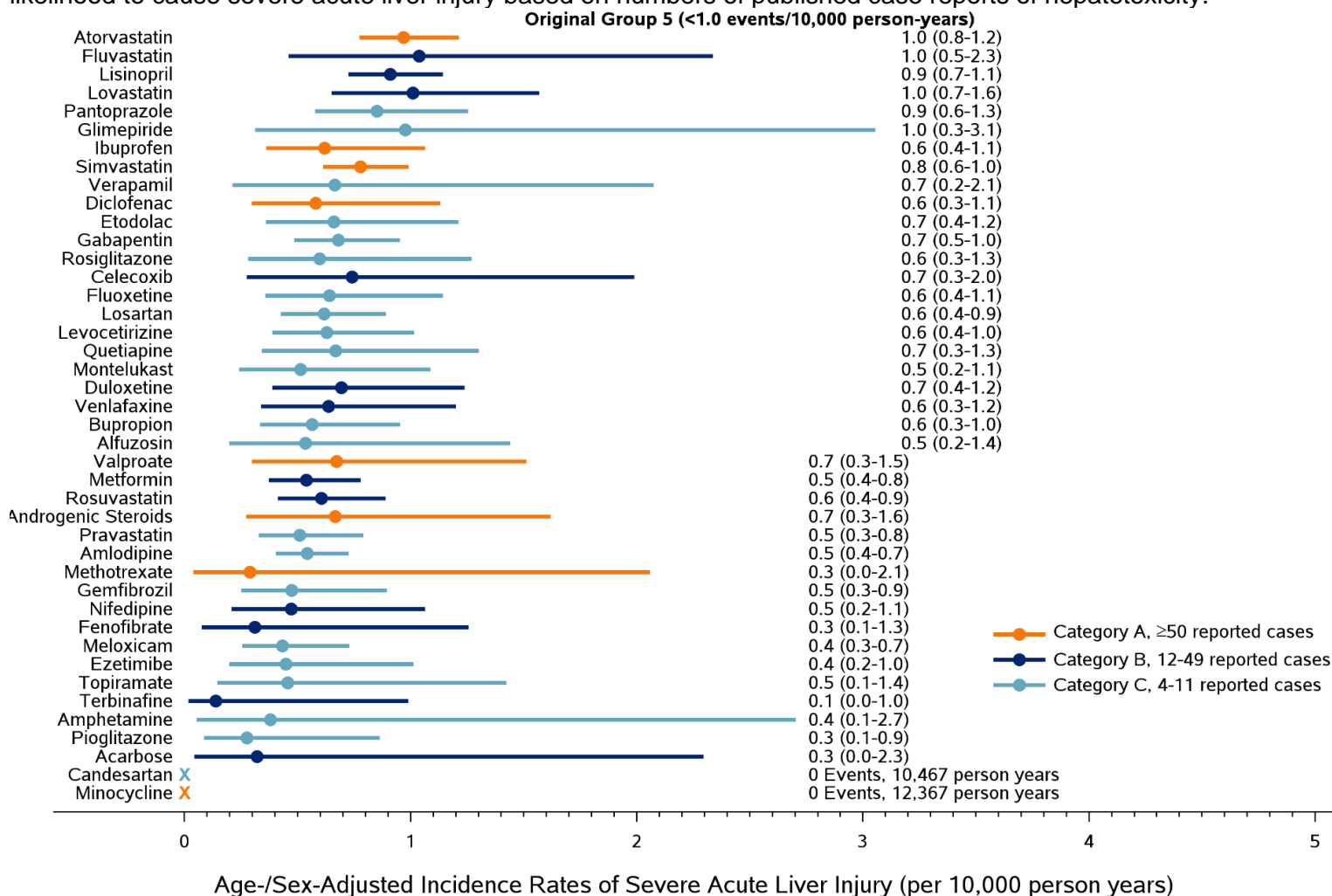
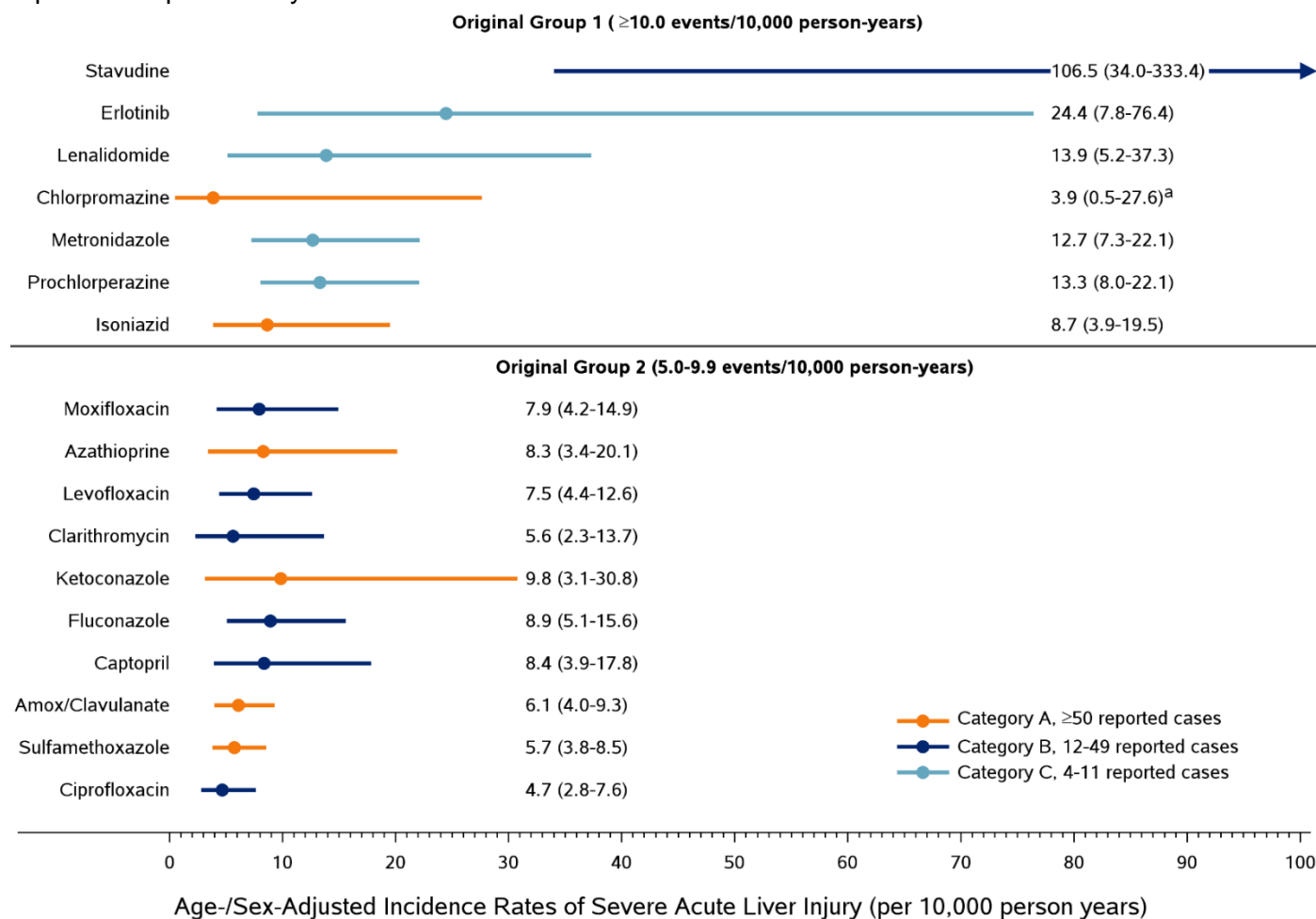
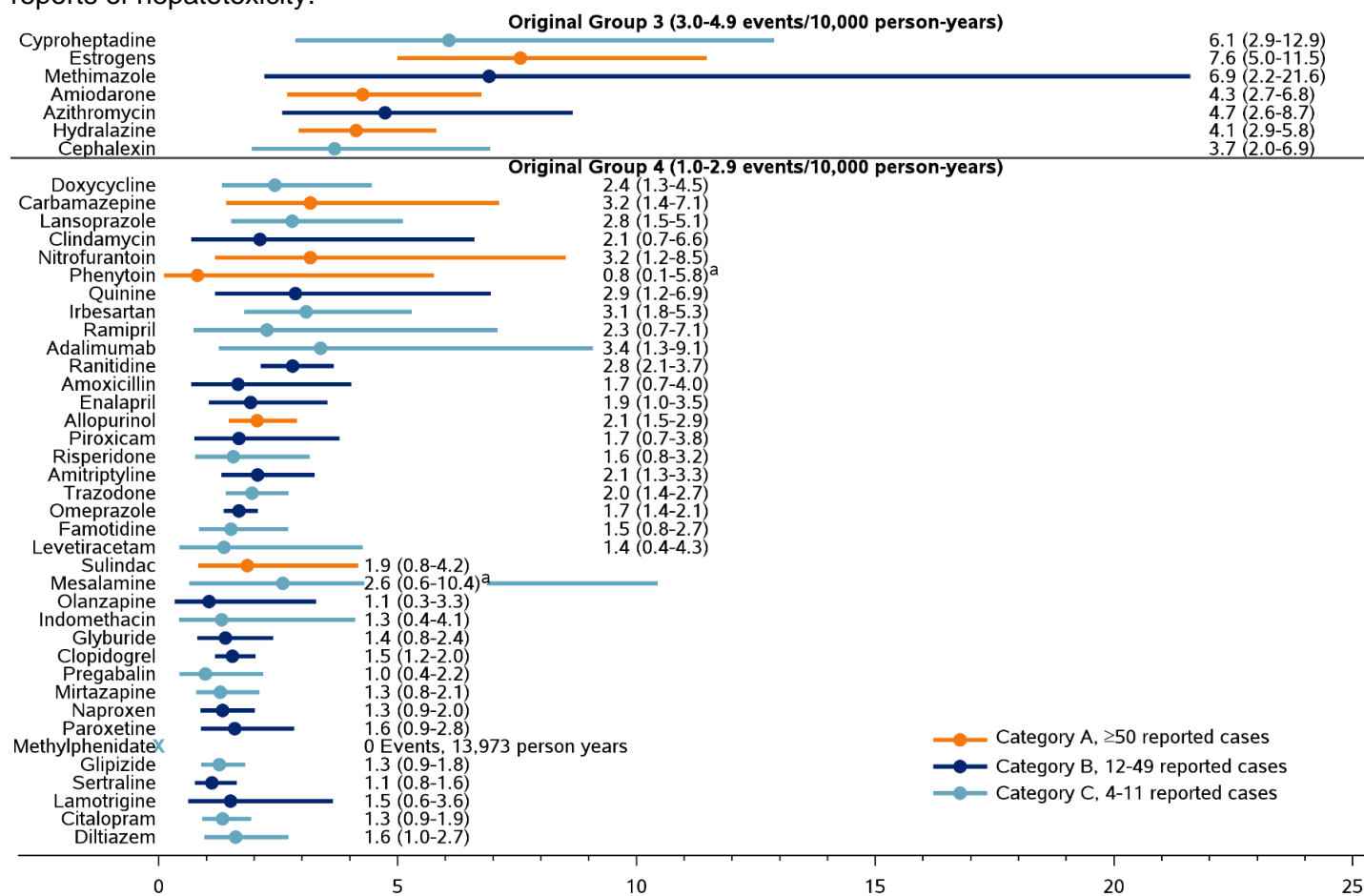


Figure 10. Rates of severe acute liver injury for Group 1-2 initiators dispensed ≥ 5 unique medications. Age-/sex-adjusted incidence rates of severe acute liver injury (per 10,000 person years and with 95% confidence intervals) are reported for medications classified in Group 1 (≥ 10.0 events/10,000 person-years) and Group 2 (5.0-9.9 events/10,000 person-years) in the primary analysis after limiting each medication initiator cohort to persons who were dispensed ≥ 5 unique medications on or within 90 days prior to the index date. Colors represent the categories of likelihood to cause severe acute liver injury based on numbers of published case reports of hepatotoxicity.



^a After exclusion of initiators on multiple hepatotoxic medications, the 95% confidence interval of the incidence rate was too wide to meet our initial criteria for classification into Groups 1-5.

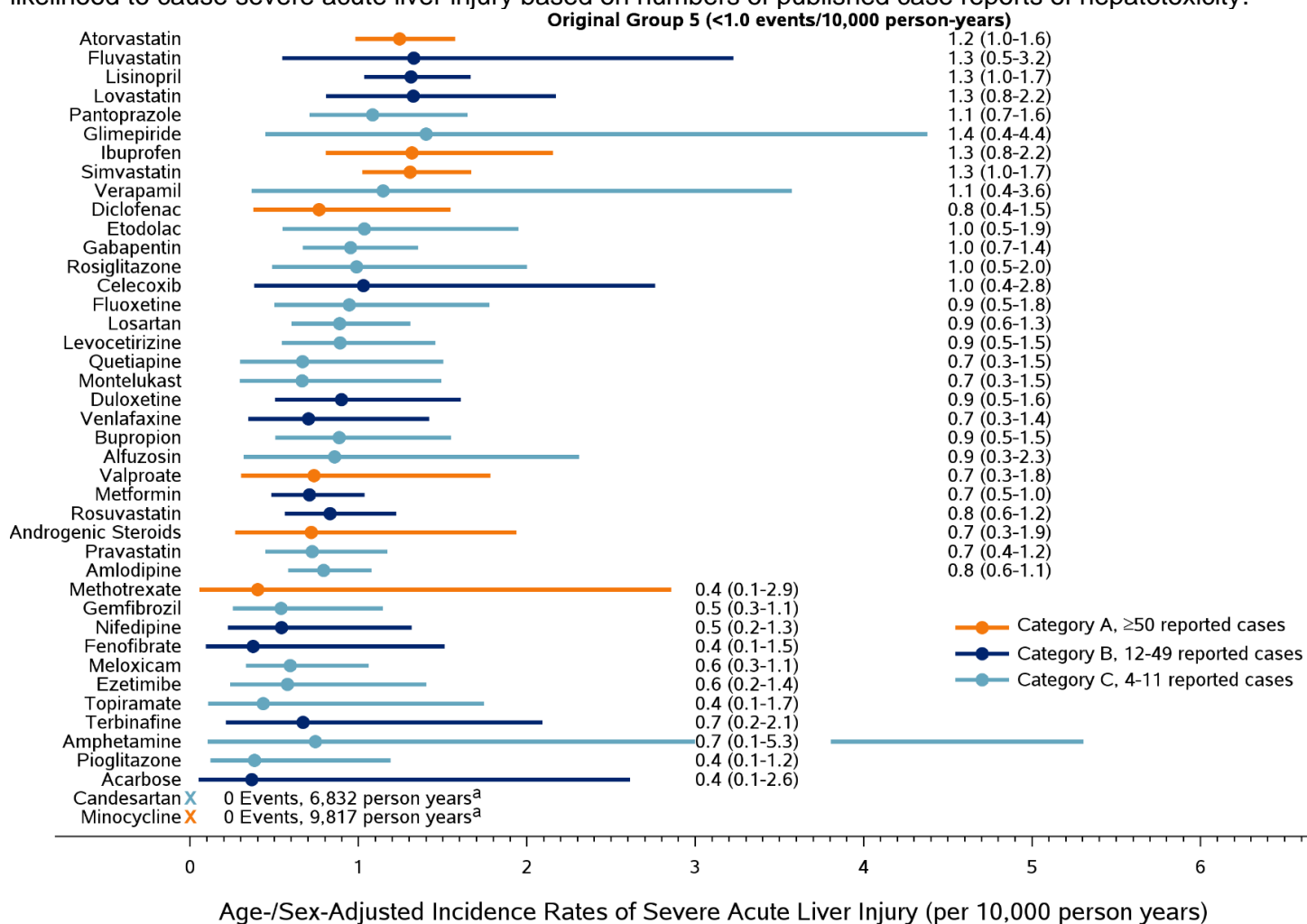
eFigure 11. Rates of severe acute liver injury for Group 3-4 initiators dispensed ≥5 unique medications. Age-/sex-adjusted incidence rates of severe acute liver injury (per 10,000 person years and with 95% confidence intervals) are reported for medications classified in Group 3 (3.0-4.9 events/10,000 person-years) and Group 4 (1.0-2.9 events/10,000 person-years) in the primary analysis after limiting each medication initiator cohort to persons who were dispensed ≥5 unique medications on or within 90 days prior to the index date. Colors represent the categories of likelihood to cause severe acute liver injury based on numbers of published case reports of hepatotoxicity.



Age-/Sex-Adjusted Incidence Rates of Severe Acute Liver Injury (per 10,000 person years)

^a After exclusion of initiators on multiple hepatotoxic medications, the 95% confidence interval of the incidence rate was too wide to meet our initial criteria for classification into Groups 1-5.

eFigure 12. Rates of severe acute liver injury for Group 5 initiators dispensed ≥5 unique medications. Age- and sex-adjusted incidence rates of severe acute liver injury (per 10,000 person years and with 95% confidence intervals) are reported for medications classified in Group 5 (<1.0 events/10,000 person-years) in the primary analysis after limiting each medication initiator cohort to persons who were dispensed ≥5 unique medications on or within 90 days prior to the index date. Colors represent the categories of likelihood to cause severe acute liver injury based on numbers of published case reports of hepatotoxicity.



^a After exclusion of initiators on multiple hepatotoxic medications, the 95% confidence interval of the incidence rate was too wide to meet our initial criteria for classification into Groups 1-5.