**Marshfield Clinic – DILI EHR algorithm implementation (March 5, 2013)**



## Baseline population

* Biobank population for eMERGE (N=4762). Age >=18 years old.

## Acute liver injury diagnosis

* Structured data (ICD-9 codes)
* Date of instance of acute liver injury code, becomes D3.

| **Acute liver injury related diagnoses and procedures** | **ICD-9 codes** |
| --- | --- |
| Disorders of bilirubin excretion | 277.4 |
| Acute and subacute necrosis of the liver | 570\* |
| Hepatic coma (hepatorenal syndrome) | 572.2 |
| Hepatorenal syndrome | 572.4\* |
| Other disorders of the liver, including chemical or drug induced | 573\* |
| Other specified disorders of biliary tract | 576.8 |
| Jaundice, unspecified, not of newborn | 782.4 |
| Hepatomegaly | 789.1\* |
| Nonspecific elevation of transaminase or lactic dehydrogenase levels | 790.4\* |
| Abnormal liver function test results | 794.8\* |

## Administration of drugs

* Structured data (MedsManager) and NLP (FreePharma Notes).
* Date of a new medication order within 90 days prior to D3, becomes D1.
* Limited to Drug Induced Iiver Injury (DILIN) study protocol medication preparations:

ciprofloxacin, clinafloxacin, levofloxacin, moxifloxacin, norfloxacin, ofloxacin, sparfloxacin,trovafloxacin, isoniazid, phenytoin, amoxicillin, valproic acid, nitrofurantoin, trimethoprim,minocycline.

## Laboratory measurements

* Upper limit of normal (ULN) is International Serious Events (iSAEC) study protocol specified.
  + ALP (Alkaline Phosphatase) ULN: 120 U/L (international units/liter).
  + ALT (Alanine Aminotransferase) ULN: 45 U/L (international units/liter).
  + Bilirubin (Indirect or Unconjugated) ULN: 40 umol/L (2.34 mg/dL).
* Threshold laboratory values for DILI
  + ALP ≥ 2x ULN.
  + ALT ≥ 5x ULN.
  + ALT ≥ 3x ULN AND Bilirubin ≥ 2x ULN.
* All laboratory values should be below thresholds for DILI (normal) between D0 and D1. (ALP < 2x ULN, and ALT < 3x ULN, and Bilirubin < 2x ULN).
* Date laboratory values reach threshold for DILI between D2 and D4, becomes D5 (not shown).

## Excluded diagnoses

* Structured data only (ICD-9 codes)
* Chronic liver disease; Sclerosing cholangitis; organ transplantation or liver operation; alcohol abuse/liver damage/toxic effects; viral hepatitis.

| **Chronic liver disease diagnosis description** | **ICD-9 code** |
| --- | --- |
| Alcoholic fatty liver | 571.0 |
| Chronic hepatitis | 571.4 |
| Chronic hepatitis, unspecified | 571.40 |
| Chronic persistent hepatitis | 571.41 |
| Other chronic hepatitis | 571.49 |
| Cirrhosis of liver without mention of alcohol | 571.5 |
| Biliary cirrhosis | 571.6 |
| Other chronic nonalcoholic liver disease | 571.8 |
| Autoimmune hepatitis | 571.42 |
| Unspecified Chronic Liver Disease without Mention of Alcohol | 571.9 |

| **Sclerosing cholangitis description** | **ICD-9 code** |
| --- | --- |
| Cholangitis | 576.1 |

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| **Organ transplantation and liver therapeutic operation descriptions** | **ICD-9 code** |
| --- | --- |
| Compl kidney transplant | 996.81 |
| Compl liver transplant | 996.82 |
| Compl heart transplant | 996.83 |
| Compl lung transplant | 996.84 |
| Complications of bone marrow transplant | 996.85 |
| Compl pancreas transplnt | 996.86 |
| Complications of other transplanted organ | 996.89 |
| Complication of intestine transplantation | 998.87 |
| Complications of transplanted organ | 998.88 |
| Complications of transplanted organ | 996.80 |
| Kidney replaced by transplant | V42.0 |
| Heart replaced by transplant | V42.1 |
| Heart valve replaced by transplant | V42.2 |
| Skin replaced by transplant | V42.3 |
| Bone replaced by transplant | V42.4 |
| Cornea replaced by transplant | V42.5 |
| Lung replaced by transplant | V42.6 |
| Liver replaced by transplant | V42.7 |
| Other specified organ or tissue replaced by transplant | V42.89 |
| Bone marrow replaced by transplant | V42.81 |
| Peripheral stem cells replaced by transplant | V42.82 |
| Pancreas replaced by transplant | V42.83 |
| Intestines replaced by transplantation | V42.84 |
| Unspecified organ or tissue replaced by transplant | V42.9 |
| Allogeneic bone marrow transplant with purging | 41.02 |
| Allogeneic bone marrow transplant without purging | 41.03 |
| Cord blood stem cell transplant | 41.06 |
| Autologous hematopoietic stem cell transplant with purging | 41.07 |
| Allogeneic hematopoietic stem cell transplant | 41.08 |
| Autologous bone marrow transplant with purging | 41.09 |
| Autologous bone marrow transplant without purging | 41.01 |
| Autologous hematopoietic stem cell transplant without purging | 41.04 |
| Allogeneic hematopoietic stem cell transplant without purging | 41.05 |
| Bone marrow transplant | 41.00 |
| Unilat lung transplant | 33.51 |
| Bilateral lung transplantation | 33.52 |
| Lung transplantation | 33.50 |
| Reimplantation of pancreatic tissue | 52.81 |
| Homotransplant of pancreas | 52.82 |
| Heterotransplant of pancreas | 52.83 |
| Autotransplantation of cells of islets of langerhans | 52.84 |
| Allotransplantation of cells of islets of langerhans | 52.85 |
| Transplantation of cells of islets of langerhans | 52.86 |
| Operations on pancreas: pancreatic transplant | 52.80 |
| Hepatotomy | 50.0 |
| Marsupialization of lesion of liver | 50.21 |
| Partial hepatectomy | 50.22 |
| Lobectomy of liver | 50.3 |
| Total hepatectomy | 50.4 |
| Auxiliary liver transplant | 50.51 |
| Other transplant of liver | 50.59 |
| Closure of laceration of liver | 50.61 |
| Other repair of liver | 50.69 |
| Percutaneous aspiration of liver | 50.91 |
| Extracorporeal hepatic assistance | 50.92 |
| Localized perfusion of liver | 50.93 |
| Other injection of therapeutic substance into liver | 50.94 |
| Unlisted proc 50.99 | 50.99 |
| Open ablation of liver lesion or tissue | 50.23 |
| Percutaneous ablation of liver lesion or tissue | 50.24 |
| Laparoscopic ablation of liver lesion or tissue | 50.25 |
| Other and unspecified ablation of liver lesion or tissue | 50.26 |
| Other destruction of lesion of liver | 50.29 |

| **Alcohol Abuse, Liver Damage, and Toxic Effects Descriptions** | **ICD-9 code** |
| --- | --- |
| Alcohol Abuse, Unspecified Drinking Behavior | 305.00 |
| Alcohol Abuse, Continuous Drinking Behavior | 305.01 |
| Alcohol Abuse, Episodic Drinking Behavior | 305.02 |
| Alcohol Abuse, In Remission | 305.03 |
| Alcoholic fatty liver | 571.0 |
| Acute alcoholic hepatitis | 571.1 |
| Alcoholic cirrhosis of liver | 571.2 |
| Alcoholic liver damage | 571.3 |
| Toxic effect of ethyl alcohol | 980.0 |
| Toxic effect of methyl alcohol | 980.1 |
| Toxic effect of isopropyl alcohol | 980.2 |
| Toxic effect fusel oil | 980.3 |
| Toxic effect of other specified alcohols | 980.8 |
| Toxic effect of unspecified alcohol | 980.9 |

| **Viral Hepatitis Descriptions** | **ICD-9 code** |
| --- | --- |
| Unspecified Viral Hepatitis Without Mention Of Hepatic Coma | 070.9 |
| Unspecified Viral Hepatitis With Hepatic Coma | 070.6 |
| Other Specified Viral Hepatitis With Hepatic Coma | 070.49 |
| Other Specified Viral Hepatitis Without Mention Of Hepatic Coma | 070.59 |
| Viral Hepatitis A Without Mention Of Hepatic Coma | 070.1 |
| Viral Hepatitis A With Hepatic Coma | 070.0 |
| Viral Hepatitis B Without Mention Of Hepatic Coma, Acute Or Unspecified | 070.30 |
| Viral Hepatitis B With Hepatic Coma, Acute Or Unspecified | 070.20 |
| Viral Hepatitis B With Hepatic Coma, Acute Or Unspecified, With Hepatitis Delta | 070.21 |
| Viral Hepatitis B, Acute Or Unspecified, With Hepatitis Delta | 070.31 |
| Acute Hepatitis C With Hepatic Coma | 070.41 |
| Hepatitis Delta Without Mention Of Active Hepatitis B Disease With Hepatic Coma | 070.42 |
| Hepatitis E With Hepatic Coma | 070.43 |
| Unspecified Viral Hepatitis C Without Hepatic Coma | 070.70 |
| Hepatitis In Viral Diseases Classified Elsewhere | 573.1 |
| Carrier Or Suspected Carrier Of Viral Hepatitis | V02.60 |
| Chronic Viral Hepatitis B Without Mention Of Hepatic Coma Or Hepatitis Delta | 070.32 |
| Viral Hepatitis B With Hepatic Coma, Chronic, Without Mention Of Hepatitis Delta | 070.22 |
| Viral Hepatitis B With Hepatic Coma, Chronic, With Hepatitis Delta | 070.23 |
| Viral Hepatitis B Without Mention Of Hepatic Coma, Chronic, With Hepatitis Delta | 070.33 |
| Other Icd9 Viral Hepatitis Carrier | V02.69 |
| Unspecified Viral Hepatitis C With Hepatic Coma | 070.71 |

## Algorithm results

* 22 DILI cases as defined by algorithm
* 1657 controls (No acute liver injury diagnoses, has exposure to drug, and no exclusion diagnoses).

## Validation steps

* Manual chart review of 10 randomly selected DILI cases (10 of 22 above).
* 1 clinical reviewer (senior research coordinator)

**Evaluation of algorithm-selected cases**

|  |  |
| --- | --- |
| **Cases** | **Counts** |
| Total algorithm selected DILI cases | 10 |
| True positive cases (TPs) | 1 |
| False positive cases (FPs) | 9 |
| Positive predictive value: TP/(TP+FP) | 10% |