**Mayo Clinic – DILI EHR algorithm implementation (March 18, 2013)**



## Baseline population

* Biobank population for eMERGE (N=6322)

## Acute liver injury diagnosis

* Structured data (ICD-9 codes) and NLP of clinical notes
* Date of first 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 (Enterprise Orders Prescribing) and NLP (Clinical Notes)
* Date of a new medication order within 90 days prior to D3, becomes D1.
* Medications include drugs from the DILI Network (DILIN; <https://dilin.dcri.duke.edu>) and NIH LiverTox database (<http://www.livertox.nih.gov/>)

## Laboratory measurements

* Upper limit of normal (ULN) is manufacturer specified.
* Threshold laboratory values for DILI
  + ALP (Alkaline Phosphatase) ≥ 2 x ULN
  + ALT (Alanine Aminotransferase) ≥ 3 x ULN
  + Bilirubin (Indirect or Unconjugated) ≥ 2 x ULN
* All laboratory values should be below thresholds for DILI (normal) between D0 and D1.
* Date laboratory values reach threshold for DILI between D3 and D1, becomes D2 (not shown)

## Excluded diagnoses

* Structured data only (ICD-9 codes)

| **Chronic liver disease diagnosis description** | **ICD-9 code** |
| --- | --- |
| Alcoholic fatty liver | 571.0 |
| Alcoholic cirrhosis of liver | 571.2 |
| Alcoholic liver damage | 571.3 |
| Chronic hepatitis | 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 |

## Validation steps

* Manual chart review of 50 algorithm-selected DILI cases and controls
* 1 highly experienced clinical reviewer (nurse coordinator for the Mayo Clinic DILIN site)
* Expert decision, determination by DILI expert (PI for Mayo Clinic DILIN site) for questionable results

NLP implementation

Case A:

There is a mention of a Signs/Symptoms or Disorder Impression Report Plan (IRP)/History of Present Illness (HPI)/Chief Complaint sections (to cover examples like autoimmune hepatitis) and relevant medication in IRP/HPI/Chief Complaint sections, where SS/Disorder and Drug must be in the same section.  
  
Ex:auto-immune hep. Due to drug x  
*Analysis (after initial run with this algorithm): If too many FPs decrease window to +/- 2 sentences surrounding the drug mentions*

Case B:  
There is a relevant SS in IRP/HPI/Chief Complaint sections or there is a Disorder (to cover examples like autoimmune hepatitis) in IRP/HPI/Chief Complaint sections and a relevant medication in Current medications, Dismissal medications or Admission medications sections.   
  
Ex:   
Sec=HPI; she complains of vomiting  
Sec=Current Medications; aspirin

Case C:  
There is an explicit mention of "drug-induced \*\*" terms, their variants or synonyms anywhere in the clinical note.  
  
Ex:   
drug-induced liver injury, etc  
But NOT cases like: auto-immune hep.

NOTE: All Named Entities must be non-negated.

Drug Window is defined as follows (for relation assertion)  
         anchor is the drug mention  
         window for SS and disorders is +/- 2 sentences surrounding the drug mention

**Examples of query diagnosis (NLP terms):**   
drug|drug induce cholestasis                             
drug|drug induce hepatotocity                            
drug|drug induce liver failure                           
cholestasis|cholestasis                          
cholestatic|cholestatic hepatitis                                
hepatic|hepatic adverse drug reaction                            
herbal|herbal hepatotoxicity                             
                                 
Autoimmune hepatitis                             
    reactive hepatitis                           
     medication induced dysfunction                              
     acute hepatitis                             
     hepatitis                           
     eosinophilia                                
  
**Key signs and symptoms (NLP terms)**   
  
fever|fever from the drug                                
rash|rash from the drug                          
itching|itching                                  
nausea|nausea                            
pain|pain in the upper right part of the abdomen                                 
dark|dark urine                                  
pale|pale stools                                 
vomiting|vomiting                                
yellow|yellow skin or eyes                               
jaundice|jaundice                                
fatigue|fatigue                          
                                 
                                 
pruritis                                 
lethargy                                 
ascites                          
Gray stools                              
abnormal/ elevated LFT                           
hepatitis or acute hepatitis                             
encephalopathy                           
abnormal/elevated liver enzymes                          
abnormal/elevated transaminases

**2) Evaluation of algorithm-selected cases**

|  |  |
| --- | --- |
|  | **Counts** |
| Total algorithm selected DILI cases | 25 |
| True positive cases (TPs) | 4 |
| False positive cases (FPs) | 21 |
| Positive predictive value: TP/(TP+FP) | 16% |

**3) Evaluation of “controls”**

|  |  |
| --- | --- |
|  | **Counts** |
| Total “controls” reviewed | 25 |
| True negative cases (TNs) | 25 |
| False negative cases (FNs) | 0 |
| Negative predictive value: TN/(TN+FN) | 100% |