Implications of Health Outcomes of Interest Definitions: Acute Liver Injury Case Study

Judy Racoosin, Patrick Ryan
on behalf of OMOP Research Team
March 24, 2011

Observational Medical Outcomes Partnership

*Established to inform the appropriate use of observational healthcare databases for active surveillance by:*

- **Conducting methodological research** to empirically evaluate the performance of alternative methods on their ability to identify true drug safety issues
- **Developing tools and capabilities** for transforming, characterizing, and analyzing disparate data sources
- **Establishing a shared resource** so that the broader research community can collaboratively advance the science
OMOP research experiment workflow

Setting

- Use of observational data for active drug safety surveillance requires using algorithms based on diagnosis codes and other clinical information to identify cases of given health outcomes of interest (HOIs)
- OMOP contractors performed systematic reviews of the literature for a range of HOIs to determine what algorithms had been previously studied and shown to have good positive predictive value (PPV) for detecting cases
- The systematic review for the HOI “acute liver injury” (ALI) did not identify any algorithms that had good PPV
- Based on the codes that were used in the ALI validation studies, OMOP investigators fashioned a series of HOI definitions
  - Diagnosis codes were grouped into “broad” and “narrow” categories
  - Requirement for relevant procedures and labs was added to some of the definitions to investigate the potential for improved capability for identifying cases
Acute liver injury (ALI) definitions

ALI 1: Occurrence of at least one broad diagnosis code

ALI 2: Occurrence of at least one narrow diagnosis code

ALI 3: Occurrence of at least one narrow diagnosis code
AND (diagnostic procedure <=30d before
OR treatment procedure >=60d after)

ALI 4: Occurrence of at least one narrow diagnosis code
AND (diagnostic procedure <=30d before
OR treatment procedure >=60d after)
AND laboratory results indicative of Hy’s law:
ALT >= 3xULN AND AST >= 3xULN AND Bilirubin >= 2xULN
within 7 days

ALI 5: Laboratory results indicative of Hy’s law:
ALT >= 3xULN AND AST >= 3xULN AND Bilirubin >= 2xULN
within 7 days

ALI 6: Laboratory results strongly indicative of Hy’s law:
ALT >= 10xULN AND AST >= 10xULN AND Bilirubin >= 2xULN
within 7 days

Impact of alternative HOI definitions
**How can OMOP’s data characterization tools refine use of HOI algorithms in active surveillance?**

- Improve accuracy of HOI case identification
- Improve the likelihood that an identified HOI case is drug-related
Natural History Analysis (NATHAN)

- OSCAR provides a systematic approach for summarizing all data within the OMOP common data model
- Natural History Analysis (NATHAN) is an extension of OSCAR, where data characteristics can be produced for a particular subpopulation of interest
  - Exposed population (e.g. patients taking antibiotics)
  - Cases (e.g. patients with acute liver injury)
  - Exposed cases (e.g. patients taking antibiotics who develop acute liver injury)
- Additional NATHAN summary statistics provide temporal assessment, relative to index date
  - Ex. conditions 30d prior to drug start
  - Ex. drug exposure any time prior to incident condition
- Use NATHAN to refine HOI algorithms in active surveillance
  - Evaluate alternative cohort definitions (HOIs)
  - Comparisons between data sources

http://omop.fnih.org/NATHAN

Factors to consider when identifying acute liver injury cases

- Demographic assessment
  - Case distribution by gender
  - Case distribution by age
NATHAN ALI cohort: gender

Proportion of cohort

<table>
<thead>
<tr>
<th></th>
<th>2: Dx Only</th>
<th>3: Dx + Proc</th>
<th>4: Dx + Proc + Lab</th>
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<td>MALE</td>
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Gender

NATHAN ALI cohort: year of birth distribution

Proportion of cohort

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<td>1920-1940</td>
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<td>1960-1980</td>
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<td></td>
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<tr>
<td>1980-2000</td>
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</table>
Factors to consider when identifying acute liver injury cases

Evidence of hepatocellular injury:
– Symptoms and Signs
  • Nausea/Vomiting
  • Abdominal pain/ Right Upper Quadrant Pain
  • Jaundice
– Laboratory tests
  • Elevated ALT/Bilirubin
  • Elevated prothrombin time (PT) or INR
– Procedures
  • Liver biopsy
  • Liver transplant following the index diagnosis

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Laboratory tests/ Diagnostic procedure

Test or Procedure Name
- Transaminase: alanine amino (ALT) (SGPT)
- Hepatic function panel
- Bilirubin: direct
- Bilirubin: total
- Prothrombin time
- Biopsy of liver, needle, percutaneous

Proportion of cohort

Proportion of cohort

Treatment procedures after index diagnosis

Color by COHORT_NAME
- Acute Liver Failure #2
- Dx Only
- Dx + Proc
- Dx + Proc + Lab

Proportion of cohort

Anytime on or after

Proportion of cohort

Anesthesia for hip replacement, total knee replacement, procedures in upper abdomen, including laparoscopy; liver transplantation; orthotopic, partial or whole, from cadaver or living donor,....
Factors to consider when identifying acute liver injury cases: pertinent negatives

Evidence of an obstructive cause

- Diagnoses
  - Pancreatic cancer
  - Common bile duct stone
- Laboratory tests
  - Elevated alkaline phosphatase
- Procedures
  - ERCP (Endoscopic retrograde cholangiopancreatography)
  - Common bile duct stenting

Pertinent negatives: diagnoses
Factors to consider when identifying drug-induced liver injury cases

Rule out alternative cause of acute liver injury

- Exposures
  - Other hepatotoxic drugs

- Diagnoses
  - Viral hepatitis
  - Autoimmune hepatitis
  - Alcoholic hepatitis
  - Hepatic cirrhosis

- Procedures
  - Liver transplant before the index diagnosis

- Laboratory tests
  - Viral serologies
  - Autoantibodies

- Treatments
  - Antiviral drugs for HBV
  - Antiviral drugs for HCV

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Alternative causes of acute liver injury: treatments for viral hepatitis

Implications for future development of HOI definitions

- There will be HOIs which have not been well validated in the literature or have algorithms identified with good PPV

- Use of a tool like NATHAN can help to refine a potential HOI definition by identifying diagnosis codes, procedure codes, and lab abnormalities that occur commonly in the population of interest and explore potential exclusion criteria

- Refinement of an HOI definition may be tested by using NATHAN to develop potential variations of an HOI algorithm and then validating the various algorithms in a database that can access source records
OMOP Contact information

Thomas Scarnecchia
Executive Director
scarnecchia@omop.org

Emily Welebob
Senior Program Manager, Research
welebob@omop.org

OMOP website: http://omop.fnih.org
Broad and narrow diagnosis code-based definitions for acute liver injury

Definition 1 - Broad:
277.4 “Disorders of bilirubin excretion”
570* “Acute and subacute necrosis of the liver”
572.2 “Hepatic coma (hepatorenal syndrome)”
572.4* “Hepatorenal syndrome”
573* “Other disorders of the liver, including chemical or drug induced”
576.8 “Other specified disorders of biliary tract”
782.4 “Jaundice, unspecified, not of newborn”
789.1* “Hepatomegaly”
790.4* “Nonspecific elevation of transaminase or lactic dehydrogenase levels”
794.8* “Abnormal liver function test results”

Definition 2 - Narrow:
570* “Acute and subacute necrosis of the liver”
572.2 “Hepatic coma (hepatorenal syndrome)”
572.4* “Hepatorenal syndrome”
573* “Other disorders of the liver, including chemical or drug induced”

Codes included as acute liver injury procedures

Diagnostic procedures

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<th>Vocabulary</th>
<th>Description</th>
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<tr>
<td>47000</td>
<td>CPT</td>
<td>Biopsy of liver, needle; percutaneous</td>
</tr>
<tr>
<td>47001</td>
<td>CPT</td>
<td>Biopsy of liver, needle; when done for indicated purpose at time of other</td>
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<tr>
<td></td>
<td></td>
<td>major procedure (List separately in addition to code for primary procedure)</td>
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<tr>
<td>87100</td>
<td>CPT</td>
<td>Biopsy of liver, wedge</td>
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<td>76205</td>
<td>CPT</td>
<td>Liver imaging (SPECT);</td>
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<td>with vascular flow</td>
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<td>50.11</td>
<td>ICD9</td>
<td>Procedure Closed (percutaneous) [needle] biopsy of liver</td>
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<td>50.12</td>
<td>ICD9</td>
<td>Procedure Open biopsy of liver</td>
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<td>50.14</td>
<td>ICD9</td>
<td>Procedure Laparoscopic liver biopsy</td>
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<td>50.13</td>
<td>ICD9</td>
<td>Procedure Percutaneous aspiration of liver</td>
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<td>50.15</td>
<td>ICD9</td>
<td>Procedure Transjugular liver biopsy</td>
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Therapeutic procedures

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<td>CPT</td>
<td>Liver allotransplantation; heterotopic, partial or whole, from cadaver or</td>
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<td>living donor, any age</td>
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<td>47135</td>
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<td>50.51</td>
<td>ICD9</td>
<td>Procedure Auxiliary liver transplant</td>
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<td>50.59</td>
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<td>Procedure Other transplant of liver</td>
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<td>38694-5</td>
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http://omop.fnih.org/AcuteLiverInjury