

**OBSERVATIONAL
MEDICAL
OUTCOMES
PARTNERSHIP**

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

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on behalf of OMOP Research Team
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Disclosure statement

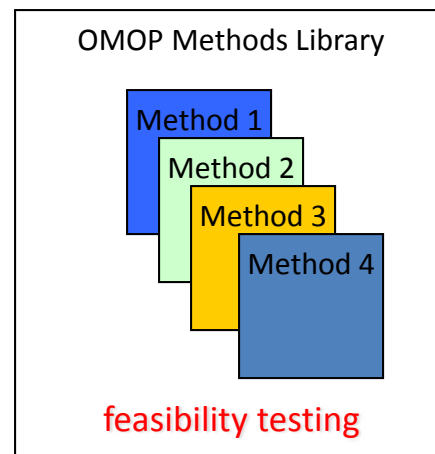
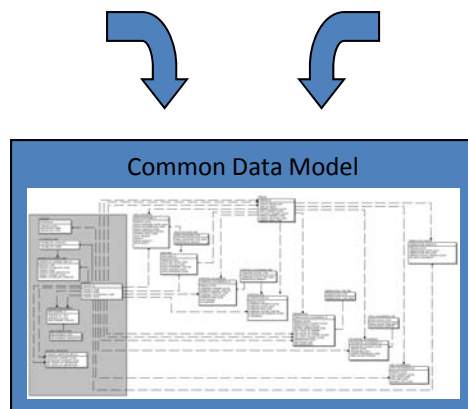
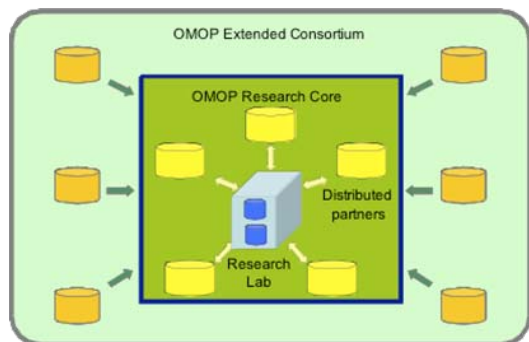
- I have no conflicts of interest to disclose
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Observational Medical Outcomes Partnership

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



Drugs

- ACE Inhibitors
- Amphotericin B
- Antibiotics
- Antiepileptics
- Benzodiazepines
- Beta blockers
- Bisphosphonates
- Tricyclic antidepressants
- Typical antipsychotics
- Warfarin

Health Outcomes of Interest

- Angioedema
- Aplastic Anemia
- Acute Liver Injury
- Bleeding
- GI Ulcer Hospitalization
- Hip Fracture
- Hospitalization
- Myocardial Infarction
- Mortality after MI
- Renal Failure

Non-specified conditions

- All outcomes in condition terminology
- 'Labeled events' as reference
 - Warning
 - Precautions
 - Adverse Reactions
 - Postmarketing Experience

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 ≤ 30 d before
OR treatment procedure ≥ 60 d after)

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

ALI 5: Laboratory results indicative of Hy's law:
ALT ≥ 3 xULN AND AST ≥ 3 xULN **AND** Bilirubin
 ≥ 2 xULN
within 7 days

ALI 6: Laboratory results strongly indicative of Hy's law:
ALT ≥ 10 xULN AND AST ≥ 10 xULN **AND** Bilirubin ≥ 2 xULN
within 7 days

ALI cohort totals



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)

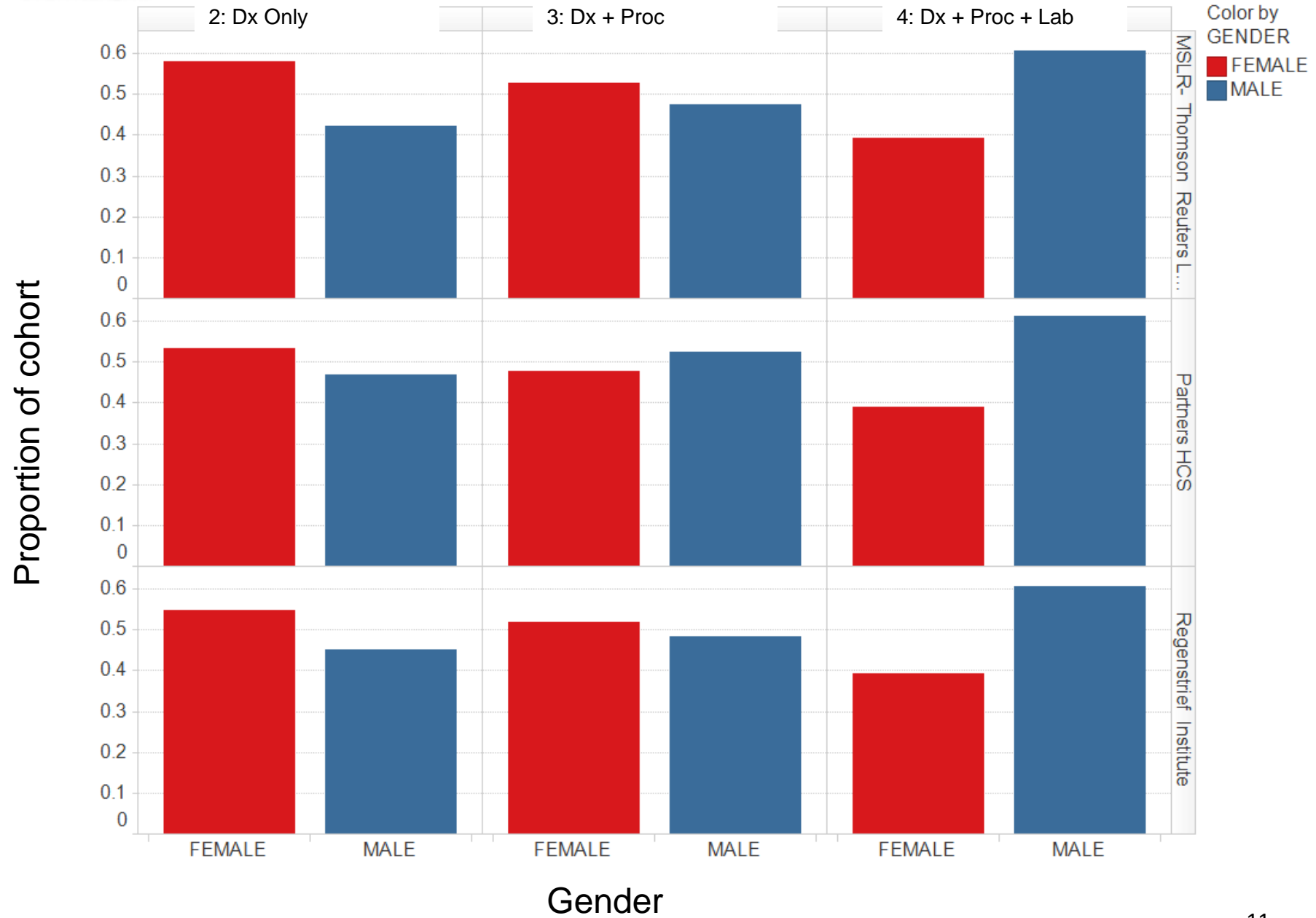
- OSCAR provides a systematic approach for summarizing all data within the OMOP common data model
- Natural History Analysis (NATHAN) is an extension of OSCAR, where data characteristics can be produced for a particular subpopulation of interest
 - Exposed population (e.g. patients taking antibiotics)
 - 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>

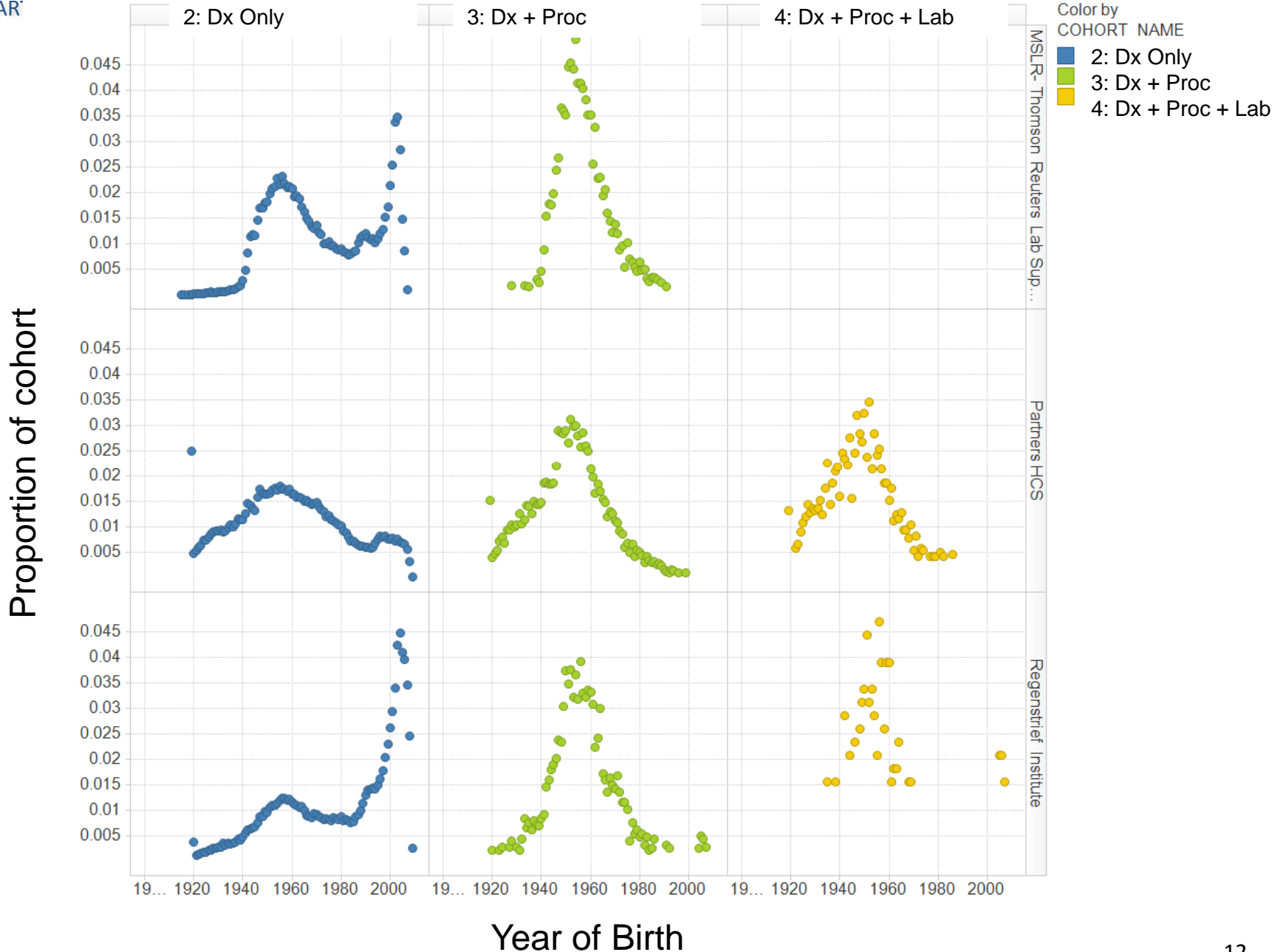
Factors to consider when identifying acute liver injury cases

- Demographic assessment
 - Case distribution by gender
 - Case distribution by age

NATHAN ALI cohort: gender



NATHAN ALI cohort: year of birth distribution

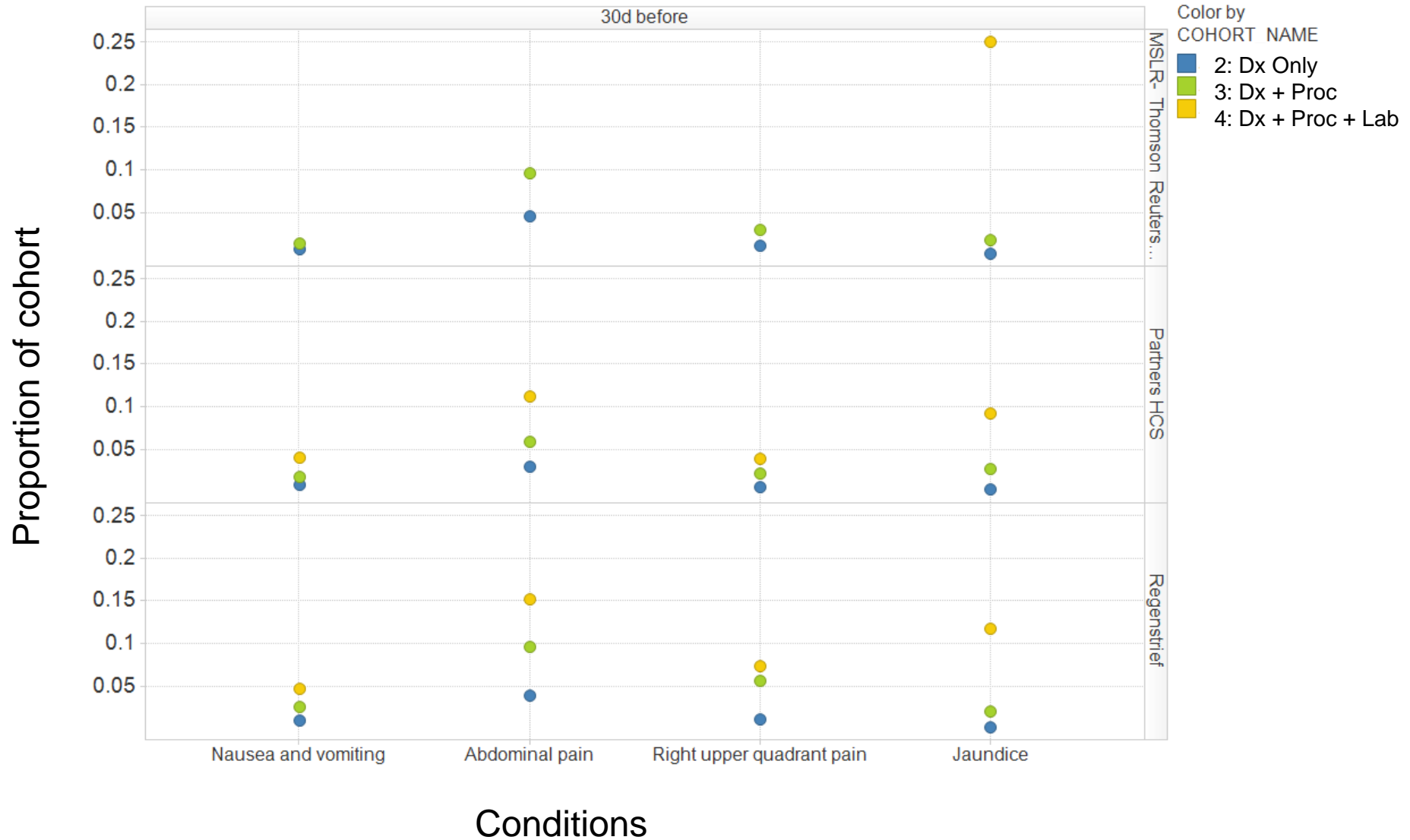


Factors to consider when identifying acute liver injury cases

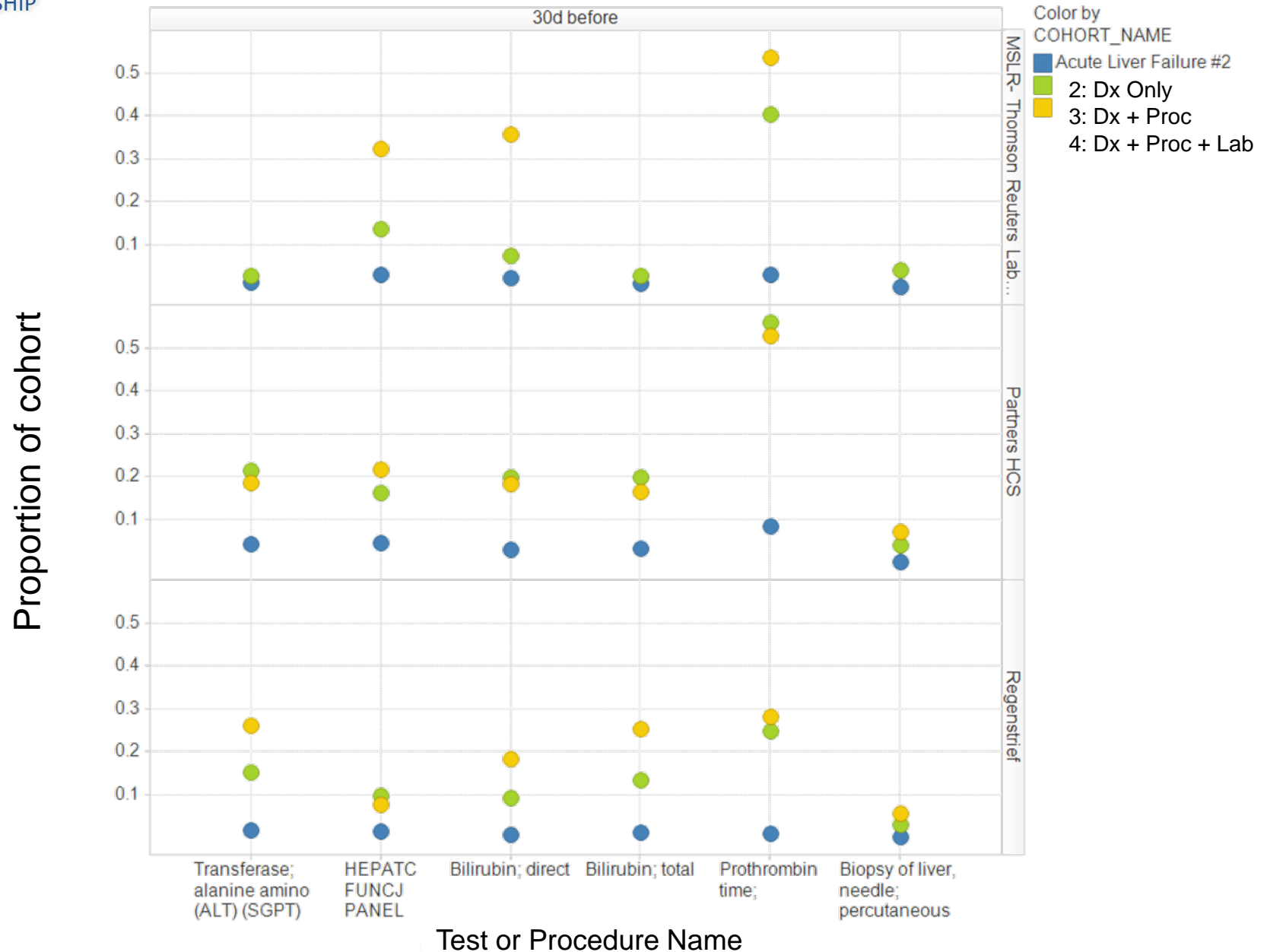
Evidence of hepatocellular injury:

- 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

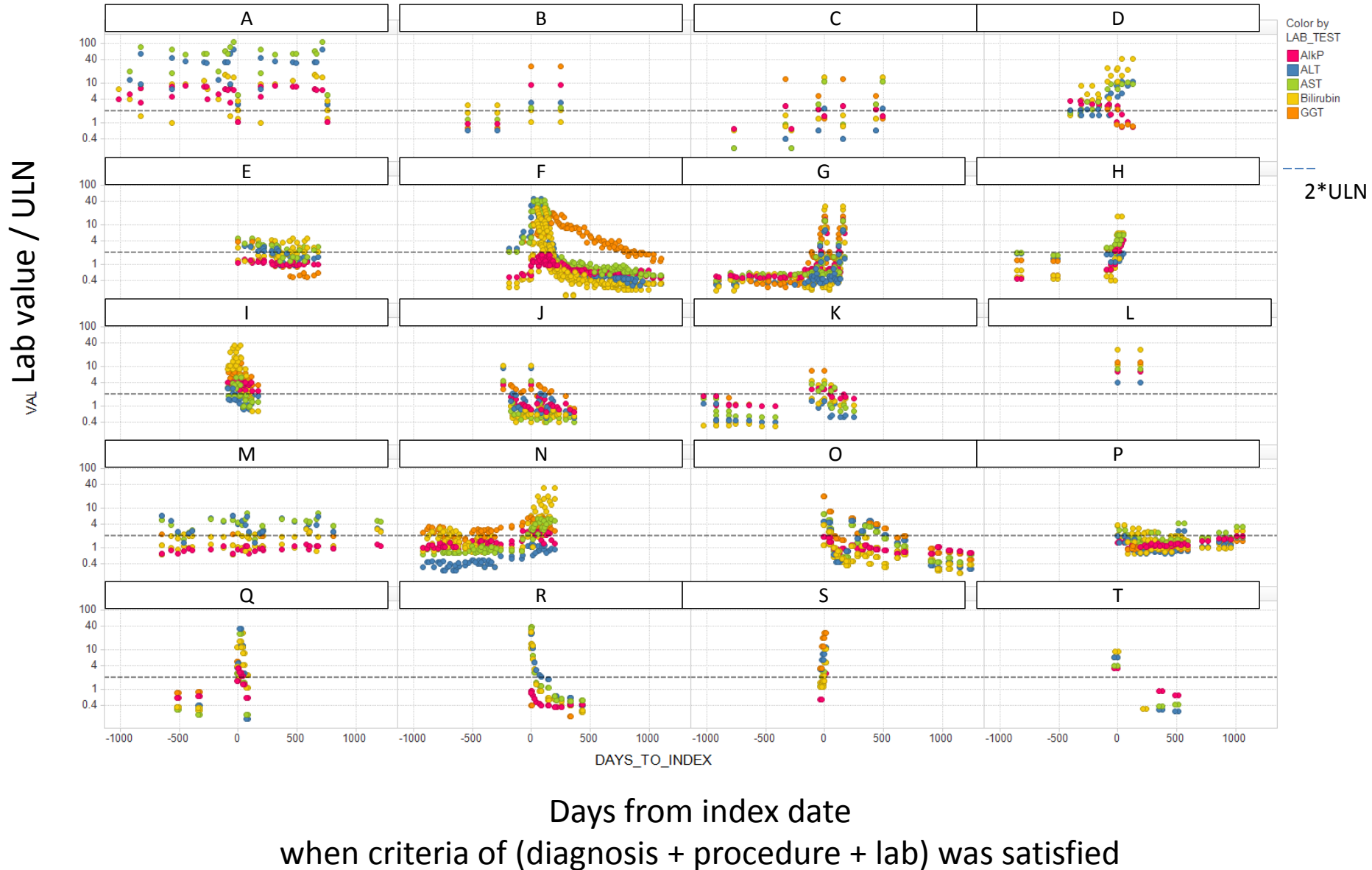
Symptoms and signs recorded as diagnosis codes



Laboratory tests/ Diagnostic procedure



Patterns of laboratory abnormalities in patients meeting the (diagnosis + procedure + lab) definition

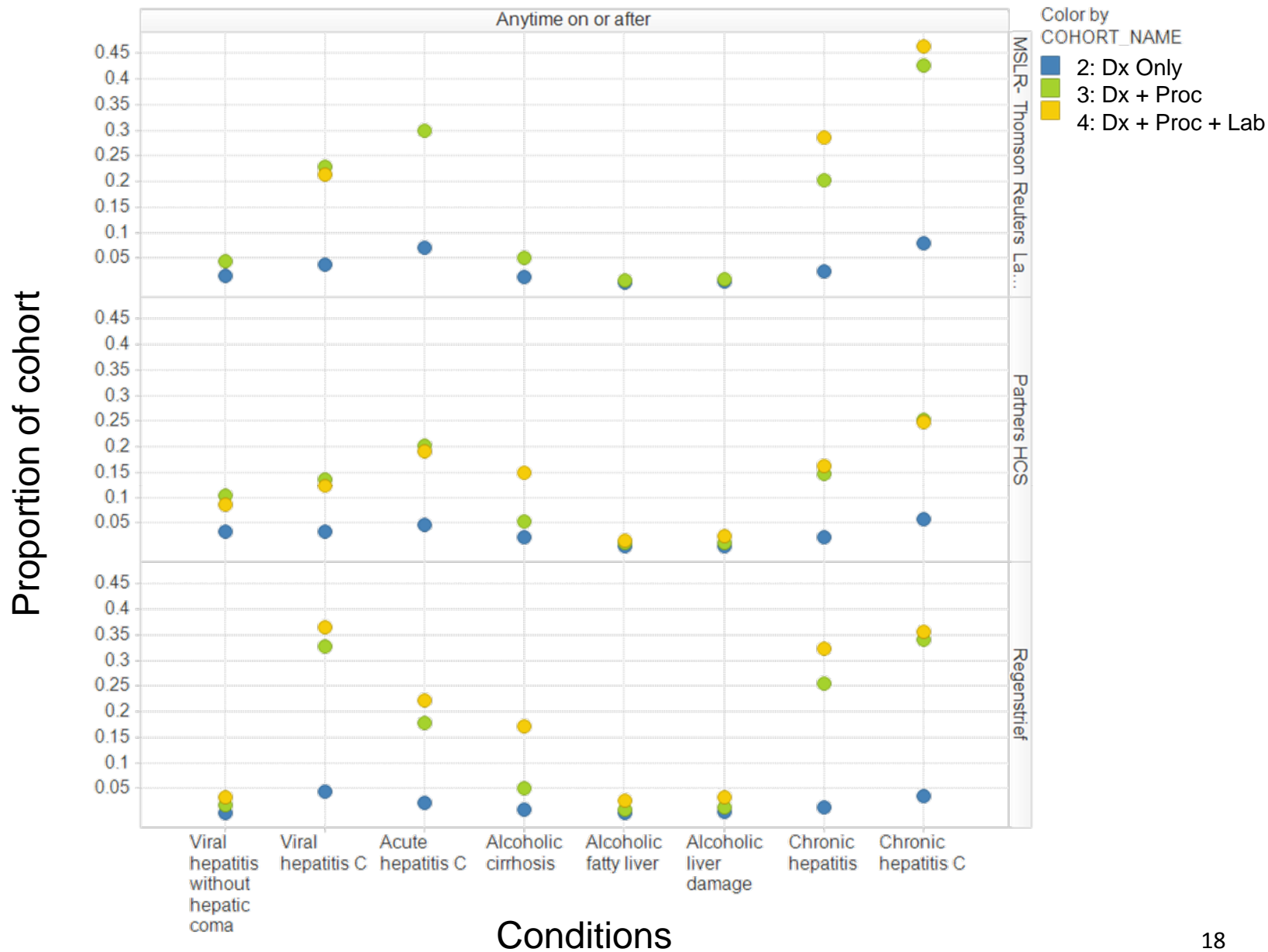


Factors to consider when identifying drug-induced liver injury cases

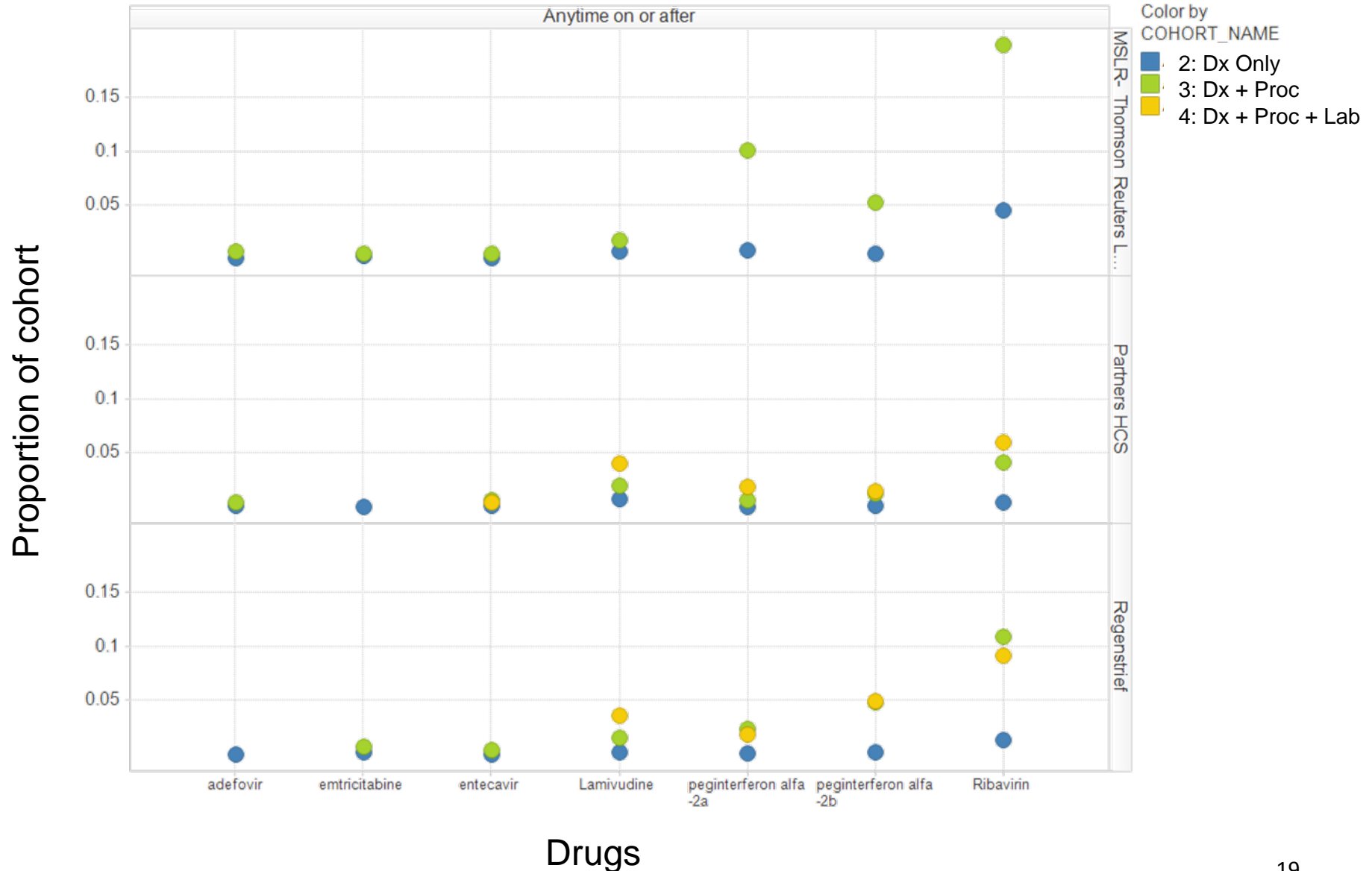
Rule out alternative cause of acute liver injury

- 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

Alternative causes of acute liver injury: diagnoses



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 exploring 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

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Backup

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

Code	Vocabulary	Description
47000	CPT	Biopsy of liver, needle; percutaneous
47001	CPT	Biopsy of liver, needle; when done for indicated purpose at time of other major procedure (List separately in addition to code for primary procedure)
47100	CPT	Biopsy of liver, wedge
78205	CPT	Liver imaging (SPECT);
78206	CPT	Liver imaging (SPECT); with vascular flow
50.11	ICD9 Procedure	Closed (percutaneous) [needle] biopsy of liver
50.14	ICD9 Procedure	Laparoscopic liver biopsy
50.12	ICD9 Procedure	Open biopsy of liver
50.91	ICD9 Procedure	Percutaneous aspiration of liver
50.13	ICD9 Procedure	Transjugular liver biopsy

Plus 34 LOINC codes for Liver CT, MR, SPECT, and US

Therapeutic procedures

Code	Vocabulary	Description
47136	CPT	Liver allotransplantation; heterotopic, partial or whole, from cadaver or living donor, any age
47135	CPT	Liver allotransplantation; orthotopic, partial or whole, from cadaver or living donor, any age
50.51	ICD9 Procedure	Auxiliary liver transplant
50.5	ICD9 Procedure	Liver transplant
50.59	ICD9 Procedure	Other transplant of liver
39694-5	LOINC	Liver Transplant RI W RNC IV
39454-4	LOINC	Liver Transplant US
38765-4	LOINC	Liver Transplant US Bx guid
30706-6	LOINC	Liver US in Surg

<http://omop.fnih.org/AcuteLiverInjury>