**Background**

Hepatic injury is one of the major drug safety issues. Non-steroidal anti-inflammatory drugs (NSAIDs) have been associated with liver injury. Objectives: To quantify exposure to NSAIDs/painkillers prior to hospital admission for acute liver injury (ALI) in the French national healthcare insurance database. SNDS was organized on hospital admissions for ALI (K71.2, 9, K72.0) over 2010-2014 were identified in SNDS (16,673,771 persons). Previous diagnoses of liver diseases/liver injury were excluded. Exposures of interest were NSAIDs (ATC codes M01A), non-steroidal polyarthritis (NSAP) (N28A, N28B), and tramadol (N02AX02) dispensed from 7 to 60 days before hospitalization, to avoid induction and inclusion of confounders. Reference populations were all the French population over the study period, extrapolated from the 1997 permanent representative sample. EGB in a case-population analysis; b) patients dispensed from EGB, same index date than the case population analysis. Results: Number of cases (years) is the number of patients with at least one interest drug dispensed over the study period (2010-2014), extrapolated to the whole French population.

**Methods**

- **Study design**
  - Case-population study of adults with a 1st hospitalization for ALI from 2010 to 2014.
  - Case-control study of adults exposed to interest drugs from 2010 to 2014.
- **Data source**: the SNDS French nationwide claims database which covers 96% of the French population and the EGB 1st permanent representative sample of SNDS.
- **Study population**
  - **Identification in SNDS among adult patients with a 1st hospitalization from 2010 to 2014 with main diagnosis of acute liver injury (ICD-10 codes K71.2, K71.9).**
  - **Reference population** identified in EGB among adult patients affiliated at least one day for each year considered to the national healthcare insurance system for salaried workers (CNAMTS).
- **Control identified in EGB among adults affiliated to the CNAMTS and hospitalized between 2010 and 2014 for a reason other than ALI.**

**Results**

- **Identification of ALI cases - Case-population analysis**
  - Source population: Patients identified in EGB between 2010 and 2014
  - n = 13,954
  - A total of 3,914 cases were dispensed any drug within 7-60 days before admission (OR 3.1 (1.8-5.1)).
  - Diagnoses of liver disease/liver injury were excluded. Exposures of interest were systemic NSAIDs (ATC codes M01A), non-steroidal polyarthritis (NSAP) (N28A, N28B), and tramadol (N02AX02) from 7 to 60 days before hospitalization.

- **Exposure of adult ALI cases**
  - 17% of cases were exposed to at least one NSAID (among NSAIDs with at least 5 exposed cases).
  - Exposure ranged from 228 cases for ibuprofen to 5 cases for nimesulide (Table 1).
  - 36.3% of cases were exposed to paracetamol and 3.4% to tramadol.

- **Incidence of hospitalization for ALI**
  - For NSAIDs, event rates per PM ranged from 300 (120-617) for meloxicam to 38 (11-88) for nimesulide and per PM from 14 (9.5-19) for celecoxib to 2 (0.6-3.6) for nimesulide.
  - For paracetamol (alone and combinations), event rate was 105 (96-117) per PM and 32 (28-35) per PM. For tramadol, event rate was 91 (77-106) and 16 (15-22) per PM.

**Conclusion**

- **Declaration of Interest Statement**
  - This study was supported by an unconditional public joint help from Direction Générale de la Santé (DGS), from Mission recherches de la Direction de la Recherche, des Etudes, des Evaluations et des Statistiques (MRES/DER), Catholic National Association Maladies des Travailleurs Salariés (CNAMTS), and part of the general call for projects by IRHP (Appel à Projets Institut de Recherche en Santé Publique) in 2013. It was conducted by Bordeaux PharmacoEpi Platform. All authors denied other relationships to disclose for this study.

- **Objectives**
  - To quantify exposure to non-steroidal anti-inflammatory drugs (NSAIDs) and analgesics prior to hospital admission for ALI in the French National healthcare insurance systems database SNDS.

- **Identification of controls - Case-control analysis**
  - Source population: Patients identified in EGB between 2010 and 2014
  - n = 13,954
  - Potential controls: All patients with at least one interest drug dispensed over the study period (2010-2014), extrapolated to the whole French population.

- **Risk of hospital admission for ALI**
  - For NSAIDs, OR was 1.4 (1.3-1.5) and ranged from 3.5 (1.9-2.4) for meloxicam to 0.6 (0.2-1.6) for nimesulide (Figure 3).
  - The OR was 1.4 (1.2-1.6) for paracetamol and 2.3 (1.9-2.8) for tramadol.

- **Methods**
  - **Identification of ALI cases – Case-population analysis**
    - Source population: Patients identified in EGB between 2010 and 2014
    - n = 13,954
  - **Identification of controls – Case-control analysis**
    - Source population: Patients identified in EGB between 2010 and 2014
    - n = 13,954
  - **Risks of hospital admission for ALI**
    - For NSAIDs, OR was 1.4 (1.3-1.5) and ranged from 3.5 (1.9-2.4) for meloxicam to 0.6 (0.2-1.6) for nimesulide (Figure 3).
    - The OR was 1.4 (1.2-1.6) for paracetamol and 2.3 (1.9-2.8) for tramadol.