

Seasonality in Acute Liver Injury in Healthcare Claims Data

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BACKGROUND

- Use of acetaminophen-containing cold and flu products fluctuates seasonally.
- There may be a corresponding seasonal pattern in the occurrence of acute liver injury (ALI), a known adverse reaction of acetaminophen use exceeding the 4 gram daily maximum.

OBJECTIVE

- Determine whether there were any clinical patterns in database hospitalizations for acute liver injury that might correspond to cold/flu season.

METHODS

Data sources

- Truven MarketScan Commercial Claims and Encounters (CCAE)
- Medicare Supplemental (MDCR)

Visual assessment

- Plot monthly rates of hospitalized diagnoses for all enrollees in the database

Statistical test

- Apply Brookhart and Rothman [1] test of intensity of seasonal occurrence

Measure

- Monthly rate of hospital visits for ALI among all enrolled in the database for that month (and the prior 6 months) in 2002-2010

Positive & negative controls

- Positive controls
 - Common cold (acute nasopharyngitis)
 - Influenza
- Negative controls
 - Breast cancer
 - Diabetes

ALI diagnosis definitions

- **Narrow**—require diagnostic procedure in prior or therapeutic procedure in following 30 days
- **Broad**—primary diagnosis for hospitalization w/o ALI dx in prior 60 days
- **Very broad**—any ALI dx w/o requirement of hospitalization

CCAE Database
102,681,594 subjects
OMOP CDM V4

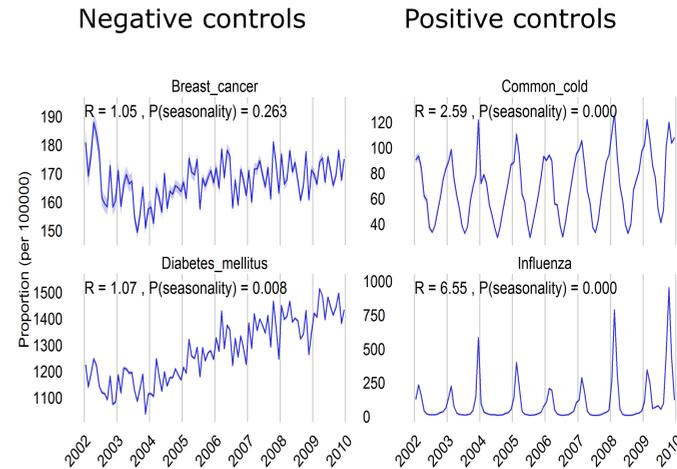


Figure 1a. Negative (left) and positive (right) controls in CCAE

MDCR Database
8,073,061 subjects
OMOP CDM V4

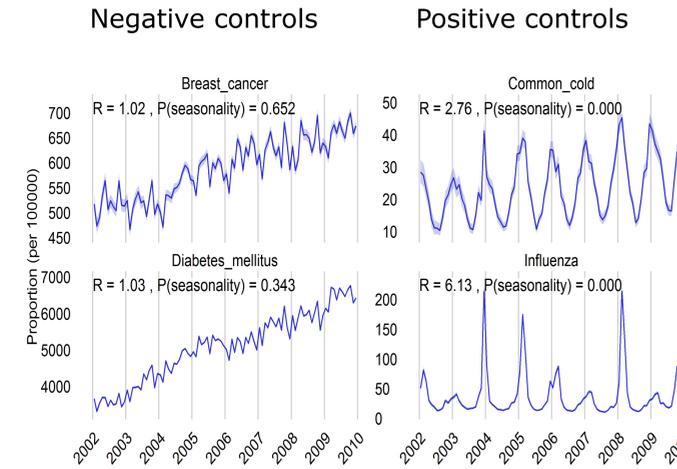


Figure 1b. Negative (left) and positive (right) controls in MDCR

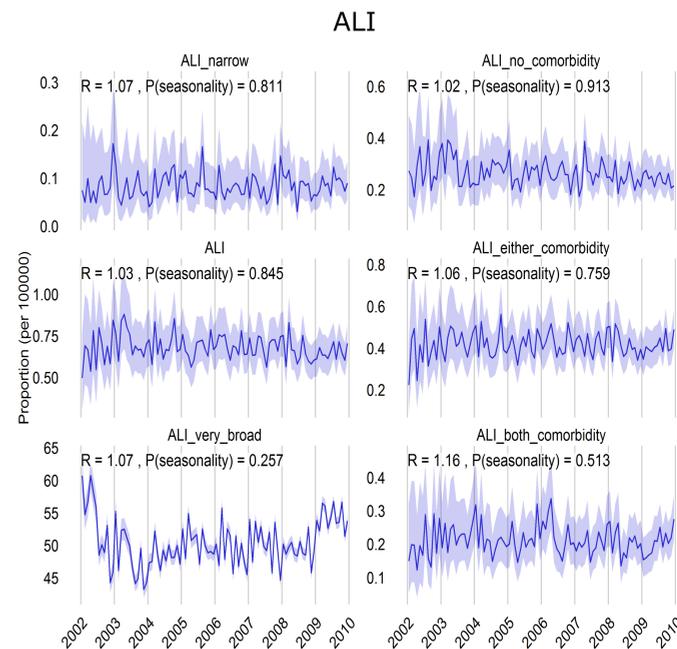


Figure 2a. Prevalence using various definitions of ALI in CCAE

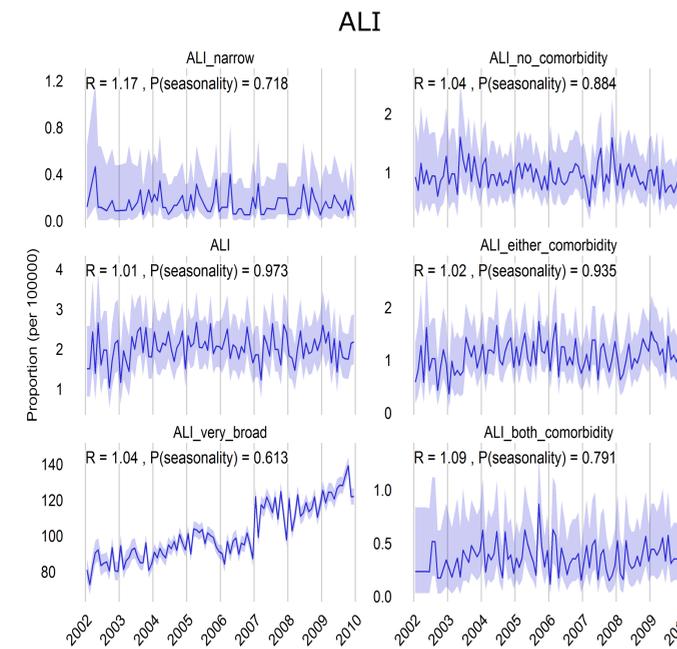


Figure 2b. Prevalence using various definitions of ALI in MDCR

ALI comorbidity subgroups

- Without hepatitis or cirrhosis
- With both hepatitis and cirrhosis
- With either hepatitis or cirrhosis

Statistical test for seasonality

- Assumes a sinusoid pattern is evidence of seasonality & included a linear component for long term trends
- The model for the expected count of events $E[N_i]$ in time period i is

$$\log(E[N_i]) = \beta_0 + \beta_1 \sin(\theta_i) + \beta_2 \cos(\theta_i) + \beta_3 \tau + \log(\varphi_i)$$

where τ is the number of months since study start date, $\theta_i = 2\pi(\text{month_of_i} - 1)/12$, $\varphi_i = \text{population_size_in_period_i} * \text{number_of_days_in_period_i} / 365.25$.

- The peak-to-low ratio of the process is given by:

$$R = \frac{\exp(\beta_0 + \sqrt{\beta_1^2 + \beta_2^2})}{\exp(\beta_0 - \sqrt{\beta_1^2 + \beta_2^2})} = \exp(2\sqrt{\beta_1^2 + \beta_2^2})$$

We compute $P(\text{Seasonality})$, the p-value corresponding to the null hypothesis that $R=1$.

RESULTS

- Figures 1a and 1b show the prevalence, R and p-values for the negative and positive controls.
- Figures 2a and 2b show this information for the various definitions of ALI.

CONCLUSIONS

- Positive and negative controls showed the expected patterns, giving some confidence in our method.
 - Cold and flu rates were significant for seasonality.
 - Breast cancer and diabetes diagnosis rates were not significant for seasonality, with 1 exception.
 - Diabetes in CCAE was significant for seasonality. This may be a utilization pattern—lower rates at year end.
- Prevalence of ALI with & without comorbidities was low, leading to wide confidence bands. Seasonal component was not significant.
- After dropping hospitalization requirement to increase precision, there was still no evidence for a seasonal component to ALI.

REFERENCE

1. Brookhart, MA, Rothman, KJ. Simple estimators of the intensity of seasonal occurrence. *BioMed Central Medical Research Methodology*. 2008, 8:67 doi:10.1186/1471-2288-8-67.

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