

THE RECENT CHANGE IN EPIDEMIOLOGY OF CHRONIC LIVER DISEASE IN JAPAN: AN ANALYSIS OF CLAIMS DATABASE

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Introduction

Background

✓ Hepatitis B or C infection has been major cause of chronic liver disease (CLD) in Japan. Actions to control infection have been performed, such as a hepatitis B immunization program to prevent vertical infection. Also, innovative medicines for hepatitis C were recently introduced. However, little is understood about nationwide epidemiological changes in the etiology of CLD.

Objective

✓ To describe, and chronologically visualize, the landscape of CLD in Japan.

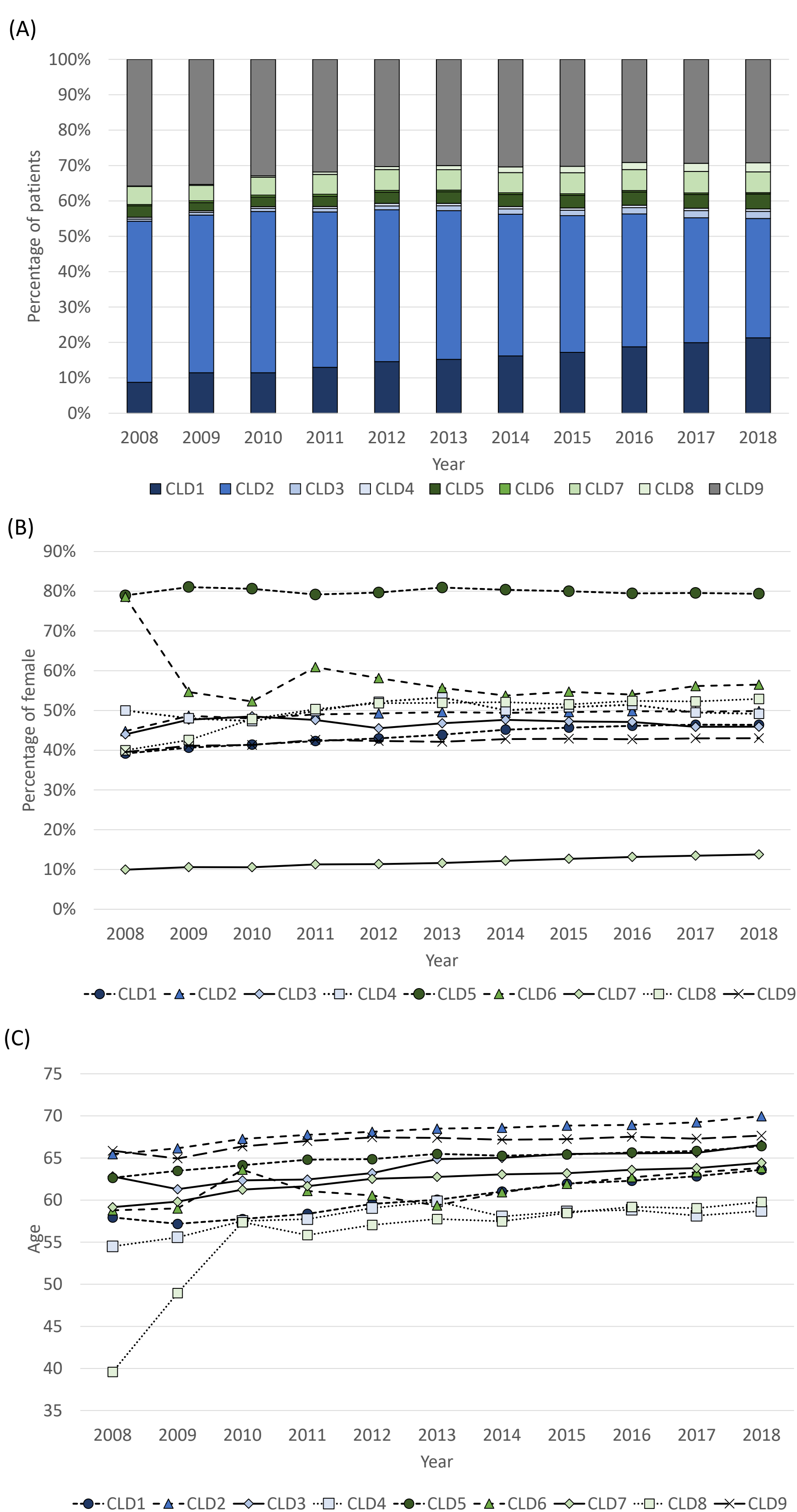
Results

Patient distribution and demographics by disease category

- ✓ There were 1,790,449 patients with CLD (mean age: 66.4, female: 45.8%) in the database.
- ✓ Hepatitis C was the highest percentage of patients among all disease categories throughout study period, but it has been decreasing from 45% in 2008 to 40% in 2015, and 33.7% in 2018 (Figure 1A).
- ✓ Hepatitis B was the second highest (besides CLD9 - others); it has been increasing from 8.7% in 2008 to 11.4% in 2009, and 21.3% in 2018 (Figure 1A).
- ✓ Other than viral hepatitis, alcoholic hepatitis was relatively high, around 6%, followed by autoimmune hepatitis, around 3-4%. Non-alcoholic steatohepatitis (NAFLD) was not high, but has increased from less than 1% prior to 2013 to 2.6% in 2018 (Figure 1A).
- ✓ Percentage of female was almost 50% for most disease categories, but high in autoimmune hepatitis (about 80%), and low in alcoholic hepatitis (about 10%) throughout the study period (Figure 1B).
- ✓ Mean age has slightly increased for all disease categories (Figure 1C).
- ✓ Hepatitis C had the highest mean age, about 70 years, and NAFLD and viral hepatitis (virus not specified) had the lowest, 59.8 years and 58.7 years, respectively, in 2018.

Figure 1. (A) Patients distribution, (B) percentage of female, and (C) mean age of patients with CLD by disease category in each year (2008-2018)

CLD1: hepatitis B, CLD2: hepatitis C, CLD3: hepatitis B and C, CLD4: viral hepatitis (virus not specified), CLD5: autoimmune hepatitis, CLD6: toxic/drug induced hepatitis, CLD7: alcoholic hepatitis, CLD8: non-alcoholic steatohepatitis, CLD9: others



Conclusions

- ✓ Hepatitis C still accounts for the largest proportion of the CLD population in Japan, but the percentage has decreased over time. Other categories of CLD have relatively grown overtime, but the change in prevalence is still unknown.
- ✓ Additional research is needed to understand whether the prevalence of any CLD disease category has been increasing or decreasing, and reasons for any prevalence changes.

Comorbidities

- ✓ Comorbidities including top 10 diagnoses for each category are shown in Table 1. Some comorbidities, such as gastro-oesophageal reflux disease, essential hypertension, gastritis and duodenitis, and other functional intestinal disorders were often diagnosed (around 30% or more) with CLD for most CLD disease categories (Table 1).
- ✓ Essential hypertension was often diagnosed for all categories, but it was especially high in those with alcoholic hepatitis (Table 1).
- ✓ Osteoporosis without pathological fracture was frequently diagnosed for those specifically with autoimmune hepatitis (Table 1).
- ✓ Disorders of lipoprotein metabolism and other lipidaemias was diagnosed relatively often in most of disease categories, but especially high, 55%, for those with NAFLD (Table 1).

Table 1. Percentage of diagnosed comorbidities in patients with CLD, by disease category (2017)

	CLD1	CLD2	CLD3	CLD4	CLD5	CLD6	CLD7	CLD8	CLD9
Gastro-oesophageal reflux disease	34%	33%	37%	29%	49%	36%	47%	29%	41%
Essential (primary) hypertension	32%	43%	39%	35%	39%	40%	48%	43%	49%
Gastritis and duodenitis	29%	31%	32%	23%	36%	32%	34%	27%	34%
Other functional intestinal disorders	27%	28%	29%	29%	32%	40%	28%	21%	36%
Gastric ulcer	23%	24%	30%	23%	32%	26%	29%	18%	29%
Disorders of lipoprotein metabolism and other lipidaemias	23%	22%	24%	30%	40%	34%	21%	55%	36%
Sleep disorders	19%	24%	23%	22%	27%	32%	30%	18%	26%
Dorsalgia	19%	22%	24%	19%	22%	26%	20%	17%	25%
Unspecified diabetes mellitus	18%	23%	27%	20%	26%	19%	22%	33%	25%
Type 2 diabetes mellitus	17%	20%	23%	20%	21%	18%	28%	40%	26%
Other diseases of liver	14%	13%	17%	21%	35%	25%	20%	49%	25%
Iron deficiency anaemia	14%	18%	23%	22%	19%	17%	22%	16%	19%
Osteoporosis without pathological fracture	13%	11%	14%	12%	42%	17%	6%	8%	13%
Other metabolic disorders	4%	7%	7%	3%	7%	4%	27%	6%	9%

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Discussions

- ✓ We showed patients distribution and demographics of patients with CLD by disease category.
 - Hepatitis C has decreased as a percentage of the total CLD cases over time, but it still accounted for the largest percentage of CLD patients. An increase in Hepatitis B was observed, but total of Hepatitis B and C (including CLD1, 2, and 3) has tended to decrease in recent years. Age and female rate tended to increase in these categories. Infection control and consequent aging of patients may be associated with these results.
 - An increase in NAFLD was observed, although the percentage was still low. It is possibly due to an improved recognition of the disease.
- ✓ Some comorbidities were often diagnosed regardless of disease categories, and others were for specific categories.
 - Essential hypertension and dyslipidaemias were often diagnosed in patients with alcoholic hepatitis and NAFLD, respectively. Particular categories of CLD and comorbidities may be associated directory, or have same other cause such as lifestyle, including eating and drinking habits.
 - Osteoporosis without pathological fracture was frequently diagnosed in patients with autoimmune hepatitis in this study. However, it may include those who were given the diagnosis due to prescription for bisphosphonate to prevent osteoporosis that can be caused by treatment with steroids.
- ✓ Limitations
 - CLD and its categories were defined based on disease name in claims. However, we have not done a validation study on it.
 - There may be different rates of undiagnosed patients actually having certain conditions among disease categories due to the availability of effective treatment. For example, effective medications are available for hepatitis C, but not for NAFLD. Rates of under diagnosis are not known, which is limitation of a database study.
 - This database consisted of data from acute-care hospitals that apply the Japanese Diagnosis and Procedure Combination per diem bundle payment system. Therefore, treatment conducted outside the hospitals was not included.

Methods

Study Design

✓ Claims based cohort study

Data Source

✓ A Japanese claims database consisting of data from acute hospitals from April 2008 to August 2018 (N=25 million) provided by Medical Data Vision (Tokyo, Japan)

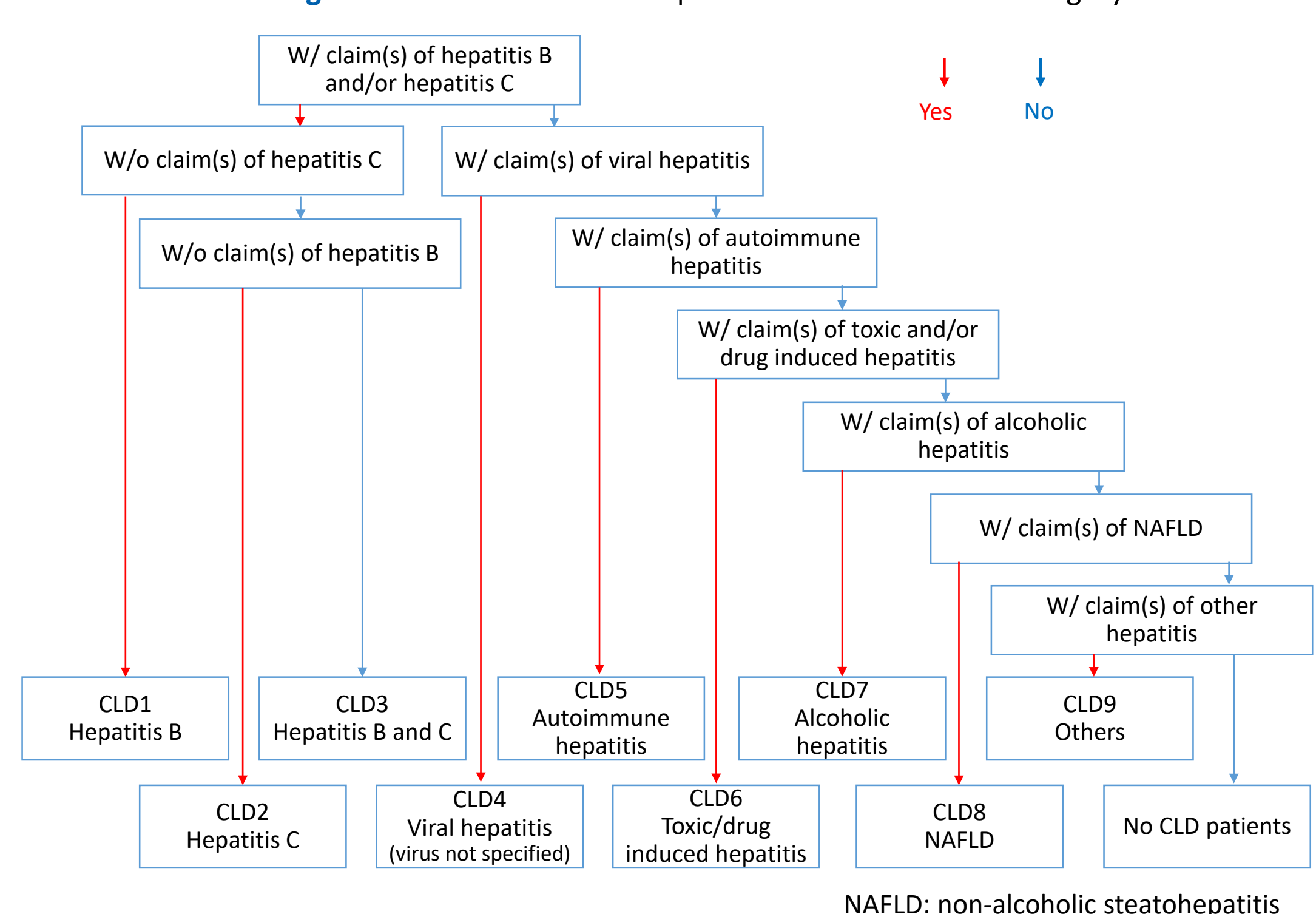
Patients

- ✓ Patients having at least one claim with any diagnosis of CLD (defined by disease name) were included as patients with CLD.
- ✓ The patients were classified into nine categories with mutually exclusive criteria as shown in Figure 2.

Analysis

- ✓ Patient distribution and demographics in each category were calculated by year (2008-2018).
- ✓ Comorbidities were analyzed based on diagnoses defined by ICD-10 3-digit code by category in 2017.

Figure 2. Classification of CLD patients for each disease category



NAFLD: non-alcoholic steatohepatitis