*Original Article*

# National trends in hospitalizations for gastrointestinal bleeding in Japan

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**Gastrointestinal bleeding (GIB) is a significant public health concern, predominantly associated with high morbidity. However, there have been no reports investigating the trends of GIB in Japan using nationwide data. This study aims to identify current trends and issues in the management of GIB by assessing Japan's national data. We analyzed National Database sampling data from 2012 to 2019, evaluating annual hospitalization rates for major six types of GIB including hemorrhagic gastric ulcers, duodenal ulcers, esophageal variceal bleeding, colonic diverticular bleeding, ischemic colitis, and rectal ulcers. In this study, hospitalization rates per 100,000 indicated a marked decline in hemorrhagic gastric ulcers, approximately two-thirds from 41.5 to 27.9, whereas rates for colonic diverticular bleeding more than doubled, escalating from 15.1 to 34.0. Ischemic colitis rates increased 1.6 times, from 20.8 to 34.9. In 2017, the hospitalization rate per 100,000 for colonic diverticular bleeding and ischemic colitis surpassed those for hemorrhagic gastric ulcers (31.1, 31.3, and 31.0, respectively). No significant changes were observed for duodenal ulcers, esophageal variceal bleeding, or rectal ulcers. The findings of this study underscore a pivotal shift in hospitalization frequencies from upper GIB to lower GIB in 2017, indicating a potential shift in clinical focus and resource allocation.**

***Key Words*: gastrointestinal bleeding, hospitalization, upper gastrointestinal bleeding, lower gastrointestinal bleeding, national database**

Gastrointestinal bleeding (GIB) represents the most common gastrointestinal-related cause of hospitalization. In the U.S., GIB accounted for over 500,000 hospital admissions in 2014, imposing an annual healthcare economic burden of nearly 5 billion U.S. dollars.[1] GIB is categorized into Upper GIB (UGIB) and Lower GIB (LGIB); UGIB refers to bleeding originating from the esophagus, stomach, or duodenum, while LGIB is epidemiologically defined as bleeding from a site distal to the Ligament of Treitz. Clinically, LGIB is often diagnosed as colonic bleeding.

Internationally, studies have reported a decreasing trend in UGIB,[2–8] while trends in LGIB have shown some variability. Specifically, data up to the early 2010s indicated an increasing trend in LGIB;[2,7,9] however, several reports based on data from the late 2010s onwards have noted a gradual decrease in LGIB.[10,11] Moreover, data suggests that LGIB has been on a decreasing trend since the early 2000s,[8,12] and various reports have been made depending on the country. In Japan, however, our recent understanding of GIB has been limited to single-center studies, registry-based reports, and one study using a specific claims database that does not include data on patients over 75 years of age,[13–15] leaving a gap in knowledge concerning national trends.

Given the variations in *Helicobacter pylori* (*H. pylori*) infection rates, demographic factors including age, antithrombotic therapy, and racial characteristics, directly extrapolating international trends to the Japanese context might be challenging. Understanding the distinct characteristics of GIB patients in Japan is crucial for identifying current issues in GIB and allocating resources appropriately.

To address the knowledge gap in the literature, this study aims to assess Japan's national trends in GIB hospitalizations, using the National Database of Health Insurance Claims and Specific Health Checkups (NDB) sampling data.

## Materials and Methods

**Study design.** This is a descriptive study based on the NDB sampling data publicly available from the Initiative for Clinical Epidemiological Research (https://icer.tokyo/). This data, edited and published by the Ministry of Health, Labour, and Welfare (MHLW), originates from the NDB sampling data, and lacks corresponding tables, making it impossible to identify individuals. Consequently, ethical approval was not required for this research.

**Data source.** The NDB is established by the MHLW and contains detailed information on almost all medical claims data in Japan.[16] It provides a comprehensive view of medical claims across the country, encompassing a wide range of information from diagnoses to various treatments such as prescriptions, injections, examinations, and surgeries for both outpatients and inpatients.[16] Given that Japan operates under a universal healthcare system,[17] the NDB covers nearly all ( $\geq$95%) hospital admissions in the country, aside from public expenditures.[18] As a sampling dataset, we procured claims data, randomly selected to cover 10% of all inpatients in January, April, July, and October from the years 2012 to 2019, from the Initiative for Clinical Epidemiological Research (https://icer.tokyo/materials/ndb_feasibility_check/). The NDB sampling data is obtained through stratified random sampling, making it a highly representative and valid sample of the nearly entire Japanese population.[19] Indeed, some comprehensive national studies have been conducted using this NDB sampling data, demonstrating its value in nationwide healthcare research.[20–24]

**Participants.** We identified hospitalized patients aged 10 and above with principal diagnoses of GIB, including hemorrhagic gastric ulcer, hemorrhagic duodenal ulcer, esophageal

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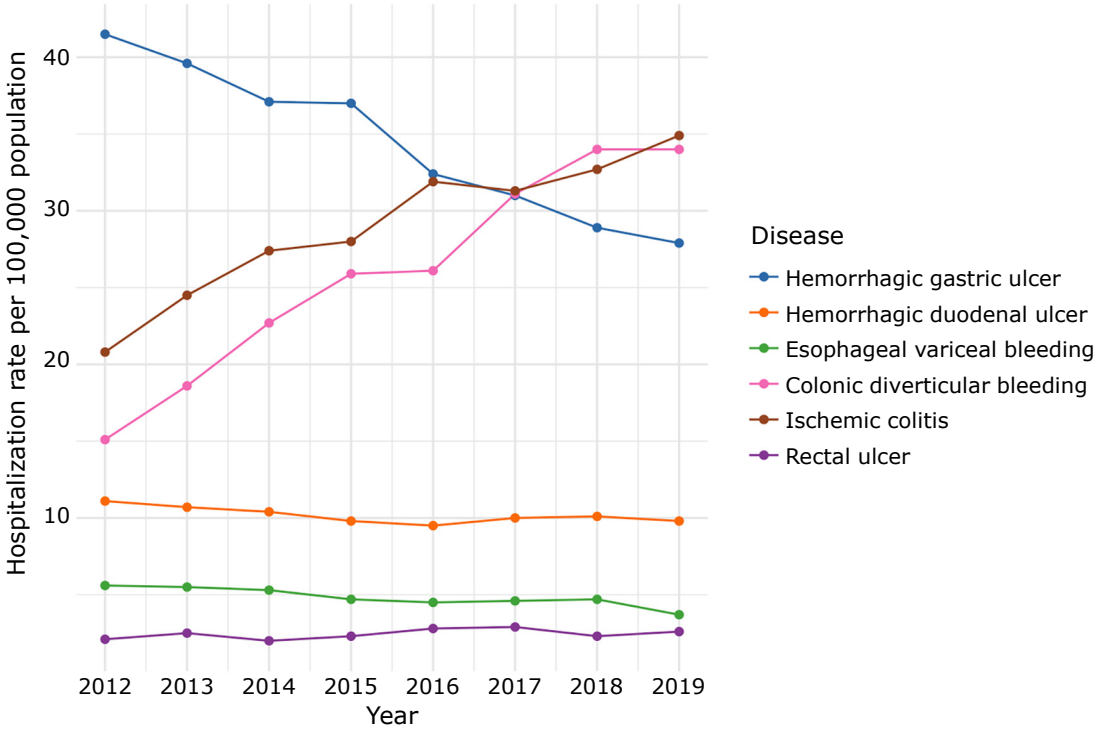


**Fig. 1.** Trends in annual hospitalization rates. See color figure in the on-line version.

variceal bleeding, colonic diverticular bleeding, ischemic colitis, and rectal ulcer. Specific billing codes were used to establish these diagnoses, and their correspondence with ICD-10 codes can be found in Supplemental Table 1*.

**Population at risk.** The population data were sourced from the Current Population Estimates as of October 1st for each respective year, provided by the Japanese Ministry of Internal Affairs and Communications (https://www.e-stat.go.jp). We focused on the entire population aged 10 and above for this study.

**Outcomes and measurements.** We investigated three primary outcomes. First, we examined the annual hospitalization rates per 100,000 for each GIB, calculated using the annual number of hospitalizations and Japan's population data for each respective year. Second, we assessed the age distribution for each disorder. Subsequently, we divided the data into two periods, 2012–2015 and 2016–2019, to evaluate any differences in age distribution between these periods.

As a secondary outcome, we assessed the seasonal variation of each disorder by examining occurrences in January, April, July, and October.

It is important to note that the numbers represented in this sample data from the NDB account for a 10% non-weighted sample from the medical receipts for these specific four months. To estimate the overall annual number of hospitalizations, these figures were multiplied by 30 for the primary outcomes and by 10 for the secondary outcomes.[23]

**Statistical analyses.** Statistical analysis was conducted using R software (ver. 4.2.1, R Foundation for Statistical Computing, Vienna, Austria).

## Results

**Hospitalization rates for GIB.** From 2012 through 2019, hospitalization rates showed the following trends (Supplemental Table 2*, Fig. 1): for hemorrhagic gastric ulcer, rates decreased from 41.5 to 27.9 per 100,000, representing a reduction to approximately two-thirds of the 2012. Hemorrhagic duodenal ulcer rates declined from 11.1 to 9.8 per 100,000. Esophageal variceal bleeding rates went down from 5.6 to 3.7 per 100,000. By contrast, colonic diverticular bleeding rates increased from 15.1 to 34.0 per 100,000, marking an increase of approximately 2.3 times the rate at 2012. Ischemic colitis rates rose from 20.8 to 34.9 per 100,000, an increase of about 1.6 times. Rectal ulcer rates showed some fluctuation but ultimately increased from 2.1 to 2.6 per 100,000. Notably, the hospitalization rate of colonic diverticular bleeding and ischemic colitis surpassed the rates of hemorrhagic gastric ulcers in 2017.

**Age distribution.** In overall age distribution, the peak age for hospitalization due to most types of GIB is between 80 and 84 years. The peak age for esophageal variceal bleeding was between 60 and 79 years, and for rectal ulcers was between 85 and 89 years (Fig. 2). Comparing the years 2012–2015 to 2016–2019, hemorrhagic gastric ulcers showed a decrease, especially in the age groups 55–84 years (Supplemental Fig. 1*). In contrast, both colonic diverticular bleeding and ischemic colitis increased, particularly in the age groups of 65–94 years (Supplemental Fig. 2*). Hemorrhagic duodenal ulcers, esophageal variceal bleeding, and rectal ulcers did not show marked age distribution trends.

**Seasonal variations.** Hemorrhagic gastric ulcers and duodenal ulcers tend to be less frequent in July, while colonic diverticular bleeding and ischemic colitis are less common in January. Specifically, for colonic diverticular bleeding, cases were fewer in January with 17,650 cases, and showed a gradual increase through April with 19,210 cases, July with 20,770 cases, and peaking in October with 23,020 cases. No significant seasonal variations were observed for esophageal variceal bleeding and rectal ulcer (Fig. 3).

## Discussion

This national data-based study revealed several trends in GIB hospitalizations in Japan. The hospitalization rate for hemor-

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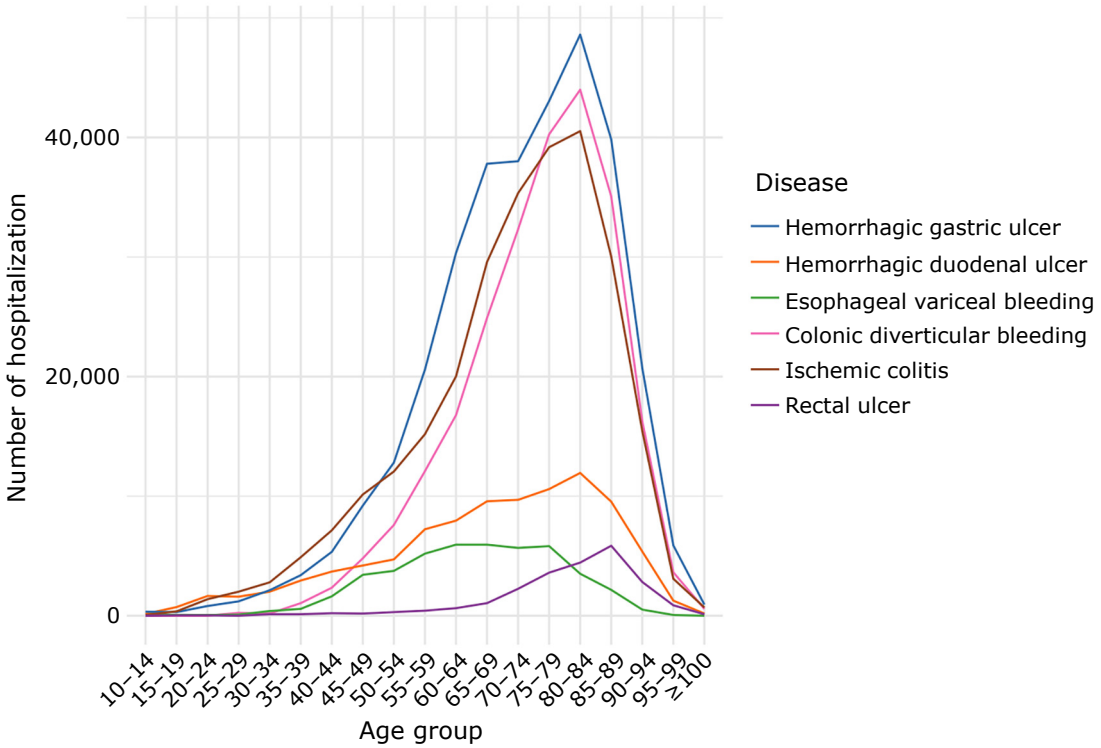


**Fig. 2.** Hospitalization volume by age group. See color figure in the on-line version.

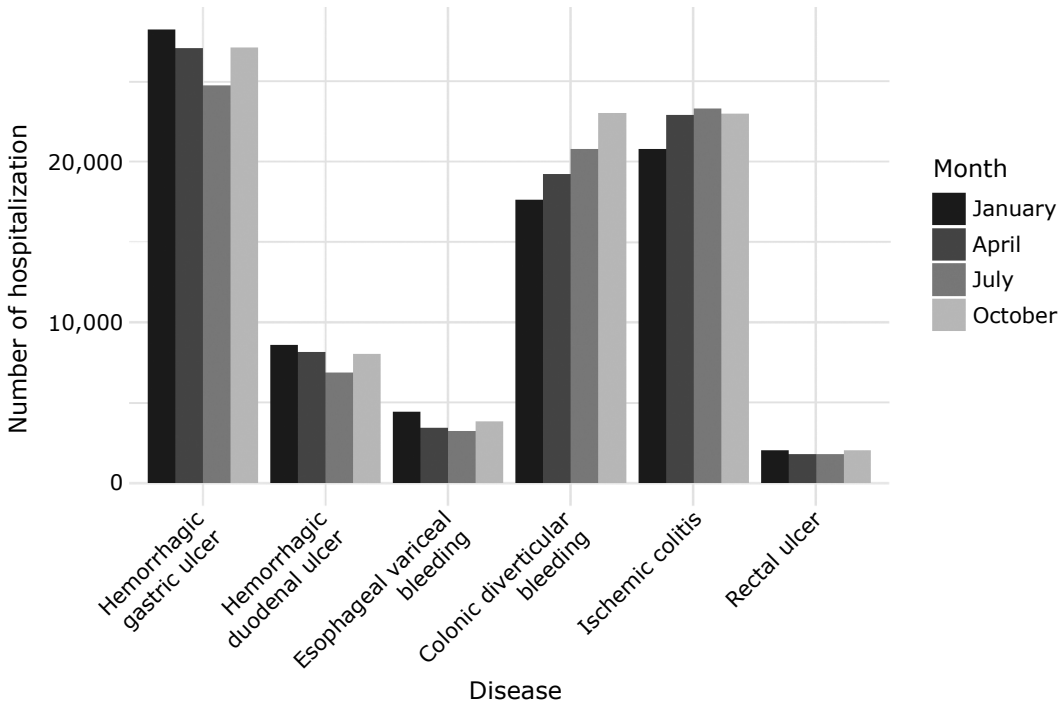


**Fig. 3.** Seasonal variations in hospitalization volume. See color figure in the on-line version.

rhagic gastric ulcers consistently decreased. In contrast, the hospitalization rates for colonic diverticular bleeding and ischemic colitis continued to increase. Moreover, the hospitalization rate for colonic diverticular bleeding and ischemic colitis surpassed those of hemorrhagic gastric ulcers in 2017. The study also provided insights into the recent age distribution of each GIB in Japan. While the causality is not clear, it highlighted the characteristic seasonal variations of each GIB.

The trends in hospitalizations for GIB vary by country. In the United States in 2018, national data showed a higher incidence of upper UGIB hospitalizations at 97.6 per 100,000 compared to LGIB at 35.5 per 100,000.[25] In contrast, Hong Kong's national


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data reported a gradual decrease in UGIB since 2009, with LGIB remaining stable, and hospitalization numbers shifting to LGIB>UGIB by 2011.10 The ratio of UGIB to LGIB decreased from 1.43 in 2009 to 0.43 in 2019.[10] Our study shows that Japan's national trend differs from the US and aligns more closely with Hong Kong's pattern. The reasons for these differences could involve a comprehensive range of factors including ethnicity, medication use, age composition, lifestyle, and healthcare systems. This underscores the importance of using national data for research, rather than applying foreign data indiscriminately.

Our research in Japan indicated a trend shift from UGIB to LGIB, paralleling findings in Hong Kong. Hong Kong studies showed a negative correlation between UGIB hospitalizations and proton pump inhibitors (PPIs) prescriptions, with aspirin increases linked to a rise in GIB, suggesting LGIB's rise due to the absence of preventive medications like PPIs.[10] This shift in Japan might be attributed to similar reasons, but our study faced limitations due to database characteristics, making it difficult to investigate population prescriptions. Considering Japan's exceptional aging society, an increase in antithrombotic prescriptions and NSAIDs could explain the LGIB trend.[13,26–29] Additionally, since 2013, *H. pylori* eradication for chronic gastritis has become insurance-covered in Japan,[30] and its widespread adoption could have accelerated the UGIB decline, given *H. pylori* infection's significant risk of ulcer formation.[2,7,31–33]

Our research also highlights seasonal trends in GIB types, with patterns such as a decrease in hemorrhagic gastric and duodenal ulcers during July and a reduction in colonic diverticular bleeding and ischemic colitis in January. This observation aligns with literature suggesting a summertime decline in hemorrhagic ulcers.[34–38] Although various theories exist, the proposed explanation involves the body's response to cold stress, leading to vascular and mucosal changes that increase peptic ulcer disease (PUD) risk.[39] On the contrary, colonic diverticular bleeding and ischemic colitis show a decrease in incidence during the summer months. The seasonal influence on colonic diverticular bleeding and ischemic colitis is less clear,[40–42] with factors such as climate and lifestyle, as well as dietary elements like certain vitamins, playing roles. This suggests that mechanisms other than cold stress, which is significant in PUD, might be at play.[39–44] The complexity and variability of these findings underscore the importance of further research to elucidate the seasonal patterns of GIB more clearly.

This study has several limitations. First, the study's identification of diseases is based on billing codes, not information from electronic medical records, which might affect accuracy. Second, while the NDB dataset includes more than 95% of health insurance coverage in Japan, it does not account for specific groups prioritized for public expenditures, such as welfare recipients or atomic bomb victims, potentially leading to a slight underestimation of the actual patient count.[18] Third, due to the characteristics of the database, this study was able to investigate GIB trends but not population prescription trends. As a result, we have not been able to evaluate the causal relationship between drug use and GIB trends. Lastly, due to the restrictions on the data available for this study, we were unable to assess GIB-related mortality or evaluate other diseases that could serve as underlying causes for GIB, such as esophageal reflux, small intestine bleeding, post-polypectomy bleeding, or tumor-related bleeding. These limitations should be considered when interpreting the study's findings.

## Conclusions

In conclusion, this national study underscores the evolving landscape of GIB in Japan, marked by a decrease in UGIB, especially hemorrhagic gastric ulcers, and a notable increase in hospitalization for LGIB, specifically colonic diverticular bleeding and ischemic colitis. This trend highlights the necessity of enhancing treatment strategies and resource allocation for LGIB management. Understanding these shifting dynamics is essential for improving patient outcomes and effectively addressing the current challenges in GIB healthcare in Japan.

## Author Contributions

CI contributed to the planning, data gathering, literature review, writing, and editing of the manuscript. TG and SS are experts in database research and provided advice on the use of the National Database data as well as revisions to the manuscript. AS provided advice on the content of the study and conducted revisions to the manuscript.


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## Conflict of Interest

No potential conflicts of interest were disclosed.

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