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# Trends in Characteristics, Management, and Outcomes of Patients Presenting with Gastrointestinal Bleeding to Emergency Departments in the United States from 2006 to 2019

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## Abstract

**Background:** Recent epidemiologic studies of trends in gastrointestinal bleeding (GIB) provide results through 2014 or earlier and assess only hospitalized patients, excluding patients presenting to emergency departments (EDs) who are not hospitalized.

**Aims:** To provide the first nationwide epidemiological evaluation of all patients presenting to EDs with GIB in the U.S.

**Methods:** We used the Nationwide Emergency Department Sample for 2006–2019 to calculate yearly projected incidence of patients presenting to EDs with primary diagnoses of GIB, categorized by location and etiology. Outcomes were assessed with multivariable analyses.

**Results:** The age/sex-adjusted incidence for GIB increased from 378.4 to 397.5/100,000 population from 2006–2019. UGIB incidence decreased from 2006 to 2014 (112.3 to 94.4/100,000) before increasing to 116.2/100,000 by 2019. LGIB incidence increased from 2006 to 2015 (146.0 to 161.0/100,000) before declining to 150.2/100,000 by 2019. The proportion of cases with ≥1 comorbidities increased from 27.4% to 35.9% from 2006 to 2019. Multivariable analyses comparing 2019 to 2006 showed increases in ED discharges (OR=1.45;95% CI=1.43–1.48) and decreases in RBC transfusions (OR=0.62;0.61–0.63), endoscopies (OR=0.60;0.59–0.61), death (OR=0.51;0.48–0.54), length of stays (RR=0.81;0.80–0.82). Inpatient cost decreased from 2012 to 2019 (RR=0.92;0.91–0.93).

**Conclusions:** Incidence of GIB in the U.S. is increasing. UGIB incidence has been increasing since 2014 while LGIB incidence has been decreasing since 2015. Despite a more comorbid

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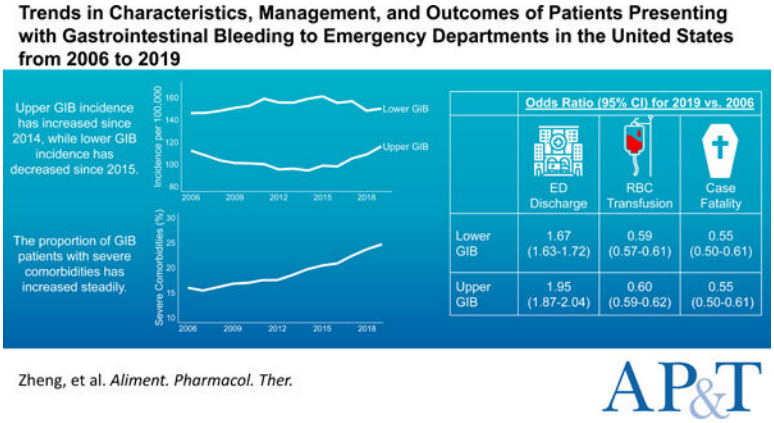
Author Contributions

N.S.Z., C.T., L.L., and D.L.S. conceived of and designed the study. N.S.Z., C.T., and D.L.S. performed data extraction. N.S.Z. and D.L.S. performed statistical analyses. N.S.Z., C.T., L.L., and D.L.S. participated in data interpretation. N.S.Z., C.T., L.L., and D.L.S. drafted the manuscript. All authors reviewed and approved the final manuscript.

**Conflict of Interest:** None.

population in 2019, case fatality rate, length of stay, and costs have decreased. More patients are discharged from the ED and the rate of RBC transfusions has decreased, possibly reflecting changing clinical practice in response to updated guidelines.

## Graphical Abstract




## INTRODUCTION

Gastrointestinal bleeding (GIB) is the most common cause of GI-related hospitalization in the United States (U.S).[1] Traditionally, studies have classified GIB into upper GIB (UGIB) and lower GIB (LGIB) based on the location of the bleeding source. UGIB refers to bleeding from the esophagus, stomach, or duodenum. LGIB has been defined epidemiologically as arising from sites distal to the Ligament of Treitz. In clinical practice, LGIB is now more commonly characterized as colonic bleeding with small bowel bleeding considered a separate diagnostic category.

Previous epidemiological studies have reported a low case fatality rate for GIB in the U.S. (<5%) and suggested decreasing incidence, but these studies only evaluated hospitalized patients and did not include patients who presented and were discharged from emergency departments (EDs).[2–6] Moreover, the most recent studies that reported on GIB trends over time evaluated patients through 2012 for UGIB and 2014 for LGIB.[2–6] Possible factors contributing to the decrease in UGIB incidence include Helicobacter pylori eradication and the increased use of proton pump inhibitors.[7] The most recent epidemiological study of LGIB in the U.S. suggested an increased hospitalization rate for LGIB from 2010 to 2014, thought to be related to an aging population and increasing frequency of antithrombotic therapy.[5, 7] Furthermore, new evidence regarding management of GIB and resultant changes in guideline recommendations (e.g., restrictive red blood cell [RBC] transfusion strategies, discharge of very low-risk patients from the ED for outpatient management) may have affected clinical practice patterns.

We believe that an updated epidemiological evaluation of the incidence and secular trends and hospital-based management and outcomes for all patients with GIB presenting to EDs in the U.S. is needed to better understand the characteristics and current state of care of patients with GIB. This study uses a large, national emergency department database to

characterize epidemiological trends for GIB incidence, management, and outcomes – and assesses whether real-world management has changed with the advent of new guideline recommendations.

## MATERIALS AND METHODS

### Data source:

This study includes data from 2006 to 2019 collected in the Nationwide Emergency Department Sample (NEDS), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality.[8] NEDS is the largest all-payer ED database in the U.S. and is a composite of the HCUP State Inpatient Database and the State Emergency Department Database, which includes information on ED visits that result in admission at that ED's hospital and those that do not, respectively. NEDS includes information on patients treated and discharged from the ED, those seen in the ED and admitted to the same hospital, and those who were transferred from the ED to another hospital. For patients who were transferred, only information from their ED visit is available. The composite database from 2019 describes an unweighted sample of 33.1 million discrete ED visits across 989 hospitals in 41 states, including the District of Columbia, and a weighted national estimate of 143.4 million ED visits. Weighted samples were used for the purposes of this study. We performed final checks to comply with HCUP privacy protections policy.

### Variables:

We identified ED visits with a primary diagnosis of GIB using the International Classification of Disease (ICD) codes (see Appendix 1). Due to the shift from the ICD Ninth Revision, Clinical modification (ICD-9-CM), to the Tenth Revision (ICD-10-CM) after the third quarter of 2015, we used ICD-9-CM from 2006 to 2015 3$^{rd}$ quarter adapted from Peery et. al 2019,[9] and ICD-10-CM from 2015 4$^{th}$ quarter to 2019 adapted from Peery et. al 2021.[1] Additional ICD codes for hemorrhoids were included from Oakland et. al 2020.[10] While there are no ICD codes specific for bleeding hemorrhoids, excluding hemorrhoids all together would exclude many patients with this common condition. The majority of ICD-9-CM codes for GIB were mapped to corresponding ICD-10-CM codes (see Appendix 2); however, given the shift we also present the incidence trends from before (2006 to 2014) and after (2016 to 2019) the complete ICD-10-CM transition. Additionally, we show incidence of acute myocardial infarction, another common ED presentation, from 2006 to 2019 in Appendix 3 as a comparison. Diagnosis of GIB were categorized into upper, lower, and unspecified GIB. We further categorized etiologies of UGIB into bleeding from ulcers, varices, and other non-variceal, non-ulcer sources. Likewise, LGIB etiologies were categorized as diverticular, hemorrhoidal, and other non-hemorrhoidal, non-diverticular sources. Since the inclusion of any hemorrhoids, bleeding or non-bleeding, may lead to an overestimation of GIB incidence, we also present a sensitivity analysis of overall GIB and LGIB incidence excluding patients with a primary diagnosis of hemorrhoids.

Demographic data included sex, age, hospital geography based on zip code (Northeast, Midwest, South, West), hospital urban-rural teaching status (urban teaching, urban non-teaching, rural non-teaching), ED volume, income quartile based on estimated median

household income of residents in the patient's zip code, and primary insurance payer (Medicare, Medicaid, private insurance, self-pay, no charge, other). Charlson Comorbidity Index (CCI) scores, which predict 10-year survival in patients with multiple comorbidities, were calculated based on ICD codes described and validated by Glasheen et. al.[11] Prior studies of gastrointestinal trends in NEDS and other HCUP databases have used CCI to characterize comorbidities.[3, 12]

## Study Outcomes:

The outcomes of interest were incidence of GIB, in-hospital RBC transfusion rate, in-hospital case fatality rate, ED discharge rate, presence of in-hospital upper or lower endoscopy, inpatient length of stay, and inpatient cost. Age- and sex-adjusted incidence were calculated to remove the confounding effects of changes in age and sex composition across time. We included patients aged ≥20 years in our analyses as population structure estimates for age and sex were only available in 5-year intervals from the U.S. Census Bureau (e.g., age=15–19, 20–25) and GIB is rare in individuals aged <20 years.[13]

For incidence, we calculated crude incidence rate for each calendar year by dividing the total number of ED visits with a primary diagnosis of GIB by the U.S. population estimate for the respective year. To adjust for changes in age- and sex population structure across different years, we used the 2010 U.S. population structure as the standard to calculate age- and sex-adjusted incidence rate by summing the multiplicative product of each age- and sex-specific incidence by the age- and sex-specific standard population divided by the total standard population. Choosing different years for the reference population structure had minimal effects on the overall results and trends (see Appendix 4).

RBC transfusions and endoscopic procedures were identified using codes from both Current Procedure Terminology (CPT) and ICD Procedure Coding System (ICD-PCS) (see Appendix 5). Case fatality rate was defined as the proportion of all-cause, in-facility deaths among the total ED visits with a primary diagnosis of GIB. The specific cause of death was not available in this database. Inpatient length of stay was a provided variable in NEDS. To evaluate inpatient healthcare costs (reported in US dollars), we converted the NEDS inpatient charge variable to inpatient cost using the HCUP hospital-level charge-to-cost ratios dataset, which was available for years 2012 to 2019.[14] NEDS-derived inpatient cost exclude provider fees. Following guidelines for inflation adjustments,[15] we adjusted calculations of inpatient healthcare costs to 2019 using the Gross Domestic Product index.[16]

## Statistical analysis:

Data extraction and preprocessing was performed using Python 3.8.5 (Python Software Foundation, Wilmington, DE, USA). Statistical analyses were performed using R v4.0.2 (R Foundation for Statistical Computing, Vienna, Austria) and STATA v17.0 (StataCorp LLC., College Station, TX, USA). We used linear regressions to analyze linear trends over 2006 to 2019 and reported p-values for linear trend for age- and sex-adjusted GIB incidence and rates of RBC transfusions, case fatality, ED discharge, and upper or lower endoscopy. Univariate and multivariate weighted logistic regressions were performed to determine if there was a relationship between the year of GIB ED visits and outcomes (RBC transfusion,

case fatality, discharge from ED, and endoscopic evaluation). Multivariate models were adjusted for age (per 5-year increase), sex, CCI score, hospital region, hospital urban-rural teaching status, ED volume, income quartile, and primary insurance payer. Patients older than 95 years were excluded from the model due to a small sample size. All statistical tests were based on two-tailed probability.

## RESULTS

The total ED visits with GIB as the primary diagnosis from the NEDS database was 168,062 in 2006 and 235,538 in 2019, with the national weighted projected cases of 784,505 in 2006 and 1,019,964 in 2019 (Table 1). From 2006 to 2019, the overall proportion of patients with UGIB, LGIB, and unspecified GIB were 26.4%, 39.1%, and 34.4%, respectively. Among patients with primary diagnosis of unspecified GIB, 2.4% had a non-primary diagnosis of UGIB and 12.7% had a non-primary diagnosis of LGIB. The disposition of all patients presenting to the ED with UGIB and LGIB is shown in Appendix 6. The distributions of age, sex, hospital region, and income quartile for GIB cases were similar across the 14-year study period. For primary payor, more patients were on Medicaid in 2019 (14.8%) than 2006 (8.9%). GIB cases with greater comorbidities (CCI ≥4) increased from 9.1% in 2006 to 15.8% in 2019 with corresponding decreases in cases with minimal or no comorbidities (CCI≤1: 2006=72.6%, 2019=64.1%).

The age- and sex-adjusted incidence for ED visits for GIB increased from 378.4/100,000 population in 2006 to 397.5/100,000 in 2019 (P-value for linear trend <0.001; Figure 1A). The increase in incidence was larger in male patients (2006 = 401.7/100,000, 2019 = 427.7/100,000; P<0.001) than in female patients (2006 = 356.5/100,000, 2019 = 369.0/100,000; P=0.021). UGIB incidence decreased from 112.3/100,000 in 2006 to 94.4/100,000 in 2014 but then increased to 116.2/100,000 by 2019 (Figure 1B). In contrast, incidence for LGIB increased from 146.0/100,000 in 2006 to a peak of 161.0/100,000 in 2015 but then declined to 150.2/100,000 by 2019. When considering the trends after the complete transition to ICD-10-CM from 2016 to 2019, there was an 18.4% (P=0.008) increase in UGIB incidence and a relatively stable LGIB incidence (−3.4%, P=0.229) (Appendix 7).We observed similar trends for UGIB and LGIB when stratifying by male and female patients. We also observed similar trends for overall GIB and LGIB incidence when excluding patients with primary diagnosis of hemorrhoids (Appendix 8): overall GIB incidence increased from 322.1/100,000 in 2006 to 373.3/100,000 in 2019 while LGIB incidence increased from 2006 to 2016 (98.5 to 108.4/100,000) before declining to 102.9/100,000 in 2019.

With regards to etiologies of UGIB (Figure 2A), incidence of variceal bleeding was relatively constant around 1.7/100,000, from 2006 to 2013 with a marked increase thereafter to 2.9/100,000 by 2019 (overall +73.6%; P=0.001). However, incidence of bleeding from ulcers decreased from 56.2/100,000 in 2006 to 40.1/100,000 in 2014 and then increased thereafter to 49.9/100,000 in 2019 (overall change −8.3%; P=0.061). Similarly, incidence of other non-variceal bleeding decreased from 56.2/100,000 in 2006 to 51.61 in 2012 before increasing to 63.3/100,000 by 2019 (+12.7%; P=0.102). Between 2016 and 2019, there were increases of 23.4% (P<0.001) in bleeding from ulcers and 16.7% (P=0.023)

in other non-variceal bleeding, but a decrease of 14.5% (P=0.390) in variceal bleeding (Appendix 9). Incidence for variceal bleeding, bleeding from ulcers, and other non-variceal bleeding stratified by age groups are shown in Appendix 10, which shows there were greater increases in UGIB incidence among younger age groups (<60 years). Incidence for more specific etiologies of UGIB from 2006 to 2019 can be found in Appendix 11.

For LGIB etiologies (Figure 2B), incidence of diverticular bleeding decreased from 37.6/100,000 in 2006 to 28.6/100,000 in 2016 and then increased to 31.2/100,000 by 2019 (overall −17.2%; P <0.001). Incidence of hemorrhoidal bleeding fluctuated but overall remained relatively unchanged from 47.5/100,000 in 2006 to 47.2/100,000 in 2019, decreasing by 0.7% (P=0.511). The incidence of other non-diverticular bleeding increased from 60.9/100,000 in 2006 to a peak of 78.2/100,000 in 2015 and then decreased afterwards to 71.8/100,000 by 2019 (+18.0%; P<0.001). Between 2016 and 2019, there was an increase of 8.8% (P=0.015) in diverticular bleeding but decreases of 4.6% (P=0.131) in hemorrhoidal bleeding and 6.8% (P=0.172) in other non-diverticular, non-hemorrhoidal bleeding (Appendix 9). Incidence for more specific etiologies of LGIB from 2006 to 2019 can be found in Appendix 11.

With a few exceptions, proportions of UGIB patients with common comorbidities were increased from 2006 to 2019, particularly for myocardial infarction (relative change=+55.2%), congestive heart failure (+43.2%), peripheral vascular disease (+61.3%), liver disease (+58.6%), and renal disease (+85.4%) (Appendix 12A). While comorbidities for LGIB patients were fewer overall than that of UGIB patients, there were notable increases from 2006 to 2019 in myocardial infarction (+42.0%), congestive heart failure (+37.3%), peripheral vascular disease (+70.0%), liver disease (+94.9%), renal disease (+103.1%), rheumatic disease (+38.0%), and HIV/AIDs (+63.5%) (Appendix 12B). Of patients with UGIB, 76.7% of variceal bleed patients had diagnosed chronic liver disease (47.1% with cirrhosis and portal hypertension) while only 9.2% (4.2% with cirrhosis and portal hypertension) and 13.7% (6.9% with cirrhosis and portal hypertension) of patients with bleeding from ulcers and other non-variceal sources had liver disease, respectively (Appendix 13). Additionally, there were large relative increases in the proportion of patients with long-term aspirin monotherapy (+449.2%), double antithrombotic therapies (+1133.8%, and triple antithromobotic therapies (+1108.6%) (Appendix 14).

The rate of RBC transfusions for all sources of UGIB decreased sharply starting around 2014 (Figure 3A). Between 2006 and 2019, the rate of RBC transfusion decreased for all sources of UGIB from 37.4% to 28.3% (relative percent change −24.4%; P<0.001) with relative decreases in variceal bleeding (−26.4%; P<0.001), bleeding from ulcers (−26.4%; P<0.001), and other non-variceal bleeding (−23.1%; P=0.005). The case fatality rate for all sources of UGIB also decreased from 2.0% to 1.4% (−29.1%; P<0.001). For variceal bleed, case fatality rate fluctuated between 6.3% in 2006 to 3.9% in 2019 with a relative decrease of −38.2% (P=0.148). The case fatality rate for bleeding from ulcers and other non-variceal bleeding was overall low in 2006 and continued to decrease through 2019 with relative decreases of −22.2% (P<0.001) and −39.0% (P<0.001), respectively (Figure 3B). Between 2006 and 2019, the rate of endoscopy decreased for all sources of UGIB from 77.4% to 69.9% (−9.7%; P<0.001). Endoscopy rates decreased for bleeding from

ulcers (−4.4%; P<0.001) and other non-variceal bleeding (−14.2%; P<0.001) but stayed relatively constant for variceal bleeding (+0.2%; P=0.126) (Figure 3C). Endoscopic rates for more specific etiologies for other non-variceal, non-ulcer sources of UGIB is shown in Appendix 15. Across the same timeframe, the rate of discharge from the ED increased for all sources of UGIB from 12.1% to 16.4% (+35.5%; P < 0.001). Discharge rate increased for bleeding from ulcers (+21.4%; P<0.001) and non-variceal bleeding (+30.8%; P<0.001) but decreased for variceal bleeding (−60.3%; P=0.050) (Figure 3D). From 2006 to 2019, average inpatient length of stay decreased for all sources of UGIB from 4.64 to 4.37 days (−5.8%; P<0.001) with relative decreases in variceal bleeding (−11.0%; P=0.036), bleeding from ulcers (−7.9%; P<0.001), and other non-variceal bleeding (−3.0%; P<0.001) (Figure 3E). From 2012 to 2019, there was a small increase in average inpatient cost for all sources of UGIB from $6,831 to $7,125 US dollars (+4.3%; P=0.136) with relative increases in bleeding in ulcers (+3.0%; P=0.313) and other non-variceal bleeding (+4.2%; P=0.083), but a relative decrease in variceal bleeding (−4.5%; P=0.143) (Figure 3F).

For LGIB, there was also a decrease in the rate of RBC transfusions starting in 2014 (Figure 4A). From 2006 to 2019, RBC transfusion rate decreased for all sources of LGIB from 13.1% to 10.0% (−23.3%; P<0.001) with relative decreases in transfusion for diverticular bleeding (−24.0%; P=0.002), hemorrhoidal bleeding (−17.6%; P=0.044), and other non-diverticular, non-hemorrhoidal bleeding (−18.8%; P<0.001). The case fatality rate was low overall for all sources of LGIB in 2006 at 0.48% and continued to decrease through 2019 to 0.29% (−40.8%; P<0.001). Relative decreases were observed for diverticular bleeding (−40.7%; P<0.001), hemorrhoidal bleeding (−41.3%; P<0.001), and other non-diverticular, non-hemorrhoidal bleeding (−43.1%; P=0.146) (Figure 4B). From 2006 to 2019, the rate of endoscopy decreased for all sources of LGIB from 26.3% to 21.6% (−17.8%; P < 0.001) with relative decreases in diverticular bleeding (−11.7%; P<0.001), hemorrhoidal bleeding (−19.1%; P<0.001), and other non-diverticular, non-hemorrhoidal bleeding (−16.5%; P<0.001) (Figure 4C). Across the same timeframe, the rate of ED discharges increased for all sources of LGIB from 57.6% to 62.1% (+7.7%; P<0.001) with relative increases for hemorrhoidal (+7.6%; P<0.001) and other non-diverticular, non-hemorrhoidal bleeding (+2.2%; P=0.001) (Figure 4D). While the rate of ED discharges for diverticular bleeding was less than 10% overall, there was a relative increase of +85.4% (P<0.001) from 2006 to 2019. From 2006 to 2019, average inpatient length of stay decreased for LGIB overall from 4.44 to 4.18 days (−5.9%; P<0.001) with a relative decrease in diverticular bleeding (−13.6%; P<0.001), but relative increases in hemorrhoidal bleeding (+12.8%; P=0.020), and other non-diverticular, non-hemorrhoidal bleeding (+1.8%; P=468) (Figure 4E). From 2012 to 2019, average inpatient cost increased for all sources of LGIB from $5,571 to $6,210 US dollars (+11.5%; P=0.011) with relative increases in bleeding in diverticular bleeding (+1.6%; P=0.322), hemorrhoidal bleeding (+26.9%; P<0.001), and other non-diverticular, non-hemorrhoidal bleeding (+20.2%; P=0.010) (Figure 4F).

Similar trends for in-hospital outcomes were observed among patients with unspecified GIB from 2006 to 2019 (Appendix 16), including decreasing RBC transfusion rate (−17.1%; P<0.001), decreasing case fatality rate (−38.6%; P<0.001), decreasing endoscopy rate (−18.5%; P=0.080), and decreasing average length of stay (−6.9%; P<0.001). Rates of ED discharge were relatively stable for unspecified GIB from 2006 to 2019 (+0.7%; P =

0.319) and there was a small increase in average inpatient cost from 2012 to 2019 (+5.0%; P=0.108). Likewise, trends in rates of RBC transfusion and case fatality were similar among patients admitted for UGIB or LGIB compared to all patients presenting to the ED with UGIB or LGIB (Appendix 17), although the proportion of admitted patients who received an endoscopy was greater and the decrease in endoscopy rates was less from 2006 to 2019.

Results of multivariate regression analyses of outcomes by year are found in Table 2. Patients presenting in 2019 for any source of GIB had increased odds of discharge from ED (odds ratio [OR] 1.45; 95% confidence interval [CI] 1.43–1.48) and reduced odds of RBC transfusions (OR 0.62; 0.61–0.63), endoscopy (OR 0.64; 0.63–0.65), and death (OR 0.53; 0.49–0.56). Additionally, they had shorter inpatient length of stays (relative ratio [RR] 0.81; 0.80–0.82) and lower inpatient costs (RR 0.92; 0.91–0.93). Likewise, patients presenting in 2019 for all sources of UGIB had increased odds of discharge from ED (OR 1.89; 1.81–1.97), reduced odds of RBC transfusion (OR=0.60; 0.58–0.61), endoscopy (OR 0.60; 0.58–0.61), and death (OR 0.57; 0.52–0.63), shorter inpatient length of stays (RR 0.85; 0.84–0.86), and lower inpatient costs (RR 0.93; 0.91–0.95). We observed similar trends for patients presenting in 2019 for all sources of LGIB for ED discharge (OR 1.63; 1.58–1.67), RBC transfusion (OR 0.60; 0.58–0.62), endoscopy (OR 0.64; 0.63–0.66), case fatality (OR 0.44; 0.37–0.53), inpatient length of stay (RR 0.86; 0.84–0.87), and inpatient cost (RR 0.98; 0.96–1.00). A notable exception to the trends was for inpatient cost for hemorrhoidal bleeding, which increased in 2019 compared to 2006 (RR 1.03; 1.09–1.18).

Further multivariate regression analyses of sociodemographic factors associated with endoscopy rate stratified by source of GI bleeding can be found in Appendix 18. Variables associated higher odds of endoscopy in patients with any source of GIB included greater age (per 5-year increase: OR 1.11; 95% CI 1.11–1.11), greater comorbidities (CCI≥4: OR 5.08; 5.03–5.13), higher incomes (≥$74,000: OR 1.13; 1.12–1.14), private insurance (OR 1.18; 1.17–1.19), or presentation at EDs with greater volume (≥50,000 visits: OR 3.90; 3.81–3.99). Patients less likely to receive an endoscopy were female (OR 0.81; 0.81–0.82), presenting at a rural hospital (OR 0.62; 0.62–0.64), or had Medicaid (OR 0.96; 0.94–0.97) or self-pay (0.82; 0.81–0.83). Similar trends were observed for UGIB and LGIB overall. Multivariate regression analyses for sociodemographic factors associated with rates of RBC transfusion and endoscopies and stratified by patients with history of myocardial infarction, history of renal disease, or Medicaid are shown in Appendix 19. Sociodemographic factors associated with increased or decreased RBC transfusion and endoscopy rates were similar to the those for all patients with GIB with a few notable exceptions. Older patients were less likely to receive an endoscopy if they had history of myocardial infarction (per 5-year increase: OR 0.97; 0.97–0.98) or renal disease (OR 0.95; 0.94–0.95), and patients across all three strata presenting at urban teaching hospitals were less likely to receive an RBC transfusion.

## DISCUSSION

We found that the overall incidence of patients presenting to the ED with GIB in the U.S. has increased from 2006 to 2019, although changes in incidence vary based on the location of GIB. Overall, UGIB incidence has been increasing since 2014 and LGIB incidence has

been decreasing since 2015. Even though patients presenting with GIB are now sicker with more comorbidities, RBC transfusion and case fatality rates have decreased from 2006 to 2019, while the proportion of patients discharged from the ED has increased.

Our results regarding declining UGIB incidence from 2006 to 2014 are supported by previous studies that used national inpatient databases to examine UGIB during this timeframe.[2–4] The most recent trend data for UGIB was in 2012 and the increasing incidence of UGIB after 2014 has not been shown previously. From 2016 to 2019, we observed increasing incidence of bleeding from ulcers and other non-variceal sources, suggesting that multiple causes may be driving this shift. The trend reversal in UGIB incidence may be a consequence of the increasing burden of comorbidities in UGIB patients from 2006 to 2019. Increased non-gastrointestinal comorbidities comprises a strong, independent risk factor for non-variceal UGIB.[17] Our study also demonstrated the increased burden of myocardial infarction, peripheral vascular disease, renal failure, and congestive heart disease over time. Antithrombotic therapies, which are often prescribed for long-term prophylaxis or management of cardiovascular disease, are known risk factors for GIB.[18, 19] We observed that increasing proportions of UGIB patients were on long-term antithrombotic therapy in our study population especially around 2014, which may be contributing to the more recent uptick in UGIB incidence. Additionally, several studies showed that the expansion of Medicaid in 2014 through the Affordable Care Act led to increased healthcare and ED utilization, especially among younger adults.[20–23] In our study, the proportion of GIB patients with Medicaid grew by 66.3% between 2006 and 2019 and we also observed greater increases in UGIB incidence among younger patients age <60 years, which may have contributed to the increase in patients presenting to the ED with UGIB after 2014.

Our findings of increasing LGIB incidence from 2006 to 2015 are supported by the most recent study of inpatient LGIB epidemiology from 2005 to 2014.[5] Decreased diverticular bleeding across that same timeframe is also consistent with other studies.[2, 6] Previous studies observed that the most common inpatient diagnosis associated with LGIB was diverticular bleeding.[2, 5] Likewise, we observed that diverticular bleeds had the lowest ED discharge rate but that bleeding hemorrhoids were a more common diagnosis associated with ED visits for LGIB than diverticular bleeds, reflecting the different patterns of LGIB etiologies in the ED versus inpatient settings. Our observation of decreasing LGIB incidence since 2015 has not been shown previously. Decreasing incidence of hemorrhoids and other non-hemorrhoidal, non-diverticular bleeding from 2016 to 2019 may be driving this trend. Since studies of LGIB incidence have been limited, further research is needed to validate these findings.

Trends in clinical practice patterns observed in this study are consistent with updates to guideline recommendations for the management of GIB. For example, the decrease in the rate of RBC transfusion around 2014 may reflect 2010 international consensus recommendations and 2012 U.S. guideline recommendations for a restrictive transfusion strategy in patients with UGIB,[24, 25] and the 2013 publication of a large randomized trial documenting improved outcomes with such a strategy.[26] Similar restrictive RBC transfusion strategies were recommended by national guidelines for LGIB in 2016.[27] The increase in ED discharge rate in our data is also consistent with updates to guideline recommendations suggesting discharge of very low risk patients with outpatient management.[24] We also

observed declining rates of endoscopy for all GIB patients but more stable rates of endoscopy among admitted patients. Therefore, this trend for endoscopies may be related to improved risk stratification and the increase in ED discharge of very low risk patients who generally do not receive endoscopy while in the ED. We also observed that patients presenting at rural non-teaching hospitals or patients who had Medicare or self-pay were less likely to receive an endoscopy, which may reflect reduced access to GI subspecialty care. Additionally, older patients with history of myocardial infarctions or renal disease were less likely to receive an endoscopy, which may be because these patients have greater contraindications to anesthesia for endoscopy. Further studies on differences in access to endoscopy across sociodemographic factors would be valuable to elucidate these findings.

Despite substantial increases in comorbidities in GIB patients presenting to the ED, case fatality continued to decrease from 2006 to 2019, which is supported by previous studies examining case fatality in both upper and lower GIB.[2–5] Similarly, average inpatient length of stay decreased from 2006 to 2019 for patients hospitalized for all sources of UGIB and for LGIB patients with diverticular bleeding. Average unadjusted inpatient cost showed small overall increases from 2012 to 2019 for UGIB (+3.0%) and LGIB (+11.5%), but multivariate regression analyses showed that inpatient costs in 2019 decreased compared to 2012 for all sources of UGIB and LGIB except for hemorrhoidal bleeding.

Value in healthcare is defined as health outcomes achieved per dollar spent.[28] This is typically measured by evaluating improvements in quality via changes in clinical outcomes and evaluating changes in cost. A previous study using the National Inpatient Sample identified trends in in-hospital mortality and costs for bariatric surgery to suggest that increased value could be attributed to the use of new surgical techniques and technologies.[29] With GIB, we found an improvement in in-hospital case fatality with overall decreasing hospital-based costs, suggesting increased value. This trend potentially reflects improvements in the management of GIB since 2006, such as integration of clinical guidelines recommending restrictive transfusion strategies and early risk assessment with discharge of very-low-risk patients from the ED. The importance of the “Triple Aim” of better health care quality, lower costs, and improved health care outcomes can be seen across different domains in healthcare.[30] This study suggests that improved healthcare delivery for patients with GIB has resulted in captured value for patients, providers, and payors.

There are several limitations to this study. First, NEDS does not include information from the hospital stay for ED patients that were transferred to another hospital, limiting longitudinal follow-up of the clinical management for these patients after their transfer. However, this did not substantially impact results because only 1.4% of patients with UGIB and 0.9% of those with LGIB were transferred to another hospital. Therefore, information regarding for these patients’ ED visit and inpatient stay were available in NEDS. Second, we do not have information about patients after their discharge from the hospital or their ED stay. Therefore, we are unable to estimate out of hospital case fatality or rates of outpatient endoscopies. Third, we did not have information on patients who may develop GIB after hospitalization for another diagnosis. Fourth, NEDS only provides encounter-level data and not patient-level data. Therefore, patients with recurrent bleeding who visited the ED more than once would have been counted as separate encounters, leading to an overestimate of

GIB incidence. This systematic overestimation should be uniform over the 14-year study period and should not affect the observed trends. Fifth, case fatality was derived from all-cause death and does not indicate death directly attributable to GIB.

Another limitation of the study was the use of ICD and CPT codes to identify diagnoses and procedures for GIB without individual chart review. These ICD codes were entered as the primary diagnosis by the patients' provider when they are discharged from the ED or the hospital. It is possible that coding patterns for GIB have increased rather than true incidence. However, since each ED visit only had one primary diagnosis code, it is unlikely that increases in coding patterns would fully explain the trends observed in this study. While the majority of GIB diagnoses in this study were likely made endoscopically, it is not possible to truly distinguish how the diagnoses were made, which may have introduced some misclassification. This is unlikely to affect most of the upper and lower GIB diagnoses as several studies have shown good positive predictive values for these codes.[31–33] However, an exception may be the ICD codes for hemorrhoids, which include bleeding hemorrhoids but is not exclusive to bleeding hemorrhoids. Some prior studies have included these codes,[10] while others have not.[1, 2] Since hemorrhoids are a common source of LGIB, we chose to include hemorrhoids in our primary analysis, although doing so may have led to an overestimation of the true incidence of LGIB. We therefore performed a sensitivity analysis excluding hemorrhoids so that we could provide the likely highest and lowest estimate of LGIB incidence. We found that the trends for LGIB incidence were similar with and without hemorrhoids. Additionally, a third of GIB diagnoses had non-specific ICD codes and could not be categorized into upper or lower GIB. We observed that a small proportion of patients with primary diagnosis of unspecified GIB had a non-primary diagnosis code for UGIB or LGIB, but NEDS does not distinguish whether non-primary diagnosis codes are from the patient's current encounter or from their past medical history. Redistribution of these unspecified cases may affect the relative proportions of upper and lower GIB. However, the observed trends in in-hospital outcomes for unspecified GIB were similar to those for upper and lower GIB. Lastly, the shift from ICD-9-CM to ICD-10-CM in 2015 may have affected coding practices. We mapped the majority of ICD-9-CM codes for GIB directly to ICD-10-CM codes, demonstrating that the updated ICD-10-CM coding scheme was unlikely to dramatically disrupt the distribution of GIB diagnoses. We also observed that trends for acute myocardial infarction from 2006 to 2019 were stable across the ICD change in 2015, suggesting that observed trends in GIB incidence were specific to GIB and were not a consequence of the ICD change only. Moreover, we observed consistent linear trends in GIB incidence after the complete shift to ICD-10-CM from years 2016 to 2019, notably for incidence of overall UGIB, bleeding from ulcer, other non-variceal bleed, and diverticular bleeding.

In summary, the overall incidence of acute GIB in the U.S. is increasing. Incidence of UGIB has been increasing since 2014 while while the incidence of LGIB is decreasing since 2015. Clinical management of GIB appears to reflect updated guideline recommendations, with decreased RBC transfusions and increased patient discharges from the ED. Despite a sicker population presenting with GIB, case fatality rate and inpatient length of stay has decreased with minimal change in healthcare costs. Our findings call for greater awareness and further investigation of underlying causes for the increasing incidence of GIB and UGIB.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Abbreviations:

| | |
|---|---|
| **GIB** | gastrointestinal bleeding |
| **UGIB** | upper gastrointestinal bleeding |
| **LGIB** | lower gastrointestinal bleeding |
| **ED** | emergency department |
| **RBC** | red blood cell |
| **NEDS** | National Emergency Department sample |
| **HCUP** | Healthcare Cost and Utilization Project |
| **ICD-9** | International Classification of Diseases, Ninth Revision |
| **ICD-10** | International Classification of Diseases, Tenth Revision |

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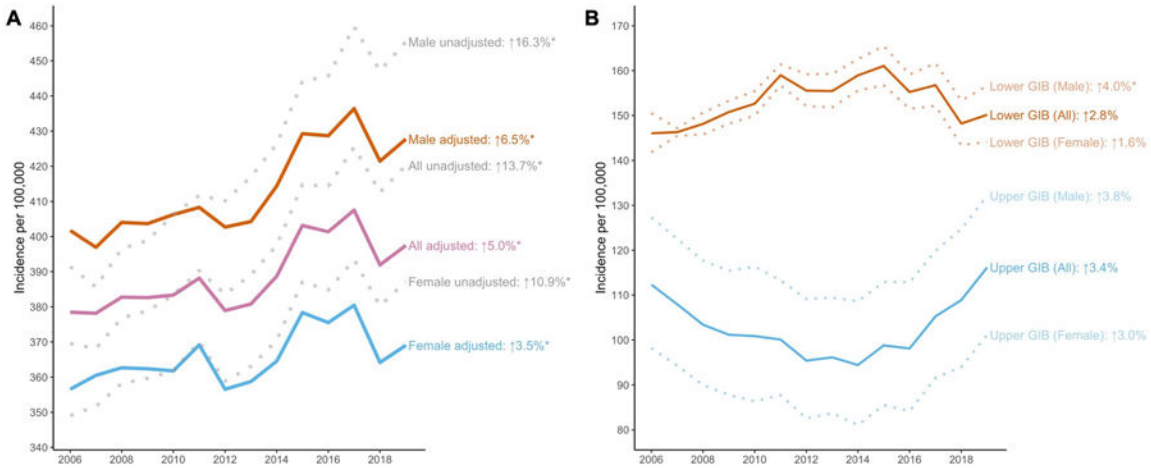


**Figure 1.**

Incidences (per 100,000 population) and percent change from 2006 to 2019 for gastrointestinal bleeding (GIB) as the primary diagnosis for emergency department visit stratified by male, female, and all (**A**) and stratified by upper and lower GIB (**B**). Percentages indicate overall percent change from 2006 to 2019. *P<0.05 for trend.

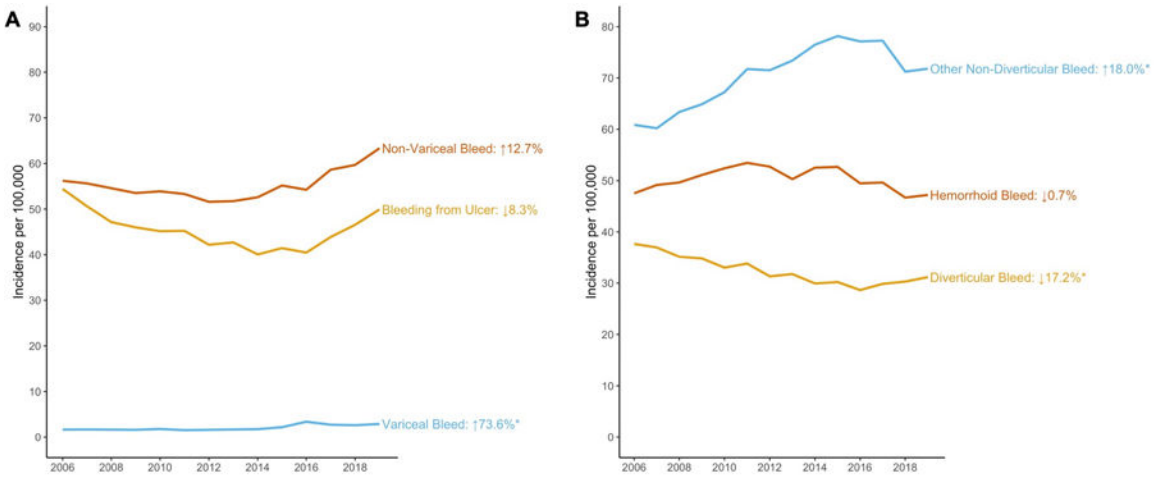


**Figure 2.**

Age- and sex-adjusted incidences (per 100,000 population) and percent change from 2006 to 2019 for different sources of upper gastrointestinal bleed (**A**) and lower gastrointestinal bleed (**B**). Percentages indicate overall percent change from baseline year of 2006 to 2019.

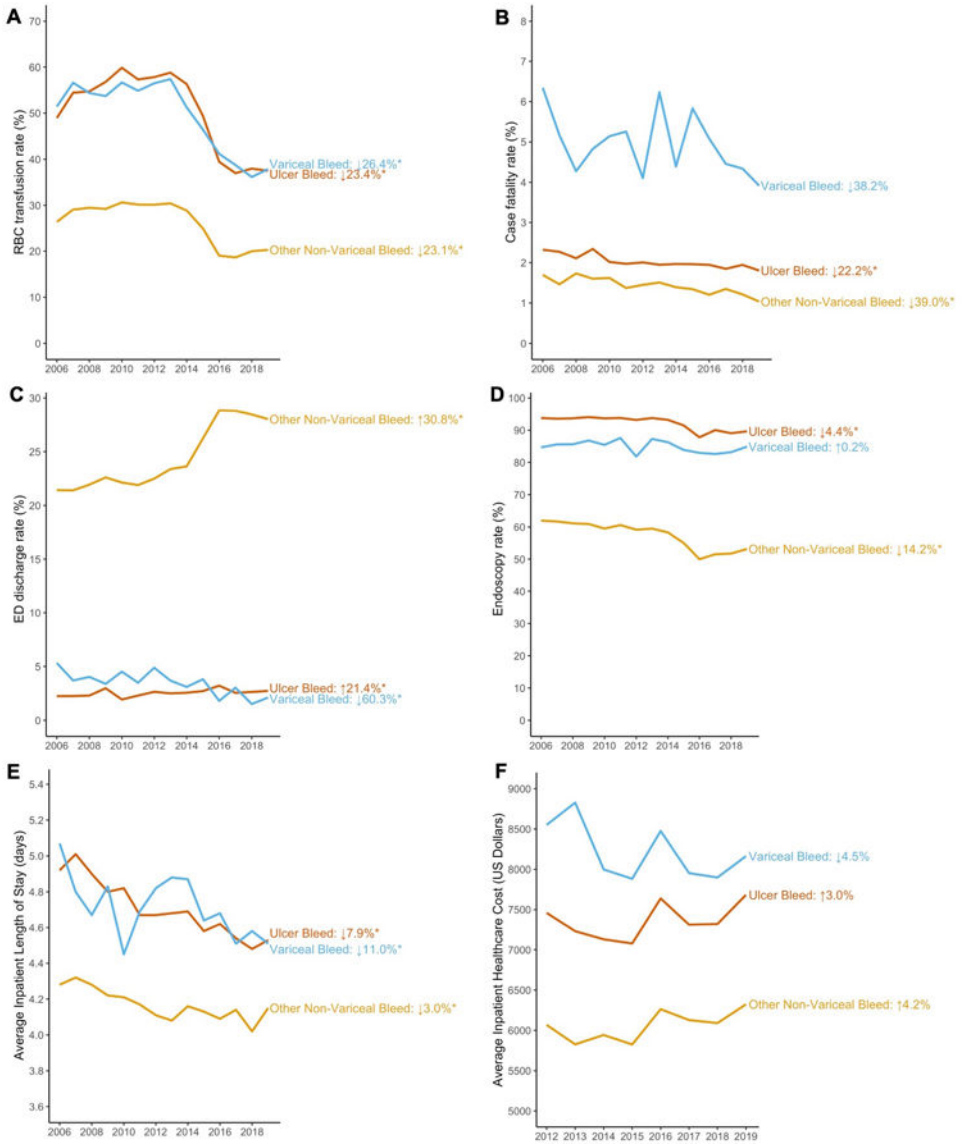


**Figure 3.**

Trends and percent change from 2006 to 2019 for in-hospital red blood cell transfusion (**A**), in-hospital case fatality (**B**), emergency department discharge (**C**), in-hospital endoscopy (**D**), inpatient length of stay (**E**), and inpatient cost (**F**) in patients with upper gastrointestinal bleeds (UGIB), stratified by different sources of UGIB. Percentages indicate overall percent change from baseline year of 2006 to 2019. *P<0.05 for trend. RBC = red blood cell; ED = emergency department; UGIB = upper gastrointestinal bleed.

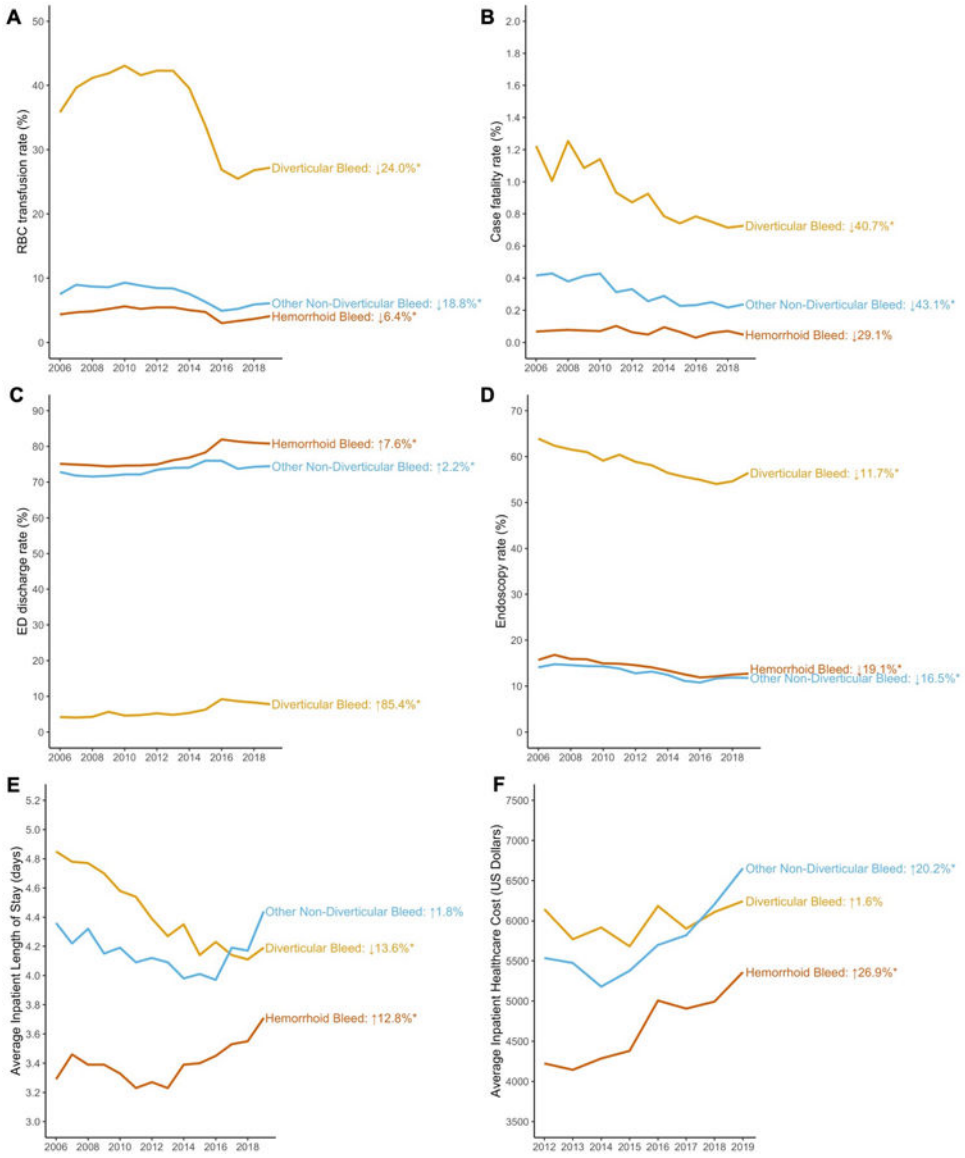


**Figure 4.**

Trends and percent change from 2006 to 2019 for in-hospital red blood cell transfusion (**A**), in-hospital case fatality (**B**), emergency department discharge (**C**), in-hospital endoscopy (**D**), inpatient length of stay (**E**), and inpatient cost (**F**) in patients with lower gastrointestinal bleeds (LGIB), stratified by different sources of LGIB. Percentages indicate overall percent change from baseline year of 2006 to 2019. *P<0.05 for trend. RBC = red blood cell; ED = emergency department; LGIB = lower gastrointestinal bleed.

**Table 1.**

Selected characteristics for gastrointestinal bleeding patients from the National Emergency Department Sample, 2006 – 2019

| Characteristics | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Total (n)** | 784505 | 790874 | 817004 | 829373 | 847464 | 870649 | 868631 | 891188 | 920404 | 972053 | 981959 | 1014717 | 995509 | 1019964 |
| **Location of Bleed (%)** | | | | | | | | | | | | | | |
| Upper | 29.6 | 28.5 | 27.0 | 26.4 | 26.3 | 25.8 | 25.3 | 25.3 | 24.4 | 24.6 | 24.5 | 25.8 | 27.8 | 29.3 |
| Lower | 38.9 | 39.0 | 38.9 | 39.5 | 39.8 | 40.9 | 40.8 | 40.5 | 40.5 | 39.5 | 38.1 | 37.9 | 37.2 | 37.1 |
| Unspecified | 31.6 | 32.6 | 34.2 | 34.1 | 33.9 | 33.3 | 33.9 | 34.2 | 35.1 | 35.9 | 37.4 | 36.3 | 35.0 | 33.5 |
| **Female (%)** | 48.8 | 49.4 | 49.1 | 49.0 | 48.7 | 48.8 | 48.5 | 48.3 | 48.2 | 48.3 | 48.0 | 47.8 | 47.6 | 47.6 |
| **Age, year (%)** | | | | | | | | | | | | | | |
| < 25 | 4.7 | 4.7 | 4.9 | 5.1 | 5.2 | 5.4 | 5.4 | 5.1 | 5.1 | 5.0 | 5.0 | 4.5 | 4.3 | 4.3 |
| 25–44 | 19.3 | 19.5 | 19.7 | 19.5 | 20.0 | 19.4 | 19.7 | 18.9 | 19.2 | 19.4 | 20.0 | 19.3 | 19.1 | 19.3 |
| 45–64 | 26.3 | 26.5 | 27.0 | 27.4 | 27.8 | 27.5 | 28.0 | 27.5 | 28.1 | 27.9 | 28.1 | 28.0 | 27.5 | 27.6 |
| ≥ 65 | 49.7 | 49.3 | 48.3 | 48.0 | 47.0 | 47.7 | 47.0 | 48.6 | 47.6 | 47.7 | 46.8 | 48.1 | 49.1 | 48.8 |
| **Region (%)** | | | | | | | | | | | | | | |
| Northeast | 19.3 | 19.3 | 19.0 | 18.4 | 18.5 | 19.0 | 18.6 | 18.7 | 17.9 | 17.0 | 17.7 | 18.3 | 18.4 | 18.4 |
| Midwest | 23.1 | 23.1 | 22.3 | 22.9 | 23.6 | 22.7 | 22.4 | 22.2 | 23.1 | 23.1 | 23.2 | 22.7 | 22.7 | 23.5 |
| South | 38.6 | 39.1 | 39.5 | 39.4 | 38.7 | 39.0 | 39.6 | 39.8 | 39.7 | 39.7 | 39.2 | 39.6 | 39.0 | 38.3 |
| West | 19.0 | 18.5 | 19.3 | 19.3 | 19.3 | 19.2 | 19.2 | 19.2 | 19.2 | 20.0 | 19.8 | 19.3 | 19.8 | 19.8 |
| **Income Quartile (%)** | | | | | | | | | | | | | | |
| $1 – 43,999 | 29.3 | 29.9 | 28.7 | 29.0 | 29.6 | 28.7 | 30.3 | 30.8 | 31.6 | 32.2 | 31.4 | 30.8 | 32.4 | 31.0 |
| $44,000 – 55,999 | 25.0 | 25.9 | 28.2 | 27.7 | 26.6 | 25.3 | 25.3 | 26.7 | 28.3 | 24.1 | 26.7 | 26.3 | 27.0 | 25.2 |
| $56,000 – 73,999 | 23.5 | 23.2 | 21.2 | 22.6 | 22.5 | 24.2 | 23.1 | 22.7 | 21.0 | 23.4 | 21.8 | 22.8 | 21.0 | 23.0 |
| $74,000+ | 20.2 | 18.6 | 19.2 | 18.2 | 19.0 | 19.6 | 19.3 | 17.6 | 16.9 | 18.5 | 18.3 | 18.6 | 18.0 | 19.1 |
| **Primary Payor (%)** | | | | | | | | | | | | | | |
| Medicare | 52.1 | 50.9 | 50.2 | 50.0 | 49.7 | 50.9 | 50.4 | 51.8 | 50.7 | 50.8 | 49.9 | 50.7 | 51.6 | 50.8 |
| Medicaid | 8.9 | 9.1 | 9.8 | 10.5 | 11.5 | 11.7 | 12.1 | 11.8 | 15.5 | 15.5 | 15.6 | 15.2 | 15.5 | 14.8 |
| Private Insurance | 24.6 | 25.3 | 25.5 | 24.4 | 23.0 | 22.3 | 21.4 | 21.2 | 21.5 | 22.8 | 23.6 | 22.8 | 22.3 | 23.1 |
| Self-Pay | 10.3 | 11.1 | 10.8 | 11.1 | 11.9 | 11.2 | 12.0 | 11.0 | 8.8 | 7.5 | 7.7 | 8.1 | 7.9 | 8.2 |
| No Charge | 0.9 | 0.6 | 0.7 | 0.9 | 0.7 | 0.7 | 0.7 | 1.0 | 0.6 | 0.5 | 0.4 | 0.5 | 0.3 | 0.4 |
| Other | 3.0 | 2.7 | 2.7 | 2.9 | 3.1 | 3.1 | 3.4 | 3.1 | 2.7 | 2.9 | 2.8 | 2.4 | 2.4 | 2.5 |

| Characteristics | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Charlson Co-morbidity Index (%)** | | | | | | | | | | | | | | |
| 0 | 50.8 | 49.9 | 49.7 | 49.1 | 49.1 | 48.3 | 48.8 | 47.2 | 47.2 | 46.8 | 47.7 | 46.3 | 45.0 | 44.6 |
| 1 | 21.8 | 22.2 | 21.9 | 21.6 | 21.6 | 21.6 | 21.4 | 21.5 | 20.9 | 20.7 | 20.1 | 20.0 | 20.0 | 19.5 |
| 2 | 11.4 | 12.5 | 12.3 | 12.5 | 12.4 | 12.6 | 12.3 | 12.8 | 12.3 | 12.1 | 11.3 | 11.3 | 11.4 | 11.2 |
| 3 | 6.9 | 7.6 | 7.8 | 8.0 | 8.0 | 8.3 | 8.2 | 8.6 | 8.5 | 8.6 | 8.4 | 8.5 | 8.8 | 8.9 |
| 4+ | 9.1 | 7.8 | 8.3 | 8.8 | 8.9 | 9.2 | 9.3 | 9.9 | 11.2 | 11.9 | 12.4 | 13.9 | 14.9 | 15.8 |

**Table 2.**

Odds ratios from multivariate weighted regressions for gastrointestinal bleeding outcomes of interest in 2019 compared to 2006

| Type of GI Bleed | RBC Transfusion OR (95% CI) | Case Fatality OR (95% CI) | ED Discharge OR (95% CI) | Endoscopy OR (95% CI) |
|---|---|---|---|---|
| Any GI Bleed | 0.62 (0.61,0.63) | 0.53 (0.49,0.56) | 0.53 (0.49,0.56) | 0.64 (0.63,0.65) |
| Upper GI Bleed | 0.60 (0.58,0.61) | 0.57 (0.52,0.63) | 1.89 (1.81,1.97) | 0.60 (0.58,0.61) |
| Variceal | 0.54 (0.45,0.66) | 0.52 (0.35,0.78) | 0.70 (0.42,1.18) | 0.60 (0.46,0.79) |
| Bleeding from ulcer | 0.59 (0.57,0.61) | 0.61 (0.54,0.69) | 1.47 (1.30,1.65) | 0.58 (0.54,0.62) |
| Other non-variceal | 0.62 (0.59,0.64) | 0.52 (0.44,0.60) | 1.93 (1.84,2.03) | 0.59 (0.56,0.61) |
| Lower GI Bleed | 0.60 (0.58,0.62) | 0.44 (0.37,0.53) | 1.63 (1.58,1.67) | 0.64 (0.63,0.66) |
| Diverticular bleed | 0.59 (0.56,0.62) | 0.45 (0.36,0.57) | 2.37 (2.14,2.62) | 0.70 (0.67,0.73) |
| Bleeding hemorrhoid | 0.82 (0.75,0.91) | 0.59 (0.27,1.30) | 1.93 (1.83,2.04) | 0.66 (0.62,0.70) |
| Other non-diverticular | 0.60 (0.56,0.65) | 0.41 (0.31,0.54) | 1.40 (1.34,1.46) | 0.65 (0.62,0.68) |

Multivariate weighted regression adjusted for age (per 5-year increase), sex, hospital region, income quartile, and Charlson Comorbidity Index score. RBC = red blood cell; OR = odds ratio; RR = relative ratio; CI = confidence interval.