

The hospitalization burden of inflammatory bowel disease in China: a nationwide study from 2013 to 2018

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Abstract

Background: The past decade has witnessed a dramatic increase in the number of patients with inflammatory bowel disease (IBD) in China. The nationwide burden of hospitalization remains unclear, however. We aimed to address this gap by conducting analysis using a nationwide database.

Methods: Population-based hospitalization rates from 2013 to 2018 were calculated by extrapolating the number of patients in the database to the national level. Surgical rates, annual hospital charges, and length of stay were also used for quantification of hospitalization burden. The Poisson regression analysis and the Cochran–Armitage trend test were conducted to analyze temporal trends as expressed as annual percentage of change (APC) with 95% confidential intervals (CIs).

Results: From 2013 to 2018, the hospitalization rates for Crohn's disease (CD) and ulcerative colitis (UC) in China increased from 2.20 (95% CI = 2.17–2.22) to 3.62 (3.59–3.65) per 100,000 inhabitants ($p < 0.0001$) with an APC of 10.68% (6.00–15.36%) and from 6.24 (6.20–6.28) to 8.29 (8.23–8.33) per 100,000 inhabitants ($p < 0.0001$) with an APC of 5.73% (2.32–9.15%), respectively. Surgical rates decreased from 7.96% (7.29–8.63%) to 5.56% (5.11–6.00%) for CD patients ($p < 0.0001$) with APC of –6.30% (–11.33 to –1.27%) and from 3.54% (3.26–3.82%) to 2.52% (2.32–2.72%) for UC patients ($p < 0.0001$) with APC of –6.35% (–16.21 to 3.51). In 2018, there were estimated 166,000 IBD patients hospitalized costing a total of \$426.37 million (\$149.91 + \$276.46 million) across the entire China.

Conclusion: The population-based hospitalization rate of IBD increased, whereas the surgical rate decreased from 2013 to 2018 in China.

Keywords: Crohn's disease, disease burden, hospitalization rate, ulcerative colitis

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Introduction

Inflammatory bowel disease (IBD) including Crohn's disease (CD) and ulcerative colitis (UC) are chronic inflammatory disorders of the gastrointestinal tract with recurrent episodes of relapse and high rates of complications.^{1,2} In the Western world, the incidence of IBD has increased from the mid-20th century.³ The prevalence of IBD now exceeds 0.5% in the Western world and is

forecasted to reach 1% of the population by 2030.^{4–7} In newly industrialized areas such as Latin America,⁸ the Middle East, and Asia, the incidence of IBD has increased dramatically from 1990,^{1,4} and the prevalence is up to 0.15% in some East Asian countries.⁹

Disease burden such as hospitalization and surgeries caused by the increasing number of IBD

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patients poses a significant challenge to the healthcare system.^{1,10} Hospital charges account for up to two-thirds of direct patient costs.^{11–13} Analyses of the hospitalization burden of IBD worldwide have indicated that the hospitalization rate in the Western industrialized world is considerably high but is mostly stable or decreasing, whereas that in newly industrialized countries is rising substantially.¹⁴

China is the largest newly industrialized countries in the world. To date, national representative epidemiological studies of IBD in China are lacking. Previous studies have only focused on certain regions or a single city or area,^{4,15–18} which precludes interpretation of the trend of IBD epidemiology and its associated burden across the entire Chinese nation. With the progress in digital healthcare in recent years,¹⁹ in this study, we used a national standardized discharge database to evaluate the hospitalization burden of IBD in China from 2013 to 2018. We aimed to analyze and report information on IBD epidemiology and disease burden over the past 5 years, which may facilitate strategies for optimal healthcare delivery to IBD patients in China and even other newly industrialized countries by providing big data analysis comparable to Western countries.

Materials and methods

Data source

The data used in this study were extracted from the Hospital Quality Monitoring System (HQMS) database from 2013 to 2018. The HQMS database is a standardized electronic data set of discharge records from tertiary hospitals in China, covering 1064 hospitals from 31 provinces (except Hong Kong and Macau) until 2018, accounting for 41.8% of tertiary centers in China. HQMS is a mandatory patient-level national database based on real-world data for hospital accreditation, under the authority of the Bureau of Medical Administration and Medical Service Supervision, National Health and Family Planning Commission of the People's Republic of China. Starting from 1 January 2013, the Bureau requested all tertiary centers in China to submit standardized electronic inpatient discharge records on a daily basis to HQMS in an automated manner. Data from HQMS were validated for its accuracy and published previously.^{20–23} HQMS includes discharge records from an

average of 18,466,820 patients per year during 2013 and 2018, which accounts for approximately 25.2% of hospitalized patients in China.

For each patient, 346 variables, including demographic characteristics, clinical diagnoses, procedures, pathology diagnoses, and expenditure breakdowns were extracted from the standardized discharge summary. As part of stringent standard practice in China, the relevant data was filed by care given doctors who are responsible for the accuracy of data acquisition from the source documents. The diagnoses were then coded based on the *International Statistical Classification of Diseases and Related Health Problems–Tenth Edition* (ICD-10) coding system by certified professional medical coders at every hospital. HQMS data reporting system performs automated data quality control on daily basis at the time of data submission to ensure the completeness, consistency, and accuracy of data. If inconsistencies were detected, the entire daily data package of the hospital will be rejected and the hospital is required to review and resubmit data.

Eligibility criteria

We included all discharge records from patients with a diagnosis of IBD in the database, with ICD-10 codes K50.x for CD and K51.x for UC accordingly. The indeterminate colitis (ICD code K52.3) was not included in this study.²⁴ We excluded discharge records lacking patient identification. All admission records with less than 24 h discharge were also excluded in order to avoid overestimation of hospitalization rate including biologics use and iron supplement.²⁵ For patients with repeated admissions, we excluded those with a diagnosis of non-IBD [such as intestinal tuberculosis (ICD-10 code A18.3) or intestinal Behçet's disease (ICD-10 code M35.2)] at the last discharge of the study period. Details of the selection process are presented in Figure 1. This manner allowed all IBD-related cases been included.

Variables and definition

Extracted variables included sex, age, location of residency (provincial level), and insurance type (rural or urban, encompassing employees' basic medical insurance or citizens' basic medical insurance as urban citizens or new rural cooperative medical care as rural residence). Surgical

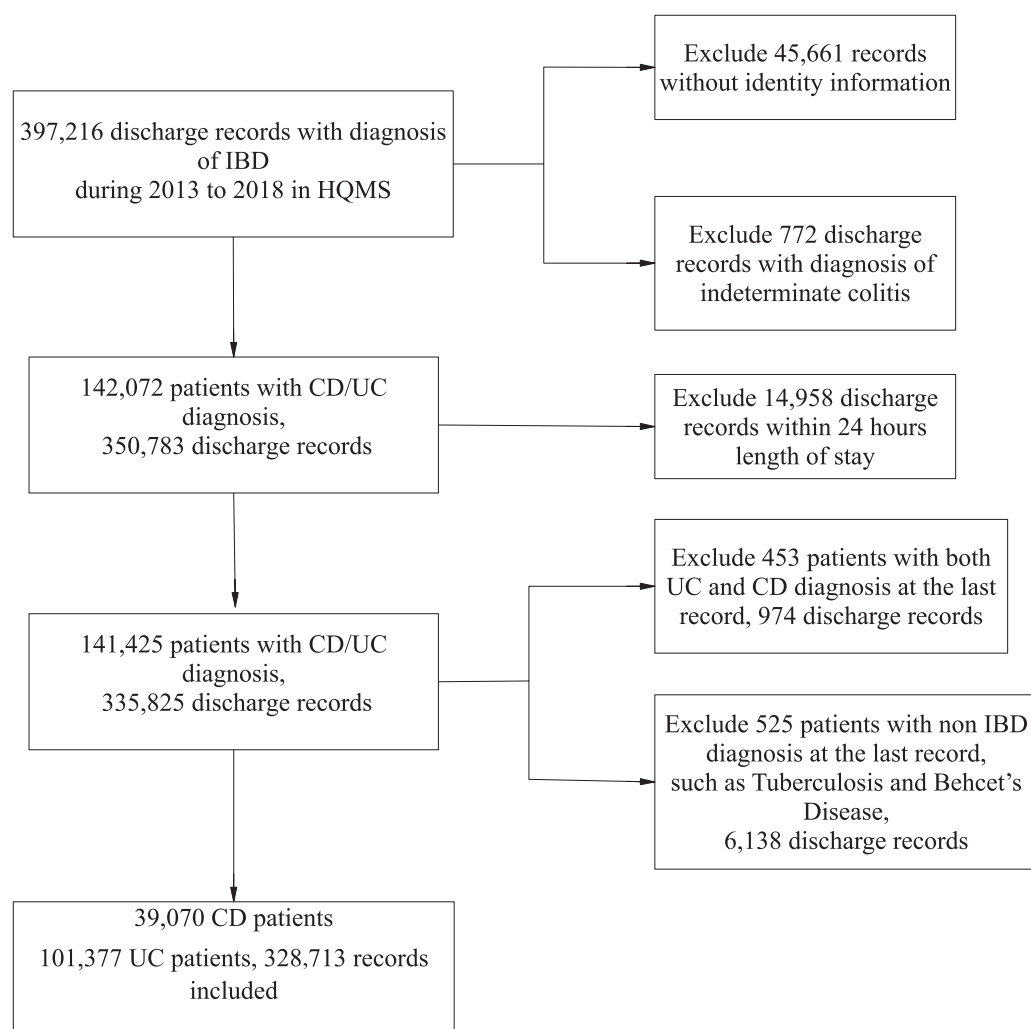


Figure 1. The flowchart of selection process.

rates (comprising bowel resection, intestinal anastomosis, fistulation, and repair of intestinal perforation;²⁵ bowel resection was subsequently analyzed separately), proportion of intestinal complications (obstructions including intestinal constriction, intussusception, volvulus, impaction, ileus, other unspecified intestinal obstructions, stenosis of rectum, and postoperative intestinal obstruction; penetration including fistula, abscess, perforation of intestine, and post-operation intestinal fistula), and perianal lesions (including anal abscess and anal fistula) based on ICD code classification (Supplementary Table 1) were used to describe the disease burden in hospitalized IBD patients.²⁶ The disease location and behavior according to the Montreal Classification was not analyzed in this study due

to lack of such information in ICD coding system. The ICD coding is verified in other studies to use in identification of surgeries and complications diagnosis in IBD patients.^{27,28} Other variables of hospitalization burden included length of stay (LOS), total charges per person year, and proportion of hospital charges covered by the national insurance program. Records without corresponding items of data were excluded from the study subsets. The demographic information of the first discharge during January 2013 and December 2018 for each individual was used as the patients' demographic features in this study, whereas the diagnosis at the last discharge was used as the diagnostic label for the patient if a change in diagnosis and evolution of the disease course occurred.

Statistical analysis

All analyses were conducted using SAS version 9.4 software (SAS Institute, Cary, NC, USA). All statistical tests were two-tailed, with $p < 0.05$ denoting the statistical significance.

General characteristics of the study population.

The chi-square test was used to detect the sex and location of residency difference in composition of hospitalized IBD patients.

Hospitalization rates and temporal trends. Population-based hospitalization rates were calculated using extrapolation data from the annual Chinese population sampling survey.^{14,25,26} The extrapolation data from the population sampling survey for each age group and urban/rural residences were used to calculate the hospitalization rate for each subgroup accordingly. The population sampling survey data and the annual number of discharged patients among all tertiary medical centers in China were obtained from the China Statistical Yearbook and China Statistical Yearbook of Sanitation and Health generated by the National Bureau of Statistics of China.^{29,30} The relevant data can be accessed at the website: <http://data.stats.gov.cn/>. Considering the majority of Chinese IBD diagnoses are occurring in tertiary hospitals due to the difficulty in differential diagnosis and uncommon incidence, national estimates of the CD and UC hospitalization rates were obtained by extrapolating the number of hospitalized CD/UC patients in the HQMS database to all tertiary centers in China using the following equation:

$$\begin{aligned} & \text{Hospitalization rate per 100,000 Chinese population} \\ & \frac{\text{Number of IBD patients in the database}}{\text{Number of patients in the database}} \times \\ & \frac{\text{Number of patients in all tertiary}}{\text{centers in China}} \\ & = \frac{\text{Chinese population by}}{\text{sampling survey}} \times 100,000 \end{aligned}$$

Adjustments for age and sex for the 2018 Chinese population were performed.^{9,31} Age- and sex-specific hospitalization rates were calculated accordingly. The CD/UC hospitalization rates in 2018 were used to determine the geographic distribution of hospitalizations. The Poisson regression analysis was conducted to analyze the temporal

trends of hospitalization rates. Annual percentage of change (APC) of the hospitalization rate was calculated using a log-linear model with 95% confidential intervals (CIs).³²

Percentage of intestinal complications, perianal diseases, and surgery. The annual percentages of bowel obstruction, intestinal penetrating diseases, perianal diseases, and surgery were calculated by dividing the number of patients presenting with these events to the number of CD patients in the database. Temporal trends for the proportions of intestinal complications, perianal diseases, and surgical rates were analyzed using the Cochran–Armitage trend test. APC with 95% CI was calculated using log-linear model.

Economic burden of hospitalization. The total hospitalization charges annually were calculated by multiplying average hospital costs per patient year with estimated number of hospitalized CD/UC patients nationwide. The total hospital charges paid by national insurance were calculated by extrapolating the average hospital charges paid by national insurance per CD/UC patient annually to national level from the estimated number of hospitalized CD/UC patients nationwide. In consideration of inflation rate, all hospital charges were adjusted by Consumer Price Index (published by the National Bureau of Statistics) to level of 2013 and expressed in US dollars according to average exchange rate between RMB and US dollars annually. We used the median and interquartile range (IQR) for the description of the LOS and hospital charges. Linear regression analysis was used to analyze the temporal trends in hospital charges and LOS.

Sensitivity analysis. To avoid overestimation by including hospitalization for other diseases (or comorbidities) in patients with IBD, we performed sensitivity analysis on hospitalized patients with primary diagnosis of IBD.

Ethical considerations

The data used in the analysis were extracted under approval of National Health Commission of the People's Republic of China. The Ethics Committee of The First Affiliated Hospital of Sun Yat-sen University approved this study. The informed consent was exempted.

Role of funding source

The funding source had no involvement in study design; the collection, analysis, and interpretation of data; the writing of the report; and in the decision to submit. The reporting of this study follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.

Results

General characteristics of the study population

In total, 39,070 CD patients and 101,377 UC patients met the inclusion criteria between January 2013 and December 2018. Table 1 presents the general demographic characteristics of included patients. The majority of CD and UC patients were males, with a significantly higher proportion in CD patients (63.7%) than in UC patients (54.3%) ($p < 0.0001$) by the chi-square test. Age groups of 20–29 years and 50–59 years comprised the highest proportions of CD and UC patients, respectively. The majority of IBD patients were from urban areas, with a significantly higher proportion in CD (73.3%) patients than in UC patients (69.2%) ($p < 0.0001$).

Hospitalization rates and temporal trends

From 2013 to 2018, the annual hospitalization rates increased from 2.20 (95% CI=2.17–2.22) to 3.62 (3.59–3.65) per 100,000 inhabitants and from 6.24 (6.20–6.28) to 8.29 (8.23–8.33) per 100,000 inhabitants for CD patients and UC patients, respectively (Figure 2). Regression analysis revealed a significant increase in the temporal trend of hospitalization rates from 2013 to 2018 in both CD and UC patients ($p < 0.0001$), with APCs of 10.68% (6.00–15.36%) and 5.73% (2.32–9.15%) for CD and UC patients, respectively. There were estimated 115,000 IBD patients ($2.20/100,000$ inhabitants $\times$ 1361 million population = 30,000 CD patients + $6.24/100,000$ inhabitants $\times$ 1361 million population = 85,000 UC patients) hospitalized totally in 2013 and 166,000 patients ($3.62/100,000$ inhabitants $\times$ 1395 million population = 50,000 CD patients + $8.29/100,000$ inhabitants $\times$ 1395 million population = 116,000 UC patients) in 2018.

Age group analysis revealed a gradual increase in hospitalization rates which peaked at age 70–79 years among UC patients (21.06 per 100,000 inhabitants in 2018; 95% CI=20.72–21.41). The hospitalization rate of CD patients peaked for the

Table 1. Demographic characteristics of included patients.

Demographic characteristics	CD (n = 39,070) ^{a,b}	UC (n = 101,377)
Sex ^c		
Male	24,892 (63.7%) ^d	55,079 (54.3%)
Female	14,178 (36.3%)	46,298 (45.7%)
Age ^e		
≤19	3990 (10.2%)	2140 (2.1%)
20–29	7982 (20.4%)	8173 (8.1%)
30–39	7149 (18.3%)	12,222 (12.1%)
40–49	7173 (18.4%)	20,810 (20.5%)
50–59	6180 (15.8%)	24,460 (24.1%)
60–69	4336 (11.1%)	21,496 (21.2%)
70–79	1815 (4.6%)	9696 (9.6%)
≥80	426 (1.1%)	2323 (2.3%)
Residence area ^f		
Urban	18,381 (72.5%)	51,616 (68.7%)
Rural	6982 (27.5%)	23,520 (31.3%)

CD, Crohn's disease; UC, ulcerative colitis.

^aN is the exact number of recorded patients in HQMS database in each category.

^b711 patients changed their diagnosis from UC to CD, and 353 patients from CD to UC.

^cDemographic features were obtained from the first discharge record of the patients during the period.

^dData were shown in number of patients (percentage).

^eThere were 19 CD patients (0.05%) and 57 UC patients (0.06%) not included in classification by age due to lack of age information.

^f13,707 CD patients (35.08%) and 26,241 UC patients (25.88%) were not included in classification by resident area due to lack of information.

age group of 20–29 years in 2018 (4.83 per 100,000 inhabitants; 95% CI=4.74–4.93), but gradually decreased in age groups thereafter. The hospitalization rates for CD and UC patients across all age groups significantly increased during the study period ($p < 0.0001$ using the Poisson regression analysis for all age groups in both CD and UC patients). The age group with the highest APC was 0–19 years for both CD [APC_{0–19} = 16.17% (11.28–21.05%)] and UC patients [APC_{0–19} = 9.50% (4.34–14.66%)] (Figure 3(a) and (b)). The hospitalization rate of male patients with CD increased from 2.61 (95% CI=2.58–2.65) to 4.51 (95% CI=4.46–4.56) per 100,000 male inhabitants ($p < 0.0001$) with an APC of

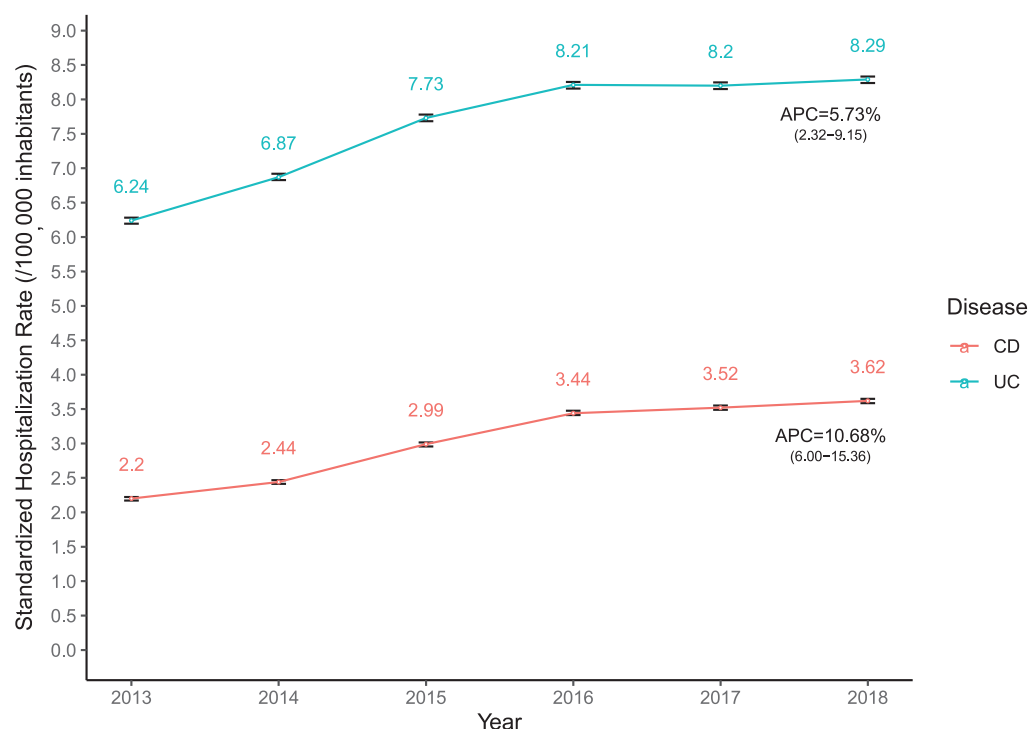


Figure 2. The temporal trends of annual hospitalization rates of patients with IBD in China from 2013 to 2018. The hospitalization rates were standardized for age and sex based on the Chinese population. APC, annual percentage of change with 95% CI in brackets; CD, Crohn's disease; UC, ulcerative colitis. The error bars indicate the 95% confidence interval of the standardized hospitalization rates. The Poisson regression analysis revealed a significantly increasing trend for both CD and UC ($p < 0.0001$).

11.73% (6.38–17.08%). The hospitalization rate of female patients with CD increased from 1.76 (95% CI=1.73–1.79) to 2.68 (95% CI=2.64–2.72) per 100,000 female inhabitants ($p < 0.0001$) with an APC of 8.93% (5.32–12.53%). The hospitalization rate of male patients with UC increased from 6.58 (95% CI=6.51–6.64) to 9.15 (95% CI=9.08–9.22) per 100,000 male inhabitants ($p < 0.0001$) with an APC of 6.72% (3.10–10.34%). The hospitalization rate of female patients with UC increased from 5.92 (95% CI=5.86–5.98) to 7.43 (95% CI=7.37–7.50) per 100,000 female inhabitants ($p < 0.0001$) with an APC of 4.58% (1.34–7.81%). The APCs of hospitalization rates for urban residents were 10.14% and 7.11% for CD and UC, respectively. In contrast, the APCs for rural residents were 5.5% and 4.2% for CD and UC, respectively (Figure 3(c) and (d)).

Sensitivity analysis showed similar trends in hospitalization rate for both CD and UC patients and under group specific calculation. The hospitalization rate peaked at age 60–69 years for UC

patients and age 20–29 years for CD patients when only including patients with primary diagnosis of IBD (Supplementary Tables 3–6).

The proportion of IBD patients in the 2018 HQMS database from 31 provinces is presented in Supplementary Table 2. The proportion of CD patients in the database was the highest in Hunan (0.1658%), followed by Jilin (0.1228%) and Jiangsu (0.1036%), whereas the proportion of UC patients was the highest in Hunan (0.1743%), followed by Shandong (0.1682%) and Xinjiang (0.1619%). CD hospitalization rates were higher in the southern coastal areas such as Jiangsu and Guangdong, whereas hospitalized UC cases were more prevalent in the Northern area of China such as Xinjiang, Inner Mongolia, and Shandong.

Percentages of intestinal complications, perianal diseases, and surgery

The proportion of CD patients with perianal diseases increased from 4.25% (95% CI=3.75–4.75) in 2013 to 6.56% (95% CI=6.08–7.04)

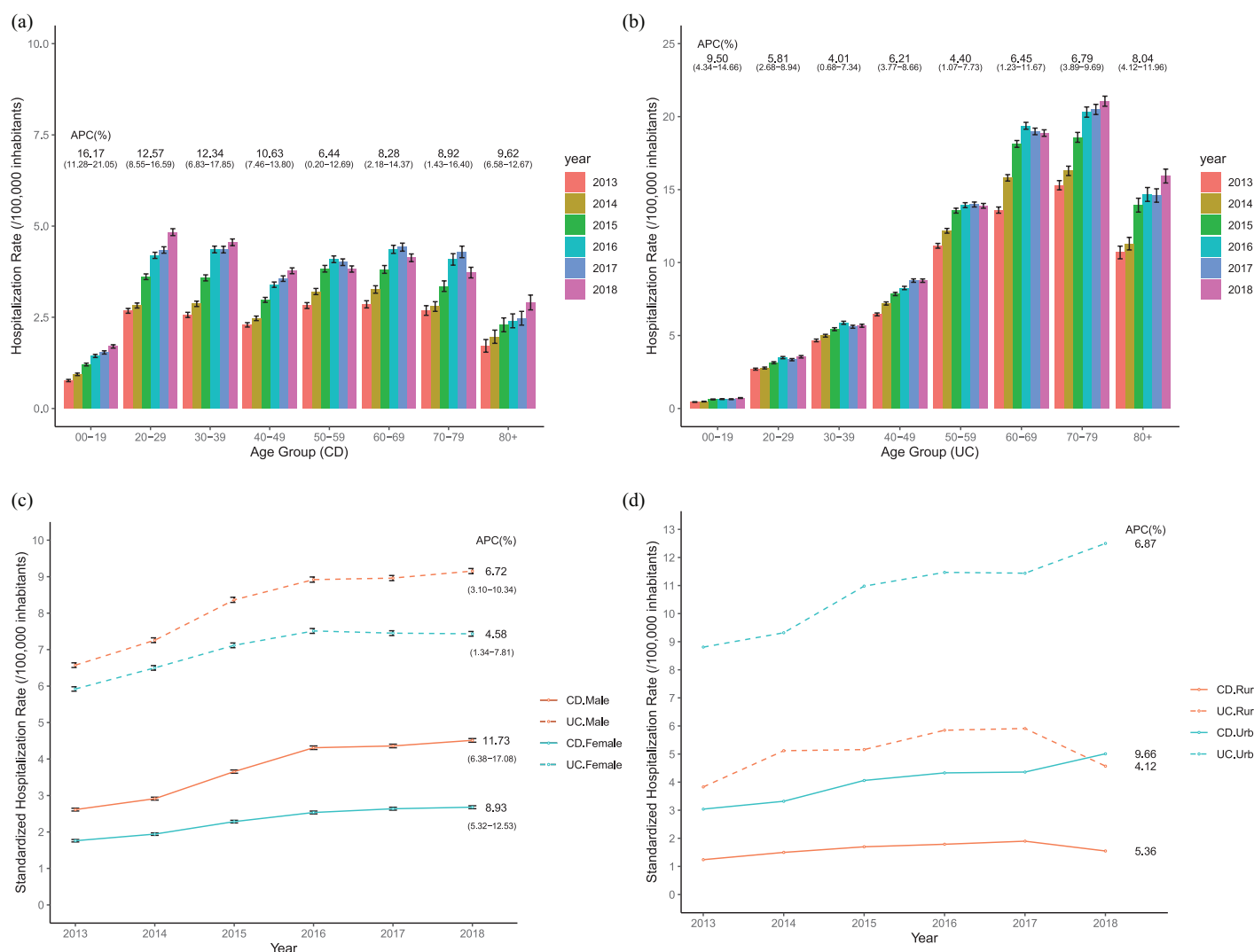


Figure 3. The temporal trends of hospitalization rates of IBD patients stratified by age, sex, and place of residence from 2013 to 2018. The sex-standardized hospitalization rates of patients with CD (a) and UC (b) grouped by age. The Poisson regression analysis revealed a significantly increasing trend for all age groups ($p < 0.0001$). (c) The temporal trends of age-standardized hospitalization rates of IBD in male and female residents from 2013 to 2018 (all $p < 0.0001$). (d) The crude hospitalization rates of IBD in urban citizens and rural residents from 2013 to 2018.

APC, annual percentage of change with 95% CI in brackets; CD, Crohn's disease; UC, ulcerative colitis. The error bars indicate the 95% confidence interval of the standardized hospitalization rates.

($p < 0.0001$) in 2018 with an APC of 9.15% (0.78–17.52) (Figure 4) (77.59% cases come from urban area). The percentages of bowel obstruction ($p = 0.085$) and penetrating disease ($p = 0.056$) in hospitalized CD patients did not significantly change over time.

The temporal trend of surgical rates for hospitalized IBD patients is presented in Figure 5. A Cochran–Armitage trend test revealed a significant decrease in intestinal surgical rates for both CD and UC patients

($p < 0.0001$) (Figure 5(a)). The surgical rates for CD patients decreased from 7.96% (95% CI=7.29–8.63) in 2013 to 5.56% (95% CI=5.11–6.00) in 2018; those for UC patients decreased from 3.54% (95% CI=3.26–3.82) in 2013 to 2.52% (95% CI=2.32–2.72) in 2018, with APC of -6.30% (-11.33 to -1.27%) and 6.35% (-16.21 to 3.51%), respectively. The resection rates for bowel resection alone decreased significantly from 2013 to 2018 for both CD patients [6.06% (95% CI=5.47–6.65) to 4.24% (95% CI=3.85–4.63), $p < 0.0001$] and UC

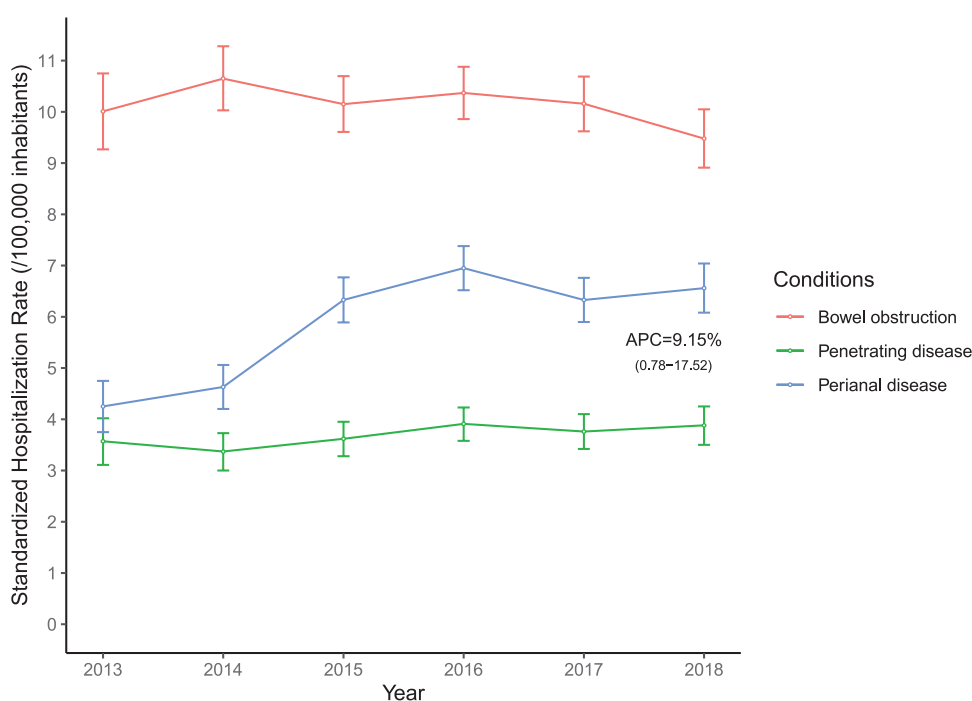


Figure 4. Temporal trends of intestinal complications and perianal diseases in hospitalized patients with CD in China from 2013 to 2018. A Cochran–Armitage trend test revealed no significant changes in rates of bowel obstruction ($p = 0.0851$) and penetrating disease ($p = 0.0562$). A significant increase in perianal disease was observed ($p < 0.0001$), with APC of 9.15% (0.78–17.52). APC, annual percentage of change with 95% CI in bracket; CD, Crohn's disease. The error bars indicate the 95% confidence interval.

patients [1.97% (95% CI=1.76–2.18) to 1.29% (95% CI=1.14–1.43), $p < 0.0001$] with APC of –6.11% (–10.95 to –1.27%) and –7.52% (–21.64 to 6.60%) (Figure 5(b)).

Sensitivity analysis on patients with primary diagnosis of IBD demonstrated similar trends in percentage of bowel obstruction, perianal diseases, and surgical rates, except for a rather increasing trend in proportion of penetrating disease among hospitalized patients with primary diagnosis of CD (Supplementary Tables 7–9).

Economic burden of hospitalization

The median annual hospital charges per patient from 2013 to 2018 are presented in Table 2. The highest hospital charges for CD patients were in 2015 (median=\$1,898.40; IQR=\$2,852.74), same as the highest charges for UC patients in 2015 (median=\$1432.79; IQR=\$1745.39). Linear regression analysis revealed a decrease in the hospital charges for CD patients ($\beta = -0.02$, $p < 0.001$) from \$1846.86 (IQR=\$2710.71) in

2013 to \$1631.15 (IQR=\$2230.79) in 2018. No significant differences in hospital charges over time were observed for UC patients ($p = 0.424$).

Using the estimated number of hospitalized patients nationwide, we calculated the hospital charges in total by extrapolation of the hospital charges per patient year. The total estimated hospitalization charges were \$312.14 million (\$104.39 million for CD patients + \$207.75 million for UC patients) in 2013 and \$426.37 million (\$149.91 million for CD patients + \$276.46 million for UC patients) in 2018. The total hospital charges afforded by national insurance program were calculated similarly (Table 2).

The median LOS for CD patients decreased from 13 days (IQR=15) to 10 days (IQR=11) ($p < 0.001$), and that for UC patients decreased from 11 days (IQR=12) to 10 days (IQR=10) ($p < 0.001$) (Table 2).

Sensitivity analysis showed no change in temporal trends in hospital charges and LOS when

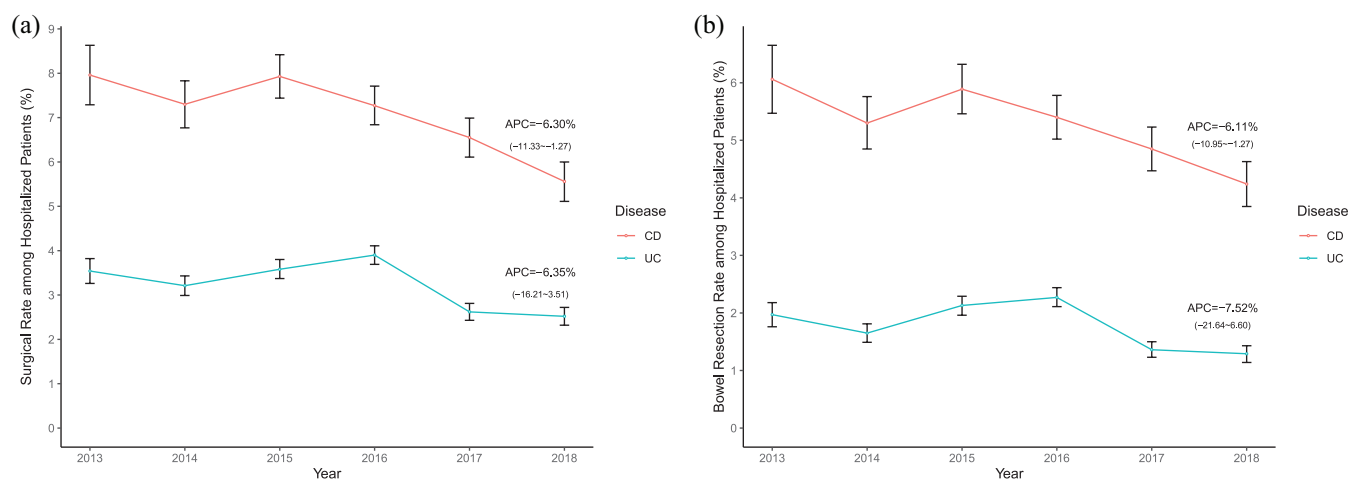


Figure 5. The temporal trends of surgical rates for hospitalized IBD patients in China from 2013 to 2018. (a) The bowel surgical rates for IBD hospitalized patients from 2013 to 2018. The Cochran–Armitage trend test results: UC, $p < 0.0001$; CD, $p < 0.0001$. (b) The bowel resection rates for IBD hospitalized patients from 2013 to 2018. The Cochran–Armitage trend test results: UC, $p < 0.0001$; CD, $p < 0.0001$. APC, annual percentage of change with 95% CI in brackets; CD, Crohn's disease; UC, ulcerative colitis. The error bars indicate the 95% confidence interval of surgical rates.

Table 2. Hospital charges and length of stay in hospitalized patients with IBD in China from 2013 to 2018.

Disease	Year					
	2013	2014	2015	2016	2017	2018
Hospital charges per patient (\$) ^a						
CD	1846.86 (2710.71) ^b	1886.44 (2749.56)	1898.40 (2852.74)	1883.53 (2812.13)	1668.44 (2421.58)	1631.15 (2230.79)
UC	1382.16 (1684.75)	1397.90 (1722.67)	1432.79 (1745.39)	1368.80 (1694.74)	1292.40 (1537.07)	1273.76 (1467.34)
Total hospital charges national level (million \$) ^c						
CD	104.39	116.33	148.80	164.61	153.59	149.91
UC	207.75	236.88	283.95	297.00	280.97	276.46
Total hospital charges covered by national insurance (million \$) ^d						
CD	45.10	52.95	71.62	75.32	78.32	76.43
UC	116.53	133.92	170.22	167.22	157.73	154.71
LOS per patient (d) ^e						
CD	13 (15)	12 (14)	12 (14)	11 (13)	10 (12)	10 (11)
UC	11 (12)	11 (12)	11 (11)	11 (11)	10 (10)	10 (10)

CD, Crohn's disease; UC, ulcerative colitis.

^aThe hospital charges were adjusted to 2013 by consumer price index: 2014, 1.02, 2015, 1.014, 2016, 1.02, 2017, 1.016, 2018, 1.021; expressed in US dollars with the average exchange rate: 2013, 1\$=6.1932¥; 2014, 1\$=6.1428¥; 2015, 1\$=6.2284¥; 2016, 1\$=6.6423¥; 2017, 1\$=6.7518¥; 2018, 1\$=6.6174¥.

^bData in this table were expressed as median (IQR), except the estimated hospital charges covered by national insurance.

^cNational level total hospital charges were calculated by estimated number of patients hospitalized multiplied by average hospital charges per patient year.

^dThe total amount of hospital charges covered presented here was extrapolated by the average amount of charges covered by insurance for single patients times the extrapolated number of annual hospitalized patients.

^eLOS indicates the length of stay in hospital.

accounting only hospitalized patients with primary diagnosis of IBD (Supplementary Table 10). The detailed information of hospital charges in each province is provided in Supplementary Table 11.

Discussion

In this study, a national hospitalization discharge database assessed the temporal trends of population-based hospitalization rates in China. A rapid increase in the hospitalization rate of IBD patients from 2013 to 2018 was observed, which may be partially attributed to the rapid increase in the incidence of IBD in China, and also could result from higher awareness of doctors in diagnosis and documentation of IBD in discharge records as well as a tendency to hospitalize enterically symptomatic patients to work up for IBD.

This study demonstrated that the hospitalization rate of IBD patients increased from 8.44 (2.20 + 6.24) in 2013 to 11.91 (3.62 + 8.29) per 100,000 inhabitants in 2018, given the large population in China, the absolute number of hospitalized IBD patients is estimated to reach 166,000 patients [(3.62 + 8.29 per 100,000 inhabitants) × 1395 million population] in 2018. In addition, the hospitalization rate of UC patients in this study was higher than that of CD patients, but the hospitalization rate of CD patients increased more rapidly. This finding was consistent with the data on trends of disease incidence in the Asia-Pacific Crohn's and Colitis Epidemiology Study (ACCESS).¹⁸ Indeed, the incidence of IBD in newly industrialized countries nowadays resembles the pattern observed in the Western world during the early 20th century, with a rapid increase in the prevalence of UC prior to CD.¹

Differences in the incidence of IBD between female and male patients in Western countries have been described previously,^{2,7} with a higher incidence of UC observed in males and a higher incidence of CD observed in females. The predominance of CD in females may be associated with the secretion of hormones involved in IBD pathogenesis, as the opposite sex distribution was observed in pediatric CD patients, and the transition of the sex distribution occurred in the 14- to 17-year-old age group of puberty.³³ Nevertheless, this hypothesis has been challenged by the studies in East Asia which have reported a predominance of adult CD patients in males.^{34,35} This study's findings argue against this explanation as we

observed a predominance of males in hospitalized CD patients in the Chinese population. The increase in hospitalization rates was also higher in male patients for both CD and UC. The reasons underlying this phenomenon in East Asia warrant further investigation.

The disease onset of IBD ranges from early childhood to over 60 years old.³⁶ The peak incidence of CD and UC occurs in patients aged 20–30 years and 30–40 years, respectively.² In this study, the age distribution of CD patients was similar to that of incident cases, whereas the age distribution of hospitalized UC patients differed slightly from incident cases with peak hospitalization rate at 70–79 years, which is consistent with other hospital-based studies.^{2,25,31,36} The reasons underpinning this distribution pattern of hospitalized UC patients remain unclear; we further conducted sensitivity analysis by including patients with only primary diagnosis of IBD to exclude hospitalization due to comorbidity in aged patients, which showed similar age distribution. Further longitudinal analysis is warranted. In addition, we observed that the highest rate of increase in hospitalizations was for individuals younger than 20 years old for both CD and UC, which concurred with studies from industrialized Western countries reporting a striking increase in the incidence of pediatric-onset IBD cases over the past two decades.³⁶

In the ACCESS inception cohort, a south-to-north gradient in UC incidence and a west-to-east gradient in CD incidence were observed.¹¹ In this study, the geographic distribution pattern of CD incidence was thought to be linked to the difference in gross domestic product in these areas.¹⁷ This study supported this finding at a nationwide scale by demonstrating that CD hospitalization rates were higher in the southern coastal areas comprising more developed cities in China. We also observed higher hospitalization rates for urban than for rural residents. The positive association between urbanization and IBD incidence may be ascribed to a Westernized diet, lifestyle, better hygiene conditions, and advances in healthcare service in urban areas.¹ We also observed that hospitalized UC cases were more prevalent in the Northern area of China, consistent with findings from previous multicenter epidemiologic studies.^{16,17}

Patients with IBD have a high morbidity of complications and surgery. Recent studies in North

America and Europe have reported a decrease in surgical rates possibly due to improvements in therapeutic strategies.^{28,37} In this study, we also observed a significant reduction in intestinal surgical rates of hospitalized IBD patients in China from 2013 to 2018. A meta-analysis demonstrated that the use of biologics could decrease the surgical rate by 33–77%,³⁸ but another population-based study reported no anticipated decline in the resection rate after the use of anti-tumor necrosis factor therapy.³⁹ The introduction of infliximab in IBD treatment dates back to 2007 in China. Whether the decreasing trend in surgical rates in this study was related to the use of biologics warrants further investigation.

The healthcare costs of IBD are considerably high in Western countries. The costs related to hospitalization and surgery may account for up to 50% of the total direct healthcare expenditure.^{11,12} Data on healthcare costs of IBD patients in newly industrialized countries are limited. A study from two centers in Shanghai, China, revealed a significant increase in the hospitalization costs per patient in both CD and UC patients in the period of 2003–2011.⁴⁰ In this study, the average annual hospitalization charges were \$1600–\$1900 per CD patient and \$1200–\$1500 per UC patient, which was lower than that in Western countries.⁴¹ The hospitalization costs for UC patients were stable during the study period, while the costs for CD patients decreased slightly. Although the individual hospitalization costs for IBD patients in China did not increase significantly, the total hospitalization charges and hospital charges afforded by the national insurance program demonstrated an increasing trend given the rise in hospitalization rates. The rising number of hospitalization costs the healthcare system \$426 million totally in 2018 and \$231 million of which afforded by national insurance program. IBD predominantly impacts quality of life in the youth, including loss of work capabilities, and will therefore pose a significant challenge to the healthcare system in China.^{41,42}

This study has several limitations. First, although comprising more than 40% of all tertiary centers in China, the hospitalization database HQMS did not encompass the entire population. There may have been a discrepancy between the actual number of hospitalized IBD cases and extrapolated number of cases used in this analysis. Also, the location of tertiary hospital mainly in urban area

will lead to less recorded rural admission records, although the majority of diagnoses of IBD are made in tertiary centers. By involving more tertiary hospitals and secondary hospitals in China, this discrepancy could be narrowed down in future analyses conducted using this database. Second, due to the limitations in study period coverage and included hospitals, it was difficult to trace the records for the exact time of diagnosis, and we were unable to conduct follow-up analyses. Third, as prescription data were not included in the HQMS database, we were unable to calculate the cost of biologics and perform correlation analyses with hospitalization rate and disease burden. Fourth, 5 year is a relatively short period for identification of population-based temporal trend. Projects with longer period up to 10 years are ongoing as the database is continuing for data inclusion. Fifth, using code-based diagnosis of IBD might have the probability of overestimation and misclassification bias. Although several prior studies have validated the use of ICD coding in the identification of individuals with IBD,⁴³ we could not conduct a validation study. The HQMS database is de-identifiable, and thus, we were not able to link a subset of the population to patient registries to address the degree of misclassification errors associated with using ICD coding within the HQMS database. Finally, this study cohort may include both incident and prevalent cases of IBD during the study period, and we were not able to differentiate incident (i.e. new diagnosis) from prevalent cases in HQMS, which is analogous to many other hospital-based studies.^{44–46}

In conclusion, this study harnessed the national hospitalization database in China and demonstrated that hospitalization rates for IBD increased, whereas surgical rates and length of hospitalization decreased from 2013 to 2018. Our results will facilitate the optimization of healthcare policies and strategies for management of patients with IBD in China, including strengthening the healthcare system for IBD patients to better account the rapid rising trend in hospitalization rate; improving and facilitating the usage of biologics to keep the trend of decreasing surgical rate and LOS; generating region-specific management of IBD patients based on geographic distribution difference in hospitalization rate of CD and UC, rural and urban area, as well as providing the better accessibility of rural patients for IBD healthcare.

Author contributions

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Rui-Ming Liang: Data curation; Formal analysis.

Jian-Yan Long: Data curation; Formal analysis; Methodology.

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Conflict of interest statement

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Data availability

The extraction data used in this study could be obtained by contact to corresponding author under the approval from the National Health Commission of the People's Republic of China.

Supplemental material

Supplemental material for this article is available online.

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