



# A nationwide analysis on the influence of obesity in inflammatory bowel disease hospitalizations

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**Background/Aims:** Proinflammatory cytokines released from adipocytes can influence the development, progression, and treatment of inflammatory bowel disease (IBD), and may be associated with worse clinical outcomes. **Methods:** For 2016–2018, we analyzed data from the Nationwide Inpatient Sample to identify adult ( $\geq 18$  years) hospitalizations with a primary discharge diagnosis of IBD. The study sample was divided based on the presence or absence of obesity. The primary outcomes included inpatient mortality, while the secondary outcomes consisted of system-based complications and disease implications on the United States healthcare system. **Results:** We identified 282,005 hospitalizations of IBD from 2016 to 2018. Of these hospitalizations, 26,465 (9.4%) had a secondary diagnosis of obesity while 255,540 (90.6%) served as controls. IBD hospitalizations with obesity had a higher mean age (47.9 years vs. 45.2 years,  $P < 0.001$ ), middle age (range, 40–65 years) predominance (37.7% vs. 28.9%,  $P < 0.001$ ), female predominance (64.1% vs. 52.5%,  $P < 0.001$ ) and higher proportion of patients with comorbidities compared to the non-obese cohort. White predominance was observed in both subgroups. No difference in the odds of inpatient mortality was noted between the 2 subgroups; however, IBD hospitalizations with obesity had higher mean total hospital charge (\$50,126 vs. \$45,001,  $P < 0.001$ ), longer length of stay (5.5 days vs. 4.9 days,  $P < 0.001$ ) and higher proportion of complications compared to the non-obese cohort. **Conclusions:** Obese IBD hospitalizations had higher length of stay, total hospital charge, and complications compared to the non-obese cohort. (**Intest Res 2022;20:342-349**)

**Key Words:** Inflammatory bowel disease; Obesity; Epidemiology; Outcomes; Nationwide Inpatient Sample

## INTRODUCTION

Inflammatory bowel disease (IBD) is a broad term characterized by the presence of chronic inflammation in the gastrointestinal tract which results from host-microbial interactions in individuals who are genetically susceptible.<sup>1</sup> It is an autoimmune condition which can be further subdivided into 2 distinct entities, namely ulcerative colitis (UC) and Crohn's dis-

ease (CD), based on the pattern of mucosal involvement and characteristics of the chronic inflammatory process.<sup>2</sup> The exact etiology of IBD is currently unknown; however, it is hypothesized that immune response dysregulation, abnormal gut microbiota, environmental factors, and genetics may play a key role in pathogenesis.<sup>3</sup> IBD may not be a leading cause of mortality in the United States (US) or worldwide, but its rising prevalence places substantial burden on the healthcare systems while also negatively impacting the patient's quality of life.<sup>4,5</sup> Obesity, defined as abnormal or excessive fat accumulation for a given height (body mass index [BMI]  $\geq 30$  kg/m<sup>2</sup>), has reached epidemic status in the US and IBD is being increasingly diagnosed in these individuals.<sup>6</sup> It has been recognized

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as a state of chronic low-grade inflammation with constant release of proinflammatory cytokines from the adipocytes.<sup>7</sup> Although researchers are actively investigating the exact mechanism implicated in the development of IBD in obese patients, there is significant paucity of data on the impact of obesity in IBD patients admitted to the hospital. The main objective of our study was to help bridge this gap in knowledge. In our study, we used the National Inpatient Sample (NIS) database to determine the epidemiology, demographic distribution, adverse outcomes, and system-based complications of IBD hospitalizations with obesity. We also further compare these characteristics with non-obese IBD hospitalizations which served as a control population. This comparative study designed helped us estimate the influence of obesity on IBD hospitalizations. Furthermore, we also discuss the geographical distribution of the disease entity across the US and detail the burden of the disease on the US healthcare system in terms of healthcare cost and resource utilization for the study period.

## METHODS

### 1. Design and Data Source

This was a retrospective cohort study design involving all adult hospitalizations with IBD in the US from 2016 to 2018. Data was extracted from the NIS database using the Stata<sup>®</sup> version 16 software (StataCorp, College Station, TX, USA) for the study period. The NIS database was developed by the Healthcare Cost and Utilization Project (HCUP), a Federal-State-Industry partnership sponsored by the Agency for Healthcare Research and Quality. It is derived from billing data submitted by individual hospitals across the US to statewide data organizations, covering 97% of the US population.<sup>8</sup> Excluding rehabilitation centers and long-term acute care hospitals, it approximates a 20% stratified sample of discharges from US community hospitals. The dataset is further weighted to obtain national estimates.<sup>9</sup> The 2016 to 2018 databases were coded using the International Classification of Diseases, 10th Revision, Clinical Modification/Procedure Coding System (ICD-10-CM/PCS). In NIS, codes are divided into a principal diagnosis which is the main ICD-10 code and secondary diagnoses which consist of any ICD-10 code other than the code for the principal diagnosis.

### 2. Study Population

The study population included all adult ( $\geq 18$  years) hospitalizations with a primary discharge diagnosis of IBD, including

both UC and CD, from 2016 to 2018. These were classified as "IBD hospitalizations" for the study. Individuals less than 18 years of age were excluded from the study. This cohort was further subdivided into 2 groups based on the presence or absence of a secondary diagnosis of obesity, defined as a BMI  $> 30$  kg/m<sup>2</sup>, using the ICD codes available from the Clinical Classifications Software Refined, developed and standardized by HCUP, were used.<sup>10</sup>

### 3. Outcome Measures

The primary outcome was comparing inpatient mortality between patients with IBD and obesity, to those without obesity. Secondary outcomes included comparing rates of acute myocardial infarction, sepsis, need for transfusion, acute renal failure, acute respiratory failure (ARF), pulmonary embolism (PE) as well as mean length of hospitalization (LOS), and mean total hospital charges (THC).

### 4. Statistical Analysis

A thorough analysis was performed using the Stata<sup>®</sup> version 16 software (StataCorp). All analyses were conducted using weighted samples for national estimates and were in adjunct with HCUP regulations. Comorbidities were calculated as proportions and the chi-square test was used to compare these characteristics between the 2 groups. A multivariate regression analysis was done to adjust for possible confounders while calculating the primary and secondary outcomes. The confounders were obtained after a thorough literature review and consisted of age, sex, race, hospital bed size, location and teaching status and grouped Charlson Comorbidity Index. A negative binomial regression model was used to adjust for count data including LOS and THC, expressed as incidence rate ratio (IRR). A threshold of 0.05 was maintained for statistical significance of the outcomes.

### 5. Ethical Considerations

The NIS database lacks patient specific and hospital level identifiers. Our study was conducted with Institutional Review Board approval from Central Michigan University College of Medicine. As the NIS database lacks patient identifiers, informed consent was waived.

### 6. Data Availability Statement

The data for the study was obtained from the NIS which is a large publicly available all-payer inpatient care database containing information on more than 7 million hospital stays across

**Table 1.** Characteristics of IBD Hospitalizations with and without the Presence of Obesity

Variable	IBD with obesity (%)	IBD without obesity (%)	P-value
Sample size (n = 282,005), No. (%)	26,465 (9.4)	255,540 (90.6)	
Crohn's disease	59.7	62.5	<0.001
Ulcerative colitis	40.3	37.5	<0.001
Women sex	64.1	52.5	<0.001
Mean age (yr)	47.9	45.2	<0.001
Age categories (yr)			<0.001
18–39	45.2	53.6	
40–64	37.7	28.9	
≥ 65	17.1	17.5	
Racial distribution			0.009
Caucasian	70.5	70.6	
African American	15.0	13.5	
Hispanic	7.7	7.9	
Others	6.8	8.0	
CCI score			<0.001
0	16.2	23.8	
1	8.5	6.1	
2	3.7	2.3	
≥ 3	71.6	67.8	
Insurance type			<0.001
Medicaid	29.7	26.3	
Medicare	19.7	19.6	
Private	46.1	48.3	
Uninsured	4.5	5.8	
Median annual income in patient's zip code (USD)			<0.001
1–43,999	27.9	25.5	
44,000–55,999	27.1	25.3	
56,000–73,999	27.2	25.3	
≥ 74,000	17.8	23.9	
Comorbidities			
Diabetes mellitus	21.7	8.2	<0.001
Hypertension	39.0	22.5	<0.001
Smoking history	40.6	36.8	<0.001
Congestive heart failure	5.6	2.5	<0.001
Chronic kidney disease	7.4	4.4	<0.001
Dyslipidemia	23.3	12.7	<0.001
Coronary artery disease	8.2	5.8	<0.001
Chronic obstructive pulmonary disease	7.8	5.2	<0.001

(Continued to the next)

**Table 1.** Continued

Variable	IBD with obesity (%)	IBD without obesity (%)	P-value
Malnutrition	10.6	13.6	<0.001
History of neoplasm	6.8	6.8	0.855
History of anemia	37.2	37.8	0.419
Hospital characteristics			
Hospital region			<0.001
Northeast	19.4	21.7	
Midwest	28.8	23.9	
South	37.9	37.9	
West	13.9	16.5	
Hospital bed size			0.190
Small	19.8	18.8	
Medium	28.5	28.1	
Large	51.7	53.1	
Urban location	93.6	93.1	0.156
Teaching hospital	74.1	72.2	0.010

IBD, inflammatory bowel disease; CCI, Charlson Comorbidity Index.

the US. The large sample size available from the NIS is ideal for developing national and regional estimates and enables analysis of large sets of population.

## RESULTS

### 1. Biodemographic Characteristics

From 2016 to 2018, we identified 282,005 hospitalizations of IBD, including both UC and CD. Of these hospitalizations, 26,465 patients (9.4%) had a secondary diagnosis of obesity while 255,540 patients (90.6%) served as controls. IBD hospitalizations with obesity were noted to be significantly older (47.9 years vs. 45.2 years,  $P < 0.001$ ) with a middle age (range, 40–65 years) (37.7% vs. 28.9%,  $P < 0.001$ ) and female predominance (64.1% vs. 52.5%,  $P < 0.001$ ) compared to patients in the non-obese subgroup. For IBD hospitalizations with obesity, Caucasians made up 70.5% of the study population followed by African American (15%), Hispanics (7.7%) and other races (6.8%). Similarly, for IBD hospitalizations without obesity, a Caucasian predominance (70.6%) in the study population was noted followed by African American (13.5%), Hispanics (7.9%) and other races (8%). Compared to IBD hospitalizations without obesity, we noted a higher percentage of patients with comorbidities such as diabetes mellitus (21.7% vs. 8.2%,  $P < 0.001$ ), dyslipidemia (23.3% vs. 12.7%,  $P < 0.001$ ), cor-

**Table 2.** Clinical Outcomes for IBD Hospitalizations with and without Obesity

Outcome	IBD with obesity (%)	IBD without obesity (%)	aOR (95% CI)	P-value <sup>a</sup>
Sample size (n = 282,005), No. (%)	26,465 (9.4)	255,540 (90.6)		
Primary outcome				
Inpatient mortality	0.28	0.30	1.03 (0.60–1.77)	0.904
Secondary outcomes				
Mean length of stay	5.5	4.9	1.12 <sup>b</sup> (1.09–1.16)	<0.001 <sup>a</sup>
Mean total hospital charge (USD)	50,126	45,001	1.32 <sup>b</sup> (1.20–1.46)	<0.001 <sup>a</sup>
Sepsis	1.5	1.2	1.34 (1.05–1.71)	0.018 <sup>a</sup>
Acute myocardial infarction	0.2	0.2	1.15 (0.61–2.66)	0.666
Transfusion of blood products	5.3	5.8	0.92 (0.81–1.05)	0.201
Acute kidney failure	10.2	7.5	1.37 (1.24–1.51)	<0.001 <sup>a</sup>
Acute respiratory failure	0.9	0.6	1.43 (1.05–1.96)	0.025 <sup>a</sup>
Acute pulmonary embolism	0.6	0.4	1.47 (1.01–2.17)	0.049 <sup>a</sup>

<sup>a</sup>Statistically significant, *P* < 0.05.

<sup>b</sup>Adjusted incidence rate ratio.

IBD, inflammatory bowel disease; aOR, adjusted odds ratio; CI, confidence interval.

onary artery disease (8.2% vs. 5.8%, *P* < 0.001), hypertension (39% vs. 22.5%, *P* < 0.001), congestive heart failure (5.6% vs. 2.5%, *P* < 0.001), chronic kidney disease (7.4% vs. 4.4%, *P* < 0.001), chronic obstructive pulmonary disease (7.8% vs. 5.2%, *P* < 0.001), and history of smoking (40.6% vs. 36.8%, *P* < 0.001) in IBD hospitalizations with obesity. However, IBD hospitalizations without obesity had more patients with malnutrition (13.6% vs. 10.6%, *P* < 0.001) than the obesity subgroup (Table 1).

## 2. Hospital Characteristics

A higher proportion of IBD hospitalizations with obesity were noted in the South (37.9%) hospital region, followed by the Midwest (28.8%), Northeast (19.4%) and West (13.9%). Most of these hospitalizations were in teaching hospitals (74.1%). Similarly, for IBD hospitalizations without obesity, the highest proportion of hospitalizations were seen in the South (37.9%), followed by the Midwest (23.9%), Northeast (21.7%) and West (16.5%) hospital regions (Table 1).

## 3. Primary Outcome

We did not find any statistical significance in the odds of inpatient mortality (0.28% vs. 0.30%: adjusted odds ratio [aOR], 1.03; 95% confidence interval [CI], 0.60–1.77; *P* = 0.904) between IBD hospitalizations with and without obesity (Table 2).

## 4. Secondary Outcomes

IBD hospitalizations with obesity were noted to have longer LOS (5.5 days vs. 4.9 days: IRR, 1.12; 95% CI, 1.09–1.16; *P* < 0.001) and higher mean THC (\$50,126 vs. \$45,001: IRR, 1.32; 95% CI, 1.20–1.46; *P* < 0.001) compared to patients without obesity (Table 2). Furthermore, inpatient complications such as sepsis (1.5% vs. 1.2%: aOR, 1.34; 95% CI, 1.05–1.71; *P* = 0.018), acute kidney failure (AKF) (10.2% vs. 7.5%: aOR, 1.37; 95% CI, 1.24–1.51; *P* < 0.001), ARF (0.9% vs. 0.6%: aOR, 1.43; 95% CI, 1.05–1.96; *P* = 0.025), and PE (0.6% vs. 0.4%: aOR, 1.47; 95% CI, 1.01–2.17; *P* = 0.049) were more frequent for IBD hospitalizations with obesity compared to those without (Table 2). From a payment perspective for IBD hospitalizations with obesity, private insurance was the largest payer (46.1%) followed by Medicaid (29.7%) and Medicare (19.7%). About 4.5% of these patients were uninsured. Additionally, a majority of IBD hospitalizations with obesity were in the \$1–\$43,999 (low) median annual income group (27.7%), followed by the \$56,000–\$73,999 (27.2%), \$44,000–\$55,999 (27.1%) and ≥ \$ 74,000 (17.8%) median annual income groups (*P* < 0.001).

## DISCUSSION

IBD is a broad term used to describe states of chronic progressive inflammation of the mucosa of the gastrointestinal tract in individuals who are genetically susceptible.<sup>11</sup> The prevalence

of IBD continues to be on the rise around the world with literature reporting an increase in the cases of IBD by 85.1% from 1990 to 2017.<sup>4</sup> Similar trends have been observed in the US with the Centers for Disease Control and Prevention (CDC) reporting an increase in the prevalence of IBD from 2 million (0.9%) in 1999 to 3 million (1.3%) cases in 2015.<sup>4</sup> Although IBD may not a leading cause of mortality, its rising prevalence, both around the world and in the US, is concerning as it significantly impacts the patient's quality of life.<sup>12</sup> Furthermore, over the last few decades, obesity has emerged as a global pandemic with rising prevalence.<sup>13</sup> The US has seen a doubling of the rates of obesity since the 1970s with over two-thirds of the American population being classified as overweight and one-third as obese.<sup>14</sup> The IBD population, which has historically been associated with malnourishment, is not immune to the rising trend of obesity with studies reporting increased diagnosis of IBD in obese populations.<sup>6</sup> The presence of obesity in IBD is an area of particular interest as it may lead to worse clinical outcomes and place undue burden on the healthcare system across the globe. Although current literature describes the association between obesity and IBD, there is significant gap in knowledge on numerous aspects of the disease entity in an inpatient setting. Therefore, this study was designed to investigate and compare the biodemographic characteristics, associations, inpatient mortality, and numerous system-based complications of obesity in IBD hospitalizations. Furthermore, we also determined the distribution of the disease entity and its burden on the US healthcare system in terms of costs and healthcare utilization.

Numerous cross-sectional studies have demonstrated that about 20%–40% of patients with IBD are overweight and around 15%–40% are obese.<sup>15</sup> In our study, we identified 282,005 hospitalizations of IBD using NIS for the 2016 to 2018 period. We report that 9.4% of these hospitalizations had a secondary diagnosis of obesity. This prevalence rate was lower than that reported in literature. It may be explained by the fact that due to increasing awareness about the disease entity, there is early recognition and intervention by physician providers, researchers, community organizations and individuals themselves.<sup>16</sup> IBD hospitalizations with obesity were significantly older with a mean age of 47.9 years compared to those without obesity. This may be because an increasing age is associated with insulin resistance and dysregulated adipokine secretion which may increase fat mass accumulation and redistribution.<sup>17</sup> This may lead to an increase in the incidence of obesity with increasing age which promotes the development of IBD. Addition-

ally, a large-scale detection power of the study may also, in part, have had a role to play in the differences noted for mean age. Furthermore, literature has described gender disparities both in the prevalence of IBD and obesity.<sup>18,19</sup> As per the CDC, the age-adjusted prevalence of severe obesity was higher in women compared to men.<sup>18</sup> Our study reflects these findings as we note a significant female predominance in IBD hospitalizations with obesity. Additionally, racial differences were noted between obese and non-obese IBD hospitalizations. However, Caucasians made up most of the study population in both cohorts. This may be because IBD is more commonly seen in Caucasians compared to any other race.<sup>20</sup>

Obesity is associated with significant morbidity and mortality particularly from cardiovascular causes and cancers.<sup>21</sup> The relationship between obesity and mortality varies substantially with the patient population, BMI, and the cause of death, and may change over time.<sup>21,22</sup> Literature reports that the obesity-related age-adjusted mortality rates have increased by 142% from 1999 to 2016 in the US disproportionately affecting men compared to women.<sup>23</sup> For patients with IBD, there is significant paucity of data on the exact mortality rates as the death may be secondary to a complication of IBD rather than the disease itself. As per literature, the 30-day mortality rate for CD and UC have been estimated to be 2.7 and 3.8 per 100 hospital stays, respectively.<sup>24</sup> Based on poor clinical outcomes associated with obesity in other chronic inflammatory diseases, it is extrapolated that obesity potentially leads to worse clinical outcomes in patients with IBD, but the studies exploring this association in-depth provide conflicting evidence.<sup>25,26</sup> In our study, the mortality rate for IBD hospitalizations with obesity was found to be 0.28%. However, we did not find any statistical significance in the odds of inpatient mortality between obese and non-obese IBD hospitalizations. The exact reason for this finding is unknown but as discussed earlier it may be because these patients die due to causes other than IBD. Furthermore, we also assessed system-based inpatient complications of these IBD hospitalizations. Compared to the non-obese cohort, IBD hospitalizations with obesity had higher proportion of patients with complications such as sepsis, AKE, ARE, and PE. Nonetheless, we advocate for the need of additional large, prospective, multi-center studies to investigate the outcomes associated with IBD hospitalizations in the presence of obesity and to further evaluate the benefit of weight reduction in these patients.

In recent years, numerous studies have estimated the burden of IBD on the US healthcare system in terms of costs and

healthcare utilization. In 2014, the mean charge for inpatient management of CD was noted to be \$11,345 and \$13,412 for UC.<sup>27</sup> From 2006 to 2015, the mean LOS for IBD hospitalizations was noted to be 6.7 days with a standard deviation of 5.8 days.<sup>28</sup> In our study, IBD hospitalizations with obesity were noted to have a mean THC of \$50,126 and LOS of 5.5 days as compared to the \$45,001 and 4.9 days for the non-obese cohort, respectively. Therefore, the presence of obesity is associated with higher costs and longer length of hospital stay in IBD hospitalizations. Hence, in these patients it becomes essential to educate and promote dietary and lifestyle changes to potentially decrease inpatient admissions and the burden of the disease on the healthcare system. Frequent outpatient follow-up with goal-oriented weight reduction may also be beneficial in these patients. Furthermore, we also assessed the geographical distribution of these hospitalizations across the US using the NIS database.<sup>29,30</sup> We noted higher proportion of IBD hospitalizations with obesity in the South, followed by the Midwest, Northeast and West hospital regions. This distribution may be because the Southern hospital regions have a higher prevalence of obesity and IBD compared to other regions of the US.<sup>31</sup> For IBD hospitalizations with obesity, from a payment perspective, private insurance was the largest payer followed by Medicaid and Medicare. Only 4.5% of these patients were uninsured. Additionally, a majority of IBD hospitalizations with obesity were in the low median annual income (\$1–\$43,999) subgroup. This may be due to consumption of low-quality, high-fat foods due to economic restraints.<sup>32</sup>

This study has several strengths along with limitations. The biggest strength of our study is the study population, which is derived from a large, national, publicly available database developed through a Federal-State-Industry partnership and contains data on inpatient admissions from all over the US. Hence, the outcomes of the study are applicable to all hospitalizations of IBD across the US. Furthermore, the study design helps us investigate, in-depth, the epidemiology, adverse outcomes, complications, and the consequences on the healthcare system for IBD hospitalizations with obesity while also comparing it with a control population. This allows for a comprehensive analysis which adds meaningful data to current literature.

However, we do acknowledge the limitations associated with our study. The NIS database lacks data on the severity of the disease and time from the diagnosis of obesity to the development of IBD. Furthermore, it does not contain data on medications used by patients with IBD or their dosage. We

also acknowledge all the all the limitations associated with using ICD codes for obesity, which was defined as a BMI >30 kg/m<sup>2</sup> in adults per the NIS database. As data was collected from NIS, all biases associated with retrospective studies are applicable to our study. Additionally, the hospitalizations selected for our study were based on the diagnosis of IBD rather than individual patients. Therefore, individuals admitted numerous times for the same chief complaint may have been included several times in the study population. Finally, NIS is an administrative database that uses a coding system to gather and store information; hence, there are possibilities for coding errors. However, despite these limitations, we believe that the large sample size, the specific study design, and a detailed analysis provide a better understanding of the topic in question. Through this study, we aimed to not only fill the gaps in literature that currently exist, but also promote intellectual conversation and promote future research on the topic.

In our study, the prevalence of obesity in IBD hospitalizations was noted to be 9.4% with a substantial female and White predominance. The mean age for IBD hospitalizations with obesity was found to be 47.9 years. Additionally, we noted higher prevalence of comorbidities such as diabetes mellitus, dyslipidemia, coronary artery disease, hypertension, congestive heart failure, chronic kidney disease, chronic obstructive pulmonary disease, and history of smoking in IBD hospitalizations with obesity compared to the non-obese cohort. Although IBD hospitalizations with obesity were noted to have higher mean THC and longer LOS, we did not find any statistical significance in the rates of mortality between the 2 subgroups. Compared to non-obese IBD hospitalizations, patient with concurrent obesity had higher rates of inpatient complications such as sepsis, AKE, ARE, and PE. In conclusion, obesity has a significant impact on IBD hospitalizations in terms of costs healthcare utilization and system-based complications.

## ADDITIONAL INFORMATION

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### Conflict of Interest

No potential conflict of interest relevant to this article was reported.

**Data Availability Statement**

We used the NIS database from 2016 to 2018, available online at <http://www.hcup-us.ahrq.gov>. The NIS is a large publicly available, all-payer inpatient care database containing data on more than seven million hospital stays yearly in the US. Its large sample size is ideal for developing national and regional estimates and enables analyses of rare conditions, uncommon treatments, and special populations.

**Author Contribution**

Conceptualization: Dahiya DS. Data curation: Dahiya DS, Kichloo A. Formal analysis: Kichloo A. Investigation: Dahiya DS, Kichloo A, Wani F, Singh J, Shaka H. Methodology, project administration, resources, supervision: Dahiya DS, Kichloo A. Validation: Dahiya DS, Kichloo A, Wani F, Singh J, Shaka H. Visualization: Dahiya DS, Kichloo A. Writing - original draft: Dahiya DS, Kichloo A. Writing - review & editing: all authors. Approval of final manuscript: all authors.

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