World Journal of Gastroenterology

Online Submissions: http://www.wjgnet.com/esps/
wjg@wjgnet.com
doi:10.3748/wjg.v19.i38.6360

World J Gastroenterol 2013 October 14; 19(38): 6360-6366
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

TOPIC HIGHLIGHT

Geoffrey C Nguyen, MD, PhD, FRCPC, *Series Editor*

Quality of care delivered to hospitalized inflammatory bowel disease patients

Adam V Weizman, Geoffrey C Nguyen

Adam V Weizman, Division of Gastroenterology, Women's College Hospital, University of Toronto, Toronto, M5S 1B2, Ontario, Canada
Geoffrey C Nguyen, Mount Sinai Hospital Centre for Inflammatory Bowel Disease, University of Toronto, Toronto, M5G 1X5, Ontario, Canada
Geoffrey C Nguyen, Division of Gastroenterology and Hepatology, Johns Hopkins School of Medicine, Baltimore, MD 21201, United States
Author contributions: Both authors contributed to the conception of the article, review of the literature, drafting and review of the manuscript, and approval of the final version.
Correspondence to: Adam V Weizman, MD, Division of Gastroenterology, Women's College Hospital, 4th Floor, 76 Grenville St, Toronto, M5S1B2, Ontario, Canada. adam.weizman@wchospital.ca
Telephone: +1-416-3237543 Fax: +1-416-3237549
Received: June 29, 2013 Revised: July 30, 2013
Accepted: August 4, 2013
Published online: October 14, 2013

Abstract

Hospitalized patients with inflammatory bowel disease (IBD) are at high risk for morbidity, mortality, and health care utilization costs. While the literature on trends in hospitalization rates for this disease is conflicting, there does appear to be significant variation in the delivery of care to this complex group, which may be a marker of suboptimal quality of care. There is a need for improvement in identifying patients at risk for hospitalization in an effort to reduce admissions. Moreover, appropriate screening for a number of hospital acquired complications such as venous thromboembolism and *Clostridium difficile* infection is suboptimal. This review discusses areas of inpatient care for IBD patients that are in need of improvement and outlines a number of potential quality improvement initiatives such as pay-for-performance models, quality improvement frameworks, and healthcare information technology.

Key words: Crohn's disease; Hospitalization; Inflammatory bowel disease; Quality improvement; Ulcerative colitis

Core tip: Hospitalized patients with inflammatory bowel disease are at risk of harm and increased utilization of healthcare resources. Variation in the care delivered to these patients is common. There is room for improvement in the quality of care focusing on reducing admissions and identifying patients at risk for inpatient complications such as venous thromboembolism and *Clostridium difficile* infection. This review outlines several aspects of inpatient care in need of improvement and discusses a number of improvement strategies that have been implemented with potential to benefit both patients and providers.

Weizman AV, Nguyen GC. Quality of care delivered to hospitalized inflammatory bowel disease patients. *World J Gastroenterol* 2013; 19(38): 6360-6366 Available from: URL: http://www.wjgnet.com/1007-9327/full/v19/i38/6360.htm DOI: http://dx.doi.org/10.3748/wjg.v19.i38.6360

INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic gastrointestinal condition characterized by relapsing inflammation. Most patients with IBD are managed in the outpatient setting, however as disease severity progresses and complications arise, hospitalization is often required. Patients admitted to hospital are at increased risk for a variety of complications including venous thrombotic events (VTE), hospital acquired infections, *Clostridium difficile*, and death[1-5]. Moreover, hospitalized patients are more likely to require surgery[5,6]. There have been

conflicting reports on trends in hospitalization rates for IBD over the last decade and the literature has revealed significant variation in care and disease outcomes among hospitalized IBD patients. The heterogeneous nature of IBD severity, location, and phenotype as well as limited evidence to guide some therapeutic domains make standardization of IBD care delivery difficult. However, given that hospitalized patients are at the highest risk for morbidity, mortality, and health care utilization costs, quality improvement initiatives aimed at reducing variation, a known surrogate marker of poor performance, are well suited to this subset of patients[7,8]. This review outlines recent trends in rates of hospitalization for IBD and highlights areas of inpatient care that are in need of improvement.

HOSPITALIZATION RATES FOR IBD

Most IBD care is delivered in the ambulatory setting. However, a significant proportion of patients will require hospitalization at some point in their disease course. Reports on overall trends in hospitalization rates for IBD over the past two decades are conflicting. Among a large cohort of patients followed across an integrated care network in Northern California, Herrinton *et al*[8] noted a 33% decline in hospitalization rates for Crohn's disease ($P = 0.02$) and a 29% decline among those with ulcerative colitis ($P = 0.0009$) from 1998-2005. However, a report using the National Hospital Discharge Survey (NHDS) showed that between the years 1970-2004, the rates of hospitalization for both Crohn's disease and ulcerative colitis in the United States increased[9]. Moreover, readmission is not uncommon, as demonstrated by Bernstein *et al*[10], whereby 20% of patients with IBD were readmitted within the same calendar year. The most important advance in IBD care over the last ten years has been the increasing use of anti-tumour necrosis factor (TNF) therapy. The true impact of this on hospitalization rate may not have been completely captured in all these reports, thus more data is needed to evaluate the impact of anti-TNF on recent hospitalization trends.

While the literature on hospitalization rates is conflicting, most studies clearly show variation in practice patterns among hospitalized IBD patients. For example, in the cohort from Northern California discussed above, variability in surgery rates and immunomodulator use depending on the number of gastroenterologists and colorectal surgeons at each site was noted among the 16 medical centers included in the study[8]. Similarly, Spiegel *et al*[11] demonstrated significant variation among community and expert gastroenterologists in a number of care areas including patients admitted to hospital with severe ulcerative colitis. Expert gastroenterologists had a lower threshold to consult a surgeon for patients with severe steroid refractory disease. Outcomes following colectomy based on surgical volumes have also been shown in several studies, with high volumes centers having lower mortality rates[12,13]. Differences in outcomes based on the type of admitting physician have also been demonstrated. Murthy *et al*[14] showed that patients with ulcerative colitis admitted to non-gastroenterologists had higher in hospital mortality rates compared to those admitted under the care of a gastroenterologist (1.1% *vs* 0.2%, $P < 0.0001$). Colectomy rates have also shown to be subject to geographic variation across the United States, with rates in the Midwest and West regions being three fold higher than those in the Northeast[15]. These studies underscore the need for improvement efforts focused on minimizing variation and bridging the gap between ideal and true performance in caring for the hospitalized inpatient with IBD.

VENOUS THROMBOEMBOLISM PROPHYLAXIS

The risk of venous thromboembolism (VTE) has been shown to be increased among patients with IBD. Multiple studies have shown patients with IBD have a 2-3.5 fold increased risk for VTE compared to the general population and a recent meta-analysis confirmed a relative risk of 2.2 (95%CI: 1.83-2.65)[1,16-18]. In fact, one study showed that among 17 chronic illnesses, only heart failure and cancer carried a greater risk of VTE than IBD[19]. Moreover, it appears the prevalence of VTE among this group of patients is rising[1]. A number of risk factors for VTE among IBD patients have been identified. In a review of the Nationwide Inpatient Sample (NIS) between 1998-2004, Nguyen *et al*[1] identified increasing age, co-morbidities, ulcerative colitis (as opposed to Crohn's disease), surgery, and the need for public heath assistance as important risk factors for the development of VTE. Disease activity has also been shown to be an important predictor, with one study showing a 4.5 fold increased risk of developing VTE during times of disease flare compared to remission[20]. Hospitalized IBD patients, particularly those with ulcerative colitis, appear to be at very high risk of VTE. Hospitalized IBD patients have been shown to have nearly a 6 fold increased absolute risk of VTE compared to an ambulatory IBD population[17] and an increased adjusted odds ratio of 1.85 (95%CI: 1.7-2.1) compared to those non-IBD patients admitted to hospital[1]. Moreover, VTE has been shown to be a marker of worse outcomes and higher health resource utilization. A review of a large database of hospital discharges in the United States found an odds ratio (OR) of 2.5 (95%CI: 1.83-3.43) for in-hospital mortality compared to IBD patients without VTE[1]. Mortality rates for ulcerative colitis were particularly high (37.4 per 1000 hospitalizations *vs* 9.9 per 1000 hospitalizations, $P < 0.0001$). Patients with IBD and VTE also had a longer average length of stay (11.7 d *vs* 6.1 d, $P < 0.0001$) and higher hospital charges compared to IBD patients without VTE.

Given the morbidity and mortality associated with inpatient VTE, the utility of VTE prophylaxis to prevent this complication is clear. Prophylaxis with heparin has been shown to significantly and safely decreased

the incidence of deep-vein thrombosis and pulmonary embolism[21]. However, despite the efficacy and ease of administering VTE prophylaxis, a significant percentage of IBD patients admitted to hospital are not receiving it and remain at risk. In a retrospective review of a tertiary IBD center in the United States, Tinsley *et al*[22] noted that the overall prophylaxis rate was only 67.6%. Variation was noted depending on the admitting service, with significantly higher rates noted among those admitted to a surgical service compared to a medical service (93.5% *vs* 57.4%). Even among those in which VTE prophylaxis was ordered, up to 34% of doses were not given. The lower prevalence for prophylaxis of IBD patients may in part be due to lack of awareness of their increased risk, as they are often young and mobile. This was suggested by a survey of gastroenterologists who were members of the American Gastroenterological Association[23]. Only 45% of respondents were aware that guidelines recommending VTE prophylaxis were published and a third surveyed reported working in a hospital with no protocols for VTE prophylaxis. Significant variation in practice was noted. However, contributors other than lack of awareness are suggested by studies of IBD experts. At a large Canadian tertiary IBD center, rates of VTE prophylaxis were lowest for patients admitted to the gastroenterology run IBD service compared to those admitted to general internal medicine or surgery[24]. Moreover, a survey of Canadian IBD experts found that almost 20% did not routinely use VTE prophylaxis and there was inconsistency among respondents regarding the indication for prophylaxis for patients in remission[25]. These studies underscore tremendous variation and suboptimal quality of care in preventing this morbid IBD related extra-intestinal manifestation. Given the uniform increased risk among hospitalized IBD patients, the presence of readily available and safe prophylactic agents, and the identification of important predictors for lack of prevention, this area of IBD care is a "low hanging fruit" that is very amenable to quality improvement initiatives.

CLOSTRIDIUM DIFFICILE TESTING

A substantial body of evidence has emerged to implicate IBD as an important risk factor for *Clostridium difficile* infection (CDI). IBD patients have been shown to have higher infection rates with CDI compared to non-IBD patients. In an analysis of administrative data using a large registry of hospital discharges in the United States, Nguyen *et al*[4] noted that patients with ulcerative colitis (UC) had a prevalence of CDI that was 8 times that of non IBD patients admitted with a gastrointestinal problem (37.3 cases/1000 discharges *vs* 4.8 cases/1000 discharges, $P < 0.001$). This finding was supported by a systematic review of 42 articles that showed CDI was more common among IBD patients than non IBD controls[26]. In addition to the higher prevalence of CDI among IBD patients, the incidence of CDI appears to be increasing over the last decade, particularly among hospitalized IBD patients. A review of discharges among hospitalized IBD patients showed that the percentage of IBD admissions complicated by CDI had increased from 1.4% to 2.9% between the years 1998 and 2007 ($P < 0.001$)[27]. This increase was most marked for the subset with UC in which CDI complicated 5.3% of admissions. Similarly, in a retrospective review of hospitalized patients, Rodemann *et al*[28] showed that while CDI rates doubled among Crohn's disease patients between the years 1998 and 2004, they tripled among those with UC.

Not only does the literature support a true rise in CDI incidence and prevalence among individuals with IBD, but CDI also may confer worse outcomes. In-hospital mortality was four fold higher among IBD patients with CDI compared to those with IBD alone in a retrospective review of the NIS[27]. Similarly, a retrospective cohort study from Ontario, Canada showed a higher in-hospital mortality rate among hospitalized UC patients with CDI compared to those with UC alone (3.3% *vs* 0.38%, $P < 0.0001$)[29]. This increased mortality rate persisted out to five years of follow up in which the cumulative 5 years mortality rate was 27% for the CDI group and 14% for those with UC alone ($P = 0.0073$). CDI has also been shown to increase length of stay and hospitalization costs among those with concomitant IBD. A review of a large administrative database of hospital discharges from the United Kingdom showed that median length of stay was 26 d among those with both CDI and IBD compared to only 5 d for those with IBD alone, a difference that was statically significant[30]. This translates into increased health care costs as shown by Nguyen *et al*[4], whereby average hospital charges were $35606 for a UC patient with CDI compared to $23856 for those with UC alone ($P < 0.0001$). The impact of CDI on colectomy is less clear. Jen *et al*[30] showed an increased risk of in-hospital colectomy among hospitalized UC patients with CDI as compared to UC alone (OR = 1.7, 95%CI: 1.4-2.1). This conflicts with the finding of Nguyen *et al*[4], who showed a lower risk of colectomy in IBD patients with CDI (OR = 0.44, 95%CI: 0.34-0.55). Studies evaluating long term risk of colectomy after CDI are also conflicting. Navaneethan *et al*[31] showed that one year following hospitalization for UC, the colectomy rate was 35% for those with CDI during that hospitalization compared to 9.9% for those without infection ($P < 0.001$). This was in keeping with a study from a large, tertiary IBD center in which one year colectomy rates for those with IBD and CDI were higher compared to those with IBD alone (44.6% *vs* 25%, $P = 0.04$)[32]. However, no difference in the risk of colectomy at 5 years was seen in the Canadian study cited above[29].

The literature supports the finding that CDI among patients with IBD is a significant and increasingly prevalent problem, particularly for those with UC. Moreover, CDI confers increased short and long term mortality risk and increased health care utilization costs and may increase short and long term risk of colectomy. The majority of CDI is diagnosed within 48 h of admission, suggesting most patients acquire CDI in the community[28]. Given the high incidence and potential poor outcomes

associated with CDI and the fact that it is most often acquired before admission, routine testing of patients presenting with exacerbation of IBD for *Clostridium difficile* is a reasonable and potentially powerful intervention. In fact, a single center study showed a reduction in the number of colectomies after routine testing on admission was introduced[33]. While more evidence evaluating the benefits of routine testing is indicated, the literature thus far supports its use. Nonetheless, it appears routine testing is not widespread. A study of 34 European countries found tremendous variation in the incidence of CDI across hospitals and suggested difference in testing behavior was most likely responsible for these results[34]. Moreover, despite the rising prevalence of CDI, there is variation in approaches management in terms of antibiotic selection and practices regarding IBD specific immunosuppressive therapy. A survey of gastroenterologists in Canada and the United States found that nearly half of respondents add antibiotics to ongoing immunosuppressive therapy while the other half routinely held all immunosuppressants during antibiotic treatment[35]. The lack of consensus even among IBD experts highlights the need for more studies aimed at bringing clarity to the commonly encountered clinical "grey area".

INTERVENTIONS AIMED AT IMPROVEMENT

In order to adequately address gaps in care, an understanding of the contributing factors to the target problem is essential. It is important to tailor a quality improvement (QI) initiative to the local context and implement according to the resources, infrastructure, and QI culture available. A variety of methods to improve identified deficiencies in the quality of care of hospitalized IBD patients are already underway and discussed in detail below.

Pay-for-performance program

Guidelines have outlined algorithmic approaches for following this complex group of patients. However, the uptake of IBD guidelines by gastroenterologists has been shown to variable[36,37]. Therefore, other improvement approaches are necessary. A pay-for-performance (P4P) funding model has been advocated by some, whereby hospital and/or physician reimbursement is tied to meeting certain predetermined care benchmarks. This model is increasingly being used, although its impact on patient outcomes remains controversial. A review of over 7000 primary care physicians in the United Kingdom Quality and Outcomes Framework Pay for Performance Program found significant improvements in outcomes of a number of chronic diseases such as diabetes and coronary artery disease[38]. Similarly, a large study from the National Health Services in England compared mortality in a region of the country that had uniformly adopted a P4P model in all hospitals to the remainder of the country which did not use this model[39]. In the 24 hospitals that did used the P4P model, an absolute reduction in mortality of 1.3% (95%CI: 0.4-2.1, $P = 0.006$) and a relative reduction of 6% (95%CI: 260-1500) was observed. However, an American study evaluating the impact of the Centers for Medicare and Medicaid Services strategy that relies primarily on financial penalties through not providing hospitals with additional payment for health care-acquired or preventable complications found no significant changes in performance before or after this policy was adopted[40]. Therefore, while P4P programs hold promise, more study is needed before there is universal adoption of these models. Moreover, there is a need to evaluate the impact of these programs on IBD patient, given their complexity and unique needs. The American Gastroenterology Association has developed IBD specific quality indicators eligible for reimbursement through the Physician Quality Reporting System (PQRS) (Table 1)[41]. The impact of the PQRS on improving the quality of inpatient IBD care needs to be further characterized.

Table 1 American Gastroenterology Association Physician Quality Reporting System inflammatory bowel disease measures

1	IBD type, location and activity all documented
2	Corticosteroid sparing therapy after 60 d
3	Bone loss assessment
4	Influenza immunization
5	Pneumococcal immunization
6	Testing for latent tuberculosis before initiating anti-TNF therapy
7	Assessment of Hepatitis B status before initiating anti-TNF therapy
8	Tobacco use: screening and cessation intervention

IBD: Inflammatory bowel disease; TNF: Tumor necrosis factor.

While not designed for the purposes of a reimbursement program, the Crohn's and Colitis Foundation of American have recently sponsored the publication of a set of quality indicators[42]. Both process and outcome indicators were developed that encompass a variety of domains in IBD care including treatment, surveillance, and health care maintenance. A number of inpatient IBD care process indicators are defined such as "IF a hospitalized patient with severe colitis is not improving on intravenous steroids within 3 d, THEN sigmoidoscopy with biopsy should be performed to exclude cytomegalovirus, AND surgical consultation should be obtained" as well as "IF a patient in whom a flare of IBD is suspected with new or worsening diarrhea THEN the patient should undergo *Clostridium difficile* testing at least once" and inpatient related outcomes measures including: (1) Number of days per year in the hospital attributable to IBD; and (2) Number of emergency room visits per year for IBD. It is important for gastroenterologists to become familiar with these quality indicators as they can be expected to become increasingly incorporated into the accreditation processes of health care institutions.

Quality improvement frameworks

As the quality improvement movement continues to build momentum, there are increasing calls for innovative changes to the way health care is delivered. System rede-

sign is a fundamental principal in QI and there has been a particular focus on healthcare provided in the hospitalized setting as this is associated with significant morbidity and cost. Examples of new frameworks in IBD care are increasing. For example, a program in Australia implemented a new model of care consisting of a designated IBD service aimed at reducing hospitalizations[43]. The service consisted of a team of gastroenterologists, a designated weekly IBD clinic, a joint gastroenterology-surgery clinic, and a nurse practitioner (NP). The NP performed a variety of tasks including standardized protocols for monitoring patients on immunomodulator and biologic therapy, a 24-h help line, routine post-discharge follow up phone calls, and a routine education session at discharge. Outcomes were compared before and after adopting this framework. Following the implementation of the IBD service, the mean number of admissions per patient, mean length of stay, and total cost for inpatient care decreased. While this simple before and after design does not clearly control for biases, it does highlight the potentially valuable role of designated chronic care teams, particularly the role of the NP. NPs have been shown to improve outcomes in other chronic diseases, however their use in IBD has lagged behind other fields[44-46]. More studies are needed to evaluate their role in participating in IBD care.

Centralizing care delivery of certain disease into designated tertiary centers of excellence has also become a model employed by some jurisdictions. A number of large studies using administrative data have shown outcomes may be improved in high volume IBD referral centers. For example, United States hospital discharges were reviewed using the Nationwide Inpatient Sample between 1998-2004[6]. IBD patients admitted to high volume centers had lower in-hospital mortality compared to non-high volume hospitals. Similarly, Ananthakrishnan *et al*[13] found that patients admitted to high volume centers were more likely to undergo IBD surgery and had lower post-operative mortality rates compared to those in average volume hospitals. These studies support the designation of IBD centers of excellence whereby complicated IBD patients can be referred to for expert opinion and management. However, these centers must have the resources in place to handle such a complex cohort of patients and to be able to accommodate a large number of referrals to be seen in a timely fashion by gastroenterology and/or surgery.

Advancing healthcare information technology

Hospitals have been increasingly incorporating healthcare information technology (HIT) into patient care. Many QI experts link HIT with improved quality, safety, efficiency, and coordination of care[47]. Hospitalized patients are at increased risk of harm in the form of hospital acquired infections, preventable complications (*e.g.,* VTE), medication errors, and lapses in communication at discharge regarding follow-up. Therefore, initiatives aimed at reducing these harms are needed, and HIT is one avenue that may achieve improvements. If designed well and appropriately adapted to the context of a given institution, an electronic heath record has the potential to improve efficiency, safety, and communication. Computerized provider order entry has the potential to decrease medication errors, link providers to clinical decision support, and address the underuse or overuse of certain resources[47]. For example, standardized admission order sets involve a collection of orders or investigations that when designed well, are effective through improving efficiency, decreasing variation, enhancing workflow, and improving communication of evidence based practices[48,49]. Fields can be customized to an admitting service (*e.g.,* general surgery, gastroenterology, *etc.*) or disease specific (*e.g.,* IBD). An IBD admission order set has the potential to address areas in which the quality of care is suboptimal. For example, including *Clostridium difficile* testing on the admission order may be expected to increase the rates of screening for IBD patients presenting to hospital with new or worsening diarrhea. While the impact of such initiative on IBD outcomes is not yet known, it would increase adherence to recently defined QI benchmarks and potentially identify a high risk group for bad outcomes[42]. Similarly, an electronic order set that automatically defaults to ordering VTE prophylaxis on admission may improve the underuse of VTE prophylaxis outlined above. The physician would deliberately have to remove this order if it is not desired. These "forcing functions" are regarded among the most effective patient safety interventions available[50]. This strategy has been shown to be effective in increasing prophylaxis rates in several studies of non-IBD patients and overcomes barriers to ordering VTE prophylaxis such as the knowledge gaps outlined above[51,52]. However, other barriers to VTE prophylaxis have also been identified that may not be adequately addressed by an order set. Moreover, evidence in support of VTE order sets in IBD is lacking. This underscores the importance of a clear understanding of the local context before implementing an initiative and to ensure that it is well tailored to the patients, resources, and providers at a given institution. Nonetheless, the theory behind order set effectiveness is sound and more study is needed to evaluate their impact on IBD outcomes.

CONCLUSION

In summary, hospitalized patients with inflammatory bowel disease are at risk of harm and increased healthcare utilization resources. More attention needs to be placed on reducing hospital admissions and re-admissions and preventable inpatient complications such as VTE. A number of potential improvement strategies may benefit both patients and providers including pay-for-performance programs, quality improvement frameworks, nurse practitioners, and healthcare information technology. While the true impact of these interventions on IBD outcomes still needs to be elucidated, quality indicators are expected to become increasingly measured in all aspects

of clinical care and it is therefore important that IBD providers familiarize themselves with these concepts.

REFERENCES

1 **Nguyen GC**, Sam J. Rising prevalence of venous thromboembolism and its impact on mortality among hospitalized inflammatory bowel disease patients. *Am J Gastroenterol* 2008; **103**: 2272-2280 [PMID: 18684186 DOI: 10.1111/j.1572-0241.2008.02052.x]

2 **Nguyen GC**, Leung W, Weizman AV. Increased risk of vancomycin-resistant enterococcus (VRE) infection among patients hospitalized for inflammatory bowel disease in the United States. *Inflamm Bowel Dis* 2011; **17**: 1338-1342 [PMID: 21560197 DOI: 10.1002/ibd.21519]

3 **Nguyen GC**, Patel H, Chong RY. Increased prevalence of and associated mortality with methicillin-resistant Staphylococcus aureus among hospitalized IBD patients. *Am J Gastroenterol* 2010; **105**: 371-377 [PMID: 19809406 DOI: 10.1038/ajg.2009.581]

4 **Nguyen GC**, Kaplan GG, Harris ML, Brant SR. A national survey of the prevalence and impact of Clostridium difficile infection among hospitalized inflammatory bowel disease patients. *Am J Gastroenterol* 2008; **103**: 1443-1450 [PMID: 18513271 DOI: 10.1111/j.1572-0241.2007.01780.x]

5 **Bassi A**, Dodd S, Williamson P, Bodger K. Cost of illness of inflammatory bowel disease in the UK: a single centre retrospective study. *Gut* 2004; **53**: 1471-1478 [PMID: 15361497 DOI: 10.1136/gut.2004.041616]

6 **Nguyen GC**, Steinhart AH. Nationwide patterns of hospitalizations to centers with high volume of admissions for inflammatory bowel disease and their impact on mortality. *Inflamm Bowel Dis* 2008; **14**: 1688-1694 [PMID: 18623172 DOI: 10.1002/ibd.20526]

7 **Wennberg J**. Small area variations in health care delivery. *Science* 1973; **182**: 1102-1108 [PMID: 4750608 DOI: 10.1126/science.182.4117.1102]

8 **Herrinton LJ**, Liu L, Fireman B, Lewis JD, Allison JE, Flowers N, Hutfless S, Velayos FS, Abramson O, Altschuler A, Perry GS. Time trends in therapies and outcomes for adult inflammatory bowel disease, Northern California, 1998-2005. *Gastroenterology* 2009; **137**: 502-511 [PMID: 19445944 DOI: 10.1053/j.gastro.2009.04.063]

9 **Sonnenberg A**. Hospitalization for inflammatory bowel disease in the United States between 1970 and 2004. *J Clin Gastroenterol* 2009; **43**: 297-300 [PMID: 18936713 DOI: 10.1097/MCG.0b013e31816244a0]

10 **Bernstein CN**, Nabalamba A. Hospitalization, surgery, and readmission rates of IBD in Canada: a population-based study. *Am J Gastroenterol* 2006; **101**: 110-118 [PMID: 16405542 DOI: 10.1111/j.1572-0241.2006.00330.x]

11 **Spiegel BM**, Ho W, Esrailian E, Targan S, Higgins PD, Siegel CA, Dubinsky M, Melmed GY. Controversies in ulcerative colitis: a survey comparing decision making of experts versus community gastroenterologists. *Clin Gastroenterol Hepatol* 2009; **7**: 168-74, 174.e1 [PMID: 18952199 DOI: 10.1016/j.cgh.2008.08.029]

12 **Kaplan GG**, McCarthy EP, Ayanian JZ, Korzenik J, Hodin R, Sands BE. Impact of hospital volume on postoperative morbidity and mortality following a colectomy for ulcerative colitis. *Gastroenterology* 2008; **134**: 680-687 [PMID: 18242604 DOI: 10.1053/j.gastro.2008.01.004]

13 **Ananthakrishnan AN**, McGinley EL, Binion DG. Does it matter where you are hospitalized for inflammatory bowel disease? A nationwide analysis of hospital volume. *Am J Gastroenterol* 2008; **103**: 2789-2798 [PMID: 18684184 DOI: 10.1111/j.1572-0241.2008.02054.x]

14 **Murthy SK**, Steinhart AH, Tinmouth J, Austin PC, Nguyen GC. Impact of gastroenterologist care on health outcomes of hospitalised ulcerative colitis patients. *Gut* 2012; **61**: 1410-1416 [PMID: 22684482 DOI: 10.1136/gutjnl-2011-301978]

15 **Nguyen GC**, Laveist TA, Gearhart S, Bayless TM, Brant SR. Racial and geographic variations in colectomy rates among hospitalized ulcerative colitis patients. *Clin Gastroenterol Hepatol* 2006; **4**: 1507-1513 [PMID: 17162242 DOI: 10.1016/j.cgh.2006.09.026]

16 **Bernstein CN**, Blanchard JF, Houston DS, Wajda A. The incidence of deep venous thrombosis and pulmonary embolism among patients with inflammatory bowel disease: a population-based cohort study. *Thromb Haemost* 2001; **85**: 430-434 [PMID: 11307809]

17 **Murthy SK**, Nguyen GC. Venous thromboembolism in inflammatory bowel disease: an epidemiological review. *Am J Gastroenterol* 2011; **106**: 713-718 [PMID: 21407182 DOI: 10.1038/ajg.2011.53]

18 **Yuhara H**, Steinmaus C, Corley D, Koike J, Igarashi M, Suzuki T, Mine T. Meta-analysis: the risk of venous thromboembolism in patients with inflammatory bowel disease. *Aliment Pharmacol Ther* 2013; **37**: 953-962 [PMID: 23550660 DOI: 10.1111/apt.12294]

19 **Huerta C**, Johansson S, Wallander MA, García Rodríguez LA. Risk factors and short-term mortality of venous thromboembolism diagnosed in the primary care setting in the United Kingdom. *Arch Intern Med* 2007; **167**: 935-943 [PMID: 17502535 DOI: 10.1001/archinte.167.9.935]

20 **Grainge MJ**, West J, Card TR. Venous thromboembolism during active disease and remission in inflammatory bowel disease: a cohort study. *Lancet* 2010; **375**: 657-663 [PMID: 20149425 DOI: 10.1016/S0140-6736(09)61963-2]

21 **Samama MM**, Cohen AT, Darmon JY, Desjardins L, Eldor A, Janbon C, Leizorovicz A, Nguyen H, Olsson CG, Turpie AG, Weisslinger N. A comparison of enoxaparin with placebo for the prevention of venous thromboembolism in acutely ill medical patients. Prophylaxis in Medical Patients with Enoxaparin Study Group. *N Engl J Med* 1999; **341**: 793-800 [PMID: 10477777 DOI: 10.1056/NEJM199909093411103]

22 **Tinsley A**, Naymagon S, Enomoto LM, Hollenbeak CS, Sands BE, Ullman TA. Rates of pharmacologic venous thromboembolism prophylaxis in hospitalized patients with active ulcerative colitis: Results from a tertiary care center. *J Crohns Colitis* 2013; Epub ahead of print [PMID: 23706933 DOI: 10.1016/j.crohns.2013.05.002]

23 **Sam JJ**, Bernstein CN, Razik R, Thanabalan R, Nguyen GC. Physicians' perceptions of risks and practices in venous thromboembolism prophylaxis in inflammatory bowel disease. *Dig Dis Sci* 2013; **58**: 46-52 [PMID: 23053902 DOI: 10.1007/s10620-012-2435-6]

24 **Ra G**, Thanabalan R, Ratneswaran S, Nguyen GC. Predictors and safety of venous thromboembolism prophylaxis among hospitalized inflammatory bowel disease patients. *J Crohns Colitis* 2013; Epub ahead of print [PMID: 23537817 DOI: 10.1016/j.crohns.2013.03.002]

25 **Razik R**, Bernstein CN, Sam J, Thanabalan R, Nguyen GC. Survey of perceptions and practices among Canadian gastroenterologists regarding the prevention of venous thromboembolism for hospitalized inflammatory bowel disease patients. *Can J Gastroenterol* 2012; **26**: 795-798 [PMID: 23166902]

26 **Goodhand JR**, Alazawi W, Rampton DS. Systematic review: Clostridium difficile and inflammatory bowel disease. *Aliment Pharmacol Ther* 2011; **33**: 428-441 [PMID: 21198703 DOI: 10.1111/j.1365-2036.2010.04548.x]

27 **Ananthakrishnan AN**, McGinley EL, Saeian K, Binion DG. Temporal trends in disease outcomes related to Clostridium difficile infection in patients with inflammatory bowel disease. *Inflamm Bowel Dis* 2011; **17**: 976-983 [PMID: 20824818 DOI: 10.1002/ibd.21457]

28 **Rodemann JF**, Dubberke ER, Reske KA, Seo da H, Stone CD. Incidence of Clostridium difficile infection in inflamma-

tory bowel disease. *Clin Gastroenterol Hepatol* 2007; **5**: 339-344 [PMID: 17368233 DOI: 10.1016/j.cgh.2006.12.027]
29 **Murthy SK**, Steinhart AH, Tinmouth J, Austin PC, Daneman N, Nguyen GC. Impact of Clostridium difficile colitis on 5-year health outcomes in patients with ulcerative colitis. *Aliment Pharmacol Ther* 2012; **36**: 1032-1039 [PMID: 23061526 DOI: 10.1111/apt.12073]
30 **Jen MH**, Saxena S, Bottle A, Aylin P, Pollok RC. Increased health burden associated with Clostridium difficile diarrhoea in patients with inflammatory bowel disease. *Aliment Pharmacol Ther* 2011; **33**: 1322-1331 [PMID: 21517920 DOI: 10.1111/j.1365-2036.2011.04661.x]
31 **Navaneethan U**, Mukewar S, Venkatesh PG, Lopez R, Shen B. Clostridium difficile infection is associated with worse long term outcome in patients with ulcerative colitis. *J Crohns Colitis* 2012; **6**: 330-336 [PMID: 22405170 DOI: 10.1016/j.crohns.2011.09.005]
32 **Jodorkovsky D**, Young Y, Abreu MT. Clinical outcomes of patients with ulcerative colitis and co-existing Clostridium difficile infection. *Dig Dis Sci* 2010; **55**: 415-420 [PMID: 19255850 DOI: 10.1007/s10620-009-0749-9]
33 **Issa M**, Weber LR, Skaros S. Decreasing rates of colectomy despite high rates of hospitalization in C difficile infection IBD patients: a tertiary referaal center experience. *Gastroenterology* 2007; **132**: A663
34 **Bauer MP**, Notermans DW, van Benthem BH, Brazier JS, Wilcox MH, Rupnik M, Monnet DL, van Dissel JT, Kuijper EJ. Clostridium difficile infection in Europe: a hospital-based survey. *Lancet* 2011; **377**: 63-73 [PMID: 21084111 DOI: 10.1016/S0140-6736(10)61266-4]
35 **Yanai H**, Nguyen GC, Yun L, Lebwohl O, Navaneethan U, Stone CD, Ghazi L, Moayyedi P, Brooks J, Bernstein CN, Ben-Horin S. Practice of gastroenterologists in treating flaring inflammatory bowel disease patients with clostridium difficile: antibiotics alone or combined antibiotics/immunomodulators? *Inflamm Bowel Dis* 2011; **17**: 1540-1546 [PMID: 21674710 DOI: 10.1002/ibd.21514]
36 **Altschuler A**, Collins B, Lewis JD, Velayos F, Allison JE, Hutfless S, Liu L, Herrinton LJ. Gastroenterologists' attitudes and self-reported practices regarding inflammatory bowel disease. *Inflamm Bowel Dis* 2008; **14**: 992-999 [PMID: 18300277 DOI: 10.1002/ibd.20416]
37 **Wagnon JH**, Leiman DA, Ayers GD, Schwartz DA. Survey of gastroenterologists' awareness and implementation of AGA guidelines on osteoporosis in inflammatory bowel disease patients: are the guidelines being used and what are the barriers to their use? *Inflamm Bowel Dis* 2009; **15**: 1082-1089 [PMID: 19137605 DOI: 10.1002/ibd.20857]
38 **Ryan AM**, Doran T. The effect of improving processes of care on patient outcomes: evidence from the United Kingdom's quality and outcomes framework. *Med Care* 2012; **50**: 191-199 [PMID: 22329994 DOI: 10.1097/MLR.0b013e318244e6b5]
39 **Sutton M**, Nikolova S, Boaden R, Lester H, McDonald R, Roland M. Reduced mortality with hospital pay for performance in England. *N Engl J Med* 2012; **367**: 1821-1828 [PMID: 23134382 DOI: 10.1056/NEJMsa1114951]
40 **Lee GM**, Kleinman K, Soumerai SB, Tse A, Cole D, Fridkin SK, Horan T, Platt R, Gay C, Kassler W, Goldmann DA, Jernigan J, Jha AK. Effect of nonpayment for preventable infections in U.S. hospitals. *N Engl J Med* 2012; **367**: 1428-1437 [PMID: 23050526 DOI: 10.1056/NEJMsa1202419]
41 http: //www.gastro.org/practice/quality-initiatives/cms-physician-qualitative-report-initiative#pqrs2012
42 **Melmed GY**, Siegel CA, Spiegel BM, Allen JI, Cima R, Colombel JF, Dassopoulos T, Denson LA, Dudley-Brown S, Garb A, Hanauer SB, Kappelman MD, Lewis JD, Lynch I, Moynihan A, Rubin DT, Sartor RB, Schwartz RM, Wolf DC, Ullman TA. Quality indicators for inflammatory bowel disease: development of process and outcome measures. *Inflamm Bowel Dis* 2013; **19**: 662-668 [PMID: 23388547 DOI: 10.1097/mib.0b013e31828278a2]
43 **Sack C**, Phan VA, Grafton R, Holtmann G, van Langenberg DR, Brett K, Clark M, Andrews JM. A chronic care model significantly decreases costs and healthcare utilisation in patients with inflammatory bowel disease. *J Crohns Colitis* 2012; **6**: 302-310 [PMID: 22405166 DOI: 10.1016/j.crohns.2011.08.019]
44 **Rudd P**, Miller NH, Kaufman J, Kraemer HC, Bandura A, Greenwald G, Debusk RF. Nurse management for hypertension. A systems approach. *Am J Hypertens* 2004; **17**: 921-927 [PMID: 15485755 DOI: 10.1016/S0895-7061(04)00867-2]
45 **Wasson J**, Gaudette C, Whaley F, Sauvigne A, Baribeau P, Welch HG. Telephone care as a substitute for routine clinic follow-up. *JAMA* 1992; **267**: 1788-1793 [PMID: 1545464 DOI: 10.1001/jama.1992.03480130104033]
46 **Piette JD**, Weinberger M, McPhee SJ. The effect of automated calls with telephone nurse follow-up on patient-centered outcomes of diabetes care: a randomized, controlled trial. *Med Care* 2000; **38**: 218-230 [PMID: 10659695 DOI: 10.1097/00005650-200002000-00011]
47 **Wachter RM**. Understanding Patient Safety. San Francisco, California: McGraw Hill, 2012: 205-227
48 **Chan J**, Shojania KG, Easty AC, Etchells EE. Does user-centred design affect the efficiency, usability and safety of CPOE order sets? *J Am Med Inform Assoc* 2011; **18**: 276-281 [PMID: 21486886 DOI: 10.1136/amiajnl-2010-000026]
49 **McGreevey JD**. Order sets in electronic health records: principles of good practice. *Chest* 2013; **143**: 228-235 [PMID: 23276846 DOI: 10.1378/chest.12-0949]
50 http: //www.effectivehealthcare.ahrq.gov/
51 **O'Connor C**, Adhikari NK, DeCaire K, Friedrich JO. Medical admission order sets to improve deep vein thrombosis prophylaxis rates and other outcomes. *J Hosp Med* 2009; **4**: 81-89 [PMID: 19219912 DOI: 10.1002/jhm.399]
52 **Maynard G**, Stein J. Designing and implementing effective venous thromboembolism prevention protocols: lessons from collaborative efforts. *J Thromb Thrombolysis* 2010; **29**: 159-166 [PMID: 19902150 DOI: 10.1007/s11239-009-0405-4]

P- Reviewers Yamamoto T, Yan YT **S- Editor** Song XX
L- Editor A **E- Editor** Zhang DN

百世登
Baishideng®

Published by **Baishideng Publishing Group Co., Limited**
Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road, Wan Chai, Hong Kong, China
Fax: +852-65557188
Telephone: +852-31779906
E-mail: bpgoffice@wjgnet.com
http://www.wjgnet.com

ISSN 1007-9327

9 771007 932045 38>