

Original Article

## Conflicts of Interest in Inflammatory Bowel Disease Articles on UpToDate

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### Abstract

**Background:** Financial conflicts of interest (FCOIs) are widespread in inflammatory bowel disease (IBD) and may be particularly important in point-of-care (POC) resources, such as UpToDate, that are used to aid clinical decision making. In this study, we determined the prevalence of industry payments from companies making biologic medications for IBD to contributors of UpToDate articles on IBD.

**Methods:** This cross-sectional analysis included UpToDate articles that mention the use of biologic medications for IBD. We collected the names of the contributors (authors and editors) and their disclosures on UpToDate. We then searched for their names on the Center for Medicare and Medicaid Open Payments database and compared the payment information from 2013 to 2018 with UpToDate's disclosures. We presented data per *episode*, which describes one instance of participation by one person in one article, regardless of whether that person contributed to multiple articles.

**Results:** We identified 23 articles on the treatment of Crohn's disease and ulcerative colitis that mentioned the use of biologic medications, with 86 total episodes. Sixty-two (72%) episodes involved FCOIs. The median payment associated with each episode was \$55 (interquartile range = \$44 to \$145,241). Contributors did not fully disclose FCOIs in 41 (48%) episodes. Deputy editors, who are required to be free of FCOIs, in general did not have substantial episodes involving FCOI.

**Conclusions:** We found that UpToDate articles on inflammatory bowel disease involve substantial FCOI, many of which are not disclosed. The presence of these FCOIs may hamper trust in the objectivity of treatment recommendations.

**Keywords:** *Conflict of interest; Inflammatory bowel diseases; Point-of-care systems*

Financial conflicts of interest (FCOI) in medicine are widespread and can influence clinical practice (1). FCOIs are important in point-of-care (POC) resources, as they are used to aid clinical decision making (2,3). UpToDate is a widely used POC resource that has been associated with improved quality of care, shorter length of stay and lower mortality rates (4). There are concerns, however, regarding the presence of physician–industry interactions among contributors (5).

As part of their conflict of interest policy, UpToDate collects information on relevant industry relationships from contributors and lists this information via a link on each article (6). Deputy editors, physicians who are not permitted to have any relevant industry relationships, are tasked with evaluating and mitigating contributors' conflicts through peer review, revision of content and replacement of contributors. Unlike several high-impact journals, however (7,8), this review process is not published or

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open to the public. As a consequence, it is challenging to assess the degree to which this process minimizes industry influence.

FCOIs in UpToDate may be especially relevant when considering expensive medications. Among such medications, we chose to examine biologic drugs in inflammatory bowel disease for several reasons. First, recent changes in recommendations for the management of Crohn's disease and ulcerative colitis have led to expanding use of biologic drugs, which now account for the majority of outpatient IBD expenditures in the United States (9–11). The guideline panels creating treatment recommendations in IBD have been shown to have a high prevalence of FCOI (12).

Second, these drugs are among the highest-grossing worldwide (13) and have substantial associated marketing expenditures (14–16). These marketing efforts can take the form of payments to physicians, which is associated with increased prescribing of biologic drugs in IBD (17). Finally, gastroenterologists tend to have more financial relationships with pharmaceutical companies and receive more industry payments compared to their colleagues (18).

Given the increasing use and high-cost of biologics, concerns about industry influence among physicians prescribing and writing guidelines about these drugs, and the widespread use of UpToDate, we aimed to quantify industry payments to authors and editors of UpToDate articles, which mentioned the use of biologic medications for Crohn's disease or ulcerative colitis.

## Methods

We conducted a cross-sectional analysis of UpToDate articles related to the treatment of Crohn's disease and ulcerative colitis that mentioned the use of biologic medications. This study

was reviewed by the St. Michael's Hospital Ethics Review Board and deemed exempt from ethics review, as it relies on publicly available information (19). The study design is summarized in Figure 1.

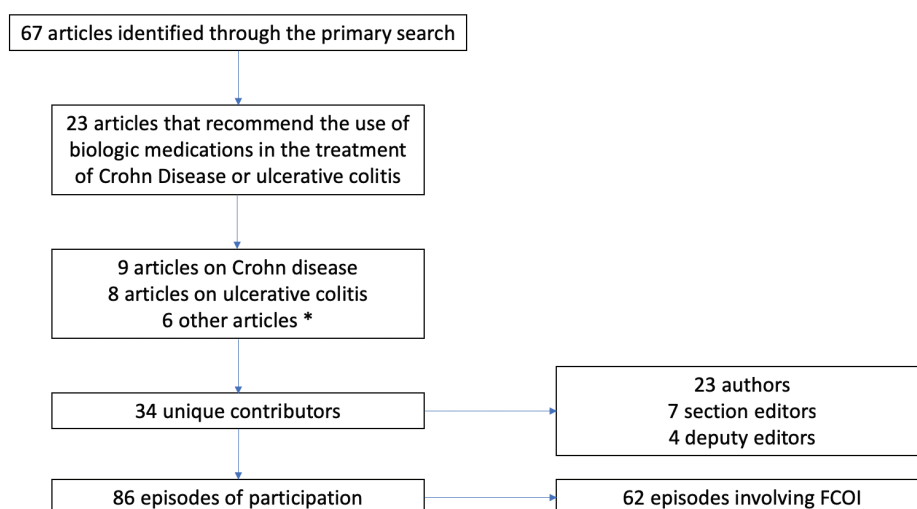
### Identification of Articles

We identified relevant articles on UpToDate, a point-of-care resource, using the search terms 'inflammatory bowel disease', 'Crohn' and 'ulcerative colitis'. Articles that mentioned TNF $\alpha$  inhibitors (infliximab, adalimumab, golimumab, certolizumab pegol),  $\alpha$ 4-integrin inhibitors (vedolizumab, natalizumab) or IL12/23 inhibitors (ustekinumab) for the treatment of IBD were included.

### Identification of Industry Payments

We use the term 'contributor', as described on UpToDate, as a physician author, section editor, or deputy editor who was involved in the creation of an article. We use the term 'episode' to describe one instance of contribution to an article by one person.

We extracted a list of contributors to each included UpToDate article and identified their disclosures, which are updated yearly and can be accessed via a link on each article. We categorized disclosures as: (i) general payments such as consulting fees, honoraria, gifts, food, and travel; (ii) research payments, including any payment to physicians for research activities and funding for a research project where the physician is named as a principal investigator; and (iii) value ownership, which represented ownership or investment in a company and the value of the ownership or investment interest gained by the physician or their immediate family members (20).



\*articles on both Crohn disease and ulcerative colitis, pouchitis, or the use of TNF $\alpha$  inhibitors

Figure 1. Study flow diagram.

We then searched for each contributor on the Centers for Medicare and Medicaid Services Open Payments (CMS-OP) database, which lists payments made by pharmaceutical companies to physicians in the United States (21). We compared payments on CMS-OP with disclosures on UpToDate to identify any additional payments beyond those that were disclosed. All CMS-OP data from January 1, 2013 to December 31, 2018 were included. Additionally, we only considered industry payments to constitute FCOI if they were made by a company producing a biologic that was mentioned in the relevant UpToDate article. For example, when examining an article that mentioned the use of adalimumab, we only included payments from AbbVie. If articles recommended the use of a biosimilar agent, we collected data on payments made by the company producing the biosimilar to contributors. We also examined a subgroup of contributors, deputy editors, who are required to be free of any financial relationships on topics they edit, as per the UpToDate conflict of interest policy (6). While we included all dates inclusive of 2013 to 2018, we did not find the

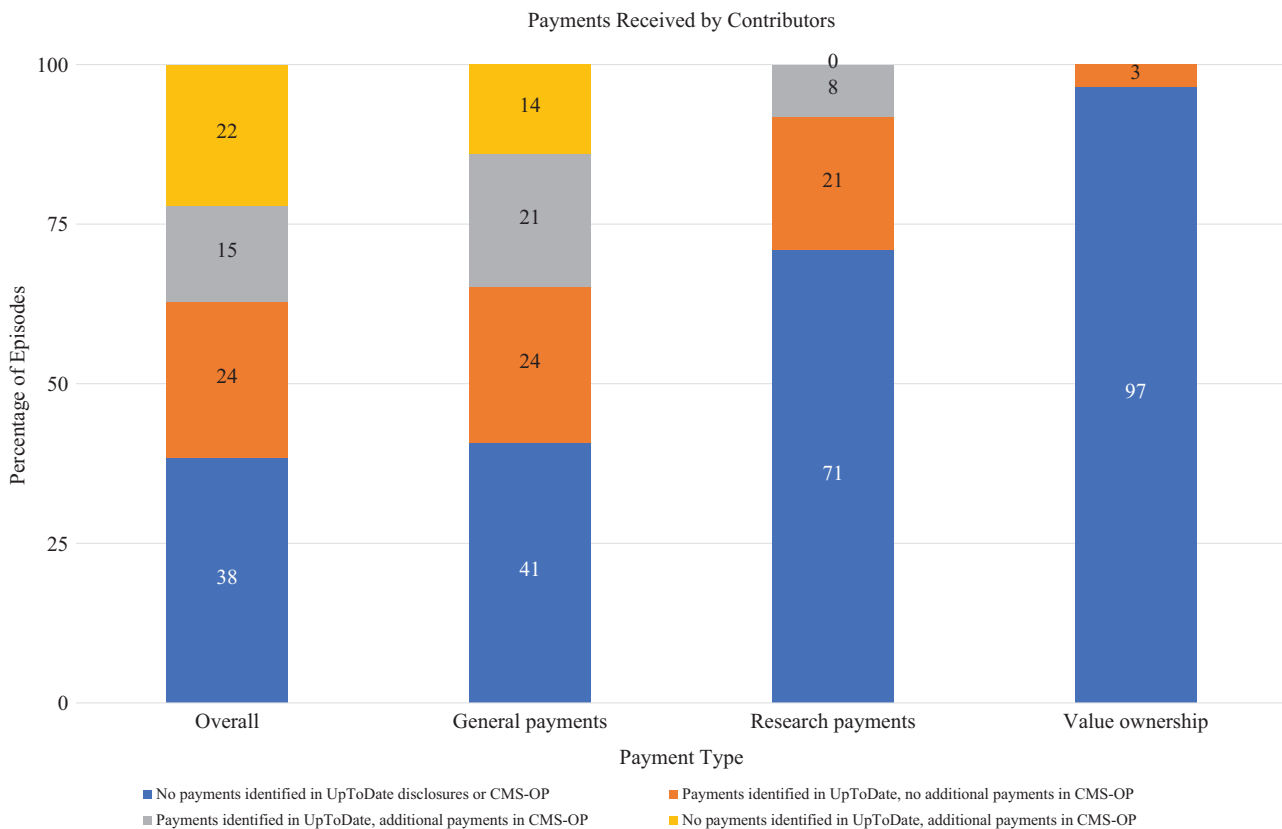
timeline within which contributors are required to disclose potential FCOI within the UpToDate policy.

**Data Analysis**

We conducted all statistical analyses using SPSS (v 24.0, SPSS Inc., Armonk, NY). We determined the frequency and distribution of the study population using descriptive analyses.

**Results**

We identified a total of 23 articles on the treatment of Crohn's disease and ulcerative colitis that mentioned the use of biologic medications. There were 34 unique contributors with 86 episodes of participation. Twenty-three (68%) contributors were authors, 7 (20%) were section editors and 4 (12%) were deputy editors. Nine (26%) contributors were female and 32 (94%) were affiliated with an academic institution. Contributors were involved in a median of 1 article (interquartile range [IQR] 1 to 3).



**Figure 2.** Data are categorized by payment type. Percentages for each category are shown within the columns. The blue bars represent episodes in which contributors had no payments identified through UpToDate disclosures or through the Centres for Medicare and Medicaid Services Open Payments (CMS-OP) search. The orange bars represent episodes in which contributors disclosed industry payments on UpToDate and had no additional payments identified through CMS-OP. The grey bars represent episodes in which contributors did not disclose industry payments on UpToDate, but had payments identified through CMS-OP. The yellow bars represent episodes in which contributors disclosed industry payments on UpToDate, and had additional payments identified through CMS-OP.

## Financial Conflicts of Interest

Through our search of disclosures listed on UpToDate and contributor profiles on CMS-OP, we found that 62 (72%) episodes involved FCOIs. Fifty-nine (68%) episodes involved general payments, 24 (28%) involved research payments and 4 (5%) involved value ownership (Figure 2). Among the 62 episodes that involved FCOIs, the median payment associated with each episode was \$55 (IQR = \$44 to \$145,241). The median payments for general and research payments were \$44 (\$27 to \$10,015) and \$0 (\$0 to \$66,379), respectively. When considering only the 59 episodes involving general payments and 24 involving research payments, the median payments were \$3403 (\$44 to \$27,440) and \$78,811 (\$35,919 to \$129,917), respectively.

As we included payment data from 2013 to 2018 on CMS-OP, not all contributors received payments for each of the 6 years. Three episodes had payment data from 1 year, 3 from 2 years, 19 from 3 years, 2 from 4 years, 6 from 5 years and 21 from 6 years. The median payment per year was \$16 (\$14 to \$26513). The median general payment per year was \$15 (\$14 to \$2035), and the median research payment per year was \$0 (\$0 to \$11,176). Contributors did not fully disclose FCOIs in 41 (48%) episodes, with a median payment value of \$31,868 (\$44 to \$187,140) per undisclosed episode. Forty-one (48%) episodes involved undisclosed general payments and nine (10%) involved undisclosed research payments, with median payment values of \$3214 (\$44 to \$31,868) and \$65,023 (\$17,715 to \$123,122) respectively. There were no instances of undisclosed value ownership.

## Deputy Editors

There were 23 episodes involving deputy editors. There were no episodes in which deputy editors declared FCOI. Through the CMS-OP search, we identified undisclosed FCOI, all general payments, among deputy editors for three (3%) episodes with a median payment of \$44 (\$0 to \$44), and a median payment per year of \$15 (0 to \$15).

## Discussion

In this cross-sectional study of inflammatory bowel disease articles on UpToDate, we found a high prevalence of financial conflicts of interest among article contributors. Many of these FCOI were not disclosed by contributors on the relevant article's disclosure page.

One potential explanation for these findings is that authors are often clinical experts who receive payments to provide education to their colleagues on new medications. In these instances, an unbiased review of the information is essential. While it is encouraging that deputy editors, who are meant to have no industry relationships on the topics they edit,

were free of financially substantial FCOI, the anonymity of UpToDate's peer review process precludes assessment of peer reviewers' potential FCOI. This may lead to a situation in which both primary authors and peer reviewers have financial relationships with commercial entities (5). Such a situation may be particularly relevant among gastroenterologists, who tend to have more financial relationships with industry compared to other physicians (18). Recently, an investigation reported that the companies producing biologic medications for IBD made more than 6 million USD in general payments to gastroenterologists in 2014 (22).

We also found several episodes of undisclosed FCOI. Several factors may impact this lack of disclosure. First, primary information on financial relationships are collected from contributors themselves. This reliance on self-reporting may lead to incomplete disclosure, as authors may not perceive payments from certain companies or from several years prior to constitute an FCOI. Second, it is not clear if there is a process to verify accuracy of disclosures using external sources such as CMS-OP or disclosures in a contributor's contemporaneous publications. Third, we did not find the dollar value of industry payments on UpToDate disclosure pages. This information is potentially important, as larger payments can be more impactful compared to smaller payments (1,23).

In this study, we encountered a lack of transparency and clarity with respect to conflict of interest policies on UpToDate. For example, we did not find any information regarding the number of years for which contributors are required to list industry payments. Additionally, we found no information within individual articles on specific companies from which payments would indicate a financial conflict. While we defined an FCOI as a payment from a company making a drug recommended within an article, we found no corollary definition on UpToDate. Several studies that have examined FCOI policies in academic journals and subspecialty medical societies have found similar results. A 2016 article reported that many organizations producing clinical practice guidelines still do not have COI policies, nor do they clearly report the steps in identifying, managing, and disclosing potential conflicts of interest (24). In another article, a review of requirements and definitions of FCOI in medical journals found that, while most journals had FCOI policies, all relied on author declarations and many did not adequately define FCOI (25).

Our study has several limitations. We could only evaluate U.S.-based contributors, as Open Payments only contains information on U.S.-based physicians. This limits the generalizability of our results. We also were not able to evaluate how industry payments may have been associated with medication recommendations, as we did not have access to preliminary drafts and peer-reviews of articles. Due to this, we also were not able to assess the potential impact of peer-review

and peer reviewers FCOIs. Finally, CMS-OP data may contain inaccuracies which are rarely corrected (26).

Based on these findings, we make several recommendations. First, UpToDate may further mitigate concerns about industry influence and bias by implementing an open peer-review process, as several large journals have (8). An open peer-review process that includes listing the peer reviewer, requesting their relevant disclosures, and publishing review reports can more accurately represent the process by which article content is determined. Additionally, UpToDate can bolster FCOI policies by requesting that contributors disclose payments for a prespecified number of years and list dollar values of payments. Another gap in transparency lies in the how deputy editors mitigate conflicts of interest for specific articles is unclear, which may be addressed by documenting and publishing the process of FCOI management for specific articles. Through measures to improve transparency, UpToDate may be able to address concerns about the objectivity of recommendations in articles.

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