

# Patterns of Opioid Use Among Patients With Inflammatory Bowel Disease: Do We Need Better Disease Control or Multidisciplinary Interventions?

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Despite multiple advances in the medical and surgical treatment of Crohn's disease (CD) and ulcerative colitis (UC) in recent decades, patients with inflammatory bowel disease (IBD) can experience significant abdominal pain, particularly during exacerbations of the disease. Pain may also manifest in the form of extra-intestinal manifestations, including pain due to arthropathies.<sup>1</sup> Treating pain in patients with IBD can be problematic, as common therapies such as non-steroidal anti-inflammatory drugs have been associated with an increased risk of disease exacerbation.<sup>2</sup> More worrisome, however, the use of opioid therapies in patients with IBD has been associated with an increased risk of several adverse outcomes, including an increased risk of mortality.<sup>3,4</sup>

In this issue of *Crohn's & Colitis* 360, Lin et al.<sup>5</sup> present their retrospective analysis of opioid use patterns among patients with CD and UC utilizing the IBM Watson Health Commercial Claims and Encounters Database (previously referred to as the Truven MarketScan data). In their analyses, opioid use was higher among patients with CD or UC when compared to a matched cohort of patients without IBD. Patients with both CD and UC who were opioid users demonstrated higher rates of healthcare resource utilization when compared to non-opioid users, including higher rates of inpatient hospitalizations and

emergency department visits. The highest rates of opioid use among patients with both CD and UC were demonstrated in the first year following diagnosis. The authors conclude that opioid use may be associated with inadequate disease control and propose that opioid-free remission could be a new endpoint in clinical trials and/or a quality measure tool in clinical practice.

This study utilized a large sample size of almost 45,000 patients with IBD, which allowed for the matched analyses including a non-IBD cohort. While a claim for a filled prescription does not guarantee that medication was taken as prescribed, prescription claims have been widely used for similar evaluations. This large sample size also allowed for important analyses of healthcare utilization, as well as the evaluation of other IBD-specific medications. In these analyses, opioid users with both CD and UC were more likely to utilize biologic therapies and conventional therapies such as immunosuppressants and corticosteroids. Despite these robust analyses, the authors did not account for prior surgeries in their multivariate analyses, an important factor which has been shown to increase the odds of receiving opioid therapy.<sup>4</sup> Although many Enhanced Recovery Pathways or Early Recovery After Surgery protocols emphasize the use of non-opioid analgesics,<sup>6</sup> evaluating the role of postoperative opioids as a risk factor for continued or chronic opioid use should be considered.

The work by Lin et al. is an important extension of prior epidemiologic studies and evaluations of opioid use among patients with IBD utilizing large administrative claims data. In a prior study utilizing the Truven MarketScan data, Noureldin et al.<sup>7</sup> found that 35% of patients with IBD developed persistent opioid use after a flare. In a nationally representative sample, Cohen-Mekelburg et al.<sup>8</sup> demonstrated an increasing prevalence of opioid use disorder-related diagnoses among patients with IBD over a 10-year period. In the Manitoba IBD Epidemiology Database, Targownik et al.<sup>3</sup> found that 5% of patients with IBD became heavy opioid users within 10 years of diagnosis, a critical finding given that heavy opioid use was strongly associated with mortality. Similarly, in a primary care database from England, Burr et al.<sup>4</sup> demonstrated a significant increase in opiate prescriptions between 1990 and 2013, with heavy use of strong opiates being associated with an increased risk of all-cause premature mortality.

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As in many other disease states, the increased use of opioids among patients with IBD is a major concern. Perhaps most troubling, those patients with IBD who are treated with opioids do not seem to derive a significant benefit with regard to pain control. In one evaluation of inpatients treated with opioids, no significant changes in daily pain scores were demonstrated; however, almost half of the patients in this population were discharged with an opioid prescription.<sup>9</sup> Similarly, in a longitudinal evaluation of outpatients with CD reporting abdominal pain, those patients initiated on opioids demonstrated no improvement in abdominal pain or quality-of-life scores when compared to patients not treated with opioids.<sup>10</sup> These findings are striking, when considering that in a retrospective cohort study of 862 hospitalized patients with IBD, those patients treated with intravenous or oral opioids were significantly more likely to receive opioids after discharge, with a positive dose–response relationship noted.<sup>11</sup> In addition to a lack of pain control, opioids may actually worsen inflammation among patients with IBD. In one murine model, opioids accelerated clinical manifestations of colitis via dysregulation of the gut microbiota.<sup>12</sup> Thus, while symptom and overall disease control will remain a critical therapeutic outcome, it is unclear if the use of opioids can reliably be utilized in this assessment.

The drivers of pain among patients with IBD, and the subsequent response or lack of response to therapy, are clearly multifactorial. Among inpatients with IBD, a prior psychiatric diagnosis, current smoking, and a prior diagnosis of irritable bowel syndrome have been significantly associated with opioid use.<sup>13</sup> In the same population, however, opioid use was not significantly associated with objective evaluation of disease severity via computed tomography or endoscopy.<sup>13</sup> Chronic pain has been demonstrated as a risk factor for worse outcomes among patients with IBD,<sup>14</sup> including an increased risk for readmission.<sup>15,16</sup> However, in these same analyses, other risk factors for worse outcomes included depression,<sup>15,16</sup> anxiety,<sup>15</sup> and tobacco abuse.<sup>15</sup> Similarly, in an analysis of prospective registry patients with sustained poor quality of life were more likely to receive opiate therapies and demonstrated a decreased time to opiate exposure.<sup>17</sup>

Given the demonstrated associations between pain, anxiety, depression, and quality of life in multiple cohort studies, a multidisciplinary approach to treating individual patients with IBD may be critical in turning the tide with regard to opioid use in the United States. Recently, new models of specialty medical care within IBD have demonstrated benefits in the management of these complex disease presentations, including the IBD Patient-Centered Medical Home.<sup>18</sup> Following enrollment in an IBD Specialty Medical Home, patients demonstrated significant decreases in healthcare resource utilization. However, the use of opioids at enrollment was significantly associated with persistent emergency department visits and hospitalizations.<sup>18</sup> Collaborative care models with heightened awareness to the role that psychosocial conditions play in the disease course may ultimately allow us to recognize those patients at greatest risk for developing chronic pain and opioid use disorders. Providers can then plan for earlier

intervention with multidisciplinary approaches including a gastroenterologist, social worker, psychologist, or psychiatrist based on an individual patient's needs, combining psychosocial interventions with non-opioid analgesic therapies as necessary.

Lin et al. have highlighted significant issues regarding opioid use among patients with CD and UC, including the high rates of opioid use when compared to non-IBD patients and the high rates of opioid use in the first year after diagnosis. To counteract the increasingly prevalent use of opioids among patients with IBD demonstrated by these authors and others, we must work proactively to identify those patients who are potentially at the greatest risk for developing chronic pain and/or an opioid use disorder early in the disease process. The increasing use of opioids is not unique to patients with IBD. However, by employing multidisciplinary approaches to reach the needs of individual patients, we can potentially act to decrease the use of chronic opioids in the treatment of IBD.

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