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Summary Report

Association Between Opioid Use and the Development of Diverticulitis

Report Authors

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Executive Summary

Opioids are commonly used to treat severe pain, but may increase the risk of diverticulitis, a serious intestinal condition. A comparative safety study was conducted to assess the risk of diverticulitis associated with short-term and long-term opioid use in patients treated for various pain indications.

The primary analysis included 23,084,410 patients with postsurgical pain indication across 5 Canadian provinces, the UK, and US. Findings indicated that starting opioid treatment within 7 days of surgery and continuing through the follow-up period was linked to higher rates of all diverticulitis and severe diverticulitis, though only the increase in severe diverticulitis was statistically significant. Additional analyses showed larger increases in diverticulitis rates for trauma and other pain indications compared to the postsurgical group.

These findings suggest health care providers may need to be particularly cautious with long-term opioid use and monitor for signs of diverticulitis, despite low overall rates in the general population. Findings should be interpreted with an understanding of the study's assumptions and limitations.

Background

Opioids are commonly used to treat severe pain but can cause constipation as a side effect, complicating treatment for patients who need pain relief. There is concern that this constipation might increase the risk of diverticulitis, a serious intestinal condition where the small pouches of the colon become inflamed and/or infected. While studies on opioids and diverticulitis are limited, observational research has suggested a potential link with some important methodological limitations.

Policy Issue

Opioid use may increase the risk of diverticulitis; however, evidence linking opioids and diverticulitis is limited. Health Canada wants to better understand the risk to assess if any regulatory actions are needed.

Policy Questions

- 1 Are adult patients who are exposed to opioids more likely to develop diverticulitis?
- 2 Is there a specific group of patients more at risk?
- 3 Does the risk of diverticulitis change according to the indication for opioid use?

Objective

The objective of this study was to assess the feasibility and then conduct an observational study to determine whether short-term and long-term opioid use are linked to an increased risk of diverticulitis in patients treated for various pain indications.

Findings

Based on the feasibility study findings, it was considered feasible to conduct a safety study comparing diverticulitis and severe diverticulitis in new users of opioids to nonusers among adults treated for pain following surgery, pain following trauma, and other indications for opioid use. The dental pain indication was not considered feasible because there were too few patients.

The comparative safety analysis included 23,084,410 individuals in the postsurgical group across 5 Canadian provinces (Alberta, British Columbia, Manitoba, Ontario, and Saskatchewan), the UK Clinical Practice Research Datalink, and the US Merative MarketScan databases. There were significant differences in the demographics and health profiles of new opioid users across jurisdictions. Overall, new users in North America tended to be younger and healthier than nonusers, while users in the UK generally had poorer health and were older, contributing to varied incidence rates for diverticulitis.

In the **postsurgical group**, starting opioid treatment within 7 days after surgery and continuing use until patients died or were lost to follow-up was linked to higher rates of diverticulitis and severe diverticulitis. Specifically, there were an additional 7.97 cases of diverticulitis and 3.36 cases of severe diverticulitis per 10,000 person-years compared to those who did not start opioids, after adjusting for external factors. These estimates remained consistent even after 730 days of continued use and nonuse. However, only the increase in the rate of severe diverticulitis was statistically significant.

Additional analyses in the **trauma and other pain indications groups** showed larger effects (5.78 and 11.08 additional severe diverticulitis events per 10,000 person-years, respectively). These findings suggest potentially stronger associations between opioid use and severe diverticulitis in some populations.

Subgroup analyses suggested an increased risk among those aged 65 years and older, highlighting the necessity of understanding these demographics when evaluating opioid use and associated risks.

Limitations

Findings should be interpreted with the understanding of the considerable assumptions and limitations of the analysis.

The main limitation of the analysis was that it might not account for all differences between opioid users and nonusers. While some health factors were balanced, use of other concomitant medications (e.g., steroids, nonsteroidal anti-inflammatory drugs, and antibiotics), alcohol use, and variations in opioid use during hospitalization were not considered. The analysis focused on new users and nonusers to reduce confounding and bias from prior use, assuming they had similar characteristics.

However, these results may not apply to other populations with different opioid use patterns. To tackle these issues, the study required patients to maintain the use of opioids (or nonuse) and some patients were censored from the analysis which could introduce bias, especially if those who continued opioid use were older or less healthy than those who did not.

There was also considerable variability in the results across different sites, likely due to differences in patient populations or prescribing practices.

Additionally, the reliance on routinely collected data might have resulted in misclassifications and missed relevant medical conditions. The study could not assess the timing of opioid use relative to surgery, which may affect recovery, but missing data were not a major concern.

Implications for Policy-Making

Findings suggest that increases in the rate of diverticulitis linked to opioid use is relatively low. However, the greater associations seen when opioids are used for pain management in patients who have experienced trauma and other pain conditions (compared to postsurgical pain) suggest health care providers may need to be particularly cautious with long-term opioid use and monitor for signs of diverticulitis, despite low overall rates of diverticulitis in the general population.

Considerations

Post-Market Drug Evaluation (PMDE) projects aim to produce health policy issue evidence and are not linked to a recommendation.

This work was intended to inform health policy. Clinical questions regarding the use of opioids for pain management should be directed to a health care professional.

For more information on CoLab and its work, visit the [CoLab website](#).

For the full scientific report, visit:

[Association Between Opioid Use and the Development of Diverticulitis](#)



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