



Beth Israel Deaconess
Medical Center



HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

Medical Management of Post-Operative Crohn's Disease

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ABSTRACT

Background: Approximately half of patients with Crohn's disease (CD) will have a bowel resection within their first ten years of diagnosis. The American Gastroenterological Association released guidelines in 2017 for post-operative Crohn's management. The goal of our study was to re-assess the data from the 2017 guidelines through 2022 and to perform a meta-analysis of current data on post-operative pharmacologic management in CD to maintain clinical and endoscopic remission. **Methods:** We performed a systematic review of the literature using Medline, Embase, and Web of Science databases to identify RCTs assessing the medical management of post-operative CD. The primary outcomes assessed were clinical and endoscopic recurrence rates at one to two years post-operatively, identified using CD Activity Index and Rutgeerts scores, respectively. Secondary outcomes were to evaluate safety data of the different pharmacologic approaches. Two independent reviewers appraised each study using a strict inclusion criterion, with a third reviewer serving to adjudicate in cases of differing opinion. We then analyzed the data through RevMan 5.3, which reported random-effects risk ratios.

Results: After initial review, a total of 8 RCTs were included in our final analysis. The odds ratios of clinical and endoscopic recurrence in the immunomodulator versus 5-ASA group were 0.68 [95% Confidence Interval (CI) 0.41-1.12, p=0.37] and 0.56 (0.31-1.01, p=0.58), respectively. The risk of serious adverse effects (AEs) was 2.50 (1.38-4.52, p=0.003). In the TNF-alpha inhibitor (TNF) versus 5-ASA group, the clinical and endoscopic recurrence odds ratios were 0.07 (0.01-0.62, p=0.02) and 0.01 (0.00-0.14, p=0.0004), respectively, while for serious AEs it was 0.53 (0.04-6.51, p=0.62). Finally, in the TNF versus immunomodulator group, the clinical and endoscopic recurrence odds ratios were 0.38 (95% CI 0.12-1.23, p=0.07) and 0.28 (95% CI 0.09-0.87, p=0.03); the risk for serious AEs was 1.44 (0.24-8.73, p=0.69).

Discussion: Our updated meta-analysis suggests that TNFs should be considered as first line treatment, as they exhibit superior rates of endoscopic remission and trend towards higher rates of clinical remission compared to immunomodulators and 5-ASA, while maintaining a similar rate of serious AEs. More studies are needed to further confirm this and to assess the role of newer medications, such as anti-integrin and interleukin-12/23 inhibitors, in maintaining remission in post-operative CD.

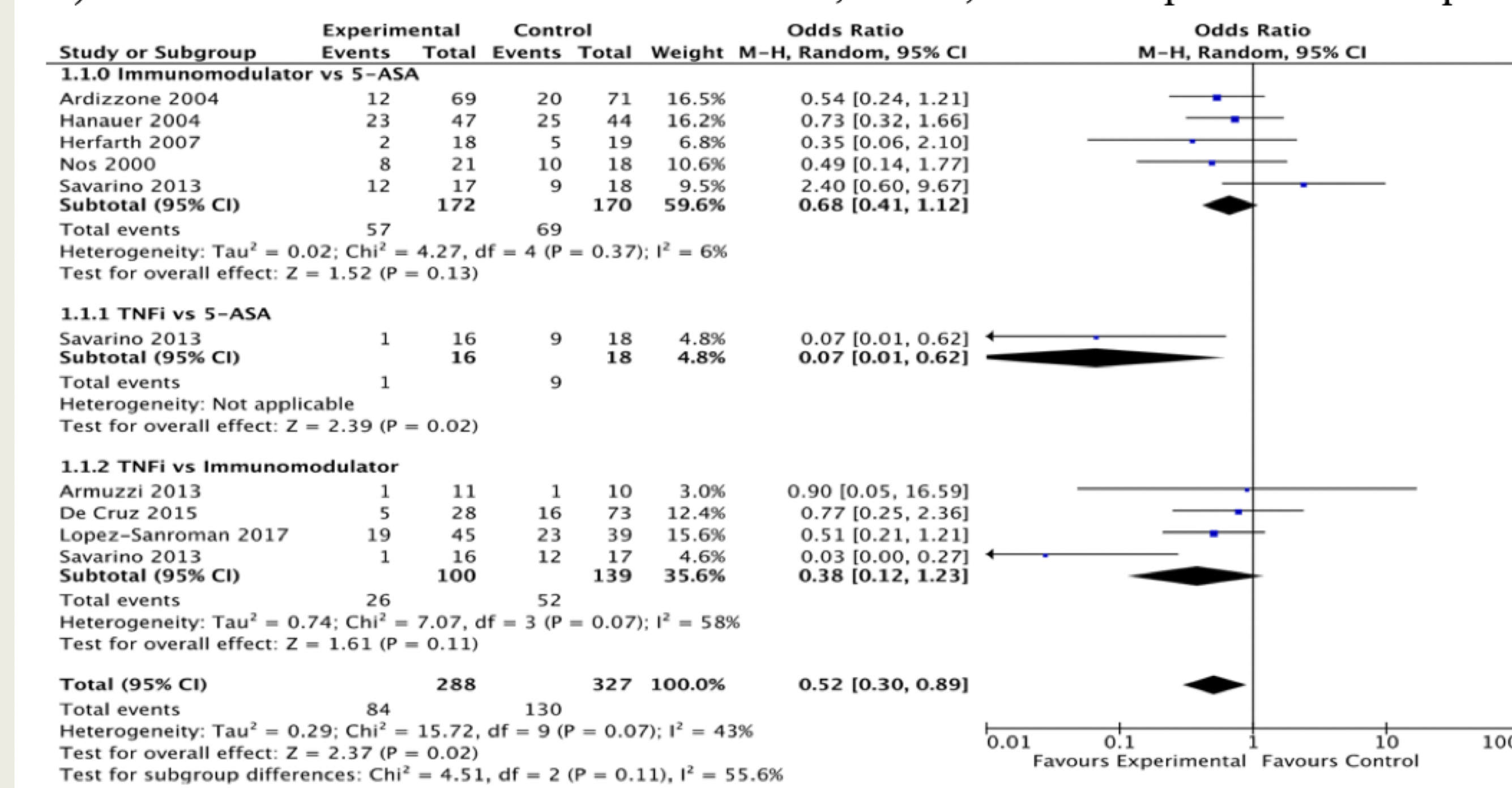
INTRODUCTION

- 50% of patients with Crohn's Disease will have surgery within ten years of diagnosis, the majority of whom will have a recurrence post-operatively and in 25% of cases require another bowel resection within the first 5 years post-operatively
- The 2017 AGA Guidelines for post-operative Crohn's Disease management outlined recommendations for pharmacologic prophylaxis after resection, with the only strong recommendation being to monitor patients endoscopically for 6 to 12 months after surgery if not receiving pharmacologic prophylaxis
- The aim of our study was to expand upon these recommendations by incorporating more updated trial data in recent years

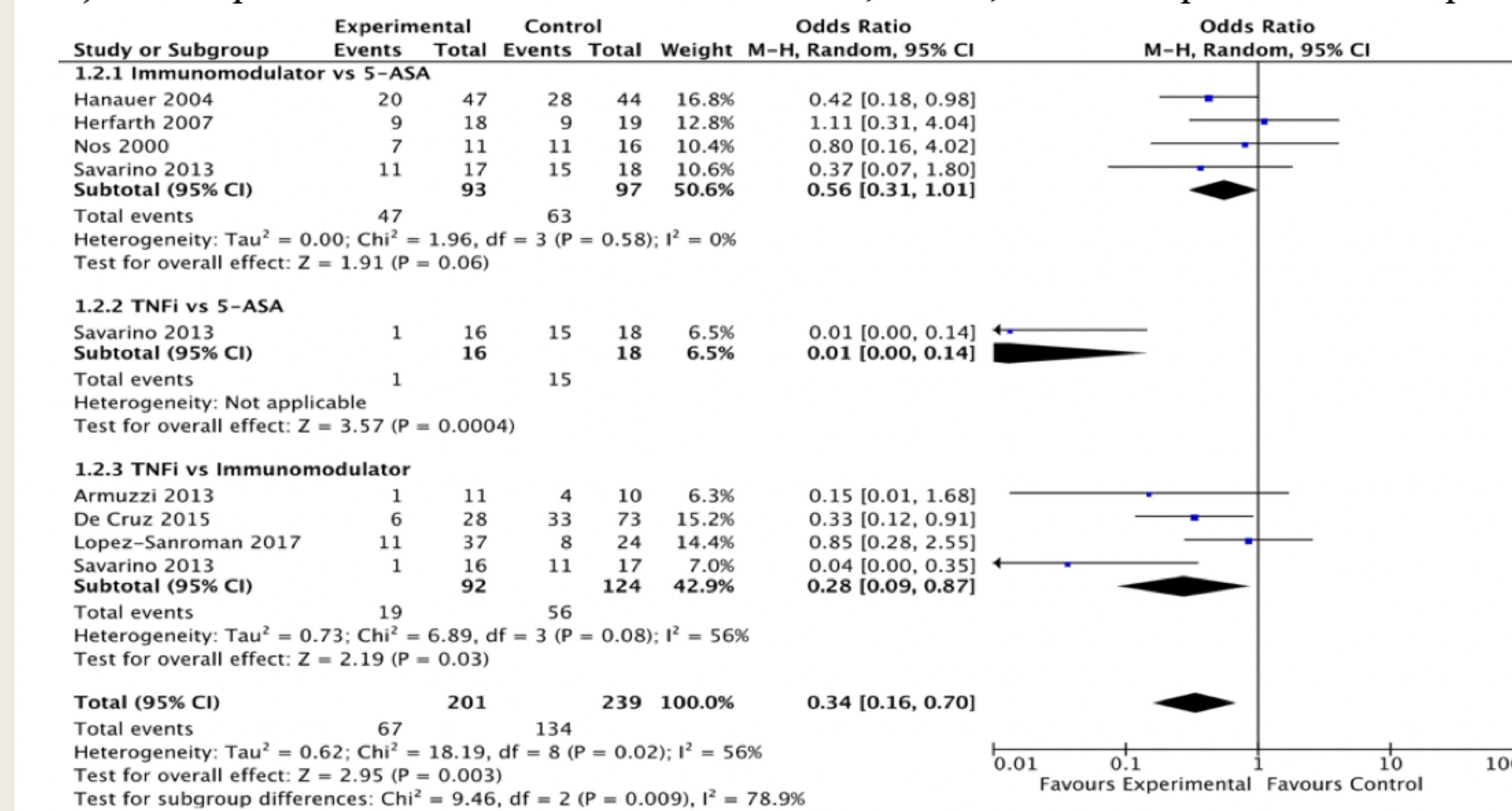
METHODS AND MATERIALS

- Performed a systematic review of the literature using Medline, Embase, and Web of Science databases
- Inclusion criteria:
 - Study Type: Randomized Controlled Trials
 - Population: Adults with Crohn's undergoing bowel resection
 - Intervention: Biologics, Immunosuppressants, and 5-ASA derivatives started prior to or during post-operative period
- Exclusion criteria:
 - Studies with no comparator arm
- Primary outcome:
 - Clinical recurrence rate: CDAI > 150
 - Endoscopic recurrence rate: Rutgeerts ≥ i2
- Secondary outcome: Rates of serious adverse effects (e.g. significant symptoms requiring hospitalization, invasive intervention, transfusion, etc.)
- Using Revman 5.3, we analyzed the data and reported random-effects risk ratios

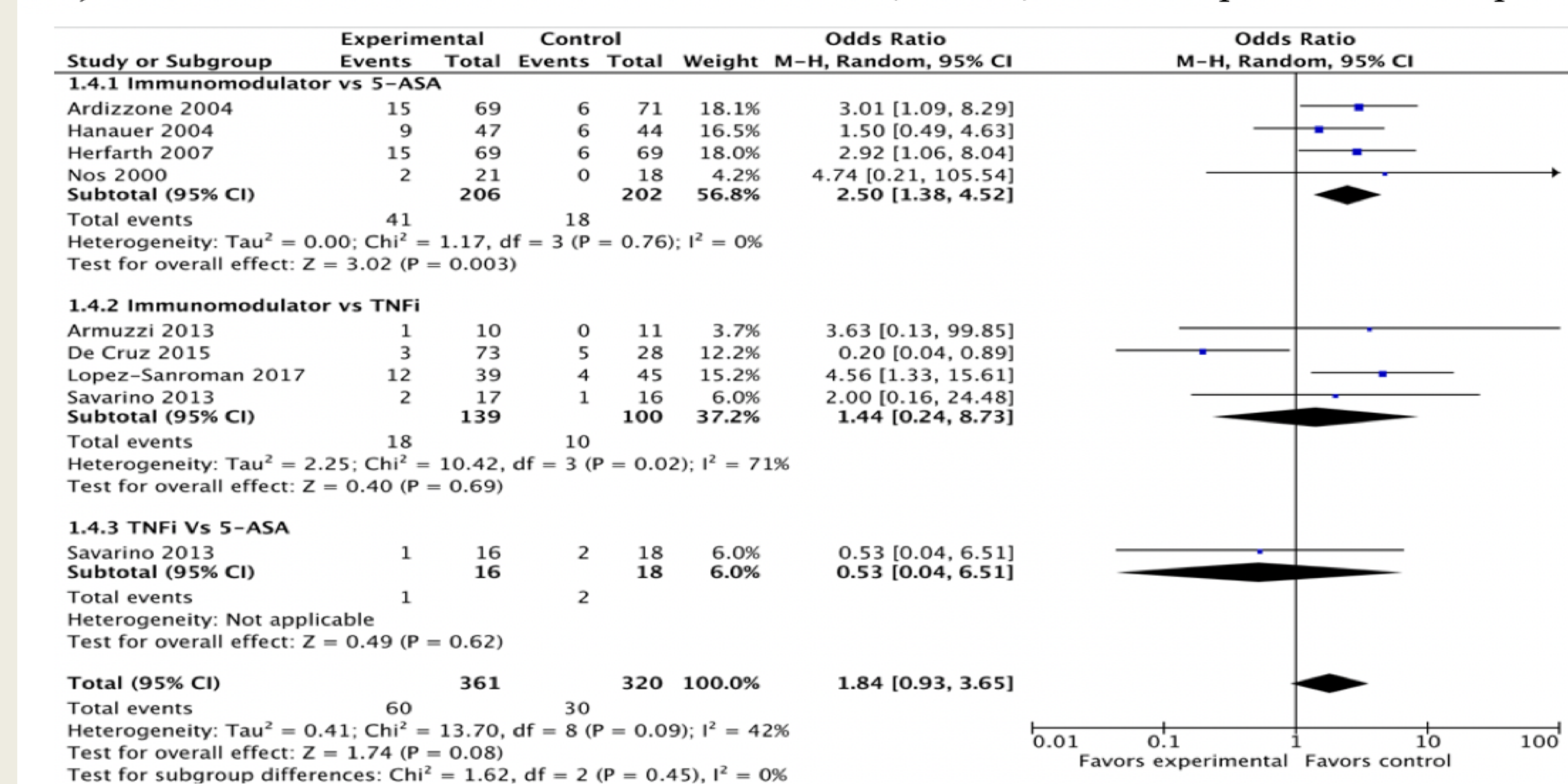
A) Clinical recurrence rates in immunomodulators, 5-ASA, and TNF-alpha inhibitor comparators



B) Endoscopic recurrence rates in immunomodulators, 5-ASA, and TNF-alpha inhibitor comparators



C) Serious adverse effects rates in immunomodulators, 5-ASA, and TNF-alpha inhibitor comparators



RESULTS

- Total of 8 RCTs were included in our final analysis
- Odds ratios with 95% Confidence Interval:
 - Clinical recurrence:
 - Immunomodulator vs 5-ASA: 0.68 (0.41-1.12, p=0.37)
 - Anti-TNF vs 5-ASA: 0.07 (0.01-0.62, p=0.02)
 - Anti-TNF vs immunomodulator: 0.38 (0.12-1.23, p=0.07)
 - Endoscopic recurrence:
 - Immunomodulator vs 5-ASA: 0.56 (0.31-1.01, p=0.58)
 - Anti-TNF vs 5-ASA: 0.01 (0.00-0.14, p=0.0004)
 - Anti-TNF vs immunomodulator: 0.28 (0.09-0.87, p=0.03)
 - Serious Adverse Events:
 - Immunomodulator vs 5-ASA: 2.50 (1.38-4.52, p=0.003)
 - Anti-TNF vs 5-ASA: 0.53 (0.04-6.51, p=0.62)
 - Anti-TNF vs immunomodulator: 1.44 (0.24-8.73, p=0.69)

DISCUSSION

- Immunomodulators maintain higher rates of endoscopic and clinical remission compared to 5-ASA but have significantly higher rates of serious adverse events
- Anti-TNFs exhibit higher rates of endoscopic and clinical remission compared to 5-ASA while maintaining a similar safety profile
- Anti-TNFs maintain higher rates of endoscopic remission and trend towards higher rates of clinical remission compared to immunomodulators while maintaining a similar safety profile

CONCLUSIONS

- Anti-TNFs should be considered as first line treatment for post-operative Crohn's Disease given their high rates of achieving endoscopic and clinical remission and relatively favorable safety profile
- More RCTs are needed to further confirm this and to assess the role of newer medications, such as anti-integrin and interleukin-12/23 inhibitors, in maintaining clinical and endoscopic remission in post-operative CD.