

**Reviewer #1:**

**Scientific Quality: Grade B (Very good)**

**Language Quality: Grade B (Minor language polishing)**

**Conclusion: Accept (General priority)**

**Specific Comments to Authors: This study reviews the extensive literature to provide clinicians with guidance on how to incorporate T2T principles into routine clinical practice for the management of CD. We look forward to the benefits of T2T approach that provides clinicians and patients with clear treatment goals and directions.**

I thank the reviewer for their favourable comments and their acknowledgement that this review has extensively assessed the published T2T literature. I would also like to thank the reviewer for their recommendation to accept this manuscript.

**Reviewer #2:**

**Scientific Quality: Grade B (Very good)**

**Language Quality: Grade A (Priority publishing)**

**Conclusion: Minor revision**

**Specific Comments to Authors: This is a nice practical guide for treat-to-target in patients with Crohn's disease. This guide will be very helpful for many inexperienced GI physicians in the treatment of CD. Review of literature was properly designed, meticulously conducted and well-written.**

This reviewer recognises that this review is likely to be very helpful for "inexperienced GI physicians in the treatment of CD." The reviewer also acknowledged that this review has been "properly designed, meticulously conducted, and well written." I thank them for these favourable comments. I would also like to thank the reviewer for their recommendation to accept this manuscript with minor revisions.

**This reviewer has some minor suggestions.**

**1, What is the author's opinion on thalidomide therapy for CD [see: Peng X, Lin ZW, Zhang M, Yao JY, Zhao JZ, Hu PJ, Cao Q, Zhi M. The efficacy and safety of thalidomide in the treatment of refractory Crohn's disease in adults: a double-center, double-blind, randomized-controlled trial. *Gastroenterol Rep (Oxf)*. 2022 Oct 20;10:goac052. doi: 10.1093/gastro/goac052. PMID: 36284737; PMCID: PMC9583847.]? Would the author include thalidomide therapy in Table 1 and relevant section in the manuscript?**

I thank the reviewer for their comment regarding the role of thalidomide in Crohn's disease. I have taken the time to read the article that they recommended. The study included 50 patients, 25 of whom were given thalidomide, with short-term outcomes out to 8 weeks reported. Whilst I acknowledge that there may be a role for thalidomide in refractory cases, it is still not a widely used for the management of Crohn's disease. Moreover, given the growing number of therapeutic agents in Crohn's disease, only a very small number of patients will require agents such as thalidomide. In fact, in most healthcare settings the use of thalidomide for Crohn's disease would be considered 'off-label'. On this basis I have opted not to include thalidomide.

**2, Suggest to discuss some of the emerging biologic therapies that are not approved by FDA but demonstrated promising efficacies in clinical trials. (e.g. For some refractory CD). Ref. Dunleavy, K. A., & Pardi, D. S. (2022). Biologics: how far can they go in Crohn's disease?. *Gastroenterology report*, 10, goac049. <https://doi.org/10.1093/gastro/goac049>**

I appreciate the reviewer's comments regarding the inclusion of emerging advanced medical therapies that are yet to be approved by the FDA. I have taken the time to read through the recommended article, and have updated the manuscript to include this reference and mention that several newer therapies are on the horizon. It is, however, important to acknowledge that the review has deliberately not included much in the way of therapeutics, rather opting to focus on the process driven aspects of T2T.

**Reviewer #3:**

**Scientific Quality: Grade D (Fair)**

**Language Quality: Grade D (Rejection)**

**Conclusion: Rejection**

**Specific Comments to Authors: It is not an interesting manuscript. Authors cannot succeed to present their idea in a clear way adding information to the existing literature.**

I thank the reviewer for taking the time to review the manuscript. I respectfully disagree with the reviewer's comments that this manuscript is uninteresting and does not add to the existing literature. As acknowledged by the two other reviewers, this manuscript brings together the existing literature to provide clinicians with much needed practical guidance regarding the clinical application of a T2T approach in patients with Crohn's disease. We have updated the final section to document strategies that may be helpful in increasing the 'real-world' uptake of a T2T approach.