



## Comparison of remicade to curcumin for the treatment of Crohn's disease: A systematic review



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### ABSTRACT

**Objective:** The aim of this study was to review the literature to assess if there is evidence to support the use of Curcumin as a safe complementary therapy in treating Crohn's Disease (CD) in conjunction with Remicade.

**Design:** Systematic searches were performed by three researchers using electronic databases (ProQuest Medical Library, CINAHL Complete, and PUBMED) to locate and identify articles to meet a predetermined set of inclusion criteria. Specifically full text, peer-reviewed articles published after 2007 were included if they studied human participants 18 years or older.

**Results:** Tumor necrosis factor-alpha (TNF-a) and Interleukin-1 (IL-1) levels increase in CD patients. Remicade reduces TNF-a in adults with CD. The issues are eventual loss of response (LOR) once IL-1 increases, and severe risks such as malignancy. CD patients using Curcumin saw a 55 point mean reduction in the Crohn's Disease Activity Index, reducing IL-1 and Crp. Plus it reduced TNF-a and PPMTase which improved colorectal cancer outcomes.

**Conclusions:** LOR of Remicade occurs when IL-1 increases, and it can cause malignancy. Research shows Curcumin reduces IL-1 and improves cancer outcomes. Future research, using both Remicade and Curcumin, would have to be done, but preliminary data would suggest using both would reduce LOR. Curcumin, even by itself, was found to be a cheap and safe way to reduce CD symptoms and inflammatory markers.

### 1. Background

Irritable Bowel Diseases (IBD) is composed of two gastrointestinal (GI) diseases, namely Crohn's Disease (CD) and Ulcerative Colitis (UC). These two diseases are considered autoimmune conditions of the GI tract and involve chronic inflammation. Other symptoms can include rectal bleeding, but are not limited to diarrhea, abdominal pain, reduced appetite, and weight loss. This systematic review focuses on CD, which affects multiple layers of the gut mucosa anywhere from the mouth all the way through the GI tract to the anus.<sup>1</sup> Due to the chronic damage of the GI tract tissue found in these diseases, they both carry a higher risk of developing colorectal cancer.<sup>2</sup>

Approximately 1.6 million people in the United States have IBD, and the disease carries annual estimated cost of \$31 billion dollars in annual direct and indirect costs. Rough estimates show that each Crohn's disease patient medical costs range from about \$8265 to \$18,963 annually.<sup>3</sup> Many people are suffering from CD and have to pay high medical costs. Crohn's patients, insurance companies, and taxpayers absorb these costs; the value of this systematic review is to find more

cost effective ways safely reduce symptoms of one IBD disease, CD.

Currently, there are medications used to reduce CD symptoms and flares. Flares or relapses are when symptoms intensify to the point of bleeding and may include problems ingesting food.<sup>4</sup> One of the medications include Remicade has been found to reduce inflammatory marker Tumor necrosis factor-alpha (TNF-a). This medication also reduced CD symptoms and long-term flares. The side effects of Remicade include, but are not limited to nausea, stomach or back pain, headache, heartburn, or fungal growth. Severe side effects can include, but are not limited to blood in the stool, chest, muscle or joint pain, blurred vision, seizures, or shortness of breath. Remicade can also cause fatal bacterial/fungal infections as well as lymphoma and skin cancer.<sup>5</sup>

Due to the possible side effects of Remicade, such as fatal infections, malignancies, blood disorders, liver toxicity and other risks that can be associated with using the medication,<sup>6</sup> finding a viable alternative or at least complementary therapies to reduce CD symptoms without side effects and death would be preferable. The key is finding alternatives, which have been found effective through current research. The main purpose of this review is to assess Remicade medication and Curcumin,

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the active component in turmeric spice, effects on the gastrointestinal (GI) tract.

## 2. Study aim and objectives

The aim of this review is to provide researchers and clinicians with clarity whether Remicade or Curcumin reduce inflammation, reduce IBD symptoms, increase remission out of a flare, and reduce colorectal cancer risk, and will conclude with a discussion side effects and health risks. The identified population for this review includes patients who are 18 years and older who have been diagnosed with CD. Specifically, we will address the following questions: How does Curcumin benefit or harm a patient when compared to Remicade treatments? Is there evidence to support using Curcumin as a complementary therapy?

## 3. Methods

### 3.1. Study method

To ensure the methodology of this systematic review is robust, we will follow the 27 checklist of PRISMA statement and the guidance outlined by the Centre for Reviews and Dissemination (CRD).<sup>7</sup> Following this guidance would ensure the methodological limitations of previous reviews outlined in the background section will be avoided. Fig. 1 provides the study flow of the search.

### 3.2. Electronic searches

Three databases ProQuest Medical, CINAHL Complete and PubMed will be searched for relevant articles published in English from commencement of databases to October 2016. The CRD guidance does not specify what constitutes a sufficient number of databases searched for a review as that number can vary from topic to topic.<sup>8</sup> In an effort to search only the articles most relevant to the research question, the inquiry was conducted based on specific inclusion and exclusion criteria.

### 3.3. Inclusion and exclusion criteria

The general inclusion criteria for all the databases searched included full-text articles that were peer-reviewed with a publication date no earlier than 2007. The inclusion criteria also consisted of human

adults that are 18 years and older who have been diagnosed with IBD because this is the population we want to find out if Curcumin could be beneficially used as a complementary therapy. The exclusion search criteria began with articles that were not full text, or peer-reviewed, had a publication date later than 2007, children under 18 years of age or involve animals. Reviewing data for animals or children of different doses and considerations than adults is irrelevant to answering the clinical question of whether Curcumin would be beneficial complementary therapy for adult CD patients.

### 3.4. Search terms

The team used the identical search terms for all three databases to locate and identify relevant articles. The search terms were divided into sets: set 1: *Crohn's AND TNF*, set 2: *cancer AND Curcumin*, set 3: *TNF AND Remicade*, set 4: *Crohn's AND Remicade*, set 5: *cancer AND Remicade*, set 6: *Curcumin*, set 7: *Remicade AND inflammation*, and set 8: *Curcumin AND C reactive protein*. The team selected 16 articles in total, five from each ProQuest Medical and CINAHL Complete and six from PubMed. All three researchers collectively searched through the articles to ensure they were the most relevant and would provide valuable information towards addressing our research question.

### 3.5. Data extraction and management

The three reviewers will independently extract data using a pre-designed data extraction form. The extracted data will be grouped in general information, study characteristics, participant characteristics, setting and intervention and outcome/result data as per CRD guidance for systematic reviews.<sup>8</sup> Any discrepancies within extracted data was discussed by four authors.

## 4. Results

This systematic review utilized three health and medical databases to search multiple sets of keywords. ProQuest Medical, CINAHL and PubMed identified 19,717 publications. The team used filters to view peer-reviewed articles on humans published since 2007. Then, the team completed a manual search of the remaining publications to eliminate articles on diseases that did not involve the gastrointestinal tract (GI) or included research related to mice that the automated filter failed to

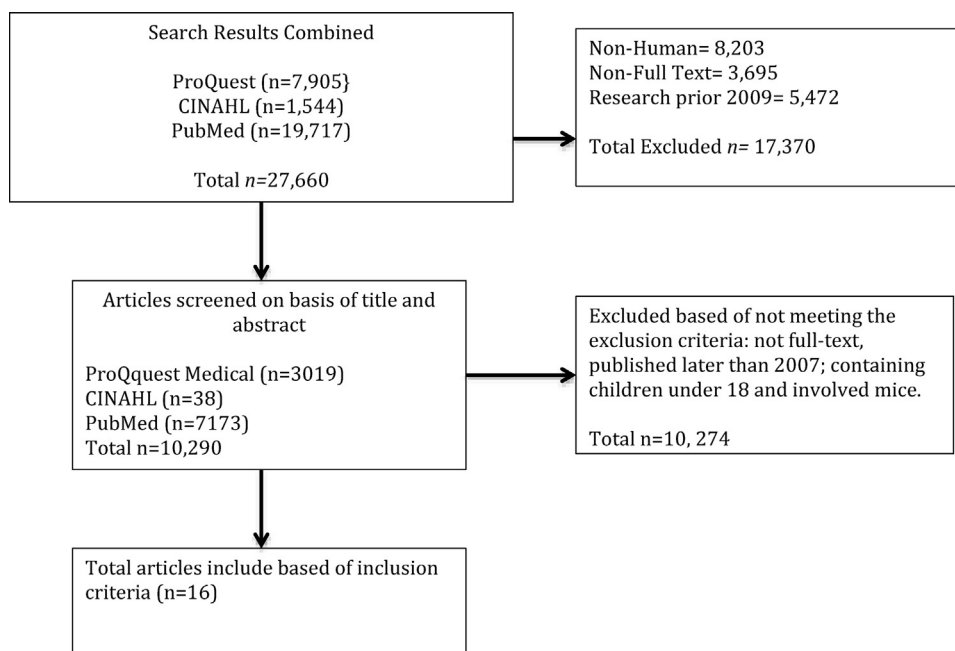


Fig. 1. Searching and selection process.

In patients 18 years and older who have been diagnosed with Crohns disease. (P), how does Curcumin benefit or harm patients (I) when compared to Remicade medication (C) is there evidence to support using Curcumin as a complementary therapy (O)?

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