

# Probiotics supplementation in colorectal cancer patients: systematic review and meta-analysis

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## Introdução

The colorectal cancer (CRC) is the second in mortality amongst other cancer types and is the third in incidence around the world, with more than 1.800.000 cases annually. The main modifiable risk factors for this type of cancer are smoking, consumption of alcohol, red meat, processed meat, low ingestion of fruits and vegetables, obesity. Many of them are related to intestinal disbiosis. The intestinal microbiota plays an important role on immune system modulation and on the pathogenesis of intestinal diseases, while it is also related to the efficacy of oncological treatments. A disbiotic microbiota will further be related with the carcinogenesis process. The CRC treatment (surgery and/or chemotherapy) is related to high morbidity, and the patients may experience gastrointestinal symptoms, such as diarrhea and abdominal bloating, as well as symptoms due to surgical procedure and prolonged hospital stay, for instance, pneumonia, pyrexia, surgical site infection, urinary tract infection and others. An associated treatment with probiotic administration, focusing on the regulation of the microbiota may benefit CRC patients, possibly reducing treatment side effects.

## Casuística e Métodos

This systematic review with meta-analysis aims to evaluate the effects of a complementary treatment with probiotics on postoperative infectious complications, pyrexia, and gastric symptoms in patients with colorectal neoplasms. Using the databases PubMed/MEDLINE, Scielo, BIREME, Cochrane Library, ClinicalTrials.gov, and the key words "probiotics" and "colorectal neoplasms", 118 articles were obtained. After a thorough review of their eligibility by separate investigators, 8 articles were included for the final analysis. The risk of bias was evaluated using the software Review Manager (RevMan) from Cochrane Collaboration, using their criteria, which investigates selection bias, performance bias, detection bias, attrition bias and reporting bias, whilst publication bias was evaluated using the funnel-plot (Begg's test). When the outcomes were comparable, the RevMan was used to calculate the summary measure, and forest-plot graphics were generated for each comparable endpoint. Outcomes were considered comparable when analysed by at least 3 different articles and data was described in a comparable way. In addition, a table was constructed with the extracted information from each study.

## Resultados

The total population from the 8 studies included was of 765, all of the studies used placebo as a comparator for the probiotic intervention and all of them had some level of blinding. Data was extracted regarding the type of strain that was used, intervention period and duration, study location, publication year, number of participants and their characteristics.

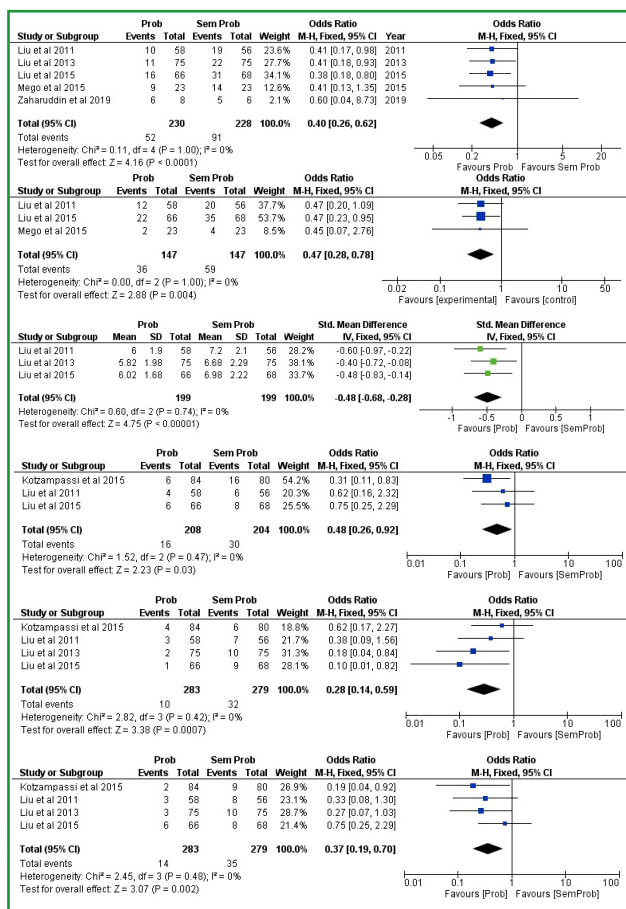
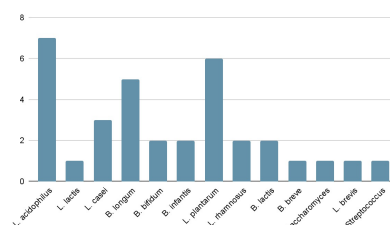
The comparable outcomes were: incidence of diarrhea (Odds Ratio (OR)= 0,40; Confidence Interval (CI) (95%)= 0,26 - 0,62), incidence of abdominal bloating (OR= 0,47; CI(95%)= 0,28 - 0,78), duration of pyrexia (Standard mean difference (SMD)= -0,48, CI(95%)= -0,68; -0,28), incidence of pneumonia (OR= 0,37; CI(95%)= 0,19 - 0,70), incidence of surgical site infection (OR= 0,48; CI(95%)= 0,26 - 0,92) and incidence of urinary tract infection (OR= 0,28; CI(95%)= 0,14 - 0,59).

The main probiotic strains used by the studies were, respectively, *L. acidophilus*, *L. plantarum*, *B. Longum* and *L. casei*. Most of the studies used a combination of probiotics.

The overall risk of bias was low and the Begg's test (funnel-plot) also showed a low publication bias risk. The heterogeneity analysis of the studies was also low ( $I^2 = 0\%$ ), resulting on a robust summary measure.

## Resultados

Below are presented the following results, respectively: 1) Absolute frequency and types of probiotic strains used on the included articles; 2) Forrest-plot for incidence of diarrhea in patients treating CRC; 3) Forrest-plot for incidence of abdominal bloating in patients treating CRC; 4) Forrest-plot for duration of pyrexia in patients treating CRC; 5) Forrest-plot for incidence of surgical site infection in patients treating CRC; 6) Forrest-plot for incidence of urinary tract infection in patients treating CRC; 7) Forrest-plot for incidence of pneumonia in patients treating CRC.



## Conclusões

The results obtained on the present study agree with other similar studies on the topic, and suggest that the use of probiotics in patients with CRC may reduce the incidence of post-operative infectious complications, gastrointestinal symptoms, and reduce the duration of pyrexia. However, the literature still lacks evidence from well conducted randomized controlled trials on the topic. During the review process it was noted that the recruitment of eligible patients was a very important limitation, for instance, a study with a recruitment period of 6 years had only 134 eligible patients. Also, a factor that may influence the results is that 6 out of 8 studies were conducted with populations from Southeast Asia. Furthermore, it needs to be clarified if the efficacy of the probiotic treatment is higher when used in combination with symbiotics or alone. Nevertheless, the main limitations found for the implementation of probiotic usage in daily clinical practice was the uncertainty regarding which probiotic strain combination is better and for how long it should be administered before and after treatment.

## Contato