

# USING ASPIRIN TO PREVENT COLORECTAL CANCER: AN EVIDENCE BASED PRACTICE

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## Introduction

Colorectal cancer (CRC) is the third most common cancer in the United States, and it is the third leading cause of cancer-related deaths when men and women are considered discretely, while it is the second leading cause when both sexes are combined. Unfortunately, CRC was expected to cause about 50,830 deaths during 2013 in U.S.[1].

Similarly, CRC is the second most common cancer type in Jordan, specifically, it is the first among Jordanian males and the second among Jordanian females; furthermore, it is the leading cause of cancer death among both genders [2]. Obviously, CRC is a major public health concern, globally and nationally. Thus, every effort should be done to improve prevention strategies, which may decrease colorectal cancer incidence, and thus, decrease the number of people who suffer from this disease and its complications.

Promising results have described aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) as possible candidates for pharmacological prevention of CRC. NSAIDs produce their clinical benefits against cancer by disturbing some mechanisms that potentially manipulate carcinogenesis, such as angiogenesis, inflammation, cell-turnover kinetics, and cell differentiation [3]. Currently, aspirin emerged to be the most promising drug because of its known cardiovascular benefit, and also because of its parallel antiplatelet effects, which are not shared with non-aspirin NSAIDs [4]. However, no authoritative recommendations have been made regarding its use for CRC prevention.

Thus, the purpose of this review is to evaluate the association between aspirin consumption and the incidence of CRC among an average incidence of CRC among an average risk adult population.

## Abstract

Colorectal cancer is a major public health concern, globally and nationally. Thus, every effort should be done to improve prevention strategies, which may decrease colorectal cancer incidence, and thus, decrease the number of people who suffer from this disease and its complications. Promising results have described aspirin and other non-steroidal anti-inflammatory drugs as possible candidates for pharmacological prevention of colorectal cancer.

The purpose of this evidence based practice is to evaluate the association between aspirin consumption and the incidence of CRC among an average risk adult population. Electronic literature search of six databases was conducted for English language articles published between 2003 and 2013, which are available as free full text articles, using MeSH terms "aspirin", "colorectal cancer", and "incidence". Studies conducted in specific high risk populations were excluded, as well as studies that measured

mortality rate, or the incidence of adenomas as an outcome, rather than measuring the incidence rate of colorectal cancer. The final sample size is seven, five studies were systematic reviews, one study was a randomized controlled trial, and the last one was a large cohort study.

The results of this paper emphasized the effectiveness of aspirin in reducing colorectal cancer; however, the duration, dose and frequency of aspirin consumption may affect this relationship. From the available evidence we can conclude that long term consumption of five years or more is essential to observe the relationship between aspirin and colorectal cancer risk. Additionally, for aspirin to be preventive, daily consumption is crucial. Finally, the optimal dose of aspirin for CRC prevention was not established.

**Key words:** aspirin, incidence, colorectal cancer, evidence based practice.

**PICO Question**

Population	Intervention	Comparison	Outcome
Adult people with average risk for developing CRC.	Regular aspirin consumption.	Not receiving aspirin.	Reduction in CRC incidence.

The PICO question is: What is the effect of aspirin consumption on the incidence of CRC among an average risk adult population?

**Methodology**

Electronic literature search of six databases: MEDLINE, CINAHL, Academic Search Complete, Education Research Complete, SocINDEX, and Science Direct was conducted for English language articles published between 2009 and 2013, which are available as free full text articles, using MeSH terms “aspirin”, “colorectal cancer”, and “incidence”. Studies conducted in specific high risk populations; such as history of CRC, familial adenomatous polyposis, or inflammatory bowel disease, were excluded, as well as studies that measured mortality rate, or the incidence of adenomas as an outcome, rather than measuring the incidence rate of CRC. The retrieved sample consisted of three studies only. So, another literature search for articles published between 2003 and 2008 was done with the same criteria mentioned above, which revealed another four studies.

The final sample size is seven; five studies were systematic reviews, one study was a randomized controlled trial, and the last one was a large cohort study. (Please refer to Table 1, appendix).

**Findings****Level IV of Evidence**

Three studies found that aspirin had a chemo-preventive benefit for colorectal cancer ([5]; [6]; [7]). These studies are systematic reviews of cohort studies and case control studies.

One study emphasized that the optimal dose of aspirin is not fully established, [7]. While, Dube et al (2007) found that the chemoprevention benefit was more evident when aspirin was used at a high dose and for longer than ten years [6]. This result is consistent with the findings of another study that showed that long term daily use of high dose aspirin was associated with lower incidence of colorectal cancer [8]. Then, Flossmann, & Rothwell (2007) specified that 300 mg or more a day of Aspirin for about five years reduced the incidence of colorectal cancer, with a latency of 10 years, [9].

**Level II of Evidence**

A randomized controlled trial with a large sample of women found that alternate day use of low-dose aspirin (100 mg) for an average of ten years did not lower risk of colorectal cancer, [10]. This may be explained by the short half life of aspirin, which makes the more frequent doses more effective to produce its effect.

**Level I of Evidence:**

A systematic review of five randomized controlled trials found that the consumption of 75-1200 mg of aspirin per day reduced the risk for colon cancer; this reduction was more pronounced when aspirin is taken for five years. Also, this study found a positive relationship between duration of aspirin consumption and its benefit in reducing CRC, [11].

Additionally, another study observed that the consumption of 300mg or more of aspirin per day for about 5 years reduced the incidence of colorectal cancer, with a latency of 10 years, [9]. However, another study observed that the low dose aspirin (325 mg and 100 mg) which was taken every other day failed to show a protective effect from CRC, [6]. Again, this result can be explained by the short half life of aspirin, especially with small doses, which makes the “every other day” frequency not appropriate to produce its effect.

**Appraisal of the Evidence****Strengths of the Evidence**

Among the strong points of this evidence is the large sample sizes of the included studies, which may enhance the generalizability of the results, and may compensate for the small sample size of the articles included in this paper. Additionally, all of the studies used in the evidence were retrieved from credible international journals.

**Limitations of the Evidence**

Not all the studies evaluated the effect of dose, duration, and frequency of aspirin consumption on the risk of CRC. Additionally, only seven studies were included in this paper; however it may be justified by the extensive literature search from multiple data bases.

**Summary and Conclusions**

The purpose of this paper was to evaluate the association between aspirin consumption and the incidence of CRC among an average risk adult population. Extensive literature search revealed seven articles met the inclusion criteria.

The results of this paper emphasized the effectiveness of aspirin in reducing CRC, however, the duration, dose and frequency of aspirin consumption may affect this relationship. From the available evidence we can

conclude that long term consumption of five years or more is essential to observe the relationship between aspirin and CRC risk. Additionally, it was obvious that for aspirin to be effective in CRC prevention daily consumption is crucial, no chemo-preventive benefit was observed when aspirin was taken every other day, which can be explained by its short half life, especially when taken in small doses. Finally, the optimal dose of aspirin for CRC prevention was not established.

## Recommendations

Clinicians should take into consideration the ability of aspirin in reducing CRC when it is taken daily for a long period of time. However, they are recommended to assess the benefit risk ratio for each patient before prescribing it.

Researchers are recommended to conduct more studies to establish the optimal dose, duration, and frequency for CRC prevention.

Educators are recommended to include the chemopreventive benefit of aspirin in their lectures, and to stimulate their students to conduct related studies.

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Author	Design	Sample	Main Findings	Level of evidence
Algra and Rothwell (2012).	Systematic review	32 case-control studies. 11 cohort studies.	Regular use of aspirin was associated with reduced risk of colorectal cancer.  Aspirin had a chemopreventive benefit for colorectal cancer. The optimal dose not fully established.	IV
Garcia-Albeniz and Chan (2011).	Systematic review	5 cohort studies. 3 case-control studies. 12 RCTs.	Aspirin's adverse effects on gastrointestinal and intracranial bleeding limit its use. Aspirin 75-1200 mg/day reduce risk for colon cancer (proximal). Effect more pronounced when aspirin is taken for 5 years Benefit increased with duration.	IV
Rothwell et al. (2010).	Systematic review	5 RCTs    2 RCTs	When duration increased, risk for rectal cancer decreased Low dose aspirin (325 mg and 100 mg every other day) failed to show a protective effect	I    I
Dube et al. (2007).	Systematic review	8 case control studies. 7 cohort studies   2 RCTs	Regular use of aspirin was associated with reduction of 22% for colorectal cancer incidence. Benefit more evident when aspirin was used at a high dose and for longer than 10 years. Aspirin (300 mg or more a day for about 5 years) reduced the incidence of colorectal cancer, with a latency of 10 years.	IV    I
Flossmann and Rothwell (2007).	Systematic review	19 case control studies. 11 cohort studies.	Same as the RCT results.	IV
Cook et al. (2005)	RCT	39,876 women	Alternate day use of low-dose aspirin (100 mg) for an average 10 years of treatment does not lower risk of colorectal cancer.	II
Jacobs et al. (2007).	Cohort study	69,810 men and 76,303 women	Long term daily use of adult-strength aspirin was associated with lower incidence of colorectal cancer.	IV

## Appendix

Table 1: This table summarizes the results obtained from the seven research articles