

The risk of cancer in ulcerative colitis

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SUMMARY STATEMENT

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REQUEST

The risk of cancer in ulcerative colitis

REQUESTED BY

Dr Richard King, Program Medical Director, General Medicine Program, Monash Medical Centre, Clayton

METHODOLOGY

Search Strategy

The Centre for Clinical Effectiveness defines the 'best available evidence' as that research we can identify that is least susceptible to bias. We determine this according to pre-defined National Health and Medical Research Council (NHMRC, 2000) criteria (see Appendix 1).

First, we search for systematic reviews, evidence based clinical practice guidelines, health technology assessments and randomised controlled trials. If we identify sound, relevant material of this type, the search stops. Otherwise, our search strategy broadens to include studies that are more prone to bias, less generalisable or have other methodological difficulties. We include case-control and longitudinal cohort studies in our critical appraisal reports. While we cite observational and case series studies, and narrative reviews and consensus statements, in our reports we do not critically appraise them. Such studies can produce accurate results but they are generally too prone to bias to allow determination of their validity beyond their immediate setting.

Details of Evidence Request

Patient (subject):	Anyone at Risk
Exposure:	Ulcerative colitis
Comparison:	No ulcerative colitis
Outcome:	Malignancy

Search terms

(see Appendix 2 for exact search strategy)

Exposure terms:	Colitis, ulcerative/, ulcerative colitis
Outcome terms:	Neoplasms, malignancy, gastrointestinal neoplasms, tumour, cancer
Other term:	Risk

Resources Searched

We searched the following databases and internet websites:

The Cochrane Library (CD-ROM) 2001 Issue 1

Medline (OVID)- 1966 to April 2000

Refinements, Searching & Reporting Constraints

We included items of evidence that were available to us on 7 May 2001. The search was restricted to humans, articles published in English in the last 5 years.

RESULTS

From our sources we identified 1 potentially relevant meta-analysis by Eaden, JA, et al (2001). After examination of the full text, the article was critically appraised.

Study Design	Number included
Systematic reviews or meta-analyses	1
Evidence-based clinical practice guidelines	0
Randomised controlled trials	0
Pseudorandomised controlled trials	0
Controlled trials, cohort or case-control analytic studies	0
Total	1

Based on our refinements, searching and reporting constraints we are reasonably confident this article represents the most relevant findings published to date.

EVIDENCE SUMMARIES

Format

Evidence summaries are presented as spreadsheets attached to this report. Each spreadsheet contains the article citation, details of the study design, patient description, scientific validity of the article, results, and pertinent remarks from the authors and Centre for Clinical Effectiveness reviewer.

REFERENCE

ARTICLE CRITICALLY APPRAISED FOR THIS REPORT

Eaden, J. A., K. R. Abrams, Mayberry JF. (2001). The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut 48 (4): 526-35.

APPENDIX 1

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Levels Of Evidence

Based on "How to use the evidence: assessment and application of scientific evidence" (National Health & Medical Research Council, Canberra, 2000):

Level I	Evidence obtained from a systematic review (or meta-analysis) of all relevant randomised controlled trials.
Level II	Evidence obtained from at least one randomised controlled trial.
Level III	-1 Evidence obtained from pseudorandomised controlled trials (alternate allocation or some other method).
	-2 Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case control studies or interrupted time series with a control group.
	-3 Evidence obtained from comparative studies with historical control, two or more single-arm studies or interrupted time series without a parallel control group.
Level IV	Evidence obtained from case series, either post-test or pretest/post-test.

APPENDIX 2

Search strategy

	Search terms for Medline and Cochrane Library
1	Exp colitis, ulcerative/ or ulcerative colitis.mp
2	Exp neoplasms/ or malignancy.mp or gastrointestinal neoplasms/
3	Neoplasm\$.mp
4	Gastrointestinal neoplasm\$.mp
5	Tumor.mp
6	Cancer.mp
7	or/2-6
8	1 and 7
9	Risk.mp or exp risk/ or risk factors/
10	8 and 9
11	Limit 10 to (clinical trial or clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or meta analysis or multicenter study or randomized controlled trial or review or review literature), human, English language and year 1995-2002

<p style="text-align: center;">Evidence Summary</p> <div style="border: 1px solid black; padding: 5px; margin: 10px 0;"> <p>Risk of colorectal cancer in ulcerative colitis</p> </div>	<p style="text-align: right;">Study 1</p> <p>Eaden, J. A., K. R. Abrams, Mayberry JF. (2001). The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut 48 (4): 526-35.</p>
<p>STUDY DESIGN & NHMRC LEVELS OF EVIDENCE</p>	<p style="text-align: center;">Meta-analysis Level I evidence</p>
<p>DESCRIPTION: Patients (subjects), Intervention, Comparisons, Outcomes, Inclusion & Exclusion Criteria</p>	<p>Patients: Those with ulcerative colitis (UC) Outcome: The risk of colorectal cancer (CRC) Inclusion & Exclusion Criteria: English language articles with a clear definition of study patient population, with well described criteria for diagnosing UC, CRC and outcomes. Studies citing cancer mortality statistics (not cancer incidence), duplicate publications and studies combining patients with UC and Crohn's disease in a common analysis were excluded.</p>
<p>VALIDITY: Methodology, rigour, selection</p>	<p>Search strategy: Articles published in English and reporting CRC risk in patients with UC were identified from Medline. Articles identified dated back to 1925. Search terms were provided. Reference list of all reviews and retrieved original studies were also searched. Assessed validity: Not clear. Included studies were placed into one of three categories prior to data extraction (crude cancer prevalence only reported; cancer incidence and duration of patient follow up reported; or cancer incidence stratified by decade and duration of patient follow up reported). Each study was read and data extracted by one of the authors. Consistent results: Sub-group analyses were performed to explore between study heterogeneity.</p>
<p>RESULTS: Generally favourable or unfavourable, specific outcomes of interest, estimate of experimental effect and precision if appropriate</p>	<p>194 studies were identified and 116 met inclusion criteria. Overall 54,478 patients were studied and a total of 1,698 CRCs were detected: 9,846 patients had total colitis, among whom 700 cancers were found.</p> <ul style="list-style-type: none"> • Prevalence: The overall prevalence of CRC in UC patients (based on 116 studies) was 3.7% (95% CI 3.2-4.2%). Thirty five of the 116 studies included adequate data on patients with total colitis. In these 35 studies there were 8,351 patients with pancolitis and 451 cases of cancer. The prevalence of cancer in this group was 5.4% (95% CI 4.4-6.5). • Incidence: Of the 116 studies, 41 reported colitis duration. The overall incidence rate of CRC for patients with colitis was 3 per 1000 person years duration (pyd) [95% CI 2/1000 to 4/1000]. Based on five studies, the overall incidence rate for any child was 6/1000 pyd (95% CI 3/1000 to 13/1000). Of the 41 studies, 19 reported results stratified into 10-year intervals of disease duration. For the first 10 years the incidence rate was 2/1000 pyd (95% CI 1/1000 to 2/1000), for the second decade the incidence rate was estimated to be 7/1000 pyd (95% CI 4/1000 to 12/1000), and in the third decade the incidence rate was 12/1000 pyd (95% CI 7/1000 to 19/1000). These incidence rates corresponded to cumulative probabilities of 1.6% (95%CI 1.2-2) by 10 years, 8.3% (95% CI 4.8-11.7) by 20 years, and 18.4% (95% CI 15.3-21.5) by 30 years. • Risk variation by geography: The overall incidence rate of CRC in the USA was 5/1000 pyd (95% CI 3/1000-7/1000), in the UK 4/1000 pyd (95% CI 3/1000-5/1000), in Scandinavia 2/1000 pyd (95% CI 1/1000-3/1000), and in other countries 2/1000 pyd (95% CI 1/1000-4/1000). The cancer risk has increased since 1955 but this finding was not statistically significant (p=0.8).
<p>AUTHOR (S) CONCLUSIONS: Limitations, implications for practice and research</p>	<p>"Using new meta-analysis techniques we determined the risk of CRC in UC by decade of disease and defined the risk in pancolitics and children. We found a non-significant increase in risk over time and estimated how risk varies with geography."</p>

<p>Evidence Summary/aetiology</p> <div style="border: 1px solid black; padding: 5px; margin: 10px 0;"> <p>Risk of colorectal cancer in ulcerative colitis</p> </div>	<p style="text-align: right;">Study 1 (cont...)</p> <p>Eaden, J. A., K. R. Abrams, Mayberry JF. (2001). The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut 48 (4): 526-35.</p>
<p>OUR COMMENTS: Opportunity for bias, weakness and strength</p>	<p>Potential for bias: Unclear how the validity of the included studies was assessed. During analyses, studies were not given equal weighting but were assigned a weight proportional to the number of cases of cancer that were included in the study. A test for heterogeneity was performed. The search was confined to Medline only (retrieval bias) and there were differences in the study design across the studies included in the review. The method of exposure (ulcerative colitis) measurement and the follow up period could also vary across the included studies. Cancer was likely to be detected among patients and reported by studies with active follow up.</p> <p>Strengths:</p> <ul style="list-style-type: none"> • According to the authors this was the first comprehensive systematic review and meta-analysis assessing the risk of CRC in ulcerative colitis. • The meta-analysis was conducted according to the guidelines produced by the NHS Centre for Reviews and Dissemination at York University. • Inclusion and exclusion criteria were stated. • Clear research question • Reported search strategy and search terms • Assessed the impact of publication bias and language biases on the study findings • Subgroup analyses were performed to explore between study heterogeneity. • The authors acknowledged the limitations of the review and the results should be treated and interpreted cautiously. <p>Weaknesses:</p> <ul style="list-style-type: none"> • Retrieved bias (search was limited to Medline and reference of the retrieved studies). • No attempted was made to identify unpublished data and the authors stated that it was very difficult to identify such unpublished data. • Unclear how the validity of the included studies was assessed. <p>In conclusion, this study is a meta-analysis. As suggested by the authors, a prospective study of patients with ulcerative colitis with complete and active follow up would provide an accurate assessment of cancer risk in these patient population.</p>