

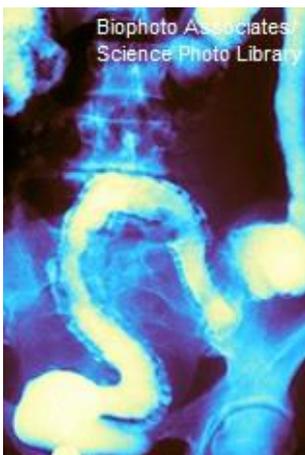


Surgery versus medical therapy in ulcerative colitis

A retrospective cohort study using US data found that elective colectomy was associated with better survival than long-term medical therapy in people with advanced ulcerative colitis, in particular in people aged 50 years or older.

Overview:

- In a US cohort of people with advanced ulcerative colitis, elective surgery was associated with lower mortality than long-term medical therapy.
- There was a significant benefit of surgery specifically in people aged 50 years or over, which was a major contributor to the overall effect.
- The data provide reassurance that surgery may be associated with positive outcomes compared with continued medical therapy and should be discussed with people who have ulcerative colitis that is difficult to control.



Background: Ulcerative colitis is a type of chronic inflammatory bowel disease where the colon and rectum become inflamed ([NHS Choices 2014](#)).

People whose disease does not respond to initial medical therapy, such as an aminosalicilate, have the option to escalate to different drugs, such as corticosteroids or immunosuppressants. However, long-term use of these drugs in people with ulcerative colitis is associated with opportunistic infections ([Toruner et al. 2008](#)) and cancer ([Bongartz et al. 2006](#)).

Alternatively, people with unresponsive disease may choose to undergo elective surgery to remove the affected portion of large bowel (colectomy). Elective colectomy may reduce the risk of mortality compared with no colectomy or emergency colectomy in people with ulcerative colitis ([Roberts et al. 2007](#)).

Current advice: The NICE guideline on [ulcerative colitis](#) recommends that a topical corticosteroid or oral prednisolone may be considered to induce remission in people who cannot tolerate or who decline aminosalicilates, or in whom aminosalicilates are contraindicated. Intravenous corticosteroids should be offered to induce remission in people admitted to hospital with acute severe ulcerative colitis.

NICE technology appraisal guidance recommends the anti-TNF drugs [infliximab](#), [adalimumab](#) and [golimumab](#), within their marketing authorisations, as options for treating moderately to severely active ulcerative colitis in adults whose disease has responded inadequately to conventional therapy or have medical contraindications for, such therapies.

[Vedolizumab](#) is recommended, within its marketing authorisation, as an option for treating moderately to severely active ulcerative colitis in adults only if the manufacturer provides the drug with the discount agreed in the patient access scheme.

The NICE guideline on [ulcerative colitis](#) recommends that the likelihood of needing surgery should be assessed in people admitted to hospital with acute severe ulcerative colitis who cannot tolerate or have contraindications to intravenous corticosteroids, and in those who do not improve despite corticosteroid treatment.

The guideline adds that people with ulcerative colitis who are considering elective surgery (and their family members or carers as appropriate) should be given information about all available treatment options, and the opportunity to discuss these options with a specialist (such as a gastroenterologist or a nurse specialist).

The NICE pathway on [ulcerative colitis](#) brings together all related NICE guidance and associated products on the condition in a set of interactive topic-based diagrams.

New evidence: A retrospective cohort study by [Bewtra et al. \(2015\)](#) assessed surgery compared with long-term medical therapy in people with advanced ulcerative colitis.

A total of 182,235 people in the USA with ulcerative colitis were identified from the databases for Medicaid (a health insurance system for people on low income), Medicare (insurance largely covering people aged 65 and older) or both.

People were eligible for the study if they had advanced ulcerative colitis (n=32,833), defined as any hospitalisation with a primary diagnosis of ulcerative colitis, 2 or more prescriptions for an oral corticosteroid within a 90-day period, or any prescription for immunosuppressant therapy (cyclosporin, tacrolimus, azathioprine, mercaptopurine [none of which are licenced for ulcerative colitis in the UK] or infliximab).

People with advanced ulcerative colitis who had undergone elective colectomy were identified using surgical codes in the databases (n=830), and each matched with up to 10 people who had received medical therapy only (n=7541). Participants were followed for up to 9 years.

The mortality rate was 34 deaths per 1000 person-years for people who had surgery and 54 deaths per 1000 person-years for medical therapy. Surgery was associated with lower mortality than medical therapy (adjusted hazard ratio [HR]=0.67, 95% confidence interval [CI] 0.52 to 0.87). This effect disappeared in sensitivity analyses that excluded people who may have had less severe disease.

A post-hoc analysis by age group showed lower mortality with surgery in people aged 50 years or older (adjusted HR=0.60, 95% CI 0.45 to 0.79). No mortality benefit with surgery was seen in people aged under 50 years (adjusted HR=1.35, 95% CI 0.69 to 2.66).

Limitations of this analysis include that participants were beneficiaries of the US Medicare or Medicaid insurance systems, or both, so the findings may not be generalisable to other populations. In addition, the source populations were followed up during different time frames (Medicaid: 2000–2005; Medicare: 2006–2011; both: 2000–2011), and the retrospective nature of the study means that the findings may have been affected by residual confounding.

Commentary by Professor Alan J Lobo, Consultant Physician and Gastroenterologist, Royal Hallamshire Hospital, Sheffield and Professor of Gastroenterology, University of Sheffield:

“The headline conclusion of this large and rigorously undertaken study is important. It supports the

view that elective surgery has an important role as an option for people with ulcerative colitis that is difficult to control. However, it is a retrospective analysis of databases used by US insurers.

“The survival benefit from surgery was driven by the benefit in people aged over 50 years. The authors explored potential explanations for the effect in this group – such as steroid or immunosuppressant use, narcotic analgesic use and infections – with no clear association found.

“The authors undertook sensitivity analyses that removed people with less severe disease, including those who received less immunosuppressant treatment. Once these less severely affected people were excluded, the effect of surgery became non-significant, suggesting that surgery was most effective in these people. The reasons for a survival benefit with surgery in people with less severe disease are not fully clear. The effect could perhaps be due to exposure to complex immunosuppressant medication and steroids in their matched, medically treated, controls.

“A careful attempt was made to match the treatment groups for comorbidity, but it is possible that patients in whom surgery carried a greater risk would be more likely to receive medical therapy. This in turn might be associated with higher mortality – confounding not captured by the comorbidity score. Because of the administrative nature of the databases examined, cause of death could not be assessed, which may have given more insight into the findings.

“These findings reinforce the NICE recommendation that surgery should be discussed with people in whom medical treatment has been ineffective in providing prolonged remission or associated with troublesome side effects. The NICE guideline also recommends that people with ulcerative colitis who are considering elective surgery should be given information about all available treatment options and the opportunity to discuss these options. Although the survival advantage is reassuring, other risks of surgery will be important to people considering surgery.

“The NICE technology appraisal of [infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis](#) considered that surgery might not be an option for all patients and was therefore not a suitable comparator for anti-TNF drugs, particularly in evaluating cost effectiveness. The findings of this study may help to inform future discussion.

“Although difficult to design, a prospective randomised trial of surgery versus continued medical treatment would clarify the effect on of each strategy on quality of life, cost and safety.”

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