
Surveillance report
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Surveillance decision

We will plan an update of the guideline on Crohn's disease. The update will focus on:

- postsurgical maintenance of remission.

We will plan an update of the guideline on ulcerative colitis. The update will focus on:

- medicines used to induce remission in people with mild-to-moderate ulcerative colitis
- treating acute severe ulcerative colitis.

During surveillance editorial or factual corrections were identified. Details are included in appendix A.1: summary of evidence from surveillance for the guideline on Crohn's disease, and appendix A.2: summary of evidence from surveillance for the guideline on ulcerative colitis.

Reason for the decision

Assessing the evidence

We found 191 studies through surveillance, 86 studies for the guideline on Crohn's disease and 105 studies for the guideline on ulcerative colitis.

Crohn's disease

Evidence that could affect recommendations was identified. Some of the new evidence identified, which covers the use of infliximab and adalimumab after surgery, was within the scope of infliximab and adalimumab for the treatment of Crohn's disease (2010) NICE technology appraisal guidance 187. In discussion with the NICE technology appraisal team it was identified that the appraisal was suitable for a partial update in the context of NICE guideline CG152. The evidence was therefore considered in the surveillance review.

Topic experts, including those who helped to develop the guideline, advised us about whether the following sections of the guideline should be updated:

Maintaining remission in Crohn's disease after surgery

- In adults and children what is the clinical and cost effectiveness of post-surgical (commencing within 3 months of any intestinal surgery for Crohn's disease) maintenance of remission for 12 months or longer of: conventional glucocorticosteroid treatment, budesonide,
5-aminosalicylate treatment, azathioprine, mercaptopurine, methotrexate, metronidazole, or combinations thereof, or nutritional treatment, compared with placebo or no treatment?

A considerable amount of new evidence (systematic reviews and randomised controlled trials) were identified which assessed the efficacy of anti-TNF therapy for maintenance of remission of Crohn's disease after surgery. Some of the evidence reported favourable outcomes associated with anti-TNF therapy, with some studies reporting that anti-TNF therapy was superior to immunomodulator therapy for postoperative maintenance of remission. Topic experts commented that the new evidence on the use of biologics after surgery increasingly reflects current practice.

Currently, NICE guideline CG152 makes recommendations on the use of immunomodulators and 5-aminosalicylates following surgically-induced remission of Crohn's disease but no recommendations are made on the post-surgical use of biologic medicines. Similarly, no recommendations are made on the post-surgical use of biologic medicines in NICE technology appraisal guidance 187.

It was considered that this question should be updated to take account of the new evidence and clarify the use of biologic medicines to maintain remission of Crohn's disease after surgery. Note: This would include a partial update and replacement of the technology appraisal guidance on infliximab and adalimumab for the treatment of Crohn's disease in the context of NICE guideline CG152. The update would cover the use of infliximab and adalimumab for post-surgical maintenance of remission.

**Decision:** This review question should be updated.

We also found new evidence that was thought to support existing recommendations or unlikely to change recommendations. This evidence was related to patient information and support, induction of remission, maintenance of remission using pharmacological interventions (without previous surgery), enteral nutrition, and surgery. Evidence on conception and pregnancy and potential risks and benefits of medical treatment was also identified but was thought to support, rather than have an impact on, recommendations.

We found evidence on the clinical and cost effectiveness of naltrexone for inducing remission in Crohn's disease, which was not covered in the guideline. However, the evidence was considered insufficient to add new recommendations in these areas at this time.

With the exception of NICE technology appraisal guidance 187 mentioned above, for any evidence relating to published or ongoing NICE technology appraisals, the guideline surveillance review deferred to the technology appraisal decision. This included evidence related to vedolizumab for
treating moderately to severely active Crohn's disease after prior therapy (2015) NICE technology appraisal guidance 352.

**Ulcerative colitis**

New evidence that could affect current recommendations was identified. Some evidence that was relevant to treating acute severe ulcerative colitis was within the scope of infliximab for acute exacerbations of ulcerative colitis (2008) NICE technology appraisal guidance 163. In discussion with the NICE technology appraisal team it was identified that the appraisal was suitable for a partial update in the context of NICE guideline CG166. Evidence relevant to infliximab and the review question was therefore considered in the surveillance review.

Topic experts, including those who helped to develop the guideline, advised us about whether the following sections of the guideline should be updated:

**Medicines used to induce remission in people with mild-to-moderate ulcerative colitis**

- In adults, children and young people with mild-to-moderate ulcerative colitis, what is the clinical and cost-effectiveness of corticosteroids, aminosalicylates and immunomodulators (mercaptopurine, azathioprine, methotrexate and tacrolimus) for the induction of remission compared to themselves (different preparations and doses), each other, combinations of preparations (oral and topical) and placebo?

Systematic reviews identified in the 4-year surveillance review reported that both beclomethasone dipropionate and budesonide MMX were superior to placebo or mesalazine for induction of remission of ulcerative colitis. Currently, NICE guideline CG166 does not make recommendations on the budesonide. Therefore assessment of the evidence on budesonide would be useful to ascertain its role in induction of remission of ulcerative colitis.

During the 4-year surveillance review, studies were identified which assessed new 5-aminosalicylate preparations. One study compared different doses of MMX mesalazine. A second study, explored the efficacy of different doses of pH-dependent release formulations. A third study reported that modified release tablets were non-inferior to enteric-coated tablets. Experts highlighted that new 5-aminosalicylate preparations are now available, and are considerably cheaper than before. This could have implications of the cost effectiveness of 5-aminosalicylates for induction of remission and therefore could impact on current guideline recommendations.
In relation to the off-label use of medications, studies which evaluated the efficacies of tofacitinib, atorvastatin, basiliximab and abatacept reported significantly greater improvements in induction of remission rates compared with placebo. Importantly, studies which assessed the off-label use of immunomodulators (tacrolimus and methotrexate) highlighted significant benefits of using these medicines for induction of remission of ulcerative colitis. Topic expert feedback was supportive of the evidence. One expert noted that evidence from studies on emergent medications have been presented at conferences and are likely to be published in the future. The published evidence identified and feedback from topic experts could have an impact on guideline recommendations.

One topic expert noted that no recommendation on the use of methotrexate was made in the original guideline as data was only available from 1 randomised controlled trial (RCT) at that time. They suggested that more evidence is now available. The expert’s observation was supported by evidence from studies identified in the 4-year surveillance review. One RCT, included in a systematic review, reported that clinical remission rates were not significantly different between patients treated by methotrexate and those treated by 6-mercaptopurine and 5-aminosalicylic acid. Another RCT reported that methotrexate induced clinical remission without steroids in a significantly larger percentage of patients compared with placebo. The identified new published evidence and topic expert feedback could impact on current recommendations therefore it is proposed that this clinical question should be updated.

**Decision:** This review question should be updated.

**Treating acute severe ulcerative colitis**

- In adults, children and young people with acute severe ulcerative colitis, what is the clinical and cost-effectiveness of corticosteroids and ciclosporin compared to each other and their combination (corticosteroids and ciclosporin) for the induction of remission?

Currently, NICE guideline CG166 makes recommendations on the use of ciclosporin in people with acute severe ulcerative colitis and cross-refers to infliximab for acute exacerbations of ulcerative colitis (2008) NICE technology appraisal guidance 163 for guidance on the use of infliximab.

Within NICE technology appraisal guidance 163 infliximab is recommended as an option for the treatment of acute exacerbations of severely active ulcerative colitis only in patients in whom ciclosporin is contraindicated or clinically inappropriate. For patients who do not meet the criterion, infliximab is recommended only in clinical trials.

Since publication of NICE technology appraisal guidance 163 two trials were completed that compared infliximab and ciclosporin. The trials conclude that there was no significant difference.
between ciclosporin and infliximab in clinical effectiveness; with one reporting no significant
difference in quality-adjusted survival between groups at 3-year follow-up. Likewise, there were no
significant differences in serious drug reaction rates, serious adverse event rates and death rates
between groups. A follow-up study of the cost effectiveness results showed that the total cost of
inflimab was considerably higher than cost of ciclosporin.

Topic experts also highlighted the need for guidance around the use of infliximab and ciclosporin
for severe ulcerative colitis. Guidance on the use of these agents is important as it is a major area of
uncertainty and guidance would help to avoid 'default' use of one or the other. For example,
inflimab may be used because of ease of administration compared to ciclosporin.

The new evidence now appears to show equivalence of the 2 therapies, and therefore how this
evidence fits in the pathway currently recommended by the guideline should be further analysed.
The new evidence identified indicate that a review of the recommendations in the guideline and
NICE technology appraisal guidance 163 is needed. It was considered that this question should be
updated to take account of the new evidence. Note: This would include a partial update and
replacement of NICE technology appraisal guidance on infliximab for acute exacerbations of
ulcerative colitis in the context of NICE guideline CG166. The update would cover the use of
inflimab and ciclosporin for acute severe ulcerative colitis.

Decision: This review question should be updated.

We found new evidence that was not thought to have an effect on current recommendations. This
evidence was related to interventions used for maintenance of remission of ulcerative colitis.

We did not find any evidence related to monitoring disease progression, pregnancy, and
information about treatment options for people who are considering surgery.

With the exception of NICE technology appraisal guidance 163 mentioned above, for any evidence
relating to published or ongoing NICE technology appraisals, the guideline surveillance review
defered to the technology appraisal decision. This included evidence related to *vedolizumab for
treating moderately to severely active ulcerative colitis (2015) NICE technology appraisal guidance
342* and *inflimab, adalimumab and golimumab for treating moderately to severely active
ulcerative colitis after the failure of conventional therapy (2015) NICE technology appraisal
guidance 329.*
Equalities

We identified no equalities issues during the surveillance process.

Overall decision

After considering all the evidence and views of topic experts, we decided that a partial update is necessary for both guidelines.

See how we made the decision for further information.
How we made the decision

We check our guidelines regularly to ensure they remain up to date. We based the decision on surveillance 4 years after the publication of NICE's guideline on Crohn's disease (CG152) in 2012 and 4 years after the publication of NICE's guideline on ulcerative colitis (CG166) in 2013.

For details of the process and update decisions that are available, see ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual.

Previous surveillance update decisions for the guidelines on Crohn's disease and ulcerative colitis are on our website.

New evidence

Crohn's disease

We found 68 studies in a search for randomised controlled trials (RCTs) and systematic reviews published between 16 April 2014 and 4 October 2016. We also considered 3 additional studies identified by members of the guideline committee who originally worked on this guideline.

We also considered evidence identified in previous surveillance 2 years after publication of the guideline. This included 15 studies identified by search.

From all sources, we considered 86 studies to be relevant to the guideline.

We also checked for relevant ongoing research, which will be evaluated again at the next surveillance review of the guideline.

See appendix A.1: summary of evidence from surveillance for details of all evidence considered, and references.

Ulcerative colitis

We found 71 studies in a search for RCTs and systematic reviews published between 8 April 2015 and 4 October 2016.

We also considered evidence identified in previous surveillance 2 years after publication of the guideline. This included 34 studies identified by search.
From all sources, we considered 105 studies to be relevant to the guideline.

We also checked for relevant ongoing research, which will be evaluated again at the next surveillance review of the guideline.

See appendix A.2: summary of evidence from surveillance for details of all evidence considered, and references.

Views of topic experts

We considered the views of topic experts, including those who helped to develop the guideline and other correspondence we have received since the publication of the Crohn's disease and ulcerative colitis guidelines.

Views of stakeholders

Stakeholders are consulted only if we decide not to update the guideline following checks at 4 and 8 years after publication. Because 4-year surveillance reviews were performed, and the decision was to update both guidelines, we did not consult on the decision.

Stakeholder consultation on a proposal to update and replace NICE technology appraisal guidance 163 and 187 in a clinical guideline would be held, in-line with technology appraisal processes.

See ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual for more details on our consultation processes.

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