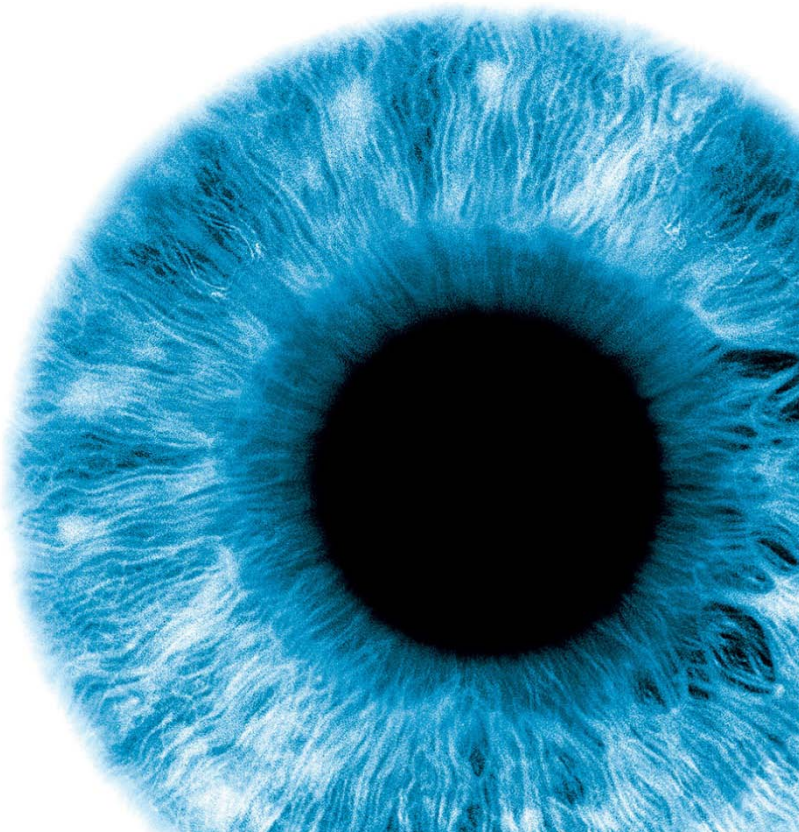
NICE National Institute for Health and Care Excellence

Acute upper gastrointestinal bleeding

Evidence Update August 2014

A summary of selected new evidence relevant to NICE clinical guideline 141 'Acute upper gastrointestinal bleeding: management' (2012)

Evidence Update 63



Contents

Introduction

Evidence Updates are intended to increase awareness of new evidence – they do not replace current NICE guidance and do not provide formal practice recommendations.

Evidence Updates reduce the need for individuals, managers and commissioners to search for new evidence. For contextual information, this Evidence Update should be read in conjunction with the relevant clinical guideline.

This Evidence Update provides a summary of selected new evidence published since the literature search was last conducted for the following NICE guidance:

[1] **Acute upper gastrointestinal bleeding. NICE clinical guideline 141 (2012)**

A search was conducted for new evidence from 23 September 2011 to 20 February 2014. A total of 6061 pieces of evidence were initially identified. After removal of duplicates, a series of automated and manual sifts were conducted to produce a list of the most relevant references. The remaining 16 references underwent a rapid critical appraisal process and then were reviewed by an Evidence Update Advisory Group, which advised on the final list of 8 items selected for the Evidence Update. See Appendix A for details of the evidence search and selection process.

Evidence selected for inclusion in this Evidence Update may highlight a potential impact on guidance: that is, a high-quality study, systematic review or meta-analysis with results that suggest a change in practice. Evidence that has no impact on guidance may be a key read, or may substantially strengthen the evidence base underpinning a recommendation in the NICE guidance.

The Evidence Update gives a preliminary assessment of changes in the evidence base and a final decision on whether the guidance should be updated will be made by NICE according to its published processes and methods.

This Evidence Update was developed to help inform the review proposal on whether or not to update NICE clinical guideline 141 (NICE CG141). The process of updating NICE guidance is separate from both the process of an Evidence Update and the review proposal.

See the NICE clinical guidelines methods guides for further information about updating clinical guidelines.

NICE Pathways

NICE pathways bring together all related NICE guidance and associated products on the condition in a set of interactive topic-based diagrams. The following NICE Pathways cover advice and recommendations related to this Evidence Update:

- Acute upper gastrointestinal bleeding. NICE Pathway

[1] NICE-accredited guidance

Quality standards

- Acute upper gastrointestinal bleeding. NICE quality standard 38

Feedback

If you would like to comment on this Evidence Update, please email contactus@evidence.nhs.uk

Key points

The following table summarises the key points for this Evidence Update and indicates whether the new evidence may have a potential impact on NICE CG141. Please see the full commentaries for details of the evidence informing these key points.

The section headings used in the table below are taken from NICE CG141.

Evidence Updates do not replace current NICE guidance and do not provide formal practice recommendations.

	Potential impact on guidance	
Key point	**Yes**	**No**
Risk assessment • The Blatchford score and the Rockall score may both be insufficient for use as a single method of risk assessment for treatment or discharge from hospital.		✓
Resuscitation and initial management • In people with upper gastrointestinal bleeding, a strategy of providing blood transfusion when the patient's haemoglobin drops to a lower threshold (7 g/dl) may be associated with lower mortality and fewer adverse events than transfusion at a higher threshold (9 g/dl). • Limited evidence suggests that tranexamic acid[2] may have beneficial effects on mortality in people with upper gastrointestinal bleeding, but may not affect bleeding or need for transfusion.		✓ ✓
Primary prophylaxis for acutely ill patients in critical care • Stress-ulcer prophylaxis for patients in critical care units may reduce gastrointestinal bleeding but may have no effects on all-cause mortality, pneumonia, or time spent in critical care. Proton pump inhibitors may be more clinically effective and more cost effective than H_2-receptor antagonists; H_2-receptor antagonists may be more clinically effective than placebo.		✓
Areas not covered by NICE CG141 • An infusion of erythromycin before endoscopy in adults with upper gastrointestinal bleeding[3] may increase visibility of the gastric mucosa and reduce second endoscopies, blood transfusions, and length of hospital stay.		✓

[2] At the time of publication of this Evidence Update, tranexamic acid did not have UK marketing authorisation for this indication and was not considered for NICE CG141.

[3] At the time of publication of this Evidence Update, erythromycin did not have UK marketing authorisation for this indication and was not considered for NICE CG141.

1 Commentary on new evidence

These commentaries focus on the 'key references' identified through the search process and prioritised by the EUAG for inclusion in the Evidence Update, which are shown in bold text. Supporting references provide context or additional information to the commentary. Section headings are taken from NICE CG141.

1.1 Risk assessment

Assessing risk with the Blatchford and Rockall scores

NICE CG141 recommends using the following formal risk assessment scores for all patients with acute upper gastrointestinal bleeding:

- the Blatchford score at first assessment, and
- the full Rockall score after endoscopy.

Chandra et al. (2012) conducted a retrospective study (n=171) to validate the Blatchford score and the Rockall score in adults who presented with upper gastrointestinal bleeding. Records for all admissions to a single US emergency department between April 2004 and July 2009 were searched to identify cases of upper gastrointestinal bleeding. The primary outcome was a composite of need for intervention (blood transfusion or haemostasis achieved by endoscopy, angiography or surgery) or death within 30 days.

Readmissions to the emergency department within 30 days were excluded and any readmissions after 30 days were considered to be a new visit. People who had not given previous authorisation to have their medical records reviewed for research purposes were excluded. Also excluded were people who lived outside the county the emergency department was located in, because population-based data for follow-up were available only for people who lived in that county. For all included cases of upper gastrointestinal bleeding, information was extracted to allow calculation of Blatchford and Rockall scores.

Most of the 171 eligible patients presented with melaena (70%), and upper gastrointestinal endoscopy was performed in 136 people (80%). The primary outcome occurred in 90 patients (53%). The Blatchford score had 54% accuracy for predicting the need for intervention or death within 30 days. The Rockall score had 53% pre-endoscopy accuracy and 61% accuracy post-endoscopy. Both scores were described as having suboptimum sensitivity and specificity.

Analysis of receiver operating characteristic curves suggested that the Blatchford score had better overall prognostic ability than the pre-endoscopy Rockall score (area under curve [AUC]=0.79 versus 0.62 respectively, p=0.0001). However, the Blatchford score and the post-endoscopy Rockall score had similar prognostic ability (AUC=0.79 versus 0.72 respectively, p=0.26).

Limitations of the study included the small sample size and retrospective single-centre design. The fairly low rates of upper gastrointestinal bleeding (171 cases in about 5 years) meant that a prospective study design may not have been pragmatic or cost effective. Several strategies were used to reduce bias in data collection, including standard protocols and forms, training and monitoring of investigators who collated the data, blinding data collectors to outcomes and blinding outcome assessors to data on predictor variables, and assessing inter-rater reliability.

This evidence suggests that the Blatchford score and the Rockall score may both be insufficient for use as a single method of risk assessment for treatment or discharge from

hospital. This finding is consistent with NICE CG141, which recommends using both the Blatchford score and post-endoscopy Rockall Score for risk assessment.

Key reference

Chandra S, Hess EP, Agarwal D et al. (2012) External validation of the Glasgow-Blatchford Bleeding Score and the Rockall Score in the US setting. American Journal of Emergency Medicine 30: 673–9

1.2 Resuscitation and initial management

Restrictive or liberal blood transfusion strategies

NICE CG141 recommends basing decisions on blood transfusion on the full clinical picture, recognising that over-transfusion may be as damaging as under-transfusion.

Villanueva et al. (2013) reported a single-centre randomised controlled trial (n=921) of liberal versus restrictive blood transfusion strategies in adults admitted with haematemesis or bloody nasogastric aspirate, or melaena. In the restrictive group, the transfusion threshold was haemoglobin of 7 g/dl with a post-transfusion target of 7–9 g/dl. In the liberal group, the transfusion threshold was 9 g/dl with a post-transfusion target of 9–11 g/dl. The primary outcome was death from any cause in the first 45 days.

Haemoglobin was measured after admission and again every 8 hours during the first 2 days, and once a day thereafter. Haemoglobin was also measured if further bleeding was suspected. In both groups, 1 unit of prestorage leukocyte-reduced packed red cells was initially transfused if haemoglobin was below the threshold, and the haemoglobin level was then measured again. A further unit of blood was administered if haemoglobin remained under the target range. All patients had emergency endoscopy within 6 hours of admission, and haemostasis was achieved using the most appropriate means.

People with massive exsanguinating bleeding, transfusion within the previous 90 days, or a Rockall score of 0 and haemoglobin of 12 g/dl or higher were excluded from the study. Also excluded were people with cardiovascular disorders including stroke and acute coronary syndromes in the previous 90 days, recent trauma or surgery, lower gastrointestinal bleeding or who had a previous decision by the treating physician that a specific treatment should not be used.

The intention-to-treat analysis included 444 patients in the restrictive group and 445 patients in the liberal group. About a third of participants (31%) had cirrhosis, and bleeding was caused by peptic ulcer in about half of participants (49%). Haemoglobin concentration was similar between groups at admission and after 45 days. The restrictive group had lower haemoglobin during the study than the liberal group.

Significantly more people in the restrictive group had no transfusion during the study (51%) than the liberal group (14%, $p<0.001$). The mean number of units transfused was also lower in the restrictive group than in the liberal group (1.5 standard deviation [SD]=2.3 units versus 3.7 SD=3.8 units respectively, $p<0.001$). Mortality at 45 days was significantly lower in the restrictive group (23 patients, 5%) than in the liberal group (41 patients, 9%, $p=0.02$). After adjustment for baseline risk factors for death, the hazard ratio for the restrictive group was 0.55 (95% confidence interval [CI] 0.33 to 0.92). Death from unsuccessful control of bleeding occurred in 3 patients in the restrictive group and 14 patients in the liberal group ($p=0.01$).

The overall rate of adverse events was lower in the restrictive group (40%) than in the liberal group (48%, $p=0.02$). Transfusion reactions and cardiac events were more common in the liberal group.

A limitation of the study was that the results may not be generalisable to all patients with acute gastrointestinal bleeding, because the sample did not include either those with a low

risk of re-bleeding or those with massive exsanguinating bleeding. Additionally, blinding was not possible because of the nature of the intervention.

A UK-based study, TRIGGER (Transfusion in Gastrointestinal Bleeding, n=936), to determine the feasibility of a phase 3 trial of transfusion strategies based on a haemoglobin threshold of 8 g/dl has announced results in a conference poster presentation. The abstract suggests that although clinically important differences were seen in the proportion of patients transfused, number of units of blood transfused and patients' clinical outcomes, the differences were not statistically significant. The authors concluded that a larger trial is needed.

This evidence suggests that in people with upper gastrointestinal bleeding, a strategy of providing blood transfusion when the patient's haemoglobin drops to a lower threshold (7 g/dl) may be associated with lower mortality and fewer adverse events than transfusion at a higher threshold (9 g/dl). This evidence is consistent with the recommendation in NICE CG141 to base decisions on blood transfusion on the full clinical picture, recognising that over-transfusion may be as damaging as under-transfusion.

Key reference

Villanueva C, Colomo A, Bosch A et al. (2013) Transfusion strategies for upper gastrointestinal bleeding. The New England Journal of Medicine 368: 11–21

Supporting reference

Jairath V, Kahan B, Gray A et al. (2014) Restrictive versus liberal blood transfusion for acute upper gastrointestinal bleeding: cluster randomised feasibility trial. Gut 63: Supplement 1 PTU-184

Tranexamic acid

NICE CG141 does not include recommendations on use of tranexamic acid for upper gastrointestinal bleeding. At the time of publication of this Evidence Update, tranexamic acid did not have UK marketing authorisation for this indication.

Gluud et al. (2012) conducted a Cochrane review of 7 randomised controlled trials (n=1654) that compared tranexamic acid with placebo for the treatment of upper gastrointestinal bleeding. The primary outcome measure was mortality, and secondary outcomes included bleeding, surgery and adverse events.

Most included studies dated from the 1970s and 1980s, with 1 study from 2001. Oral administration of tranexamic acid was used in 3 trials; the rest used intravenous dosing for up to 2 days or until endoscopy with oral dosing afterwards. Treatment lasted from 2 days to 7 days, with daily dosing of 4–8 g; the total dose administered ranged from 16 g to 42 g.

Overall, 41 (5%) of 829 patients who received tranexamic acid died compared with 68 (8%) of 825 patients who received placebo (random effects risk ratio=0.61, 95% CI 0.42 to 0.89, p=0.01). However, in further analyses (worst case scenario and sequential analysis), no significant effect of tranexamic acid on mortality was seen. Bleeding and need for transfusion did not differ significantly between groups. The reporting of adverse events was unclear in most studies, but in 3 trials reporting thromboembolic events (n=1048) there were no significant differences between groups.

Limitations of the study included that trials were old and only 1 trial used endoscopic treatment in line with current clinical practice, and about 20% of patients dropped out of studies, but loss to follow-up was not reported adequately in most studies.

Limited evidence suggests that tranexamic acid may have beneficial effects on mortality in people with upper gastrointestinal bleeding, but may not affect bleeding or need for transfusion. This evidence is unlikely to have an impact on NICE CG141, which does not include recommendations on tranexamic acid. Additional randomised controlled trials are needed to determine the effect of tranexamic acid when combined with current clinical

practice. The international multicentre randomised controlled trial. HALT-IT (Haemorrhage ALleviation with Tranexamic acid– IntesTinal system) of tranexamic acid for the treatment of gastrointestinal bleeding is underway.

Key reference

Gluud LL, Klingenberg SL, Langholz E (2012) Tranexamic acid for upper gastrointestinal bleeding. Cochrane Database of Systematic Reviews issue 1: CD006640

1.3 Timing of endoscopy

No new key evidence for this section was selected for inclusion in this Evidence Update.

1.4 Management of non-variceal bleeding

No new key evidence for this section was selected for inclusion in this Evidence Update.

1.5 Management of variceal bleeding

No new key evidence for this section was selected for inclusion in this Evidence Update.

1.6 Control of bleeding and prevention of re-bleeding in patients on NSAIDs, aspirin or clopidogrel

No new key evidence for this section was selected for inclusion in this Evidence Update.

1.7 Primary prophylaxis for acutely ill patients in critical care

Acid-suppression therapy for stress-ulcer prophylaxis

NICE CG141 recommends offering acid-suppression therapy (H_2-receptor antagonists or proton pump inhibitors [PPIs]) for primary prevention of upper gastrointestinal bleeding in acutely ill patients admitted to critical care. If possible, the oral form of the drug should be used.

Krag et al. (2014) did a systematic review and meta-analysis of 20 randomised trials (n=1971) in adults admitted to a critical care unit comparing stress-ulcer prophylaxis with PPIs or H_2-receptor antagonists with a placebo or no prophylaxis. The primary outcome analysed was all-cause mortality, and secondary outcomes were gastrointestinal bleeding and pneumonia. All 20 included trials assessed a H_2-receptor antagonist (mainly ranitidine and cimetidine), but only 2 trials assessed a PPI (both omeprazole, n=249).

Mortality did not differ significantly between the prophylaxis groups and those on no prophylaxis or placebo (relative risk [RR]=1.00, 95% CI 0.84 to 1.20, p=0.87; 15 trials, n=1604). Pneumonia also showed no significant difference between groups (RR=1.16, 95% CI 0.84 to 1.58, p=0.28; 7 trials, n=1008). Gastrointestinal bleeding was significantly lower with stress-ulcer prophylaxis than with placebo or no prophylaxis (RR=0.41, 95% 0.31 to 0.53, p=0.01; 20 trials, n=1971). However, trial sequential analysis did not show a significant effect of stress-ulcer prophylaxis on gastrointestinal bleeding. Subgroup analysis of trials of H_2-receptor antagonists versus PPIs showed no increase in effect for PPIs for mortality, gastrointestinal bleeding, or pneumonia. No included trial was assessed to be at low risk of bias, which is a potential limitation of this study.

Barkun et al. (2012) conducted a systematic review and meta-analysis of PPIs compared with H_2-receptor antagonists (13 trials, n=1587) for stress-ulcer prophylaxis in adults in critical care units. The primary outcome was clinically significant bleeding, and the secondary outcomes were pneumonia, all-cause mortality and days in the critical care unit.

Overall, the occurrence of gastrointestinal bleeding was lower with PPIs than with H_2-receptor antagonists (odds ratio [OR]=0.30, 95% CI 0.17 to 0.54; 13 trials, n=1587). No significant differences were seen between groups for pneumonia (OR=1.05, 95% CI 0.69 to 1.62; 7 trials, n=1017), all-cause mortality (OR=1.19, 95% CI 0.84 to 1.68; 8 trials, n=1260), or days in the critical care unit (weighted mean difference [WMD]=−0.12 days, 95% CI −1.90 to 1.66 days; 3 trials, n=339). The results were maintained in several sensitivity analyses that accounted for the definition of bleeding, whether the trial was published fully or only as an abstract, recent or older publication dates, and whether patients received enteral or nasogastric feeding.

The meta-analysis was limited by the poor quality of many included trials, use of varying definitions of bleeding, and variation in the critical care setting across trials. However, no heterogeneity or publication bias was noted.

Alhazzani et al. (2013) conducted a systematic review and meta-analysis focusing on the same patients, interventions and outcomes as the review by Barkun et al. (2012), reported above. Alhazzani et al. (2013) additionally looked for the incidence of *Clostridium difficile* infection as a secondary outcome, but no studies reported this outcome. Of 14 included studies (n=1720), 12 were the same as those included in Barkun et al. (2012).

Alhazzani et al. (2013) found that the risk of bleeding was significantly lower for PPIs than for H_2-antagonists, for both clinically important bleeding (RR=0.36, 95% CI 0.19 to 0.68, p=0.002; 12 trials, n=1614) and overt bleeding (RR=0.35, 95% CI 0.21 to 0.59, p<0.0001; 14 trials, n=1720). No significant differences between groups were seen for pneumonia, all-cause mortality, or days in the critical care unit. A funnel plot indicated that some small trials with negative results may have been missing. Risk of bias was low in 3 trials, unclear in 5 trials and high in 6 trials.

Barkun et al. (2013) conducted a US-based cost-effectiveness analysis of PPIs and H_2-receptor antagonists. Patients in critical care units who were at high risk of developing stress-ulcer-related bleeding were identified from a national database. The Nationwide Inpatient Sample 2008 included data for 1000 hospitals in 42 states. These data were used to estimate hospital costs (including drug costs) and length of stay at 2010 US dollar prices.

Overall, 94,865 patients had no complications, with a mean length of stay of 14 days at a cost of $41,600. Stress-ulcer bleeding was seen in 1088 patients, with a mean hospital stay of 24 days at a cost of $65,500. Ventilator-associated pneumonia was seen in 235 patients, with a mean stay in hospital of 42 days at a cost of $137,700.

A decision-tree model covering a 2-month period was developed that assumed that all patients at risk of stress-ulcer bleeding received either PPIs (oral or intravenous bolus of omeprazole 40 mg daily) or H_2-antagonists (intravenous famotidine 40 mg twice daily). Patients could then progress to 'no complications' or to have the complications of either stress-ulcer bleeding or ventilator-associated pneumonia.

Probabilities were calculated from a literature search that included the same 13 studies as the systematic review and meta-analysis by Barkun et al. (2012). The probability of stress-ulcer bleeding was assumed to be 1.34% for people on PPIs and 6.61% for those on H_2-receptor antagonists. The probability of ventilator-associated pneumonia was assumed to be 10.33% for people on PPIs and 10.32% for H_2-receptor antagonists. No reported values for quality-adjusted life years were identified, so cost effectiveness was assessed by complications averted.

In the base-case analysis, the cost of treating a patient who had no complications with PPIs was $58,700 compared with $63,921 for H_2-receptor antagonists. In a sensitivity analysis, the incremental cost effectiveness ratio was affected most if the rate of pneumonia rose to over 11.6% in the PPI group or dropped below 9% in the H_2-antagonist group. PPIs became more

expensive, but their greater effect on bleeding meant that they remained more effective than H_2-receptor antagonists.

Taken together, these studies suggest that stress-ulcer prophylaxis for patients in critical care units may reduce gastrointestinal bleeding but may have no effects on all-cause mortality, pneumonia, or time spent in critical care. PPIs may be more clinically effective and more cost effective than H_2-receptor antagonists; H_2-receptor antagonists may be more clinically effective than placebo. Trials of PPIs compared with placebo are needed, so no impact on NICE CG141 is expected.

Additional information is available from independent critical appraisal reports produced for the Centre for Reviews and Dissemination. The Database of Abstracts of Reviews of Effects has a critical appraisal report on Alhazzani et al. (2013) and a report on Krag et al. (2014). The NHS Economic Evaluation Database has a critical appraisal report on Barkun et al. (2013).

Key references

Alhazzani W, Alenezi F, Jaeschke RZ et al. (2013) Proton pump inhibitors versus histamine 2 receptor antagonists for stress ulcer prophylaxis in critically ill patients: a systematic review and meta-analysis. Critical Care Medicine 41: 693–705

Barkun AN, Adam V, Martel M et al. (2013) Cost-effectiveness analysis: stress ulcer bleeding prophylaxis with proton pump inhibitors, H2 receptor antagonists. Value in Health 16: 14–22

Barkun AN, Bardou M, Pham CQ et al. (2012) Proton pump inhibitors vs. histamine 2 receptor antagonists for stress-related mucosal bleeding prophylaxis in critically ill patients: a meta-analysis. The American Journal of Gastroenterology 107: 507–20

Krag M, Perner A, Wetterslev J et al. (2014) Stress ulcer prophylaxis versus placebo in critically ill patients: a systematic review of randomised clinical trials with meta-analysis and trial sequential analysis. Intensive Care Medicine 40: 11–22

1.8 Information and support for patients and carers

No new key evidence for this section was selected for inclusion in this Evidence Update.

Areas not currently covered by NICE CG141

Erythromycin for improved endoscopic imaging

NICE CG141 does not include recommendations on use of erythromycin as a prokinetic agent to improve endoscopy results. At the time of publication of this Evidence Update, erythromycin did not have UK marketing authorisation for this indication.

Theivanayagam et al. (2013) did a systematic review of 7 randomised controlled trials (n=558) assessing an infusion of erythromycin before endoscopy in adults with upper gastrointestinal bleeding. The primary outcomes assessed were visualisation of gastric mucosa and need for second endoscopy. Secondary outcomes were units of blood transfused, length of hospital stay, and duration of endoscopy. Trials using nasogastric lavage were included only if this procedure was done in both groups.

Erythromycin was associated with a greater chance of adequate visualisation of the gastric mucosa than no erythromycin (OR=3.43, 95% CI 1.81 to 6.50, p<0.01; 7 trials, n=558). Second endoscopy was needed in fewer patients who received erythromycin compared with those who did not (OR=0.47, 95% CI 0.26 to 0.83, p=0.01; 7 trials, n=558).

Erythromycin was also associated with lower need for blood transfusion (WMD=−0.41 units of blood transfused, 95% CI −0.82 to −0.01, p=0.04; 5 trials, n=504) and shorter hospital stay (WMD=−1.51 days, 95% CI −2.45 to −0.56, p<0.01; 4 trials, n=335). However, the duration of

endoscopy was not affected by administration of erythromycin (WMD=−1.36 minutes, 95% CI −4.69 to 1.97, p=0.42; 4 studies, n=463).

Limitations of the study included that gastric visualisation was based on endoscopists' assessment and definitions varied across studies. In this meta-analysis, gastric visualisation was simplified to either adequate or inadequate. Trials also used differing doses of erythromycin – 125 mg, 250 mg, or weight-based dosing – although this variation did not seem to affect results.

This evidence suggests that an infusion of erythromycin before endoscopy in adults with upper gastrointestinal bleeding may increase visibility of the gastric mucosa and reduce second endoscopies, blood transfusions, and length of hospital stay. However, these findings should be confirmed in a large randomised controlled trial, so no impact on NICE CG141 is expected.

Key reference

Theivanayagam S, Lim RG, Cobell WJ et al. (2013) Administration of erythromycin before endoscopy in upper gastrointestinal bleeding: a meta-analysis of randomised controlled trials. The Saudi Journal of Gastroenterology 19: 205–10

2 New evidence uncertainties

During the development of the Evidence Update, the following evidence uncertainties were identified for the UK Database of Uncertainties about the Effects of Treatments (UK DUETs).

Primary prophylaxis for acutely ill patients in critical care

- Cost effectiveness of proton pump inhibitors versus placebo for stress ulcer prophylaxis in critically ill patients

Further evidence uncertainties for upper gastrointestinal bleeding can be found in the UK DUETs database and in the NICE research recommendations database.

UK DUETs was established to publish uncertainties about the effects of treatments that cannot currently be answered by referring to reliable up-to-date systematic reviews of existing research evidence.

Appendix A: Methodology

Scope

The scope of this Evidence Update is taken from the scope of the reference guidance:

- Acute upper gastrointestinal bleeding. NICE clinical guideline 141 (2012)

Searches

The literature was searched to identify studies and reviews relevant to the scope. Searches were conducted of the following databases, covering the dates 23 September 2011 (the end of the search period of NICE clinical guideline 141) to 20 February 2014:

- CDSR (Cochrane Database of Systematic Reviews)
- CENTRAL (Cochrane Central Register of Controlled Trials)
- CINAHL (Cumulative Index to Nursing and Allied Health Literature)
- DARE (Database of Abstracts of Reviews of Effects)
- EMBASE (Excerpta Medica database)
- HTA (Health Technology Assessment) database
- MEDLINE (Medical Literature Analysis and Retrieval System Online)
- MEDLINE In-Process
- NHS EED (Economic Evaluation Database)
- PsycINFO

The Evidence Update search strategy replicates the strategy used by NICE CG141 (for key words, index terms and combining concepts) as far as possible. Where necessary, the strategy is adapted to take account of changes in search platforms and updated indexing language.

Table 1 provides details of the MEDLINE search strategy used, which was adapted to search the other databases listed above. The search strategy was used in conjunction with validated Scottish Intercollegiate Guidelines Network search filters for RCTs and systematic reviews.

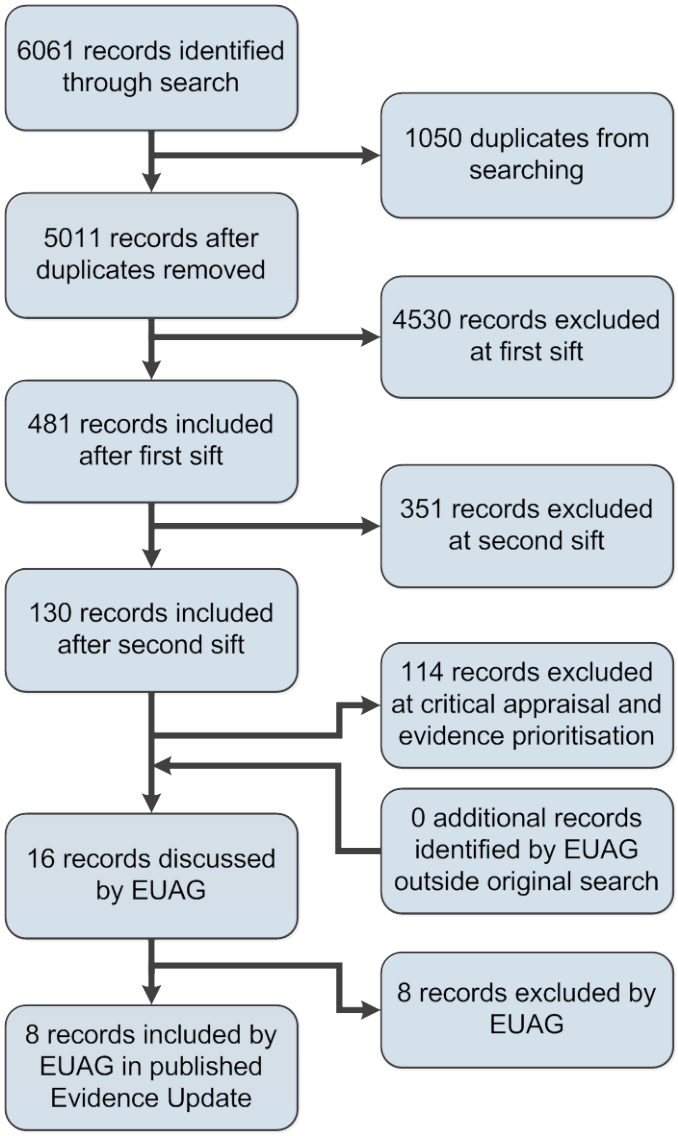
Figure 1 provides details of the evidence selection process. The list of evidence excluded after review by the Chair of the EUAG, and the full search strategies, are available on request from contactus@evidence.nhs.uk

See the NICE Evidence Services website for more information about how NICE Evidence Updates are developed.

Table 1 MEDLINE search strategy (adapted for individual databases)

1	exp Gastrointestinal hemorrhage/
2	exp "Esophageal and gastric varices"/
3	(hemateme* or haemateme*).ti,ab.
4	((oesophag* or esophag* or gastric) adj3 (varic* or varix)).ti,ab.
5	((GI or stomach or gastric or gastrointest* or gastro-intest* or varic* or varix or ulcer* or duod* or oesoph* or esophag*) adj3 (bleed* or blood* or lesion* or haemorrhag* or hemorrhag* or rebleed*)).ti,ab.
6	or/1-5

Figure 1 Flow chart of the evidence selection process



EUAG – Evidence Update Advisory Group

Appendix B: The Evidence Update Advisory Group and Evidence Update project team

Evidence Update Advisory Group

The Evidence Update Advisory Group is a group of topic experts who reviewed the prioritised evidence from the literature search and advised on the development of the Evidence Update.

Dr Kelvin Palmer – Chair

Consultant Gastroenterologist, Western General Hospital, Edinburgh

Dr Stephen Atkinson

Academic Clinical Fellow in Gastroenterology and Hepatology, Imperial College Healthcare NHS Trust, London

Mr Daniel Greer

Pharmacist Lecturer and Practitioner, University of Leeds and Leeds Teaching Hospitals Trust

Dr Markus Hauser

Consultant Physician, Gloucestershire Hospitals NHS Foundation Trust

Dr Simon McPherson

Consultant Vascular and Interventional Radiologist, Leeds Teaching Hospitals Trust

Dr David Patch

Consultant Hepatologist, Royal Free Hospital, London

Evidence Update project team

Marion Spring

Associate Director

Dr Chris Alcock

Clinical Lead – NICE Evidence Services

Chris Weiner

Consultant Clinical and Public Health Adviser

Cath White

Programme Manager

Swapna Mistry

Project Manager

Steve Sharp
Information Specialist

Lynne Kincaid
Medical Writer