NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

QUALITY STANDARDS PROGRAMME

Quality standard topic: Acute upper gastrointestinal bleeding

Output: Briefing paper

Introduction

This briefing paper presents a structured evidence review to help determine the suitability of recommendations from the key development sources listed below, to be developed into a NICE quality standard. The draft quality statements and measures presented in this paper are based on published recommendations from these key development sources:

Gastrointestinal bleeding: the management of acute upper gastrointestinal bleeding. NICE clinical guideline 141 (2012; NICE accredited). Available from www.nice.org.uk/guidance/CG141

Structure of the briefing paper

The body of the paper presents supporting evidence for the draft quality standard reviewed against the three dimensions of quality: clinical effectiveness, patient experience and safety. Information is also provided on available cost-effectiveness evidence and current clinical practice for the proposed standard. Where possible, evidence from the clinical guideline is presented. When this is not available, other evidence sources have been used.

1 Risk assessment

1.1 NICE CG141 Recommendations 1.1.1 [KPI] and 1.1.2

1.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.1.1 Use 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. 1.1.2 Consider early discharge for patients with a pre-endoscopy Blatchford score of 0
Proposed quality statement	People with acute upper gastrointestinal bleeding are offered a formal risk assessment, using the Blatchford score at first assessment, and the full Rockall score after endoscopy, with early discharge considered for those with a pre-endoscopy Blatchford score of 0
Draft quality measure	**Structure:** Evidence of local arrangements to ensure that people with acute upper gastrointestinal bleeding are offered a formal risk assessment, using the Blatchford score at first assessment, and the full Rockall score after endoscopy, with early discharge considered for those with a pre-endoscopy Blatchford score of 0. **Process:** a) The proportion of people with acute upper gastrointestinal bleeding who receive a Blatchford score at first assessment Numerator – The number of people in the denominator who receive a Blatchford score at first assessment Denominator – The number of people with acute upper gastrointestinal bleeding b) The proportion of people with acute upper gastrointestinal bleeding who receive a full Rockall score after endoscopy Numerator – The number of people in the denominator who receive a full Rockall score after endoscopy Denominator – The number of people with acute upper gastrointestinal bleeding c) The proportion of people with acute upper gastrointestinal bleeding with a pre-endoscopy Blatchford score of 0 who are considered for early discharge Numerator – The number of people in the denominator who are considered for early discharge Denominator – The number of people with acute upper gastrointestinal bleeding with a pre-endoscopy Blatchford score of 0

1.1.2 Clinical and cost-effectiveness evidence

The evidence upon which this recommendation is made is predominantly of low to very low quality by GRADE criteria. The evidence review included a total of 19 case review studies (plus an additional study which was consulted for baseline characteristics of another included study).

The evidence indicated that there was a choice between the Blatchford and the Rockall scores: these had been more extensively evaluated than any other scoring system, and performed well. Across the available studies, the Blatchford score appeared to be the better predictor of re-bleeding, and comparable with the Rockall for prediction of mortality.

The Rockall score was recognised as being well validated and already in widespread usage. Furthermore, there is a post-endoscopy Rockall score and although this is clearly not useful as a means of selecting patients for early discharge and later endoscopy, it is a useful score for prediction of mortality and patients at high risk of re-bleeding. However, the Blatchford score has emerged more recently, and in direct comparison to the Rockall score is a better predictor of re-bleeding and / or need for intervention. Although it was recognised that Units well versed in use of the Rockall might not wish to change, the guideline concluded that the evidence in favour of the Blatchford score in pre-endoscopy assessment could not be ignored and that its use should be recommended.

No health economic evidence was available to review. It was felt that there was unlikely to be significant incremental cost implications attached to the implementation of any of the scoring systems considered; however, it was noted that early discharge of patients with a pre-endoscopy Rockall or Blatchford score of 0, could result in reduced hospital stay and associated cost.

1.1.3 Patient experience

No patient experience information is presented, however it may be advantageous for some patients to be returned home earlier.

1.1.4 Patient safety

A patient safety incident is any unintended or unexpected incident which could have or did lead to harm for one or more patients receiving NHS care (see Appendix A). A comprehensive analysis of recent reported incidents (please see full accompanying report from the patient safety function at the NHS Commissioning Board Special Health Authority) identifies the following priority areas relating to patient safety:

- There is an incident in the sample that recognises the need for risk assessment, although in this case it had not been done.

It is clearly undesirable to routinely encourage the early discharge of patients where there is a risk of mortality or re-bleeding, but there are also obvious practical benefits to early discharge where this is safe. CG141 found that the lower scores on both scales were associated with little risk of adverse outcomes, but is not able to make a confident recommendation above a score of 0.

1.1.5 Current practice

NICE CG141 concludes that the most widely used scoring system in the UK is the Rockall score, which is recognised as being well validated and already in widespread usage.

The 2007 UK comparative audit of upper gastrointestinal bleeding and the use of blood from the British Society of Gastroenterology[1] (BSG) asks “Does your hospital routinely calculate and document a risk score (e.g. Rockall or Blatchford scores) for patients with suspected upper GI bleeding?” 50% said yes, 49% said no.

1.1.6 Current indicators

No current indicators are presented.

2 Timing of endoscopy – Immediate endoscopy for unstable patients

2.1 NICE CG141 Recommendation 1.3.1 [KPI]

2.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.3.1 Offer endoscopy to unstable patients with severe acute upper gastrointestinal bleeding immediately after resuscitation.
Proposed quality statement	People with unstable severe acute upper gastrointestinal bleeding are offered endoscopy immediately after resuscitation
Draft quality measure	**Structure:** Evidence of local arrangements to ensure people with unstable severe acute upper gastrointestinal bleeding are offered endoscopy immediately after resuscitation **Process:** The proportion of people with unstable severe acute upper gastrointestinal bleeding who receive endoscopy immediately after resuscitation Numerator – The number of people in the denominator who receive endoscopy immediately after resuscitation Denominator – The number of people with unstable severe acute upper gastrointestinal bleeding

2.1.2 Clinical and cost-effectiveness evidence

PLEASE NOTE THAT THE EVIDENCE PRESENTED IN THIS SECTION DISCUSSES TIMING OF ENDOSCOPY FOR BOTH HIGH-RISK (DRAFT STATEMENT 2) AND STABLE (DRAFT STATEMENT 3) PATIENTS

The optimal timing for endoscopy relates to the severity of bleeding.

The available clinical evidence in relation to the timing of endoscopy for either stable patients or unstable/high risk is predominantly of very low quality. The evidence for timing of endoscopy (early versus late) includes a total of 3 randomised control trials with timing to endoscopy ranging from 2 to 12 hours after admission to the emergency department compared to later endoscopy. The results of the review were analysed according to whether the patient population included patients at risk (according to hemodynamic factors, had co-morbid illnesses or those with variceal bleeding etc) or whether the study only used a ‘stable’ low risk patient population. The clinical papers did not show any consistent significant differences between timing strategies, and deliberations centred mainly on the health economic data.

One study considering health economics was identified. Due to the limited applicability of the identified study to the UK NHS setting, it was decided to

build an original economic model to compare four different strategies, three of which would allow for earlier endoscopy than currently observed in the UK's current practice. This model assessed the trade-off between the additional costs of implementing a wider service (key cost identified was additional staff hours), versus the potential savings which through early discharge and reduced length of stay. Data from the 2007 BSG audit[1] were used and 4 service models were identified:

- Endoscopy available 8am-5pm, Monday to Friday only;
- Endoscopy available 8am-5pm on Monday to Friday, and 8am-12pm on weekends;
- Endoscopy available 8am-5pm everyday, with oncall services between 5pm and 12am;
- Endoscopy available 8am-5pm everyday, with oncall services between 5pm-8am.

The evidence showed that for stable patients with low risk of mortality and rebleeding, endoscopy within the first 24 hours is likely to be more cost effective than endoscopy later than 24 hours. This is based in part on evidence with minor limitations and partial applicability, and in part on evidence with direct applicability and with potentially serious limitations.

The economic model suggested that the first two strategies listed above were optimal from a health economic point of view, and the provision of endoscopy services on weekend mornings in addition to those provided 8am-5pm on the weekday is likely to be cost-effective, provided that

- this allows all patients to be endoscoped within 24 hours of presentation and
- that the provider expects approximately 330 or more presentations of acute upper gastrointestinal bleed per year.

The economic analysis is based upon NHS costs, models of care and representative UK audit data – and therefore directly applicable. However as it is based on observational data, it potentially has serious limitations.

For the stable patient group, the output of the health economic model posed a problem, as offering endoscopy to patients within 24 hours only if they find themselves in a hospital with an annual caseload above 330 cases per year, and not if they are in a smaller unit, would be inequitable. The consensus view was that endoscopy within 24 hours should ideally be offered to all patients

[1] British Society of Gastroenterology (2007) "UK Comparative Audit of Upper Gastrointestinal Bleeding and the Use of Blood"

rather than a subgroup. However, it was noted there is a trade-off between staff costs of a daily service to provide a quick discharge and “hotel” costs of the wait to a slower discharge of a weekday service noting that smaller providers would need to explore these factors in deciding how best to provide services for stable patients. It is worth noting that the majority of endoscopies in the UK currently occur in units dealing with more than 330 cases per year.

Despite a lack of formal evidence on this issue (particularly as it would be unethical to delay an intervention for unstable patients), the experience of the guideline group for CG141 is that urgent endoscopy for unstable and high risk patients reduces mortality, length of hospital stay and transfusion requirements, and that this is intuitively the correct recommendation.

2.1.3 Patient experience

The advantages to patients and carers in terms of the peace of mind associated with rapid diagnosis (and intervention where appropriate) were acknowledged by CG141. Delayed endoscopy lengthens hospital stay.

2.1.4 Patient safety

A patient safety incident is any unintended or unexpected incident which could have or did lead to harm for one or more patients receiving NHS care (see Appendix A). A comprehensive analysis of recent reported incidents (please see full accompanying report from the patient safety function at the NHS Commissioning Board Special Health Authority) identifies the following priority areas relating to patient safety:

- There are incidents in the sample supporting that for a variety of reasons patients aren’t being offered immediate endoscopy. These include issues relating to access to endoscopy services as well as availability of clinicians.

Also, endoscopy is associated with complications, and whilst these are uncommon in the context of diagnostic endoscopy in relatively fit individuals, they are relatively common in patients who are actively bleeding and may be life threatening in unstable patients with medical co-morbidities. Patients should therefore be optimally resuscitated before endoscopy to minimise their risk of complications and the procedure should not be undertaken whenever possible until cardiovascular stability is achieved.

2.1.5 Current practice

The principle diagnostic test for patients with acute upper gastrointestinal bleeding is endoscopy. Endoscopy defines a specific cause for bleeding in more than 80% of cases, provides prognostic information and facilitates delivery of a range of haemostatic therapies.

CG141 states that patients who present with relatively trivial bleeding, who have no cardiovascular instability and are free from major medical co-morbidities, are at low risk of death yet are almost invariably admitted to hospital and may wait several days for semi-elective endoscopy.

The BSG audit[1] found 50% of patients had an endoscopy within 24 hours, 20% 24-71 hours, and 17% 72+ hours, with percentages almost exactly the same for those with a pre-endoscopy Rockall score of 3 or more (medium-high risk), therefore having a medium-high risk pre-endoscopy Rockall score appears to have no impact on the time to endoscopy.

2.1.6 Current indicators

No current indicators suggested.

3 Timing of endoscopy – endoscopy within 24 hours of admission

3.1 NICE CG141 Recommendations 1.3.2 and 1.3.3 [KPIs]

3.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.3.2 Offer endoscopy within 24 hours of admission to all other patients with upper gastrointestinal bleeding. 1.3.3 Units seeing more than 330 cases a year should offer daily endoscopy lists. Units seeing fewer than 330 cases a year should arrange their service according to local circumstances
Proposed quality statement	People with [non-urgent] acute upper gastrointestinal bleeding are offered endoscopy with 24 hours of admission.
Draft quality measure	**Structure:** a) Evidence of local arrangements to ensure people with non-urgent acute upper gastrointestinal bleeding are offered endoscopy within 24 hours of admission b) Evidence of local arrangements to ensure [units] seeing more than 330 cases a year offer daily endoscopy lists **Process:** The proportion of people with non-urgent acute upper gastrointestinal bleeding who receive endoscopy within 24 hours of admission Numerator – The number of people in the denominator who receive endoscopy within 24 hours of admission Denominator – The number of people with stable acute upper gastrointestinal bleeding

3.1.2 Clinical and cost-effectiveness evidence

Please see 2.1.2

3.1.3 Patient experience

Please see 2.1.3.

3.1.4 Patient safety

Please see 2.1.4.

3.1.5 Current practice

Please see 2.1.5.

3.1.6 Current indicators

Please see 2.1.6.

4 Management of non-variceal bleeding – endoscopic treatment

4.1 NICE CG141 Recommendation 1.4.2 [KPI]

4.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.4.2 For the endoscopic treatment of non-variceal upper gastrointestinal bleeding, use one of the following: • a mechanical method (for example, clips) with or without adrenaline • thermal coagulation with adrenaline • fibrin or thrombin with adrenaline.
Proposed quality statement	People with non-variceal upper gastrointestinal bleeding are offered [endoscopic treatment]
Draft quality measure	**Structure:** Evidence of local arrangements to ensure people with non-variceal upper gastrointestinal bleeding are offered endoscopic treatment **Process:** The proportion of people with non-variceal upper gastrointestinal bleeding who receive one of the following: a mechanical method (for example, clips) with or without adrenaline; thermal coagulation with adrenaline; fibrin or thrombin with adrenaline. Numerator – The number of people in the denominator who receive one of the following: a mechanical method (for example, clips) with or without adrenaline; thermal coagulation with adrenaline; fibrin or thrombin with adrenaline. Denominator – The number of people with non-variceal upper gastrointestinal bleeding

4.1.2 Clinical and cost-effectiveness evidence

The evidence review for this in CG141 considers whether combinations of endoscopic treatments alone are more clinically/cost effective than adrenaline injection alone in patients with non-variceal upper gastrointestinal bleeding.

Three approaches to endoscopic therapy for non-variceal bleeding were examined in clinical trials. The trials focused upon peptic ulcer bleeding and have included patients with active, arterial haemorrhage and other major stigmata of recent haemorrhage (a visible vessel and adherent blood clot), but it is reasonable to conclude that other causes of non-variceal bleeding including selected patients with Mallory Weiss tears or those with vascular malformations may also respond to endoscopic therapy. The three approaches were:

1. Injection into the bleeding point of either dilute adrenaline (to induce vasoconstriction of the bleeding artery) or thrombin (to thrombose the bleeding artery)

2. Coagulation of the bleeding point, either by diathermy or direct application of heat (the 'heater probe' or Argon Plasma Coagulation).

3. Mechanical occlusion of the bleeding point, principally by endoscopic application of clips.

Randomised clinical trials generally show that each of these approaches can control active bleeding, reduce the rate of re-bleeding and need for blood transfusion compared to patients not receiving endoscopic therapy. It is more difficult to show survival benefit, although this has been demonstrated in meta-analyses. Trials have failed to show superiority of any one approach and clinical experience has shown that these three approaches should not be regarded as competitors; rather they should be considered to be complementary. For example it may be relatively easy to inject or coagulate a bleeding ulcer at the junction of the first and second part of the duodenum, but very difficult to apply a clip, whilst an obvious protruding vessel within a lesser curve gastric ulcer can be a relatively easy target for clip application. Endoscopists should therefore have a range of therapies that can be tailored according to clinical need.

Nine randomised control studies were identified and one Cochrane review was cross-referenced. Four of those compared adrenaline in combination with a mechanical endoscopic method, two used the adrenaline and thermal combination and three further studies investigated adrenaline with thrombin injection; all of these compared the combined treatments to adrenaline alone. The aim of all these papers was to assess a combination of endoscopic procedures were the more effective means than adrenaline injection alone to improve outcomes in patients with non-variceal UGIB. One further study was included which compared to adrenaline combinations to each other (adrenaline plus thermal versus adrenaline plus mechanical). The formal evidence was usually of low or very-low quality by GRADE criteria, but it was felt that the studies had been reasonably well-performed allowing for the difficulties of performing RCT's in acutely ill patient groups.

It was considered whether to recommend any particular combination as being superior to others but this was not possible. Technically, the guideline development group agreed that there can be situations where it easier to use one method than another (where hemoclip as monotherapy can be very effective), but this is not consistent between patients, depending on variables such as site and depth of the bleeding ulcer. They therefore felt that use of a combination of treatment modes should be recommended, but that different

forms of treatment should be available for use in the varied situations which an endoscopist might face.

Mortality data was available for this question and did not show a significant difference between combination and single modes of treatment for bleeding ulcers. However, it was uncertain whether the numbers in the studies were sufficiently powered to show a mortality difference given the relatively low mortality rates observed in the study populations. The studies showed that re-bleeding rates were significantly lower when two forms of treatment were employed, rather than one or either treatment used alone. Securing initial haemostasis was not significantly improved with combination therapy, but the need for further emergency procedures after initial endoscopy was reduced; this outcome is likely to be influenced strongly by both immediate haemostasis and the rate of re-bleeding.

Length of hospital stay tended to be less when combination treatments were used, but was not significantly reduced.

No formal health economic evidence was found. The treatment modalities which might be used in addition to adrenaline injection are not likely to be significantly different in terms of unit cost, as they are considered to have similar resource use. The reductions in re-bleeding and the need for further emergency interventions found with the use of combination treatments compared to adrenaline alone imply that the additional cost of adjunctive treatment may be at least partially offset by reduced down stream health related resource use and associated cost.

4.1.3 Patient experience

No patient experience information is presented.

4.1.4 Patient safety

A patient safety incident is any unintended or unexpected incident which could have or did lead to harm for one or more patients receiving NHS care (see Appendix A). A comprehensive analysis of recent reported incidents (please see full accompanying report from the patient safety function at the NHS Commissioning Board Special Health Authority) finds that there are no incidents in the sample supporting this statement.

Adverse effects of the different forms of treatment were not compared in the papers. The experience of the guideline group for CG141 is that these are very rare. The group discussed whether they could define a safe upper dose of adrenaline, but concluded that there was no secure data on which to base such a recommendation.

4.1.5 Current practice

The BSG audit[1] asks “Were any therapeutic endoscopic procedures undertaken?” 23% stated yes, 75% stated no. It concludes that the use of therapeutic endoscopy and medical therapies after endoscopy is disappointingly low.

4.1.6 Current indicators

No current indicators are presented.

5 Management of non-variceal bleeding – Proton pump inhibitors

5.1 NICE CG141 Recommendations 1.4.4

5.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.4.4 Offer proton pump inhibitors to patients with non-variceal upper gastrointestinal bleeding and stigmata of recent haemorrhage shown at endoscopy
Proposed quality statement	People with non-variceal upper gastrointestinal bleeding and stigmata of recent haemorrhage shown at endoscopy are offered proton pump inhibitors
Draft quality measure	**Structure:** Evidence of local arrangements to ensure people with non-variceal upper gastrointestinal bleeding and stigmata of recent haemorrhage shown at endoscopy are offered proton pump inhibitors **Process:** The proportion of people with non-variceal upper gastrointestinal bleeding and stigmata of recent haemorrhage shown at endoscopy who receive proton pump inhibitors Numerator – The number of people in the denominator receive proton pump inhibitors Denominator – The number of people with non-variceal upper gastrointestinal bleeding and stigmata of recent haemorrhage shown at endoscopy

5.1.2 Clinical and cost-effectiveness evidence

NICE CG141 considers whether all patients should receive acid suppressing drugs when they present with haematesis or melaena, or whether these drugs should only be used in patients who, at endoscopy, have either active bleeding or major stigmata of recent haemorrhage. The first approach ensures that all patients at greatest risk of uncontrolled bleeding receive potentially effective drug therapy, but this is probably wasteful since approximately 80% of ulcers stop bleeding without any form of intervention and do not re-bleed. Powerful acid suppression may therefore be unnecessary in these patients, at least in improving the prognosis of the acute event, although standard doses of PPIs or H2 receptor antagonists clearly have a role in ulcer healing.

32 RCTs were identified and two Cochrane meta-analyses were cross-referenced, and additionally one Health Technology Appraisal. There were two main clinical questions for this section:

- Are Proton Pump Inhibitors (PPIs) the most clinical / cost effective pharmaceutical treatment, compared to H2-receptor antagonists (H2-

RAs) or placebo, to improve outcome in patients presenting with likely non-variceal Upper Gastrointestinal Bleeding (UGIB) prior and after endoscopic investigation?

- Are proton pump inhibitors administered intravenously more clinical / cost effective than the same agents administered in tablet form for patients with likely non-variceal upper gastrointestinal bleeding?

CG141 does not explore the cost-effectiveness of PPIs versus H2-RAs or placebo pre-endoscopy, as it concludes from the clinical review that there is no benefit from these agents when given routinely pre-endoscopy. In consideration of the use of acid suppressing drugs post-endoscopy, two studies were included as relevant. In regard to the use of acid suppression treatment pre and post-endoscopy, seven studies were selectively excluded due to their limited applicability to the UK setting. Results from the analysis by one study showed that, for patients with likely non-variceal upper gastrointestinal bleeding, the most cost-effective strategy is to offer oral PPI before and after endoscopy, in hospital and at discharge. In addition, haemostatic therapy should be offered at endoscopy to patients with major stigmata of recent haemorrhage. This superior strategy presents, at 28 days, a cost-effectiveness ratio of £24,300 per QALY gained, which is slightly higher than the NICE threshold of £20,000 per QALY gained. When looking at the cost-effectiveness ratio from the lifetime analysis of £140 per LY gained, and considering the utility scores applied to the 28-day analysis (0.45 when the patient is hospitalised and 0.78 when at home), the cost-effectiveness ratio in cost per QALY gain is lower than the NICE threshold of £20,000. However, the mortality rates used in this analysis were considered high, thereby potentially biasing the results.

Results from another paper showed that, for patient with high-risk peptic ulcer haemorrhage in whom successful endoscopic haemostasis was performed, oral PPI is the preferred option compared with IV PPI and IV H2 receptor antagonist. IV PPI is not cost effective compared with oral PPI, even under conservative assumptions favouring IV PPI. The superiority of oral PPI compared with IV PPI is mainly explained by the lower cost of the treatment, a shorter hospital stay, and a higher QALY gained in shortening the hospital length of stay. The reduced length of hospital stay may have in part been driven by the assumption IV PPI administration requires an extra day to oral PPIs. H2 receptor antagonists were found to be more costly and less effective than PPI strategies. This analysis was developed from a US perspective; therefore the applicability of the results to the UK NHS is questionable.

When PPIs are considered specifically in the context of routine administration prior to endoscopy in patients with suspected non- variceal bleeding, there is no statistically or clinically significant evidence that acid suppression therapy is beneficial in relation to any of the considered outcomes.

When the results of the endoscopy are known, the considered evidence demonstrates statistically and clinically significant benefit of proton pump inhibitors, compared to placebo. Benefit was seen across all outcomes except mortality where there was a trend in favour of PPI which did not reach statistical significance. Proton pump inhibitors were also demonstrably superior to H2 receptor antagonists when considering re-bleeding, surgery and length of hospital stay but not mortality and blood transfusion requirements.

The evidence from Leontiadis et al (2007) suggests that giving oral PPI pre-endoscopy is a cost effective strategy when compared with doing nothing or giving intravenous PPIs prior to endoscopy. However, in light of the findings of the clinical review, the guideline development group felt that the model could have potentially serious limitations. There is no available evidence that makes a direct comparison between the administration of oral and iv. PPI prior to endoscopy. The best available evidence used in the Leontiadis model compares the interventions to placebo and infers that oral PPIs are superior to iv PPI; as one trial showed a trend of decreased risk of mortality for the former, and another single trial showed a trend towards increased risk in the latter. However, the guideline development group noted this contrasted to the evidence in the clinical review which made a direct comparison of oral versus iv administration of PPIs post-endoscopy, where there was not a significant difference in outcome between the two interventions. Using the overview of evidence provided by the clinical review, it was questioned whether there was sufficient evidence to be able to subgroup on the basis of administration of the PPI prior to endoscopy, as had been done in the one study.

In the clinical review, where the interventions had not been sub grouped, there was not a clinical or statistical difference between placebo and PPI in outcome, including those which would infer downstream cost.

CG141 notes that a ‘do nothing’ approach prior to endoscopy would not incur acquisition costs of the drug itself, and that there was no conclusive evidence that downstream costs would be higher with this approach.

In consideration of the cost effectiveness of H2-receptor antagonist to PPIs given post-endoscopy, the available analysis by one paper demonstrates the superior cost-effectiveness of proton pump inhibitors over H2-receptor antagonists.

The guideline notes that proton pump inhibitors administered pre-endoscopy reduce the incidence of major stigmata or recent haemorrhage. However the evidence suggests that this does not translate into improved clinical outcomes.

The guideline development group debated and agreed that acid suppression therapy should not be use as a 'holding measure' to replace or delay early endoscopic therapy.

Overall, CG141 is able to recommend the use of PPI when there is evidence of recent bleeding at endoscopy. In patients with non-variceal upper GI bleeding where endoscopy does not demonstrate stigmata of recent haemorrhage clinicians should consider existing NICE guidance, including that relating to the management of dyspepsia and osteoarthritis, and offer acid suppression therapy as indicated in that guidance.

The considered evidence does not demonstrate a statistically or clinically significant difference between oral and intravenous proton pump inhibitors across all outcomes. CG141 concludes either route of administration could be cost effective. Although direct comparisons exist, the quality of evidence comparing oral and intravenous proton pump inhibitors is of very low quality, and consequently it is inadequate to allow firm conclusions to be drawn.

5.1.3 Patient experience

No patient experience information is presented.

5.1.4 Patient safety

A patient safety incident is any unintended or unexpected incident which could have or did lead to harm for one or more patients receiving NHS care (see Appendix A). A comprehensive analysis of recent reported incidents (please see full accompanying report from the patient safety function at the NHS Commissioning Board Special Health Authority) identifies the following priority areas relating to patient safety.

- There is evidence that proton pump inhibitors are prescribed but being omitted and delayed in administration or that there is a failure to prescribe a PPI when it is indicated.

5.1.5 Current practice

BSG audit[1]: Intravenous PPIs were started in 70% of patients with an ulcer who received endoscopic therapy at the first endoscopy (460/656), and were also administered to 16% of patients where no ulcer was documented (147/928).

Intravenous (iv) PPI was given to 48% (3225/6750) of all patients in the audit (including those who did not have an endoscopy). 89% (2885/3225) of these were given iv PPI prior to any endoscopy. 6% (308/5004 - denominator is those having endoscopy) were given or continued on iv PPI despite not receiving endoscopic therapy nor having an endoscopic high risk lesion.

This suggests high levels of inappropriate use of iv PPI.

5.1.6 Current indicators

No current indicators are presented.

6 Management of non-variceal bleeding – treatment after first or failed endoscopic treatment (repeat endoscopy)

6.1 NICE CG141 Recommendation 1.4.5

6.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.4.5 Consider a repeat endoscopy, with treatment as appropriate, for all patients at high risk of re-bleeding, particularly if there is doubt about adequate haemostasis at the first endoscopy.
Proposed quality statement	People with non-variceal upper gastrointestinal bleeding who have received first or failed endoscopic treatment [who are at high risk of re-bleeding] are [considered for] repeat endoscopy [with treatment as appropriate?]
Draft quality measure	**Structure:** Evidence of local arrangements to ensure people with non-variceal upper gastrointestinal bleeding who have received first or failed endoscopic treatment are considered for repeat endoscopy **Process:** The proportion of people with non-variceal upper gastrointestinal bleeding, who are at high risk of re-bleeding and who have received first or failed endoscopic treatment, who are considered for repeat endoscopy Numerator – The number of people in the denominator are considered for repeat endoscopy Denominator – The number of people with non-variceal upper gastrointestinal bleeding, who are at high risk of re-bleeding and who have received first or failed endoscopic treatment

6.1.2 Clinical and cost-effectiveness evidence

By GRADE criteria the evidence on this question was low to moderate. It was felt that these studies had been reasonably well performed, but also noted that they were several years old and that techniques for arresting bleeding at endoscopy have improved in recent years. The chances of being able to secure haemostasis at first endoscopy are therefore greater that when these studies were performed, which would tend to reduce the benefit of a routine second procedure.

Mortality is clearly the most important outcome, but the GDG were not expecting, nor did they find, any difference in mortality based on routine performance of a second endoscopy. The debate centred around risk and identification of re-bleeding within the first 30 days of endoscopy, with a reduction in those undergoing a second endoscopy. There were no other

significant differences, although in general the trends favoured a second endoscopy for most outcomes. The potential benefit of a repeat endoscopy is the early identification of re-bleeding (or continued bleeding). Endoscopy is a generally safe procedure, and therefore the potential harm involved in this question is principally that related to delay in treating any re-bleeding.

The only economic paper available suggested that a routine second look endoscopy was not cost-effective, but that selective elective re-endoscopy was worthwhile in patients in whom the risk of re-bleeding was high (based on a Baylor score, which is not used in the UK but which the GDG felt to be equivalent to a high risk patient using the post-endoscopy Rockall score). The study was performed in the USA and is therefore not directly transferable to a UK population.

The guideline notes that the evidence dealt with re-endoscopy within 24 hours. To provide this would necessitate availability of endoscopy services at weekend, and this is not routinely available in the UK at present. The set-up cost of a recommendation in favour of routine re-endoscopy would be considerable and not justified by the current evidence. However, the GDG also noted that provision of endoscopy services is an important consideration for other recommendations within this guideline. If endoscopy service provision increases in line with other recommendations in the guideline, the incremental cost of providing second look endoscopy will be less. In light of the cumulative evidence and recommendations made in previous chapters, the GDG came to a consensus that the increased levels of endoscopy service required to enable a second look endoscopy in high risk patients was likely to be cost effective.

The guideline development group were not unanimous in their assessment of this evidence, some feeling that the reduction in re-bleeding and the health economic benefits should lead to a positive recommendation in favour of second-look endoscopy, others feeling that the benefits were not sufficient to justify a considerable change in current practice (at present, unless a patient has clearly bled again, repeat endoscopy would only be arranged if the endoscopist feels that the first procedure is unlikely to have secured anything more than temporary haemostasis). They agreed to couch a recommendation in terms which encourages a more pro-active approach in patients at high risk of re-bleeding, but without making this obligatory

In patients with non-variceal upper gastrointestinal bleeding after first endoscopic treatment, is a routine second-look endoscopy more clinically / cost effective than routine clinical follow-up?

6.1.3 Patient experience

No patient experience information is presented.

6.1.4 Patient safety

A patient safety incident is any unintended or unexpected incident which could have or did lead to harm for one or more patients receiving NHS care (see Appendix A). A comprehensive analysis of recent reported incidents (please see full accompanying report from the patient safety function at the NHS Commissioning Board Special Health Authority) identifies the following priority areas relating to patient safety.

- There is an incident in the sample supporting this statement

Repeated endoscopic therapies could increase the risk of ulcer perforation.

Failed primary haemostasis and re-bleeding are associated with high mortality; in the National UK audit[1] there was a 30% post operative mortality in patients undergoing emergency surgery for uncontrolled ulcer bleeding. Death is rarely due to exsanguination but occurs in the majority of cases either because of decompensation of medical co-morbidity (cardiac events in patients with coronary artery disease, stroke in patients with cerebrovascular disease, renal failure in patients with pre-existing kidney disease etc) or because of a post operative complication after emergency surgery. Management of these critically ill patients is best undertaken by a multi-disciplinary team in a high dependency setting with discussion involving gastroenterologists, surgeons and, where available, interventional radiologists.

6.1.5 Current practice

Failed primary haemostasis and re-bleeding are associated with high mortality; in the National UK[1] audit there was a 30% post operative mortality in patients undergoing emergency surgery for uncontrolled ulcer bleeding

The BSG audit[1] finds that in all categories, the number of repeat endoscopies was low, with less than a third of cases getting repeat procedures. The reasons for these low levels of therapy and repeat procedures need investigation.

CG141 notes that the evidence dealt with re-endoscopy within 24 hours. To provide this would necessitate availability of endoscopy services at weekend, and this is not routinely available in the UK at present. The set-up cost of a recommendation in favour of routine re-endoscopy would be considerable and not justified by the current evidence.

6.1.6 Current indicators

No current indicators are presented.

7 Management of non-variceal bleeding – Treatment after first or failed endoscopic treatment (interventional radiology)

7.1 NICE CG141 Recommendation 1.4.7 [KPI]

7.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.4.7 Offer interventional radiology to unstable patients who re-bleed after endoscopic treatment. Refer urgently for surgery if interventional radiology is not promptly available.
Proposed quality statement	People with unstable non-variceal acute upper gastrointestinal bleeding who re-bleed after endoscopic treatment are offered interventional radiology, or urgent referral for surgery if interventional radiology is not [promptly] available
Draft quality measure	**Structure:** Evidence of local arrangements to ensure people with unstable acute upper gastrointestinal bleeding who re-bleed after endoscopic treatment are offered interventional radiology, or urgent referral for surgery if interventional radiology is not [promptly] available **Process:** a) The proportion of people with unstable acute upper gastrointestinal bleeding who re-bleed after endoscopic treatment who receive interventional radiology Numerator – The number of people in the denominator who receive either interventional radiology, or urgent referral if interventional radiology is not [promptly] available Denominator – The number of people with unstable acute upper gastrointestinal bleeding who re-bleed after endoscopic treatment b) The proportion of people with unstable acute upper gastrointestinal bleeding who re-bleed after endoscopic treatment, and for whom interventional radiology is not [promptly] available, who receive urgent referral for surgery Numerator – The number of people in the denominator who receive urgent referral for surgery Denominator – The number of people with unstable acute upper gastrointestinal bleeding who re-bleed after endoscopic treatment, and for whom interventional radiology is not [promptly] available.

7.1.2 Clinical and cost-effectiveness evidence

Evidence from 5 observational studies (not pooled) with 70, 91, 46, 97 and 88 participants respectively, were used for the comparison between embolisation and surgery for patients in whom first line treatment failed to achieve

haemostasis. The guideline recognised that a truly randomised study on this question would be very difficult to perform because the two procedures are so different and each would appear to have definite advantages in certain circumstances, and because skill and experience of the radiologists and surgeons would have to be taken into account. The studies had all the well recognised problems that follow with non-controlled data.

A difference was noted in re-bleeding rates, in favour of surgery rather than embolisation under radiological guidance, but all other outcome measure showed no difference between the two treatment modalities. It was not felt that this outcome alone, measured at 3-days post-procedure, was sufficient evidence to prompt a clear recommendation.

It was noted that, even if the slight difference in favour of surgery was accepted, surgical procedures are not advisable in some circumstances because the patient poses too great an anaesthetic/operative risk.

No health economic evidence was available for this question.

Given the absence of any good quality controlled evidence, CG141 considers the practical issues which would follow from any recommendation. It notes that some people were poor operative risks, for a variety of possible reasons, and that successful embolisation was potentially the safer procedure. There was a strong consensus view that this should be tried first (encompassing all professional groups and the patient representatives). However, at present not all hospitals can offer appropriate interventional radiology. The guideline development group did not wish to make a recommendation which would prevent timely surgery when an appropriately skilled interventional radiologist was not available, and formed a recommendation which emphasises the need for prompt action whichever treatment modality is to be employed.

7.1.3 Patient experience

No patient experience information is presented.

7.1.4 Patient safety

A patient safety incident is any unintended or unexpected incident which could have or did lead to harm for one or more patients receiving NHS care (see Appendix A). A comprehensive analysis of recent reported incidents (please see full accompanying report from the patient safety function at the NHS Commissioning Board Special Health Authority) identifies the following priority areas relating to patient safety:

- There is evidence to support that patients are urgently referred for surgery but the incidents do not clarify if they have previously had endoscopic treatment.

7.1.5 Current practice

The BSG audit[1] finds that 3% of people with upper gastrointestinal bleeding had surgery or radiological intervention to control.

7.1.6 Current indicators

No current indicators are presented.

8 Management of variceal bleeding – prophylactic antibiotic therapy

8.1 NICE CG141 Recommendation 1.5.2 [KPI]

8.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.5.2 Offer prophylactic antibiotic therapy at presentation to patients with suspected or confirmed variceal bleeding.
Proposed quality statement	People with suspected or confirmed variceal [acute upper gastrointestinal] bleeding are offered prophylactic antibiotic therapy at presentation
Draft quality measure	**Structure:** Evidence of local arrangements to ensure people with suspected or confirmed variceal acute upper gastrointestinal bleeding are offered prophylactic antibiotic therapy at presentation **Process:** The proportion of people with suspected or confirmed variceal acute upper gastrointestinal bleeding who receive prophylactic antibiotic therapy at presentation Numerator – The number of people in the denominator who receive prophylactic antibiotic therapy at presentation Denominator – The number of people with suspected or confirmed variceal acute upper gastrointestinal bleeding

8.1.2 Clinical and cost-effectiveness evidence

Nine randomised control studies were identified and one Cochrane review was cross-referenced. The GRADE quality for the reviewed outcomes was generally low to very low. However, the guideline development group felt that these studies were well conducted given the difficulties of research in this acutely ill patient group.

One health economic study was identified that included the relevant comparison. A randomised controlled trial with a cost component was identified. The study was felt to have potentially serious limitations, particularly with randomisation. Additionally the study did not include a quality of life assessment and only considered the antibiotic cost. This and the short timeframe meant potential benefits of antibiotic prophylaxis noted in the clinical review may not have been fully captured. It was also noted that this relatively old study did not explore the potential cost associated with antibiotic resistance.

The study supported the cost effectiveness of prophylactic antibiotic administration to patients with Child's C cirrhosis, considered at high risk of infection, due to reduced incidence of infection and associated costs of

antibiotic treatment. It was also noted antibiotic prophylaxis reduced the incidence of re-bleeding and the associated costs of transfusion and hospital stay.

Overall it was felt that the use of antibiotics in this setting was likely to be cost effective and even cost saving.

It was felt that the evidence demonstrated a significant beneficial effect for prophylactic antibiotic therapy for patients with variceal bleeding. However, concern was expressed that widespread use of antibiotic therapy could lead to increased rates of antibiotic resistance. Indeed there was some anecdotal evidence from some clinicians that this was occurring. Additionally members of the guideline development group worried that increasing the prevalence of antibiotic use in this patient group risked a corresponding rise in the prevalence of Methicillin-resistant staphylococcus aureus (MRSA) and Clostridium difficile infections. Although these were not reported as specific outcomes in any of the trials evaluated, the guideline development group was somewhat reassured that the rates of significant infections with these organisms were unlikely to be greatly increased in the studies since these showed lower overall rates of infections and duration of hospital stay with prophylactic antibiotic use. Additionally it was felt that overall the number of patients admitted with variceal bleeding was small when considered in the context of all patients admitted to hospital on antibiotic therapy. Nonetheless it was felt a watchful eye needed to be kept on the situation.

8.1.3 Patient experience

No patient experience information is presented.

8.1.4 Patient safety

A patient safety incident is any unintended or unexpected incident which could have or did lead to harm for one or more patients receiving NHS care (see Appendix A). A comprehensive analysis of recent reported incidents (please see full accompanying report from the patient safety function at the NHS Commissioning Board Special Health Authority) found:

- No evidence could be identified to inform this quality statement.

The hospital mortality of patients presenting with acute variceal bleeding is closely related to the severity of liver disease, rising to 30% in those with Childs-Pugh cirrhosis (Grade C). Bleeding can be very severe and, particularly in patients with advanced cirrhosis, cause renal failure that has a very poor prognosis. These patients are also prone to develop infection. This is related to defective immunological function and to trans-location of bacteria from the gastrointestinal tract into the peritoneal cavity leading to spontaneous bacterial peritonitis. Infection has adverse effects on renal function and

commonly precipitates hepatorenal failure, characterised by oligurea, sodium and fluid retention and death

The benefits of preventing infection, particularly spontaneous bacterial colonisation, have to be balanced against the risks of complications such as Clostridium Difficile infection and development of resistant bacterial species

8.1.5 Current practice

No current practice information is presented.

8.1.6 Current indicators

No current indicators are presented.

9 Management of variceal bleeding – endoscopic treatment

9.1 NICE CG141 Recommendation 1.5.3 and 1.5.5

9.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.5.3 Use band ligation in patients with upper gastrointestinal bleeding from oesophageal varices 1.5.5 Offer endoscopic injection of N-butyl-2-cyanoacrylate to patients with upper gastrointestinal bleeding from gastric varices.
Proposed quality statement	People with bleeding from upper gastrointestinal oesophageal or gastric varices are offered [endoscopic treatment] OR TWO SEPARATE STATEMENTS People with upper gastrointestinal bleeding from oesophageal varices are offered band ligation People with gastric varices are offered endoscopic injection of N-butyl-2-cyanoacrylate
Draft quality measure	**Structure:** Evidence of local arrangements to ensure people with bleeding from upper gastrointestinal oesophageal or gastric varices are offered [endoscopic treatment] **Process:** a) The proportion of people with upper gastrointestinal bleeding from oesophageal varices who receive band litigation Numerator – The number of people in the denominator who receive band litigation Denominator – The number of people with upper gastrointestinal bleeding from oesophageal varices b) The proportion of people with upper gastrointestinal bleeding from gastric varices who receive endoscopic injection of N-butyl-2-cyanoacrylate Numerator – The number of people in the denominator who receive endoscopic injection of N-butyl-2-cyanoacrylate Denominator – The number of people with upper gastrointestinal bleeding from gastric varices

9.1.2 Clinical and cost-effectiveness evidence

Band ligation

CG141 asks the following clinical question:

In patients with confirmed oesophageal varices is band ligation superior to injection sclerotherapy in terms of re-bleeding and death?

Seventeen randomised controlled trials compared ligation with injection sclerotherapy in patients with bleeding oesophageal varices, by GRADE criteria the evidence on this question was low to very low.

A significant mortality benefit for band ligation over injection sclerotherapy was seen. Band ligation was also significantly superior to injection sclerotherapy when considering the outcomes of re-bleeding, numbers of additional procedures required to control bleeding, total units of blood transfused, and the number of sessions of treatment required to eradicate varices.

One health economic study, which was also included in the clinical review, was identified that included the relevant comparison.

The only economic paper addressing this topic favoured injection sclerotherapy over band ligation. No quality of life analysis was performed. The results of the clinical study on which the economic analysis was based ran contrary to all others in the clinical evidence analysis. It was felt that the clinical study had potentially serious limitations including a baseline inequivalence favouring sclerotherapy, since those in the band ligation group had a greater prevalence of very large varices.

In discussion the GDG did not feel that there was significant cost difference between a session of band ligation or sclerotherapy. Given the finding that fewer band ligation sessions were required to eradicate varices it was felt that its widespread adoption would be cost-saving.

It was felt that band ligation should be first-line therapy in all patients with upper gastrointestinal bleeding due to oesophageal varices. However the guideline development group did not feel that there was sufficient evidence to make a recommendation against the use of injection sclerotherapy because, very occasionally in a patient with particularly dramatic bleeding it might not be possible to secure haemostasis by banding, in which case sclerotherapy might reasonably be attempted.

N-butyl-2-cyanoacrylate

PLEASE NOTE THAT THE EVIDENCE PRESENTED IN THIS SECTION DISCUSSES ENDOSCOPIC INJECTION OF N-BUTYL-2-CYANOACRYLATE, AND TIPS IF BLEEDING FROM GASTRIC VARICES IS NOT CONTROLLED BY ENDOSCOPIC INJECTION OF N-BUTYL-2-CYANOACRYLATE.

The clinical question used to develop this recommendation was:

In patients with confirmed gastric variceal bleeding which initial treatment (endoscopic injection of glue or thrombin and/or transjugular intrahepatic portosystemic shunts [TIPS]) is the most clinical and cost effective to improve outcome?

Four randomised control studies were identified. Three of those had a study population consisting of patients with variceal bleeding of either oesophageal or gastric origin. These studies were included in the review as a mixed variceal subgroup (oesophageal and gastric) and therefore represent indirect evidence. The fourth study featured only patients with gastric varices and was therefore directly applicable; it used injection of glue as a comparator to TIPS treatment. This is classified as direct evidence since the patient population directly matched the group specified in the protocol. The aim of all papers was to assess whether TIPS is more effective than alternative treatments (sclerotherapy, banding, and glue injection) to improve outcomes. The GRADE quality categories were noted. In general the guideline felt that these studies were well conducted given the difficulties of research in this acutely ill patient group. They noted however that the studies performed in the 1990's will have used uncovered stents not purposely designed for TIPS, and therefore may not reflect the benefits which can be achieved now.

Overall the studies showed no mortality difference between TIPS and endoscopic therapy for bleeding gastric varices (endoscopic treatment typically comprises endoscopic injection of N-butyl-2-cyanoacrylate). However, the GDG noted a difference between the studies, in that one study employed TIPS at presentation, whereas in other studies it was only used after other attempts to control acute bleeding. The former study showed a mortality benefit from early TIPS.

There appeared also to be advantages to the use of TIPS in terms of re-bleeding and total blood transfusion requirements (both statistically significant although the improvement in re-bleeding rate was modest).

The outcome measure "unresolved varices" appeared to favour endoscopic injection of N-butyl-2-cyanoacrylate. However, it was felt that this measure was of debatable value since sclerotherapy can lead to encasement of varices and thus give a spurious impression of resolution.

There was no noteworthy difference in length of hospital stay

One health economic study was identified that included the relevant comparators of endoscopic glue injection and TIPS. Unfortunately this was a retrospective study from a Unit in which patients were treated with TIPS until 1999 and then treated using sclerotherapy, with the obvious potential for confounding by other time-related changes in medical management (and indeed other non-medical factors, since time to discharge was an important

component of the results and this may have been influenced by increasing pressures on hospital beds). Moreover, there was no Quality of Life measurement within the study. The guideline development group agreed that TIPS is a more expensive procedure than sclerotherapy.

The guideline development group were of the opinion that TIPS is the preferred option for bleeding gastric varices, and the available evidence supports this view. In practice patients will always have an endoscopy to assess the source of bleeding, and an attempt to stop the bleeding at that endoscopy is clearly appropriate rather than leaving the bleeding site alone and proceeding to immediately arrange TIPS. However, the GDG felt that TIPS should be the next procedure if bleeding continues.

The guideline development group were aware that there are other materials than N-butyl-2-cyanoacrylate which might be used or have been used for endoscopic sclerotherapy procedures. However, these are currently either not available or are more expensive. Moreover, most of the evidence reviewed related to N-butyl-2-cyanoacrylate.

At present not all hospitals receiving patients with GI bleeding have the facility to perform TIPS. The expense of the procedure and of setting up the facility at all sites was discussed, noting the relative rarity of bleeding gastric varices among causes of upper GI bleeding. The GDG felt that it would be preferable to establish networks in localities or regions, designed to permit rapid transfer of appropriate patients to centres with the relevant expertise. However, this need should not prevent them making a recommendation in favour of availability of TIPS.

9.1.3 Patient experience

No patient experience information is presented.

9.1.4 Patient safety

A patient safety incident is any unintended or unexpected incident which could have or did lead to harm for one or more patients receiving NHS care (see Appendix A). A comprehensive analysis of recent reported incidents (please see full accompanying report from the patient safety function at the NHS Commissioning Board Special Health Authority) found:

- There are incidents in the sample that describe complications of patients having had band ligation and injection of varices.
- No incidents involving endoscopic injection in the context of varices were found

Injection sclerotherapy can cause oesophageal strictures in an appreciable minority of cases, and this is not observed with band ligation

The incidence of encephalopathy was increased after TIPS in comparison to treatment with endoscopic injection of N-butyl-2-cyanoacrylate. The encephalopathy is not necessarily acute and obvious; the guideline development group were aware of case series demonstrating chronic low-grade mental impairment.

Concerns have been raised about sepsis after TIPS, but the studies did not demonstrate any significant increase

9.1.5 Current practice

The 2007 BSG audit[1] found that for one-third (35%, (517-335)/517) of patients presenting with AUGIB with oesophageal varices at the first endoscopy, no endoscopic therapy was provided. This is not in line with the BSG guidelines for the management of variceal haemorrhage. However, this may be consistent with the findings of the organisational audit, that 26% of consultant endoscopists performing out of hours endoscopy, are not able to perform all therapeutic procedures. This is an area that needs attention and might be a measure for the quality of the out of hours endoscopy service for future audits.

The audit found that variceal banding was used consistently more often than variceal sclerotherapy (6% vs. 1% at first endoscopy), and 0.1% received glue injection at first endoscopy.

What endoscopic therapeutic procedures were administered? (Q77,Q78)	National Audit FIRST Endoscopy (5004)		SECOND Endoscopy (590)		THIRD Endoscopy (91)		Your site FIRST Endoscopy (21)	
	%	N	%	N	%	N	%	N
Data known		4942		580		91		20
Any therapeutic procedure	24	1172	43	250	51	46	29	6
Ulcer base injection	14	684	16	92	13	12		4
BICAP / heater probe	4	186	5	31	4	4		
Endoclip(s) applied	3	148	5	29	8	7		
Glue injection	0.1	7	1	6	4	4		
APC	2	93	4	23	4	4		
Variceal sclerotherapy	1	53	3	19	9	8		
Variceal banding	6	283	15	91	20	18		2
Others	2	77	6	34	7	6		
More than one of above (excluding variceal therapies)	6	315	8	47	5	5		

Source: BSG audit[1]

9.1.6 Current indicators

No current indicators are presented.

10 Management of variceal bleeding – TIPS

10.1 NICE CG141 Recommendations 1.5.4 [KPI] and 1.5.6

10.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.5.4 Consider transjugular intrahepatic portosystemic shunts (TIPS) if bleeding from oesophageal varices is not controlled by band ligation. 1.5.6 Offer TIPS if bleeding from gastric varices is not controlled by endoscopic injection of N-butyl-2-cyanoacrylate.
Proposed quality statement	People with uncontrolled bleeding from gastric varices are offered transjugular intrahepatic portosystemic shunts (TIPS), with consideration given to offer TIPS to those with uncontrolled bleeding from oesophageal varices.
Draft quality measure	**Structure:** Evidence of local arrangements to ensure people with uncontrolled bleeding from gastric varices are offered transjugular intrahepatic portosystemic shunts (TIPS), with consideration given to offer TIPS to those with uncontrolled bleeding from oesophageal varices **Process:** a) The proportion of people with uncontrolled bleeding from gastric varices who receive transjugular intrahepatic portosystemic shunts (TIPS) Numerator – The number of people in the denominator who receive TIPS Denominator – The number of people with uncontrolled bleeding from gastric varices b) The proportion of people with uncontrolled bleeding from oesophageal varices who are [considered for] transjugular intrahepatic portosystemic shunts (TIPS) Numerator – The number of people in the denominator who are [considered for] TIPS Denominator – The number of people with uncontrolled bleeding from oesophageal varices

10.1.2 Clinical and cost-effectiveness evidence

Consider TIPS

This recommendation is based on the following clinical question:

What is the evidence that TIPS is better than repeat endoscopic therapy or balloon tamponade in patients where the variceal bleed remains uncontrolled?

No studies were identified that directly address any treatment comparisons specified in the protocol for patients with uncontrolled variceal bleeding. No economic evaluations were identified that compared TIPS to repeat endoscopy or balloon tamponade in patients where variceal bleeding remained uncontrolled.

In the absence of formal evidence comparing the options when initial endoscopic treatment has failed, the guideline development group debated the question in the light of their clinical experience. They were also aware of case series showing that TIPS can be successful in these cases, and also of (older) series showing that a surgical approach tends to have a high mortality. The results of conservative, supportive management alone were felt to be unacceptably poor. They recognised the difficulties in providing TIPS for all of these extremely unwell patients if this required transfer between hospitals, but felt that a recommendation should be made which prompted clinicians to consider TIPS as an option. They noted that this would be consistent with the recommendation for early consideration of TIPS specifically for gastric variceal bleeding.

It was acknowledged that TIPS is a relatively expensive procedure, compared to endoscopic methods or balloon tamponade for control of bleeding.

Offer TIPS if bleeding from gastric varices is not controlled by endoscopic injection of N-butyl-2-cyanoacrylate

Please see section 9.1.2 for evidence.

10.1.3 Patient experience

No patient experience information is presented.

10.1.4 Patient safety

A patient safety incident is any unintended or unexpected incident which could have or did lead to harm for one or more patients receiving NHS care (see Appendix A). A comprehensive analysis of recent reported incidents (please see full accompanying report from the patient safety function at the NHS Commissioning Board Special Health Authority) found there were no incidents in the sample supporting this statement.

The guideline development group for CG141 believe that TIPS can be an appropriate treatment in this scenario. They debated again the relatively limited availability of TIPS and acknowledged the potential risks of transferring a patient with uncontrolled variceal bleeding to another centre, agreeing that ultimately this is a decision which can only be made on an individual patient basis.

10.1.5 Current practice

No current practice information is presented.

10.1.6 Current indicators

No current indicators are presented.

11 Control of bleeding and prevention of re-bleeding in patients on NSAIDs, aspirin or clopidogrel – Aspirin

11.1 NICE CG141 Recommendation 1.6.1 [KPI]

11.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.6.1 Continue low-dose aspirin for secondary prevention of vascular events in patients with upper gastrointestinal bleeding in whom haemostasis has been achieved.
Proposed quality statement	People with acute upper gastrointestinal bleeding [who take aspirin and] in whom haemostasis has been achieved should continue on low-dose aspirin [for secondary prevention of vascular events]
Draft quality measure	**Structure:** Evidence of local arrangements to ensure people with acute upper gastrointestinal bleeding, [who take aspirin and] in whom haemostasis has been achieved should continue on low-dose aspirin [for secondary prevention of vascular events] **Process:** The proportion of people with acute upper gastrointestinal bleeding in whom haemostasis has been achieved who [continue] on low-dose aspirin for secondary prevention of vascular events Numerator – The number of people in the denominator continue on low-dose aspirin Denominator – The number of people with acute upper gastrointestinal bleeding [who take aspirin] in whom haemostasis has been achieved

11.1.2 Clinical and cost-effectiveness evidence

PLEASE NOTE THAT THE EVIDENCE PRESENTED IN THIS SECTION DISCUSSES CONTROL OF BLEEDING AND PREVENTION OF RE-BLEEDING IN PATIENTS ON BOTH ASPIRIN AND CLOPIDOGREL

A single RCT was found investigating the continuation or discontinuation of low dose aspirin in the setting of acute gastrointestinal bleeding. By GRADE criteria the evidence for outcomes from this study was of predominantly moderate to high quality for the outcomes considered. The paper looked at patients taking aspirin as secondary prophylaxis; where primary prophylaxis was the indication, the patient was excluded from the study. The GDG also noted that aspirin was stopped for 56 days, but that a difference between study arms was apparent at 30 days.

This RCT was conducted in Asia and the GDG discussed the applicability to a UK population. However, they were satisfied that this appeared to be a well

performed study, and felt that the effects of aspirin in the Hong Kong population are sufficiently similar to the UK to allow extrapolation.

No trials were found investigating the continuation or discontinuation of clopidogrel, dipyridamole or non-steroidal anti-inflammatory drugs in the setting of acute gastrointestinal bleeding.

Mortality, either from gastrointestinal bleeding or vascular events, was the most important outcome. Evidence was available for aspirin, but not for clopidogrel or NSAID's, and showed that mortality was higher when aspirin was stopped in patients presenting with acute GI bleeding. The occurrence of vascular events (cerebro- or cardiovascular) and re-bleeding rates were also felt to be particularly important. Here the evidence was as expected, and showed that there were fewer acute ischemic events when aspirin was continued, but a greater rate of proven re-bleeding. Neither of these outcomes reached statistical significance.

No evidence specific to clopidogrel was found, an evidence gap which will become more important since this agent is likely to be prescribed more frequently in the near future as it becomes less expensive and familiarity with its benefits increases. Due to the lack of evidence it was felt that it could not make any general recommendation for clopidogrel. The prescription of clopidogrel to maintain the patency of coronary artery stents was considered to be a special and potentially high-risk situation requiring discussion with a cardiologist to decide upon the most appropriate course of management. Where clopidogrel was prescribed for a non-cardiac indication the treating physician may need to seek advice from an alternative specialist.

No relevant economic evaluations were identified that compared discontinuation with continuation of medication for patients presenting with UGIB already on NSAIDs, clopidogrel, aspirin or dipyridamol (single or combination).

11.1.3 Patient experience

In all cases it was felt very important to involve patients, and their carers, in discussions relating to the potential risks and benefits of continuing or stopping any of these medications.

11.1.4 Patient safety

A patient safety incident is any unintended or unexpected incident which could have or did lead to harm for one or more patients receiving NHS care (see Appendix A). A comprehensive analysis of recent reported incidents (please see full accompanying report from the patient safety function at the NHS Commissioning Board Special Health Authority) foundL

- No evidence in the NRLS could be identified to inform this quality statement.

11.1.5 Current practice

95% (5262/5547) of new admissions with AUGIB had a record of the medications at the time of their presentation.

NEW ADMISSIONS	National Audit (5262 with record)		Your site	
	%	N	%	N
Aspirin	27	1406	47	9
Warfarin	7	372	5	1
NSAID	12	648	16	3
SSRI antidepressant	9	480	0	0
Clopidogrel	5	243	0	0
Dipyridamole	1	66	5	1
Low molecular weight heparin	1	55	0	0
Proton Pump Inhibitor	30	1575	26	5

* Note the above table considers 'not known' as 'no'

Source: BSG audit[1]

It is well known that there is high use of low dose aspirin as prophylaxis for cardiovascular diseases, and in this audit over a quarter of all patients with AUGIB had received aspirin in the preceding week.

11.1.6 Current indicators

No current indicators are presented.

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

12.1 NICE CG141 Recommendation 1.6.3

12.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.6.3 Discuss the risks and benefits of continuing clopidogrel (or any other thienopyridine antiplatelet agents) in patients with upper gastrointestinal bleeding with the appropriate specialist (for example, a cardiologist or a stroke specialist) and with the patient.
Proposed quality statement	People with acute upper gastrointestinal bleeding [who take clopidogrel or any other thienopyridine antiplatelet agents] are advised on the risks and benefits of continuing clopidogrel (or any other thienopyridine antiplatelet agents) by the appropriate specialist
Draft quality measure	**Structure:** Evidence of local arrangements to ensure people with acute upper gastrointestinal bleeding [who take clopidogrel or any other thienopyridine antiplatelet agents] are advised on the risks and benefits of continuing clopidogrel (or any other thienopyridine antiplatelet agents) by the appropriate specialist **Process:** The proportion of people with acute upper gastrointestinal bleeding [who take clopidogrel or any other thienopyridine antiplatelet agents] who are advised on the risks and benefits of clopidogrel (or any other thienopyridine antiplatelet agents) by the appropriate specialist Numerator – The number of people in the denominator who are advised on the risks and benefits of continuing clopidogrel (or any other thienopyridine antiplatelet agents) by the appropriate specialist Denominator – The number of people with acute upper gastrointestinal bleeding who take clopidogrel or any other thienopyridine antiplatelet agents

12.1.2 Clinical and cost-effectiveness evidence

Please see section 11.1.2 for clinical and cost effectiveness evidence.

12.1.3 Patient experience

Please see 11.1.3 for patient experience evidence.

12.1.4 Patient safety

A patient safety incident is any unintended or unexpected incident which could have or did lead to harm for one or more patients receiving NHS care (see Appendix A). A comprehensive analysis of recent reported incidents (please see full accompanying report from the patient safety function at the NHS Commissioning Board Special Health Authority) found:

- Significant issues with clopidogrel and prasugrel were identified concerning omission and delay and over anticoagulation.

12.1.5 Current practice

Please see 11.1.5 for current practice evidence.

12.1.6 Current indicators

Please see 11.1.6 for current indicators.

Appendix A: Definition of patient safety

The patient safety function at the NHS Commissioning Board Special Health Authority defines patient safety in the following terms:

Every day more than a million people are treated safely and successfully in the NHS, but the evidence tells us that in complex healthcare systems things will and do go wrong, no matter how dedicated and professional the staff. When things go wrong, patients are at risk of harm, and the effects are widespread and often devastating for patients, their families and the staff involved. Safety incidents also incur costs through litigation and extra treatment, and in 2009/10 the NHSLA paid out approximately £827, 000,000 in litigation costs and damages. These incidents are often caused by poor system design rather than the error of individuals i.e. ‘they are an accident waiting to happen’.

In short patient safety could be summarised as ‘The identification and reduction of risk and harm associated with the care provided to patients ‘or ‘Preventing patients from being harmed by their treatment’. Examples of this might be ‘operating on or removing the wrong organ, ten times the dose of an opioid, giving a colonoscopy to the wrong patient with the same name as someone else in the waiting room etc.’ These risks are unlikely to be identified through clinical trials or traditional evidence bases and so other evidence sources, such as the National Reporting and Learning System, need to be analysed to highlight the risks and improve system development. This does not however give an accurate picture of prevalence in that way that methods such as casenote review may do.