

**105****Management of acute upper and  
lower gastrointestinal bleeding***A national clinical guideline**September 2008*

# KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS

## LEVELS OF EVIDENCE

- 1<sup>++</sup> High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
- 1<sup>+</sup> Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
- 1<sup>-</sup> Meta-analyses, systematic reviews, or RCTs with a high risk of bias
- 2<sup>++</sup> High quality systematic reviews of case control or cohort studies  
High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
- 2<sup>+</sup> Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
- 2<sup>-</sup> Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
- 3 Non-analytic studies, eg case reports, case series
- 4 Expert opinion

## GRADES OF RECOMMENDATION

*Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.*

- A** At least one meta-analysis, systematic review, or RCT rated as 1<sup>++</sup>, and directly applicable to the target population; or  
A body of evidence consisting principally of studies rated as 1<sup>+</sup>, directly applicable to the target population, and demonstrating overall consistency of results
- B** A body of evidence including studies rated as 2<sup>++</sup>, directly applicable to the target population, and demonstrating overall consistency of results; or  
Extrapolated evidence from studies rated as 1<sup>++</sup> or 1<sup>+</sup>
- C** A body of evidence including studies rated as 2<sup>+</sup>, directly applicable to the target population and demonstrating overall consistency of results; or  
Extrapolated evidence from studies rated as 2<sup>++</sup>
- D** Evidence level 3 or 4; or  
Extrapolated evidence from studies rated as 2<sup>+</sup>

## GOOD PRACTICE POINTS

- Recommended best practice based on the clinical experience of the guideline development group.

NHS Quality Improvement Scotland (NHS QIS) is committed to equality and diversity. This guideline has been assessed for its likely impact on the six equality groups defined by age, disability, gender, race, religion/belief, and sexual orientation.

For the full equality and diversity impact assessment report please see the “published guidelines” section of the SIGN website at [www.sign.ac.uk/guidelines/published/numlist.html](http://www.sign.ac.uk/guidelines/published/numlist.html). The full report in paper form and/or alternative format is available on request from the NHS QIS Equality and Diversity Officer.

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Scottish Intercollegiate Guidelines Network

**Management of acute upper and lower  
gastrointestinal bleeding**  
A national clinical guideline



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purpose of implementation in NHSScotland

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# 1 Introduction

## 1.1 THE NEED FOR A GUIDELINE

Acute gastrointestinal (GI) bleeding (or haemorrhage) is a common major medical emergency, accounting for approximately 7,000 admissions to hospitals in Scotland each year. In a 2007 UK-wide audit, overall mortality of patients admitted with acute GI bleeding was 7%. In contrast the mortality in patients who bled during admissions to hospital for other reasons was 26%.<sup>1</sup> In an audit undertaken in the West of Scotland the incidence of acute GI bleeding was higher than that reported elsewhere at 170/100,000 people with a mortality of 8.2%.<sup>2</sup> These differences may relate to different case ascertainment in the two audits.

Over the last ten years there has been a number of improvements in diagnosis and management. The increased involvement of acute care specialists during resuscitation and follow up, improved diagnostic and therapeutic endoscopy, advances in diagnostic and therapeutic radiology, the use of powerful ulcer healing drugs, more selective and less invasive surgical approaches may all improve outcome for patients. These changes have altered the diagnostic and treatment pathways for patients presenting with non-variceal and variceal upper GI bleeding and those with acute colonic bleeding. There is a need to examine the evidence to clarify which diagnostic and management steps have proven benefit. The major objectives of all involved in the management of bleeding patients are to reduce mortality and the need for major surgery. A secondary objective is to prevent unnecessary hospital admission for patients presenting with bleeding that is not life threatening.

## 1.2 REMIT OF THE GUIDELINE

### 1.2.1 OVERALL OBJECTIVES

This guideline provides recommendations based on current evidence for best practice in the management of acute upper and lower GI bleeding. It includes the assessment and management of variceal, non-variceal, and colonic bleeding in adults. The guideline deals with the management of bleeding that is of sufficient severity to lead to emergency admission to hospital. Bleeding of lesser severity is subject to elective investigation and is not considered here. The management of patients under the age of 14 is not covered by this guideline.

### 1.2.2 TARGET USERS OF THE GUIDELINE

This guideline will be of interest to a range of medical professionals including acute physicians, gastroenterologists, gastrointestinal surgeons, endoscopists, pharmacists, anaesthetists and nurses. It will also be of interest to patients who have suffered from acute GI bleeding and to their carers.

### 1.3 DEFINITIONS

#### Upper and lower gastrointestinal bleeding

Upper gastrointestinal bleeding (or haemorrhage) is that originating proximal to the ligament of Treitz; in practice from the oesophagus, stomach and duodenum. Lower gastrointestinal bleeding is that originating from the small bowel and colon. This guideline focuses upon upper GI and colonic bleeding since acute small bowel bleeding is uncommon.

#### Haematemesis (*and coffee-ground vomitus*)

Haematemesis is vomiting of blood from the upper gastrointestinal tract or occasionally after swallowing blood from a source in the nasopharynx. Bright red haematemesis usually implies active haemorrhage from the oesophagus, stomach or duodenum. This can lead to circulatory collapse and constitutes a major medical emergency. Patients presenting with haematemesis have a higher mortality than those presenting with melaena alone.<sup>2</sup>

Coffee-ground vomitus refers to the vomiting of black material which is assumed to be blood. Its presence implies that bleeding has ceased or has been relatively modest.

#### Melaena

Melaena is the passage of black tarry stools usually due to acute upper gastrointestinal bleeding but occasionally from bleeding within the small bowel or right side of the colon.

#### Hematochezia

Hematochezia is the passage of fresh or altered blood per rectum usually due to colonic bleeding. Occasionally profuse upper gastrointestinal or small bowel bleeding can be responsible.

#### Shock

Shock is circulatory insufficiency resulting in inadequate oxygen delivery leading to global hypoperfusion and tissue hypoxia. In the context of GI bleeding shock is most likely to be hypovolaemic (due to inadequate circulating volume from acute blood loss). The shocked, hypovolaemic patient generally exhibits one or more of the following signs or symptoms:

- a rapid pulse (tachycardia)
- anxiety or confusion
- a high respiratory rate (tachypnoea)
- cool clammy skin
- low urine output (oliguria)
- low blood pressure (hypotension).

It is important to remember that a patient with normal blood pressure may still be shocked and require resuscitation.

#### Varices

Varices are abnormal distended veins usually in the oesophagus (oesophageal varices) and less frequently in the stomach (gastric varices) or other sites (ectopic varices) usually occurring as a consequence of liver disease. Bleeding is characteristically severe and may be life threatening. The size of the varices and their propensity to bleed is directly related to the portal pressure, which, in the majority of cases, is directly related to the severity of underlying liver disease. Large varices with red spots are at highest risk of rupture.

#### Endoscopy

Endoscopy is the visualisation of the inside of the gastrointestinal tract using telescopes. Examination of the upper gastrointestinal tract (oesophagus, stomach and duodenum) is known as gastroscopy or upper gastrointestinal endoscopy. Examination of the colon (large bowel) is called colonoscopy.

#### Triage

Triage is a system of initial assessment and management whereby a group of patients is classified according to the seriousness of their injuries or illnesses so that treatment priorities can be allocated between them.



## 1.4 STATEMENT OF INTENT

This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.

### 1.4.1 ADDITIONAL ADVICE TO NHSSCOTLAND FROM NHS QUALITY IMPROVEMENT SCOTLAND AND THE SCOTTISH MEDICINES CONSORTIUM

NHS QIS processes multiple technology appraisals (MTAs) for NHSScotland that have been produced by the National Institute for Health and Clinical Excellence (NICE) in England and Wales.

The Scottish Medicines Consortium (SMC) provides advice to NHS Boards and their Area Drug and Therapeutics Committees about the status of all newly licensed medicines and any major new indications for established products.

SMC advice and NHS QIS validated NICE MTAs relevant to this guideline are summarised in the section on implementation.

## 2 Assessment and triage

### 2.1 ASSESSING GASTROINTESTINAL BLEEDING IN THE COMMUNITY

The assessment of GI bleeding from any cause in the community involves the identification of patients who require urgent admission, patients who require to be referred for outpatient assessment and patients who can be managed at home without involvement of hospital services. No studies were identified that were undertaken in primary care settings to address optimal referral practice. The decision to refer must be based upon clinical experience, common sense and extrapolation of guidance derived from risk assessment studies undertaken in secondary care settings.

### 2.2 ASSESSING GASTROINTESTINAL BLEEDING IN HOSPITAL

The purpose of this section is to assist individual units to develop guidelines and protocols based on available evidence which are suitable for their local circumstances. Patients referred to hospital are initially assessed in a variety of settings including emergency departments, acute assessment units, gastroenterology departments, dedicated GI bleeding units or surgical wards.

Acute GI bleeding is a medical emergency. Initial triage and assessment are generic with emphasis on identifying the sick patient with life threatening haemodynamic compromise and initiating appropriate resuscitation (see section 4.2). Certain clinical features associated with GI bleeding have been studied in attempts to identify patients at increased risk of morbidity and death. Although acute upper and lower GI bleeding are distinct entities, the site of bleeding is not always immediately apparent; for example, 15% of patients with severe haematochezia have a source of bleeding in the upper GI tract.<sup>3</sup> Despite this, the literature on upper and lower GI bleeding is largely separate and this section on assessment is similarly subdivided.

#### 2.2.1 RISK FACTORS ASSOCIATED WITH POOR OUTCOME

##### Acute upper gastrointestinal bleeding

There is a lack of good quality studies on the initial assessment of patients with acute upper GI bleeding (UGIB). Limited evidence is available from cohort and case series which identify risk factors associated with poor outcome (variously defined) but usually without formal scoring. Studies confirm an extremely high fatality in inpatients of 42%.<sup>4,5</sup>

3

The following factors are associated with a poor outcome, defined in terms of severity of bleed, uncontrolled bleeding, rebleeding, need for intervention and mortality. These factors should be taken into account when determining the need for admission or suitability for discharge.

- **Age** - mortality due to UGIB increases with age across all age groups. Odds ratio (OR) for mortality is from 1.8 to 3 for age > 60 years (compared to patients aged 45-59 years), and from 4.5 to 12 for age > 75 years (compared to patients ≤ 75 years).<sup>2,4,6</sup>
- **Comorbidity** - the absence of significant comorbidity is associated with mortality as low as 4%.<sup>2,4,6,7</sup> Even one comorbidity almost doubles mortality (OR 1.8) and the presence of cardiac failure (OR 1.8) or malignancy (OR 3.8) significantly worsens prognosis.
- **Liver disease** - cirrhosis is associated with a doubling of mortality and much higher risk of interventions such as endoscopic haemostasis or transfusion.<sup>8</sup> The overall mortality of patients presenting with varices is 14%.<sup>1</sup>
- **Inpatients** have approximately a threefold increased risk of death compared to patients newly admitted with GI bleeding. This is due to the presence of comorbidities in established inpatients rather than increased severity of bleeding.<sup>4,5</sup>
- **Initial shock** (hypotension and tachycardia) is associated with increased mortality (OR 3.8) and need for intervention.<sup>2,4,7</sup>

3

2-

3

3

3

2

- **Continued bleeding** after admission is associated with high risk of intervention (OR 1.8)<sup>7</sup> and up to a 50-fold increased mortality.<sup>6</sup> | 3
- **Haematemesis** - the presence of initial haematemesis doubles mortality.<sup>2,7</sup> | 3
- **Haematochezia** - the presence of haematochezia doubles rebleeding, mortality and surgery rates.<sup>9</sup> | 3
- **Elevated blood urea** is associated with a need for intervention.<sup>10</sup> | 3

Non-steroidal anti-inflammatory drugs (NSAIDs)<sup>2,11</sup> and anticoagulants<sup>2,12</sup> do not adversely affect the clinical outcomes of patients presenting with UGIB. | 3

There is conflicting evidence on the value of nasogastric aspiration. A bloody aspirate may indicate a high-risk lesion (sensitivity 48%, specificity 76%) but no evidence has been identified that it alters outcome.<sup>13,14</sup> | 3

#### Acute lower gastrointestinal bleeding

There is limited evidence available on the initial assessment of patients with acute lower gastrointestinal bleeding (LGIB). One general review of management<sup>15</sup> and one guideline were identified.<sup>16</sup> Other evidence comes from case series and epidemiology, and from expert opinion. Two uncontrolled case series analyse early predictors of severity, one prospective<sup>17</sup> and one retrospective.<sup>18</sup> The available evidence identifies the following factors associated with uncontrolled bleeding and/or death. | 3  
4

- **Age** - acute lower GI bleeding occurs most often in the elderly. The precise relationship between age and mortality is statistically less well defined than for UGIB.<sup>15,18,19</sup> | 3
- **Acute haemodynamic disturbance** (OR 3 to 4.3) and gross rectal bleeding on initial examination (OR 2.3 to 3) are important predictors of subsequent severe bleeding.<sup>17,18</sup> | 3
- **Comorbidity** - the presence of two comorbid conditions doubles the chance of a severe bleed (OR 1.9).<sup>18</sup> | 3
- **Specific drugs** – patients taking aspirin or NSAIDs are at increased risk of severe lower GI bleeding (OR 1.8 to 2.7).<sup>18,20</sup> | 3
- **Inpatients** who are hospitalised for another condition and who subsequently bleed after admission have a mortality rate of 23% compared with 3.6% in those admitted to hospital because of rectal bleeding ( $p < 0.001$ ).<sup>19</sup> | 3

The patient's history is important for accurate assessment of risk and can give important clues to the diagnosis and need for admission. For example, a history of previous LGIB from a known diagnosis of diverticular disease (the commonest cause of LGIB accounting for 23-48% of cases) predicts a further episode with a 10% chance of recurrence at one year and 25% at four years. Diverticular bleeds resolve spontaneously in 75% of cases.<sup>19</sup> | 3

### 2.2.2 PRE-ENDOSCOPIC RISK ASSESSMENT

#### Acute upper gastrointestinal bleeding

Simple and widely validated scoring systems to identify patients at high risk of rebleeding, death and active intervention are needed for optimum management.

The Rockall scoring system was principally designed to predict death based on a combination of clinical and endoscopic findings. Given that many of the risk factors for rebleeding are identical to those for mortality and that rebleeding itself is independently predictive of death, the Rockall score may also be used to estimate rebleeding risk.<sup>21</sup> The initial (pre-endoscopic) Rockall score is derived from age (0 to 2 points), shock (0 to 2 points) and comorbidity (0 to 3 points). The minimum score of 0 is assigned to patients with age < 60 years who have no evidence of shock and or comorbidity. A score of 0 identifies 15% of patients with acute UGIB at presentation who have an extremely low risk of death (0.2%) and rebleeding (0.2%), and who may be suitable for early discharge or non-admission (see *Table 1*).<sup>21</sup> | 3

Table 1: Rockall numerical risk scoring system

Variable	Score				
	0	1	2	3	
Age	< 60 years	60-79 years	≥ 80 years		<b>Initial score criteria</b>
Shock	'no shock', SBP* ≥ 100 mm Hg, pulse < 100 beats per minute	'tachycardia', SBP ≥ 100 mm Hg, pulse ≥ 100 beats per minute	'hypotension', SBP < 100 mm Hg,		
Comorbidity	no major comorbidity		cardiac failure, ischaemic heart disease, any major comorbidity	renal failure, liver failure, disseminated malignancy	
Diagnosis	Mallory-Weiss tear, no lesion identified and no SRH	all other diagnoses	malignancy of upper GI tract		<b>Additional criteria for full score</b>
Major stigmata of recent haemorrhage (SRH)	none, or dark spot only		blood in upper GI tract, adherent clot, visible or spurting vessel		

\*SBP - systolic blood pressure \*SRH - Stigmata of recent haemorrhage  
 Maximum additive score prior to diagnosis = 7  
 Maximum additive score after diagnosis = 11.

If the initial (pre-endoscopic) score is above 0 there is a significant mortality (score 1: predicted mortality 2.4%; score 2: predicted mortality 5.6%) suggesting that only those scoring 0 can be safely discharged at this stage.<sup>21</sup> 3

One prospective study which validated the initial (pre-endoscopic) Rockall score confirmed a mortality of less than 1% in patients with a score of 0 or 1, including one death in the score 0 group, emphasising that no predictive score is totally reliable for the individual.<sup>22</sup> The study also showed a general relationship between increasing initial Rockall score across the range of values and mortality, and suggested that patients could be triaged to different models of care based on their score. 3

A further prospective study of 358 patients assessed the validity of the initial Rockall risk scoring system in predicting rebleeding and mortality in patients with oesophageal varices or peptic ulcers.<sup>23</sup> The study showed zero mortality for patients with peptic ulcer or varices presenting with acute UGIB who had an initial (pre-endoscopic) score of 0 to 1 and confirmed a significant relationship between hospital mortality and those scoring 2 and above. The rebleeding rates were not given. 3

The Blatchford risk score was derived to predict death and the need for treatment (transfusion, endoscopic treatment, surgery).<sup>10</sup> The full score was validated internally on 197 patients and performed better than the Rockall score in predicting the need for treatment.<sup>10</sup> 3

The Blatchford system is theoretically attractive since it aspires to identify patients who need intervention at the time of presentation to hospital, but it has yet to be tested against alternatives such as the Rockall score and, crucially, lacks any external validation. It cannot be recommended for clinical use.

An abbreviated Blatchford score (a fast track screening tool which measured urea, haemoglobin, blood pressure and pulse rate) was shown to be extremely sensitive in identifying 99% of patients requiring treatment, but lacked specificity as it identified only 32% of patients who did not require treatment.<sup>10</sup>

3

Another pre-endoscopy risk stratification system, designed at Addenbrooke's Hospital, is based on simple clinical data available at admission.<sup>7</sup> This allocates patients to high-, medium- and low-risk groups but currently cannot be recommended because it lacks external validation.

3

No evidence has been identified that the application of any particular risk scoring system calculated at the time of admission to hospital alters the outcome for patients admitted with acute upper GI bleeding. The initial Rockall score is the only pre-endoscopic formal scoring system with any external validation. A more general protocol based on available evidence and the guideline development group's expert opinion is included in Table 2.

Table 2: Acute upper gastrointestinal bleeding – initial assessment protocol

<b>Consider for discharge or non-admission with outpatient follow up if:</b>
<ul style="list-style-type: none"> <li>▪ age &lt; 60 years, and;</li> <li>▪ no evidence of haemodynamic disturbance (systolic blood pressure <math>\geq</math> 100 mm Hg, pulse &lt; 100 beats per minute), and;</li> <li>▪ no significant comorbidity (especially liver disease, cardiac disease, malignancy), and;</li> <li>▪ not a current inpatient (or transfer), and;</li> <li>▪ no witnessed haematemesis or haematochezia.</li> </ul>

All such patients will have an initial Rockall score of 0. If aged >60 years Rockall score becomes 1 and the patient should probably be admitted but considered for early discharge. Each patient must be assessed individually and clinical judgement should be used to guide these considerations.

<b>Consider for admission and early endoscopy (and calculation of full Rockall score) if:</b>
<ul style="list-style-type: none"> <li>▪ age <math>\geq</math> 60 years (all patients who are aged &gt;70 years should be admitted), or;</li> <li>▪ witnessed haematemesis or haematochezia (suspected continued bleeding), or;</li> <li>▪ haemodynamic disturbance (systolic blood pressure &lt; 100 mm Hg, pulse <math>\geq</math> 100 beats per minute), or;</li> <li>▪ liver disease or known varices.</li> </ul>

### **Acute lower gastrointestinal bleeding**

The triage and initial assessment of patients with acute lower GI bleeding is extremely variable across different settings and in different regions. There are no predictive models or scoring systems which can accurately assess risk at the point of initial triage and assessment, or later. Many factors associated with poor clinical outcomes are known and have been used here to formulate general guidance based on available evidence and the guideline group's experience and opinion (see Table 3).

Table 3: Acute lower gastrointestinal bleeding – initial assessment protocol

<b>Consider for discharge or non-admission with outpatient follow up if:</b>
<ul style="list-style-type: none"> <li>▪ age &lt; 60 years, and;</li> <li>▪ no evidence of haemodynamic compromise, and;</li> <li>▪ no evidence of gross rectal bleeding, and;</li> <li>▪ an obvious anorectal source of bleeding on rectal examination/sigmoidoscopy.</li> </ul>
<b>Consider for admission if:</b>
<ul style="list-style-type: none"> <li>▪ age ≥ 60 years, or;</li> <li>▪ haemodynamic disturbance, or;</li> <li>▪ evidence of gross rectal bleeding, or;</li> <li>▪ taking aspirin or an NSAID, or;</li> <li>▪ significant comorbidity.</li> </ul>

2.2.3 POST-ENDOSCOPIC RISK ASSESSMENT

**Acute upper gastrointestinal bleeding**

The full Rockall score comprises the initial score plus additional points for endoscopic diagnosis (0 to 2 points), and endoscopic stigmata of recent haemorrhage (SRH) (0 to 2 points) giving a maximum score of 11 points (see Table 1).

Around a third of the original cohort of patients with UGIB studied by Rockall scored ≤ 2 on the full Rockall score. These patients had low mortality (0.1%) and rebleeding (4.3%) in the acute phase. Early endoscopy identifies a substantial number of patients at low risk of rebleeding or death who should be considered for early discharge and appropriate outpatient follow up, with consequent resource savings.<sup>24</sup>

3

The full Rockall score has been validated in a number of studies. One study analysed 951 Dutch patients with acute UGIB.<sup>25</sup> The overall mortality was 14%, indicating a group with higher baseline risk than Rockall’s original cohort. The Rockall score performed well in predicting mortality but less well in predicting rebleeding. The mortality in patients with full Rockall score < 2 was zero, and mortality in patients with full Rockall score of < 3 was 0.8%. The rebleeding rate in patients with full Rockall score < 3 was 6.7%. This study suggests that patients with a full Rockall score < 3 should be considered for early discharge.

3

One Italian study prospectively validated the full Rockall score in patients with non-variceal UGIB. The study found zero mortality in patients with a full Rockall score < 3, but, like the Dutch study, showed that prediction of rebleeding was poor.<sup>26</sup>

3

A further prospective study confirmed that the full Rockall score predicted mortality and rebleeding in patients with ulcer and varices with low scores but was unsatisfactory in predicting mortality in patients with peptic ulcers with high scores. A full score < 3 was associated with zero mortality in patients with ulcers or varices.<sup>23</sup>

3

The usefulness of the full Rockall score for the triage of patients at higher risk of death has been considered. One study showed a progressive increase in mortality from 2% with full Rockall score 2 to 39% in patients with full Rockall score > 8. There was a similar gradual increase in rebleeding from 5% to 47%. There was no obvious cut-off at which a different model of care could be suggested.<sup>24</sup>

3

Another study showed a mortality risk of 11% and rebleeding risk of 16% in those with a full Rockall score of 5.<sup>25</sup> This rose to a mortality risk of 46% and rebleeding risk of 27% in patients who scored ≥ 8. Prediction of rebleeding by Rockall score was statistically unsatisfactory.

3

The reported rates for both mortality and rebleeding have been shown to vary markedly from the original Rockall rates at higher scores suggesting that the Rockall score may be unreliable in the statistical prediction of mortality at higher levels and is unlikely to be of value in triaging patients to standard or intensive care.<sup>21</sup>

3

## 2.2.4 SUMMARY

The initial Rockall scoring system is an appropriate tool for assessment prior to endoscopy and is predictive of death and rebleeding in patients with ulcers or varices.<sup>21-23</sup> Patients presenting with an initial (pre-endoscopic) score of 0 (age < 60 years, no shock, no comorbidity) have an extremely low risk of death or rebleeding and should be considered for non-admission or early discharge with appropriate outpatient follow up.<sup>21,22</sup>

3

**D All patients presenting with acute upper gastrointestinal bleeding should have an initial (pre-endoscopic) Rockall score calculated. Patients with a Rockall score of 0 should be considered for non-admission or early discharge with outpatient follow up.**

A full (post-endoscopic) Rockall score is predictive of mortality in unselected patients with acute UGIB.<sup>23-26</sup> This includes both patients with bleeding ulcers and varices.<sup>23</sup> It is less satisfactory in predicting rebleeding.<sup>24,25</sup>

3

Approximately 30% of all patients undergoing early endoscopy will have a Rockall score < 3. These patients have an extremely low predicted mortality (< 1%) and rebleeding rate (approximately 5%) and should be considered for early discharge and outpatient follow up.<sup>24,25</sup>

3

**D In patients with initial (pre-endoscopic) Rockall score > 0 endoscopy is recommended for a full assessment of bleeding risk.**

**D Patients with a full (post-endoscopic) Rockall score < 3 have a low risk of rebleeding or death and should be considered for early discharge and outpatient follow up.**

There is a general relationship between increasing Rockall score and both mortality and rebleeding at Rockall score above 2,<sup>24</sup> however this varies across studies.<sup>23,25</sup> No studies have addressed the validity of triaging patients to different models of care, such as high dependency unit (HDU) according to Rockall score, and at present the Rockall score is not recommended as a tool for this purpose.

3

**D The Rockall score should be taken into account with other clinical factors in assigning patients to different levels of care. It should not be used in isolation to assign patients to high dependency care.**



### 3 Organisation of services

No evidence for the management of patients with GI bleeding within primary care was identified. Current practice is based upon immediate referral to an acute admitting unit.

In the majority of UK hospitals patients with UGIB are admitted to general medical wards and patients with LGIB are admitted to surgical units. Over the last 10 to 15 years several models of care have been introduced in an attempt to improve the outcomes of these patients. The most prominent is the dedicated GI bleeding service.

#### 3.1 DEDICATED GI BLEEDING UNIT

Several cohort studies were identified which described the management of upper GI bleeding. The majority of these studies were conducted prior to the routine use of endoscopic interventions to control bleeding and are therefore less relevant to current practice. However, there was an improved mortality associated with these bleeding units in which patients with acute gastrointestinal bleeding are managed by dedicated teams. Improved outcome may have been due to protocolised care, prompt resuscitation and close medical and surgical liaison.

Four cohort studies<sup>27-30</sup> and one single cohort study<sup>31</sup> that examined the role of bleeding units were identified from the "post-endoscopic intervention" era. Four of these studies were rejected due to a high risk of bias.<sup>27-30</sup>

One study was of adequate methodological quality.<sup>31</sup> This study described the effectiveness of a dedicated upper gastrointestinal bleeding unit in the UK. The outcomes from 900 patients admitted to the unit were described. Once stratified by Rockall scoring into low, moderate and high risk of death, outcomes were compared with those from the National Audit of UGIB<sup>4</sup> by calculating standardised mortality ratios (SMRs) (see Table 4).

This study expresses the relationship between outcomes in the two groups as a standardised mortality ratio. This compares actual numbers of deaths to expected numbers, adjusting for age and sex. In this case, the actual numbers of deaths in the study sample was compared to the expected number of deaths derived from the larger population of the UK audit. A population with an SMR of 1 has the same mortality as the reference population, an SMR less than 1 indicates lower mortality and an SMR more than 1 indicates greater mortality.

Table 4: A comparison of mortality data from a dedicated GI bleeding unit and a National Audit

Patient group	SMR	95% confidence interval
All	0.63	0.48 to 0.78
Low-risk (full Rockall score 0-3)	0.35	0.00 to 1.04*
Medium-risk (full Rockall score 4-6)	0.56	0.34 to 0.78
High-risk (full Rockall score $\geq 7$ )	0.70	0.49 to 0.91

\* Not significant

This study suffers from uncertain case ascertainment in the reference group, nevertheless the large number of patients and inclusion of a high proportion of patients with varices (a high risk group) make the conclusions of interest.

**D Patients with acute upper gastrointestinal haemorrhage should be admitted, assessed and managed in a dedicated gastrointestinal bleeding unit.**



This evidence supports a dedicated GI bleeding unit with the following features:

- a dedicated ward area,
- nursing staff experienced in the care of UGIB, with the ability to monitor vital signs at least hourly,
- all patients with suspected UGIB admitted to unit,
- unit guidelines for the management of UGIB,
- consultant gastroenterology 24 hour on-call service,
- ability to perform immediate interventional endoscopy if needed,
- ability to manage central venous access,
- shared care between gastroenterology and the referring consultant.

## 4 Resuscitation and initial management

### 4.1 AIRWAY, BREATHING AND CIRCULATION

Patients with acute GI bleeding should have continual assessment and appropriate management of airway, breathing and circulation. These patients are at particular risk of airway compromise. Staff involved in the care of these patients should be competent in the recognition of airway compromise and its management with basic airway manoeuvres. They should also be able to call upon staff trained in advanced airway manoeuvres when appropriate.

### 4.2 FLUID RESUSCITATION

Shock is associated with a greater risk of death in patients with acute GI haemorrhage (see section 2.2.1). A key part of their initial management is the recognition of shock and early aggressive resuscitation.

#### 4.2.1 INITIAL RESUSCITATION

The guideline on the management of massive blood loss from the British Committee for Standards in Haematology recommends rapid volume expansion to maintain tissue oxygenation and perfusion.<sup>32</sup> Transfusion of red cells is likely to be required after 30-40% of the circulation volume is lost (see Table 5).

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Table 5: Classification of hypovolaemic shock by blood loss in adults

	Class I	Class II	Class III	Class IV
<b>Blood loss, volume (ml)</b>	< 750	750-1500	1500-2000	> 2000
<b>Blood loss (% of circulating blood)</b>	0-15	15-30	30-40	> 40
<b>Systolic blood pressure</b>	No change	Normal	Reduced	Very reduced
<b>Diastolic blood pressure</b>	No change	Raised	Reduced	Very reduced/ unrecordable
<b>Pulse (beats per minute)</b>	Slight tachycardia	100-120	120 (thready)	> 120 (very thready)
<b>Respiratory rate</b>	Normal	Normal	Raised (> 20/min)	Raised (> 20/min)
<b>Mental state</b>	Alert, thirsty	Anxious or aggressive	Anxious, aggressive or drowsy	Drowsy, confused or unconscious

Adapted from Baskett, PJF. ABC of major trauma. Management of Hypovolaemic Shock. BMJ 1990; 300: 1453-1457.

**D**

- Shocked patients should receive prompt volume replacement.
- Red cell transfusion should be considered after loss of 30% of the circulating volume.

#### 4.2.2 COLLOID AND CRYSTALLOID FLUIDS

No studies of sufficient quality comparing crystalloid and colloid fluid restoration were identified in patients with GI bleeding. Evidence from a broader population of critically ill patients was considered. One meta-analysis and one large RCT of sufficient quality were identified.

A Cochrane review demonstrated no statistical difference between crystalloids and a wide range of colloids (hydroxyethylstarch, modified gelatins, dextrans and colloid in hypertonic crystalloid).<sup>33</sup> This review includes the Saline versus Albumin Fluid Evaluation (SAFE) study which showed no difference in outcomes between the use of 4.5% human albumin solution and normal saline in the resuscitation of critically ill ICU patients.<sup>34</sup>

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**B** Either colloid or crystalloid solutions may be used to achieve volume restoration prior to administering blood products.

#### 4.2.3 USE OF MAJOR HAEMORRHAGE PROTOCOLS

The use of protocols may form an integral part of the management of patients within a UGIB unit (see section 3.1). Major haemorrhage protocols have become more common in practice in the last 10 years. No evidence was identified describing the use of major haemorrhage protocols in the management of patients with acute gastrointestinal haemorrhage.

Units which manage acutely bleeding patients should have a major haemorrhage protocol in place.

### 4.3 EARLY PHARMACOLOGICAL MANAGEMENT

#### 4.3.1 UNSELECTED PATIENTS WITH GASTROINTESTINAL BLEEDING BEFORE ENDOSCOPY

Maintaining gastric pH above 6 optimises platelet aggregation and clot formation.<sup>35</sup> Patients at high risk for rebleeding receive endoscopic therapy to achieve haemostasis and are subsequently treated with high-dose acid suppression to promote the formation of blood clots over the arterial defect that is responsible for bleeding (see section 5.3.2). Although there is evidence of improved clinical outcome associated with post-endoscopic pharmacological management of patients at high risk of rebleeding,<sup>36</sup> there is a lack of evidence to support pre-endoscopic treatment with proton pump inhibitors (PPI).

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In one meta-analysis, PPI treatment before diagnosis by endoscopy in unselected outpatients with upper gastrointestinal bleeding showed no benefit in terms of mortality, rebleeding or need for surgery.<sup>37</sup> Pooled mortality rates were low for both the PPI group (6.1%) and the control group (5.5%). Comorbidities were not recorded. The low mortality rate may be partly explained by the exclusion of inpatients, a group with high mortality rate, from the main study in the meta-analysis. Overall 37.3% of patients on PPI and 39.6% of patients in the control group required endoscopic haemostatic treatment.

1++

Pooled rebleeding rates were 13.9% for PPI treatment and 16.6% for control treatment, indicating that there was no statistically significant effect of PPI treatment on pooled rebleeding rates (OR 0.81, 95% confidence interval (CI) 0.61 to 1.09). Pooled rates for surgery were 9.9% for PPI treatment and 10.2% for control treatment. PPI treatment did not significantly affect surgical intervention rates (OR 0.96, 95% CI 0.68 to 1.35).

One RCT suggested that high-dose omeprazole infusion (80 mg bolus followed by 8 mg/hour) prior to endoscopy accelerated the signs of resolution of bleeding and reduced the need for endoscopic therapy.<sup>38</sup> This study may not be generalisable to Scotland as it was carried out in an Asian population. The treatment effect is higher in Asian patients who are more sensitive to PPI treatment (see section 5.3.2). The study also excluded patients on long-term aspirin therapy. The optimum dose and route of PPI is unclear and requires to be evaluated in a non-Asian population.

1++

Pre-endoscopic therapy did not affect clinical outcome and should not be considered an alternative to early endoscopy (see section 4.4.1). Endoscopic therapy is indicated for only high-risk lesions (active arterial bleeding, non-bleeding visible vessels and adherent clots). Those with a clean ulcer base or pigmented spots do not require intervention (see section 5.2). In this trial, although more ulcers with clean bases were observed in the omeprazole group than in the placebo group ( $p = 0.001$ ), there was no difference in the numbers of non-bleeding visible vessels, clots and pigmented spots.

1<sup>++</sup>

Pre-endoscopic therapy with high-dose PPI may reduce the numbers of patients who require endoscopic therapy, but there is no evidence that it alters important clinical outcomes and there is insufficient evidence to support this practice.

**A Proton pump inhibitors should not be used prior to diagnosis by endoscopy in patients presenting with acute upper gastrointestinal bleeding.**

The early pharmacological management of patients with suspected variceal bleeding is discussed in section 6.2.1.

**4.4 EARLY ENDOSCOPIC INTERVENTION**

Endoscopy is an effective intervention for acute GI bleeding (see sections 5.2 and 6.1). The optimal timing of endoscopy has not been clearly established and there is no consistent definition of an “early” or “delayed” procedure. The literature describes early endoscopy as ranging from one to 24 hours after initial presentation.<sup>39,40</sup>

**4.4.1 TIMING OF ENDOSCOPY**

**Acute upper gastrointestinal bleeding**

Current clinical practice involves endoscopy being undertaken in working hours within 24 hours of presentation. Early endoscopy allows risk to be estimated for bleeding patients. Low-risk patients who can be discharged from hospital at an early stage, may be identified thus reducing costs of admission.<sup>40</sup> No evidence was identified that urgent early endoscopy affects mortality, although a systematic review suggested that early endoscopy is associated with a reduced transfusion need and a reduction in length of stay in high-risk patients with non-variceal bleeding.<sup>41</sup> Timing in these studies varied from four hours to 12 hours.

2<sup>+</sup>

A small subgroup of patients is unstable because of active bleeding (active haematemesis and/or melaena, tachycardia and/or hypotension). Early endoscopy and endoscopic therapy (< 24 hours from admission) is associated with reduced transfusion requirements, a reduction in rebleeding and a lower need for surgery compared to patients receiving later endoscopy.<sup>41-43</sup>

2<sup>+</sup>  
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Endoscopy should be undertaken in a dedicated endoscopy area with the help of appropriately trained endoscopy assistants. Optimum resuscitation is essential before endoscopy in order to reduce the potential cardiorespiratory complications of the procedure.<sup>43</sup>

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**Acute lower gastrointestinal bleeding**

One RCT comparing urgent colonoscopy with elective colonoscopy found little difference in outcome between the two groups although a definite source of bleeding was found more often in urgent colonoscopies.<sup>44</sup>

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A large cohort study showed that length of hospital stay was shorter in patients who underwent colonoscopy within 24 hours of admission than those undergoing colonoscopy after 24 hours.<sup>45</sup> A further cohort study suggested that colonoscopy be deferred until patients are haemodynamically stable, have adequate bowel preparation to optimise diagnostic accuracy and upper GI bleeding has been excluded by upper endoscopy. A higher diagnostic yield was found in patients with less severe bleeding.<sup>46</sup>

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Most patients who present with haematochezia are investigated when stable. Urgent colonoscopy is only considered in actively bleeding and shocked patients. It should only be done once resuscitation has been optimised.

**C Early endoscopic examination should be undertaken within 24 hours of initial presentation, where possible.**

## 5 Management of non-variceal upper gastrointestinal bleeding

The reported rates of non-variceal gastrointestinal bleeding due to specific causes vary considerably, reflecting differing methodologies and definitions, and variations in case ascertainment. The most common cause of significant non-variceal bleeding is universally reported to be peptic ulcer disease, which accounts for up to half of all cases found at emergency endoscopy (see Table 6).<sup>1,4</sup>

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Table 6: Major causes of upper gastrointestinal bleeding

Cause of bleeding	Relative frequency (% of those in whom any abnormality was identified at endoscopy)
Peptic ulcer	44
Oesophagitis	28
Gastritis/erosions	26
Erosive duodenitis	15
Varices	13
Portal hypertensive gastropathy	7
Malignancy	5
Mallory Weiss tear	5
Vascular malformation	3

NB. In approximately 20% of patients presenting with apparent acute upper gastrointestinal bleeding endoscopy does not reveal a cause.

### 5.1 RISK STRATIFICATION

Endoscopic stigmata are integral to the Rockall scoring system (see section 2.2.3). Ulcers with clean base, black or red spots have negligible rebleeding risk.<sup>47,48</sup> The risk of rebleeding from patients who have adherent blood clot is approximately 35% whilst that for non-bleeding visible vessels is 40-50%.<sup>42,43,49</sup> Patients who are shocked and have active bleeding at endoscopy have an 80% risk of continuing to bleed or rebleed unless endoscopic intervention is undertaken.

### 5.2 ENDOSCOPY

Whilst the rate of rebleeding, requirements for blood transfusion and need for surgical intervention are significantly reduced by endoscopic therapies (see sections 5.2.1 to 5.2.4), the impact upon reduced mortality is generally not significant (number needed to treat, NNT 35-500).<sup>42</sup> This may be because the major determinant of survival is the number and severity of medical comorbidities rather than achievement of haemostasis.<sup>2,21</sup> Only high risk lesions (active arterial bleeding, non-bleeding visible vessels or an adherent blood clot) should be treated endoscopically since only these are at risk of further bleeding.<sup>43</sup> Black or red spots or a clean ulcer base with oozing do not merit endoscopic intervention since these lesions have an excellent prognosis without intervention.<sup>43</sup>

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**D Endoscopic therapy should only be delivered to actively bleeding lesions, non-bleeding visible vessels and, when technically possible, to ulcers with an adherent blood clot.**

5.2.1 INJECTION

Endoscopic injection of fluid around and into the bleeding point reduces the rate of rebleeding in patients with non-bleeding visible vessels from approximately 50% to 15-20%.<sup>42</sup> Rebleeding following injection into ulcers with adherent blood clot is also significantly reduced from approximately 35 to 10%.<sup>49,50</sup> The commonest injection fluid is 1:10,000 adrenaline (epinephrine).

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One RCT compared the effect of different volumes of injected adrenaline on haemostasis and complication rates in patients with actively bleeding ulcers.<sup>51</sup> There were no significant differences in the rate of initial haemostasis between three groups with 20, 30 and 40 ml endoscopic injections of a 1:10,000 solution of adrenaline. The rate of peptic ulcer perforation was significantly higher in the group receiving 40 ml adrenaline ( $p < 0.05$ ). The rate of recurrent bleeding was significantly higher in the 20 ml adrenaline group (20.3%) than in the 30 ml (5.3%) and 40 ml (2.8%) adrenaline groups ( $p < 0.01$ ). There were no significant differences in the rates of mortality, surgical intervention, the amount of transfusion requirements, or the days of hospitalisation between the three groups. The proportion of patients who developed epigastric pain associated with endoscopic injection, was significantly higher in the 40 ml adrenaline group (67%) than in the 20 ml (3%) and 30 ml (7%) adrenaline groups ( $p < 0.001$ ). This study concludes that the optimal injection volume of adrenaline for endoscopic treatment of an actively bleeding ulcer is 30 ml.

1++

Another RCT showed that injection of a large volume (> 13 ml) of adrenaline can reduce the rate of recurrent bleeding in patients with high-risk peptic ulcers and is superior to injection of lesser volumes of adrenaline (5-10 ml) when used to achieve sustained haemostasis.<sup>52</sup>

1++

Injection of sclerosants (polydochanol, sodium tetradecyl sulphate (STD) or ethanolamine) and absolute alcohol is also effective but is associated with a significantly increased risk of complications including mucosal perforation and necrosis compared with adrenaline.<sup>42</sup>

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5.2.2 THERMAL

Coagulation using the heater probe or multipolar coagulation has similar clinical efficacy to injection.<sup>53</sup>

1++

Complications, including mucosal perforation are rare.<sup>54-56</sup> Therapy should be administered until the treated area is black and cavitated.

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5.2.3 MECHANICAL

A meta-analysis compared the efficacy of endoscopic clipping versus injection or thermocoagulation in the control of non-variceal gastrointestinal bleeding. Patients ( $n = 1,156$ ) were randomised in 15 RCTs.<sup>57</sup> Definitive haemostasis was higher with clipping (86.5%) than injection (75.4%; relative risk, RR 1.14, 95% CI 1.00 to 1.30). Use of clips significantly reduced rebleeding (9.5%) compared with injection (19.6%; RR 0.49, 95% CI 0.30 to 0.79) and the need for surgery (2.3% v 7.4%; RR 0.37, 95% CI 0.15 to 0.90). Clipping and thermocoagulation had comparable efficacy (81.5% and 81.3%; RR 1.00). No differences in mortality were reported between any interventions.

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5.2.4 COMBINATION THERAPIES

Two meta-analyses have demonstrated that combinations of endoscopic therapy are superior to the use of a single modality therapy, and combination treatment does not increase the risk of complications.

One meta-analysis of 16 RCTs reported that adding a second endoscopic intervention (thermal, mechanical or injection) following an endoscopic adrenaline injection reduced the further bleeding rate from 18.4% to 10.6% (OR 0.53, 95% CI, 0.40 to 0.69) and emergency surgery from 11.3% to 7.6% (OR 0.64, 95% CI, 0.46 to 0.90). Mortality fell from 5.1% to 2.6% (OR 0.51, 95% CI 0.31 to 0.84).<sup>58</sup>

1++

Another meta-analysis showed that definitive haemostasis was higher with injection combined with clipping (88.5%) compared with injections alone (78.1%, RR 1.13, 95% CI 1.03 to 1.23), leading to a reduction in rebleeding (8.3% v 18.0%; RR 0.47, 95% CI 0.28 to 0.76) and reduced requirement for surgery (1.3% v 6.3%; RR 0.23, 95% CI 0.08 to 0.70). There was no difference in mortality between single and combination therapies.<sup>57</sup> 1++

**A** Combinations of endoscopic therapy comprising an injection of at least 13 ml of 1:10,000 adrenaline coupled with either a thermal or mechanical treatment are recommended in preference to single modalities.

5.2.5 REPEAT ENDOSCOPY

The value of second look endoscopy following endoscopic treatment for peptic ulcer bleeding was examined in a meta-analysis of four RCTs involving a total of 785 patients. Patients who underwent second look endoscopy with further treatment when major SRH were found, had a reduced rate of rebleeding (12% v 18.2%; OR 0.64, 95% CI 0.44 to 0.95, p < 0.001) compared to those who underwent a single procedure (NNT = 16). This was not associated with reduced mortality or surgical operation rate.<sup>59</sup> 1++

A second meta-analysis of 10 studies, including 1,202 patients, also showed reduction of rebleeding in patients undergoing second look endoscopy (11.4% v 15.7%; OR 0.69; 95% CI 0.49 to 0.96).<sup>57</sup> 1++

These findings show that repeat endoscopy has significant advantages in terms of reducing rebleeding but does not confer survival benefit. Repeat endoscopy is safe and complications are rare.

**B** Endoscopy and endo-therapy should be repeated within 24 hours when initial endoscopic treatment was considered sub-optimal (because of difficult access, poor visualisation, technical difficulties) or in patients in whom rebleeding is likely to be life threatening.

5.2.6 REBLEEDING FOLLOWING ENDOSCOPIC THERAPY

Patients who rebleed after endoscopic therapy have increased mortality and require urgent intervention.<sup>6,7,60</sup> 1++

Optimum management is based upon clinical judgement, local expertise and is best undertaken following discussion between physicians and surgeons.

One trial randomised 100 patients who rebled following endoscopic therapy for ulcer bleeding to operative surgery or repeat endoscopic treatment. Thirty day mortality and transfusion requirements were low and similar in the two groups although more complications occurred in patients randomised to surgery.<sup>61</sup> This trial was undertaken in a tertiary referral centre by expert endoscopists and its conclusions may not be generalisable to less specialist units. 1++  
1+

The use of digital subtraction angiography to assist in the localisation of bleeding point and simultaneous superselective coil transcatheter embolisation using coils and polyvinyl alcohol, and gelatine sponge, has been reported in small cohort studies. These indicate high rates of technical success (98%), no rebleeding within 30 days (68-76%), and low (4-5%) complication rates (hepatic/splenic infarction, duodenal ischaemia).<sup>62-64</sup> One retrospective study reported similar success rates with embolisation using N-butyl-cyanoacrylate.<sup>65</sup> 3

A single retrospective comparison between embolisation and surgery showed no difference in rebleeding or mortality despite the more advanced age and greater prevalence of heart disease in the embolisation group.<sup>66</sup>



Embolisation has been used for a wider variety of causes of non-variceal upper GI haemorrhage, such as oesophageal haemorrhage,<sup>67</sup> GI surgery,<sup>68</sup> pancreatitis,<sup>69</sup> and haemobilia.<sup>70</sup>

A retrospective review of 163 patients with acute upper gastrointestinal haemorrhage and transcatheter embolisation reviewed factors associated with clinical success and concluded such treatment had a positive impact on survival independent of clinical condition<sup>64</sup> while a further review indicated early rebleeding was associated with abnormal coagulation and use of coils alone.<sup>71</sup>

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**D Non-variceal upper gastrointestinal haemorrhage not controlled by endoscopy should be treated by repeat endoscopic treatment, selective arterial embolisation or surgery.**

### 5.3 PHARMACOLOGICAL THERAPY

The recommendations made in this section are based on evidence available to support therapeutic management decisions in patients who present with non-variceal upper gastrointestinal bleeding. The recommendations cover the prevention of recurrent ulcer bleeding and do not address primary prophylaxis of gastrointestinal bleeding.

Approximately one third of patients who present with a bleeding ulcer will develop recurrent bleeding within two years and 40-50% within 10 years if left untreated after ulcer healing.<sup>72</sup>

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#### 5.3.1 HELICOBACTER PYLORI

##### Prevention of rebleeding

The role of *Helicobacter pylori* (H pylori) eradication in reducing the recurrence rate of uncomplicated peptic ulcer disease is well established.<sup>73</sup> In bleeding peptic ulcers, H Pylori eradication therapy also has a role in the prevention of recurrent bleeding.

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One systematic review which contained two meta-analyses compared H pylori eradication therapy to antisecretory non-eradication therapy and concluded that eradication of H pylori is more effective than antisecretory non-eradicating therapy (with or without long term maintenance antisecretory therapy) in preventing recurrent bleeding from peptic ulcer.<sup>72</sup> The NNT with eradication to prevent one episode of rebleeding was 6 when compared with no long term maintenance and 20 when compared with long term antisecretory therapy. Studies included follow up of at least six months. Studies excluded patients taking NSAIDs in order to remove complications attributable to these drugs.

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There is evidence to support discontinuing acid suppressing therapy after one week eradication therapy in uncomplicated peptic ulcer disease, however, the duration of ulcer healing treatment in patients with bleeding peptic ulcer varied within the trials included in the meta-analyses. One RCT confirmed that following successful eradication and three weeks of omeprazole 20 mg daily in patients with bleeding ulcers, there was no difference in terms of ulcer recurrence or H pylori re-infection during a mean follow up of 56 months between groups randomised to 16 weeks maintenance with antacid, colloidal bismuth subcitrate 300 mg four times daily, famotidine 20 mg twice daily or placebo.<sup>74</sup> This study confirmed there is no requirement for maintenance therapy beyond a four week treatment course and, in the absence of evidence to support a shorter treatment course, three weeks of a usual healing dose of PPI should be given following the one week H pylori eradication regimen.

There is no evidence to suggest that H pylori eradication influences the rate of rebleeding in the acute phase of peptic ulcer bleeding. One prospective cohort study showed that early H pylori eradication had no effect on the rate of rebleeding within three weeks of the index bleed.<sup>75</sup> This study suggests there is no need to treat patients before oral intake is established.

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**Testing for H pylori**

The presence of H pylori should be sought at the time of endoscopy. As PPI therapy is reported to reduce the sensitivity of H pylori testing, mucosal biopsies should be obtained from the antrum and body of the stomach at the initial endoscopy prior to commencing PPI therapy.<sup>76</sup> High-dose PPI therapy decreases the detection rate of H pylori infection to a greater extent than regular dose therapy (p=0.001).<sup>77</sup>

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2++

The accuracy of diagnostic tests for H pylori has been evaluated less thoroughly in patients with peptic ulcer bleeding compared with patients with dyspepsia or uncomplicated peptic ulcer. A meta-analysis suggested that endoscopic methods have a reduced sensitivity of H Pylori detection in patients with upper gastrointestinal bleeding; the rapid urease test providing a high number of false negative results.<sup>76</sup> Non-invasive methods seem to be less influenced by upper gastrointestinal bleeding. Meta-analysis illustrated that the urea breath test has the optimal sensitivity and specificity compared with both biopsy based methods and serology or stool tests, but there may be practical difficulties in asking nauseated patients to drink the test solution and to blow into the tube.

2++

The rapid urease test is the best test as it is quick, easy to perform and inexpensive. The use of PPIs are associated with false negative rapid urease results, therefore when negative for this test, additional biopsies should be examined histologically.<sup>76</sup> When biopsies are not obtained, the 13C-urea breath test is indicated since this minimises false negative results.<sup>76,78</sup> Delayed non-invasive testing (two weeks after stopping PPI therapy) at the outpatient clinic has improved detection of H pylori in those who tested negative at initial endoscopy.<sup>79</sup>

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The results of stool antigen tests are controversial. Pooled sensitivity (0.87) and specificity (0.7) suggest further studies using the more specific monoclonal enzyme-linked immunosorbent assay stool antigen test are required before this method can be recommended to diagnose H pylori in patients with upper gastrointestinal bleeding.<sup>76</sup>

2++

The H pylori infection rate in patients with bleeding peptic ulcers has been calculated as 79.8% (95% CI, 78% to 81%) from 32 studies of 3,597 patients.<sup>80</sup> Delayed testing suggests the prevalence may be higher.<sup>78,79</sup> There is no evidence to support empirical eradication of H pylori in patients with bleeding peptic ulcers. Practitioners should consider the small risk of antibiotic complications if this approach is taken.

**A Patients with peptic ulcer bleeding should be tested for Helicobacter pylori (with biopsy methods or urea breath test) and a one week course of eradication therapy prescribed for those who test positive. A further three weeks ulcer healing treatment should be given.**

**A In non-NSAID users, maintenance antisecretory therapy should not be continued after successful healing of the ulcer and Helicobacter pylori eradication.**

**B Biopsy samples to test for presence of Helicobacter pylori should be taken at initial endoscopy prior to commencing proton pump inhibitor therapy. Biopsy specimens should be histologically assessed when the rapid urease test is negative.**

- Successful Helicobacter pylori eradication should be confirmed by breath test or biopsy to minimise the risk of rebleeding from peptic ulcer.
- Second line treatment should be prescribed in the case of eradication failures.

Helicobacter pylori testing to confirm successful eradication should only be taken after proton pump inhibitor and antibiotic therapy has been completed and discontinued since testing within two weeks of these treatments may result in false negative findings.

Follow up endoscopy should be performed to confirm healing of gastric ulcers if there is suspicion of malignancy.

## 5.3.2 ACID SUPPRESSION AND AGENTS TO ARREST BLEEDING

**Acid suppression**

Patients at high risk of rebleeding (active arterial bleeding, non-bleeding visible vessels, adherent clots) receive endoscopic therapy to achieve haemostasis. The aim of additional acid suppression therapy in this group of patients is to maintain intragastric pH above 6 to stabilise clots and prevent rebleeding.<sup>35</sup> The aim of acid suppression therapy in patients in whom there is no indication for endoscopic therapy, is to commence usual therapeutic doses of oral PPI to initiate the ulcer healing process. This section focuses on the effectiveness of acid suppressing agents in terms of mortality, rebleeding or need for surgery in those patients with high-risk peptic ulcer bleeding.

A meta-analysis of 24 RCTs involving 4,373 patients confirmed that PPIs significantly reduce the rate of rebleeding (NNT = 13), the need for surgery (NNT = 34) and requirement for further endoscopic treatment (NNT = 10).<sup>36</sup> However, PPIs did not significantly affect overall mortality. An updated meta-analysis and further subgroup analysis of the same patients reported that reduction in mortality was significant when analysis was confined to seven trials in high-risk patients (active bleeding or non-bleeding visible vessel) who received endoscopic treatment.<sup>36</sup> The reduction in mortality remained significant when analysis was confined to four trials that used high-dose PPI treatment (omeprazole 80 mg bolus injection followed by 8 mg/hour intravenous infusion for 72 hours) following endoscopic treatment. There was no effect on mortality in the other three trials that used lower-dose intravenous or oral PPI treatment. The trials included in the meta-analysis used either H<sub>2</sub> receptor antagonists or placebo as control treatment. Mortality benefit was greatest in Asian patients (NNT = 34) and in patients with active bleeding or a non-bleeding visible vessel (NNT = 50). The optimum dose and route of PPI is unclear and should be evaluated in a non-Asian population (see section 4.3.1).

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PPIs are not licensed for the reduction in rate of rebleeding in patients with bleeding peptic ulcers.

**A** **High-dose intravenous proton pump inhibitor therapy** (eg omeprazole or pantoprazole 80 mg bolus followed by 8 mg/hour infusion for 72 hours) **should be used in patients with major peptic ulcer bleeding** (active bleeding or non-bleeding visible vessel) following endoscopic haemostatic therapy.

**Tranexamic acid**

The role of fibrinolytic inhibitors in gastrointestinal bleeding is unclear. Two meta-analyses including trials undertaken prior to the current practice of endoscopic treatment were identified.<sup>81,82</sup> Studies were small and heterogeneous, varied in methodology and the doses of tranexamic acid used. Pooled analysis suggested that tranexamic acid did not significantly reduce the rate of rebleeding or need for surgery but significantly reduced mortality (5% v 8%; RR 0.61, 95% CI 0.42 to 0.89). No evidence was identified that evaluated tranexamic acid as an adjunct to endoscopy. Tranexamic acid may be of benefit but large randomised trials are required to investigate its role in the management of upper gastrointestinal bleeding.

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1<sup>++</sup>

There is insufficient evidence to make a recommendation for the use of tranexamic acid in the treatment of non-variceal gastrointestinal bleeding.

**Somatostatin and its analogues**

The role of somatostatin in non-variceal gastrointestinal bleeding is unclear. Small individual trials show inconsistent results, vary in methodology and are heterogeneous. One meta-analysis, undertaken prior to current practice of endoscopic treatment compared somatostatin 250 mcg/hour or octreotide with H<sub>2</sub> receptor antagonists or placebo controls.<sup>83</sup> Somatostatin reduced the risk of continued or rebleeding (NNT = 5) and the risk of need for surgery (NNT = 8).

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There is insufficient evidence to make a recommendation for the use of somatostatin or its synthetic analogues in the treatment of non-variceal gastrointestinal bleeding.

5.3.3 CONTINUATION OF THERAPY FOR OTHER MEDICAL CONDITIONS

Prior to the bleeding episode, patients may have been taking medication which, if continued may increase the risk of rebleeding. This section describes evidence available to support risk minimisation strategies when medicines associated with upper gastrointestinal complications are used.

- ☑ Medicines known to increase the risk of upper gastrointestinal complications should, where possible, be given in monotherapy and at the lowest effective dose to minimise the risk of upper gastrointestinal complications.

**Non-steroidal anti-inflammatory drugs (NSAIDs)**

There is a fourfold increase in acute upper gastrointestinal bleeding and perforation in people who take NSAIDs (aspirin and non-aspirin NSAIDs) compared to people not taking these medications. Clinical factors reported to increase the risk of developing NSAID associated upper gastrointestinal complications include a history of ulcer or GI bleeding, increasing age, concomitant anticoagulation or corticosteroid therapy and high-dose NSAID use.<sup>84</sup> Patients with advanced age or a history of complicated ulcer disease have higher baseline risk for further gastrointestinal complications whether or not they take NSAIDs.

2++

Users of NSAIDs with a history of ulcer complications have a greater absolute increased risk of upper gastrointestinal bleeding than those without a history of ulcers. An incidence rate of 25-30 per 1,000 patient years was shown in NSAID users with a previous history of complicated ulcer. The risk associated with the NSAID persists for approximately two months after the treatment is stopped.<sup>84</sup>

2++

A number of studies have examined the role of gastroprotective agents in minimising the risk of recurrent bleeding in patients who require continuing NSAID treatment.

One RCT examined the use of 400 mcg/day misoprostol in combination with 500 mg/day naproxen or 1,000 mg/day of the cyclo-oxygenase 2 (COX-2) selective inhibitor nabumetone alone for 24 weeks.<sup>85</sup> The proportion of patients suffering major gastrointestinal events at 24 weeks was similar in both groups (31.1% in the naproxen/misoprostol group compared with 28.9% in the nabumetone group, p=0.93). This study suggested that neither misoprostol (400 mcg/day) nor nabumetone adequately reduces the risk of recurrent ulcer complications. Both drugs have a similar risk of complications. No studies were found where higher doses of misoprostol (associated with a high incidence of diarrhoea) were used in prevention of recurrent ulcer complications.

1+

Gastroprotection and eradication of H pylori infection were assessed in another RCT which compared omeprazole 20 mg daily with H pylori eradication for the prevention of recurrent UGIB in both users of low-dose aspirin (80 mg) and in patients with arthritis taking naproxen 500 mg twice daily.<sup>86</sup> After six months, the probability of recurrent bleeding among aspirin users was 1.9% after eradication therapy and 0.9% on omeprazole (absolute difference 1%; 95% CI -1.9 to 3.9%). Among naproxen users, the probability of recurrent bleeding was 18.8% after eradication therapy and 4.4% on omeprazole (absolute difference 14.4%; 95% CI 4.4 to 24.4%, p=0.005).

1+

Omeprazole (20 mg daily) is superior to eradication of H pylori in preventing recurrent bleeding in patients who are taking non-aspirin NSAIDs. Eradication of H pylori alone is as effective as maintenance treatment with omeprazole in preventing recurrent upper gastrointestinal bleeding in patients taking low-dose aspirin.

**COX-2 Inhibitors**

The safety of a COX-2 inhibitor in comparison to a combination of a non-selective NSAID and a PPI has been evaluated in three randomised controlled trials that assessed the frequency of recurrent bleeding and ulcer complications in patients with previous peptic ulcer bleeding. Patients were similar with no other risk factors.

Similar rates of rebleeding ulcers were found at six months: 6.4% in those taking diclofenac 75 mg twice daily in combination with omeprazole 20 mg daily, and 4.9% in those taking celecoxib 200 mg twice daily.<sup>87</sup> In a similar study, the probability of recurrent ulcers was 24% in the celecoxib group versus 32% in the diclofenac plus omeprazole group.<sup>88</sup> Another study compared celecoxib 200 mg daily to naproxen 750 mg daily in combination with lansoprazole 30 mg daily after healing of complicated NSAID ulcers and eradication of *H pylori*.<sup>89</sup> This study did not demonstrate that COX-2 inhibitors alone are safer than a combination of non-selective NSAID in combination with a PPI. After 24 weeks 4/120 (3.7%) in the celecoxib group compared with 7/122 (6.3%) in the naproxen and lansoprazole group developed ulcer complications (absolute difference -2.6%; 95% CI -9.1% to 3.7%).

1++

One RCT compared a combination of celecoxib 200 mg twice daily and esomeprazole 20 mg twice daily with celecoxib alone for prevention of recurrent ulcer bleeding in patients with previous NSAID induced ulcer bleeding who continued NSAID treatment.<sup>90</sup> No patients in the combination group and 12 patients (8.9%) in the celecoxib group had recurrent ulcer bleeding in the 13 month follow up period.

1++

The optimum dose of PPI for prevention of NSAID induced ulcer complications is unclear. A study involving patients at increased risk of developing GI complications (age over 60 and/or previous peptic ulcer disease) but not a previous history of recent GI haemorrhage, compared non-selective NSAIDs and COX-2 inhibitors in combination with esomeprazole 20 mg, 40 mg or placebo.<sup>91</sup> This study demonstrated that esomeprazole 20 mg is as effective as 40 mg daily for ulcer prevention. Subgroup analysis from this study of patients who did not have ulcer complications, suggested that a COX-2 inhibitor in combination with a PPI was no more effective than a non-selective NSAID plus PPI in ulcer prevention. The combination of COX-2 inhibitor and PPI has not been compared to non-selective NSAID and PPI in patients with a history of ulcer bleeding.

1+

Although the rate of rebleeding varies among different studies, patients at the highest risk of NSAID induced ulcer complications (those with a history of ulcer bleeding) have an increased risk of recurrent bleeding when taking a combination of NSAID and a PPI or COX-2 inhibitor alone.

It is not possible to recommend a COX-2 inhibitor in combination with a PPI in all high risk patients who are not at cardiovascular risk. Further studies are required to compare the rates of recurrent bleeding in patients receiving a combination of COX-2 inhibitor and PPI with a combination of non-selective NSAID and PPI.

Patients who have a history of ulcer bleeding and require NSAID treatment for arthritic conditions are usually elderly and have coexisting medical conditions, frequently including cardiovascular disease. The cardiovascular risk associated with both COX-2 inhibitors and non-selective NSAIDs should be taken into account when assessing individual need for an NSAID and in selecting choice, dose, route of administration and duration of therapy.

**A Patients with healed bleeding ulcers who test negative for *Helicobacter pylori* require concomitant proton pump inhibitor therapy at the usual daily dose if NSAIDs, aspirin or COX-2 inhibitors are indicated.**

- In patients in whom cardiovascular risk is a concern, naproxen with a proton pump inhibitor is recommended when alternative analgesic therapies fail.
- COX-2 inhibitors are not recommended in patients with cardiovascular risk.



**Aspirin and clopidogrel**

At a daily dose of 75 mg, aspirin is associated with a twofold increase in risk of upper GI complications compared to people not taking aspirin (RR 2.0, 95% CI 1.6 to 2.6). The risk is not reduced with enteric coated formulations.<sup>92</sup>

4

One RCT provided evidence that H pylori eradication therapy alone is as effective as maintenance treatment with omeprazole in preventing rebleeding in low-dose aspirin users.<sup>86</sup> The probability of recurrent bleeding was 1.9% after eradication therapy and 0.9% on omeprazole (absolute difference 1%; 95% CI -1.9 to 3.9%). A further RCT assessed whether the combination of lansoprazole 30 mg daily with H pylori eradication adds any benefit to H pylori eradication alone in prevention of rebleeding in aspirin users.<sup>93</sup> After 12 months, addition of lansoprazole 30 mg daily reduced the frequency of rebleeding (adjusted hazard ratio 9.6, 95% CI 1.2 to 76.1).

1+

The safety of clopidogrel in comparison to a combination of aspirin with esomeprazole has been evaluated in two RCTs involving patients with previous aspirin-induced peptic ulcer bleeding.<sup>94,95</sup> H pylori eradication and ulcer healing were confirmed before randomisation. In one trial the cumulative incidence of recurrent bleeding during the 12 month period was 8.6% (95% CI 4.1 to 13.1) in the clopidogrel group and 0.7% (95% CI 0 to 2.0) in those taking aspirin 80 mg plus esomeprazole 20 mg twice daily (difference 7.9%; 95% CI 3.4 to 12.4, p=0.001).<sup>95</sup>

1++

The second trial employed a dose of 100 mg aspirin and esomeprazole 20 mg once daily compared with clopidogrel 75 mg daily.<sup>94</sup> No patients in the aspirin plus esomeprazole group and nine patients in the clopidogrel group developed recurrent ulcer complications. A greater absolute difference in cumulative incidence was observed, 13.6% (95% CI 6.3 to 20.9, p=0.0019). Esomeprazole 20 mg once daily is an effective dose in the prevention of recurrent ulcer bleeding. In patients with a history of aspirin-induced ulcer bleeding, the combination of aspirin plus esomeprazole is superior to clopidogrel in the prevention of recurrent ulcer bleeding.

1++

All data comparing the recurrence of gastrointestinal bleeding associated with NSAIDs (aspirin and non-aspirin NSAIDs) with or without PPI are derived from studies where ulcer healing and eradication of H pylori was confirmed before randomisation.

- A**
  - **Aspirin and NSAIDs should be discontinued when patients present with peptic ulcer bleeding.**
  - **Once ulcer healing and eradication of *Helicobacter pylori* are confirmed, aspirin and NSAIDs should only be prescribed if there is a clear indication.**

**Selective serotonin reuptake inhibitors**

A review of cohort and case control studies provides weak evidence that selective serotonin reuptake inhibitor (SSRI) use may be associated with an increased risk of upper gastrointestinal bleeding especially in those patients at high risk and those taking concomitant NSAIDs or aspirin.<sup>96</sup> The relative risk is less with other antidepressants.

2+

- D** **Selective serotonin reuptake inhibitors should be used with caution in patients who have an increased risk of gastrointestinal bleeding, especially in patients taking NSAIDs or aspirin. A non-SSRI antidepressant may be an appropriate choice in such patients.**

**Anticoagulants**

The risk of recurrent bleeding in those patients taking oral anticoagulants and with a history of GI bleeding is unknown and data must be extrapolated from studies of patients with no history of gastrointestinal bleeding. Concurrent use of oral anticoagulants in NSAID users has been shown in a cohort study to increase the risk of hospitalisation for bleeding ulcer approximately threefold compared with NSAID users not taking oral anticoagulants.<sup>97</sup> This increase was similar to that found in users of anticoagulants compared with non-users of anticoagulants. These data suggest that anticoagulant use is associated with a threefold increase in risk of bleeding ulcer. The relative risk of bleeding ulcer in patients taking a combination of anticoagulants and NSAIDs compared with non-users of either drug was 12.7 (95% CI 6.3 to 25.7).<sup>97</sup>

2+

**Corticosteroids**

The risk of recurrent bleeding in those patients taking oral corticosteroids and with a history of GI bleeding is unknown. Concurrent use of oral corticosteroids in NSAID users has been shown in a case control study to increase the relative risk of peptic ulcer or ulcer complications from 3.6 (95% CI 2.9 to 4.3) in those receiving NSAID monotherapy to 8.5 (95% CI 3.9 to 13.9).<sup>92</sup> Extrapolation of these data suggests that the risk of gastrointestinal bleeding associated with NSAIDs might be doubled in patients receiving corticosteroids.

2+

**D** Oral anticoagulants or corticosteroids should be used with caution in patients at risk from gastrointestinal bleeding, especially in those taking aspirin or NSAIDs.

## 6 Management of acute variceal upper gastrointestinal bleeding

Variceal haemorrhage occurs from dilated veins (varices) at the junction between the portal and systemic venous systems. These tend to be in the distal oesophagus and/or the proximal stomach, but isolated varices may be found in the distal stomach, large and small intestine. The majority of patients with variceal bleeding have chronic liver disease. Patients with variceal haemorrhage will often present with overt upper GI bleeding with haematemesis and/or melaena, but may also present with a decompensation of chronic liver disease including encephalopathy or with anaemia.

Around 11% of patients undergoing endoscopy for upper GI bleeding have variceal bleeding,<sup>1</sup> of which the large majority have bleeding oesophageal varices (see Table 7). Variceal haemorrhage has a poor prognosis (see section 2.2.1) and prompt recognition and treatment are required.

Table 7: Relative frequency of variceal gastrointestinal bleeding

Variceal bleeding	Relative frequency (%)
oesophageal varices	90
gastric varices	8
ectopic varices	2

The outcome for patients with variceal haemorrhage is closely related to the severity of the underlying liver disease.<sup>98</sup> The severity of liver disease is stratified by Childs-Pugh grade (see Table 8). In patients with alcoholic liver disease who were treated with injection sclerotherapy for bleeding oesophageal varices mortality was reported at 32% for Childs A, 46% for Childs B and 79% for Childs C patients three years after endoscopic therapy. Survival rates declined in all patients as length of follow up increased.<sup>98</sup> There is evidence that outcomes from variceal haemorrhage are improving over time as new treatment strategies (eg variceal band ligation and vasoactive drugs) are introduced.<sup>99,100</sup>

Table 8: Childs-Pugh grading of chronic liver disease

Clinical/laboratory findings	Score		
	1	2	3
Encephalopathy	None	Mild (grade 1-2)	Severe (grade 3-4)
Ascites	None	Mild/Slight	Moderate/Large
Bilirubin (micromol/l)	< 34	34-51	> 51
Albumin (g/l)	≥ 35	28-35	< 28
Prothrombin time prolongation (secs) or international normalised ratio (INR)	< 4 < 1.3	4-6 1.3 – 1.5	> 6 > 1.5

Chronic liver disease is classified into Child-Pugh class A to C, employing the total score from the above table.

Total Points	Child-Pugh class
5-6	A
7-9	B
10-15	C



Patients presenting with variceal haemorrhage should be assessed and resuscitated as for any other patient with evidence of UGIB. Variceal haemorrhage may be suspected when there is a history of previous variceal bleeding, known liver disease or when clinical assessment identifies 'stigmata' of chronic liver disease or portal hypertension. These include the presence of jaundice, ascites, splenomegaly (enlargement of the spleen), encephalopathy, caput medusae (dilated periumbilical veins) and spider naevi. The initial approaches to treating patients presenting with variceal haemorrhage are endoscopic treatment, pharmacological therapy, and balloon tamponade.

## 6.1 ENDOSCOPIC THERAPY FOR ACUTE VARICEAL HAEMORRHAGE

Variceal haemorrhage is confirmed at the time of upper gastrointestinal endoscopy. In patients with suspected variceal haemorrhage endoscopy should be performed once appropriate resuscitation has been undertaken.<sup>101,102</sup>

4

### 6.1.1 OESOPHAGEAL VARICES

A meta-analysis of seven RCTs showed that variceal band ligation therapy was superior to sclerotherapy in terms of rebleeding (OR 0.52, 95% CI 0.37 to 0.74), all-cause mortality (OR 0.67 CI 0.46 to 0.98), and death due to bleeding (OR 0.49, CI 0.24 to 0.996) in patients with bleeding oesophageal varices.<sup>103</sup>

1++

In a subsequent randomised trial better control of variceal bleeding was achieved with ligation than sclerotherapy (97% v 76%,  $p=0.12$ ). Complications were greater in the sclerotherapy group (29% v 5%,  $p=0.007$ ), particularly in regard to sepsis and oesophageal ulceration.<sup>104</sup>

1+

Variceal band ligation has been shown to be superior to sclerotherapy in patients who are also prescribed somatostatin.<sup>105</sup> The advantage was seen in immediate haemostasis (OR 2.4, 95% CI 1.1 to 4.9), and in significantly greater six week survival without continued acute bleeding, rebleeding or death ( $p=0.01$ ).

1+

A meta-analysis of vasoactive drug treatment versus sclerotherapy indicated similar rates of haemostasis, rebleeding and mortality for both interventions, with greater adverse events in the sclerotherapy group (RR 0.14, 95% CI 0.07 to 0.22).<sup>106</sup>

1++

One trial compared somatostatin with variceal band ligation in the management of active variceal bleeding. The ligation group had a significantly lower failure rate (4.8% v 31.7%,  $p=0.0001$ ).<sup>107</sup>

1+

**A Patients with confirmed oesophageal variceal haemorrhage should undergo variceal band ligation.**

Banding may be technically difficult in cases of continued bleeding, and sclerotherapy may then be necessary.<sup>102,108,109</sup>

4

### 6.1.2 GASTRIC VARICES

Gastric varices can be classified according to their position and their association with oesophageal varices. Gastric varices which are in continuity with oesophageal varices extending less than 5 cm along the lesser curve of the stomach are classified gastro-oesophageal (GOV) Type 1. Those which are in continuity with oesophageal varices but which extend further towards the fundus are classified GOV Type 2. Isolated gastric varices (IGV) are classified according to whether they are found in the fundus (IGV Type 1) or elsewhere in the stomach (IGV Type 2).

Two RCTs have compared the efficacy and complications of cyanoacrylate injection and banding ligation for the management of bleeding gastric varices.

In the first of these studies endoscopic obturation using cyanoacrylate was more effective and safer than band ligation.<sup>110</sup> Initial haemostatic rate (defined as no bleeding for 72 hours after treatment) was 87% in the injection group and 45% in the ligation group ( $p=0.03$ ). Rebleeding rates were significantly higher in the ligation group (54%) than the injection group (31%,  $p=0.0005$ ). Treatment-induced ulcer bleeding occurred in two patients (7%) in the injection group and eight patients (28%) in the ligation group ( $p=0.03$ ). The amount of blood transfusions required was also higher in the ligation group than the injection group ( $4.2 \pm 1.3$  v  $2.6 \pm 0.9$  units, respectively,  $p<0.01$ ). Nine patients in the injection group and 14 patients in the ligation group died ( $p=0.05$ ). 1+

In the second study there was no difference in control of bleeding, but the rebleeding rate was significantly less in those treated with cyanoacrylate (OR 2.45).<sup>111</sup> 1+

The majority of patients in both studies had GOV Type 1 rather than fundal varices (GOV Type 2 or IGV Type 1). The benefits of cyanoacrylate injection therapy were not limited to any specific type of gastric varix in the first study. In the second study the reduction in rebleeding was most clearly seen in patients with IGV Type 1.

A further RCT, involving only IGV Type 1 compared cyanoacrylate with alcohol injection and suggested an advantage in the use of cyanoacrylate for controlling acute bleeding.<sup>112</sup> 1+

A retrospective study compared cyanoacrylate injection with transjugular intrahepatic portosystemic stent shunt (TIPSS) for acute gastric variceal haemorrhage.<sup>113</sup> This study suggested that cyanoacrylate was more cost effective than TIPSS. There were no significant differences in mortality or rebleeding between the two treatments. Most patients had GOV Type 1 varices. 3

Although not subject to RCTs, thrombin injection of gastric varices has been described for the management of acute bleeding. The largest of these studies reported a 94% initial haemostasis rate with a low (8%) six week mortality.<sup>114</sup> 3

**B Patients with confirmed gastric variceal haemorrhage should have endoscopic therapy, preferably with cyanoacrylate injection.**

## 6.2 VASOACTIVE DRUG THERAPY FOR ACUTE VARICEAL HAEMORRHAGE

Two systematic reviews considered the use of either terlipressin<sup>115</sup> or somatostatin and its analogues<sup>116</sup> for the management of acute variceal haemorrhage.

In the first systematic review seven RCTs compared terlipressin with placebo.<sup>115</sup> There was a statistically significant mortality benefit in favour of terlipressin with a relative risk of 0.66 (95% CI 0.49 to 0.88). The NNT for terlipressin to prevent one death was 8.3. 1++

The systematic review of somatostatin and its analogues identified 21 RCTs comparing these drugs with placebo.<sup>116</sup> There was no reduction in mortality (relative risk 0.97, 95% CI 0.75 to 1.25, for the trials with a low risk of bias, and 0.80, 95% CI 0.63 to 1.01, for the other trials), although there was an improvement in initial haemostasis with drug therapy (relative risk 0.68; 95% CI 0.54 to 0.87). 1++

Neither meta-analysis presented results according to whether the drugs were used before or after endoscopy. In clinical practice the decision to use drug treatment is based either on suspicion of variceal haemorrhage or endoscopic confirmation of variceal haemorrhage. In addition, neither review separated those trials which used vasoactive drug treatment in combination with, or instead of endoscopic therapy. Therefore, trials relating to these differing clinical situations were reviewed separately.

### 6.2.1 VASOACTIVE DRUG THERAPY PRIOR TO ENDOSCOPY

In the studies reviewed, vasoactive drug treatment was initiated prior to an endoscopic diagnosis of variceal haemorrhage. Most patients went on to receive endoscopic treatment with either variceal band ligation or sclerotherapy.

**Terlipressin**

One RCT randomised patients with suspected bleeding varices to a combination of terlipressin plus glyceryl trinitrate (GTN) or placebo.<sup>117</sup> Bleeding control was significantly better in the terlipressin/GTN group than in the control group ( $p=0.034$ ). Mortality due to bleeding episodes was significantly lower in the terlipressin/GTN group than in the placebo group at day 15 ( $p=0.035$ ) but this effect was not maintained over a longer timescale. The dose of terlipressin was 1-2 mg intravenously repeated at four and eight hours after the initial treatment. 1+

**Somatostatin and analogues**

Two RCTs tested the efficacy of somatostatin compared with placebo prior to endoscopy. One of these trials demonstrated an improvement in the rate of haemostasis with drug treatment (RR 0.63; 95% CI 0.46 to 0.97), but did not show reduced rebleeding or mortality.<sup>118</sup> Treatment failed in 35 somatostatin and 57 placebo recipients ( $p=0.004$ ); death or use of rescue therapy occurred in nine and 19 patients, respectively ( $p=0.05$ ). The treatment used was 250 mcg/hour after a 250 mcg bolus given intravenously. 1+

The other RCT showed no difference in rates of haemostasis, rebleeding or mortality between somatostatin treated patients and placebo patients.<sup>119</sup> 1+

No evidence was identified for the pre-endoscopic use of octreotide, an analogue of somatostatin.

One RCT studied the effects of treatment with vapreotide, another somatostatin analogue, before endoscopic treatment in 227 patients with cirrhosis who were hospitalised for acute upper gastrointestinal bleeding.<sup>120</sup> Patients were randomised to either vapreotide (a 50 mcg intravenous bolus followed by an infusion at a rate of 50 mcg/hour for five days) or placebo. At the time of endoscopy, active bleeding was evident in 31% of patients in the vapreotide group and 46% of patients in the placebo group ( $p=0.03$ ). During the five day infusion survival and control of bleeding was achieved in 66% of patients in the vapreotide group and 50% of patients in the placebo group ( $p=0.02$ ). The patients in the vapreotide group received significantly fewer blood transfusions ( $2.0 \pm 2.2$  v  $2.8 \pm 2.8$  units,  $p=0.04$ ). Overall mortality rates at 42 days were not significantly different in the two groups. 1+

**A** Prior to endoscopic diagnosis, terlipressin should be given to patients suspected of variceal haemorrhage.

6.2.2 VASOACTIVE DRUG THERAPY AFTER ENDOSCOPIC DIAGNOSIS OF ACUTE VARICEAL HAEMORRHAGE

**Terlipressin**

Two studies compared terlipressin with placebo after endoscopic confirmation of variceal haemorrhage.<sup>121,122</sup> One study demonstrated an improvement in haemostasis (OR 0.29; 95% CI 0.09 to 0.94).<sup>122</sup> In the other study 60% of acute variceal bleeding episodes were controlled with terlipressin compared with 37% in patients given placebo (not significant). 1+

Terlipressin has been compared with vasopressin in two studies.<sup>123,124</sup> One study showed that terlipressin more effectively achieved haemostasis (OR 0.09, 95% CI 0.002 to 0.48).<sup>123</sup> The other study showed no significant difference in therapeutic effect. The use of vasopressin is limited by its side effect profile, in particular with regard to ischaemia and arrhythmias.<sup>108</sup> 1+  
4

In one study comparing terlipressin with octreotide, the rate of haemostasis was greater for octreotide (OR 2.74, 95% CI 1.01 to 6.14), with a trend to a reduction in rebleeding with terlipressin (OR 0.38, 95% CI 0.14 to 1.01). Neither drug had a survival advantage.<sup>125</sup> Another study showed no differences in haemostasis, rebleeding or mortality.<sup>126</sup> 1+

**Somatostatin**

Only one study has compared somatostatin with placebo after endoscopic confirmation of variceal haemorrhage.<sup>127</sup> Somatostatin was delivered at an infusion rate of 250 mcg/hour after a 250 mcg bolus. This study showed similar rates of rebleeding and mortality in the two arms. 1+

One RCT using high-dose somatostatin (750 mcg bolus followed by 500 mcg/hour) demonstrated improved survival (93% v 70%) and haemostasis (82% v 60%) rates for patients with active bleeding at endoscopy compared with 250 mcg/hour regimens.<sup>128</sup> Infusions continued for two days. 1+

Two studies have compared terlipressin with somatostatin. There were no significant differences in haemostasis, rebleeding or survival.<sup>129,130</sup> 1+

**Vasoactive drug treatment in combination with endoscopic treatment**

In a meta-analysis of eight RCTs the combination of somatostatin, octreotide or vapreotide with endoscopic therapy was superior to endoscopic therapy alone (haemostasis OR 1.12, 95% CI 1.02 to 1.23; early rebleeding OR 1.28, 95% CI 1.18 to 1.39) although there was no survival benefit.<sup>131</sup> All but one of these studies used sclerotherapy as endoscopic treatment. The remaining trial showed that a combination of variceal band ligation plus octreotide (50 mcg bolus; 50 mcg/hour for five days) more effectively achieved haemostasis by day 5, compared to octreotide alone (RR 1.58; 95% CI 1.19 to 2.08).<sup>132</sup> 1+

Four further studies were identified that have investigated the combination of octreotide and sclerotherapy with sclerotherapy alone.<sup>133-136</sup> The doses of octreotide in these studies was similar (25-50 mcg/hour for two days ± a 50 mcg bolus).

Two of these showed an improvement in haemostasis (RR 0.26, 95% CI 0.08 to 0.9 and RR 0.47, 95% CI 0.22 to 0.97 respectively) with the endoscopy/drug combinations.<sup>133,134</sup> Two studies demonstrated reduced rebleeding (RR 0.15, 95% CI 0.03 to 0.63 and RR 0.22, 95% CI 0.05 to 0.99 respectively),<sup>134, 135</sup> but none showed improved survival with combination therapy. 1- 1+

One study showed no benefit for the combination of octreotide and sclerotherapy over sclerotherapy alone in haemostasis, rebleeding or survival.<sup>136</sup> 1+

An RCT using high-dose somatostatin (500 mcg bolus followed by 500 mcg/hour) demonstrated a reduction in rebleeding for Childs B and C patients (OR 0.3, 95% CI 0.1 to 0.9) compared with 250 mcg/hour regimens when both regimens were combined with sclerotherapy. Infusions continued for five days.<sup>137</sup> 1+

One study of terlipressin showed a lower mortality (OR 0.26, 95% CI 0.08 to 0.82) and improved haemostasis for patients in the terlipressin arm (OR 0.19, 95% CI 0.06 to 0.6).<sup>138</sup> In this study patients received 2 mg terlipressin or placebo every four hours for 24-36 hours prior to endoscopic sclerotherapy. This study is exceptional amongst trials of vasoactive drugs in that it shows an improvement in survival, although survival was not a primary end point. 1+

**A** After endoscopic treatment of acute oesophageal variceal haemorrhage patients should receive vasoactive drug treatment (terlipressin for 48 hours, octreotide, or high-dose somatostatin each for three to five days).

**6.3 ANTIBIOTIC THERAPY**

A meta-analysis showed that antibiotic use significantly reduces the mortality of patients who develop acute UGIB in association with chronic liver disease (OR 0.73, 95% CI 0.55 to 0.95).<sup>139</sup> 1++

One RCT compared oral norfloxacin with intravenous ceftriaxone. This showed no difference in mortality between these drugs, although there were significantly fewer septic episodes in patients treated with ceftriaxone.<sup>140</sup> 1+

**A** Antibiotic therapy should be commenced in patients with chronic liver disease who present with acute upper gastrointestinal haemorrhage.

## 6.4 BALLOON TAMPONADE

Six randomised controlled trials examined the use of balloon tamponade in acute variceal haemorrhage.<sup>118,141-145</sup> These studies compared balloon tamponade with different pharmacological treatments (terlipressin ± GTN, octroetide and somatostatin). Balloon tamponade did not improve survival and was associated with the development of significant complications. None of these studies examined the use of balloon tamponade prior to endoscopic diagnosis of variceal haemorrhage. 1+

One study compared balloon tamponade with prompt endoscopic sclerotherapy.<sup>145</sup> Although there was no difference in mortality or rebleeding, the transfusion requirement ( $p < 0.01$ ) and complication rates (14% v 39%;  $p < 0.05$ ) were lower in the endoscopic treatment group. 1+

## 6.5 MANAGEMENT OF BLEEDING VARICES NOT CONTROLLED BY ENDOSCOPY

On occasion acute variceal bleeding will continue despite the combination of endoscopic therapy and drug therapy. Expert opinion recommends managing such patients in two stages: initial emergency therapy to arrest the blood loss, and second line therapy to address the underlying cause.<sup>102</sup> 4

Rates of haemostasis associated with balloon tamponade are reported to be 80-95% in patients with either oesophageal or gastric varices. The complications of balloon tamponade including pneumonia, oesophageal tears and discomfort were noted to be greater than drug treatments or sclerotherapy.<sup>146</sup> 4

Balloon tamponade is a temporary measure that can control massive variceal bleeding which does not respond to endoscopic therapy. Definitive endoscopic, TIPSS or surgical treatment can subsequently be administered once the patient has been stabilised.<sup>102</sup>

A retrospective study with a historical control group demonstrated an overall improvement in survival with TIPSS compared with oesophageal transection for the management of torrential variceal haemorrhage (mortality 42% v 79%).<sup>147</sup> 2+

One RCT suggested that an H-graft porto-caval shunt may be more effective than TIPSS for uncontrolled variceal haemorrhage, but the proportion of patients treated by surgical shunting on an emergency or urgent basis was much lower than those treated with TIPSS (20% v 37%).<sup>148</sup> 1+

As surgical shunts are rarely performed and require specialised surgical skills TIPSS should be considered the therapy of choice.

**C Transjugular intrahepatic portosystemic stent shunting is recommended as the treatment of choice for uncontrolled variceal haemorrhage.**

**D Balloon tamponade should be considered as a temporary salvage treatment for uncontrolled variceal haemorrhage.**

## 7 Prevention of variceal rebleeding

Once acute bleeding is successfully controlled, the recurrence of variceal rebleeding can be as high as 50% within the first day of the acute episode and 80% within one year.<sup>149,150</sup> Due to the high risk of mortality, consideration must be given to secondary prophylaxis of variceal haemorrhage.

4

### 7.1 VASOACTIVE DRUG THERAPY

#### 7.1.1 OESOPHAGEAL VARICES

A meta-analysis of 895 patients in 12 trials comparing propranolol with placebo in the secondary prevention of variceal haemorrhage found propranolol monotherapy more effective than placebo in reducing risk of death (pooled risk difference -5%, 95% CI -9% to 1%,  $p=0.002$ ) and rebleeding (pooled risk difference -25%, 95% CI -39% to -10%,  $p<0.001$ ).<sup>151</sup>

1+

The combination of beta blocker and nitrate is superior to beta blocker therapy alone and of equal efficacy to variceal band ligation.<sup>152-154</sup>

1+

There is no evidence that octreotide has any role in the secondary prevention of variceal bleeding.

#### 7.1.2 GASTRIC VARICES

No placebo controlled studies have been identified that examine the efficacy of non-selective beta blocker drugs in preventing rebleeding from gastric varices.

### 7.2 ENDOSCOPIC THERAPY

#### 7.2.1 OESOPHAGEAL VARICES

Secondary prevention of variceal bleeding can be achieved with endoscopic sclerotherapy or band ligation.

In a meta-analysis of secondary prevention studies (1,111 patients) sclerotherapy was shown to be superior to placebo in reducing the risk of rebleeding, (OR 0.63, 95% CI 0.49 to 0.79) and death (OR 0.77, 95% CI 0.61 to 0.98). Nine trials involving a total of 787 patients compared sclerotherapy to beta blocker drugs and found rebleeding to be significantly reduced in the group receiving sclerotherapy (OR 0.71, 95% CI 0.51 to 0.99), despite considerable heterogeneity in the data analysed ( $p=0.07$ ).<sup>155</sup>

1+

This meta-analysis also showed band ligation to be more effective than sclerotherapy in preventing rebleeding (OR 0.49, 95% CI 0.31 to 0.78).<sup>155</sup>

1+

In another meta-analysis of seven RCTs involving 547 patients which compared variceal sclerotherapy to band ligation, band ligation was associated with a lower rebleeding rate (OR 0.52, 95% CI 0.37 to 0.74) and mortality (OR 0.67, 95% CI 0.46 to 0.98) and had significantly fewer complications (OR 0.10, 95% CI 0.03 to 0.29).<sup>103</sup>

1++

A meta-analysis of eight RCTs compared combination sclerotherapy and band ligation to band ligation alone in the prevention of rebleeding.<sup>156</sup> No difference was found in rebleeding (RR = 1.05, 95% CI 0.67 to 1.64,  $p=0.83$ ) or death rates (RR = 0.99, 95% CI 0.68 to 1.44) but a high stricture rate was noted in those treated with combination therapy.

1+



In two RCTs the combination of nadolol (a non-selective beta blocker) and variceal band ligation was shown to be superior to band ligation alone for reduction in rebleeding. The variceal bleeding recurrence rates were 12% and 14% in the ligation plus beta blocker groups and 29% and 38% in the ligation only groups respectively ( $p=0.001$  and  $p=0.006$ ).<sup>157,158</sup>

1+

**A** Variceal band ligation combined with a beta blocker is recommended as secondary prevention for oesophageal variceal haemorrhage.

**A** In patients unsuitable for variceal band ligation combination of non-selective beta blocker and nitrate is recommended as secondary prevention for oesophageal variceal haemorrhage.

## 7.2.2 GASTRIC VARICES

One RCT suggested that endoscopic injection therapy with histoacryl glue is not more effective than non-selective beta blockers in secondary prevention of variceal haemorrhage.<sup>159</sup>

1+

## 7.3 PORTOSYSTEMIC SHUNTS

### 7.3.1 OESOPHAGEAL VARICES

A meta-analysis of 22 trials compared portosystemic shunts (TIPSS and surgical shunts) versus endoscopic therapy.<sup>160</sup> Shunt therapy reduced the rate of rebleeding (OR 0.24, 95% CI 0.18 to 0.30) but this was at the cost of an increased incidence of chronic hepatic encephalopathy (OR 2.07, 95% CI 1.20 to 3.62) with no differences in mortality. Higher shunt dysfunction and reintervention was observed in TIPSS patients (59%, range 18% to 72%) compared to those receiving a distal splenorenal surgical shunt operation (7.8%, range 3.8% to 13.9%).

1++

Surgical shunts and TIPSS have similar rates of rebleeding and encephalopathy but TIPSS is associated with a higher rate of shunt dysfunction.<sup>161</sup>

1+

One RCT found that polytetrafluoroethylene covered stents had lower shunt dysfunction and a reduced reintervention rate compared to uncovered stents.<sup>162</sup>

1+

One RCT showed that a combination of propranolol and nitrates was less effective than TIPSS in preventing variceal rebleeding. Hepatic encephalopathy was less prevalent and treatment costs were lower in patients receiving the drug combination whilst survival and changes in the Child-Pugh scores were similar in both groups.<sup>163</sup>

1-

As surgical shunts are not readily available and require specialised surgical skills, and because many patients with chronic liver disease are unfit for major surgery, TIPSS should be considered to prevent rebleeding when combination pharmacological and band ligation therapy are not available, cannot be tolerated or fail.

**A** Transjugular intrahepatic portosystemic stent shunts should be considered to prevent oesophageal variceal rebleeding in patients with contraindications, intolerance to or failure of endoscopic and/or pharmacological therapy.

### 7.3.2 GASTRIC VARICES

One RCT has demonstrated that TIPSS is more effective than cyanoacrylate injection in preventing rebleeding from gastric varices, with similar survival and frequency of complications.<sup>164</sup> After a median follow up of 33 months, rebleeding from gastric varices was recorded in 11% of patients who received TIPSS and in 38% of patients who received cyanoacrylate injection (OR 3.6, 95% CI 1.2 to 11.1,  $p=0.014$ ). Blood transfusion requirements were lower in the TIPSS group than in the cyanoacrylate group ( $p<0.01$ ). There was no significant difference between groups in survival or frequency of complications.

1++

**B** Transjugular intrahepatic portosystemic stent shunts should be considered to prevent gastric variceal rebleeding.

## 8 Management of lower gastrointestinal bleeding

Lower gastrointestinal bleeding of modest severity is a common problem in primary care. This guideline addresses the management of bleeding that is of sufficient severity to warrant emergency admission to hospital. Bleeding of lesser severity, subject to elective investigation, is not considered. This section considers the management of the small group of patients admitted with severe colonic haemorrhage.

Around 25% of patients presenting with GI haemorrhage in hospital have bleeding that originates in the lower GI tract. A large majority of these (80-85%) will stop bleeding spontaneously without any specific treatment.<sup>165</sup> These patients should receive resuscitation and transfusion, if required, to restore circulatory volume. Colonic imaging is an appropriate investigation to exclude neoplasia and determine an underlying cause.

Although lower GI haemorrhage is defined as bleeding that originates from a source distal to the ligament of Trietz, approximately 15% of patients with acute severe haematochezia will have an upper GI source of bleeding identified on upper endoscopy.<sup>3</sup> Small bowel sources account for 0.7-9.0% of cases of severe hamatochezia.<sup>15</sup>

The incidence of underlying causes of lower GI bleeding varies between age groups. The most common causes are listed in Table 9.<sup>19</sup>

Table 9: Major causes of colonic bleeding

Major causes of colonic bleeding
diverticular disease
vascular malformations (angiodysplasia)
ischaemic colitis
haemorrhoids
inflammatory bowel disease (eg ulcerative proctitis, Crohn's disease)
neoplasia (carcinoma or polyps)
radiation enteropathy

A case series of 88 patients with radiation-induced rectal bleeding following radiotherapy for gynaecological malignancies showed that most patients presented with bleeding within one year (69% of patients). Within two years of radiotherapy 96% of patients had presented with rectal bleeding and the remaining 4% presented later than two years. Sigmoidoscopy showed active proctitis and occasionally bleeding was severe.<sup>166</sup>

A history of pain and weight loss in combination with bleeding suggests cancer. Most rectal cancers are palpable. Rectal examination in patients presenting with haematochezia is essential to detect ongoing bleeding and enable diagnosis of local anorectal conditions (accounting for 14% of acute LGIB).<sup>167</sup> The majority of these are haemorrhoids which can cause severe bleeding. Rectal examination and proctoscopy will allow confident diagnosis of trivial anorectal conditions in a healthy young person permitting safe discharge and outpatient follow up.

- All patients with rectal bleeding should have a full history taken, abdominal examination and should undergo digital rectal examination and proctoscopy.



## 8.1 LOCALISING BLEEDING

Localisation of the site and determination of the cause of bleeding in acute colonic haemorrhage allows treatment to be appropriately focused. Localisation techniques utilise endoscopic, radiological and nuclear scintigraphic modalities.

The quantity of evidence on which this practice is based is limited. Few studies have compared diagnostic modalities.

### Colonoscopy

One RCT compared urgent colonoscopy (within eight hours) with standard colonoscopy (within 48 hours) and found improved diagnosis with urgent colonoscopy but not improved outcomes.<sup>44</sup> | 1+

### Computed tomography angiography/angiography

Cohort studies have showed that computed tomography angiography (CTA) may have a role prior to angiography.<sup>168</sup> One study compared multislice CTA with flexible sigmoidoscopy, and found favourable results for CTA but concluded that further work was needed to define sensitivity and specificity.<sup>169</sup> | 3

### Nuclear scintigraphy

Several single-cohort studies examined the role of technetium-labelled red blood cell scintigraphy in the preoperative localisation of acute LGIB. In contrast to CT angiography, whilst the site of bleeding may be identified by scintigraphy, this modality cannot determine the underlying cause.<sup>170-173</sup> | 3

A single-cohort study showed that technetium-labelled red blood cell scintigraphy in acute lower GI haemorrhage is more useful with patients with active significant haemorrhage (>2 units transfused in previous 24 hours).<sup>174</sup> | 3

**D** The cause and site of massive lower gastrointestinal haemorrhage should be determined following the early use of colonoscopy and use of computed tomography scanning, computed tomography angiography or digital subtraction angiography.

**D** Nuclear scintigraphy should be considered to assist in localisation of bleeding in patients with significant recent haemorrhage.

## 8.2 INTERVENTIONS

In patients with poor localisation and ongoing bleeding, early catheter mesenteric angiography and embolisation using superselective techniques is often attempted. The quantity of evidence on which this practice is based is limited. There are few studies that allow direct comparison between modalities.

### 8.2.1 COLONOSCOPIC HAEMOSTATIC TECHNIQUES

A number of case series and cohort studies were identified that describe the effectiveness of colonoscopic haemostatic techniques (adrenaline injections, bipolar coagulation or endoscopic hemoclipping).<sup>175-178</sup> | 3

In patients who were identified to be bleeding secondary to diverticulosis, colonoscopic haemostatic techniques were associated with:

- high technical success in 90-100% of cases
- clinical success rates of 70-100% of cases
- no significant complications.

In patients who had bleeding following colonoscopic polypectomy or colonoscopic biopsy colonoscopic haemostatic techniques were associated with:

- high technical success in 99-100% of cases
- clinical success rates of 95-100% of cases
- no significant complications.<sup>177,178</sup>

3

**D In patients with massive lower gastrointestinal haemorrhage, colonoscopic haemostasis is an effective means of controlling haemorrhage from active diverticular bleeding or post-polypectomy bleeding, when appropriately skilled expertise is available.**

8.2.2 EMBOLISATION

Several single-cohort studies were identified that analysed embolisation and superselective embolisation in the treatment of lower GI haemorrhage.<sup>63,179-184</sup>

3

Embolisation was associated with:

- high technical success in 89-100% of cases
- clinical success rates of 80-91% of cases (complete 68%, partial in 16%). Delayed rebleeding (in another bowel segment) in 27%
- some complications - in one study, 11% of patients required colectomy for colonic ischaemia.<sup>181</sup>

**D In patients with massive lower gastrointestinal haemorrhage, if colonoscopy fails to define site of bleeding and control haemorrhage, angiographic transarterial embolisation is recommended as an effective means of controlling haemorrhage.**

8.2.3 SURGERY

Eight cohort studies and two case control studies were identified that investigated the surgical management of lower GI haemorrhage.<sup>185-194</sup>

2+  
2-

Surgery was associated with:

- rebleeding rates of 0 - 18% of cases
- mortality rates of 0 - 33% of cases.

In the cohort studies the rebleeding and mortality rates for blind segmental resection were considerably higher than those for either directed segmental resection or subtotal colectomy.<sup>193,194</sup>

2+

Two case control studies comparing subtotal colectomy with segmental colectomy have produced conflicting conclusions regarding the supremacy of one technique over the other.<sup>192, 193</sup> In these studies, where preoperative localisation was not possible, a subtotal colectomy was a safe procedure with acceptable functional results.

**D Localised segmental intestinal resection or subtotal colectomy is recommended for the management of colonic haemorrhage uncontrolled by other techniques.**

## 9 Provision of information

This section reflects the issues likely to be of most concern to patients and their carers. These points are provided for use by health professionals when discussing GI bleeding with patients and carers and in guiding the production of locally produced information materials.

### 9.1 AREAS OF CONCERN TO PATIENTS

The following section suggests questions which may arise and information which may be desired by patients at different stages of their illness.

#### 9.1.1 AT TIME OF PRESENTATION

- what is happening?
- why has this happened and how serious is this?
- will I have to be admitted to hospital and if so for how long?

#### 9.1.2 AT TIME OF INITIAL ASSESSMENT

- what is an endoscopy/colonoscopy?
- will I be sedated?
- could there be complications and if so, what are they?

#### 9.1.3 AT TIME OF TREATMENT

- what risks are there in any of the procedures?
- what alternatives are there?
- what if I do not agree to the procedure, what will happen?
- do I have to sign a consent form?
- what is the prognosis in both short term and long term?
- will I have to have medication and what are the possible side effects of taking this medication?
- assuming other medical conditions exist, will I be able to continue with my normal medication and if not, what alternatives do I have?

#### 9.1.4 AFTER TREATMENT

- will I have a re-occurrence of the bleed?
- will I have to attend an outpatients clinic? How do I get an appointment?

## 9.2 SOURCES OF FURTHER INFORMATION

### **British Liver Trust**

Helpline: 0800 652 7330  
[www.britishlivertrust.org.uk](http://www.britishlivertrust.org.uk)

The British Liver Trust is a charity that provides information and support for people with liver disease.

### **Digestive Disorders Foundation (CORE)**

[www.digestivedisorders.org.uk](http://www.digestivedisorders.org.uk)

CORE is a charity which funds research in order to prevent, cure or treat gut and liver disorders. It also provides information for patients and their families in the form of leaflets, factsheets and newsletters.

### **Helicobacter Foundation**

[www.helico.com](http://www.helico.com)

The Helicobacter Foundation is a website providing information on diagnosis, treatment and basic science concerning the Helicobacter Pylori bacterium.

### **NHS24**

Tel: 08454 24 24 24: Textphone: 18001 08454 24 24 24.  
[www.nhs24.com](http://www.nhs24.com)

NHS24 is a nurse-led helpline providing confidential healthcare advice and information.

### **National Library for Health Clinical Knowledge Summaries**

[www.cks.library.nhs.uk](http://www.cks.library.nhs.uk)

If you are feeling unwell, or are looking after someone who feels unwell, and you are unsure what to do, you can find out more about a condition or treatment by looking at the information on this website.

### **Royal Infirmary of Edinburgh**

Endoscopy, Centre for Liver and Digestive Disorders,  
The Royal Infirmary of Edinburgh,  
51 Little France Crescent, Edinburgh EH16 4SA  
Tel: 0131 536 1000  
[www.mph.ed.ac.uk/endo/patientinfo.htm#leaflets](http://www.mph.ed.ac.uk/endo/patientinfo.htm#leaflets)

## 10 Implementing the guideline

This section provides advice on the resource implications associated with implementing the key clinical recommendations, and advice on audit as a tool to aid implementation.

Implementation of national clinical guidelines is the responsibility of each NHS Board and is an essential part of clinical governance. Mechanisms should be in place to review care provided against the guideline recommendations. The reasons for any differences should be assessed and addressed where appropriate. Local arrangements should then be made to implement the national guideline in individual hospitals, units and practices.

### 10.1 RESOURCE IMPLICATIONS OF KEY RECOMMENDATIONS

This section is based on discussions with the guideline development group regarding current resource use in Scotland and the likely impact of implementing the recommendations made in the guideline. Where current practice will not change as a result of the recommendations it is unlikely there will be resource implications.

#### 10.1.1 UNSELECTED PATIENTS WITH GASTROINTESTINAL BLEEDING BEFORE ENDOSCOPY

**A** Proton pump inhibitors should not be used prior to diagnosis by endoscopy in patients presenting with acute upper gastrointestinal bleeding.

#### 10.1.2 ACID SUPPRESSION AND AGENTS TO ARREST BLEEDING

**A** High dose intravenous proton pump inhibitor therapy should be used in patients with major peptic ulcer bleeding following endoscopic haemostatic therapy.

Implementation of these recommendations should lead to a significant decrease in the use of PPI therapy for these patients across NHSScotland, leading to reductions in the cost to the drugs budget.

#### 10.1.3 DEDICATED GI BLEEDING UNIT

**D** Patients with acute upper gastrointestinal haemorrhage should be admitted, assessed and managed in a dedicated gastrointestinal bleeding unit.

There are approximately 7,000 admissions per annum in Scotland for acute GI bleeding.

Current practice varies from dedicated GI bleeding units to ad hoc management in surgical or GI units. As a result, the exact resource implications across NHSScotland are unclear.

The guideline development group estimates that, in some areas, the features of a dedicated GI bleeding unit identified in the guideline can be achieved with reorganisation of existing services. This is likely to have training and awareness raising elements. For areas where the features are not currently available, such as availability of 24 hour interventional endoscopy, then there may be significant resource implications associated with additional staffing.

For areas where there is a low caseload and a local GI bleeding unit is unfeasible, implementation of this recommendation will require collaboration with other sites. This may encourage the development of clinical networks for the management of GI bleeding.

## 10.2 AUDITING CURRENT PRACTICE

A first step in implementing a clinical practice guideline is to gain an understanding of current clinical practice. Audit tools designed around guideline recommendations can assist in this process. Audit tools should be comprehensive but not time consuming to use. Successful implementation and audit of guideline recommendations requires good communication between staff and multidisciplinary team working.

The guideline development group has identified the following as key points to audit to assist with the implementation of this guideline:

- Hospital audit of outcomes before/after adoption of suggested protocols for initial assessment.
- The proportion of patients with non-variceal gastrointestinal bleeding who are tested for H pylori which is subsequently eradicated.
- In what proportion of patients is antisecretory therapy continued unnecessarily following eradication of H pylori in non-NSAID users?
- What proportion of patients with and without major peptic ulcer bleeding are prescribed high-dose intravenous PPI?

## 10.3 ADVICE TO NHSSCOTLAND FROM THE SCOTTISH MEDICINES CONSORTIUM

There is no relevant SMC advice.

# 11 The evidence base

## 11.1 SYSTEMATIC LITERATURE REVIEW

The evidence base for this guideline was synthesised in accordance with SIGN methodology. A systematic review of the literature was carried out using a search strategy devised by a SIGN Information Officer. Databases searched include Medline, Embase, Cinahl, PsycINFO and The Cochrane Library. For most searches the year range covered was 2000-2007, but some went back to 1990. Internet searches were carried out on various websites including the New Zealand Guidelines Programme, NELH Guidelines Finder, and the US National Guideline Clearinghouse. The Medline version of the main search strategies can be found on the SIGN website, in the section covering supplementary guideline material. The main searches were supplemented by material identified by individual members of the development group.

### 11.1.1 LITERATURE SEARCH FOR PATIENT ISSUES

At the start of the guideline development process, a SIGN Information Officer conducted a literature search for qualitative and quantitative studies that addressed patient issues of relevance to gastrointestinal bleeding. The search was run in Medline, Embase, CINAHL and PsycINFO, and the results were summarised and presented to the guideline development group.

A number of themes were identified from the literature, the main ones being 'Patient Anxiety', 'Doctor-Patient Relationships' and 'Patient Education and Information'.

A copy of the Medline version of the patient search strategy is available on the SIGN website.

## 11.2 RECOMMENDATIONS FOR RESEARCH

The guideline development group was not able to identify sufficient evidence to answer all of the key questions asked in this guideline. The following areas for further research have been identified:

- Existing risk assessment scores should be validated in populations other than those with which they were developed.
- Research is required to clarify the management of GI bleeding in the community. This should include the natural history of the bleeding episodes, modes of presentation, indications for admission, outpatient referral and appropriate follow up methods.
- Research is required to determine whether an initial Rockall Score of 0 or 1 could be used for GP triage to identify the group not requiring admission.
- Research is required to determine the risks of rebleeding and cardiovascular mortality in patients presenting with ulcer bleeding who are taking aspirin.
- Research is required to determine the role of tranexamic acid in the treatment of non-variceal gastrointestinal bleeding following endoscopic haemostasis.
- Research is required to determine the optimum dose of PPI to use in European patients to prevent rebleeding in high-risk patients.
- Research is required to determine the optimum dose of PPI to be used in combination with a non-selective NSAID or COX-2 inhibitor in the prevention of recurrent peptic ulcer bleeding in high-risk patients who need to continue anti-inflammatory treatment.
- Is there a need to test for H pylori in patients with bleeding peptic ulcer or can empirical eradication therapy be prescribed? Is there a need to confirm eradication success? What is the rate of recurrent bleeding in those who fail eradication?
- What is the diagnostic yield of gastric cancer resulting from following up endoscopy to confirm ulcer healing?



- Can aspirin be reintroduced with PPI infusion immediately after haemostasis?
- Further studies are required to determine if concomitant PPI is useful in reducing the recurrence of peptic ulcer bleeding in high-risk patients taking clopidogrel.
- Does somatostatin or its analogues have a role in treatment of non-variceal gastrointestinal bleeding following endoscopic haemostasis?

### 11.3 REVIEW AND UPDATING

This guideline was issued in 2008 and will be considered for review in three years. Any updates to the guideline in the interim period will be noted on the SIGN website: [www.sign.ac.uk](http://www.sign.ac.uk)

## 12 Development of the guideline

### 12.1 INTRODUCTION

SIGN is a collaborative network of clinicians, other healthcare professionals and patient organisations and is part of NHS Quality Improvement Scotland. SIGN guidelines are developed by multidisciplinary groups of practising clinicians using a standard methodology based on a systematic review of the evidence. The views and interests of NHS Quality Improvement Scotland as the funding body have not influenced any aspect of guideline development, including the final recommendations. Further details about SIGN and the guideline development methodology are contained in "SIGN 50: A Guideline Developer's Handbook", available at [www.sign.ac.uk](http://www.sign.ac.uk)

### 12.2 THE GUIDELINE DEVELOPMENT GROUP

Dr Kelvin Palmer (Chair)	<i>Consultant Gastroenterologist, Western General Hospital, Edinburgh</i>
Dr Robin Balfour	<i>General Practitioner, Edinburgh</i>
Dr Chris Cairns	<i>Consultant in Anaesthesia and Intensive Care, Stirling Royal Infirmary</i>
Ms Lilian D'Arcy	<i>Lay Representative, Edinburgh</i>
Dr Ewan Forrest	<i>Consultant Gastroenterologist, Glasgow Royal Infirmary</i>
Mr Malcolm Green	<i>Lay Representative, Edinburgh</i>
Dr Graeme Houston	<i>Consultant Radiologist, Ninewells Hospital, Dundee</i>
Ms Moira Kinnear	<i>Principal Pharmacist, Western General Hospital, Edinburgh</i>
Mr Colin MacKay	<i>General Upper GI Surgeon, Victoria Infirmary, Glasgow</i>
Ms Sheila Mair	<i>Gastroenterology Nurse Practitioner, Hairmyres Hospital, East Kilbride</i>
Mr James Mander	<i>Consultant Colorectal Surgeon, Western General Hospital, Edinburgh</i>
Dr John Morris	<i>Consultant Gastroenterologist, Glasgow Royal Infirmary</i>
Dr Moray Nairn	<i>Programme Manager, SIGN</i>
Dr Roddy Neilson	<i>Consultant Haematologist, Falkirk and District Royal Infirmary</i>
Dr William Ruddell	<i>Consultant Physician, Forth Valley Acute Hospital Trust</i>
Ms Joanna Kelly	<i>Information Officer, SIGN</i>

The membership of the guideline development group was confirmed following consultation with the member organisations of SIGN. All members of the guideline development group made declarations of interest and further details of these are available on request from the SIGN Executive.

Guideline development and literature review expertise, support and facilitation were provided by the SIGN Executive.

### 12.2.1 PATIENT INVOLVEMENT

In addition to the identification of relevant patient issues from a broad literature search, SIGN involves patients and carers throughout the guideline development process in several ways. SIGN recruits a minimum of two patient representatives to guideline development groups by inviting nominations from the relevant “umbrella”, national and/or local patient focused organisations in Scotland. Where organisations are unable to nominate, patient representatives are sought via other means, eg from consultation with health board public involvement staff.

Further patient and public participation in guideline development was achieved by involving patients, carers and voluntary organisation representatives at the National Open Meeting (see section 12.4.1). Patient representatives were invited to take part in the peer review stage of the guideline and specific guidance for lay reviewers was circulated. Members of the SIGN patient network were also invited to comment on the draft guideline section on provision of information.

## 12.3 ACKNOWLEDGEMENTS

SIGN is grateful to the following former members of the guideline development group who have contributed to the development of this guideline.

Mr David Chong	<i>Consultant Surgeon, Glasgow Royal Infirmary</i>
Dr Brian McLelland	<i>Strategy Director, Scottish National Blood Transfusion Service, Edinburgh</i>
Professor Ashley Mowat	<i>Consultant Gastroenterologist, Aberdeen Royal Infirmary</i>
Mr Rowan Parks	<i>Senior Lecturer in Surgery, The University of Edinburgh</i>
Ms Janice Ross	<i>Nurse Endoscopist, Stirling Royal Infirmary</i>

## 12.4 CONSULTATION AND PEER REVIEW

### 12.4.1 NATIONAL OPEN MEETING

A national open meeting is the main consultative phase of SIGN guideline development, at which the guideline development group presents its draft recommendations for the first time. The national open meeting for this guideline was held on 4 May 2007 and was attended by representatives of all the key specialties relevant to the guideline. The draft guideline was also available on the SIGN website for a limited period at this stage to allow those unable to attend the meeting to contribute to the development of the guideline.

### 12.4.2 SPECIALIST REVIEW

This guideline was also reviewed in draft form by the following independent expert referees, who were asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. The guideline group addresses every comment made by an external reviewer, and must justify any disagreement with the reviewers' comments.

SIGN is very grateful to all of these experts for their contribution to the guideline.

Dr Alan Begg	<i>General Practitioner, Townhead Surgery, Montrose</i>
Dr Rob Boulton-Jones	<i>Consultant Physician and Gastroenterologist, Victoria Infirmary, Glasgow</i>
Dr Rodney Burnham	<i>Registrar, Royal College of Physicians, London</i>
Dr Nicholas Church	<i>Consultant Gastroenterologist, Queen Margaret Hospital, Dunfermline</i>
Ms Ruth Forrest	<i>Lead Clinical Pharmacist, ITU and Theatres, Western Infirmary, Glasgow</i>

Dr Andrew Fraser	<i>Consultant Gastroenterologist, Aberdeen Royal Infirmary</i>
Professor Peter Hayes	<i>Professor of Hepatology, Royal Infirmary of Edinburgh</i>
Dr Stuart Hislop	<i>Consultant Gastroenterologist, Royal Alexandra Hospital, Paisley</i>
Dr Mark Hudson	<i>Consultant Hepatologist, Freeman Hospital, Newcastle upon Tyne</i>
<i>Dr Peter Hutchison</i>	<i>General Practitioner and Primary Care Cancer Facilitator, Dumfries</i>
Dr David Johnston	<i>Consultant Gastroenterologist, Ninewells Hospital, Dundee</i>
Professor John Kinsella	<i>Head of Section of Anaesthesia, Pain and Critical Care Medicine, Glasgow Royal Infirmary</i>
Mr Colin J McKay	<i>Consultant Pancreatic/Upper GI Surgeon, Glasgow Royal Infirmary</i>
Dr Peter Mills	<i>Consultant Gastroenterologist, Gartnavel General Hospital, Glasgow</i>
Dr Tim Reilly	<i>Consultant Physician and Gastroenterologist, Hairmyres Hospital, East Kilbride</i>
Ms Nicola Ring	<i>Lecturer, Department of Nursing and Midwifery, University of Stirling</i>
Dr James Rose	<i>Consultant Physician / General Medicine, Ayr Hospital</i>
Mr Alan Timmins	<i>Principal Pharmacist, Queen Margaret Hospital, Dunfermline</i>

#### 12.4.3 SIGN EDITORIAL GROUP

As a final quality control check, the guideline is reviewed by an editorial group comprising the relevant specialty representatives on SIGN Council to ensure that the specialist reviewers' comments have been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. The editorial group for this guideline was as follows.

Dr Keith Brown	<i>Chair of SIGN; Co-Editor</i>
Dr Rajan Madhok	<i>Royal College of Physicians and Surgeons of Glasgow</i>
Mrs Fiona McMillan	<i>Royal Pharmaceutical Society of Great Britain</i>
Dr Safia Qureshi	<i>SIGN Programme Director; Co-Editor</i>
Dr Graeme Simpson	<i>Royal College of Physicians of Edinburgh</i>
Dr Sara Twaddle	<i>Director of SIGN; Co-Editor</i>

## Abbreviations

<b>A&amp;E</b>	accident and emergency
<b>AAU</b>	acute assessment unit
<b>CI</b>	confidence interval
<b>CT</b>	computed tomography
<b>COX-2</b>	cyclo-oxegenase 2
<b>CTA</b>	computed tomography angiography
<b>DSA</b>	digital subtraction angiography
<b>GI</b>	gastrointestinal
<b>GIH</b>	gastrointestinal haemorrhage
<b>GOV</b>	gastro-oesophageal varix
<b>GTN</b>	glyceryl trinitrate
<b>HDU</b>	high dependency unit
<b>H pylori</b>	Helicobacter Pylori
<b>IGV</b>	isolated gastric varix
<b>INR</b>	international normalised ratio
<b>LGIB</b>	lower gastrointestinal bleeding
<b>MTA</b>	multiple technology assessment
<b>NNT</b>	number needed to treat
<b>NHS QIS</b>	NHS Quality Improvement Scotland
<b>NICE</b>	National Institute for Health and Clinical Excellence
<b>NSAID</b>	non-steroidal anti-inflammatory drug
<b>OR</b>	odds ratio
<b>PPI</b>	proton pump inhibitor
<b>RCT</b>	randomised controlled trial
<b>RR</b>	relative risk
<b>SAFE</b>	Saline versus Albumin Fluid Evaluation trial
<b>SBP</b>	systolic blood pressure
<b>SIGN</b>	Scottish Intercollegiate Guidelines Network
<b>SMC</b>	Scottish Medicines Consortium
<b>SMR</b>	standardised mortality ratio
<b>SRH</b>	stigmata of recent haemorrhage
<b>SSRI</b>	selective serotonin reuptake inhibitor
<b>STD</b>	sodium tetradecyl sulphate
<b>TIPSS</b>	transjugular intrahepatic portosystemic stent shunt
<b>UGIB</b>	upper gastrointestinal bleeding

# Annex 1

## Key questions used to develop the guideline

THE KEY QUESTIONS USED TO DEVELOP THE GUIDELINE	
ASSESSMENT	
Key question	See guideline section
1. In patients presenting in the pre-hospital setting with acute GI bleeding, are there any subgroups that do not need immediate referral to hospital, and can they be managed in the community setting?	2.1
2. In patients presenting in hospital with GI bleeding, what signs, symptoms and features can be used to determine those at high risk and requiring immediate intervention, and those at low risk who can be safely discharged? a) hematemesis b) shock c) age d) medical comorbidities e) patients on aspirin, warfarin, SSRI, NSAIDs, steroids f) basic tests (HB, urea, renal function, creatinine)	2.2.1
3. In patients with GI bleeding, (with or without liver disease) is there an accurate scoring system for determining which patients are high risk and require immediate intervention?	2.2.2 and 2.2.3
4. In patients with GI bleeding who require immediate intervention, what is the most appropriate model of care in terms of length of hospital stay, mortality, rebleeding, need for surgery and blood transfusion? a) dedicated GI bleeding service b) resuscitation and triage by acute team (ITU v general ward)	3.1
5. What follow up is necessary in patients with a GI bleed who are sent home from A&E to ensure optimum outcome in terms of mortality, rebleeding, need for surgery or transfusion? a) outpatient endoscopy b) omission of causative drugs ie NSAIDs, aspirin, SSRI, warfarin c) treatment with proton-pump inhibitors d) referral/review by GP or GI outpatient department	4.3.1, 5.3.1 and 5.3.3

INITIAL MANAGEMENT AND RESUSCITATION	
Key question	See guideline section
6. In patients with (variceal and non-variceal) GI bleeding requiring urgent fluid resuscitation which solution is more effective in terms of mortality, risk of rebleeding and subsequent organ failure; and what are the indications for it to be given? a) colloid b) crystalloid c) blood	4.2
7. Does the use of a major haemorrhage protocol reduce mortality in patients with GI bleeding?	4.2.3
8. Does IV PPI alter outcome (mortality, need for transfusion, surgery, need for endoscopic intervention) if given at the initial assessment stage?	4.3.1
9a) In patients with GI bleeding, does endoscopy within 8 hours of admission improve outcome (mortality, rebleeding)?  9b) In patients with GI bleeding, does endoscopy within 24 hours of admission improve outcome (mortality, rebleeding)?	4.4.1
10. For early endoscopy (within 24 hours) does grade, speciality, medical or nursing or level of experience affect: a) diagnostic rate b) complication rate c) intervention rate d) outcome (rebleeding, mortality, length of stay)	4.4.1
NON-VARICEAL UPPER GI BLEEDING	
(Including all patients who at endoscopy have evidence of bleeding from oesophagus, stomach, duodenum which is not due to varices)	
Key question	See guideline section
11. In this patient group, which of the following endoscopic findings predict rebleeding (and which predict no rebleeding), need for surgical operation, transfusion, death? a) visible vessel spurting blood (spurting haemorrhage) b) visible vessel not spurting blood c) no visible vessel d) black/red spots in ulcer base e) clean ulcer base f) adherent blood clot	2.2.3 and 5.1
12. In this patient group, which patients benefit from endoscopic therapy, in terms of re-bleeding, mortality, need for surgery or transfusion?	5.2
13. In this patient group, what is the optimum (ie improves mortality, risk of re-bleeding) endoscopic therapy for non-variceal bleeding? a) injection sclerotherapy, ( <i>with what agent?</i> ) b) thermal c) mechanical (clips, bands) d) combined	5.2.1 to 5.2.4



14. What is the evidence that the following drugs improve mortality and risk of re-bleeding in patients with non-variceal bleeding? a) proton-pump inhibitor b) H <sub>2</sub> receptor antagonists c) somatostatin analogues (octreotide) d) tranexamic acid	5.3
15. Is there evidence that H pylori testing and treatment affects early outcomes (rebleeding, surgery, mortality) or late outcomes (recurrent bleeding, recurrent symptoms). If so, when and how should it be done?	5.3.1
16. What is the evidence that one or more of the following drugs alters the risk of rebleeding in patients with a previous bleed? a) aspirin b) SSRIs c) NSAIDs d) steroids e) clopidogrel f) warfarin g) PPI/ H <sub>2</sub> receptor antagonists	5.3.3
17. In this group of patients, does a second-look endoscopy affect outcomes (further bleeding), in: a) the acute situation b) interval endoscopy (after discharge, 2-3 months)	5.2.5
VARICEAL UPPER GI BLEEDING (Including patients suspected of having variceal bleed, but not yet confirmed by endoscopy)	
<b>Key question</b>	<b>See guideline section</b>
18. In this group of patients, what is the evidence that any intervention (tube or drug) alters pre-endoscopic continued bleeding, blood transfusion requirement, finding of active bleeding or immediate survival at the time of eventual endoscopy? a) drugs: vasopressin, glypressin, somatostatin analogues, octreotide b) tubes: balloon tamponade, sengstaken tube/Minnesota	6.2.1 and 6.4
19. In this group of patients, what is the optimum time to perform an endoscopy to reduce mortality? ( <i>less or more than 8 hours</i> )	4.4.1

VARICEAL UPPER GI BLEEDING (Including patients with <b>confirmed variceal haemorrhage</b> )	
<b>Key question</b>	<b>See guideline section</b>
20. In patients with confirmed variceal bleed at time of endoscopy, which of the following therapies should be used for improved survival and transfusion requirements, and haemostasis? a) sclerotherapy b) variceal banding c) drugs – glypressin, octreotide, vasopressin, nitrates, somatostatin analogues	6.1 and 6.2.2
21. In patients where variceal bleed remains uncontrolled after or during endoscopic treatment, what is the evidence that the following therapies improve survival and risk of rebleeding? a) TIPSS b) balloon tamponade c) repeat endoscopy d) drugs – glypressin, octreotide, vasopressin, nitrates, somatostatin analogues	6.5
22. In patients where the variceal bleed is successfully controlled after endoscopic treatment, what is the evidence that the following treatments (or combination of) reduce the risk or rebleeding and mortality? (and hepatorenal failure) a) glypressin b) antibiotics c) nitrates d) beta-blockers e) somatostatin analogues (octreotide) f) banding g) TIPSS h) repeat endoscopy	7
COLONIC BLEEDING	
<b>Key question</b>	<b>See guideline section</b>
23. What is the most accurate diagnostic tool in patients presenting with lower massive/major GI bleeding? a) colonoscopy b) angiography c) contrast enhanced CT d) operative endoscopy e) radio nucleotide scan f) capsule endoscopy	8.1
24. Which of the following interventions influence the outcomes (rebleeding, mortality, perforation, transfusion requirements, repeat surgery) of colonic bleeding? a) clipping b) laser c) embolisation d) surgery	8.2
25. In patients presenting with major/massive bleeding, what is the value of localising the precise anatomical site of bleeding in terms of rebleeding, repeat surgery, mortality and bowel function?	8.1

## Annex 2

### Drug licensing status

All drugs recommended in this guideline are licensed for the indication included in the recommendation with the following exceptions:

Section	Drug
5.3.2	Proton pump inhibitors are not licensed for the reduction in rate of rebleeding in patients with bleeding peptic ulcers.
6.2.1	Somatostatin and vapreotide are not licensed for use in the management of variceal bleeding.
6.2.2	Somatostatin and octreotide are not licensed for use in the management of variceal bleeding.
7.2.1	With the exception of propranolol, beta blockers are not licensed for secondary prevention of oesophageal variceal haemorrhage.

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