National Institute for Health and Clinical Excellence

Acute upper gastrointestinal bleeding
Guideline Consultation Comments Table
13th December 2011 – 14th February 2012

Type	Stakeholder	Order No	Document	Page No	Line No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
PR	NETSCC, HTA	1	Full	general		**1.1 Are there any important ways in which the work has not fulfilled the declared intentions of the NICE guideline (compared to its scope – attached)** - None identified	Thank you for your comment.
PR	NETSCC, HTA	2	Full	1		The title is too broad. The guidelines seem to only concentrate on upper GI bleeding "peptic ulcer bleeding and bleeding from varices" (P14 Line 39). I cannot find in the other guidelines other causes of upper GI bleeding covered.	Thank you for your comment. The title of the guideline is appropriate since the guideline does make recommendations that encompass the management of other causes of GI bleeding, for example those which relate to resuscitation and massive bleeding (see chapter 6 in the full guideline). However, we agree that the emphasis is on the most important causes of upper gastrointestinal bleeding which in the UK are peptic ulcers or variceal bleeding.
PR	NETSCC, HTA	3	Full	general		The scope asks for primary care, as well as secondary and tertiary. I can find no reference to primary care. All assumes patients are in hospital. This is also interesting considering the RCGP name attached to it.	Thank you for your comment. We ensured a GP was recruited to the GDG. Our intention was to include primary care in the risk assessment chapter but unfortunately there was no literature specific to primary care. A note to this effect has been added to the other considerations section of the LETR in section 5.6..
PR	NETSCC, HTA	4	Full	general		Validity seems to fit with NICE guidelines manual	Thank you for your comment.
PR	NETSCC, HTA	4	Full	4	19	A single GP was part of the team – which seems odd considering the scope asked for primary, secondary and tertiary care settings to be considered.	Thank you for your comment. We thought this was appropriate given the predicted nature of the published guidance.
PR	NETSCC, HTA	5	Full	18	21	The declared inclusion criteria should also state "peptic ulcer bleeding and bleeding from varices"	Thank you for your comment. The inclusion criteria are correct. The main focus was on peptic ulceration and varices as that is where

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							most of the evidence was found.
PR	NETSCC, HTA	6	Full	general		The issue of including references that have 'potentially serious or very serious limitations' I consider needs to be revisited as to whether this is appropriate.	Thank you for your comment. The inclusion of such studies and downgrading the evidence accordingly is the method employed in GRADE. We can then assess our confidence in the findings according to the overall GRADE rating rather than by study.
PR	NETSCC, HTA	7	Full	25	3	Search strategies complete and appropriate. Both randomized and observational studies were included – these were appropriate.	Thank you for your comment.
PR	NETSCC, HTA	8	Full	general		The recommendations are balanced and complete based on the scope of the work.	Thank you for your comment.
PR	NETSCC, HTA	9	Full	32	3	Table 5. The MID are based on consensus. How were these arrived at? How many contributed to the consensus? Was there heterogeneity on these?	Thank you for your comment. There was good agreement within the room; formal consensus methods were not required.
PR	NETSCC, HTA	10	Full	general		I feel that the references that fit into the different levels should be highlighted if they fit into the categories of very serious, potentially serious and minor limitations. As these affect the evidence validity.	Thank you for your comment. This is not specified in technical manual.
PR	NETSCC, HTA	10	Full	104	39	How is the concept of early and delayed endoscopy ("within 12 hrs of admission") chosen? Why is this not related, on history, to onset of bleeding rather than admission (a human construct)?	Thank you for your comment. The included studies referred to time from admission to endoscopy, and compared endoscopy with the earlier timeframe of 2-12 hours from admission to a later timeframe. The concept of early endoscopy was developed by the GDG based on time intervals used in the available evidence, which used time of admission. We acknowledge your point that admission is a human construct, however the evidence available did not provide sufficient data regarding the time of onset to inform decision making.
PR	NETSCC, HTA	11	Full	general		**4.1 Is the whole report readable and well presented? Please comment on the overall style and whether, for example, it is easy to**	Thank you for your comment.

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						understand how the recommendations have been reached from the evidence. Yes the content is provided, the depth and detail is appropriate however most 'users' never get to actually read into such extensive documents, they stop at the guidelines if they seem reasonable	
PR	NETSCC, HTA	12	Full	26	21	Why only one person doing this? You should have a t least two, with some double assessments to check for the precision and validity of each person-s assessments.	Thank you for your comment. We do have a quality assurance process in place. The main reviewer on the guideline was quality assured by a second reviewer (i.e. 15% of sifts, checklists and whole reports). We have added this to section 3.3 of the full guideline.
PR	NETSCC, HTA	13	Full	27	11	Use of meta-analysis with a standard approach and software is appropriate.	Thank you for your comment.
PR	NETSCC, HTA	14	Full	27	17	Statistical heterogeneity in what?	Thank you for your comment. This refers to the heterogeneity between individual study results. This has been added to the text.
PR	NETSCC, HTA	15	Full	27	26	Did you compare the random-effect model with fixed effects for all analyses? This would be more powerful.	Thank you for your comment. The use of random effects models is outlined in section 3.3.2 of the guideline. Comparisons between fixed and random effects models throughout the guideline is not part of NICE methodology.
PR	NETSCC, HTA	16	Full	general		It would be useful to provide the guidelines as diagrams as the visual format improves communication and use	Thank you for your comment. Please refer to the NICE pathway at www.nice.org.uk
PR	NETSCC, HTA	16	Full	27	29	Estimating the standard deviation using the 95% CI method is appropriate.	Thank you for your comment.
PR	NETSCC, HTA	17	Full	27	29	Using the p-value will lead to some potential serious underestimating the standard error. Did you consider contacting any authors? Did you consider using this method for all reports? This would give consistency.	Thank you for your comment. The use of p-values to estimate standard errors was not used in this guideline therefore the reference to this was removed from this section.

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PR	NETSCC, HTA	18	Full	27	32	The use of conservative p-values is appropriate.	Thank you for your comment.
PR	NETSCC, HTA	19	Full	27	37	The sensitivity and specificity methods seem appropriate.	Thank you for your comment.
PR	NETSCC, HTA	20	Full	28	6	Define single and double blinding.	Thank you for your comment. Blinding is covered in the study limitation section (section 3.3.7) and we have covered the type of blinding in more detail in the table in this section.
PR	NETSCC, HTA	21	Full	28	17	Use of ITT is appropriate.	Thank you for your comment.
PR	NETSCC, HTA	22	Full	28	24	I disagree. It is entirely feasible that you will have a motivated group who participate in a trial. They are less likely to drop out and therefore the final result will be closer to the true effect of the intervention. Whilst in a general population, more may drop out and you will be closer to the effect of the control group.	Thank you for your comment. Most methodologists believe that ITT analysis will bias results towards no difference, in comparison to per protocol analysis for instance. It is therefore a more conservative approach. This is the methodology that is also used by the Cochrane collaboration.
PR	NETSCC, HTA	23	Full	42	5	What is "multivariant analysis"?	Thank you for your comment. The line should read 'multivariate', the guideline has been amended.
PR	NETSCC, HTA	24	Full	52 -54		Tables 11, 12, 13. I am unclear why these scored as "Low" for Quality. Is this because they are not an RTC. But how do you develop such a study design for looking at this?	Thank you for your comment. We have now added a section regarding the adaptation of the GRADE table for risk scoring analysis in the methods section (section 3.3.11) that is explaining this process in more detail. As you pointed out we agree that different study designs are appropriate for this section and this is reflected in the study limitation rating.
PR	NETSCC, HTA	25	Full	64	3	Appropriate question for this.	Thank you for your comment.
PR	NETSCC, HTA	26	Full	64	21	Table 16. Brandarian 2004 – unclear how this study was performed – was it a comparison of different interventions? How define "early" intervention?	Thank you for your comment. On closer inspection we agree that the table was not very clear. The table has been amended to describe the study intervention more clearly.

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PR	NETSCC, HTA	27	Full	66		Table 17. Why is absolute risk not calculable?	Thank you for your comment. This was due to zero events in the control group and this has been added to the footnote.
PR	NETSCC, HTA	28	Full	88	22	How are the interpretations such as "Only 25 patients randomized" made? These should be quantified with a power level – as this is continuous I do not see how this sentence can be written.	Thank you for your comment. 'Only' has now been removed from this sentence.
PR	NETSCC, HTA	29	Full	169		Table 49. Why was a pooling not attempted? ("when first line treatment has failed (data was not pooled)"). Particularly for mortality – and this would help to address the issue of imprecision.	Thank you for your comment. These observational studies and their study populations are not sufficiently similar to pool the data in a meta-analysis.
PR	NETSCC, HTA	30	Appendix H	general		Forest plots look appropriate.	Thank you for your comment.
PR	NETSCC, HTA	31	Appendix J	578		Where was the evidence for : "It was assumed that deaths occurred at midday and discharges occurred at 4pm.". This may have an impact. You could have tried imputation?	Thank you for your comment. The assumption regarding the time of death and discharge was necessary as no time was recorded in the dataset used. These assumptions were considered reasonable by clinical experts within the group.
PR	NETSCC, HTA	32	Appendix J	578		Why did you use categories ("Ten of the eleven categories to which patient records were assigned were: endoscoped in[0-4 hours (h), 4-12 h, 12-24 h, 24- 48 h, 48 – 72 h, 4- 5 days (72-120h), 6- 10 days (120-240h), 11-15 days (240h-360h), 16-20 days (360h-480h) and 21-28 days (480h-672h)].").. Why doid you not use the real values, rather than throwing away information.	Thank you for your comment. The data was categorized in order for the competing risks model outlined in Appendix J to become computationally manageable within the time given to guideline development. The competing risks statistical model was the preferred method of analysis to stratify for a group of risk factors contained within each Rockall score.
PR	NETSCC, HTA	33	Appendix J	578		The discussion on confounding is correct. The method for dealing with this is also appropriate.	Thank you for your comment.
PR	NETSCC, HTA	35	Full	31	34	I don't understand what the relevance e of the CI crossing a threshold has. This is also based on the	Thank you for your comment. The threshold is the minimal important difference (MID) and is

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						precision of the effect.	the smallest difference between intervention and comparison that would lead the patient or clinician to consider a change in the management. When CIs cross the MID we would be less confident that this effect has been achieved and the evidence for this outcome is then downgraded. This is explained in the methodological introduction to the guideline.
PR	NETSCC, HTA	36	Full	31	45	This is appropriate for inference.	Thank you for your comment.
PR	NETSCC, HTA	37	Full	37	21	The summary does not give the way in which the scores are to be used. Add "Consider patients with a pre-endoscopy Rockall or Blatchford score of 0 for early discharge".	Thank you for your comment. This is a separate recommendation please see p38 of the full guideline.
PR	NETSCC, HTA	38	Full	42	19	The score was developed in "west of Scotland". Is this appropriate, e.g. socioeconomically, ethnically, for the rest of UK?	Thank you for your comment. Yes this is appropriate for the rest of the UK – it has been tested in several other Centres.
PR	NETSCC, HTA	39	Full	61	33	Why when stated "the Blatchford score appeared to be the better predictor of re-bleeding, and comparable with the Rockall for prediction of mortality." Did the recommendation not state that the Blatchford pre-endoscopy should be used? This should be changed to Blatchford is better. What is the reason that the group decided otherwise?	Thank you for your comment. We agree that the evidence supports the use of Blatchford rather than clinical Rockall before endoscopy. After a discussion with the GDG this recommendation has been revised in light of your comment and now reads "Use the following formal risk assessment scores for all patients with acute upper gastrointestinal bleeding: • the Blatchford score at first assessment, and • the full Rockall score after endoscopy."
PR	NETSCC, HTA	40	Full	71	18	The recommendation "in stable patients clinicians should exercise caution when deciding if and when to transfuse." Is not clear enough. What does the group think should be done? Or is there no evidence either way?	Thank you for your comment. This is not a recommendation; it is part of the LETR and sets out the thought processes of the GDG.

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PR	NETSCC, HTA	41	Full	71	18	The recommendation "The appropriate use of blood transfusions in UGIB is essential and is likely to be cost-effective." – has no basis in evidence. I do not see how this can be backed up.	Thank you for your comment. This recommendation was based on GDG consensus.
PR	NETSCC, HTA	42	Full	176	22	Appropriate recommendation.	Thank you for your comment.
PR	NETSCC, HTA	44	Full	4	19	I struggled to find the input given by the general practitioner. What is the expertise of the GP in relation to upper GI bleeding? Build the credibility.	Thank you for your comment. All GDG members contributed to all of the discussion. Details of the GDG membership can be found on page 10 of the full guideline.
PR	NETSCC, HTA	45	Full	4	26	Limitations of lack of RCTs discussed appropriately.	Thank you for your comment.
PR	NETSCC, HTA	46	Full	14	17 18	Presentation of melaena fairly common in primary care. This seems to be ignored.	Thank you for your comment. The guideline uses the generalised term of acute upper gastrointestinal bleeding recognising that it encompasses all possible presentations, including melaena. Melaena is therefore not ignored in the guideline.
PR	NETSCC, HTA	47	Full	26	40	The inclusion of other causes of bleeding may cause confusion. Why are they not included in the other questions? This seems to confuse.	Thank you for your comment. With regards to review question 16, the GDG agreed that studies with a mixed patient population, i.e. patients with gastric varices and also patients with oesophageal varices should be permitted as indirect evidence. This was because it was thought there would be a limited evidence base covering gastric varices alone (in comparison to that for oesophageal varices).
PR	NETSCC, HTA	48	Full	37	24	Is this correctly known as the "Glasgow-Blatchford score"?	Thank you for your comment. The Blatchford score is not generally referred to as the Glasgow-Blatchford score.
PR	NETSCC, HTA	49	Full	65		Table 16. Small detail - Hearnshaw, 2010 looked at 16-17 year olds not included in these	Thank you for your comment. You are correct; it was not possible to look at 16-17 year olds in

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						recommendations.	the study.
PR	NETSCC, HTA	50	Full	226	14	Table 65. This one study is from China (I think). How does this have an effect on inference?	Thank you for your comment. The other considerations section of the LETR has been amended to reflect the fact that the GDG did not believe that this effected the applicability of the study.
PR	NETSCC, HTA	52	Full	4	10	For example page 4. Use of language such as "than ever before" adds a certain informality that you may wish to avoid.	Thank you for your comment. This is the foreword, not a technical part of the guideline.
PR	NETSCC, HTA	53	Full	26		Section 3.3. Missing parentheses.	Thank you for your comment. The guideline has been amended accordingly.
PR	NETSCC, HTA	54	Full	32		Table 5. ARR and RRR are not defined and are not in the abbreviations table at the front of the document. What does the last column title mean?	Thank you for your comment. These abbreviations refer to the absolute risk reduction and the relative risk reduction. We have changed the column titles to reflect this and added a note below the table to explain how the columns are derived. It has also been added to the abbreviations table at the front of the document.
PR	NETSCC, HTA	55	Full	33	3	What is OIS? It is not in the abbreviations.	Thank you for your comment. This sentence has been removed from the guideline.
PR	NETSCC, HTA	56	Full	general		Various sopelling errors – use a spell check e.g. P151 "radomised".	Thank you for your comment. The guideline has been amended accordingly.
PR	NETSCC, HTA	58	Full	general		Research recommendations were not clear – these need summarizing and adding.	Thank you for your comment. No research recommendations were identified during the GDG meetings.
PR	NETSCC, HTA	59	Full	general		All scores (Blatchford and Rockall) should be explored using latent variable methods. The arbitrary cut-offs may be based on simplistic numbering systems, but there may be far more appropriate ways that can be discovered using	Thank you for your comment. The bi-variate diagnostic meta analysis was run and explained in more detail in section 3.3.2 in the full guideline with a detailed description in Appendix L of the guideline. The latent variable method was not used

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						sophisticated statistical approaches.	because the scoring systems are based on multivariate analyses of clinical parameters and clinical cut-offs are therefore not arbitrary. These cut-off values are designed to maximise sensitivity in order to rule out patients who are likely to experience a severe adverse event. A latent variable method would lead to a score that would maximise both sensitivity as well as specificity which would therefore not be suitable for this review question.
PR	NETSCC, HTA	60	Full	general		Comparing Addenbrooke with the other scoring systems is required.	Thank you for your comment. Addenbrookes scoring system is not externally validated so was not used. There were no direct comparison studies. The LETR has been amended to include more detail.
PR	NETSCC, HTA	62	Full	general		Overall clearly written. Some specific issues raised earlier on clarity.	Thank you for your comment.
PR	NETSCC, HTA	63	Full	general		Primary care/community setting entirely excluded. Not sure this was the original plan, but the title is too broad and confusing for all GPs.	Thank you for your comment. We ensured a GP was recruited to the GDG. Our intention was to include primary care in the risk assessment chapter but unfortunately there was no literature specific to primary care. A note to this effect has been added to the other considerations section of the LETR in section 5.6.
SH	British Society for Paediatric Gastroenterology, Hepatology and Nutrition	1	Full	general		1. The guideline is indirectly relevant to children because although aetiologies and managements are not the same they follow the same principles and actually ovelap to some degree. 2. The Rockall score or Glasgow-Blatchford score have not been adapted for children and have no equivalent - perhaps it is time to develop one? 3. The numbers of annual procedures performed to identify a unit with daily scope services (>330/yr) is	Thank you for your comments. We agree that the clinical management of, and service provision for, children will differ than that for adults and we acknowledge all the points you make here. However, because the guideline scope stipulated a population aged 16 years and over, issues specific to paediatrics are not included in the guideline.

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						far too high for a paediatric criterion. Nevertheless the implicit referral network relationship (Units <330/yr refer to units >330/yr) requires to be developed in paediatrics but at lower referral levels. The question of networks in paediatric GI is to be considered by the British Society for Paediatric Gastroenterology, Hepatology and Nutrition on behalf of the DoH. 4. Relationships between paediatric gastroenterologists and paediatric surgeons must be considered as paediatric surgeons are usually the first line for referral of children with GI bleeding into hospital. This should also be considered as part of the function of a network. 5. Adult methods of managing non-variceal bleeding (NVB) are not available in many (or most) paediatric centres. 6. TIPS is not available for or suitable for some children due to their size or pathology. 7. Low dose aspirin (or low molecular weight heparin) is not used after variceal bleeding in children - this should be the subject of a study if sufficient numbers could be recruited. 8. The guidelines for use of blood products are similar for children to adults. 9. Octreotide is used instead of terlipressin as first line in acute variceal bleeding in children. The treatments are of similar efficacy. 10. To guarantee endoscopy within 24 hours in all paediatric patients with GI bleeding is a standard	

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						we aspire to, but currently cannot achieve without more resources including access to theatre space and associated facilities. 11. Children under 10-12 Kg undergo primary sclerotherapy rather than banding of varices.	
SH	British Society of Gastroenterology	1	FULL	4	3	British Society of Gastroenterology	Thank you for your comment.
SH	British Society of Gastroenterology	2	FULL	4	13	Change 'possible' to 'probable'	Thank you for your comment. We believe that 'possible' is more appropriate than 'probable' given the available evidence.
SH	British Society of Gastroenterology	3	FULL	14	2 -3	incidence should be 50-150/100,000 (10,000 in text).	Thank you for your comment. We have amended the introduction to read 84-172/100,000 to accurately reflect the range estimates included in the studies.
SH	British Society of Gastroenterology	4	FULL	14	8	Delete the sentence starting 'Disappointedly [sic]……'	Thank you for your comment. This sentence has been deleted from the introduction.
SH	British Society of Gastroenterology	5	FULL	15	28 -36	This paragraph needs to expand upon the statement that 'facilities should be available for urgent endoscopy in unstable, actively bleeding patients'. The ability to guarantee an endoscopy within 24 hours is insufficient. All hospitals should have access to an experienced endoscopist 24 hours a day to handle the most serious GI bleeds (those with evidence of continued active bleeding and who remain haemodynamically unstable despite resuscitation). This group of patients require an endoscopy within the first few hours of admission and the only way this can be achieved is for all hospitals to have a formal system in place that provides access to endoscopists with the skills to manage these patients, including the technical ability to deal with bleeding ulcers and varices. This system must operate 24 hours a day, 7 days a week. These points should be emphasised in this	Thank you for your comment. This is an introduction to the guideline and it would be inappropriate at this point to pre-empt the recommendations made in the full guideline.

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						paragraph	
SH	British Society of Gastroenterology	6	FULL	37 -38		There is confusing use of 2 nomenclatures for haemoglobin level - in some sections (eg p37, 38) it is g/l, in others (eg section 6, p63 et seq) it is g/dl. Better to use one and stick to it.	Thank you for your comment. We agree and have ensured g/dl is now used throughout the guideline.
SH	British Society of Gastroenterology	7	FULL	63		There is confusing use of 2 nomenclatures for haemoglobin level - in some sections (eg p37, 38) it is g/l, in others (eg section 6, p63 et seq) it is g/dl. Better to use one and stick to it.	Thank you for your comment. We agree and have ensured g/dl is now used throughout the guideline
SH	British Society of Gastroenterology	8	FULL	37	13	Before 'the development' change 'of' to 'or'	Thank you for your comment. This sentence has now been changed.
SH	British Society of Gastroenterology	9	FULL	37	15	Delete 'Affects an'	Thank you for your comment. This sentence has now been changed.
SH	British Society of Gastroenterology	10	FULL	37	27 -29	Surely a cut off of 0.8g/l is wrong (incompatible with life!!) - should be 80g/l or 8g/dl - see p37, lines27-29 and p38 lines 30-32. This appears in the recommendations in the brief guidance also.	Thank you for your comment. We agree and have ensured g/dl is now used throughout the guideline.
SH	British Society of Gastroenterology	11	FULL	37	31	'Urgent' needs to be defined. Within 24 hours or waiting overnight is insufficient for the most unstable patients. Arrangements should be in place to provide an urgent endoscopy outside normal working hours.	Thank you for your comment. We agree, although it is difficult to put a realistic figure on an "urgent" procedure which covers all circumstances. We have amended the recommendation to try to address the comment.
SH	British Society of Gastroenterology	12	FULL	37	35	See below comments on calculation of number of cases seen per year to justify daily endoscopy lists for patients with GI bleeding	Thank you for your comment.
SH	British Society of Gastroenterology	13	FULL	38	30 -32	Surely a cut off of 0.8g/l is wrong (incompatible with life!!) - should be 80g/l or 8g/dl - see p37, lines27-29 and p38 lines 30-32. This appears in the recommendations in the brief guidance also.	Thank you for your comment. We agree and have ensured g/dl is now used throughout the guideline.
SH	British Society of Gastroenterology	14	FULL	39	21	See comments in above two boxes	Thank you for your comment.

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					-27		
SH	British Society of Gastroenterology	15	FULL	39	14 -26	Band ligation should be mentioned first (moved up to line 15)	Thank you for your comment. The order of the recommendations have now been changed.
SH	British Society of Gastroenterology	16	FULL	39 -40 154 160-161		p39-40, p154 (Table 45), p160-161: there seems to be contradiction in statements regarding the use of iv PPIs between cost economic analyses on p154 and 160-161. In the first, oral PPIs are superior, in the second iv PPIs are superior to 2nd look endoscopy in selected cases, yet the GDG do not support iv PPIs. The evidence reviewed seems to concern iv PPIs in 'all comers' non-variceal bleeders after endoscopy vs oral PPIs, but current practice is to give iv PPIs for 72 hours in high risk cases identified by endoscopy (visible vessels/bleeding ulcers treated by endotherapy). Are they saying that this is no longer recommended? If so, they do not seem to present the evidence for/against use of iv PPIs in high risk situations - not sure if there is evidence comparing with oral PPIs in these high risk cases. Also the cost economic analysis on p154 assumes 48 hours inpatient stay for oral PPIs vs 72 for iv PPIs which seems nonsensical. There is old evidence from the 1970's suggesting patients with serious bleeds be kept in for 72 hours after which the risk of rebleed drops to <5% They should review the evidence for duration of admission in high risk bleeders and make a recommendation.	Thank you for your comment. We have concluded that PPIs are required in this group of patients. The points you raise regarding the economic evidence were discussed as outlined in the LETR. There is no convincing evidence that one route of administration is superior to another. In response to this comment and comment number 146, additional detail has been added to this LETR's "other considerations" section (2nd LETR in section 8.2.6) regarding the study reported dosages and the timeframes that the studies used.
SH	British Society of Gastroenterology	17	FULL	154		assumes 48 hours inpatient stay for oral PPIs vs 72 for iv PPIs which seems nonsensical. There is old evidence from the 1970's suggesting patients with serious bleeds be kept in for 72 hours after which the risk of rebleed drops to <5% They should review the evidence for duration of admission in	Thank you for your comment. In response to your comment and comment 88, the "Other considerations" section of the LETR has been amended to give further detail on the dosage regimen that the studies reported. It states "A regimen of an 80mg bolus of Omeprazole or

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						high risk bleeders and make a recommendation. Finally, if oral PPIs are recommended for all instead of iv PPIs, we should be given guidance on the dose - they say 'high dose for 48 hours' but what is high dose and on what evidence is this based?	Pantoprazole followed by a 72 hour infusion of 8mg per hour was used in the majority of studies. In contrast studies of orally administered proton pump inhibitor drugs used comparable dosage but a shorter duration of therapy. We are therefore unable to recommend a specific dosage regimen". The evidence did not suggest superiority of one route of administration over another and therefore the GDG were unable to specify the route of administration in the recommendation.
SH	British Society of Gastroenterology	18	FULL	57 -60		the evidence shows that the Blatchford score performs better than 'pre-endoscopy' Rockall in predicting re-bleed and need for intervention. The Blatchford score has been independently validated and compared x7 to pre-endo Rockall and performs better, so surely the recommendation should say so?! The pre-endoscopy Rockall is easier to calculate and it may be that a form of words could be found to reflect the better performance of Blatchford, and suggest considering using this in pre-endoscopy assessment but accepting the pre-endo Rockall is acceptable but not quite as good??	Thank you for your comment. We agree that the evidence supports the use of Blatchford rather than clinical Rockall before endoscopy. After a discussion with the GDG this recommendation has been revised and now reads "Use the following formal risk assessment scores for all patients with acute upper gastrointestinal bleeding: • the Blatchford score at first assessment, and • the full Rockall score after endoscopy."
SH	British Society of Gastroenterology	19	FULL	113 -116		Timing of Endoscopy and link to evidence. The conclusions arise from the review of evidence which is largely based on three studies (528 participants) which the guideline acknowledges are of very low quality. This makes any comment on the absence of statistical significance in mortality meaningless. The guideline correctly acknowledges that it is not surprising that studies have been of insufficient	Thank you for your comment regarding the limitations in the evidence. Thank you for your comment regarding differences found in mortality with weekend and holiday service provision. The paper commented on delay to diagnostic endoscopy in relation to the day of the week the patient presented, but did not provide further detail regarding the

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						power to demonstrate a statistically significant difference in mortality between those trusts that provide 24 hour cover and those that do not. However, data from Wales has shown a 13% higher case fatality for patients admitted with GI bleeding at weekends and 41% higher for those admitted on public holidays (Button et al, Aliment Pharmacol Ther. 2011 Jan;33(1):64-76. doi: 10.1111/j.1365-2036.2010.04495.x.) and more recently published data suggest an increased mortality for a variety of diagnoses in a variety of hospitals over the weekends (Freemantle et al, J R Soc Med 2012: 1 – 11. DOI 10.1258 /jrsm.2012.120009). These reports constitute a useful surrogate indicator of the effects of a reduced access to the right clinical skills outside normal working hours The discussion relating to the potential benefits of endoscoping patients within 12 hours should therefore acknowledge that recommendations cannot be based on published studies but needs to accept the 'expert opinion' (indeed common sense) view that a patient who remains haemodaynamically compromised despite measure to resuscitate with features suggesting on-going profuse GI bleeding cannot wait more than 12 hours for endoscopy. The recommendations need to be more explicit with regard to the endoscopic management of unstable patients. Critically the word 'urgent' must be defined, as this determines whether or not the 50% of hospitals in the UK (BSG Survey) that currently do not have a formal GI bleed rota will need to put in place systems that ensure 24 hour access to clinicians with the skills to manage these patients.	impact of time of endoscopy to the outcomes under review. Additionally this study was based on audit data and was not an RCT. This has now been added to the list of excluded studies in the appendix. As such this paper was not included in the review; however, we agree that reduced access to the right clinical skills outside normal working hours is an important consideration. Thank you for your comments regarding the need to define urgent. The recommendation has been revised in light of your suggestions. Thank you for your comments regarding the NCGC model. The clinical and cost effectiveness of network arrangements was not prioritised as a clinical question and the cost effectiveness analysis did not consider the transfer of patients or network arrangements as a strategy to increase economies of scale for smaller providers. However, the GDG discussed this as a potential strategy for smaller providers to follow as a means to providing endoscopy in a timely manner. This discussion is noted in the economic section and in other considerations of the Linking Evidence To Recommendations section of this chapter.

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						The first recommendation should be changed to: "Perform urgent endoscopy in all unstable patients with evidence of continuing upper gastrointestinal bleeding despite resuscitation measures". The NCGC model suggests that units seeing more than 330 cases of upper GI bleeding per year should offer daily endoscopy lists while those with fewer than 330 may consider alternative strategies such as networks. The figure of 330 is likely to be close to the national average (assuming 60,000 cases per year and 200 units in the country) and could result in around half of all endoscopy units failing to provide a local service that would allow endoscopy within 24 hours. Has the cost effectiveness analysis looked at the cost of transferring between one and two patients per day by ambulance, with a trained nurse escort (and potentially a medical escort) to a neighbouring endoscopy unit? This would almost certainly affect the health economic analysis and considerably lower the figure. (The commentary acknowledges that the number of 330 is conservative and does not capture all the potential benefits of daily endoscopy lists.)This number should be revised after recalculating the true cost of the 'network' model.	
SH	British Society of Gastroenterology	20	FULL	117 -133		no comment is made on the suggested volume (nor dilution) of adrenaline - presumably 1 in 10,000 but not stated anywhere. There is some evidence regarding volume - better with higher volumes of 20-30 mls - should this not be reviewed and a recommendation made?	Thank you for your comment. This was not included in the scope.
SH	British Society of Gastroenterology	21	FULL	152	32	Typo: 'stigmata' (not stimata) – typo appears three times in document	Thank you for your comment. The guideline has been amended accordingly.
SH	British Society of Gastroenterology	22	FULL	160	4	The recommendation "Offer proton pump inhibitor with non-variceal…….shown at endoscopy" does	Thank you for your comment. We agree with your comment. We do not specify this but it is

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						not acknowledge that PPI therapy is of proven value in treating peptic ulcers. All patients with ulcers should be offered oral PPI therapy.	entirely compatible with the recommendation.
SH	British Society of Gastroenterology	23	FULL	162	7	Delete 'be'	Thank you for your comment. The guideline has been amended accordingly.
SH	British Society of Gastroenterology	24	FULL	180		Management of variceal bleeding – the initial emphasis on TIPS and gastric variceal haemorrhage is curious. The commonest presentation is bleeding from oesophageal varices and this should be discussed before the management of gastric varices and TIPS.	Thank you for your comment. The order of the recommendations has now been changed.
SH	British Society of Gastroenterology	25	FULL	general		A recent BSG survey has shown that around half the trusts in the UK do not have a formal GI bleed rota. At these sites, patients with GI bleeding are usually managed by surgical teams even though the majority of on-call surgical consultants do not possess the required technical skills to deal with bleeding lesions. It should be emphasised that formal systems ensuring 24/7 access to staff with the right skills to manage patients with acute GI bleeding is essential. The guidelines mention a number of different models that would provide acceptable cover arrangements to ensure these patients are managed appropriately. However, it is likely many trusts would fail to put in place formal measures to provide such cover without significant changes to the recommendations.	Thank you for your comment. We state that all unstable acutely bleeding patients must receive urgent endoscopy but we have to recognise the difficulties of providing a 24/7 service in remote and rural communities and cover will need to be ensured according to local need and commissioning arrangements. Following public consultation on the guideline and finalisation of the recommendations, NICE undertakes a series of activities' to encourage implementation. In the clinical benefits and harms section of the LETR, we state "for high risk patients requiring urgent endoscopy, particularly if out-of-hours, the GDG emphasised the importance of appropriate facilities and trained staff and that the safety and quality of any endoscopic procedure should not be compromised by its timing". To further acknowledge your point about staff skills and training we have also highlighted that staff should be trained under the "other considerations" section of the LETR; stating "arrangements for urgent therapeutic endoscopy in actively bleeding, haemodynamically unstable patients must be put in place. How this is done will depend upon local circumstances. In referral

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							centres fully trained teams could provide 24/7 endoscopic cover, supported by surgery and interventional radiology".
SH	BSPGHAN	1	full	general		Although children below 16 are excluded, many children age 16-18 (who are included) may be looked after by Paediatric Gastroenterology services rather than in adult medical departments. The figures for mortality and morbidity are likely to be substantially lower in this age group, and it is unclear whether the studies concerned were powered adequately for consideration of this age-group.	We agree with your comment. Unfortunately it was impossible to identify the subjects aged 16 and 17 within the studies and almost all studies excluded children.
SH	BSPGHAN	2	full	13	39	The practice of withholding acid suppression therapy until after endoscopy in non-variceal bleeding is not usual paediatric practice, and may be dangerous as the availability of urgent endoscopy may be less, due to the usual need for general anaesthesia. I would question whether there is a sufficient evidence base for such a statement for 16-18 year olds, managed in paediatric units.	Thank you for your comment. Unfortunately it was impossible to identify the subjects aged 16 and 17 within the studies and almost all studies excluded children. There is no evidence that early use of PPIs improve outcome. Patients with severe acute gastrointestinal bleeding need endoscopic therapy not PPIs.
SH	BSPGHAN	3	full	General		This guideline did not intend to include children (and we note that there was no paediatric representation on the group). There is an urgent need for a guideline to encompass young people and children. Adult practitioners may need clear guidelines as may be undertaking procedures on young people under 16 in some regions. BSPGHAN and BAPS (British Association of Paediatric Surgery) are currently consulting about the provision for diagnosis and management of acute upper GI bleeding in children and discussing how to formalise paediatric	Thank you for your comment. We don't disagree, however this was beyond the scope of the guideline. We recommend you submit your suggestion to NICE as a potential topic for a future guideline.

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						networks. There is less provision for children for management of GI bleeding in regions and there needs to be a formalised network to ensure improved standards of care and equity of access to services. Adult gastroenterologist may have to provide emergency cover for older children in a few areas. Very few regions operate "out of hours "services for GI bleeding for children due to insufficient skilled operator in all regions. There needs to be improved networking local networking to cover for OOH, access to endoscopy lists, and to allow a critical mass of expertise (with adequate equipment) to build up in key centres. A paediatric document should encompass the specific techniques used in the 3 supra regional hepatology centres and cover the techniques for children with portal hypertension eg management of variceal bleeding, procedures such as TIPPS and specialised drugs.	
SH	Department of Health	1	Full	general		The Department of Health has no substantive comments to make, regarding this consultation.	Thank you for your comment.
SH	Gloucestershire Hospitals NHS Foundation Trust	1	Full	General		Our comments our as follows: The guidelines in general are acceptable, however we would wish to see PPI offered prior to endoscopy if a patient has dyspepsia or upper GI bleeding in association with a NSAID. We recognise that this does not affect mortality/outcome of GI bleed, but it is a treatment for dyspepsia and treatment of NSAID upper GI complications. In the case of painless upper GI bleeding the PPI is less relevant	Thank you for your comment. We specifically haven't considered dyspepsia as it is already the subject of a NICE guideline (CG17). The guideline covers the evidence base of the management of patients who are taking NSAIDs and experiencing an upper GI bleed in chapter 10 of the full guideline.
SH	MHRA	1	Full	general		We confirm that we will not be participating in this guideline.	Thank you for your comment.
SH	NHS Blood and Transplant	1	Full	71	18	We contest the strong statement the guideline has made: "Do not offer blood transfusion to patients who have a haemoglobin level of more than 0.8g/litre". We believe this statement is misleading,	Thank you for your comment. The recommendation has been revised in light of your comment. The recommendation now reads "Base decisions on blood transfusion on the full

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						not representative of the evidence base and potentially even harmful to patients. There is singular lack of high quality evidence to inform this statement. The observational data presented is all subject to confounding and should not be used to inform a bold statement in a guideline. The RCT evidence is clearly summarised in a Cochrane meta-analysis (Jairath et al, reference 41). Other RCTs suggesting this threshold to be safe have been conducted in younger patients with less co-morbid illness and do not have the unique problem of rebleeding, which occurs in 15% if patients with UGIB. 25% of patients with UGIB are over the age of 80 and almost 1/3 has cardio-vascular disease. It is unknown whether or not this group benefit from a transfusion threshold of 8g/dL or 10g/dL. A recommendation of 8g/dL, in the absence of a well conducted RCT, could result in an excess of cardiovascular events and even death if followed as a result of this guideline. We believe this statement should be revised to the following: "Although a transfusion threshold of 8 g/dL is safe in other patient cohorts, it is unclear whether this can be translated to patients with UGIB, in the absence of a well conducted randomised controlled trial".	clinical picture, recognising that over transfusion may be as damaging as under transfusion".
SH	NHS Blood and Transplant	2	Full	38	28	As above	Thank you for your comment.
SH	NHS Direct	1	Full	GENERAL		NHS Direct welcome the guideline and have no comments on the consultation. No identified impact on telephone assessment.	Thank you for your comment.
SH	Nottingham University Hospitals NHS Trust	1	NICE	5	7	Clinical Rockall score or Blatchford score at first assessment. The two scores have different roles. The role of Blatchford is purely for triaging patients with a score of 0 for out-patient endoscopy rather than admission (Stanley AJ et al., Lancet 2009;373:	Thank you for your comment. The recommendations have been amended and now reads "Use the following formal risk assessment scores for all patients with acute upper gastrointestinal bleeding:

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						42-47). Rockall 0 score doesn't have similar robust data to support it's use. This should be corrected under 1.1.1 at line 8, page 7.	• the Blatchford score at first assessment, and • the full Rockall score after endoscopy."
SH	Nottingham University Hospitals NHS Trust	2	NICE	9	17 -20	The economic model requires a number of assumptions that may not be true. We give two examples. One of the key assumptions is that death within 28 days does not occur following GI bleeding following discharge from hospital (Appendix 1.2.6). This is incorrect as demonstrated by Crooks C et al. (Gastroenterology. 2011;141(1):62-70.) where 15% of deaths occurred outside hospital within this period. Given the importance of mortality estimates in this model it is severely compromised by this error. In addition, the Markov transition state diagram indicates that the model includes probabilities based on timing units of 0-4 hours, 4-12 hours, 12-24 hours etc and the effect of such intervention on death or discharge. The model is then cycled over 1 hourly intervals. The evidence underpinning the assumptions taken to make this hourly model are simply not supported by the available evidence (as clearly outlined in the full review document). These are only two examples that suggest that making a definitive statement about timing of endoscopy (NICE guidance recommendation 1.3.2) with respect to number of cases and daily endoscopy lists cannot be supported.	Thank you for your comment and examples of assumptions which are of concern. All assumptions made in the model were discussed with clinical members and agreed as reasonable for the purposes of developing a model to aid decision making. All assumptions were explicitly acknowledged (and clearly outlined in the full document) so that the GDG could take them into account when interpreting the model results. We acknowledge that Crooks et al (2011) report that of the deaths which occurred within a 28 day period, 15% of these occurred after discharge from hospital and therefore would not be captured in the NCGC model. Unfortunately, the paper does not report data to estimate the probability of death post discharge according to the timing of endoscopy or risk group. Further, no information is provided regarding the time of death post discharge. If all post discharge deaths occurred at 28 days, the base case model results would be unaffected, The case fatality that occurs post discharge would not influence the length of hospital stay or cost, a key driver of the cost effectiveness in this analysis. As outlined in appendix section I.4, the number of deaths, as recorded as a secondary outcome, was lowest in the everyday strategy. If we were to assume case fatality post discharge had the same risk factors as death within

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							hospital, it is likely that the majority of deaths post discharge would occur in the weekday strategy rather than in the everyday strategy. Overall assumptions in the economic model would lead to a conservative estimate regarding the number of cases required annually to make the everyday strategy cost effective, as noted in the discussion in appendix I. Therefore the developers felt it reasonable to make a strong recommendation to regarding what providers who see over this number of cases should do (i.e. implement daily endoscopy lists), and a weaker recommendation of what providers under this number should consider doing.
SH	Nottingham University Hospitals NHS Trust	3	NICE	5	21 -25	The recommendation derived from superficial review of literature is incomplete. The meta-analysis showed that the dual therapy modality therapy is only superior when compared with adrenaline injection alone. When compared with mechanical therapy alone (heater probe or clips), dual therapy wasn't superior. In addition, dual modality treatment is associated with statistically significant HIGHER perforation rate (Marmo R. Et al., Am J Gastroenterol 2007;102:279-89). So, a blanket recommendation that starts with adrenaline injection followed by another mechanical modality is inappropriate and contrary to the evidence base. This should also be corrected in section 1.4.1, page 9, lines 13-16.	Thank you for your comment. A clear recommendation with regards to mechanical methods alone could not be made since it was not part of the clinical question. However, the recommendation was amended in light of your comment to state that mechanical methods could be used as a single treatment rather than in combination with another modality.
SH	Nottingham University Hospitals NHS Trust Nottingham University Hospitals NHS Trust	4	NICE	8	23	1.2.9. Offer terlipressin to patients with suspected variceal bleeding. Clarify as to how do you suspect this. Recommendation should say- those with decompensated cirrhosis or those known to have varices.	Thank you for your comment. After discussion with the GDG, it was decided that the original wording of the recommendation was appropriate and allowed for clinical judgement and history of the patient. .

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SH	Nottingham University Hospitals NHS Trust	5	NICE	8	24	1.2.9. Stop treatment... sentence should be modified as... after definitive haemostasis has been achieved or after 5 days of maximum treatment....	Thank you for your comment. The recommendation has been amended. The recommendation now reads: Offer terlipressin to patients with suspected variceal bleeding when they first present. Stop treatment after definitive haemostasis has been achieved, or after 5 days, unless there is another indication for its use ."
SH	Nottingham University Hospitals NHS Trust	6	NICE	9	21 -23	1.4.2. Do not offer acid suppression drugs before endoscopy. This recommendation is supported by a systematic review which showed increased all cause mortality in association with IV PPI therapy in upper GI bleeding. Khuroo MS et al., J Gastroenterol Hepatol. 2005;20(1):11-25.	Thank you for your comment.
SH	Nottingham University Hospitals NHS Trust	7	FULL	14	1 -46	The only work referenced in the introduction is the recent national audit, however the information quoted from the audit is supported by larger population based studies. For example the authors of the audit compare their estimated mortality results to existing population based studies to provide validity, and these studies should therefore at least be acknowledged in the statements relating to mortality in the introduction. Indeed the published audit itself acknowledges its susceptibility to selection bias stating that *"it is probable that some cases of AUGIB were not captured in the current audit since the number of recorded cases varied greatly between contributing hospitals with some institutions collecting relatively small numbers of patients in comparison to hospitals that served similar populations*." (Hearnshaw SA, Logan RFA, Lowe D, et al. GUT. 2011:doi:10.1136/gut.2010.228437)	Thank you for your comment. We have amended the introduction by adding further reference to the Crooks, Rockall, Blatchford and Button studies in the first paragraph.
SH	Nottingham	8	FULL	14	3	The statement for the occurrence of upper	Thank you for your comment. We have

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	University Hospitals NHS Trust					gastrointestinal haemorrhage is not referenced and could be supported by a number of population based studies of the incidence of non variceal haemorrhage. The most recent of which have reported incidence as **84-103/100,000 in England** (Crooks C, Card T, West J. Gastroenterology. 2011;141(1):62-70.) **and** (Rockall TA, Logan RF, Devlin HB, Northfield TC. BMJ. 1995;311(6999):222 – 6; **and 99-172/100,000 in Scotland** (Blatchford O, Davidson LA, Murray WR, Blatchford M, Pell J. BMJ. 1997;315(7107):510-514; Taha AS, Angerson WJ, Knill-Jones RP, Blatchford O. Aliment Pharmacol Ther. 2005;22(4):285-289.), **and 134/100,000 in Wales** (Button LA, Roberts SE, Evans PA, et al. Alimentary Pharmacology & Therapeutics. 2011;33(1):64-76).	amended the introduction by adding further reference to the Crooks, Rockall, Blatchford and Button studies in the first paragraph.
SH	Nottingham University Hospitals NHS Trust	9	FULL	14	4	The statement that socially deprived communities are most often affected is not referenced, yet this has been clearly demonstrated in each part of the UK in population based studies**: in England** (Crooks CJ, West J, Card TR. Gut. 2011: doi:10.1136/gutjnl-2011-300186), **in Scotland** (Blatchford O, Davidson LA, Murray WR, Blatchford M, Pell J. BMJ. 1997;315(7107):510-514) **, and in Wales** (Button LA, Roberts SE, Evans PA, et al. Alimentary Pharmacology & Therapeutics. 2011;33(1):64-76).	Thank you for your comment. We have amended the introduction by adding the suggested references to the first paragraph.
SH	Nottingham University Hospitals NHS Trust	10	FULL	14	7	The statement for mortality does not define over what period of time it is being measured and it is crucial that it does. As mentioned in point 1, with the concerns about selection bias in the audit the mortality should at a minimum be reported as a range reflecting estimates from larger population based studies that the audit itself referenced (Button LA, Roberts SE, Evans PA, et al. Alimentary Pharmacology & Therapeutics. 2011;33(1):64-76) & (Crooks C, Card T, West J.	Thank you for your comment. We have amended the introduction to make it clear that the audit referred to hospital mortalities. The incidence of mortality mentioned has been amended to reflect the range of estimates from the studies that have been referenced.

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						Gastroenterology. 2011;141(1):62-70.).	
SH	Nottingham University Hospitals NHS Trust	11	FULL	14	9	The statement that mortality has not improved since the 1950s contradicts with the conclusion of the recent national audit published in GUT. The mortality in the recent audit (Hearnshaw SA, Logan RFA, Lowe D, et al. GUT. 2011:doi:10.1136/gut.2010.228437) was lower than that of the 1995 audit (Rockall TA, Logan RF, Devlin HB, Northfield TC. BMJ. 1995;311(6999):222 – 6) suggesting that 28 day mortality has indeed improved. However as there were methodological issues in comparing mortality between audits with different methodology and poor case ascertainment, studies using longitudinal data should also be referenced (as the published audit itself does) for Scotland (Kang JY, Elders A, Majeed A, Maxwell JD, Bardhan KD. Aliment Pharmacol Ther. 2006;24(1):65-79.), Wales (Button LA, Roberts SE, Evans PA, et al. Alimentary Pharmacology & Therapeutics. 2011;33(1):64-76) and in England (Crooks C, Card T, West J. Gastroenterology. 2011;141(1):62-70.) which showed that after adjusting for changes in co-morbidity and age there has been a steady linear reduction in mortality over the last decade.	Thank you for your comment. This sentence has been deleted from the introduction. We have also amended the introduction by adding the suggested references to the first paragraph.
SH	Nottingham University Hospitals NHS Trust	12	FULL	14	35	The proportion of bleed events that are variceal bleeds is stated here as12% which is quoted from the recent audit. However this was higher than has been found in many other studies that have reported the proportion of variceal haemorrhage admissions in the UK at 3-6% (Rockall TA, Logan RF, Devlin HB, Northfield TC. BMJ. 1995;311(6999):222 – 6), (Blatchford O, Davidson LA, Murray WR, Blatchford M, Pell J. BMJ. 1997;315(7107):510-514), (Button LA, Roberts SE, Evans PA, et al. Alimentary Pharmacology & Therapeutics. 2011;33(1):64-76), (Crooks C, Card	Thank you for your comment. We have amended the 6th paragraph of the introduction to address this comment.

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						T, West J. Gastroenterology. 2011;141(1):62-70.). Longitudinal hospital admission data showed no change in variceal haemorrhage admissions over the last decade (Crooks C, Card T, West J. Gastroenterology. 2011;141(1):62-70.).	
SH	Nottingham University Hospitals NHS Trust	13	FULL	14	41 -46	This guideline focuses on the management of variceal and peptic ulcer bleeds at the exclusion of other causes. However the justifications for this are over stated; that those other causes are rare or have good outcomes. The majority of cases in the recent audit were due to oesophagitis, duodenitis, gastritis or had no abnormality seen, with 28 day mortality for having one of these diagnoses in isolation 4-6%. This is not that dissimilar to the 9% reported for peptic ulcer and probably reflects the large contribution co-morbidity makes to mortality after bleeding(Sung JJY, Tsoi KKF, Ma TKW, et al. Am J Gastroenterol. 2009;105(1):84-89). Therefore the only reason that can be given to limit the guidelines to peptic ulcer and variceal haemorrhage is the lack of data for other causes.	Thank you for your comment. We found no direct evidence in this area.
SH	Nottingham University Hospitals NHS Trust	14	FULL	15	7 -8, 31-34	When discussing the assessment and management of upper gastrointestinal haemorrhage it is important to state that historically, i.e. before endoscopic therapy, conservative medical management resulted in over 70% of peptic ulcer bleeds and 44% of variceal bleeds resolving with no further bleeding (Ward-McQuaid J, Pease J, Smith AME, Twort R. Gut. 1960;1(3):258), (Johnston SJ, Jones PF, Kyle J, Needham CD. BMJ. 1973;3(5882):655-660). Therefore the outcome of the majority of patients presenting with acute upper gastrointestinal haemorrhage will not be improved by acute endoscopic interventions beyond providing reassurance that they are in a low risk group and allowing earlier discharge (as discussed on page 114). For the remainder therapeutic endoscopy has	Thank you for your comment. This has been noted.

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						proven benefit in reducing re-bleeding. The number of patients who die from exsanguinations is low with current management (Sung JJY, Tsoi KKF, Ma TKW, et al. Am J Gastroenterol. 2009;105(1):84-89).	
SH	Nottingham University Hospitals NHS Trust	15	FULL	32	3	The end points in table 1 need to be better defined. Presumably the mortality, re-bleeding and surgery are within 28 days of bleeding? However, it is not clear. The figures given are solely based on the audit and which, as previously discussed, do not reflect the range of reported values from larger UK population based studies. As this figure is used as a criterion for the minimal important difference, it needs to be better supported by published data e.g. 10%, (Button LA, Roberts SE, Evans PA, et al. Alimentary Pharmacology & Therapeutics. 2011;33(1):64-76), 10.5% - (Crooks C, Card T, West J. Gastroenterology. 2011;141(1):62-70.)	Thank you for your comment. The MID is not derived from any specific data, but by expert consensus (see methodological introduction to the Guideline)
SH	Nottingham University Hospitals NHS Trust	16	FULL	71	14 -18	The evidence presented in the guideline document is as the authors state of low or very low quality, and is also limited in quantity. The grounds for choosing a hard value at which to state transfusion becomes appropriate are therefore questionable. This is particularly so as (as the guideline development group are aware) an RCT to better address this issue is shortly to commence. If there is evidence sufficient for the guideline as it is to go forward, that study will not be of restricted and liberal, but of normal and excessive transfusion. It may also be that such confidence in guidance before the trial may damage recruitment to it. Though we concur that excessive use of transfusion is a clear problem we would suggest that the evidence better supports, and the trial will be better supported by a statement that. 1. Evidence is currently insufficient to	Thank you for your comment. The recommendation has been revised in light of your comment. The recommendation now reads "Base decisions on blood transfusion on the full clinical picture, recognising that over transfusion may be as damaging as under transfusion".

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						confidently answer this question. 2. What limited data there are, suggest that transfusion of those with haemoglobin above 8 may not be helpful, and may even cause harm. Whether a cut off of 7, 8 or 9 grams per dl is more appropriate has however not been addressed in the available studies. And guidance to 1. Transfuse patients with massive bleeding with blood, platelets and clotting factors in line with the local protocols for managing massive bleeding. 2. Base decisions on blood transfusion to patients with acute upper gastrointestinal bleeding on the full clinical picture, recognising that over transfusion may be as damaging as under transfusion.	
SH	Royal College of General Practitioners	1	NICE	general		These clearly are hospital based guidelines. It might be useful to have the Rockall or Blatchford score explicitly stated as most GPs probably would not know what they mean. From a general practice perspective, communication in the form of accurate and timely written information is of importance. This particularly applies to drugs provided on discharge particularly when it's important to manage co-morbidity such as cardiovascular or cerebrovascular disease. Follow up arrangements should be clearly specified.	Thank you for your comment. This level of detail is not normally put in the NICE version. Further details of the scoring systems are available in the chapter on risk scoring in the full guideline.
SH	Royal College of Nursing	1	Full	General		The Royal College of Nursing welcomes this draft guideline. They are well written, easy to understand and we	Thank you for your comment.

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						consider that GI practice will benefit from them.	
SH	Royal College of Paediatrics and Child Health	1	Full	General		Although children below 16 are excluded, many children age 16-18 (who are included) may be looked after by Paediatric Gastroenterology services rather than in adult medical departments. The figures for mortality and morbidity are likely to be substantially lower in this age group, and it is unclear whether the studies concerned were powered adequately for consideration of this age-group.	We agree with your comment. Unfortunately it was impossible to identify the subjects aged 16 and 17 within the studies and almost all studies excluded children.
SH	Royal College of Paediatrics and Child Health	2	Full	General		The GDG did not include a paediatrician.	Thank you for your comment. The guideline population was people aged 16 and over, therefore the GDG did not seek a paediatrician member.
SH	Royal College of Paediatrics and Child Health	4	Full	39	37	The practice of withholding acid suppression therapy until after endoscopy in non-variceal bleeding is not usual paediatric practice, and may be dangerous as the availability of urgent endoscopy may be less, due to the usual need for general anaesthesia. I would question whether there is a sufficient evidence base for such a statement for 16-18 year olds, managed in paediatric units.	We agree with your comment. Unfortunately it was impossible to identify the subjects aged 16 and 17 within the studies which included patients of this age range. . In general the GDG feel that the priority in managing upper GI bleeding is prompt endoscopic therapy and hope that the recommendations in the Guideline will lead to delays being minimised, which in turn will lead to prompt administration of PPI's if these are indicated. .
SH	Royal College of Paediatrics and Child Health	5	Full	86	26	Terlipressin – unlicensed for use in children but BNF for Children gives doses for children aged 12-18 years. Little evidence for its use in younger children presented.	Thank you for your comment.
SH	Royal College of Paediatrics and Child Health	6	Full	117	11	Not sure of meaning of "diluted adrenaline". Little evidence can be given on use of fibrin and thrombin in children < 16 years.	Thank you for your comment. The introduction has been amended.
SH	Royal College of Paediatrics and Child Health	7	Full	134	1	Reasonable experience of use of PPIs in children but there are considerable practical difficulties in administering accurate doses, eg if to be given down nasogastric tubes; doses available.	Thank you for your comment. With respect to children, we agree that their clinical management may differ from that of adults, however cannot comment further as such management was beyond the scope of the guideline. In respect to young people,

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							unfortunately we could not isolate this group in the literature available.
SH	Royal College of Paediatrics and Child Health	8	Full	231	11	The question of continuation of aspirin for secondary preventionof vascular events in children must be reasonably uncommon. Aspirin is unlicensed in children < 16 years but "low dose" antiplatelet doses are available in the BNF for Children. Again practical difficulties in giving accurate doses.	Thank you for your comment. This was outside the scope of the guideline.
SH	Royal College of Physicians	1	Full	general		The RCP has had sight of the response due to be submitted on the above consultation by the British Society of Gastroenterology (BSG). We wish to endorse those comments	Thank you for your comment.
SH	South Asian Health Foundation	1	Full	General		Should there be something in the guideline about adequate history and examination of upper GI bleeds – often patients with a low haemoglobin are assessed as such without checking for chronicity/melaena etc.	Thank you for your comment. We agree that a history and examination are standard clinical practice and of course important, but they are part of basic medicine.
SH	South Asian Health Foundation	2	Full	general		Likewise, should there be something in the guideline about relevant blood tests on admission (eg, FBC, U&E, coag, crossmatch) etc.	Thank you for your comment. We agree that a history and examination are standard clinical practice and of course important, but they are part of basic medicine.
SH	South Asian Health Foundation	3	NICE	9	1.4.2	Is the role of proton pump inhibitors so clearcut before endoscopy – although it can reduce endoscopic stigmata, in some settings (eg, where endoscopy is not possible immediately or a massive bleed), it has a role	Thank you for your comment. Evidence of this is given in the full guideline.
SH	South Asian Health Foundation	4	NICE	10	1.5	Should some comment be made about treating the underlying liver disease for varices (eg, alcohol cessation)	Thank you for your comment. This is outside our remit.
SH	South Asian Health Foundation	5	NICE	11	1.6	Should some comment be made about use of gastroprotectants (eg, PPIs) in secondary prevention of non-variceal bleeding?	Thank you for your comment. This is outside the remit of the scope.
SH	South Asian Health Foundation	6	NICE	11	1.7	Should some comment be made about increasing risks of bleeding with increased antithrombotic use (anticoagulants, antiplatelets and fibrinolytics) and NSAIDs/coxibs and appropriate risk stratification for	Thank you for your comment. This is outside the remit of the scope.

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						these is required?	
SH	South Asian Health Foundation	7	NICE	11	1.7	Also, surprised that H.pylori is not mentioned in these guidelines in the context of secondary prevention even though it is covered in other guidelines	Thank you for your comment. This is outside the remit of the scope.
SH	South Asian Health Foundation	8	NICE	11	1.7.3	Should it be made more explicit that the discussion about clopidogrel (and other newer antithrombotics) depends on absolute vascular risks?	Thank you for your comment. No, this is not a subject of the guideline.
SH	South Asian Health Foundation	9	NICE	11	1.8	We agree that establishing good communication between clinical staff and patients and their family and carers at the time of presentation, throughout their time in hospital and following discharge is important, esp. in ethnic minority patients and other inequalities (eg, deprivation) in which this can be an especial issue.	Thank you for your comment.
SH	The British Society of Interventional Radiology (BSIR) and the Faculty of Clinical Radiology, The Royal College of Radiologists (RCR)	1	Full	General		Whilst these guidelines are in the most part accurate and realistic, we would suggest that the phrase "offer Interventional Radiology *if available* as second line treatment for non variceal bleeding" should be changed. The evidence supports Interventional Radiology as the second line treatment and we feel that NICE should be stressing that centres accepting patients with Upper GI bleeding should be offering all diagnostic and treatment modalities. Leaving the guidance stating 'if available' will continue to perpetuate the 'postcode lottery' for this treatment. We would refer NICE to the "Upper GI Bleeding Toolkit" on the Academy of Medical Royal Colleges website (http://aomrc.org.uk/projects/upper-gastrointestinal-bleeding-toolkit.html) which could be referred to if business cases for Interventional Radiology have to be made.	Thank you for your comment. We acknowledge your comment and the differences between an evidence based guideline such as this and a policy document such as you have referenced. We have reworded the recommendation to emphasize interventional radiology as second line treatment. It now rereads "Offer interventional radiology to unstable patients who re-bleed after endoscopic treatment. Refer urgently for surgery if interventional radiology is not promptly available". However, the developers are very aware that treatment should be prompt and of the increased cost of service provision that would be required to offer interventional radiology in all centres. As such, it is felt it remains inappropriate to mandate interventional radiology in all centres without further supportive evidence.
SH	The British Society of Interventional	2	Full	General		*Our comment above applies also to variceal bleeding. The phrase "Consider TIPs" does not*	Thank you for your comment and drawing our attention to this reference. The review question

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	Radiology (BSIR) and the Faculty of Clinical Radiology, The Royal College of Radiologists (RCR)					*follow on entirely from the evidence. In particular we would refer NICE to the following randomised study that clearly demonstrated the survival benefits of early TIPs. We would urge NICE to consider this paper:* *June 24, 2010, García-Pagán J.C., Caca K., Bureau C., et al. N Engl J Med 2010; 362:2370 - 2379 Early use of TIPS in patients with Cirrhosis and Variceal Bleeding.*	was focused on patients with gastric variceal bleeding. The reference that you cite focuses on patients with oesophageal varices and excludes patients who have gastric varices. This is why it was excluded. Please see section K.7.1 in the Appendices for studies excluded from this review.
SH	United Kingdom Clinical Pharmacy Association (UKCPA)	1	Full	General		There is a huge gap with the omission of any advice on the use of continuous infusions of PPI. This is exacerbated by the terminology used to describe the modes of administration. SIGN 105 contains much more specific information in this area (sect. 5.3.2) recommending the dose of 72 hours continuous infusion in patients with major bleeding following endoscopic homoeostasis, However the NICE guidelines only discuss the use of IV route in general terms, not stating that it is the continuous infusion that is preferred. Indeed, mention is made on some occasions to IV infusions, but it is not clear if 30min infusion or continuous infusion is intended. There can be considerable inappropriate use of continuous infusions, for example following surgical repair of prior to endoscopy. Clarification would be very helpful to underpin appropriate use of IV PPI.	Thank you for your comment. This was not part of the protocol. Specific doses are not generally given in NICE recommendations. The LETR has been amended to reflect this.

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