Transfusion
Consultation on draft guideline - Stakeholder comments table
1 June-13 July 2015

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page	Line	Comments	Developer's response
Amgen UK	Full	General	General	We are concerned that for the management of patients suffering from chemotherapy induced anaemia the guideline does not explicitly refer to the recently published NICE guidance on Erythropoiesis-stimulating agents (epoetin and darbepoetin) for treating anaemia in people with cancer having chemotherapy, TA323. Although TA 323 is listed in the condition specific list (section 3.3.3.2), we feel it would be more appropriate to explicitly exclude chemotherapy induced anaemia from the scope of this guideline similarly to other specialist areas already covered by NICE guidance (anaemia in chronic kidney disease, upper gastrointestinal bleeding, and trauma and massive haemorrhage).	Thank you for your comment. We have edited the 'Linking evidence to recommendations' section for this recommendation and the following statement has been added to the 'other considerations' section: The GDG noted that EPO is recommended for use in some non-surgical patients where it had been prescribed for other causes, for example, chronic renal disease and in people with anaemia having chemotherapy to treat cancer.
Amgen UK	Full	13	31-35	Explicitly add a point related to management of chemotherapy induced anaemia referring to TA323: For guidance on managing anaemia in patients receiving chemotherapy, see the NICE guidance TA323	Thank you for your comment. We agree and this has now been added to the 'other considerations' section of the EPO 'Linking evidence to recommendations' table.
Amgen UK	Full	19		Explicitly add a point related to management of chemotherapy induced anaemia referring to TA323: *For guidance on managing anaemia in patients receiving chemotherapy, see the NICE guidance TA323*	Thank you for your comment, this has been added to the 'other considerations' section of the EPO 'Linking evidence to recommendations' table.
British Blood Transfusion Society	Full	General	General	As an original Stakeholder we were asked to consult on the guidelines below. These have been circulated to the relevant Council members and I can report that there were no	Thank you for reviewing the guideline.

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				additional comments. Please let me know if there are any queries.	
BCSH Transfusion Task Force	Full	General	General	The language overall is complex and not easy to follow. To understand the guidelines one needs to read and understand the way the literature has been selected and analysed. This appears to have been done by a different team; it would be interesting to know what it cost to generate this huge document. In the sections read we do not find anything that was not already contained in the various BCSH guidelines.	Thank you for participating in the consultation process. We have included a glossary to help explain complex terminology. NICE produces guidelines in several formats for end users. Among these formats is Information for Patients version of the guideline which is drafted with a lay-reader in mind. More information on how NICE guidelines are developed can be found at: https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-guidelines/nice-clinical-guidelines. The guideline development group worked with a team at the National Clinical Guideline Centre comprising of Information Scientists, Systematic Reviewers and Health Economists to produce the guideline. The Department of Health commissioned NICE to develop a cross cutting clinical guideline on the assessment and management of blood transfusion. There are a number of generic costs associated with guideline production. Typically the development of a standard NICE clinical guideline takes 26 months from the time that the topic is referred to the publication date. At any one time we will have a portfolio of guidelines at various stages of development with many organisations and individuals involved in the various stages. The guideline committee include healthcare

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					professionals, technical experts and patients and carers who have relevant expertise and experience. NICE pay travel and subsistence costs to the committee when necessary in line with their policy, to enable attendance at committee meetings. Remuneration for committee members can be found discussed in the 'Information for applicants' documents listed against current vacancies on our website and a current 'information for applicant' document can be found here and expense costs can be found from page 6. More information on how NICE guidelines are developed can be found at: https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-guidelines/nice-clinical-guidelines Your observation related to the BCSH guidelines is noted.
BCSH Transfusion Task Force	Full	General	General	The reference numbers do not match the reference list.	Thank you for your comment, this has been amended.
BCSH Transfusion Task Force	Full	General	General	There are 3 key areas for further research listed. A number of sections have low evidence, and yet none of these have recommendations for further research - need more robust evidence	For each review area the GDG considered whether it was better to make a practice recommendation or a recommendation for research. In some cases where there was no reliable evidence there was good consensus within the GDG of what a recommendation for practice should say and that it was more valuable to make a practice recommendation than wait for future research.
BCSH Transfusion Task Force	Full	General	General	Incorrect spelling of Erythropoietin	Thank you for your comment, this has been amended.
BCSH Transfusion	Full	General	General	Was there no involvement from the Royal College	Thank you for your comment. The Royal College of

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Task Force				of Pathologists ?	Pathologists are one of the registered stakeholders for the guideline and therefore have had the opportunity to input at the scope development stage and comment on the draft guideline.
BCSH Transfusion Task Force	Full	12	9	"offer" seems a strange way of wording – suggest "recommend"	Thank you for your comment. NICE reflects the strength of its recommendations in the wording used across its guidance. The Institute, uses 'offer' (or similar wording such as 'measure', 'advise', 'commission' or 'refer') to reflect a strong recommendation, usually where there is clear evidence of benefit. On this occasion the group agreed that 'offer' was the best option for the guideline.
BCSH Transfusion Task Force	Full	12	11	"offer" seems a strange way of wording – suggest "recommend"	Thank you for your comment. NICE reflects the strength of its recommendations in the wording used across its guidance. The Institute, uses 'offer' (or similar wording such as 'measure', 'advise', 'commission' or 'refer') to reflect a strong recommendation, usually where there is clear evidence of benefit. On this occasion the group agreed that 'offer' was the best option for the recommendation.
BCSH Transfusion Task Force	full	12	27	What about the threshold of platelets 20 and fever for transfusion	Thank you for your comment. No evidence was found to routinely raise the threshold for patients with fever. It was the consensus of the GDG not to raise the threshold for prophylactic platelet transfusions. This has been noted in the 'other considerations' section of the 'Linking evidence to recommendations' table.
BCSH Transfusion Task Force	Full	13	21	What about the threshold of platelets 20 and fever for transfusion	Thank you for your comment. No evidence was found to routinely raise the threshold for patients

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					with fever. It was the consensus of the GDG not to raise the threshold for prophylactic platelet transfusions. This has been noted in the 'other considerations' section of the 'Linking evidence to recommendations' table.
BCSH Transfusion Task Force	Full	13	23	Intravenous iron wouldn't routinely be needed both before AND after surgery – depends on degree of blood loss if the preop dose was enough to make the patient iron replete	Thank you for your comment. We agree and this has now been amended to 'before or after surgery'.
BCSH Transfusion Task Force	Full	13	27	Would only consider iv iron preop if the interval to surgery is short in surgery that cannot safely be postponed not routinely	Thank you for your comment. The point about the possibility of postponing surgery in patients with IDA has been included in the 'other considerations' section of the 'Linking evidence to recommendations' table for this recommendation.
BCSH Transfusion Task Force	Full	14	10	Probably should comment for how long after a transfusion to monitor patient's condition	Thank you for your comment, the following statement has been added to the 'Linking evidence to recommendations' statement (LETR): Trusts should develop a policy for the frequency of observations based on the clinical state of the patient. The GDG discussed time frames in the 'other considerations' section of this part of the chapter. It is stated in the LETR that the group agreed that the 'frequency of monitoring would depend on the type of patient receiving a transfusion, for example, children and unconscious patients may require more frequent monitoring during blood transfusions'. We have however, edited our LETR to include a reference to the BSCH guidelines on 'Investigation and management of acute transfusion reactions' and 'the administration of blood components'.

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BCSH Transfusion Task Force	Full	14	12	Suggest that restrictive transfusion threshold is inappropriate in all patients with known coronary disease whether acute or otherwise	Thank you for your comment, however, we did not identify any data to support this and have discussed this in the section linking evidence to recommendations.
BCSH Transfusion Task Force	Full	14	19	Suggest that restrictive transfusion threshold is inappropriate in all patients with known coronary disease whether acute or otherwise	Thank you for your comment, however, we did not identify any data to support this.
BCSH Transfusion Task Force	Full	14	34	Maximum of 100 as long as there is no platelet dysfunction or anti-platelet treatment	Thank you for your comment. The 'other considerations' section of this LETR makes it clear that platelet dysfunction, if present, should be taken into account.
BCSH Transfusion Task Force	Full	15	22	Don't think the risk of central venous cannulation is the same as bone marrow aspirate – while both have low risk of bleeding don't think I'd be comfortable putting in a central venous catheter if platelet count less than 30 – if error happens getting platelets in a timely manner may be difficult – no problems on the other hand with doing a BM	Thank you for your comment. No relevant evidence was identified but it was a consensus opinion of the GDG to make this recommendation. Obtaining platelets in a timely manner is a logistic issue for the hospital and the blood supplier and is beyond the scope of this guideline.
BCSH Transfusion Task Force	Full	16	42	Not sure that would use "implications" when explaining to a patient that if they've been transfused they can no longer be a blood donor – they need to do what is best for themselves first of all so would reword that sentence or use a different example of transfusion implications – same comment applies to pg 13 line 15	Thank you for your comment. We have edited this bullet to read: '…that they are no longer eligible to donate blood'.
BCSH Transfusion Task Force	Full	20	13	Sentence repeats itself	Thank you for your comment, this has been edited.
BCSH Transfusion Task Force	Full	65	6	Recommendation 1 – doesn't consider those patients who refuse a transfusion, or patients with complex alloimmunisation	Thank you for your comment. The recommendation for EPO has now been reworded and a statement that EPO may be considered in patients who refuse blood transfusions and when appropriate blood type

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					is not available because of the patient's red cell antibodies, has now been included in the recommendation. Please also see the other considerations section in the 'Linking evidence to recommendations' table.
BCSH Transfusion Task Force	Full	47	13	Limited to surgical patients – what about medical patients?	Thank you for your comment. We have not included any investigations and treatment of anaemia in medical patients as they are outside the scope of the guideline.
BCSH Transfusion Task Force	Full	68	1	Recommendation 3 – Consider IV iron – if 'consider' is defined as 'other options may be similarly cost effective' if oral iron is not tolerated, what other options are there? – ? should be changed to 'offer' 'Where the interval to surgery is considered short' could be changed to 'where the interval between detection of anaemia and surgery is predicted to be too short for oral iron'	Thank you for your comment. We feel that the wording accurately reflects the strength of the evidence. 'Consider' in the context of NICE recommendations indicates that the GDG could not make a strong recommendation based on the evidence because the balance between benefits and harms was less definitive. The only alternative to using IV iron in this subgroup is to do nothing, and this may be preferable in some situations (for example some subgroups of patients are contraindicated). We agree the wording could be improved to ' and the interval between the diagnosis of anaemia and surgery is predicted to be too short for oral iron to be effective'.
BCSH Transfusion Task Force		123		Monitoring for acute reactions – this section adds nothing at all to what is already known, recommended and practiced	Thank you for participating in the consultation process. The technical team found very little evidence for this area and the recommendations are a reflection of the GDG's consensus on the topic.
BCSH Transfusion Task Force		142	general	Think electronic decision support has great potential and agree that more research is needed. Research should include how this would be	Thank you for your comment. We agree that this is an important area for research however the trial we would propose initially would focus on clinical and

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				implemented, how would the algorithms used be arrived at, how would possible conflicts with clinical judgement be handled, and what would be the legal status of overriding an 'electronic' decision – could affect cost effectiveness if leading to litigation.	cost effectiveness including outcomes of inappropriate transfusion, rates of transfusion, mortality and transfusion errors as a priority. The GDG felt that decision support is meant to be a guide, and not intended to override the individual judgement of clinicians.
BCSH Transfusion Task Force		142		'other considerations' missing reference – should be 8.5.1	Thank you for your comment, this has been edited.
BCSH Transfusion Task Force	Full	192		Scale of 1-7 seems incorrect as 5 and 7 are the same	Thank you for your comment, we have amended the guideline, scale 7 has been edited.
BCSH Transfusion Task Force	Full	205		Was there any evidence for the recommendation that there is no need to increase the threshold for prophylactic platelet transfusion in haematology patients with fever/antibiotics	Thank you for your comment. No evidence was found to routinely raise the threshold for patients with fever. It was the consensus of the GDG not to raise the threshold for prophylactic platelet transfusions. This has been noted in the 'other considerations' section of the 'Linking evidence to recommendations' table.
BCSH Transfusion Task Force	Full	206		The use of >50 platelet count for neuroaxial block is not according to current guidelines?	Thank you for your comment. The recommendation is in line with the Obstetric Anaesthetists' Association guidelines (2013) and emphasises that patients need to be individually assessed if there are additional factors likely to increase the risk of bleeding.
BCSH Transfusion Task Force	Full	207	26	See Comment 10 above re prophylactic platelets pre central venous cannulation	Thank you for your comment.
BCSH Transfusion Task Force	Full	223		Tables (e.g. 113) need headers on each page rather than assuming we will all remember what the columns are. Overall the review showed, as already published, that there is insufficient evidence upon which to base recommendations. There is far too much reliance on the opinions of the GDG.	Thank you for your comment. We have acknowledged there was very little evidence in this area. Also, the table headers are now repeated on each page

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BCSH Transfusion Task Force	Full	237		The paragraph on page 237 …that FFP should be considered for situations where a patient has clinically significant bleeding and abnormal coagulation test results… should be in BOLD. The following paragraph is disappointing as much FFP is transfused to neonates without good evidence. The 2nd sentence in the paragraph (para starting 'There was no specific evidence available for the use of FFP in the paediatric population') is very difficult to follow and needs rewording. I do not agree that the same standards should apply as to adults when considering neonates since the National Comparative Audit of FFP use showed that many hospitals did not have normal ranges for infants, and are therefore very likely to be transfusing FFP to infants on the basis of using wrong normal ranges and misunderstanding the meaning of results	Thank you for your comment. We have reworded the section slightly to make it clearer. Neonates were not included in the scope of the guideline. We have added a research recommendation on doses of FFP.
BCSH Transfusion Task Force	Full	238		The recommendation was based on the indirect evidence and consensus opinion of the GDG members'. So this is a very weak recommendation and surely better not to make a recommendation at all rather than put into print something for which there is really inadequate evidence. A different group of experts might come to a different conclusion.	Thank you for our comment. The GDG felt it was reasonable to make a recommendation, in spite of the lack of evidence, on the basis of their knowledge and experience. They noted that not making a recommendation here would leave a gap and in this case, expert guidance was better than none at all. We acknowledge that a different expert group may arrive at a different conclusion, however, the GDG were confident that this recommendation reflected best practice.
BCSH Transfusion Task Force	Full	239	32	Same comment as above, relying on 'knowledge and experience of the GDG' and 'abnormal coagulation tests' not defined…none of this helps	Thank you for your comment. The GDG felt it was reasonable to make a recommendation for both adults and children, in spite of the lack of evidence,

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				the clinician decide. Same worry about extending this to children who have a different haemostatic system with a different setting. It is simply not appropriate to extend a non-evidence based recommendation such as this to a different population.	on the basis of their knowledge and experience. They noted that not making a recommendation here would leave a gap and in this case, expert guidance was better than none at all. They have however, also opted to include a research recommendation on this topic. Additionally, the GDG has emphasised in the introduction of the guideline, the difficulty faced when extrapolating evidence from adults to small children. Please note that infants and neonates are not included in the guideline.
BCSH Transfusion Task Force	Full	247		FFP transfusion doses – again the evidence is weak and recommendations are based on GDG, page 247, it is naïve to state that 'a dose of at least 15ml/kg' would 'increase the likelihood of providing a sufficient quantity of coagulation factors to reduce bleeding'. This is absolutely not true, for example, in reversal of deficiency of factors II, IV, IX and X related to vitamin K antagonists.	Thank you for your comments. The recommendation on dose has been removed and replaced with a research recommendation.
BCSH Transfusion Task Force	Full	250-265		Cryoprecipitate section. Essentially no evidence for the questions asked. Recommendations based on GDG's knowledge and experience. The recommendations look sensible and in line with current practice.	Thank you for participating in the consultation process, we appreciate your feedback.
BCSH Transfusion Task Force	Full	292	28	This comments on donating own blood prior to surgery – whilst I appreciate that this is not a recommendation, and is a summary of another evidence paper, PAD is not a recommended procedure – could this inclusion cause confusion?	Thank you for your comment. The reference to donating blood before surgery is stating one of the findings in the literature review on this topic. Recommendations are highlighted and it is clear that this procedure is not being recommended.
BCSH Transfusion Task Force	Full	295	1	Recommendation 46 – need to add that they will no longer be able to donate blood	Thank you for your comment. We have amended the recommendation to include the following bullet point has been added: '…that explains that they are

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					no longer eligible to donate blood.'
BCSH Transfusion Task Force	Full	250-265		Cryoprecipitate section. Essentially no evidence for the questions asked. Recommendations based on GDG's knowledge and experience. The recommendations look sensible and in line with current practice.	Thank you for participating in the consultation process, we appreciate your feedback.
Department of Heath	General	General	General	Thank you for the opportunity to comment on the draft for the above clinical guideline. I wish to confirm that the Department of Health has no substantive comments to make, regarding this consultation	Thank you for participating in the consultation process.
Institute of Biomedical Science	General	General	General	Thank you for inviting the Institute of Biomedical Science (IBMS) to contribute to the consultation on the NICE Draft Guideline on Transfusion. The IBMS is the UK professional body for biomedical science. It represents approximately 20,000 members employed mainly in NHS laboratories, NHS Blood and Transplant, Public Health services, private laboratories, research, industry and higher education. In its capacity as a standard setting organisation, and also an HCPC approved education provider the Institute supports the recommendations in the Guideline from the perspective of the laboratory and biomedical science, however most relates to clinician judgement and is therefore not directly within our remit.	Thank you for your comment.
Intensive Care Society	Full	General	General	We were disappointed there was a specific section relating to transfusion practice in ICU specifically. We appreciate that the principles elsewhere in the document are transferable, but it would have been	Thank you for your comment. We were unable to go into the detail of having recommendations for specific units or settings, due to time and evidence constraints. However, the recommendations are

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				beneficial to have a separate ICU section as transfusion is such a common practice there.	applicable to ICU.
Intensive Care Society	Full	General	General	It would be very useful to have specific statements for patient groups where some clinicians hold the erroneous vie that aiming for a ridiculously high Hb value is clinically beneficial. Examples include patients with burns, cardiac surgery patients and vascular surgery patients. Even if the evidence is not substantial it would nevertheless be worthwhile to have some sort of a statement to stop these patients being over-transfused.	Thank you for your comment. We believe the recommendations on transfusion thresholds are very clear – recommending the use of restrictive transfusions as well as key exceptions.
Lancashire Teaching Hospitals NHS Foundation Trust (Rosemere Cancer Centre)	Short	General	General	Previously oncology patients were excluded from these guidelines as there is a lot of evidence out there to support a HB of 110+g/l for patients receiving curative radiotherapy in head and neck or cervical cancer. Also, patients receiving chemotherapy don't have any impact on QOL if HB increased from 70 to 90g. We are aware there is some guidance out there to support use of ESA's in the treatment of chemotherapy induced anaemia (although it is extremely slow to be implemented) but it would be good to have some mention of oncology patients being excluded from this guidance (as patients on dialysis etc are currently and used to be in the previous document)	Thank you for your comment. We agree this is an important clinical area. As this is a cross cutting guideline focussing on the general principles of transfusion and the appropriate use of blood, no specific clinical condition was excluded, including oncology patients. However the detailed management of specific clinical conditions was not considered for inclusion as they would be covered by other NICE guidance.
National Blood Authority Australia on behalf of the Patient Blood Management Steering	Short	4	General	Suggest include what guideline does not cover in short version – as per full Page 20 lines 2-13 or abbreviated version Page 23 lines 24-26	Thank you for your comment the introduction to the short version has been edited to explain what is NOT covered by the guideline.

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Committee					
National Blood Authority Australia on behalf of the Patient Blood Management Steering Committee	Short	General	General	Suggest including Algorithm from full document (page 19) in short version	Thank you for your comment. The algorithm has now been added to the short version of the guideline.
National Blood Authority Australia on behalf of the Patient Blood Management Steering Committee	Short	General	General	Suggest including a section on "Implementation of the guidelines" – could include links to other useful resources	Thank you for your comment, this information is highlighted on the NICE website for the information of users.
National Blood Authority Australia on behalf of the Patient Blood Management Steering Committee	Short	General	General	Suggest including section 3.3.3 from full document (page 23-24) i.e. Relationship to other NICE guidelines	Thank you for your comment, this information is highlighted on the NICE website for the information of users.
National Blood Authority Australia on behalf of the Patient Blood Management Steering	Short	6	11	Suggest including term "alternatives" ie. …about the risks, benefits and alternatives for the interventions…	Thank you for your comment, this is standard text for all NICE guidelines.

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Committee					
National Blood Authority Australia on behalf of the Patient Blood Management Steering Committee	Short	8	General	Suggest provide a statement that the priorities must be suggested in the context of the full list of recommendations – this is particularly important for 1.2.2	Thank you for your comment. There is an explanation for how the key priorities for implementation are chosen in the NICE guidelines manual. The GDG selected them from the full list of recommendations, prioritising them on the basis of those that would have the greatest impact on practice in the NHS.
National Blood Authority Australia on behalf of the Patient Blood Management Steering Committee	Short	8 13	6-7 7-8	1. Suggest including people with iron deficiency without anaemia and those at risk of developing iron deficiency anaemia. eg. have suboptimal iron stores in whom substantial blood loss is anticipated – these should be treated with preoperative iron therapy. The literature review conducted for the Australian Patient Blood Management Guidelines: Module 2 Perioperative (http://www.blood.gov.au/pbm-module-2) has the following recommendations and practice points: Recommendation: In surgical patients with, or at risk of, iron-deficiency anaemia, preoperative oral iron therapy is recommended (Grade B). Practice point: Surgical patients with suboptimal iron stores (as defined by a ferritin level <100 µg/L) in whom substantial blood loss (blood loss of a volume great enough to induce anaemia that would require therapy) is anticipated, should be treated with preoperative iron therapy. http://www.blood.gov.au/pubs/pbm/module2/3-clinical-guidance/3.4.2-effect-of-erythropoiesis-stimulating-agents.html	1. Thank you for your comment. The identification of patients with iron deficiency without anaemia is beyond the scope of this guideline. 2. Thank you for your comment. The majority of the studies included in the evidence review included patients treated with both pre-operative and post-operative iron and so these were not evaluated separately. The GDG discussed the available evidence and agreed that for all patients with pre-operative iron deficiency anaemia, treatment with oral iron should continue after surgery as this is likely to be effective. 3. Thank you for your comment, we agree and have included this point in the 'Linking evidence to recommendations' table for this section of the guideline.

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				2. Suggest clarification of use of oral iron after surgery - the literature review conducted for the Australian Patient Blood Management Guidelines: Module 2 Perioperative found that" The effect of postoperative oral iron was investigated in patients found to be anaemic postcardiac98–100 and noncardiac surgery.101,102 The effect on haemoglobin concentration was minimal. This finding is not unexpected, because the acute inflammatory response after surgery is associated with reduced iron absorption. This resulted in the following recommendation: In patients with postoperative anaemia, early iron therapy is not clinically effective; its routine use in this setting is not recommended (Grade B). http://www.blood.gov.au/pubs/pbm/module2/3-clinical-guidance/3.4.1-effect-of-iron-therapy.html 3. Whilst "diagnosis of anaemia" was out of scope of the guideline, suggestion should be given to a statement about the importance of early identification, assessment and management of anaemia and iron deficiency. (There are a number of recommendations and practice points from above reference).	
National Blood Authority Australia on behalf of the Patient Blood Management	Short	8 14	16-19 11-13	This recommendation may be taken out of context if not aligned directly with recommendations 1.2.1 and 1.2.3. Suggest clarification or linkage.	Thank you for your comment. The key priorities for implementation do need to be read in conjunction with the full list of recommendations.

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Steering Committee					
National Blood Authority Australia on behalf of the Patient Blood Management Steering Committee	Short	9	3-10	Suggest rephrase and/or link to 1.3.7 and 1.3.8 to clarify. Eg. Offer prophylactic platelet transfusion to patients with a platelet count below 10x109 per litre who are not bleeding or having invasive procedures or surgery. This does not apply to patients who have: • chronic bone marrow failure • autoimmune thrombocytopenia • heparin-induced thrombocytopenia • thrombotic thrombocytopenic purpura (1.3.7); and patients having: • procedures with a low risk of bleeding, such as adults having central venous cannulation or any patients having bone marrow aspiration and trephine biopsy (1.3.8)	Thank you for your comment. The GDG considered patients undergoing invasive procedures and surgery separately from patients not having such procedures and think that the clarity of the recommendations is clearer as two rather than one.
National Blood Authority Australia on behalf of the Patient Blood Management Steering Committee	Short	10 19	2 23	Suggest adding "and the likelihood of the risks occurring"	Thank you for your comment. We think it is understood that an explanation of the risks and benefits of transfusion would include details on the 'likelihood' of those risks and benefits.
National Blood Authority Australia on behalf of the Patient Blood Management Steering Committee	Short	14	17-19	Suggest adding "not due to a reversible cause"	Thank you for your comment. The recommendation states that this is for patients with chronic anaemia who require regular transfusions and therefore requires no additional explanation.

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National Blood Authority Australia on behalf of the Patient Blood Management Steering Committee	Short	14	27	Suggest clarifying line 27 in line with single unit guideline to…and give a further unit, followed by reassessment if needed.	Thank you for your comment. We believe the current wording is clear.
National Blood Authority Australia on behalf of the Patient Blood Management Steering Committee	Short	17	1.5	Suggest reference to use of fibrinogen concentrate	Thank you for your comment. Fibrinogen concentrate is outside the scope of the guideline.
National Blood Authority Australia on behalf of the Patient Blood Management Steering Committee	Short	19	7	Suggest including in "Patient Safety" Monitoring for delayed transfusion reactions.	Thank you for your comment. The scope covered monitoring of signs and symptoms of acute transfusion reactions only.
National Blood Authority Australia on behalf of the Patient Blood Management Steering Committee	Full	General	General	Thanks for the opportunity It looks comprehensive and sensible. I was unable to find anything about how the guideline would be implemented, how practitioners will be notified about the guideline and what the processes are for updating clinical and governance knowledge for those responsible for treating patients who may need blood products.	Thank you for your comment. Implementation issues, including notification of practitioners about the guideline and updating clinical and governance knowledge are not covered in detail in this guideline. The NICE implementation team will look at this, once the guideline is finalised and will produce some useful tools and guidance.
National Blood Authority Australia	Full	General	General	From an Australian perspective it was disappointing that although Patient centred care is highlighted the	Thank you for your comment. It is possible to structure a transfusion guideline in many different

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on behalf of the Patient Blood Management Steering Committee				guidelines are still product focussed transfusion guidelines and not patient focussed Patient Blood Management Guidelines	ways, this guideline was largely structured around the use of different blood components. However, we believe that the guideline focuses on patient outcomes as much as the evidence allows.
National Blood Transfusion Committee	Short	General	General	[redacted] The scope of the document needs clearly announcing in the short form to avoid misunderstanding about the lack of recommendations for patients with massive haemorrhage. The confusion party arises from the definition of massive haemorrhage on page 11 which a reader might suppose to indicate that this was central to the guideline. Patients with bone marrow failure are mentioned in various sections but receive short shrift. 1.2.1 and 1.2.2 do not exclude these patients but the guidance is clearly inappropriate for transfusion dependant patients as recognised in 1.2.4. Treatment of patients with inherited anaemia may be dealt with in other guidance but should either be included or specifically excluded. At the moment neither is clear from the short document. [redacted]	Thank you for your comment. The introduction on both versions of the guideline have been edited to include a description of what is included and what is excluded from the scope of the guideline. In addition, further detail on particular groups of patients who require special consideration are discussed in the relevant 'Linking evidence to recommendations' tables.
National Blood Transfusion Committee	Short	General	General	The risks of blood transfusion are divisible into those directly due to faults in the component e.g. infected units, and those due to misuse of the component, e.g. TACO or ABO incompatibility. When quoting mortality and morbidity rates in the	Thank you for your comment. We have taken the data on 'risk of major morbidity and mortality' directly from the 2014 SHOT report and attributed it clearly to the report in the full version of the guideline only, as future edits will see references removed from the

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				introduction this is not made clear, and the figures taken from the SHOT report 2013 appear to include all deaths and major morbidity even if the event was only 'possibly' attributed to transfusion. The figure includes deaths (n=5) due to delayed or under-transfusion. It is arguable whether the failure to use a treatment modality should be counted against that modality and used as an argument for not using it. The figures vary over the years and I would suggest using a cumulative risk over 5 years rather than a single year figure, excluding deaths due to failure to transfuse and giving a range based on all possible, probable and definite deaths, up to only the definitely related deaths. The present risk statements therefore overestimate the risk and do not allow for improvements due to better management of the transfusion process. This distinction is important when considering the risks of transfusion against the risks of not transfusing. [redacted]	short version of the guideline. However, we take your point and will amend the sentence. We have also added a sentence to address your point about removing the deaths and major morbidity due to delayed transfusion (there were no deaths or major morbidity reported for under transfusion). The section now reads: 'The Serious Hazards of Transfusion (SHOT) scheme estimated that in 2014 the risk of transfusion-related death was 5.6 per million blood components issued, and the risk of transfusion-related major morbidity was 63.5 per million blood components issued,2 although the attribution of transfusion as the direct cause of death or major morbidity was not always certain. Removing cases where patient harm was caused by delayed transfusion rather than transfusion itself reduces the risk of transfusion-related death to 4.5 per million blood components issued, and the risk of transfusion-related major morbidity was 61.9 per million blood components issued.'
National Blood Transfusion Committee	Short	13	7	1.2.2 does not appear to take account of the recently published TITRE2 trial. The excess mortality seen in the restrictive arm of this trial in cardiac surgery far outweighs the very modest longer term risk for transfusion. It should also be noted that the best evidence other trials showed equivalence for restrictive and liberal transfusion arms and that in the best post operative trial in patients with prior cardiac risk, but not acute coronary syndrome (FOCUS Trial), the restrictive	Thank you for your comment. We have now included the TITRe2 trial in the RBC thresholds review in our guideline. We have added this to the meta-analysis of all the studies included in the RBC thresholds review. The evidence showed that there was clinically important benefit with restrictive strategies with respect to the number of patients transfused and number of units transfused. The evidence suggested that there was no difference between the groups with respect to mortality, adverse events,

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				threshold for transfusion was 80g/L. The TRICC trial is no longer suitable evidence as the red cell component quality has improved considerably since 1996-9. Therefore this recommendation should be more specific and note that a transfusion trigger of 80g/L is as safe as 100g/L in patients having non-cardiac operations and with a history or high risk of cardiovascular co-morbidity. For patients undergoing cardiac surgery a post-operative threshold of 90g/l should be considered. To recommend a flat threshold of 70g/L does not take account of the best evidence available. [redacted]	new cardiac events, length of hospital stay, quality of life and infection, but there was some uncertainty. The GDG discussed the applicability of the transfusion threshold recommendations for those patients with and those without cardio-vascular morbidity; and we have now expanded the 'Linking evidence to recommendations' section to reflect this.
National Blood Transfusion Committee	Short	14	21	1.2.5 and 1.2.6 are suitable for a minority of patients, those receiving top up transfusions after a bleed or surgery. However a more useful approach would be to advise careful dosing based on estimated blood volume and target Hb with risk assessment for volume induced heart failure (TACO). I am not aware of any evidence for a single unit policy, and none is given in the full document. It is unusual to make a strong recommendation without evidence, but we are aware of increasing risks of TACO associated with red cell transfusion. Prevention requires a risk adapted policy rather than a blanket policy. [redacted]	Thank you for your comment. The GDG discussed your concerns and considered these recommendations applicable to most patients needing transfusions, not just in the surgical/perioperative or post-bleed settings. As suggested in your comment, it is important to customise transfusions for individual patients and to minimise the risk of TACO, and a single unit policy with assessment of the patient after each unit addresses these issues.
National Blood Transfusion Committee	Short	13	4	1.1.1 This recommendation should allow use in those with religious objection to transfusion. It is an odd contradiction that a recent NICE guideline on erythropoietin suggests use in cancer patients having chemotherapy in order to avoid transfusion. In this group there is strong evidence of serious	Thank you for your comment. The recommendation for EPO has now been reworded and a statement has now been included in the recommendation that EPO may be considered in patients who refuse blood transfusions and when appropriate blood type is not available because of the patient's red cell

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				harm from epo which in the NICE assessment is lost because the evidence is taken from a meta-analysis including poor trials, whereas here the argument is largely economic and ignores those for whom transfusion is not possible due to religious beliefs. [redacted]	antibodies. Please also see the other considerations section in the 'Linking evidence to recommendations' table.
National Blood Transfusion Committee	Short	16	23	1.3.10 Platelet dose. Larger platelet doses given to patients having chemotherapy for haematological disease have been shown to give a longer interval between transfusion but not to reduce bleeding. Where a patient is at home it may be entirely appropriate to give a larger dose of platelets to avoid the need for an early return to hospital. This may well be justified on economic grounds if the cost of patient transport/ day patient care much outweighs the cost of an extra unit of platelets, on quality of life grounds, and on medical grounds where a visit to hospital may have other risks such as during a viral outbreak. This recommendation should be adjusted to account for these circumstances. [redacted]	Thank you for your comment. We have added the following text to the 'other considerations' section of the LETR for recommendation 27: Haematology departments could consider giving larger doses of platelets to outpatients with chronic thrombocytopenia to extend the interval between transfusions and minimise the number of attendances for platelet transfusions. The recommendation states 'do not routinely' give more than a single dose, which should be standard best clinical practice, however in exceptional circumstances, for example such as those stated above, different doses could be considered.
National Blood Transfusion Committee	Full	General	General	Myself and my colleagues in vascular surgery have concerns about the use of tranexamic acid in conjunction with cell salvage for vascular patients. Unfortunately I have not been able to see the evidence for this as the website for the NICE guidance keeps locking me out but instinctively the use of tranexamic acid for patients whose major complications following major surgery are thrombotic events, and where blood loss of 500-1000ml is usually controlled, seems	Thank you for your comment. The review evaluated the literature relating to the risk of thrombotic complications with the use of tranexamic acid following major surgery , including vascular surgery, and the evidence, although non-significant, suggested that there were fewer complications with the use of tranexamic acid (RR 0.48 [0.18, 1.23] in the high risk group and RR 0.69 [0.44, 1.07] in the moderate risk group). We apologise that you were unable to see the evidence due to web issues.

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				counterintuitive. Contact [redacted]	Please refer tables 35 and 42 in the full guideline for details.
National Blood Transfusion Committee	Short	13	4/5	Do not offer erythropoietin to reduce the need for blood transfusion in patients having surgery. Suggestion – add the word 'routinely' (or specify may be appropriate for those with religious objections to transfusion). Contact East of England Regional Transfusion Committee	Thank you for your comment. We agree. The recommendation for EPO has now been reworded and a statement that EPO may be considered in patients who refuse blood transfusions and when appropriate blood type is not available because of the patient's red cell antibodies, has now been included in the recommendation. Please also see the other considerations section in the 'Linking evidence to recommendations' table.
National Blood Transfusion Committee	Full	General	General	In the economic evaluation of EPO were costs used those at time of publications or present costs which are relatively cheaper	Thank you for your comment. The economic evaluations included in the erythropoietin review use costs at the time of their publication. We have however accounted for this by presenting the current publically and nationally available costs (sourced from British National Formulary) and discussing these costs alongside the published evidence in the Linking Evidence to Recommendations 'Economic evidence section' (section 5.5 full guideline).
National Blood Transfusion Committee	Short	13	9/10	Consider IV iron before and after surgery for patients with iron-deficiency anaemia. Suggestion – should be a link about assessment of functional iron deficiency. Contact East of England Regional Transfusion Committee	Thank you for your comment. We acknowledge that this is an important point but diagnosis of anaemia is out of the scope of this guidance.
National Blood Transfusion Committee	Full	General	General	1.1.3 functional iron defy should not be lumped in with absolute iron deficiency	Thank you for your comment. We agree and this recommendation has now been reworded.
National Blood	Short	13	23-25	Offer tranexamic acid to adults undergoing surgery	Thank you for your comment. The review did not

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Transfusion Committee				who are expected to have a least moderate blood loss. Suggestion – This needs further clarification as to • Timings (e.g. intra or post op) • Exclusions & contradictions Contact East of England Regional Transfusion Committee	evaluate the timings of administration of tranexamic acid and therefore we are unable to comment on these issues. The GDG did not note any specific exclusions or contraindications to the use of tranexamic acid other than that described in the summary of product characteristics which every clinician is expected to follow.
National Blood Transfusion Committee	Short	13	26-28	Consider tranexamic acid for children undergoing surgery who are expected to have at least moderate blood loss. Suggestion – Also children with ITP Contact East of England Regional Transfusion Committee	Thank you for your comment. The recommendation does include children with ITP.
National Blood Transfusion Committee	Short	14	11-16	Use of restrictive RBC transfusion thresholds. Suggestion – Add 'in optimal circumstances' and 'consider patient's symptoms' Contact East of England Regional Transfusion Committee	Thank you for your comment. WE have now added details regarding the signs and symptoms to be assessed to the LETR.
National Blood Transfusion Committee	Short	14	24-27	After each single unit RBC transfusion, clinically re-assess and check Hb levels. Suggestion – add 'where practical' Contact East of England Regional Transfusion Committee	Thank you for your comment. We believe the current wording is clear.
National Blood Transfusion Committee	Short	15	14-16 (1.3)	Offer prophylactic platelet transfusion to patients with platelets <10 x 109 /L who are not bleeding or having evasive procedures. Suggestions - Add "or to haematology patients with sepsis and a platelet count of <20 x 10 9/L" Contact East of England Regional Transfusion	Thank you for your comment. No evidence was found to routinely raise the threshold for fever or sepsis. As noted in the LETR the GDG discussed this and agreed that the threshold for prophylactic platelet transfusions should not be routinely increased in haematology patients with fever or

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				Committee	haematology patients who have been administered antibiotics.
National Blood Transfusion Committee	Short	15	1-16	Situation with Sepsis needs clarification Contact East of England Regional Transfusion Committee	Thank you for your comment. No evidence was found to routinely raise the threshold for sepsis. As noted in the LETR the GDG discussed this and agreed that the threshold for prophylactic platelet transfusions should not be increased in haematology patients with fever or haematology patients who have been administered antibiotics. However, the GDG recommended that a higher threshold should be considered for patients thought to be at high risk of bleeding because of the presence of specific combinations of clinical and laboratory factors such as sepsis, haemostatic abnormalities, and/or the administration of therapeutic doses of anticoagulants or anti-platelet drugs.
National Blood Transfusion Committee	Short	16	10-15	Do not routinely offer platelet* transfusions with chronic bone marrow failure. Suggestion - Insert the word "stable" before chronic Contact East of England Regional Transfusion Committee *NB the statement is about prophylaxis	Thank you for your comment. We do not agree. The addition of the word 'stable' does not provide any added value to this recommendation and could potentially be confusing because it may imply that patients with unstable chronic bone marrow failure should routinely receive platelet transfusion.
National Blood Transfusion Committee	Full	General	General	It would be good to have a recommendation on a 'cut off' Haemoglobin prior to surgery. Contact – South West Regional Transfusion Committee	Thank you for your comment. The focus of the recommendations are on the avoidance of transfusion before surgery, using measures to identify the cause of the anaemia and treating the cause accordingly.
National Blood Transfusion Committee	Full	General	General	Where expert opinion is provided we suggest that this is corroborated more widely. For example we disagree that it is a majority patient preference to	Thank you for your comment. The GDG discussed this and agreed that it was likely to be patients' preference to receive oral iron rather than IV iron.

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				receive oral rather than IV iron. Personal comment from South West Contact – South West Regional Transfusion Committee	
National Blood Transfusion Committee	Full	General	General	We accept the relatively good evidence for the use of tranexamic acid (TXA) when ≥ 500ml blood loss is anticipated. This remains one of the outcome measures in an incomplete national obstetrics trial (WOMAN trial due to report 2016/17) and ask whether its use in obstetrics should be restricted until this additional data becomes available. Contact – South West Regional Transfusion Committee	Thank you for your comment. The recommendation is based on current evidence and the expert opinion of GDG members. Future updates of the guideline will assess any new relevant evidence for inclusion.
National Blood Transfusion Committee	Full	General	General	We disagree with the recommendation that Intra-operative Cell Salvage (IOCS) in combination with TXA should not be offered routinely for any other than high risk surgery. The trial and economic data for IOCS + TXA in moderate risk surgery appears to support its use and the criteria for its rejection appears to be that TXA alone has a greater incremental advantage. This should not exclude the use of IOCS in moderate risk surgery provided it confers an additional advantage. Contact – South West Regional Transfusion Committee	Thank you for your comment. There was insufficient evidence to justify recommending the use of IOCS+TXA in the moderate risk group. Data was only available for one outcome (number of patients transfused) and as a result, both interventions (IOCS+TXA and ICS alone) were not included in the network meta-analysis and economic model.
National Blood Transfusion Committee	Full	General	General	There is no distinction in the economic case between blood collection and combined collection and processing IOCS – the full cost is only incurred when there is sufficient blood collected to justify its re-infusion. Likewise the effect of experience and the resulting clinical discretion on both quality and	Thank you for your comment. In appendix M of the guideline (section M.2.3.7.2), we discuss the distinction between collection and combined collection and processing in the costing of intraoperative cell salvage: "The consumable for ICS is a kit that is made up of two parts. The first part of

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				economic outcomes cannot be assessed by available data. Contact – South West Regional Transfusion Committee	the kit which allows for the collection of blood is required for all patients. If sufficient blood is collected (approximately one unit of blood) then a second part of the kit is used which allows for the washing and re-infusion of the salvaged blood. In the high risk of bleeding subgroup, it was assumed that all patients would require both parts of the kit (collection and re-infusion)." Please note we did not include intraoperative cell salvage in the moderate risk group analysis (due to insufficient clinical effectiveness data). Had we included it, then we would have considered the possibility that not all patients would be re-infused and explored the costs accordingly.
National Blood Transfusion Committee	Full	General	General	In practice there must be sufficient trained and experienced staff to perform IOCS and if moderate risk surgery is excluded this would effectively terminate IOCS in all but specialist centres which perform frequent high risk procedures. On our site we have excellent training and governance in IOCS but this could not be sustained for an occasional high risk bleed. Contact – South West Regional Transfusion Committee	Thank you for your comment. There was insufficient clinical and cost-effectiveness evidence for the use of IOCS alone or in combination with TXA to recommend its use in moderate risk surgery.
National Blood Transfusion Committee	Full	General	General	I have one comment to make re: warfarin reversal. Given that the BCSH guidelines* are quite strongly recommending that FFP is not used for warfarin reversal (because alternatives for each possible situation are better / less risky) I expected to see a similar statement to this effect in the NICE guideline.	Thank you for your comment. We have amended the recommendations in the FFP section (1.4.2) to include a statement that FFP should not be used in patients requiring reversal of anticoagulation.

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				The practice of using FFP to reverse warfarin in patients who are not bleeding prior to an invasive procedure, for example is still prevalent and the draft NICE guideline does not appear to specifically rule it out. *From the 2004 BCSH guideline for the use of fresh frozen plasma, cryoprecipitate and cryosupernatant "FFP has only a partial effect, is not the optimal treatment, and should never be used for the reversal of warfarin anticoagulation in the absence of severe bleeding" Contact – South Central Regional Transfusion Committee	
National Blood Transfusion Committee	Full	General	General	There are alternative strategies for dissemination other than electronic data, eg The AFFINITIE programme of audit and feedback and the NIHR Programme Grants for Applied Research (PgfRA), which might be cost effective. Should this be acknowledged? Contact – South Central Regional Transfusion Committee	Thank you for your comment. We have not looked at strategies for implementing good transfusion practice apart from electronic decision support as these were outside the scope of the guideline. These issues were not prioritised at the scoping stage.
National Blood Transfusion Committee	Short	General	General	The guideline overall is not specific enough and therefore looks like a wasted opportunity. I would say that it would not help Trust's get the message out about transfusions, as it lacks specifics. Where would it fit? The PBM document and the BCSH guidelines are much more beneficial than this document. Contact – South Central Regional Transfusion Committee	Thank you for your participation in the consultation process. Unlike many other guidelines we have conducted systematic reviews of the clinical and economic evidence in every area covered by the guideline and have produced a novel economic model on alternatives to transfusion for surgical patients. NICE produces rigorous, independent and objective evidence based guidelines and also produces quality standards based on recommendations which are designed to drive and

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					measure priority quality improvements.
National Blood Transfusion Committee	Short	General	General	e.g Patient safety on page 19 section 1.7.1. It needs more details - what vital signs? Emphasis on the 15 minutes after the start of a unit. Contact – South Central Regional Transfusion Committee	Thank you for your comment, we have added the following statement to the 'Linking evidence to recommendations' table in the 'other considerations' section: 'frequency of monitoring would depend on the type of patient receiving a transfusion, for example, children and unconscious patients may require more frequent monitoring during blood transfusions'. We have also, edited our 'Linking evidence to recommendations' table to include a reference to the BSCH guidelines on 'Investigation and management of acute transfusion reactions' and 'the administration of blood components' events'.
National Blood Transfusion Committee	Short	General	General	There is no definition for acute coronary syndrome - this is a term referred to on several occasions throughout. Contact – South Central Regional Transfusion Committee	Thank you for your comment. We agree and a definition of acute coronary syndrome has now been added to the LETR and to the glossary.
National Blood Transfusion Committee	Full	General	General	Wealth of information and evidence but there are other areas of transfusion which aren't discussed, nor feature in research recommendations eg no mention of the need for research in the areas of PCC, FFP, Cryoprecipitate, Fibrinogen and PCC. Electronic Decision Support is one way of addressing practice, but many other options for change exist, which may be cost efficient. Contact – South Central Regional Transfusion Committee	Thank you for your comment. We are unable to cover everything in the guideline in the time we have so we worked with stakeholders during scoping to prioritise the areas we should cover. In areas where there was no evidence the GDG chose whether to make a recommendation for practice or for research. In some cases the GDG felt it was possible and beneficial to make a consensus based practice recommendation rather than wait for future research.
National Blood	Short	General	General	I am pleased to note we don't have to make any	Thank you for your comment. This information is

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Transfusion Committee				real changes! 2. As very few people will read the full document I feel the short version does not contain enough detail 3. What about major haemorrhages? If we applied some of the calculations mentioned a patient could bleed out before being recognised as having a MH 4. It's a shame reversal of NOACs weren't included as staff are going to use this as part of a one stop shop but I guess that's not within the remit. South Central Regional Transfusion Committee	highlighted on the NICE website for easier access for users. The full guideline is also available on the website when readers need more detail. Major haemorrhage and reversal of NOACs were outside of the scope of the guideline.
National Blood Transfusion Committee	Full	General	General	Lots of information and evidence but there are other areas of transfusion which aren't discussed. Other thoughts about NICE guidance which I can't see. -It would be useful for NICE to give some practical guidance/targets on structure of transfusion in terms of governance within hospital, -guidance on HTC powers within the trust or what powers they should have, -What type of invention trust should employ for department breaking/not following transfusion regulations (sanctions), -Activation of major haemorrhage a national approach to activation with common number to use e.g. 2222 -The transfusion support that each trust should have per 100 000 population (in terms of TP and haematology input)	Thank you for your comment. We are unable to cover everything in the guideline in the time we have, so we worked with stakeholders during scoping to prioritise the areas we should cover.

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				-Introduction of electronic tracking in hospitals with high/medium blood use for safety of patients South Central Regional Transfusion Committee	
National Blood Transfusion Committee	Short	13		I'm concerned with the advice given on page 13 regarding IV iron. There is no evidence yet (we are all involved in PREVENTT). I have also highlighted this concern with [redacted] North West Regional Transfusion Committee	Thank you for your comment. The GDG has reviewed the existing evidence for IV iron and has made recommendations accordingly. If further evidence is published this could be included in the next update to the guideline.
National Blood Transfusion Committee	Full	General	General	We discussed the NICE guidelines at transfusion committee. The main comment is that although we recognise that the guideline does not aim to cover all specialist indications, we were surprised that use of platelets in cardiac surgery was completely omitted, since this is the second largest use for platelet transfusion. Contact – [redacted]	Thank you for your comment. The additional issue of dysfunctional platelets (for example cardiac surgery) has been added to the 'trade-off between clinical benefits and harms' section of this recommendation.
National Blood Transfusion Committee	Short	General	General	I have read the short guideline. My only comment is that there is a lot of stuff about safeguarding children and patient centred care that is not really relevant to the guideline. I feel the section on 'Safeguarding Children' p4 is worthy but not of any use in a guideline that will be referred to by clinicians wanting advice on transfusion who are hardly likely to suddenly think 'Oh yes- this anaemia is being caused by neglect, I must initiate the safeguarding process!'. While i recognise the need for a section on Patient Centred Care really what this section is about is *Consent.* This section would be better laid out by explaining the obligation to make clinical decisions	Thank you for your comment. The text on safeguarding children has now been removed from our final version. With reference to patient centred care, this is standard text used across all NICE guidance and 'consent' was not included in the scope of this guideline.

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				in conjunction with the patient, to explain the risks and benefits to the patient and obtain consent for transfusion. Then the legal situation relating to children under the age of 16 and to adults lacking capacity could be explained. These are my personal thoughts, not that of the UHL transfusion committee Contact – [redacted] East Midland Regional Transfusion Committee	
National Blood Transfusion Committee	Full	General	General	The guideline states not to use prophylactic cryoprecipitate in patients with a low fibrinogen who are not bleeding but we would argue that this should be used in the case of newly diagnosed APL (acute promyelocytic leukaemia) patients with a low fibrinogen and low platelets who have DIC and are at a high risk of haemorrhagic complications	Thank you for your comment. The LETR has been amended to include the following statement under 'other considerations': An exception to this recommendation are patients with acute promyelocytic leukaemia, who have disseminated intravascular coagulation with a combination of low fibrinogen and severe thrombocytopenia and who are at high risk of haemorrhagic complications
National Blood Transfusion Committee	Short	General	General	My only comment is regarding patients with BM failure (disease related or chemo induced) which deserves a mention in addition to the group of patients with coronary syndromes, major haemorrhage in 1.2.1. Hb threshold of 70 and single unit top ups do not help symptoms and are inconvenient for pts with no erythropoetic activity. I suppose these patients may get covered by 1.2.4 'Consider setting individual thresholds and haemoglobin concentration targets for each patient who needs regular blood transfusions for chronic	Thank you for your comment. We agree and we have addressed the issue of haematology patients requiring regular blood transfusions for chronic anaemia in recommendation 1.2.4. We did not specifically consider the question of restrictive vs. liberal transfusion in patients with acute haematological disease. The guideline is cross cutting and is on the principles of transfusion. Clinicians will still need to use their judgements for individual circumstances.

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				anaemia' This was discussed at a recent NCRI AML WP mtg when Simon Stanworth approached the group to ask the 'restrictive vs liberal' transfusion question in AML trials. There was unanimous concern re the Hb 70 threshold for pts getting intensive chemo and not expected to recover counts for weeks and plan is to revisit it with higher threshold ? 80 Contact - [redacted]	
National Blood Transfusion Committee	Full	General	General	Just another small point from me. I may have missed something in the small print and I realise the guideline seems prioritised to surgery, hence the level of Hb being emphasised as the key to decision making. I try to teach the medical students in a tutorial that Hb level is one of many factors involved in the decision to transfuse (cause, acute or chronic, symptoms, bone marrow function also important etc) For example, I would suggest that patients who have a documented reversible cause for anaemia (e.g. B12 deficiency, folate deficiency, iron deficiency, autoimmune haemolysis) should have treatment of the underlying cause and avoid transfusion unless they have signficant cardio-respiratory symptoms regardless of the Hb (i.e. even if <70). These chronic anaemias are often well tolerated and patients can be relatively asymptomatic even at low Hbs. I would be	Thank you for your comment. The guideline only covers alternatives to transfusion specifically for patients having surgery and other groups are outside the scope. The recommendations on platelets, red blood cells, FFP, cryoprecipitate and PCC do apply to non-surgical patients. The introductions to both versions of the guideline have been edited to include a description of what is included and what is excluded from the scope of the guideline. In addition, further details on particular groups of patients who require special consideration are discussed in the relevant 'Linking evidence to recommendations' tables. We have addressed the possibility of unnecessary transfusions in patients with chronic anaemia by making a recommendation stating that individual thresholds and haemoglobin concentration targets should be considered.

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				concerned if this is not emphasised that unnecessary transfusions may occur in some of these patients. Contact [redacted]	
National Blood Transfusion Committee	Full	General	General	Summary of comments from the East Midlands as requested Don't like their recommendation against preop Epo—so much for our preop anaemia clinics! Surely there is a case in perhaps more selected patient besides the categories they mention—those with anaemia of inflammation who don't normalise their Hb to IV Fe, those with Hb <100, those for whom there is no time to optimise solely with Fe, those who can't have cell salvage, etc….really a whole host exceptions. But they've r/ved the cost analyses and I haven't, I guess. RBC transfusions—should they be given **preprocedure prophylactically**? I say not, but there is no mention of this VERY common practice (at least in NUH). Don't like their recommendations on platelet transfusions. **Rec 23 should apply to 22**.	Thank you for your comment. EPO The recommendation for EPO has now been reworded and a statement that EPO may be considered in patients who refuse blood transfusions and when appropriate blood type is not available because of the patient's red cell antibodies, has now been included in the recommendation. Please also see the other considerations section in the 'Linking evidence to recommendations' table. Pre-procedure transfusion. Thank you for your comment, this is now mentioned in the chapter introduction. The thrust of this section is on the management of anaemia without the need for transfusion before, during or after the procedure. Recommendations 22 and 23 Thank you for your comment. Both recommendations are 'consider' recommendation at the discretion of the clinician given the

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					circumstances of the patient. Recommendation 23 describes some specific criteria which clinicians should use to determine if the patient has a high risk of bleeding and in consequence a higher threshold for prophylactic platelet transfusions should be used.
				And what procedures are "**low risk of bleeding**"—I include ascitic drains, pleural taps, for instance. Central venous lines is an important mention—they need to include tunnelled lines (Hickman), which will be mentioned in the next plt transfusion guidelines.	Procedures for low risk of bleeding Thank you for your comment. An example of procedures for low risk of bleeding is provided in the 'Linking evidence to recommendations' statement for recommendations 22 and 23 as well as being provided in recommendation 26.
				Don't care for the woolly **FFP guidelines**—no mention as to cause of prolonged PT/PTT and the appropriateness of using FFP in an attempt (usually futile) to correct or the necessity to correct. They should also mention a maximum dose, as 15 ml/kg in an high body wt patients can cause fluid overload. The cryo bit is better. Don't like the PCC recommendations—but since these are guidelines rather than guidance, each Trust can adapt. Our ED isn't keen to give PCC to every person with a head injury ?bleed because 1.often there is no bleed 2.sometimes the bleed is very small and they don't always reverse, depending on the INR 3. This will mean a lot of patients with potentially unnecessarily reversed warfarin for whom reanticoagulation is a problem,	FFP Guidelines Thank you for your comment. We have now included text, reminding clinicians of the cause of prolonged PT/PTT. Cause of abnormal coagulation Thank you for your comment. We have now included a statement in the LETR that the cause of an abnormal coagulation screen should be investigated. FFP Dose We have removed the recommendation around dose and have included a research recommendation on this topic.

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				especially patients with metallic valves. The bit about transfusion reactions and consent is good and offers additional support for those of us who are pushing for proper informed consent. RBC triggers are acceptable After each unit in adults, not children, a repeat formal Hb is not always necessary. POC testing would suffice. **EPO** should not be didactaly withdrawn from the pre op settings, more defined usage would seem reasonable. Agree with TXA. Agree with 42. 46. I do not agree this needs to be on the GP discharge letter. it confers no benefiit. Also, crucialy, the use of ICE type investigation applications should be encouraged for blood group and prouct requests. This will reduce the frequency of rejected smaples by about 20% thoughout the UK. I am rolling this out accros my trust. We have a	EPO Thank you for your comment, the evidence indicated that the use of EPO is not clinically and cost effective and therefore has not been recommended. Some exceptions to this recommendation are discussed in the 'Linking evidence to recommendations' section. Patient information recommendation Thank you for your comment, the GDG felt that it was good practice to keep patients informed of their treatment. ICE investigations Thank you for your comment. Laboratory electronic systems were outside the scope of the guideline.

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				robust validated solution. I would hope to present this to the next NBTC for comment. Contact [redacted]	
National Blood Transfusion Committee		General	General	Dear colleagues We read with interest the excellent document by NICE on Transfusion that is currently out for opinion and would like to comment on the use of Iron therapy in the perioperative setting:- SUMMARY Two problems exist on the role of iron therapy to treat anaemia in the surgical setting. Firstly the ability to define iron deficiency in this setting, second the efficacy and effect of iron therapy to prevent transfusion. Both remain 'known unknowns' and currently it is not possible to offer recommendations on iron therapy practise for surgical patients in the NHS without waiting for specific research in this area, for fear of adverse events or patient harm. We would urge NICE to recommend that:- • In patients undergoing surgery, preoperative anaemia is screened and identified in a timely manner. • Anaemia is investigated and where appropriate elective surgery delayed pending investigations. • Oral Iron should be prescribed to those patients with iron deficiency and anaemia further, where possible, the elective	Thank you for your comment and suggestions. We acknowledge the importance of proper screening and diagnosis of anaemia as a prerequisite for surgery and we have now added a sentence to highlight this in the introduction to the guideline. However, the diagnosis and other aspects relating to delaying of surgery highlighted in your comment were not evaluated as part of this guideline as they are out of the scope of this guidance. The guideline only evaluated the effectiveness of iron therapy as an alternative to blood transfusion in surgical patients.

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				operation delayed until anaemia is corrected. • Hospitals should develop a surgical Patient Blood Management team and program of care. • Post operatively, oral iron is not prescribed as it has little effect in the post-operative period. • Further research is needed on the role of intravenous iron therapy in the preoperative patient to determine the impact on need for blood transfusion and patient outcomes. • Further research is needed on the role of iron therapy to patients with post-operative anaemia to determine if there an effect on recovery and patient rehabilitation. • BACKGROUND The World Health Organisation defines anaemia as insufficient Red Blood Cell (RBC) mass circulating in the blood <13g/dL for men and <12g/dL for women (1). Anaemia is associated with impaired physical function, reduced quality of life, infection, patient morbidity and mortality (2). Pre-operative anaemia is common, affecting 30-60% of all patients undergoing major elective surgery (3). In the surgical setting anaemia compounds the stress of operation; anaemia is an independent risk factor for blood transfusion, in-patient complications, delayed hospital discharge and poorer recovery (4).	

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				DIAGNOSIS OF IRON DEFICIENCY ANAEMIA The cause for anaemia in surgical patients is often multifactorial; due to blood losses, nutritional anaemia, anaemia of chronic disease (cancer and/or inflammatory disease) or a combination of these aetiologies. Two main types of anaemia affect surgical patients, iron deficiency anaemia (IDA) and anaemia of chronic disease (ACD), the latter is more common in chronically ill and hospitalised patients (5). ACD can be difficult to diagnose, often being regarded as a diagnosis of exclusion, key feature is a disruption of normal iron homeostasis initiated by a cytokine mediated immune response, such as in chronic inflammatory disease, during infection or following surgery (5, 6,). Consequently, despite the presence of normal, or even increased, body iron stores, these cannot be mobilised or utilised, leading to a state of functional iron deficiency (FID). FID is well recognised in renal and cardiac disease and increasingly recognised as a cause for anaemia in the general surgical patient (7, 8). However, the diagnosis of anaemia due to FID remains an uncertain area in non-renal failure populations, there is no consensus for a definition of iron deficiency in the surgical patient and there is no clear trial data indicating which patients would benefit from iron therapy. Indeed in those trials included in a recent Cochrane Database review of iron therapy for the treatment of anaemia in non-CKD populations (9) the definitions of anaemia and	

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				iron deficiency were extremely varied (10). Data in the surgical population was notably lacking and here was no evidence on how to define iron deficiency anaemia in surgical patients. Consequently as it is not possible to accurately diagnose or define iron deficiency anaemia in the surgical patient we urge NICE not to issue broad recommendations for treatment. IRON THERAPY The role of iron therapy to treat anaemia has considerably changed since the development of modern intravenous iron preparations in the last 5-8 years. Intravenous (IV) iron is the standard of care to treat anaemia in patients with renal failure. Its use has widened to routinely treat anaemia in patients with inflammatory bowel disease and cardiac disease. Introduction of new IV iron preparations that can be administered as a single treatment in a relatively short (15 minute) time without need for test dose, with low risk' has facilitated small trials of obstetric, gynaecological, orthopaedic and obesity surgery. These studies have observed that IV iron in selected populations may increase Hb levels before operation, and this may result in lower transfusion rates (11-18). In a recent Cochrane systematic review, 4745 participants were randomly assigned in 21 trials (9). Trials were conducted in a wide variety of clinical settings. The comparison between oral iron and inactive control revealed no evidence of clinical benefit in terms of mortality (RR 1.05, 95% CI 0.68	

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				to 1.61; four studies, N = 659; very low-quality evidence), but that oral iron lowered the proportion of participants who required blood transfusion (RR 0.74, 95% CI 0.55 to 0.99; three studies, N = 546; very low-quality evidence). In patients receiving parenteral iron; haemoglobin levels were higher than with oral iron (MD -0.50 g/dL, 95% CI -0.73 to -0.27; six studies, N = 769; very low-quality evidence) but there were no significant differences in the proportion of participants requiring blood transfusion between parenteral iron and oral iron groups (RR 0.61, 95% CI 0.24 to 1.58; two studies, N = 371; very low-quality evidence) or between parenteral iron groups and inactive controls (RR 0.84, 95% CI 0.66 to 1.06; eight studies, N = 1315; very low-quality evidence), data were imprecise. In adult patients oral iron may work in the general population to prevent transfusion However there is the data is less clear in surgical patients. Indeed in the setting of preoperative surgical patients there are only three small RCTs totalling 110 patients and no significant reduction in transfusions was reported (16, 19–21). Further postoperatively, there are several RCTs, four in orthopaedics alone (22-25), all showing no benefit for post-operative oral iron therapy. For intravenous iron only one trial exists that is heterogeneous with no impact on transfusion outcomes (26). There is no evidence of effect for oral iron in the post-operative patient.	

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				These are important points to make as, while there is no good evidence either of efficacy or effect of iron therapy, the role of iron therapy is not without risk. Oral Iron is associated with increased risk of side effects (27) and intravenous iron is associated with a potential increased risk of infection (28). NIHR research in this field of medicine should be supported to determine the efficacy of intravenous iron to treat anaemia and prevent the need for blood transfusion in the surgical patient also to ensure that the rates of adverse events in patients receiving the intervention are not related to patient harm (29). Intravenous iron therapy should not be recommended outside the setting of a clinical trial without clear evidence of efficacy to reduce transfusion or effect on patient outcomes in surgical patients. REFERENCES 1. Kramer&Zimmerman. Nutritional Anemia Book. Zimmerman K, editor. Basel, Switzerland: Sight and Life Press; 2007. 2. Spahn DR. Anemia and patient blood management in hip and knee surgery: a systematic review of the literature. Anesthesiology. 2010 Aug;113(2):482-95. 3. Shander A, Knight K, Thurer R, Adamson J, Spence R. Prevalence and outcomes of anemia in surgery: a systematic review of the literature. Am J Med. 2004 Apr 5;116 Suppl 7A:58S-69S. 4. Munoz M, Garcia-Erce JA, Diez-Lobo AI,	

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				Coloproctology of Great Britain and Ireland Annual Meeting Harrogate United Kingdom. Conference Start: 20090608 Conference End: 20090611. Conference Publication: (Supplement S1):31. 21. Ng O, Keeler B, Mishra A, Simpson A, Neal K, Brookes MJ, Acheson AG. Cochrane Database Syst Rev. 2015 Apr 2. NJ0192 Iron therapy for pre-operative anaemia http://www.cochrane.org/CD011588/INJ_iron-therapy-for-pre-operative-anaemia 22. Mundy GM1, Birtwistle SJ, Power RA. The effect of iron supplementation on the level of haemoglobin after lower limb arthroplasty. J Bone Joint Surg Br. 2005 Feb;87(2):213-7. 23. Weatherall M1, Maling TJ. Oral iron therapy for anaemia after orthopaedic surgery: randomized clinical trial. ANZ J Surg. 2004 Dec;74(12):1049-51. 24. Sutton PM1, Cresswell T, Livesey JP, Speed K, Bagga T. Treatment of anaemia after joint replacement. A double-blind, randomised, controlled trial of ferrous sulphate versus placebo. J Bone Joint Surg Br. 2004 Jan;86(1):31-3. 25. Parker MJ. Iron supplementation for anemia after hip fracture surgery: a randomized trial of 300 patients. J Bone Joint Surg Am. 2010 Feb;92(2):265-9. doi: 10.2106/JBJS.I.00883. 26. Bisbe E, Moltó L, Arroyo R, Muniesa JM, Tejero M. Randomized trial comparing ferric	

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				carboxymaltose vs oral ferrous glycine sulphate for postoperative anaemia after total knee arthroplasty. Br J Anaesth. 2014 Sep;113(3):402-9. doi: 10.1093/bja/aeu092. Epub 2014 Apr 29. 27. Tolkien Z, Stecher L, Mander AP, Pereira DI, Powell JJ. Ferrous sulfate supplementation causes significant gastrointestinal side-effects in adults: a systematic review and meta-analysis. PLoS One. 2015 Feb 20;10(2):e0117383. doi: 10.1371/journal.pone.0117383. eCollection 2015. 28. Litton E, Xiao J, Ho KM. Safety and efficacy of intravenous iron therapy in reducing requirement for allogeneic blood transfusion: systematic review and meta-analysis of randomised clinical trials. BMJ. 2013 Aug 15;347:f4822. doi: 10.1136/bmj.f4822. Review. 29. Richards T, Clevenger B, Keidan J, Collier T, Klein AA, Anker SD, Kelly JD. PREVENTT: preoperative intravenous iron to treat anaemia in major surgery: study protocol for a randomised controlled trial. Trials. 2015 Jun 4;16(1):254. doi: 10.1186/s13063-015-0774-2. [redacted]	
National Blood Transfusion Committee	Short	General	General	We have just had the PIWG meeting and would like the NBTC to include in their feedback to NICE that the word 'provide' does not seem like a strong enough word with respect to the patient information	Thank you for your comment. The general principles regarding patient information are covered in the patient experience guideline and therefore we do not think a change is needed to the recommendations in

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				recommendations. We suggest that the word 'must' should precede each of the 3 recommendations, particularly in light of the new law on consent that should also be taken into account in this guidance. [redacted] on behalf of the Patient Information Working Group of the NBTC	this guideline. We have however added a link to the patient experience guideline to the NICE version.
NHS Blood & Transplant	Short	General	General	Mostly this is very clear, and the recommendations make sense. The NICE format takes a bit of getting used to! I think most people will just read the summary and dip into the evidence- so the summary needs to be truly standalone. Therefore I think it needs: -a short statement on scope, esp what isn't included. Most readers would expect something on neonates, which I assume were out of scope. Since it's organised by product, similarly worth saying that plasma products are excluded. Page 2 has a statement on safeguarding and medicines which seem a bit random- perhaps they have to be in all NICE guidance but need some context at least. Also safeguarding applies to vulnerable adults as well as children. There are lots of links to other NICE guidelines but none to other national guidelines. It should be explained why eg BCSH guidance is not referred to.	Thank you for your comment and for your participation in the consultation process. The scope is highlighted in the appendices of the full version of the guideline and the excluded and included topics have now been highlighted in the introductions of both the short version and full guideline. Page 2: Safeguarding. Thank you for your comment. This has now been removed from the guideline. Generally, NICE guidelines only refer to other NICE guidelines. Other relevant guidelines such as the BCSH are referenced in the specific sections where there were alluded to.

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				Four publications are included as footnotes on pages 2 and 3, but no other references are included in the summary- this seems odd- is this because these references don't crop up in the original evidence?	Footnotes: Thank you for your comment. In keeping with the style of the short version of the guideline, all references have now been removed from this section.
				Pages 8 to 10- key priorities. A statement as to why these are the priorities would be helpful. I realise these are copied from later in the document, but this has led to some anomalies: - the section headed 'intravenous and oral iron' has nothing on oral iron.	Pg 8-10. Thank you for your comment. The criteria for selecting the key priorities for implementation are described in the NICE guidelines manual and can be accessed online at http://publications.nice.org.uk/the-guidelines-manual-pmg6/. The topic headings in the key priorities correspond to the headings in the full list of recommendations from which the specific recommendations were selected as key priorities. The full list of recommendations should be referred to for a complete picture.
				- red cells- p8 advises on the threshold for restrictive transfusion, but nothing on when restrictive should be used.	Red Cells – p8. Thank you for your comment. Guidance on when restrictive thresholds should be used can be found in the full list of recommendations for this section of the guideline.
				- p8 (and p14). This feels too bald a statement in this summary section. Suggest reword as either 'single unit transfusions as initial treatment' or include more guidance on assessment. Is this irrespective of Hb? What if it's 2 or 3 g/dl?	P8 (and p14) We believe the wording is clear as initially drafted. Further guidance on checking haemoglobin levels can be found in the full list of recommendations for this section of the guideline. Additionally, the LETR makes it clear that these recommendations do not apply to patients with

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					active bleeding. For other patients e.g. those with Hb concentrations 20-30g/L below the threshold, the GDG considered that elective red cell transfusions should be administered one unit at a time in adults (and the equivalent in children and low weight adults) with re-assessment of the clinical state and Hb concentration before the next transfusion is administered, specifically to avoid over-transfusion and its clinical consequences such as transfusion-associated circulatory overload.
				P13. Section on I/V iron refers to situation where interval to surgery is considered 'short' - either needs defining or reword as 'too short for oral iron to raise the Hb'.	Pg 13. Thank you for your comment- this has now been reworded. The LETR explains the duration of iron therapy as being two weeks prior to date of surgery.
				P14- cell salvage. Not sure what 'major obstetric procedures' is intended to cover- presumably not routine C section. Maybe give an example.	Pg 14 cell salvage Thank you for your comment. 'Major obstetric procedures' is intended to cover any major obstetric surgery where the patient is expected to lose greater than 1000ml of blood. This is classified in the guideline as the high risk group.
				P14 (and bottom of p20). Red cell thresholds and targets. Reads a bit oddly in that thresholds are same as lower end of targets so not clear whether transfusion is recommended close to the threshold or not.	P14 (and bottom of p20). Red cell thresholds and targets. We think it is clear and does not need rewording because if a patient has a haemoglobin level equivalent to the target they would not to start or continue red blood cell transfusion. Both thresholds and targets are recommended in ranges

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					and transfusion at a lower threshold will correspond to a lower target range and vice versa.
				P18 cryoprecipitate. Have forgotten whether NICE covers anywhere other than England. If so, are we sure that pooled cryo is what the Blood Service provides?	Pg 18. Thank you for your comment. The guidelines are applicable to England and Wales. The NHSBT provide pooled cryoprecipitate for England and North Wales.
				P19. Monitoring patients- no reference to BCSH guidance. I think this is dangerously vague in that the timing of the first observation during transfusion is not specified, nor that it is needed after start of each separate pack.	Pg 19. Thank you for your comment. We have now added references to the BCSH guidelines in the LETR for the relevant recommendations.
				P19 Electronic systems. I think this should be a lot stronger. Why so hesitant?	Pg 19. Thank you for your comment. The GDG were not comfortable in making a stronger recommendation on electronic patient identification systems based on the strength of evidence.
				P19 Patient information. No reference to SaBTO work and guidance which is unfortunate---	Pg. 19 Thank you for your comment. We have noted all references considered by the GDG during discussion, including the leaflets produced by NHSBT, in the LETR of the relevant recommendations. We do not refer to specific organisations or publications in the recommendations.
				The membership and conflicts of interest occupies	NICE prides itself on transparency regarding all

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				20 per cent of the document. Hopefully will be shorter in final printed version! Look forward to seeing other comments. [redacted]	aspects of guideline development, including membership and any conflicts of interest. Thank you.
NHS Blood & Transplant	Full	189 219		Congratulations on the production of a guideline which has a clear - remit, presentation of evidence and recommendations. I have only 2 comments for the platelet section, as below. 1) Prophylaxis not pre-procedure. At the bottom of page 189 it clearly states that haematology and non-haematology patients are clinically very different. The text and recommendation for prophylaxis (not pre-procedure) do not mention this and imply that the same threshold should apply to both. 2) Prophylaxis pre procedure. On page 219 it states that more than one dose may be required in advance of major surgery. The recommendations however only advise more than one dose if bleeding is in a critical site. Could the recommendation for more than one dose be altered to accommodate low counts and major surgery. This would likely improve guideline acceptance and compliance. [redacted] Consultant Haematologist - NHSBT and NBT (North Bristol Trust)	Thank you for your comment. 1) All the studies relating to prophylactic use of platelets were in haematology and none in non-haematology patients and it was the consensus of the GDG that the same recommendation applies to both types of patient with the exception of some specified patient groups. 2) The 'other considerations' section has been rewritten to address this point.
NHS Blood & Transplant	Short	General	General	the recommendations state for red cells	Thank you for your comment. We have now expanded the LETR to include detail regarding

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				1.Use restrictive red blood cell transfusion thresholds for patients who need red blood cell transfusions and who do not have major haemorrhage or acute coronary syndrome.(recommendation 13) 2. When using a restrictive red blood cell transfusion threshold, consider a threshold of 70 g/litre and a haemoglobin concentration target of 70-90 g/litre after transfusion. (recommendation 14) 3. Consider a red blood cell transfusion threshold of 80 g/litre and a haemoglobin concentration target of 80-100 g/litre after transfusion for patients with acute coronary syndrome. (recommendation 15) 4. Consider setting individual thresholds and haemoglobin concentration targets for each patient who needs regular blood transfusions for chronic anaemia.(recommendation 16) Personally I think that for recommendation 13 in the exclusion it MUST also be explicit that those with chronic anaemic may be excluded and in recommendation 16 it should be explicit that those with chronic anaemia include those with inherited Hb disorders as these require different targets and thinking eg	situations where transfusion to a higher haemoglobin concentration may be considered, including patients with inherited haemoglobin and/or red cell abnormalities. We have also edited the recommendation to state as follows: Use restrictive red blood cell transfusion thresholds for patients who need red blood cell transfusions and who do not have major haemorrhage, acute coronary syndrome or require regular transfusions for chronic anaemia.

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				those with sickle cell disease may well have a level of HbS which is the trigger rather than the Hb level those with thalassaemia are usually transfused or hypertransfused with a minim threshold for transfusion of 95-100g/litre the level of evidence for recommendation 16 in thalassaemia is I admit not great - I am looking through it for the UK Forum on Hb disorders for the transfusion recommendations in the Standards of Care for Thalassaemia and although the evidence is limited (and quite old) there is clear clinical consensus that transfusion thresholds should be of the order suggested above My worry is that it would be potentially dangerous for patients with these disorders if this guidelines went out as is - eg there may well be patients with thalassaemia or sickle cell disease (looked after by a haematologist - or their juniors - who has only one or two patients and little experience) who are not transfused appropriately by doctors misunderstanding or misinterpreting red cell thresholds on the basis of this document or plain not getting beyond the first recommendation or two it would be interesting to know what other people in the field both within NHSBT and outside think - maybe I am being overly pedantic - and I see that Shubha and Karen Madgwick were involved in the	

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				writing group so that I am sure that they considered this other than that I think its very good! [redacted] [redacted] NHSBT	
NHS Blood & Transplant	Short	General	General	Thank you for circulating the draft NICE guidelines for blood transfusion. I have a few comments that you might want to consider: 1.1.1 Erythropoietin: While the statement is correct for most patients, would it not be appropriate to allow pre-operative use of EPO in Jehovah's Witnesses, if required? 1.2.2 Red cells: the recommendation of a threshold of 70 g/l, aiming at post-transfusion haemoglobin of 70-90 g/l, sounds strange. Would we be satisfied if a patient's haemoglobin increased from 69 to 72 g/l?? Suggest changing the target haemoglobin to 80-90 g/l. 1.2.3 As above; suggest changing target to 90-100 g/l. 1.3.8 advises against prophylactic PLT transfusion in patients "having central venous cannulation". I think this needs some clarification, as a PICC line insertion may not have the same risk as a tunnelled line insertion. I found this difficult to understand especially in the light of paragraph 1.3.3. [redacted] Consultant Haematologist King's College Hospital/NHSBT	Thank you for your comments. 1.1.1 - We agree and would like to bring to your attention that this was considered by the GDG and a statement that EPO may be considered in patients who refuse blood transfusions has now been included in the recommendation; please also see the other considerations section in the 'Linking evidence to recommendations' table. 1.2.2 and 1.2.3 - It is the opinion of the GDG that once the haemoglobin is above the threshold for transfusion, (such as 70) it is not necessary to transfuse further units at that time. 1.3.8 - Please see recommendation 1.3.5 Where it states that the specific procedure being undertaken should be considered when deciding what threshold for prophylactic platelet transfusion should be used before a procedure. Recommendation 1.3.3 refers to patients not having invasive procedures.
NHS Blood & Transplant	Short	2	20 - 21	Research Recommendations: one point of feedback is the research priority list. This is a very short list, given many gaps in the evidence and sections. Why were patients with cardiac disease mentioned, but	Thank you for your comment. We agree, there are many areas of research that need to be conducted, but we felt the ones we highlighted were most important. The GDG considered whether it was best

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				the statement on providing individualised transfusion support in haematology patients not mentioned for research. Likewise on electronic support, but not other areas. One might imagine this list reflects the committee membership and therefore full disclosure of conflicts and interests (which may not be just financial) should be added	for us to make a good practice recommendation for the NHS in the areas lacking in evidence or make no recommendation and wait for future research. In several areas, the GDG felt that whilst evidence was lacking there was good consensus about what good practice should be. Areas for further research were identified by the guideline committee throughout development following the appraisal of the evidence. An additional research recommendation on FFP was added during the consultation. The full disclosure of conflicts of interests is included in the appendix of the guideline.
NHS Blood & Transplant	Full	General	General	The numbers after the references in the main text do not tally with the reference list p495 – 509. For example, on page 48, Aufricht 1994 (17) – but in the reference section on page 496, reference number 17 is Campbell et al (2014). In fact, I cannot see the reference for Aufricht at all !	Thank you for your comment. The reference list is correct in the full guideline. Each document has its own reference list, and only the references cited in that document will appear in the list.
NHS Blood & Transplant	Full	General	General	There is a lack of evidence for a number of points and recommendations, due to the evidence acceptance criteria. They have not included relevant literature covered in other guidelines because it does not fit their criteria, but that leaves recommendations stating 'no evidence was identified.	Thank you for your comment. The GDG agreed that for each clinical question the evidence would be searched for and reviewed according to pre-specified criteria of hierarchy based quality of evidence. We looked for highest quality evidence in the first instance; if this was not available or where the GDG felt that lower quality evidence would be helpful, we have searched for lower quality evidence. The details of this can be found in the protocols in appendix C. The GDG noted that lower quality evidence for some questions was likely to be

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					unreliable and therefore may not assist in making recommendations. The GDG considered that performing a systemic review of all lower quality studies would have taken a huge amount of resources and would not have added a great deal to the guideline. In areas where no clinical evidence was identified, the GDG members used their collective experience to make consensus recommendations. However, the GDG members also identified areas where evidence to answer their review questions was lacking and have used this information to formulate recommendations for future research.
NHS Blood & Transplant	Full	General	General	Phrasing of some recommendations could give more clarity. NICE guidelines are generally interpreted by hospitals and implemented in the exact way they are written whereas with some other guidelines they use more clinical interpretation. For example 'Do not use cell salvage alone' I feel could be phrased better.	Thank you for your comment. We have edited the recommendation for greater clarification. It now states: Do not routinely use cell salvage without tranexamic acid.
NHS Blood & Transplant	Full	General	General	The phrasing of the recommendations is derived from how strong the evidence for that recommendation is, but as some points are poorly evidenced due to the NICE evidence acceptance criteria this may not necessarily reflect recommendations / guidance from other organisations i.e. BCSH or some of the literature. for example if the evidence is strong they put 'offer', if it's weak 'consider', but they may not have accepted all the evidence so the strength of recommendation may not be a true reflection.	Thank you for your comment. We feel that the wording does accurately reflect the strength of the evidence. Even if we were to include observational studies for some questions, due to the limitations of this type of study, the evidence would be unreliable. We would therefore still have a lack of confidence in the results and the recommendation is likely to still say 'consider'.

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NHS Blood & Transplant	Full	General	General	The introduction of the guidelines is referenced and talks about risks, SHOT, TACO etc, but yet there is no mention of this and 'no evidence available' for the recommendation of single unit including adverse events (section 10).	Thank you for your comment. The introduction of the guideline references and talks about the risks and adverse events associated with transfusion in general. However, with respect to the review evaluating the effectiveness of single unit red cell transfusions, we did not find any evidence for the same and this has been noted in the 'Linking evidence to recommendations' section.
NHS Blood & Transplant	Full	General	General	Economic considerations - did not include consideration of additional laboratory and clinical workload of taking / testing additional samples (perhaps purposefully?)	Thank you for your comment. We acknowledge that we have not taken all possible additional costs into account because there are many, much of the data are difficult to capture and they are difficult to cost. We have indicated which ones we have accounted for and have made it clearer that we did not include consideration of the additional laboratory and clinical workload of taking / testing additional samples. However, the GDG were confident that the cost impact would not be large enough to affect the recommendations and we have made this more explicit in the 'Linking evidence to recommendations' table.
NHS Blood & Transplant	Full	General	General	There are several references to England and Wales – should this be England and North Wales?	Thank you for your comment. We have now amended the references to England and Wales to England and North Wales when referring to the NHSBT blood products.
NHS Blood & Transplant	Full	General	General	There are instances where 10^9 is noted as 109 throughout the document	Thank you for your comment. This has been edited throughout the document.
NHS Blood & Transplant	Full	General	General	Platelet dose guidance (13) is lacking evidence to support recommendation for low dose (single unit) transfusions. No evidence provided for bleeding patients. QOL, LOS and standardised dosing in	Thank you for your comment. There is evidence to support the use of single dose platelet transfusions, as described in the 'trade-off between clinical benefits and harms' section of the LETR for this

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				studies may lead to uncertainty in practice.	recommendation.
NHS Blood & Transplant	Full	General	General	I think there is a case for further research into the use of FFP in massive haemorrhage and I think this should be one of the research recommendations. There also must be some questions about why there is no information about using FFP in Massive haemorrhage in the guidelines.	Thank you for your comment. Massive haemorrhage is outside the scope of this guideline. We would also like to highlight that a research recommendation has now been made on FFP.
NHS Blood & Transplant	Full	General	General	Why is Electronic Decision Support a research recommendation when surely there must be more important research needed?	Thank you for your comment. The group thought this was an important area for research as there was not enough evidence to make recommendations for clinical practice. Due to potentially high set up costs it will be useful to establish both the clinical and cost effectiveness of such systems. The GDG discussed the impact of this research and noted that reduction in inappropriate blood transfusion will reduce risk to patients, and improve clinical outcomes. Reduction in overall use of blood products will reduce costs to the NHS, and increase availability for the population. The study would provide evidence to guide whether the electronic decision support systems for blood transfusion should be introduced across the NHS.
NHS Blood & Transplant	Short	20 and 21		There are 3 key areas for further research listed. Whilst I understand that these are 3 areas where there was not enough evidence to make a recommendation at all, considering most other aspects of this guideline states that evidence is of low – moderate quality, I do think that other more important and influential areas of research should be considered here. Whilst I appreciate that Electronic Decision Support may assist clinicians – would this tool not need to	Thank you for your comment. We agree, there are many areas of research that need to be conducted, but we felt the ones we highlighted were most important. The GDG considered whether it was best for us to make a good practice recommendation for the NHS in the areas lacking in evidence or make no recommendation and wait for future research. In several areas, the GDG felt that whilst evidence was lacking there was good consensus about what good practice should be. Areas for further research were

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				be backed by more robust evidence?	identified by the guideline committee throughout development following the appraisal of the evidence. We have also added a new research recommendation on FFP. Regarding EDS, a practice recommendation was not made due to the lack of evidence and a research recommendation drafted.
NHS Blood & Transplant	Full	12	14	The use of cell salvage for all routine and, where possible, emergency obstetric procedures reduces blood use and standardises the practice and increases expertise of staff using equipment.	Thank you for your comment but intraoperative cell salvage was only found to be clinically and cost-effective for patients expected to lose a very high volume of blood.
NHS Blood & Transplant	Full	19	General	*Algorithm* The box that states 'have other alternatives to blood transfusion been considered?' should have a no option that directs to appropriate guidance for treatment/diagnosis of iron deficiency etc	Thank you for your comment. We have changed the algorithm. We have deleted the 'yes' box and made the question into a statement: 'Consider alternatives to blood transfusion. For example….' Thank you for your suggestion.
NHS Blood & Transplant	Full	20	12-13	Repetition of transfusion associated circulatory overload	Thank you for your comment. This has been edited.
NHS Blood & Transplant	Full	13 and 65	19 6	Spelling of the word 'Erythropoietin' to be corrected	Thank you for your comment, this has been edited throughout the guideline.
NHS Blood & Transplant	Full	65	6	Recommendation 1 – I think that this should be changed to 'Do not routinely offer EPO' – should it be considered in those patients who refuse a transfusion, or to patients with complex alloimmunisation	Thank you for your comment. We agree. The recommendation for EPO has now been reworded and a statement has now been included in the recommendation that EPO may be considered in patients who refuse blood transfusions and when appropriate blood type is not available because of the patient's red cell antibodies.
NHS Blood & Transplant	Full	47	13	Why is the iron review question only limited to surgical patients – what about medical patients? (we know most blood is used in medicine – a lot of it inappropriately)	Thank you for your comment. We have not included any investigations and treatment of anaemia in medical patients as these are outside the scope of the guideline.

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NHS Blood & Transplant	Full	68	1	Recommendation 3 – Consider IV iron – is 'consider' a strong enough recommendation? (I agree that should be consider if other cost-effective options are available, but if oral iron is not tolerated, what other options are there?) – I suggest this should therefore be changed to 'offer'. Also – I think 'where the interval to surgery is considered short' could be changed to 'where the interval between detection of anaemia and surgery is predicted to be too short for oral iron'	Thank you for your comment. We feel that the wording accurately reflects the strength of the evidence. 'Consider' in the context of NICE recommendations indicates that the GDG could not make a strong recommendation based on the evidence because the balance between benefits and harms was less definitive. We agree the wording could be improved to ' and the interval between the diagnosis of anaemia and surgery is predicted to be too short for oral iron to be effective. '.
NHS Blood & Transplant	Full	114	39	Recommendation 7 - Will be challenging to implement as further advice regarding dose would be required for widespread use in children	Thank you for your comment. We note this but we did not specifically consider dose of tranexamic acid either for adults and children.
NHS Blood & Transplant	Full	118	1	Recommendation 8 – I am concerned that this recommendation implies that smaller trusts can interpret this as Cell salvage provision is not warranted in their organisation. This would reduce choice for patients particularly whose religion does not support allergenic transfusion	Thank you for your comment. The recommendation advises against the use of cell salvage on its own without tranexamic acid as the evidence suggested that it was not clinically or cost effective when used on its own. Cell salvage can still be used in smaller trusts in combination with tranexamic acid in patients who are expected to lose a very high volume of blood or indeed patients who do not wish to receive a transfusion and this recommendation should therefore not impact patient choice in this regard.
NHS Blood & Transplant	Full	120	1	Recommendation 9 - will be challenging to implement in obstetrics until/dependent on the publication of results from the "WOMAN" trial NB: page 21 states that 'pregnant women' were excluded from the scope of this guideline	Thank you for your comment. The recommendation is based on current evidence and the expert opinion of GDG members. Further updates of the guideline will include any new relevant evidence.
NHS Blood &	Full	127	2	Recommendation 10 – very vague re timings	Thank you for your comment, we have added the

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Transplant					following statement to the 'Linking evidence to recommendations' table in the 'other considerations' section: 'frequency of monitoring would depend on the type of patient receiving a transfusion, for example, children and unconscious patients may require more frequent monitoring during blood transfusions', than a stable conscious patient receiving an elective transfusion and so the GDG opted not to state specific timings within the recommendation.
NHS Blood & Transplant	Full	144 and 150	18 6	Table 66 – as the review question is 'ensuring patient safety' should the comparison outcomes also include 'Evidence of incorrect and inadequate use (near miss). There is evidence of staff employing 'work arounds' where electronic devices are not robust enough. Recommendation 12 should also be changed to state 'Hospitals should consider using robust electronic ……'	Thank you for your comment. The GDG agreed that the outcome on incorrect labelling, including incorrect blood samples and rejected blood samples would cover evidence of near miss cases. In addition to the above, the outcome evaluating incorrect blood component transfused covers evidence of incorrect and inadequate use. Thank you for your comment. We think the recommendation is clearer as is stated.
NHS Blood & Transplant	Full	176	27	1. It takes time to embed the education/rationale on the use of restrictive transfusion both with clinicians and the lab staff. Lab staff may need more support with empowerment to assist this is implemented. This would be a responsibility of the transfusion practitioner to ensure the correct education was being delivered 2. Examples of good practice of lab algorithms to support BMS empowerment to implement	Thank you for your comment. We agree, however training issues are outside the scope of the guideline.
NHS Blood & Transplant	Full	179	1	1. Again the biggest impact is the expected level of education required to implement effectively and	Thank you for your comment. This impact on education has been noted and passed onto the

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				audit. It may result on more check Hb's being performed to ensure a satisfactory target haemoglobin is reached. Impact on the TP and the haematology lab if more FBC's are tested 2. As above, but pretty much standard practice in most Trusts I suspect	NICE costing and implementation team. We acknowledge that we have not taken all possible additional costs into account because there are very many, much of the data are difficult to capture and they are difficult to cost. We have indicated which ones we have accounted for and will make it clearer that we did not include consideration of the additional laboratory and clinical workload of taking / testing additional samples. However, the GDG were confident that the cost impact would not be large enough to affect the recommendations and we have made this more explicit in the 'Linking evidence to recommendations' table.
NHS Blood & Transplant	Full	186	1	Recommendation 18: statement to both clinically assess and check haemoglobin, and give further transfusions if needed. I wonder if this would be better phrased without the 'and', but a full stop to encourage the process reassess, then stop, evaluate and if required give further transfusions. i.e *...clinically reassess and check haemoglobin levels. Give further transfusions if needed*.	Thank you for your comment. We believe the current wording is clear.
NHS Blood & Transplant	Full	221	1	Could it be stated that you can take the post platelet count 10 minutes after the transfusion – Reference: O'Connell B, Lee EJ, Schiffer CA. The value of 10-minute post transfusion platelet counts. Transfusion 1988; 28: 66-67	Thank you for your comment. We have added the following text to the LETR statement: Traditionally this assessment is carried out at 1 hour and 24 hours post-transfusion but the initial assessment of the effectiveness of the transfusion can be achieved by sampling 10 minutes after the transfusion.
NHS Blood & Transplant	Full	223	5	Needs to say *-25°C*, currently says *25°C*	Thank you for your comment, this has been edited.
NHS Blood & Transplant	Full	223	8	FFP sourced, "as far as possible" from male donors……does this include MBFFP?	Thank you for your comment. This does include MBFFP and the GDG is aware.

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NHS Blood & Transplant	Full	223	10	Specify as *01/01/1996*	Thank you for your comment, this has been edited.
NHS Blood & Transplant	Full	223	11	Include reference to SD FFP as an alternative non-UK sourced plasma	Thank you for your comment, the introduction has been edited to include the following text: imported FFP is pathogen inactivated, either single donor methylene blue treated (provided by NHSBT) or pooled solvent detergent treated (commercially available 'Octaplas').
NHS Blood & Transplant	Full	223	17	Include statement that FFP is not to be used for volume replacement	Thank you for your comment. We have included a statement in the LETR to this effect.
NHS Blood & Transplant	Full	223	110	*…prothrombin ration (PT)* – should this read *…prothrombin time (PT)*; this occurs twice in this table	Thank you for your comment, this has been edited.
NHS Blood & Transplant	Full	225	6	Reads as *…fresh frozen plasma FFP* – should read either *fresh frozen plasma* or *FFP*	Thank you for your comment, this has been edited.
NHS Blood & Transplant	Full	226	1	*…asses* should read *…assess*	Thank you for your comment, this has been edited.
NHS Blood & Transplant	Full	227	112	Intervention/comparison column for the Trimble study, reads *…FFP I unit* should be *…FFP 1 unit*	Thank you for your comment, this has been edited.
NHS Blood & Transplant	Full	237	30	MBFFP is £178 per bag	Thank you for your comment. The cost we have referenced in the guideline is from the NHSBT 2013/2014 price list, which was the available price list at the time of presenting this information to the guideline committee. A reference has been added to the 'Linking evidence to recommendations' section to clarify this. As stated in section 4.4.4 of the full guideline, *'the UK NHS costs reported in the guideline are those that were presented to the GDG and were correct at the time recommendations were drafted. They may have changed subsequently*

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					before the time of publication. However, we have no reason to believe they have changed substantially'.
NHS Blood & Transplant	Full	238	31	MBFFP is £178 per bag	Thank you for your comment. The cost we have referenced in the guideline is from the NHSBT 2013/2014 price list, which was the available price list at the time of presenting this information to the guideline committee. A reference has been added to the 'Linking evidence to recommendations' section to clarify this. As stated in section 4.4.4 of the full guideline, *'the UK NHS costs reported in the guideline are those that were presented to the GDG and were correct at the time recommendations were drafted. They may have changed subsequently before the time of publication. However, we have no reason to believe they have changed substantially'*.
NHS Blood & Transplant	Full	240	32	MBFFP is £178 per bag	Thank you for your comment. The cost we have referenced in the guideline is from the NHSBT 2013/2014 price list, which was the available price list at the time of presenting this information to the guideline committee. A reference has been added to the linking evidence to recommendations statements to clarify this. As stated in section 4.4.4 of the full guideline, *'the UK NHS costs reported in the guideline are those that were presented to the GDG and were correct at the time recommendations were drafted. They may have changed subsequently before the time of publication. However, we have no reason to believe they have changed substantially'*.
NHS Blood & Transplant	Full	General – 14	General	Section 14 – FFP transfusion: thresholds and targets – Only 3 fairly vague recommendations – nothing on replacement of single factor deficiency,	Thank you for your comment, the GDG recognises that not all clinical indications for the use of FFP are covered by this guideline and a statement to this

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				multiple factor deficiency, DIC, TTP or reversal of warfarin.	effect has been added to the 'Linking evidence to recommendations' section.
NHS Blood & Transplant	Full	General – section 14	General	Section 14 – FFP transfusion : thresholds and targets – much of the evidence is deemed to be of low quality ??acceptable	Thank you for your comment. Much of the evidence was of low quality. The recommendations were based on indirect evidence and the opinion of GDG members. We have now included a further research recommendation on this topic.
NHS Blood & Transplant	Full	250	7 , 8	A standard adult dose of cryoprecipitate is 10 units available in the UK as pools of 5 single units. - I am not sure if this will cause confusion as people might order 10 pools. Will explaining 'A standard adult dose of cryoprecipitate is 2 pooled units (in the UK each pooled unit is made up of 5 single units)'	Thank you for your comment. We have amended the text in the Linking evidence to recommendations table.
NHS Blood & Transplant	Full	287	2	Evidence summary – I found this table quite confusing and difficult to follow – unclear whether summary of papers or individual results. Contradictory findings, which jumped about, but nothing to indicate which papers.	Thank you for your comment. We apologise if the summary table is unclear. The table is a summary of the findings relating to each theme which emerged from the individual studies. A narrative summary of each theme is presented in section 20.4. It is important to report all findings, even if contradictory, as the basis of qualitative synthesis is to acknowledge all perspectives and relate them to context. The studies, along with their individual findings are referenced separately in the evidence tables.
NHS Blood & Transplant	Full	292	28	Comments on donating own blood prior to surgery – but no mention that this is NOT a recommended procedure (BCSH PAD guideline)	Thank you for your comment. The reference to donating blood before surgery is stating one of the findings in the literature review on this topic. Recommendations are highlighted and it is clear that this procedure is not being recommended.
NHS Blood &	Full	292	29 - 35	Mode of information delivery – no mention that	Thank you for your comment. We do mention this

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Transplant				57.7% of patients felt that the best source of information was directly from the HCP.	finding in the summary of evidence table under the theme 'Mode of information delivery'. We acknowledge the validity of this point and the wording of the recommendation reflects this by emphasising dialogue between the health care professional. ('Provide verbal and written…')
NHS Blood & Transplant	Full	295	1	Recommendation 46 – add that they can no longer donate blood	Thank you for your comment. We have amended the recommendation to include the following bullet point : '…that explains that they are no longer eligible to donate blood.'
NHS Blood & Transplant	Full	20 – 285-286	25 129)	I am also aware of the following papers which have not been included: Vetter et al (2014) http://www.ncbi.nlm.nih.gov/pubmed/24842177 Cheung et al (2014) http://onlinelibrary.wiley.com/doi/10.1111/tme.12141/pdf	Thank you for your comment and for highlighting these studies. We have excluded the study Vetter et al 2014 as this is a survey of patient's perception of risk of blood transfusion and associated patient characteristics. The study did not report what information people may want. Please refer to the excluded studies list for further details. We have now included the study Cheung et al. 2014 in our review. This was not picked up during the initial searches due to poor indexing in the search databases. The recommendations remain unchanged even after addition of the study.
NHS England	General	General	General	Thank you for the opportunity to comment on the above Clinical Guideline. I wish to confirm that NHS England has no substantive comments regarding this consultation.	Thank you for participating in the consultation process.
Northern Ireland Transfusion Committee	Full	13	3	Prothrombin complex concentrate transfusions – prothrombin complex concentrate is deemed as a blood product (not a blood component) so therefore 'infusions' is more appropriate term here as	Thank you for your comment. You are correct. For recommendation 42, we will omit the word 'transfusions' as it is superfluous....so it will read 'Consider the immediate administration of

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				opposed to 'transfusions'. (This same comment is applicable in other sections of the document when prothrombin complex concentrate is being discussed).	prothrombin complex concentrate to reverse warfarin....'. We will make the appropriate changes in the rest of the guideline.
Northern Ireland Transfusion Committee	Full	15	4	50X109 per litre – 9 needs to be superscript font	Thank you for your comment. This has now been amended.
Northern Ireland Transfusion Committee	Full	17	1	Document discussion in the patient's notes – suggest adding 'or complete relevant section on the 'Transfusion Records' where these are used.	Thank you for your comment. We do not think it is necessary to be specific about where the discussion is documented in the patient's records as this may vary. The key point is that the discussion is documented.
Northern Ireland Transfusion Committee	Full	17	2	Is this going to be possible – the Electronic Care Record (ECR) in WHSCT has a section that can be completed regarding details of blood components or blood products administered – however is a copy of this discharge letter permitted to be given to the patient?	Thank you for your comment. It is certainly permitted and indeed is good practice for patients to be provided with copies of discharge letters and other correspondence relating to their healthcare.
Northern Ireland Transfusion Committee	Full	17	24	"blood products' – is this term supposed to be 'blood components' which refers to Fresh Frozen Plasma, Platelets, Cryoprecipitate as well as Red Cells?	Thank you for your comment, this has now been changed to components.
Northern Ireland Transfusion Committee	Full	19	General	*Algorithm* Consider using term 'blood component transfusion' as opposed to 'blood transfusion' in boxes in upper section as information in lower section relates to 'blood components' not just 'blood transfusion'.	Thank you for your comment. We have left the reference to 'blood transfusion' in the upper section (first top left and first top right boxes, and third top left box) because in the lower section we are referring not only to blood components, but also to blood products. To reflect this, we have amended the fourth and the six boxes from the top to 'blood component / product'.
Northern Ireland	Full	19	General	*Algorithm*	Thank you for your comment. The full stop has been

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Transfusion Committee				Full stop not required after procedures – 4th bullet point under Platelets recommendations.	removed.
Northern Ireland Transfusion Committee	Full	19	General	*Algorithm*) required after giving example of platelet count - 5th bullet point section under Platelets recommendations.	Thank you for your comment. A) has been added after '50-75X10^9 per litre'.
Northern Ireland Transfusion Committee	Full	19	General	*Algorithm*) not required last bullet point (5th bullet point section under Platelets recommendations).	Thank you for your comment. The) has been removed after the last sub-bullet after haemostasis.
Northern Ireland Transfusion Committee	Full	19	General	*Algorithm* Suggest heading to be Fresh Frozen Plasma (FFP) recommendations and then rest of text in box could use the term 'FFP'. In same section need to decide if using transfusion or transfusions when referring to FFP as both terms used.	Thank you for your comment. We have changed the title from 'FFP recommendations' to 'Fresh Frozen Plasma (FFP) recommendations'. However, we have decided not to use the abbreviation FFP in the text as abbreviations are not used in the original recommendations.
Northern Ireland Transfusion Committee	Full	20	11	Superscript 'b' should be before full stop not after.	Thank you for your comment. This has been amended.
Northern Ireland Transfusion Committee	Full	20	11 -13	Change to "The most common cause of death associated with transfusion was transfusion associated circulatory overload (TACO)"	Thank you for your comment. This has been amended.
Northern Ireland Transfusion Committee	Full	20	16	Insert another bullet point that "some patients are transfused unnecessarily"	Thank you for your comment. We have accepted you suggestion and edited the introduction to reflect this change.
Northern Ireland Transfusion Committee	Full	23	25	Change to "This guideline will not cover neonates and infants up to one year of age, foetuses, pregnant women or patients with haemoglobinopathies"	Thank you for your comment. We agree and have amended the introduction and the section on 'what this guideline covers' accordingly.

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Stakeholder	Document	Page	Line	Comments	Developer's response
Northern Ireland Transfusion Committee	Full	25	13	Change to " A total of 21 review questions were considered in this guideline"	Thank you for your comment. This has been amended.
Northern Ireland Transfusion Committee	Full	25	General	*Table 1 point 5* Standardize term to "intravenous iron" or to "IV iron" in document	Thank you for your comment, for consistency, where it appears first in the guideline it is noted as 'intravenous' and IV iron thereafter.
Northern Ireland Transfusion Committee	Full	28	General	*Table 1 point 14* In second column put "FFP" in brackets	Thank you for your comment. This has been amended.
Northern Ireland Transfusion Committee	Full	29	General	*Table 1 point15* Re phrase second column to "What is the clinical- and cost-effectiveness of different target levels of post-transfusion haemostasis tests with the prophylactic transfusion of cryoprecipitate?"	Thank you for your comment. We believe the wording is clear as it stands.
Northern Ireland Transfusion Committee	Full	30	20	Need % after 52.	Thank you for your comment. This has been amended.
Northern Ireland Transfusion Committee	Full	30	25	First time to see number reference in document and it is 291??	Thank you for your comment. The reference list is generated alphabetically by author and therefore the numbers will not appear in numerical order in text.
Northern Ireland Transfusion Committee	Full	31	General	*Table 1 point19* Re phrase middle column to "What information and support would patients and their family members or carers value about transfusion and by what means would they prefer to receive it?"	Thank you for your comment. The wording of this question was agreed with the GDG at the time of reviewing the evidence. We would not re-phrase questions at this stage of the guideline development process.
Northern Ireland Transfusion	Full	31	4	"parameters stipulated within **the**…"	Thank you for your comment. This has now been amended.

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Committee					
Northern Ireland Transfusion Committee	Full	48	13 15	Standardize term to "erythropoietin" or 24'EPO'.	Thank you for your comment. This amendment has been made.
Northern Ireland Transfusion Committee	Full	62	8	Change "blood units" to "red cell units"	Thank you for your comment. This amendment has been made.
Northern Ireland Transfusion Committee	Full	63	35	Change "number of units transfused" to "number of red cell units transfused"	Thank you for your comment. The evidence statement wording reflects the outcome as written in the protocol. The protocol does not specify red cell units transfused as different studies may report number of whole blood units transfused or not specify red cells. Therefore we are not able to make this suggested amend.
Northern Ireland Transfusion Committee	Full	63	4 12 32	Remove extra full stops	Thank you for your comment. This has been amended.
Northern Ireland Transfusion Committee	Full	63	30	Space needed between iron and but.	Thank you for your comment. This has been amended.
Northern Ireland Transfusion Committee	Full	67	General	*Table, 2nd column, 3rd paragraph* "stay" is omitted from sentence beginning "The evidence showed clinically important benefit for oral iron for the outcome length of hospital…"	Thank you for your comment. This has been amended.
Northern Ireland Transfusion Committee	Full	68	General	*Table "Other considerations" 4th paragraph* "post-surgical patients may be more likely to be truly responsive to iron therapy as the mechanism of developing anaemia is usually blood loss." Does this statement make the assumption that blood loss reduces iron stores?	Thank you for your comment. Yes, the statement makes the assumption that blood loss reduces iron stores. We have edited the other considerations section in the 'Linking evidence to recommendations' table to reflect that there is another perspective, that is, oral iron is of limited effectiveness after surgery because of post-operative inflammation. The GDG

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Stakeholder	Document	Page	Line	Comments	Developer's response
					discussed the available evidence and agreed that for all patients with pre-operative iron deficiency anaemia, treatment with oral iron should continue after surgery as this is likely to be effective.
Northern Ireland Transfusion Committee	Full	70	General	*Table 2nd column, 1st sentence* Amend to "Both oral and intravenous iron…"	Thank you for your comment. This has been amended.
Northern Ireland Transfusion Committee	Full	72	7	Consider adding 'TXA' after tranexamic acid at this point as term is used during chapter and I do not appear to see where it has been defined until later on in chapter 6.4.1.	Thank you for your comment. This has been amended as suggested.
Northern Ireland Transfusion Committee	Full	72	5	Change to "This has driven a requirement to transfuse blood components appropriately and to use alternative to transfusion"	Thank you for your comment. The original sentence is clear and so this change has not been made.
Northern Ireland Transfusion Committee	Full	72	7	Change to "Cell salvage and tranexamic acid have both been used in surgical patients to reduce the requirement for transfusion of allogeneic red cells"	Thank you for your comment. This has been amended as suggested.
Northern Ireland Transfusion Committee	Full	72	10 11	Change to "is collected an then transfused back to the patient."	Thank you for your comment. This has been amended as suggested.
Northern Ireland Transfusion Committee	Full	72	14 -16	Move these lines to line 11. "During surgery a cell saver device is used to collect and process shed blood before transfusing it back to the patient. Blood collected in drains postoperatively may also be transfused back to the patient.	Thank you for your comment. The group agreed that the original sentence/ paragraph is clear and so this change has not been made.
Northern Ireland Transfusion Committee	Full	72	12 -19	Condense these lines into one paragraph. e.g. "This technique has been used for many years to reduce the volume of donated red cell transfusions given to patients during and after surgical procedures. It has also contributed to a marked reduction in the overall use of allogeneic red cells in	Thank you for your comment. The group agreed that the original sentence/ paragraph is clear and so this change has not been made.

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Stakeholder	Document	Page	Line	Comments	Developer's response
				surgical patients in England during the last 15 years"	
Northern Ireland Transfusion Committee	Full	72	25 26	Re word "Tranexamic acid (TXA) is a synthetic derivative of the amino acid lysine that inhibits clot breakdown by blocking plasminogen binding sites; i.e. it is an antifibrinolytic drug.	Thank you for your comment. The group agreed that the original sentence/ paragraph is clear and so this change has not been made.
Northern Ireland Transfusion Committee	Full	72	32 33	Re word "A Cochrane review reported that antifibrinolytics reduce blood loss during surgery and the requirement for allogeneic red cell without increasing the risk of post-operative complications.	Thank you for your comment. This introduction has been amended and the sentence you referred to removed.
Northern Ireland Transfusion Committee	Full	74	15	Change beginning of sentence to "To this end, the evidence was reviewed…"	Thank you for your comment. This has been amended as suggested.
Northern Ireland Transfusion Committee	Full	74	19	Re word "The GDG stratified the population according to baseline risk of requiring a blood…"	Thank you for your comment. This has been amended as suggested.
Northern Ireland Transfusion Committee	Full	75	6 -8	Re phrase "Since cell salvage is not a feasible option in the low risk surgery group the effectiveness of tranexamic acid alone was compared with standard treatment in this group."	Thank you for your comment. The group agreed that highlighting the reason why cell salvage is not feasible in the low risk group is important here and so the suggested amendment has not been made.
Northern Ireland Transfusion Committee	Full	76	2 3	The GDG agreed that all doses and routes of administration of tranexamic acid **should** be evaluated together.	Thank you for your comment. This has been amended as suggested.
Northern Ireland Transfusion Committee	Full	76	20	Space needed between study and interventions.	Thank you for your comment. There already is a space between these two words.
Northern Ireland Transfusion Committee	Full	76	10	Change "reducing blood transfusion requirements." to "reducing donated red cell transfusion requirements"	Thank you for your comment. The word allogeneic has been added prior to blood transfusion requirements to clarify this sentence.
Northern Ireland Transfusion	Full	82 -91	General	*Tables 27 to 46* In all tables 27 to 46 change "Units of allogeneic	Thank you for your comment. The studies did not all report red cell transfusion, for example, in some

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Stakeholder	Document	Page	Line	Comments	Developer's response
Committee				blood transfused" to "Units of allogeneic red cells transfused"	cases they report whole blood transfusion and therefore we are not able to make this suggested amendment.
Northern Ireland Transfusion Committee	Full	104	7 8	Re phrase to "Cell salvage is a procedure whereby blood loss during or after surgery is collected, processed and then transfused back to the patient, with the aim of reducing the requirement for allogeneic blood transfusion."	Thank you for your comment, this has been amended as suggested.
Northern Ireland Transfusion Committee	Full	104	36 37	Re phrase to "Adults undergoing surgery with a low risk of bleeding (<0.5 litres) were not included in the analysis as cell salvage would not be a feasible option."	Thank you for your comment, the sentence has been reworded.
Northern Ireland Transfusion Committee	Full	104	42	Re phrase to "on the proportion of patients transfused and the volume of red cells transfused"	Thank you for your comment. The group agreed that the original sentence is clear and accurately reflects the model methodology; and so this change has not been made.
Northern Ireland Transfusion Committee	Full	106	4	Re phrase to "The cost of transfusion of a unit of red cells was taken to be £192.17 .."	Thank you for your comment. The sentence has been reworded to include the words red blood cells.
Northern Ireland Transfusion Committee	Full	106	8	Re phrase to "the cost of the first unit of red cells".	Thank you for your comment. The sentence has been reworded to include the words 'red blood cells'.
Northern Ireland Transfusion Committee	Full	112	27 28	Is there sufficient evidence base to stand over this statement about non-significant reduction of thrombotic events secondary to TXA, for example in high risk surgeries where anastomotic site ischaemia is critical e.g. Oesophagectomy? Should there still be caution in use of TXA for some major elective surgical procedures in the absence of bleeding > 1,000 ml?	Thank you for your comment. The review evaluated the literature relating to the risk of thrombotic complications with the use of tranexamic acid following major surgery and the evidence, although non-significant, suggested that there were fewer thrombotic complications with the use of tranexamic acid (RR 0.48 [0.18, 1.23] in the high risk group and RR 0.69 [0.44, 1.07] in the moderate risk group). Please refer tables 35 and 42 in the full guideline for

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Stakeholder	Document	Page	Line	Comments	Developer's response
					details. Based on this evidence the GDG agreed that there was no need for additional caution.
Northern Ireland Transfusion Committee	Full	114	39	On the basis of comment 51 suggest change to Recommendation 6. to "Offer tranexamic acid to adults undergoing surgery who are expected …"	Thank you for your comment. Recommendation 6 is already phrased the way you suggested in this comment.
Northern Ireland Transfusion Committee	Full	123	13	Change to "observations on patients being transfused blood components or blood products"	Thank you for your comment. This introduction has been edited and no longer includes this sentence.
Northern Ireland Transfusion Committee	Full	123	19	3rd box – large bullet point not required.	Thank you for your comment. This formatting error has been amended.
Northern Ireland Transfusion Committee	Full	124	5	Change to "as well as the parameters (clinical signs) being monitored"	Thank you for your comment. This sentence has been reworded.
Northern Ireland Transfusion Committee	Full	127	General	"reactions occur during the first minutes of transfusion.(**ref**)" Insert reference here	Thank you for your comment. The reference has now been added.
Northern Ireland Transfusion Committee	Full	130 -133	General	*Table 64* Change "blood transfusions" to "red cell transfusions"	Thank you for your comment. This change has been made in some instances. In others, the study reported transfusion of different blood components not only red cells.
Northern Ireland Transfusion Committee	Full	130 -140	General	*Table 64 & 65* Convert g/dl to g/L for haemoglobin values	Thank you for your comment this has been amended for consistency throughout the guideline's 'Linking evidence to recommendations' tables and introductions.
Northern Ireland Transfusion Committee	Full	128	General	*2nd column* Complete (see section **xx7.2**, clinical evidence review for details)"	Thank you for your comment. This has now been amended.
Northern Ireland	Full	144	3	Re phrase to "the biggest risk of an adverse event	Thank you for your comment. This amendment has

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Stakeholder	Document	Page	Line	Comments	Developer's response
Transfusion Committee				occurring in the transfusion process is still human error."	been made.
Northern Ireland Transfusion Committee	Full	144	3 4	Change "A majority of these errors are made by staff who have been deemed competent in the process." to "Human error has not been averted by competency based assessments in transfusion related procedures." (As only staff that are competency assessed should be involved in the blood transfusion process, then of course it will be the majority of staff who are assessed who are making the errors)	Thank you for your comment. We have removed this sentence because it is superfluous to this brief introduction.
Northern Ireland Transfusion Committee	Full	144	9	patient's wristbands Change to "patient's identification band"	Thank you for your comment. This amendment has been made.
Northern Ireland Transfusion Committee	Full	152 153	General	*Table 69 & 70* Should there be a population restriction to "children over the age of 1 year"? as per initial exclusion criteria for this NICE guideline?	Thank you for our comment. We have not specified this cut off in each PICO as the restriction is specified clearly in section: 3.3.2 What this guideline does not cover: 'This guideline will not cover neonates and infants up to 1 year of age; and foetuses.'
Northern Ireland Transfusion Committee	Full	153	13 14	Change "blood transfusion" to "red cell transfusion"	Thank you for your comment. This has been amended to red blood cells.
Northern Ireland Transfusion Committee	Full	154	2	Change "blood" to "red cells"	Thank you for your comment. This has been amended to red blood cells.
Northern Ireland Transfusion Committee	Full	155	General	*Table 72* Change units of Hb to g/L	Thank you for your comment. We agree and have now changed the units to g/L in the full guideline. The units in tables (GRADE tables, evidence tables) reflect the reporting in the actual studies and remain

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Stakeholder	Document	Page	Line	Comments	Developer's response
					unchanged.
Northern Ireland Transfusion Committee	Full	176	General	*Recommendation 13* I could not find a definition of "acute coronary syndrome in this section or in Medical glossary. Is a restrictive red cell transfusion threshold recommended for patients with stable ischaemic heart disease or other conditions such as chemotherapy?	Thank you for your comment. We have now added the current definition 'acute coronary syndrome 'in the LETR section of the recommendation and also in the glossary.
Northern Ireland Transfusion Committee	Full	176	General	Does this guideline exclude red cell transfusion triggers and post transfusion Hb range for patients who have major haemorrhage?	Thank you for your comment. The management of patients who have major haemorrhage are out of the scope of the guideline.
Northern Ireland Transfusion Committee	Full	185	General	*Recommendation 17* Re-phrase to "Consider single-unit red blood cell transfusions for adults (or equivalent volumes, **calculated according to** body weight, for children or adults who weigh under 50 kg) …"	Thank you for your comment. We feel the wording of the recommendation is clear as it stands.
Northern Ireland Transfusion Committee	Full	186	General	*Recommendation 18* Same re phrasing suggested as 68	Thank you for your comment. We feel the wording of the recommendation is clear as it stands.
Northern Ireland Transfusion Committee	Full	188	15	"recommendations for platelet count and **particularly for platelet dose**"	Thank you for your comment. There is considerable non-compliance for both so we do not think a change is needed to the text.
Northern Ireland Transfusion Committee	Full	202	General	*Recommendation 21* Best to clarify this by making a second sentence for clinical conditions when platelet transfusion is contraindicated, ie "invasive procedures or surgery. Prophylactic platelet transfusions are contraindicated in patients with	Thank you for your comment we have edited the recommendation to indicate that prophylactic platelet transfusions should be offered to patients with a platelet count below $10x10^9$ per litre who are not bleeding or having invasive procedures or surgery, and who do not have any of the listed conditions.

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Stakeholder	Document	Page	Line	Comments	Developer's response
				Chronic bone marrow failure.." etc	
Northern Ireland Transfusion Committee	Full	205	General	*Recommendation 23* Does this higher threshold of 50-75 include those patients who are actually bleeding and undergoing surgery or another procedure?	Thank you for your comment. Patients who are actually bleeding are covered in an earlier recommendation (1.3.1 and 1.3.2).
Northern Ireland Transfusion Committee	Full	218	General	*Recommendation 27* Re phrase to " Do not routinely transfuse more than a single dose of platelets" Use of word transfusion at end of sentence is misleading.	Thank you for your comment. We have edited as per your suggestion.
Northern Ireland Transfusion Committee	Full	220	General	*Recommendation 28* Re phrase to "Consider transfusion of more than a single dose of platelets in patients with severe thrombocytopenia and bleeding in a critical site, e.g. brain, spine, eye"	Thank you for your comment. The recommendation states 'central nervous system, including eyes' and we think that this wording is sufficient.
Northern Ireland Transfusion Committee	Full	221	General	*Recommendation 29* Re phrase to "Reassess the patient's clinical status and check the platelet count after each platelet transfusion, to see if another dose of platelets is indicated"	Thank you for your comment. We have edited the recommendation to include part of your suggested edit.
Northern Ireland Transfusion Committee	Full	246	General	*Recommendation 33* Re phrase to " The minimum dose of fresh frozen plasma to transfuse is 15 ml / kg body weight"	Thank you for your comment. We have removed the recommendation around dose and have made a research recommendation on this topic. Details related to dose are discussed in the 'Linking evidence to recommendations' section.
Northern Ireland Transfusion Committee	Full	246	General	Should the guidelines include a statement that there is poor correlation between results of coagulation tests and degree of bleeding? Any evidence assessed to see if thromboelastometry gives more reliable assessment of coagulopathy?	Thank you for your comment. These issues were outside the scope of the guideline.
Northern Ireland	Full	263	General	*Recommendation 38*	Thank you for your comment. We did not specify that

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Stakeholder	Document	Page	Line	Comments	Developer's response
Transfusion Committee				Re phrase to "The minimum dose of cryoprecipitate is 2 pools for an adult and 5-10 ml/kg body weight to a maximum of 2 pools for children"	the 2 pools should be the minimum as that implies that it could be usual to give more than 2 pools in the first instance. Instead we stated the usual dose of 2 pools and made a recommendation advising that patients should be reassessed and offered further doses if needed.
Northern Ireland Transfusion Committee	Full	266	5	Change to "bleeding occurs (for example, in the brain or intestine) or, if urgent surgery is necessary"	Thank you for your comment. This amendment has been made.
Northern Ireland Transfusion Committee	Full	268	General	*Recommendation 40* Should this recommendation include a prompt to administer vitamin K along with prothrombin complex concentrate?	Thank you for your comment. We did not evaluate the effectiveness of vitamin K along with prothrombin complex concentrate so we are unable to recommend it. However, the GDG discussed the use of vitamin K with prothrombin complex concentrate and this is highlighted in the 'Linking evidence to recommendations' table in that chapter.
Northern Ireland Transfusion Committee	Full	271	General	*Recommendation 42* Re phrase to "Consider immediate prothrombin complex concentrate transfusions to reverse warfarin anticoagulation in patients having emergency surgery, taking the extent of anticoagulation and the bleeding risk into account.	Thank you for your comment. We feel the wording is clear as it stands.
Northern Ireland Transfusion Committee	Full	273	General	*Recommendation 43* Re phrase to Re-assess the patient's clinical status and monitor the international normalised ratio (INR) to confirm that warfarin anticoagulation has been adequately reversed and to determine whether additional prothrombin complex concentrate is indicated.	Thank you for your comment. We do not think that the suggested rewording is appropriate as reassessment of the patient's clinical status is not required to determine whether warfarin anticoagulation has been reversed.
Northern Ireland Transfusion	Full	295	3	*Recommendation 46 line 3* Re phrase to	Thank you for your comment. The wording of the recommendation is clear and therefore the GDG do

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Stakeholder	Document	Page	Line	Comments	Developer's response
Committee				**"what blood components or blood products they received"**	not see the need to edit it further.
PREVENTT TSC	Full	General	General	We read with interest the excellent document from NICE on Transfusion that is currently out for opinion and would like to comment on the use of iron therapy in the perioperative setting (reference P8 lines 5-7, P13 lines 6-16) The role of iron therapy to treat anaemia and/or prevent the need for blood transfusion in the surgical patient remains unclear for two key reasons. Firstly the ability to define iron deficiency in this setting, and secondly the lack of evidence on the efficacy and effect of iron therapy to prevent transfusion. Currently it is not possible to offer recommendations on iron therapy practise for surgical patients in the NHS without waiting for the results of ongoing NIHR research in this area. We would urge NICE to modify its recommendations on the use of iron in the perioperative settings as follows:- • In patients undergoing surgery, preoperative anaemia is screened and identified in a timely manner. • Anaemia is investigated and where appropriate elective surgery delayed pending investigations. • Oral iron should be prescribed to those patients with iron deficiency and anaemia further, where possible, the elective operation delayed until anaemia is corrected.	Thank you for your comment and suggestions. We acknowledge the importance of proper screening and diagnosis of anaemia as a prerequisite for surgery and we have now added a sentence to highlight this in the introduction to the guideline. The diagnosis of anaemia and other aspects relating to delaying of surgery highlighted in your comment were not evaluated as part of this guideline as they are out of the scope of this guidance. However, we have made a note of this in the section on 'other considerations' in the 'Linking evidence to recommendations' table.

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Stakeholder	Document	Page	Line	Comments	Developer's response
				• Hospitals should develop a surgical Patient Blood Management team and program of care. • Post operatively, oral iron is not prescribed as it has little effect in the post-operative period. • Further research is needed on the role of intravenous iron therapy in the preoperative patient to determine the impact on need for blood transfusion and patient outcomes. • Further research is needed on the role of iron therapy to patients with post-operative anaemia to determine if there an effect on recovery and patient rehabilitation. BACKGROUND The World Health Organisation defines anaemia as insufficient Red Blood Cell (RBC) mass circulating in the blood <13g/dL for men and <12g/dL for women (1). Anaemia is associated with impaired physical function, reduced quality of life, infection, patient morbidity and mortality (2). Pre-operative anaemia is common, affecting 30-60% of all patients undergoing major elective surgery (3). In the surgical setting anaemia compounds the stress of operation; anaemia is an independent risk factor for blood transfusion, in-patient complications, delayed hospital discharge and poorer recovery (4). DIAGNOSIS OF IRON DEFICIENCY ANAEMIA The cause for anaemia in surgical patients is often multifactorial, including blood losses, nutritional anaemia, anaemia of chronic disease (cancer	

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				and/or inflammatory disease) or a combination of these aetiologies. Two main types of anaemia affect surgical patients, iron deficiency anaemia (IDA) and anaemia of chronic disease (ACD), the latter is more common in chronically ill and hospitalised patients (5). ACD can be difficult to diagnose, often being regarded as a diagnosis of exclusion. A key feature of ACD is a disruption of normal iron homeostasis initiated by a cytokine mediated immune response, such as in chronic inflammatory disease, during infection or following surgery (5, 6,). Consequently, despite the presence of normal, or even increased, body iron stores, these cannot be mobilised or utilised, leading to a state of functional iron deficiency (FID). FID is well recognised in renal and cardiac disease and increasingly recognised as a cause for anaemia in the general surgical patient (7, 8). However, the diagnosis of anaemia due to FID remains an uncertain area in non-renal failure populations, and there is no consensus for a definition of iron deficiency in the surgical patient and no clear trial data indicating which of these patients would benefit from iron therapy. Indeed in those trials included in a recent Cochrane Database review of iron therapy for the treatment of anaemia in non-CKD populations (9) the definitions of anaemia and iron deficiency were extremely varied (10). Data in the surgical population was notably lacking and there was no evidence on how to define iron deficiency anaemia in surgical patients.	

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Stakeholder	Document	Page	Line	Comments	Developer's response
				Consequently as it is not possible to accurately diagnose or define iron deficiency anaemia in the surgical patient we urge NICE not to issue broad recommendations for treatment. IRON THERAPY The role of iron therapy to treat anaemia has considerably changed since the development of modern intravenous iron preparations in the last 5-8 years. Intravenous (IV) iron is the standard of care to treat anaemia in patients with renal failure. Its use has widened to routinely treat anaemia in patients with inflammatory bowel disease and cardiac disease. Introduction of new IV iron preparations that can be administered as a single treatment in a relatively short (15 minute) time without need for test dose, with low risk' has facilitated small trials of obstetric, gynaecological, orthopaedic and obesity surgery. These studies have observed that IV iron in selected populations may increase Hb levels before operation, and this may result in lower transfusion rates (11-18). In a recent Cochrane systematic review, 4745 participants were randomly assigned in 21 trials (9). Trials were conducted in a wide variety of clinical settings. The comparison between oral iron and inactive control revealed no evidence of clinical benefit in terms of mortality (RR 1.05, 95% CI 0.68 to 1.61; four studies, N = 659; very low-quality evidence), but oral iron did lower the proportion of participants who required blood transfusion (RR	

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Stakeholder	Document	Page	Line	Comments	Developer's response
				0.74, 95% CI 0.55 to 0.99; three studies, N = 546; very low-quality evidence). In patients receiving parenteral iron, haemoglobin levels were higher than with oral iron (MD -0.50 g/dL, 95% CI -0.73 to -0.27; six studies, N = 769; very low-quality evidence) but there were no significant differences in the proportion of participants requiring blood transfusion between parenteral iron and oral iron groups (RR 0.61, 95% CI 0.24 to 1.58; two studies, N = 371; very low-quality evidence) or between parenteral iron groups and inactive controls (RR 0.84, 95% CI 0.66 to 1.06; eight studies, N = 1315; very low-quality evidence), data were imprecise. In adult patients oral iron may work in the general population to prevent transfusion However the data is less clear in surgical patients. Indeed in the setting of preoperative surgical patients there are only three small RCTs totalling 110 patients and no significant reduction in transfusions was reported (16, 19–21). Postoperatively, there are several RCTs, four in orthopaedics alone (22-25), all showing no benefit for post-operative oral iron therapy. For intravenous iron only one trial exists that is heterogeneous and showed no impact on transfusion outcomes (26). There is no evidence of effect for oral iron in the post-operative patient. These are important points as, while there is no good evidence either of efficacy or effect of iron therapy, iron therapy is not without risk. Oral iron is	

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Stakeholder	Document	Page	Line	Comments	Developer's response
				recognised to have significant gastro-intestinal side effects (27) and intravenous iron is associated with a potential increased risk of infection (28). NIHR research in this field of medicine should be supported to determine the efficacy of intravenous iron to treat anaemia and prevent the need for blood transfusion in the surgical patient and to ensure that the rates of adverse events in patients receiving the intervention are not causing patient harm (29). Intravenous iron therapy in the perioperative setting should not be recommended outside of a clinical trial without clear evidence of efficacy to reduce transfusion or effect on patient outcomes in surgical patients. REFERENCES Kramer&Zimmerman. Nutritional Anemia Book. Zimmerman K, editor. Basel, Switzerland: Sight and Life Press; 2007. 30. Spahn DR. Anemia and patient blood management in hip and knee surgery: a systematic review of the literature. Anesthesiology. 2010 Aug;113(2):482-95. 31. Shander A, Knight K, Thurer R, Adamson J, Spence R. Prevalence and outcomes of anemia in surgery: a systematic review of the literature. Am J Med. 2004 Apr 5;116 Suppl 7A:58S-69S. 32. Munoz M, Garcia-Erce JA, Diez-Lobo AI, Campos A, Sebastianes C, Bisbe E. [Usefulness of the administration of	

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Stakeholder	Document	Page	Line	Comments	Developer's response
				intravenous iron sucrose for the correction of preoperative anemia in major surgery patients]. Med Clin (Barc). 2009 Mar 7;132(8):303-6. 33. Weiss G, Goodnough LT. Anemia of chronic disease. N Engl J Med. 2005 Mar 10;352(10):1011-23. 34. Nemeth E, Rivera S, Gabayan V, Keller C, Taudorf S, Pedersen BK, et al. IL-6 mediates hypoferremia of inflammation by inducing the synthesis of the iron regulatory hormone hepcidin. J Clin Invest. 2004;113(9):1271-6. 35. Anker SD, Comin Colet J, Filippatos G, et al. Ferric Carboxymaltose in Patients with Heart Failure and Iron Deficiency. New England Journal of Medicine 2009; 361: 2436–48. 36. Hsu C-Y, McCulloch CE, Curhan GC. Epidemiology of anemia associated with chronic renal insufficiency among adults in the United States: results from the Third National Health and Nutrition Examination Survey. Journal of the American Society of Nephrology 2002; 13: 504–10. 37. Gurusamy KS, Nagendran M, Broadhurst JF, Anker SD, Richards T. Iron therapy in anaemic adults without chronic kidney disease. Cochrane Database Syst Rev. 2014 Dec 31;12:CD010640. doi: 10.1002/14651858.CD010640.pub2.	

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				38. Clevenger B, Richards T.Pre-operative anaemia. Anaesthesia. 2015 Jan;70 Suppl 1:20-8, e6-8. doi: 10.1111/anae.12918. 39. Theusinger OM, Leyvraz PF, Schanz U, Seifert B, Spahn DR. Treatment of iron deficiency anemia in orthopedic surgery with intravenous iron: efficacy and limits: a prospective study. Anesthesiology. 2007 Dec;107(6):923-7. 40. Cuenca J, Garcia-Erce JA, Munoz M, Izuel M, Martinez AA, Herrera A. Patients with pertrochanteric hip fracture may benefit from preoperative intravenous iron therapy: a pilot study. Transfusion. 2004 Oct;44(10):1447-52. 41. Garcia-Erce JA, Cuenca J, Munoz M, Izuel M, Martinez AA, Herrera A, et al. Perioperative stimulation of erythropoiesis with intravenous iron and erythropoietin reduces transfusion requirements in patients with hip fracture. A prospective observational study. Vox Sang. 2005 May;88(4):235-43. 42. Cuenca J, Garcia-Erce JA, Martinez F, Perez-Serrano L, Herrera A, Munoz M. Perioperative intravenous iron, with or without erythropoietin, plus restrictive transfusion protocol reduce the need for allogeneic blood after knee replacement surgery. Transfusion. 2006 Jul;46(7):1112-9.	

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Stakeholder	Document	Page	Line	Comments	Developer's response
				43. Bisbe E, Rodriguez C, Ruiz A, Saez M, Castillo J, Santiveri X. [Preoperative use of intravenous iron: a new transfusional therapy]. Rev Esp Anestesiol Reanim. 2005 Nov;52(9):536-40. 44. Kim YH, Chung HH, Kang SB, Kim SC, Kim YT. Safety and usefulness of intravenous iron sucrose in the management of preoperative anemia in patients with menorrhagia: a phase IV, open- label, prospective, randomized study. Acta Haematol. 2009;121(1):37-41. 45. Serrano-Trenas JA, Ugalde PF, Cabello LM, Chofles LC, Lazaro PS, Benitez PC. Role of perioperative intravenous iron therapy in elderly hip fracture patients: a single-center randomized controlled trial. Transfusion. 2011 Jan;51(1):97-104. 46. Diez-Lobo AI, Fisac-MartÍN MP, Bermejo-Aycar I, Munoz M. Preoperative intravenous iron administration corrects anemia and reduces transfusion requirement in women undergoing abdominal hysterectomy. Transfusion alternatives in transfusion medicine. 2007;9(2):114-9. 47. Lidder PG, Sanders G, Whitehead E, Douie WJ, Mellor N, Lewis SJ, et al. Pre-operative oral iron supplementation reduces blood transfusion in colorectal surgery – a prospective, randomised, controlled trial.	

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				Annals of The Royal College of Surgeons of England 2007;89(4):418–21. 48. Noble E, Edwards T, Durran A, Mellor N, Hosie KB. A prospective blinded placebo controlled randomised trial of intravenous iron supplementation in patients undergoing colorectal cancer surgery. Colorectal disease 2009; Conference: Association of Coloproctology of Great Britain and Ireland Annual Meeting Harrogate United Kingdom. Conference Start: 20090608 Conference End: 20090611. Conference Publication: (Supplement S1):31. 49. Ng O, Keeler B, Mishra A, Simpson A, Neal K, Brookes MJ, Acheson AG. Cochrane Database Syst Rev. 2015 Apr 2. NJ0192 Iron therapy for pre-operative anaemia http://www.cochrane.org/CD011588/INJ_iron-therapy-for-pre-operative-anaemia 50. Mundy GM1, Birtwistle SJ, Power RA. The effect of iron supplementation on the level of haemoglobin after lower limb arthroplasty. J Bone Joint Surg Br. 2005 Feb;87(2):213-7. 51. Weatherall M1, Maling TJ. Oral iron therapy for anaemia after orthopaedic surgery: randomized clinical trial. ANZ J Surg. 2004 Dec;74(12):1049-51. 52. Sutton PM1, Cresswell T, Livesey JP, Speed K, Bagga T. Treatment of anaemia after joint replacement. A double-blind,	

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				randomised, controlled trial of ferrous sulphate versus placebo. J Bone Joint Surg Br. 2004 Jan;86(1):31-3. 53. Parker MJ. Iron supplementation for anemia after hip fracture surgery: a randomized trial of 300 patients. J Bone Joint Surg Am. 2010 Feb;92(2):265-9. doi: 10.2106/JBJS.I.00883. 54. Bisbe E, Moltó L, Arroyo R, Muniesa JM, Tejero M. Randomized trial comparing ferric carboxymaltose vs oral ferrous glycine sulphate for postoperative anaemia after total knee arthroplasty. Br J Anaesth. 2014 Sep;113(3):402-9. doi: 10.1093/bja/aeu092. Epub 2014 Apr 29. 55. Tolkien Z, Stecher L, Mander AP, Pereira DI, Powell JJ. Ferrous sulfate supplementation causes significant gastrointestinal side-effects in adults: a systematic review and meta-analysis. PLoS One. 2015 Feb 20;10(2):e0117383. doi: 10.1371/journal.pone.0117383. eCollection 2015. 56. Litton E, Xiao J, Ho KM. Safety and efficacy of intravenous iron therapy in reducing requirement for allogeneic blood transfusion: systematic review and meta-analysis of randomised clinical trials. BMJ. 2013 Aug 15;347:f4822. doi: 10.1136/bmj.f4822. Review. 57. Richards T, Clevenger B, Keidan J, Collier	

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Stakeholder	Document	Page	Line	Comments	Developer's response
				T, Klein AA, Anker SD, Kelly JD. PREVENTT: preoperative intravenous iron to treat anaemia in major surgery: study protocol for a randomised controlled trial. Trials. 2015 Jun 4;16(1):254. doi: 10.1186/s13063-015-0774-2.	
Royal College of General Practitioners	Full	General	General	This is a comprehensive piece of work. It will be very useful to those involved in transfusion activities.	Thank you for participating in the consultation process.
Royal College of Nursing	Full	General	General	No comments to submit to inform on the above guideline consultation at this time.	Thank you for participating in the consultation process.
Royal College of Paediatrics and Child Health	Full	10.1 69	152	I = exchange transfusion in this (and subsequent) PICO – typo? It's written as makes sense for a top-up transfusion.	Thank you for your comment. The population for this review question excluded patients who received exchange transfusions as noted in the PICO table. The interventions (I) include restrictive and liberal haemoglobin thresholds which are compared to one another.
Royal College of Surgeons Edinburgh	Full	General	General	Cardiac surgical patients are different in a way that cardiopulmonary bypass is utilised for their surgery and bleeding is encountered more frequently leading to blood transfusion. It is surprising that this GDG does not include a cardiac surgeon.	Thank you for your comment. Unfortunately we had to keep the group to a manageable size and couldn't have all specialities. We had some difficulty recruiting any surgeons to the group as there was a lack of response to our adverts. However we did manage to recruit a surgeon in the end (although not cardiac). The Society for Cardiothoracic Surgery in Great Britain and Ireland are stakeholders and has contributed to this stakeholder consultation.
Royal College of Surgeons Edinburgh	Full	13 65	19 6	This guideline does not exclude patients who refuse blood components (eg: Jehovah's witness…Pg 21 Line 2 - 13) and therefore, the recommendation of not offering pre-operative erythropoietin to this group of patients undergoing cardiac surgery with	Thank you for your comment. This was considered by the GDG and a statement that EPO may be considered in patients who refuse blood transfusions, has now been included in the recommendation for EPO.

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Stakeholder	Document	Page	Line	Comments	Developer's response
				cardiopulmonary bypass is concerning.	Please also see the other considerations section in the 'Linking evidence to recommendations' table.
Royal College of Surgeons Edinburgh	Full	13-14 120	41 1	Recommendation to consider intra-operative cell salvage and Tranexamic acid for 'complex cardiac surgery' could be changed to 'cardiac surgery with use of cardiopulmonary bypass'.	Thank you for your comment. This recommendation refers to patients undergoing surgical procedures where blood loss is expected to be greater than 1 litre. The GDG have clarified the wording of these surgical procedures to 'cardiac and complex vascular surgery'. Complex cardiac surgery includes more than just cardiac surgery with the use of cardiopulmonary bypass.
Royal College of Surgeons Edinburgh	Full	155	1	Recently published TITRe2 RCT with over 2000 patients has not been included in this draft (Murphy et al., Liberal or Restrictive Blood transfusion after cardiac surgery, N Engl J Med 2015; 372:997-1008). It reported significantly higher mortality in the restrictive group compared to the liberal group with no difference in total cost.	Thank you for your comment. The TITRe2 study was not included as it was published after the cut-off date for searches for evidence for the guideline. We have now reviewed this evidence and have included this study in the RBC thresholds review in our guideline. The evidence showed clinically important benefit with restrictive strategies with respect to the number of patients transfused and number of units transfused. The evidence suggested that there was no difference between the groups with respect to mortality, adverse events, new cardiac events, length of hospital stay, quality of life and infection, but there was some uncertainty. We would like to highlight that the inclusion of the TITRe2 trial in the meta-analysis did not have an impact on the current recommendations.
Royal College of Surgeons Edinburgh	Full	14 176 179	11 -13 27 1	Use of restrictive protocol (Transfusion threshold; Hb < 70 g/L) in patients undergoing cardiac surgery will be harmful.	Thank you for your comment. The GDG discussed the applicability of the transfusion threshold recommendation with respect to patients undergoing cardiac surgery and this is reflected in the LETR for this recommendation.

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Stakeholder	Document	Page	Line	Comments	Developer's response
Royal College of Surgeons Edinburgh	Full	14-15	General	Often, patients undergoing cardiac surgery after an acute coronary syndrome have dysfunctional platelets due to antiplatelet agents which cannot be stopped. Platelet transfusion recommendations in this guideline are purely based on platelet counts. Maybe the guideline should mention the role of platelet function studies/thromboelastography to aid transfusion in this group of patients.	Thank you for your comment. We agree with your comment. The LETR has been edited to include the following: 'and platelet function studies for example in patients undergoing cardiac surgery (refer to NICE guidelines on TEG).'
Royal College of Paediatrics and Child Health	Full	13 , 14	176 - 180	The conclusion reached is based around bleeding (usually acutely) or critical illness as a cause for anaemia. Marrow suppression from chemotherapy is very poorly investigated (1 trial comparing 10 vs 12 triggers – well out of date with current practice) and has a strikingly different aetiology. This is not explored in the 'linking' sections of the references. Should there not also be a research recommendation considering the appropriate values to start transfusions from, and the dose to give, in those with solid and haematological malignancies?	Thank you for your comment. In this guideline we were not able to go into detail about different clinical conditions. We agree that there are a number of specific clinical conditions such as haematology where further clinical trials of thresholds for red cell transfusions could be considered (both in adults and children). However, the GDG did not prioritise this for its research recommendations.
Royal College of Paediatrics and Child Health	Full	21	202	The recommendation in the no-bleeding pt (excluding the ITP/HIT/TTP gang) to give prophylactic plts <10 ignores the studies in chemo patients where fever was used to trigger at plts <20 in the trial protocol (Rebulla 1997) and I'm not sure if this was considered in non-compliance issues within the studies where not mentioned, as it's not explicitly discussed. It's in the final issues area – explicitly NOT increasing the threshold in the setting of fever/antibiotics – but the justification is not explained.	Thank you for your comment. No evidence was found to routinely raise the threshold for patients with fever, and this was a consensus recommendation by the GDG.

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Stakeholder	Document	Page	Line	Comments	Developer's response
Royal College of Paediatrics and Child Health	Full	10	-	No comment is made as to how weight-based doses of red cells should be accomplished for children.	Thank you for your comment. The GDG discussed this and noted in the LETR that for children likely to require repeated single-unit equivalent transfusions in order to bring their Hb up to the recommended target, a higher volume may be considered (up to a maximum of a single unit) in order to reduce donor exposure. The GDG noted that there are formulae in common use to guide the appropriate transfusion volume per kilogram weight for a given rise in Hb.
Scottish Clinical Transfusion Advisory Committee	Full	General	General	Although I realise why the Guideline Summary has a lot of repetition	Thank you for your comment. Some repetition is unavoidable.
Scottish Clinical Transfusion Advisory Committee	Full	19		RBC recommendations – the 3rd bullet point is a duplicate of the 2nd bullet point Flow chart is excellent but very "wordy"	Thank you for your comment, we have removed the duplication. This flowchart is based on the guideline's recommendations, so we are unable to use shorter phrasing.
Scottish Clinical Transfusion Advisory Committee	Full	20	11	Extra Space between "common cause"	Thank you for your comment, this has been amended.
Scottish Clinical Transfusion Advisory Committee	Full	20	20	Could there be more emphasis on Identification of patients as this is more oftent than not the reason for errors in the transfusion process	Thank you for your comment. Patient identification was only considered in relation to electronic means for patient identification. The GDG did discuss the importance of accurate patient identification when considering the evidence presented for this review. Their discussions are summarised in the linking evidence to recommendations section of the chapter and states: '….Moreover, mandatory competency training could be linked to the transfusion process.

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Stakeholder	Document	Page	Line	Comments	Developer's response
					All staff should be aware of the steps of the patient identification process and the rationale for it, and know how to revert to a manual system of cross checking and verification if the need arises. The GDG also noted that there is always a chance of human error, even in staff who have been trained and assessed as being competent in the transfusion process. The electronic systems help in minimising the chance of human error.'
Scottish Clinical Transfusion Advisory Committee	Full	20	24, 55	Should this be per 1000 population rather than 100,000	Thank you for your comment, this has been amended.
Scottish Clinical Transfusion Advisory Committee	Full	20	33	Should the patient be mentioned first before cost and waste	Thank you for your comment. We have edited the text as per your suggestion.
Scottish Clinical Transfusion Advisory Committee	Full	40	23	Text not clearly defined in the diagram	Thank you for your comment, this has been amended.
Scottish Clinical Transfusion Advisory Committee	Full	97	3	Graph (figure 3) looks blurred compared to one below Figure 4 – figure 5 same comment (?is it due to PDP format)	Thank you for your comment. This has now been amended.
Scottish Clinical Transfusion Advisory Committee	Full	123	12	Would it be better to state that Trusts /hospitals should have a policy for when monitoring should take place in addition to the comments made	Thank you for your comment, we have added the following statement to the 'Linking evidence to recommendations' table in the 'other considerations' section: 'frequency of monitoring would depend on the type of patient receiving a transfusion, for example, children and unconscious patients may

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Stakeholder	Document	Page	Line	Comments	Developer's response
					require more frequent monitoring during blood transfusions'.
Scottish Clinical Transfusion Advisory Committee	Full	261	General	Different fonts in table	Thank you for your comment, this has been amended throughout the guideline.
Scottish Clinical Transfusion Advisory Committee	Full	281	General	Different fonts in table.	Thank you for your comment. This has been amended throughout the guideline.
Scottish National Blood Transfusion Service, Better Blood Transfusion Team	Full	13	39	I would be concerned that this statement may discourage some from considering or pursuing the initial development of cell salvage as an alternative to transfusion. I appreciate that the evidence indicates that cell salvage in combination with TXA is more appropriate. Could the statement be worded more positively eg Routinely offer TXA alongside cell salvage (unless contraindicated)?	Thank you for your comment. The GDG were keen to make a strong recommendation to discourage the use of cell salvage on its own based on the evidence of clinical and cost effectiveness. The evidence supports the recommendation not to use cell salvage without tranexamic acid. We appreciate your suggestion regarding wording this positively, but believe that the next recommendation to use cell salvage in combination with tranexamic acid addresses this to an extent.
Scottish National Blood Transfusion Service, Better Blood Transfusion Team		19		RBC recommendations – the 3rd bullet point is a duplicate of the 2nd bullet point	Thank you for your comment, this has been edited.
Scottish National Blood Transfusion Service, Better Blood Transfusion Team		20	24,25	Is this correct? The comparative RCC transfusion rate usually used is number of RCC per 1,000 population (rather than 100,000)	Thank you for your comment this has been amended.
Scottish National		123	13	Suggest this statement refers to blood components	Thank you for your comment, this has been edited.

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Stakeholder	Document	Page	Line	Comments	Developer's response
Blood Transfusion Service, Better Blood Transfusion Team				rather than blood products	
Scottish National Blood Transfusion Service, Better Blood Transfusion Team		127	2	Other considerations (2nd para): suggest better to state that 'the majority of *serious* acute transfusion reactions occur during the first minutes of transfusion.'	Thank you for your comment. We have edited this as suggested.
Scottish National Blood Transfusion Service, Better Blood Transfusion Team		259	36	Other considerations (para 9): sentence is incomplete	Thank you for your comment. The sentence has been completed and now reads as follows: Each pool of Methylene Blue cryoprecipitate contains six single units.
Scottish National Blood Transfusion Service, Better Blood Transfusion Team		295	46	Transfusion related information is currently not well or consistently documented in discharge summaries in our organisation: this would perhaps be improved if the standard letter template used included a specific prompt for this information.	Thank you for your comment. We are unable to design documentation for use in hospitals nationwide – this would be outside NICE's remit, however we have added a sentence to the 'other considerations' section of the 'Linking evidence to recommendations' table, suggesting that provision of information to GPs about receipt of transfusions in-hospital could be provided automatically on electronic discharge summaries.
Serious Hazards of Transfusion (SHOT)	Full	General	General	General comments – there is a great deal of repetition, even within the short version and in summary sections. The guideline is difficult to read and not easily accessible to the general reader. To understand it, It requires one to read in detail the methodology.	Thank you for your comment. We're sorry you felt that that guideline was difficult to read. We use a standard template so that for each section readers know where to find the evidence that was the basis for each recommendation. Sometimes, in order to be complete, these means there can appear to be some repetition.

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Stakeholder	Document	Page	Line	Comments	Developer's response
				Tables should have headings for the columns on every page.	We have also revised the tables throughout the document and each page now includes a header row.
				Overall this guideline is disappointing. It does not seem to say anything which is not already included in the several carefully written expert guidelines from the British Committee in Haematology, only one of which is referenced.	We believe that we have added to the field by performing systematic reviews and analysis of the economic literature in the areas we've covered. We've also performed a network meta-analysis and produced an economic model, which are novel pieces of work.
				Several references are made to application of the recommendations for adults to also be applicable to children but this is worrying. While this may be appropriate for older children, say from 10 yrs and upwards, the under-5 years group are significantly different in many ways, particularly in relation to haemostasis and thrombosis risks.	With regards to recommendations for children, the GDG have extrapolated from adult recommendations to children when deemed appropriate. With regards to recommendations for children, the GDG have extrapolated from adult recommendations to children when deemed appropriate. With regards to recommendations for children, the GDG have extrapolated from adult recommendations to children when deemed appropriate.
				The one area of particular value is the section on patient information and consent and the resulting recommendations. Since the publication of the SaBTO recommendation there has been discussion about whether it is feasible to obtain consent and it	With regards to recommendations for children, the GDG have extrapolated from adult recommendations to children when deemed appropriate. With any guideline we are unable to cover all areas

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Stakeholder	Document	Page	Line	Comments	Developer's response
				is important to have the back up of this guidance. Additional comments from members of the group: I am unsure what the real purpose of this document was-an economic evaluation or a guideline or a mix of both. It states "The remit for this guideline is: to develop a cross cutting clinical guideline on the assessment for and management of transfusion. " Does it really achieve this aim? The document is hard to use and without going through with a tooth comb, I am unclear if there are any substantial differences from the existing BCSH guidance. You remember the muddle there used to be over anti-D with RCOG and BCSH guidelines both existing, slightly out of sync. Also I very much dislike the listing of conditions where a specific component should NOT be used, as the fact that these are NOT indications is very unclear on quick scanning Is the term 'one platelet dose' understood by the reader for whom this is aimed? It is defined in the detailed text but may benefit from earlier explanation There is no mention of consent which has been much discussed by SaBTO- I am not sure why or maybe I am out of date	of a field and transfusion is no exception. At scoping, registered stakeholders helped us prioritise the areas that would most benefit from an analysis of the clinical and economic literature and recommendations from NICE. Regarding 'one platelet dose', the description is included in the 'Linking evidence to recommendations' section for platelet transfusion doses.

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Stakeholder	Document	Page	Line	Comments	Developer's response
				I am unclear why PCC is included! Overall I suppose it is a useful review of the woefully inadequate literature on transfusion but I am not clear what purpose the document serves as to my mind it does not really address the aim as stated	The matter of patient consent is outside the scope of the guideline; however, it is mentioned in the section on 'patient-centred care' in the short version. PCC was highlighted by stakeholders for inclusion in the guideline during the scoping stage and was therefore included. We are glad that you think the review is useful and we believe that if the recommendations are implemented fully then care for patients will be improved.
Serious Hazards of Transfusion (SHOT)	Full	General	General	General comments – there is a great deal of repetition, even within the short version and in summary sections. The guideline is difficult to read and not easily accessible to the general reader. To understand it, It requires one to read in detail the methodology. Tables should have headings for the columns on every page. Overall this guideline is disappointing. It does not seem to say anything which is not already included in the several carefully written expert guidelines from the British Committee in Haematology, only one of which is referenced.	Thank you for your comment. We're sorry you felt that the guideline was difficult to read, we use a standard template so that for each section readers know where to find the evidence that was the basis for each recommendation. Sometimes, in order to be complete, these means there can appear to be some repetition. We believe that we have added to field by performing systematic reviews and analysis of the economic literature in the areas we've covered. We have also performed a network meta-analysis and produced an economic model, which are novel pieces of work.

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Stakeholder	Document	Page	Line	Comments	Developer's response
				Several references are made to application of the recommendations for adults to also be applicable to children but this is worrying. While this may be appropriate for older children, say from 10 yrs and upwards, the under-5 years group are significantly different in many ways, particularly in relation to haemostasis and thrombosis risks. The one area of particular value is the section on patient information and consent and the resulting recommendations. Since the publication of the SaBTO recommendation there has been discussion about whether it is feasible to obtain consent and it is important to have the back up of this guidance. Additional comments from members of the group: I am unsure what the real purpose of this document was-an economic evaluation or a guideline or a mix of both. It states "The remit for this guideline is: to develop a cross cutting clinical guideline on the assessment for and management of transfusion. " Does it really achieve this aim? The document is hard to use and without going through with a tooth comb, I am unclear if there are any substantial differences from the existing BCSH guidance. You remember the muddle there used to be over anti-D with RCOG and BCSH guidelines both existing, slightly out of sync. Also I very much dislike the listing of conditions where a specific component should NOT be	With regards to recommendations for children, the GDG have extrapolated from adult recommendations to children when deemed appropriate. With any guideline we are unable to cover all areas of a field and transfusion is no exception. At scoping registered stakeholders helped us prioritise the areas that would most benefit from an analysis of the clinical and economic literature and recommendations from NICE.

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Stakeholder	Document	Page	Line	Comments	Developer's response
				used, as the fact that these are NOT indications is very unclear on quick scanning Is the term 'one platelet dose' understood by the reader for whom this is aimed? It is defined in the detailed text but may benefit from earlier explanation There is no mention of consent which has been much discussed by SaBTO- I am not sure why or maybe I am out of date I am unclear why PCC is included! Overall I suppose it is a useful review of the woefully inadequate literature on transfusion but I am not clear what purpose the document serves as to my mind it does not really address the aim as stated	Regarding 'one platelet dose', the description is included in the 'Linking evidence to recommendations' section for platelet transfusion doses. The matter of patient consent is outside the scope of the guideline, however it is mentioned in the section on 'patient-centred care' in the short version. PCC was highlighted by stakeholders for inclusion in the guideline during the scoping stage and was therefore included. We are glad that you think the review is useful and we believe that if the recommendations are implemented fully then care for patients will be improved.
Serious Hazards of Transfusion (SHOT)	Short	4	11-20	Sections on 'Safeguarding children' and 'Medicines' don't make sense in this publication.	Thank you for your comment. This has been amended.
Serious Hazards of Transfusion (SHOT)	Short	19	13	Consider including recommendation from SHOT (p26 Annual SHOT Report 2013) about giving patients a 24 hour contact number to report any	Thank you for your comment. We are unable to provide this level of detail in our guideline, but if hospitals/trusts wish to do so, they may implement

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Stakeholder	Document	Page	Line	Comments	Developer's response
				symptoms post transfusion.	this locally.
Serious Hazards of Transfusion (SHOT)	Full	12	21-22	Brackets say - (or equivalent volumes, calculated based on body weight, for children or adults who weigh under 50 kg) With respect to 'adults who weigh under 50 kg' there is no reference for this as a separate guideline. If that doesn't exist anywhere, maybe it should actually be included as a specific recommendation within this guideline. Also, this is not consistently mentioned throughout the paper when referring to body weight calculations for children e.g. p19 FFP recommendations.	Thank you for this comment. We have amended the recommendation and the 'Linking evidence to recommendations' statement to refer to a less specific body weight for adults. It was felt that this dosage recommendation was not relevant for FFP, as dose for this component is calculated in ml/kg for all age groups.
Serious Hazards of Transfusion (SHOT)	Full	20	2	Figures given for NHS Blood and Transplant components issued. Does NICE include all of Wales and if so should these figures include components supplied by the Welsh Blood Service?	Thank you for your comment. The figures for transfusion are for NHSBT only and are used to provide an indication of the volume of blood used.
Serious Hazards of Transfusion (SHOT)	Full	20	6	Estimate given as "the number of patients transfused is likely to be 10 – 20% less" – how was this figure derived? Reduction in blood usage may not equate to a reduction in the number of patients transfused, but might reflect the amount of blood given to each patient.	Thank you for your comment. The figure is a reflection of the known reduction in red cell use in England over this period. These data are provided in reference 4 of the introduction of the full version (Goodnough T 2015). We agree this reduction will be due to a combination of both a reduction in patients transfused and units/patient.
Serious Hazards of Transfusion (SHOT)	Full	20	20	'Accurate patient identification is a crucial step. – this seems to be the only place where patient identification is mentioned NOT in conjunction with a recommendation for electronic patient	Thank you for your comment. Patient identification was only considered in relation to electronic means for patient identification in the scope of this guideline. The GDG did discuss the importance of

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				identification. The guideline should mention the importance of positive patient identification when there is no electronic system available. SHOT data repeatedly show failures in this are a major reason for wrong transfusions, both at the time of taking the pre-transufsion blood sample, and at the time of setting up the transfusion. It is our experience that many hospital staff do not understand how to do this, i.e. to ask the patient to say their name and date of birth and not simply say 'are you Joe Bloggs?'.	accurate patient identification when considering the evidence presented for this review. Their discussions are summarised in the linking evidence to recommendations section of the chapter and states: '….Moreover, mandatory competency training could be linked to the transfusion process. All staff should be aware of the steps of the patient identification process and the rationale for it, and know how to revert to a manual system of cross checking and verification if the need arises. The GDG also noted that there is always a chance of human error, even in staff who have been trained and assessed as being competent in the transfusion process. The electronic systems help in minimising the chance of human error.'
Serious Hazards of Transfusion (SHOT)	Full	20	33	Reference 'e' against number "20%[e]" is incorrect. That figure is not derived from SHOT data and is not quoted in that referenced SHOT Report. Perhaps needs to quote a National Comparative Audit publication?	Thank you for your comment. This has been amended. It is now quoted from the NHS Blood & Transplant. National Comparative Audit of Blood Transfusion programme.
Serious Hazards of Transfusion (SHOT)	Short	3	2	What is meant by 'common'? I do not think blood transfusion is common in clinical practice – this statement needs to be in relation to something.	Thank you for your comment, the following sentence goes on to detail the facts and figures for use of Transfusion in the UK.
Serious Hazards of Transfusion (SHOT)	Short	3	13	Suggest use updated numbers from current SHOT report (data for 2014) published on June 27th, page 24, risk of transfusion-related death (imputability 1-3) 5.6 per million components issued (approx 1 in 180,000) and major morbidity 63.5 per million components issued (approx 1 in 16,000)	Thank you for your comment. All quoted statistics have been updated.
Serious Hazards of	Short	3	16	The para under this contains points from NCA	Thank you for your comment. Final edited versions

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Transfusion (SHOT)				which should also be referenced. Only the first bullet point relates to data from SHOT.	of the Short guideline will not feature any references. However, the reference has been updated in the full version of the guideline.
Serious Hazards of Transfusion (SHOT)	Short	15	3	The restriction on use of platelet transfusions in TTP and HIT applies here also and this recommendation reads as if it may be acceptable to use platelet transfusions in these circumstances	Thank you for your comment we have edited the recommendation to indicate that prophylactic platelet transfusions should be offered to patients with a platelet count below $10x10^9$ per litre who are not bleeding or having invasive procedures or surgery, and who do not have any of the listed conditions.
Serious Hazards of Transfusion (SHOT)	Short	15	22	Many would not agree with this blanket recommendation for threshold of 50 for transfusion of platelets for 'invasive procedures'. I would use a more variable threshold depending on the cause of thrombocytopenia and the nature of the procedure	Thank you for your comment. The wording of recommendations 22, 23 and 24 are to be read together and indicate that 50 x 10^9/L is not a 'blanket' recommendation.
Serious Hazards of Transfusion (SHOT)	Short	16	10	'Do not routinely…' – this is an inappropriate introduction to the idea of transfusion of platelets to patients with TTP or HIT where platelet transfusions are contra-indicated, and in ITP also. People unfamiliar with these conditions may not understand the importance of not giving platelets inappropriately. It can be dangerous in TTP and HIT.	Thank you for your comment. The rationale is described in the 'trade-off between clinical benefit and harm' section and includes the point that there are exceptions to the recommendation including major bleeding, hence the 'do not routinely' wording.
Serious Hazards of Transfusion (SHOT)	Short	17	12	What is the definition of 'abnormal coagulation'? The relationship between derangements of standard coagulation tests and bleeding is poor, particularly in children and people with liver disease.	Thank you for your comment. The GDG acknowledges the lack of evidence. An abnormal PT or APTT ratio of above 1.5 is suggested as an abnormal result and this has now been clarified in all relevant 'Linking evidence to recommendations' section in this chapter. We have also now acknowledged the poor relationship between derangements of standard coagulation tests and bleeding.

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Serious Hazards of Transfusion (SHOT)	Full	20	12-13	This does not make sense '..for example TACO'	Thank you for your comment, this has been edited.
Serious Hazards of Transfusion (SHOT)	Full	20	16	The first bullet point data derived from SHOT not NCA, other bullet points correctly derived from NCA	Thank you for your comment. We have indicated that the data for this section comes from SHOT as well as the NCA.
Serious Hazards of Transfusion (SHOT)	Full	294		'currently NHSBT does not provide information in booklets which are specific to children of different ages' – this is a bit surprising as work was done on this a few years ago in the 'appropriate use of blood' group resulting in two books for children of different ages with pictures etc. What has happened to these? Models may also exist in Children's hospitals. Was this source of evidence considered, particularly in making the recommendations?	Thank you for your comment. We have amended this typo and changed it to'…the NHSBT does provide information in booklets...'
Sheffield Children's Hospital	Full	1.3.3	1.3.3	'give prophylactic platelet transfusion if level less than 10.' Should one of the exceptions to this be ITP as our experience is that children without symptomatic bleeding are not usually transfused in ITP at a level of 10.	Thank you for your comment. We've already excluded autoimmune thrombocytopenia (also known as ITP) in this recommendation.
Sheffield Children's Hospital	Full	General	General	There is no paediatric definition of major haemorrhage in this guideline	Thank you for your comment. There is a definition of major haemorrhage included for both adults and children in the short version of the guideline and we have added this to the glossary of the full guideline.
Society for Cardiothoracic Surgery in Great Britain and Ireland	Full	General	General	There is a lack of consistency with respect to the objectives of the guidelines. The principal objectives for the iron/ erythropoietin therapy recommendations appear to be to reduce transfusion. The principal objective for the red cells appears to be to improve clinical outcomes. The	Thank you for your comment. The overall objectives of the guideline were to ensure patient safety, improve clinical outcomes and optimise use of blood products for transfusion. Certain reviews of the guideline had one or more of these as their primary objective, for example, the section on alternatives to

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				principal objective for the platelet guidelines appears to be a reduction in bleeding. This reflects the limitations of the data and the studies included, but this should not then be directly translated into limitations within the recommendations.	blood transfusion gave equal importance to the optimisation of blood products and clinical outcomes. Accordingly, outcomes were finalised a priori for each review based on the objective of that review and the blood product being evaluated. These were classified as critical or important in each review protocol after discussion with the GDG (please refer to the top row in the 'Linking evidence to recommendations' table for each recommendation). The availability, or lack of data, did not influence the objective of the review. However, the availability/ lack of evidence did influence the strength of the recommendation and this is reflected in the wording of the recommendations and explained in the section on 'quality of evidence' in the 'Linking evidence to recommendations' statement.
Society for Cardiothoracic Surgery in Great Britain and Ireland	Full	General	General	Transfusion in isolation is not a clinically important endpoint. For example there are multiple blood management interventions that have been shown in high quality trials to reduce transfusion rates and also to increase mortality (aprotinin, recombinant activated factor VII, restrictive transfusion thresholds in cardiac surgery). This is not considered in any of the recommendations. The principal objective of any of the interventions should be to improve clinical outcomes that are important to patients. Transfusion should be a secondary consideration.	Thank you for your comment. The overall objectives of the guideline were to ensure patient safety, improve clinical outcomes and optimise use of blood products for transfusion. In line with the above objectives, the GDG discussed the outcomes and agreed that the number of people transfused and the number of units transfused were critical outcomes. Whilst recognising that these are not clinical outcomes the GDG felt that these outcomes gave useful information about the use of a scare resource and were a surrogate for clinical outcomes. The GDG noted the evidence for each of the outcomes, including its quality and strength, and then discussed the trade-offs between benefits and harms for each recommendation. This brought

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					together evidence across outcomes for each review and summarised the GDG's discussion on the rationale for the recommendation. For details, please refer to the section on 'trade-offs between clinical benefits and harms' in the 'Linking evidence to recommendations' table for each recommendation.
Society for Cardiothoracic Surgery in Great Britain and Ireland	Full	General	General	The only conclusion that should be made where the available evidence is of low quality, and there is uncertainty as to clinical benefit, is that more research is required. However despite this being the case in almost every question evaluated by the guideline committee only 3 suggestions are made for further research.	The methodology of NICE guidelines allows the GDG to make consensus based recommendations in the absence of evidence. For each review the GDG considered whether it was better to make a practice recommendation in the absence of evidence or make a recommendation for research. There are several cases where the GDG felt it was better to make a practice recommendation as there was a general consensus of what good practice should be rather than wait for future research.
Society for Cardiothoracic Surgery in Great Britain and Ireland	Full	General	General	The economic analyses appear to be predominantly focused on the balance between the cost of the intervention and the costs of the transfusions avoided (threshold analyses). This increases the likelihood that the evaluation of cost effectiveness will not be accurate. This reflects the lack of high quality health economic analyses that have been undertaken with respect to blood management interventions but again these limitations should not be directly translated into limitations of the recommendations.	Thank you for your comment. We have included published economic analyses that meet our inclusion criteria and these have included some 'threshold analyses'. The limitations of such analyses have been accounted for in the overall rating of these studies and any uncertainty will have been discussed in the 'Linking evidence to recommendations' statements. The limitations of the recommendations do not solely reflect the limitations of the existing body of economic evidence, they will also be a reflection of the strength and quality of the clinical evidence.
Society for Cardiothoracic Surgery in Great	Full	General	General	There are a significant number of recommendations that are based solely on the opinion of the experts on the panel. This is only apparent after careful	NICE no longer grades recommendations but instead, we have stated where a recommendation was consensus based in the section 'Linking

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Britain and Ireland				reading however. These would normally be classed as recommendations based on Class C evidence. This should be made much clearer in the guidelines summary, as is the case in other guidelines.	evidence to recommendations' for each recommendation.
Society for Cardiothoracic Surgery in Great Britain and Ireland	Full	General	General	The guidelines are inconsistent; Erythropoietin was found to be effective at reducing transfusion rates but did not improve clinical outcomes and was not recommended. Conversely restrictive red cell transfusion was also found to reduce transfusion without improving clinical outcomes and was recommended. The distinction between the weight of evidence for these two recommendations is not clear. The main rationale appears to be that EPO is not cost effective but that restrictive transfusion is; but as stated above the economic judgements do not appear to be based on health economic analyses that considered all the health resource use influenced by the intervention but largely on threshold analyses.	Thank you for your comment. NICE recommendations are based on clinical and cost effectiveness. Please note, the outcomes 'number of patients transfused' and 'units transfused' were critical outcomes and the GDG thought they were appropriate surrogate outcomes for reliably assessing the effectiveness of the transfusion strategies. The recommendation for EPO has now been reworded and a statement that EPO may be considered in patients who refuse blood transfusions and when appropriate blood type is not available because of the patient's red cell antibodies, has now been included in the recommendation. EPO was not recommended (except for patients listed in the exceptions), as although EPO reduced transfusions, the clinical evidence also suggested evidence of harm with higher mortality and thrombosis compared to placebo. In addition, the GDG considered, based on the available published economic evidence and additional threshold analysis that EPO was unlikely to be cost-effective. The consideration of all the economic evidence is detailed in the 'Linking evidence to recommendations' table.

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					The use of restrictive red blood cell transfusion was recommended as it reduced transfusion and did not negatively impact health outcomes. Therefore it was considered likely to be cost-effective and was recommended.
Society for Cardiothoracic Surgery in Great Britain and Ireland	Full	General	General	The distinction between offer and consider in the guidelines is poorly defined and appears inconsistent. For example, erythropoietin (EPO) is not to be offered to patients although it reduces transfusion, but does not improved clinical outcomes, and is more costly. Conversely intravenous iron can be considered, although it reduces transfusion, but does not improve clinical outcomes and is more costly.	Thank you for your comment. The recommendation for EPO has now been reworded and a statement that EPO may be considered in patients who refuse blood transfusions and when appropriate blood type is not available because of the patient's red cell antibodies, has now been included in the recommendation. The recommendation is based on evidence of harm with the use of EPO (it may be associated with higher mortality and thrombosis) and the fact that it was not cost effective. The use of intravenous iron was not associated with adverse events and was considered to be cost-effective based on existing published economic evidence (less costly and more effective than current practice)**.** NICE reflects the strength of its recommendations in the wording used across its guidance. The Institute, uses 'offer' (or similar wording such as 'measure', 'advise', 'commission' or 'refer') to reflect a strong recommendation, usually where there is clear evidence of benefit. 'Consider' in the context of NICE recommendations indicates that the GDG could not make a strong recommendation based on the evidence because

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					the balance between benefits and harms was less definitive. Accordingly, the group agreed to make a 'consider' recommendation for the use of Intravenous iron.
Society for Cardiothoracic Surgery in Great Britain and Ireland	Full	25	16	Review question: What is the clinical- and cost-effectiveness of 11 oral iron, IV iron and erythropoietin in reducing blood 12 transfusion requirements in surgical patients? The main aim of any clinical intervention is to improve clinical outcomes that are important to patients. Transfusion in itself does not meet this definition but is defined as a critical outcome with greater importance than infection, thrombosis, bleeding or quality of life.	Thank you for your comment. The aim of this review was to assess the effectiveness of oral iron, IV iron and erythropoietin as an alternative to blood transfusion. To this effect, the GDG agreed that clinical outcomes such as mortality and quality of life were critical and these have been evaluated in the review. However, the GDG noted that the number of patients receiving transfusions and the number of units transfused, although not clinical outcomes, were critical to assess the effectiveness of the interventions being evaluated. The number of transfusions was also critical to the assessment of cost effectiveness.
Society for Cardiothoracic Surgery in Great Britain and Ireland	Full	65	6	1. Do not offer erythropoietin to reduce the need for blood transfusion in patients having surgery. The GRADE quality evidence for the data presented in these analyses was either Low (mortality), or Very Low (transfusion, adverse events, infection and thrombosis), with a high risk of bias. There was uncertainty in relation to the clinical benefits, but no clear evidence of harm. The cited economic analyses were not based on these trials but were based on the negative findings of 2 small studies (one based on a US healthcare payer perspective) with potentially serious limitations. Conversely 2 additional; studies cited (references 77 and 293) appeared to show that EPO was	Thank you for your comment. The recommendation for EPO has now been reworded and a statement that EPO may be considered in patients who refuse blood transfusions and when appropriate blood type is not available because of the patient's red cell antibodies, has now been included in the recommendation. Although there was uncertainty, the clinical evidence did show an increase in mortality and thrombosis associated with the use of EPO in comparison with placebo. As highlighted in the 'Linking evidence to

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				dominant. From the text it appears that the economic evidence was based on the balance of costs of the drug versus the transfusions avoided; this is not a comprehensive health economic analysis. It is not clear from the data why the panel would then make such a strong recommendation that EPO should not be offered based on this evidence. The evidence identifies uncertainty that should be addressed by a clinical trial.	recommendations' section, the GDG considered all four economic studies as well as the additional threshold analysis conducted which incorporated the current UK costs of transfusion and EPO. All four published studies were considered to have potentially serious limitations, not only the first two analyses cited in your comment. Of note these first two economic analyses were indeed based on evidence that was not included in the clinical review, however the negative findings were a result of the high cost of EPO relative to the small benefit in terms of QALYs. Furthermore, had these studies incorporated all the findings reported in the clinical review, such as an increased mortality and thrombotic events, EPO would likely be even less cost-effective. The two other economic analyses, which concluded EPO was dominant, included unit costs for EPO which were considered to be much lower than the current nationally and publically available costs in the UK. In addition, sensitivity analyses from these studies indicated uncertainty with the conclusions regarding cost-effectiveness. Finally, we agree that this threshold analysis was not comprehensive as it did not incorporate all the clinical outcomes reported from the clinical evidence. Had we included these, EPO would be even less cost effective as the clinical evidence reported an increase in mortality and thrombosis associated with the use of EPO.
Society for Cardiothoracic	Full	66	1	2. Offer oral iron before and after surgery to patients with iron-deficiency anaemia.	Thank you for your comment. This recommendation is based on low quality evidence as well as the

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Surgery in Great Britain and Ireland				This recommendation is based on two trials that recruited 154 patients, that were considered Very Low GRADE evidence, and that did not show any statistically significant reduction in transfusion (uncertainty). The effect on clinical outcomes was not reported. The economic analysis is based on the cost comparison between the numbers of units of red cells avoided and the iron supplement in a RCT of 45 patients, and not on a health economic analysis. It appears that this recommendation is not based on evidence but on opinion; this is not stated in the guideline.	consensus expert opinion of the GDG members. This has been highlighted wherever relevant in the guideline. Although of low quality, the evidence showed that there was benefit with respect to clinical and cost effectiveness with oral iron and the group were keen to make a recommendation in this regard.
Society for Cardiothoracic Surgery in Great Britain and Ireland	Full	69	1	3. Consider intravenous iron before and after surgery for patients with iron- deficiency anaemia who: cannot tolerate or absorb oral iron, are diagnosed with functional iron deficiency, are diagnosed with iron-deficiency anaemia and the interval to surgery is considered short, are unable to adhere to oral iron treatment The evidence summary, based on 2 studies (n=280) suggested that this intervention reduced transfusion (GRADE, Low), but did not result in improvements in clinical outcomes. The economic analysis in favour of intravenous iron was supported by a published economic model (reference 184) that was derived from literature data and expert opinions and not from a trial. It is also not clear how these findings were extrapolated to include patients with functional iron deficiency, a condition that is poorly defined, and was not specified in any of these trials. This recommendation appears to be	Thank you for your comment. This recommendation is based on low quality evidence as well as the consensus expert opinion of the GDG members. Please refer to the 'Linking evidence to recommendations' statement for this recommendation which also discusses the economic considerations and the relevant literature. The GDG did discuss the issues of Functional Iron Deficiency and Iron therapy in this context. And this has also been noted in the LETR for this section. We acknowledge your concerns and please note that this recommendation has now been amended to read as follows: Consider intravenous iron before or after surgery for patients who: • have iron-deficiency anaemia and cannot tolerate or absorb oral iron, or are unable to adhere to oral iron treatment (see the NICE guideline on medicines adherence)

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				based on expert opinion rather than the evidence, although this is not immediately clear.	• are diagnosed with functional iron deficiency • are diagnosed with iron-deficiency anaemia, and the interval between the diagnosis of anaemia and surgery is too short for oral iron to be effective.
Society for Cardiothoracic Surgery in Great Britain and Ireland	Full	118	1	8. Do not routinely offer cell salvage alone. This recommendation was based on a network meta-analysis. However the major limitation of this analysis was the low quality of the trials that were included. Should the strength of this recommendation be downgraded given that it is not supported by a single high quality trial, and that there was no evidence of an important clinical benefit for either tranexamic acid or cell salvage in any of the analyses in this section with the exception of a mortality benefit for tranexamic acid in high risk groups (Table 35)? The certainty of this recommendation is also challenged by the conclusion that this question must be addressed by further research (p112, line 1).	Thank you for your comment. We acknowledge your concerns and believe these are adequately reflected in the wording of the recommendation with the use of the word 'routinely'. Although of low quality, the evidence unequivocally showed that there was no benefit with respect to clinical and cost effectiveness by using cell salvage alone in the absence of tranexamic acid and the group were keen to make a recommendation in this regard.
Society for Cardiothoracic Surgery in Great Britain and Ireland	Full	176	27	13. Use restrictive red blood cell transfusion thresholds for patients who need red blood cell transfusions and who do not have major haemorrhage or acute coronary syndrome. Significant heterogeneity in these analyses implies that there may be important subgroups where restrictive transfusion is not beneficial; for example the recommendation does not reflect the findings of the recent TITRE2 study that demonstrated increased mortality in cardiac surgery patients randomised to a restrictive transfusion threshold of	Thank you for your comment. We agree with your comment and the next recommendation highlights specific subgroups where a higher threshold for red blood cell transfusion may be considered. We have now included the TITRe2 trial in the RBC thresholds review in our guideline. The results of the TITRe2 trial have now been evaluated as part of the meta-analysis of all the studies included in the RBC thresholds review.. The evidence showed clinically important benefit with restrictive strategies with respect to the number of patients transfused and

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				7.5g/dL (New England Journal of Medicine 2015;372:997-1008).	number of units transfused. The evidence suggested that there was no difference between the groups with respect to mortality, adverse events, new cardiac events, length of hospital stay, quality of life and infection, but there was some uncertainty. The inclusion of this study in the meta-analysis has not led to a change in the existing recommendations.
Society for Cardiothoracic Surgery in Great Britain and Ireland	Full	179	1	14. When using a restrictive red blood cell transfusion threshold, consider a threshold of 70 g/litre and a haemoglobin concentration target of 70–90 15 g/litre after transfusion. Nine of the 33 trials evaluated (references 60, 123, 124, 133, 150/ 170, 238, 270, 307, 309) assessed restrictive thresholds as low as 7g/dL, not the majority as stated. Trials that evaluated very restrictive thresholds were conducted in patients cared for in highly monitored environments. It does not appear that the evidence shows very restrictive thresholds are safe in patients in their generality.	Thank you for your comment. The rationale for recommending a restrictive threshold of 70g/L is described in the 'trade-off between clinical benefit and harm' section of the LETR for this recommendation. The GDG noted that those trials that used the most restrictive thresholds (Hb 70g/L) tended to have been conducted in the sickest patient groups, for example critically ill patients in ICU. The GDG considered that the safety of Hb triggers of 70g/L in these situations, especially for younger patients and those without cardiovascular co-morbidity supported this threshold for most patients. We have now added this text to the LETR.
Society for Cardiothoracic Surgery in Great Britain and Ireland	Full	180	1	15. Consider a red blood cell transfusion threshold of 80 g/litre and a haemoglobin concentration target of 80–100 g/litre after transfusion for patients with acute coronary syndrome. This recommendation is not supported by evidence, but on expert opinion. This should be more clearly stated in the document. Similarly, the statement that a higher haemoglobin threshold for transfusion may have clinical benefit such as those with brain injury and chronic cardiovascular disease are not supported by	Thank you for our comment. The GDG felt it was reasonable to make a recommendation for patients with ACS, in spite of the lack of evidence, on the basis of their knowledge and experience. The rationale for this recommendation is described in the 'trade-off between clinical benefit and harm' section of the LETR. The GDG also discussed the haemoglobin threshold for patients with chronic cardiovascular disease and the following statement has now been added to the

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				evidence. In fact in the FOCUS trial where the great majority of patients had cardiovascular disease there was no benefit (or harm) from restrictive transfusion. The research recommendation however identifies chronic cardiovascular disease with coronary ischaemia at baseline as a key research area. Neither of these terms is consistent with modern definitions of cardiovascular disease and these might be better defined.	LETR section of the recommendation: The GDG noted that for many of the studies comparing restrictive with liberal strategies in patient groups with a high incidence of, or risk of, concurrent chronic cardiovascular disease the restrictive transfusion trigger was 80 g/L or greater. This was notably the case in the FOCUS trial (Carson 2011), which was undertaken in elderly patients with a prevalence of known cardiovascular disease undergoing emergency hip fracture repair. The GDG also noted that in a post-hoc analysis of the sub-group of patients in a large study of critically ill patients who had ischaemic heart disease (Hebert 1999), and in an a priori defined sub-group of patients with cardiovascular disease enrolled in a trial of restrictive versus liberal transfusion triggers for managing septic shock (Holst 2014), the mortality was lower with liberal transfusion. The restrictive transfusion trigger was 70 g/L in both of these trials. The GDG also took into account the findings of a recent large trial in patients undergoing cardiac surgery (Murphy 2015) in which mortality was lower in the liberal groups. The GDG therefore acknowledged the insufficient evidence for patients with coronary artery disease. For these patients the GDG agreed that clinical judgement was needed on an individual patient basis using information about disease severity and cardiovascular status (for example blood pressure and heart rate). Although restrictive strategies may be safe, the actual transfusion threshold and target haemoglobin may

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					need to be higher than used for patients without coronary disease.
Society for Cardiothoracic Surgery in Great Britain and Ireland	Full	236	17	30. Only consider fresh frozen plasma transfusion for patients with clinically significant bleeding but without major haemorrhage if they have abnormal coagulation test results (for example, prothrombin time ratio or activated partial thromboplastin time ratio above 1.5). This suggested threshold used in this guideline was based on the findings of a single large observational analysis in ICU patients. This analysis was subject to bias from unmeasured confounders and the likelihood of higher INRs in sicker patients. Furthermore the relevance of this recommendation to other clinical settings is not clear. In cardiac surgery for example the INR does not discriminate between those who bleed and those that do not bleed.	Thank you for your comment. For this recommendation, the GDG considered evidence from two studies (one RCT and one cohort study) in cardiac surgery patients and one cohort study in ICU patients. However the evidence was noted to be indirect to the review question (see item on quality of evidence in 'Linking evidence to recommendations' section) and the recommendation was based largely on the consensus expert opinion of the GDG. The GDG discussed this and felt that whilst general, the recommendation was applicable to other clinical settings where we found no evidence.
Society for Cardiothoracic Surgery in Great Britain and Ireland	Full	239	1	32. Consider prophylactic fresh frozen plasma transfusions for patients with abnormal coagulation who are having invasive procedures or surgery with a risk of clinically significant bleeding. This recommendation is based on expert consensus and is at odds with a Cochrane review that does not support the use of prophylactic FFP in patients undergoing cardiac surgery. The main limitation of this recommendation is that there no clear consensus as to what constitutes abnormal coagulation using existing data and definitions.	Thank you for your comment. There is little evidence to indicate the value of prophylactic FFP in patients with abnormal coagulation undergoing invasive procedures or surgery. However, the GDG drew on its experience to form the consensus opinion that the benefits of FFP to minimise severe bleeding outweigh the risks associated with its transfusion. The Cochrane review does not compare FFP transfusion at different INR levels as stated in our review protocol and therefore evidence from this was not included. Moreover, it was specific to cardiac surgery patients and the GDG agreed that findings from this specific group were not

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					generalisable to other patients. .
Stanningley Pharma Ltd	Full	12	8-9	The suggestion of offering oral iron to those patients with iron deficiency anaemia fails to address the issues of patients who are iron deficient but not anaemic. If patients already have IDA it would seem wise if possible to potentially postpone surgery until this is resolved. In addition it may be that IV iron is a superior option in cases of IDA. It is unlikely that a patient with IDA will be able to absorb sufficient oral iron to correct the IDA and to place sufficient iron into stores to allow the correction of the low Hb caused by surgical blood loss. Those patients with normal Hb and low iron stores (non-anaemic ID) are likely to remain anaemic post surgery. This being the case offering appropriate iron supplementation both pre and post surgery to all patients would seem wise. A form of words would need to be added to potentially exclude those patients with Haemochromatosis. Recent work in Cardiac patients has shown a significant association between low iron and poor outcome regardless of Hb. Inducing ID by not supplementing with iron post blood loss may well be a contributor to post-surgical morbidity and mortality.	Thank you for your comment. The point about the possibility of postponing surgery in patients with IDA has been included in the 'other considerations' section of the 'Linking evidence to recommendations' table for this recommendation. The use of IV iron in patients with IDA is made in the next recommendation. No evidence was found to support a recommendation for the routine use of iron in all surgical patients.
Stanningley Pharma Ltd	Full	13	21-22	See comment 1 above	Thank you for participating in the consultation process.
Stanningley Pharma Ltd	Full	13	23-24	See comment 1 above	Thank you for participating in the consultation process.
Stanningley Pharma Ltd	Full	13	25	If time allows suggest trying alternative oral iron preparations. Here OTC Haem iron preparations	Thank you for your comment. Consideration of different types of oral iron was

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				may be considered as Haem iron is better absorbed. Oral iron preparations such as Ferric Maltol are currently undergoing trial and have shown promise in those patients unable to tolerate Ferrous iron.	beyond the scope of this guideline.
Stanningley Pharma Ltd	Full	13	26	FID would benefit from a fuller definition here. The idea of FID is well understood in a renal setting but potentially little understood elsewhere. For example a ferritin level is often the only marker of iron stores available and is known to be highly unreliable. To be able to determine patients true iron status requires more tests than ferritin alone. It would be helpful to highlight that an elevated ferritin may not be a useful marker of iron availability and suggest using either red cell hypochromia or retuculocyte Hb. This is covered in detail in Nice NG8. Though less reliable a measurement of TSAT is helpful as if below 20% this potentially indicates low iron availability regardless of ferritin level (assuming this is below 800). In such situation oral or IV iron may be appropriate depending upon the circumstances which again would benefit from discussion. The recently updated Nice guidance https://www.nice.org.uk/guidance/ng8 may be helpful	Thank you for your comment. Definitions of FID and Iron Deficiency are included in the glossary of the guideline. The management of anaemia in medical patients are out of the scope of the guideline. The diagnosis of anaemia is also out of scope.
Stanningley Pharma Ltd	Full	13	27-28	See comment 1 above.	Thank you for participating in the consultation process.
Stanningley Pharma Ltd	Full	19	General	Suggest modification to the algorithm See comment 1-6 above	Thank you for participating in the consultation process.
Stanningley Pharma Ltd	Full	24	1	Please note CG114 has recently been updated by NG8. https://www.nice.org.uk/guidance/ng8	Thank you for your comment, the hyperlink and the guideline numbering have been updated.

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Stanningley Pharma Ltd	Full	47	4-6	Though effective in the long term oral iron may be less appropriate than IV iron in situations where significant blood loss is anticipated.	Thank you for your comment. Management of iron deficiency anaemia for patients with anticipated significant blood loss is outside the scope of the guideline.
Stanningley Pharma Ltd	Full	47	6-7	It may be worthwhile highlighting the risks associated in using IV iron products vs. oral therapy. In addition higher dose less frequent administration of IV iron may be more appropriate in this setting. This is likely to be more convenient to patients and reduce costs to the NHS significantly.	Thank you for your comment. We have edited the introduction. The benefits and harms of oral and intravenous iron were discussed by the GDG and this is highlighted in the 'Linking evidence to recommendations' section of this chapter. The scope of this guideline does not cover different dosing or frequency of IV or Oral Iron.
Stanningley Pharma Ltd	Full	47	7	The use of oral and IV iron in combination is not covered by the oral or IV iron products SMPC's. Their use in combination would seem to be pointless.	Thank you for your comment. We have edited the introduction. We have not recommended that oral and IV iron be used in combination.
Stanningley Pharma Ltd	Full	58	19	Few hospitals would be likely to pay list price for EPO as it is heavily often discounted.	Thank you for your comment. Only publically and nationally available costs can be referenced in NICE guidelines. We are aware that EPOs are often discounted However it is difficult to assess the extent of these discounts at a national level and therefore only the list prices were presented. However, we can be fairly certain that the discount is not large enough for EPO to be cost-effective: one of the economic evaluations suggested that the cost of EPO would need to reduce by 95%.
Stanningley Pharma Ltd	Full	62	2-6	The BNF price is unhelpful due to significant discounting of EPO in hospitals	Thank you for your comment. Only publically and nationally available costs can be referenced in NICE guidelines. We are aware that EPOs are often discounted However it is difficult to assess the extent of these discounts at a national level and therefore only the list prices were presented. However, we can

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					be fairly certain that the discount is not large enough for EPO to be cost-effective: one of the economic evaluations suggested that the cost of EPO would need to reduce by 95%.
Stanningley Pharma Ltd		62	20	The use of higher dose IV iron products could potentially reduce dosing to a single administration which could be given at a pre-surgery assessment.	Thank you for your comment. The scope of this guideline does not cover different dosing or frequency of IV or Oral Iron. The GDG felt that oral iron would be the first option for patients and the rationale is noted in the 'Linking evidence to recommendations' section of the full guideline.
Stanningley Pharma Ltd	Full	62	21	The true societal cost of a unit though not easy to determine is likely to be considerably higher.	Thank you for your comment. All costing and original economic modelling in the guideline reflect the NICE reference case and an NHS and personal social services (PSS) perspective. Therefore the cost of transfusing a unit of blood does not take into account the societal cost but only that of the NHS and PSS.
Stanningley Pharma Ltd	Full	66	1	Please see comment 1 above	Thank you for your comment.
Stanningley Pharma Ltd	Full	66	1	Comment is made re. the success of oral iron therapy being largely dependent upon patient compliance. This being the case it may be worthwhile highlighting the potential merits of OTC Haem. Iron products. Due to the low cost of such interventions research is limited due to the low returns.	Thank you for your comment. Although the scope of the guideline includes the use of self-administered oral iron, this recommendation was directed toward health care professionals and does not address the use of OTC haematology iron products.
Stanningley Pharma Ltd	Full	66	1	Though oral iron may be effective IV iron ensures compliance and this alone may be a reason to recommend IV iron therapy in some patients.	Thank you for your comment. We agree with your statement and have recommended that clinicians: Consider intravenous iron before or after surgery for patients who: • have iron-deficiency anaemia and cannot tolerate or absorb oral iron, or are unable to

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					adhere to oral iron treatment (see the NICE guideline on medicines adherence) • are diagnosed with functional iron deficiency • are diagnosed with iron-deficiency anaemia, and the interval between the diagnosis of anaemia and surgery is predicted to be too short for oral iron to be effective.
Stanningley Pharma Ltd	Full	66	1	Two weeks therapy with oral iron prior to surgery should be seen as a minimum. As a % of content very little iron is absorbed from oral iron preparations.	Thank you for your comment. The GDG also discussed the relevance of the duration of iron therapy prior to surgery. The GDG agreed that oral iron would be useful in raising haemoglobin levels if prescribed for a period of approximately 2 weeks. It was noted that this introduces logistic challenges of identifying patients with iron deficiency at sufficient time pre-surgery for the intervention to be given. The group was also concerned about absorption rates and recommended that clinicians consider intravenous iron before and after surgery for patients who: ▫ have iron-deficiency anaemia and cannot tolerate or absorb oral iron, or are unable to adhere to oral iron treatment (see the NICE guideline on medicines adherence) ▫ are diagnosed with functional iron deficiency ▫ are diagnosed with iron-deficiency anaemia, where the interval between detection of anaemia and surgery is predicted to be too short for oral iron to be effective in treating the anaemia
Stanningley	Full	68	1	Could a statement be added here to include the use	Thank you for your comment. The group was also

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Pharma Ltd				of IV iron in those patients where the anticipated surgical blood loss is such that oral iron alone is unlikely to be able to deliver sufficient iron to the stores?	concerned about absorption rates and recommended that clinicians consider intravenous iron before and after surgery for patients who: ▯ have iron-deficiency anaemia and cannot tolerate or absorb oral iron, or are unable to adhere to oral iron treatment (see the NICE guideline on medicines adherence) ▯ are diagnosed with functional iron deficiency ▯ are diagnosed with iron-deficiency anaemia where the interval between detection of anaemia and surgery is predicted to be too short for oral iron to be effective in treating the anaemia
Stanningley Pharma Ltd	Full	68	1	Comment is made regarding the safety of IV iron preparations. It may be worthwhile referencing the latest guidance from the MHRA. https://www.gov.uk/drug-safety-update/intravenous-iron-and-serious-hypersensitivity-reactions-strengthened-recommendations	Thank you for your comment. We agree and have replaced our original reference with your suggestion.
Stanningley Pharma Ltd	Full	66	1	Comment is made regarding the issues of identifying patients earlier. In the case of the use of IV iron even a day offers the opportunity to give up to 2,000mg of iron IV. This is sufficient to provide enough iron to enable the patient to have sufficient iron in stores to correct quite severe blood loss given enough time. 200mg of IV iron is regarded as sufficient to lead to a 1g/dl increase in Hb level.	Thank you for your comment. The group agrees that IV iron is able to increase iron stores quickly, and therefore recommended that clinicians consider intravenous iron before and after surgery for patients who: ▯ have iron-deficiency anaemia and cannot tolerate or absorb oral iron, or are unable to adhere to oral iron treatment (see the NICE guideline on medicines adherence) ▯ are diagnosed with functional iron deficiency

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					• are diagnosed with iron-deficiency anaemia where the interval between detection of anaemia and surgery is predicted to be too short for oral iron to be effective in treating the anaemia
Stanningley Pharma Ltd		68	1	Though using oral or IV iron to help correct anaemia is important it is also important to correct low iron levels independent of Hb level. Low levels of iron independent of Hb level have been shown to be associated with increased morbidity and mortality especially in those patients with conditions such as CHF. In addition the use or either oral or IV iron therapy has been show to lead improvements in such patients in terms of function/QOL and even a trend in terms of survival.	Thank you for your comment. This has now been done. Please see below: Thank you for your comment. We agree that the use of oral iron and intravenous iron are important and effective ways to correct anaemia. The use of oral and intravenous iron for other clinical conditions was not addressed specifically by this guideline; however, the GDG did consider and refer readers to the following guidance: • NICE guidance on Chronic Kidney Disease and Anaemia Management in Chronic Kidney Disease • NICE technology appraisal on the same topic. • NICE guideline on acute upper gastrointestinal bleeding.
Stanningley Pharma Ltd	Full	308		Suggest widening the definition of FIA as it may be present in conditions other than CKD. The definition below may be of help. *Functional iron deficiency (FID) is a state in which there is insufficient iron incorporation into erythroid precursors in the face of apparently adequate body iron stores, as defined by the presence of stainable iron in the bone marrow together with a serum ferritin value within normal limits (Macdougall et al,*	Thank you for your comment. A definition for FID has been added to the glossary.

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				1989).	

Registered stakeholders: **http://www.nice.org.uk/guidance/indevelopment/gid-cgwave0663/documents**