The British Rhinological Society multidisciplinary consensus recommendations on the hospital management of epistaxis

INTEGRATE (THE NATIONAL ENT TRAINEE RESEARCH NETWORK)*

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Abstract

Objective: Epistaxis is a common ENT emergency in the UK; however, despite the high incidence, there are currently no nationally accepted guidelines for its management. This paper seeks to recommend evidence-based best practice for the hospital management of epistaxis in adults.

Methods: Recommendations were developed using an Appraisal of Guidelines for Research and Evaluation ('AGREE II') framework. A multifaceted systematic review of the relevant literature was performed and a multidisciplinary consensus event held. Management recommendations were generated that linked the level of supporting evidence and a Grading of Recommendations Assessment, Development and Evaluation ('GRADE') score explaining the strength of recommendation.

Recommendations: Despite a paucity of high-level evidence, management recommendations were formed across five management domains (initial assessment, cautery, intranasal agents, haematological factors, and surgery and radiological intervention).

Conclusion: These consensus recommendations combine a wide-ranging review of the relevant literature with established and rigorous methods of guideline generation. Given the lack of high-level evidence supporting the recommendations, an element of caution should be used when implementing these findings.

Key words: Epistaxis; Assessment; Cautery; Packing; Hematology; Surgery

Introduction

Epistaxis is the most common acute presentation to ENT services in the UK, with around 25 000 acute presentations each year.¹ Despite this high incidence, there are currently no nationally accepted guidelines for its management.² A recent multi-centred pilot audit undertaken by INTEGRATE (The National ENT Trainee Research Network) demonstrated a wide variation in management practice.³

This multidisciplinary consensus guideline aimed to develop agreed evidenced-based, multidisciplinary recommendations for the management of epistaxis. This guideline was subsequently utilised as the 'gold standard' for the national audit of epistaxis management.⁴

Materials and methods

Recommendations were developed using an Appraisal of Guidelines for Research and Evaluation ('AGREE II') framework,⁵ a method successfully utilised for the 2009 hereditary haemorrhagic telangiectasia guidelines.⁶ Consensus member disagreement was managed using

an adaptation of the method utilised within RAND Corporation/University of California Los Angeles ('RAND/UCLA') appropriateness studies.⁷ The use of established guideline generation methodology sought to provide rigour in development, despite an expected paucity in high-level evidence.

Scope and purpose

Representatives from the ENT-UK Clinical Audit and Practice Advisory Group and the British Rhinological Society approached INTEGRATE, highlighting the requirement for nationally accepted standards of care in epistaxis management. This guideline seeks to recommend evidence-based best practice for the hospital management of epistaxis cases, of all severity, occurring in adults, within the context of commonly associated co-morbidities known to affect outcome. Guidance on the management of epistaxis in paediatric patients, and in those with hereditary haemorrhagic telangiectasia and other specific haematological conditions, is beyond the scope of this document.

Accepted for publication 24 July 2017

^{*}See Authorship and participation section for full list of collaborators.

Stakeholder involvement

An organising committee was composed of eight junior clinicians, including a nominated chair and two executive senior members. The organising committee were responsible for developing the consensus methodology and co-ordinating a multifaceted systematic review of the relevant literature.

A separate multidisciplinary consensus panel was composed of patients, ENT surgeons and representative experts from allied specialties involved in epistaxis management from across the UK. An open invite was extended to all consultant members of the British Rhinological Society and ENT-UK to participate in the consensus panel as ENT representatives. Allied specialty consultants and patient representatives were invited individually following identification by the steering committee as appropriate experts in their fields. Individuals specialising in health economics, emergency medicine, haematology, interventional radiology, general ENT and rhinology all contributed to the guidelines (Table I).

Rigour of development

For the purposes of this consensus, epistaxis management was divided by the steering committee into five domains: initial assessment, cautery, intranasal agents, haematological factors, and surgery and radiological intervention. Each domain was assigned co-authors from locations throughout the UK. Within the domains, a total of 15 systematic reviews were conducted,^{8–12} with the support of the University of Cambridge, the University of Exeter and the Defence Military Library. A robust yet pragmatic methodology was followed, including validated assessment of bias,^{13,14} capturing all relevant published evidence of level 3 and above.

The data synthesis and full-text articles included were made available to the consensus panel members,

prior to domain co-authors presenting their findings at a guidelines conference held in Leeds on 19 May 2016. A consensus panel discussion was held following each domain presentation, facilitated by the consensus panel chair, which sought to generate management recommendations. These discussions were digitally recorded and converted to a written consensus matrix by the steering committee. Each recommendation was then linked with: the level of evidence¹⁵ supporting each statement, and a Grading of Recommendations Assessment, Development and Evaluation ('GRADE') score¹⁶ explaining the strength of recommendation in the context of the evidence plus the perceived harm and benefit. The draft matrix was then returned to the consensus panel electronically for two separate rounds of comments and subsequent adjustment.

Disagreement within the consensus panel was managed using an adaptation of the method utilised within RAND Corporation/University of California Los Angeles appropriateness studies.⁷ Following final consensus matrix adjustment, consensus panel members independently assigned an agreement rating from 0-10 for each recommendation. A rating of 0 represented complete disagreement with the statement and 10 represented absolute agreement. Panel members were asked to abstain from comment when the specific recommendation was felt to be outside their clinical remit. Recommendations achieving a median rating of less than 7 were excluded from the consensus matrix. Disagreement was defined as statements achieving a median rating of 7 or higher but with individual ratings of less than 4. In these cases, outlying panel members were given the opportunity to revise their score if desired. All retained statements were reported with their median consensus agreement rating, range of ratings and an asterisk annotated where ratings were revised following disagreement.

TABLE I CONSENSUS PANEL MEMBERS											
Name	Specialty	Affiliation									
Dr Sura Priyesh Dr Adam Reuben Mr Sean Carrie Miss Claire Hopkins Mr Paul Chatrath Mr Paul Nix Mr Russell Cathcart Miss Victoria Ward Mr Paul White Mr Rami Salib Mr Carl Philpott Dr Jason Mainwaring Dr Tim Nokes Dr Andrew Sutton Patient A Patient B Dr Robert Lenthall Dr Will Adams	Emergency Medicine Emergency Medicine ENT (Chairperson) ENT ENT ENT ENT ENT ENT ENT ENT Haematology Haematology Health Economics Unit Patient Radiology Radiology Radiology	Kings College Hospital, London Royal Devon & Exeter Hospital Freeman Hospital, Newcastle upon Tyne Guy's & St Thomas' Hospital, London Imperial College Healthcare NHS Trust, London Leeds General Infirmary Jersey General Hospital, St Helier Mid Yorkshire Hospitals NHS Trust, Wakefield Ninewells Hospital, Dundee Southampton General James Paget University Hospital, Great Yarmouth Royal Bournemouth & Christchurch Hospitals NHS Foundation Trust Derriford Hospital, Plymouth Health Economics Unit, Leeds N/A N/A Queens Medical Centre, Nottingham Derriford Hospital, Plymouth									

N/A = not applicable

It is anticipated that the consensus recommendations will be updated following the completion of each cycle of the epistaxis management national audit.⁴

Recommendations

Initial assessment

Despite low and very low quality of evidence, a number of strong recommendations were made (Table II). This was achieved because of the lack of perceived risk of recommendation versus consensus agreed benefit. Recommendations centred round the use of a structured airway, breathing and circulation ('ABC') approach to patient assessment and management, and the recording of key co-morbidities where there was evidence available to support their impact on patient outcome.

Very low quality or absent evidence limited the strength of recommendation regarding the use of well-established first aid techniques, and specific statements regarding the clinical examination methods and investigation of patients presenting with epistaxis. Despite these limitations, there were consistently high agreement rating levels, with minimal disagreement in the accepted recommendations.

Cautery

Low and very low quality evidence again limited the strength of recommendations made regarding intranasal cautery (Table III). Strong recommendations were made supporting cautery as a first-line treatment in all patients, on the basis that cautery should only be targeted at identified points of bleeding. Weak recommendations were made regarding: the need for specific cautery training, the use of topical vasoconstrictors, electrocautery in preference to chemical (silver nitrate) cautery, and advanced clinical examinations when a bleeding point cannot be identified with anterior rhinoscopy. There were high median agreement ratings for all statements, with no disagreement.

Intranasal agents

In contrast to other domains, this area of management was supported, in places, by moderate and high quality evidence (Table IV). This allowed the strong recommendation of non-dissolvable anterior nasal packs as an effective haemostatic intervention in stipulated clinical scenarios, when placed by individuals specifically trained in their use. Consensus opinion strongly supported the use of targeted cautery following the removal of non-dissolvable packs, despite no supporting evidence. This was based on a perceived significant benefit balanced against any potential harm or cost. The consensus panel weakly recommended the use of Rapid Rhino[®] packs over Merocel[®] packs as the non-dissolvable pack of choice, and made weak recommendations regarding the length of time a pack should remain in situ and how long patients should be observed following pack removal. Despite median agreement ratings largely

between 8 and 9.5, there were several instances of disagreement.

Recommendations regarding the use of dissolvable packs and haemostatic agents were limited by: a paucity of high quality evidence, the diversity of available products and a lack of clarity regarding when to employ these products. Three of the four recommendations received low agreement ratings of 7 or 7.5, and there was a single instance of disagreement.

Antithrombotic therapy and haematological factors

Despite no epistaxis-specific supporting evidence, several weak recommendations were made regarding the management of warfarin, direct oral anticoagulants and heparin (Table V).^{17,18} These centred around the extrapolation of generic national guidelines and maintaining a low threshold for seeking case-specific haematological advice. Despite recommendations of weak strength, there were universally high levels of median agreement rating, with no instances of disagreement.

Similarly, there was no evidence to recommend an epistaxis-specific treatment strategy for the management of ongoing antiplatelet therapy (Table VI).^{19,20} Consensus opinion recommended the continuation of such agents in uncomplicated cases, and the involvement of allied specialties in complex or refractory cases. Levels of agreement were high, with no disagreement.

Transfusion strategies for epistaxis were again based on evidence unrelated to the condition. Despite this, a number of strong recommendations were made for the use of elements of the British Committee for Standards in Haematology guidelines for the management of major haemorrhage.¹⁹ Median agreement ratings were 10 for recommendations, with one instance of disagreement.

Tranexamic acid use in epistaxis benefited from moderate quality evidence; however, findings were inconsistent. As a result, weak recommendations for its use were made, with median rater agreement of 7 and 8, with disagreement in both epistaxis-specific statements. National guidelines exist for the use of tranexamic acid in defined major haemorrhage; it was strongly recommended that this guidance be followed when relevant, with a median agreement rating of 10 without disagreement.

Surgery and radiological intervention

Weak strength recommendations were made regarding the role of surgical and radiological intervention in epistaxis (Table VII). Recommendations were limited by the lack of quality evidence in this area. Despite this, consensus agreement was high for the identified clinical scenarios requiring treatment escalation, and regarding the recommendation for surgery over radiological intervention. However, interventional radiologists were outnumbered by ENT surgeons on the consensus panel, which may have biased the median agreement rating.

TABLE II INITIAL ASSESSMENT RECOMMENDATIONS											
Recommendation	Is evidence specific to	Level of evidence	Quality of evidence	Strength of recommendation	Agree score (ement 0-10)	Comments				
	epistaxis?	(Oxford CEBM)	(GRADE)	(GRADE)	Median	Range					
Initial assessment & management of epistaxis patients should											
- An 'ABC' approach should be adopted	-	-	-	Strong	10	-	Consensus panel opinion; this internationally recognised approach to patient assessment was felt to benefit our enistaxis natients				
 Initial assessment should be conducted in a location with appropriate facilities to assess, resuscitate & perform initial management, such as an emergency department 	_	_	-	Weak	9	6-10	Consensus panel opinion				
 Initial assessment should be conducted by a competent practitioner who has undergone epistaxis-specific training & has relevant experience 	_	_	-	Weak	9.5	7-10	Consensus panel opinion				
 Use of an oral ice pack is a first aid measure which should be considered 	Yes	2a	Very low	Weak	8	2-10	2 non-RCT studies assessed nasal airflow as a surrogate to epistaxis outcome. Tendency for reduced Doppler flow marginally greater with oral ice, but no evidence of effect on epistaxis				
 Direct nasal pressure is a first aid measure which should be considered 	_	_	_	Weak	8	8-10	Consensus panel opinion				
The following patient factors may affect outcome, & their presence or absence should be recorded in all epistaxis											
– Duration of epistaxis	Yes	3a	Very low	Weak	8	7-10	Limited non-RCT data of low quality. Patient reporting				
- History of sustained ambulatory hypertension	Yes	3a	Very low	Strong	8	7-10	Multiple non-RCT studies of low quality. Inconsistent reports				
- History of diabetes mellitus	Yes	3a	Low	Strong	8	4-10	Multiple non-RCT studies of low quality. Consistent findings				
- History of bleeding diathesis	Yes	3a	Very low	Strong	9	7-10	Multiple non-RCT studies of low quality. Sparse subgroup				
- History of ischaemic heart disease	Yes	3a	Low	Strong	8	7-10	Multiple non-RCT studies of low quality. Consistent findings				
- History of anticoagulation	Yes	3a	Moderate	Strong	10	8-10	of worse outcomes in ischaemic heart disease patients Multiple large-scale non-RCT studies. Consistent findings of effect size >2 on outcomes in patients taking oral				
- History of antiplatelet therapy	Yes	3a	Low	Strong	10	8-10	anticoagulants Multiple non-RCT studies of low quality. Consistent findings of worse outcomes in patients taking antiplatelet medication				
- Site of bleeding (anterior or posterior)	Yes	3a	Low	Strong	10	5-10	Multiple non-RCT studies of low quality. Inconsistent definition of posterior epistaxis; however, consistent findings of worse outcomes in posterior bleed epistaxis cases				
							Continued				

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Recommendation	Is evidence specific to	Level of evidence	Quality of evidence	Strength of recommendation	Agreen score ((ment)-10)	Comments
	epistaxis?	(Oxioid CEBM)	(GRADE)	(GRADE)	Median	Range	
nvestigations:							
 There are no routine investigations for epistaxis patients There should be a low threshold for requesting a full blood count &/or venous blood gas to estimate haemoglobin concentration. A 'group & save' should be considered on a case by case basis 	_	_		Weak Weak	8 8	0–10 3–10	Consensus panel opinion Consensus panel opinion
 Coagulation studies should be reserved for patients taking anticoagulant medication, or those with confirmed or suspected bleeding diatheses 	Yes	2c	Very low	Weak	8	8-10	Single small non-RCT study. Limited evidence to support recommendation. Failure to investigate may result in undiagnosed coagulopathy
- Anterior rhinoscopy with headlight following nasal decongestion should be attempted in all patients to locate point of bleeding	-	_	_	Weak	10	8-10	Consensus panel opinion
All other investigations should be considered on case-by-case basis	-	-	-	Weak	10	8-10	Consensus panel opinion

Oxford CEBM = Oxford Centre for Evidence-Based Medicine; GRADE = Grading of Recommendations Assessment, Development and Evaluation; ABC = airway, breathing and circulation; RCT = randomised controlled trial

TABLE III CAUTERY RECOMMENDATIONS												
Recommendation	Is evidence specific to epistaxis?	Level of evidence (Oxford	Quality of evidence (GRADE)	Strength of recommendation (GRADE)	Agree score (ment D-10)	Comments					
		CEDM)			Median I							
Cautery should be considered first-line treatment for all acute epistaxis cases. This recommendation is based on:	_	_	_	Strong	9	6–10	Large body of low-level evidence consistently demonstrates a multifaceted benefit over packing as first-line treatment, with lower rates of recurrence compared to first aid measures alone					
- Lower recurrence rates for cautery vs packing	Yes	3a	Low	-	_	_	Multiple non-RCT studies consistently show a significant effect size >2. However, often concerns regarding small sample size & allocation methodology					
 Reduced admission rates & length of stay with cautery 	Yes	2a	Low	-	-	-	Multiple non-RCT studies consistently show a significant effect size >2. However, often concerns regarding small sample size & allocation methodology					
- Lower pain scores for cautery vs packing	Yes	2b	Low	-	-	-	Single non-RCT study demonstrating large, significant difference in VAS pain scores comparing cautery with packing					

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- Potential economic benefit	Yes	2a	Very low	-	-	-	Two non-RCT studies demonstrating significant reduction in cost; however, limited methodology without health economics rigour
A vasoconstrictor agent should be used prior to attempting cautery unless contraindicated	Yes	3b	Low	Weak	9	8-10	Single non-RCT study demonstrating significant improvement in outcome. No power calculation. Difficult to accept as generalisable. Insufficient evidence to strongly recommend this intervention; however, it was consensus opinion that vasoconstrictor or local anaesthetic be used prior to cautery
Cautery should only be performed on a visually identified point of bleeding	_	-	-	Strong	9.5	5-10	No specific studies to support this recommendation. Indiscriminate cautery is felt to be of no benefit to patient & may lead to adverse events
Cautery should be performed by care practitioner appropriately trained & experienced in its use	_	_	_	Weak	9	5-10	Consensus panel opinion
Electrocautery should be used in preference to silver nitrate cautery by suitably trained & experienced care practitioners where available. This recommendation is based on:				Weak	8	5-10	Multifaceted low to very low quality evidence to suggest improved outcomes. Insufficient to justify strong recommendation
- Lower treatment failure & recurrence rates	Yes	2b	Very low	-	-	-	1 potentially underpowered RCT failed to demonstrate a difference. 1 poorly designed non-RCT concluded improved outcomes with electrocautery
- Reduced rates of nasal packing	Yes	2c	Low	-	_	_	Single non-RCT study showed an effect size <0.5. No power calculation. As an isolated study, difficult to ascertain whether generalisable
- Reduced rates of hospital admission	Yes	2c	Very low	-	-	-	Single non-RCT study showed a significant effect. No power calculation. As an isolated study, difficult to ascertain whether generalisable
– Similar pain score	Yes	2c	Very low	-	-	-	Single non-RCT study demonstrated no significant difference in VAS pain score between the 2 methods of cautery
Where anterior rhinoscopy fails to identify a bleeding point, rigid endoscopy or microscopy should be employed (by a suitably trained & experienced care practitioner)	Yes	2a	Low	Weak	10	7–10	Multiple non-RCT studies consistently demonstrate high bleeding point localisation rate & treatment success. Studies suggest an ability to localise bleeding point in 98% & 87% respectively, with initial treatment success rates of 92% & 93% respectively. Limited evidence insufficient to support strong recommendation given significant infrastructure & training burden associated with use of more specialised equipment

Oxford CEBM = Oxford Centre for Evidence-Based Medicine; GRADE = Grading of Recommendations Assessment, Development and Evaluation; RCT = randomised controlled trial; VAS = visual analogue scale

		INTRANA	TABLE SAL AGENT R	CIV ECOMMENDATIONS			
Recommendation	Is evidence specific to epistaxis?	lence Level of Qu ic to evidence evi (is? (Oxford (Gi CEBM)		Strength of recommendation (GRADE)	Agreement score (0–10)		Comments
						Range	
 Non-dissolvable intranasal packs: Non-dissolvable anterior nasal packs should be considered when: uncontrolled bleeding persists despite first aid measures; cautery has been attempted or deemed inappropriate; or patient is geographically distant from specialist services & local skill set does not include intranasal cautery 	Yes	la	Moderate	Strong	9.5	8-10	Multiple RCTs consistently demonstrated effect, with important limitations in trial methodology. There is moderate level evidence & strong consensus panel opinion that benefits of appropriate non-dissolvable pack use outweigh harm & cost in epistaxis management, whilst acknowledging that successful cautery can reduce requirement of said devices
 When indicated, non-dissolvable nasal packs should be inserted by care providers specifically trained & experienced in their use 	Yes	1b	Strong	Strong	10	8-10	Evidence from a single RCT with low risk of bias supported by multiple non-RCT studies that consistently demonstrate benefit of specific training on practical ability & patient outcomes. Evidence & consensus panel opinion support benefit of specific training & experience, considered to outweigh potential harm & cost
 Rapid Rhino & Merocel packs are as equally effective as haemostatic interventions, & so both are advocated for epistaxis cessation 	Yes	1a	Moderate	Strong	9	9–10	Multiple RCTs & non-RCT studies (with important limitations) consistently demonstrate no significant differences between bleeding cessation for Merocel vs Rapid Rhino. Evidence & consensus panel opinion consider that both products can equally achieve haemostasis
 Rapid Rhinos result in less patient discomfort on insertion & removal compared to Merocel packs, & are therefore preferred 	Yes	la	Moderate	Weak	8.5	2–10	2 RCTs with important limitations demonstrated a significant difference in VAS pain scores on insertion & removal of Merocel vs Rapid Rhino packs. There was no significant difference in pain score whilst packs were in situ. Moderate evidence suggests an inferior patient subjective experience with Merocel packs compared to Rapid Rhino. Consensus panel felt magnitude of benefit was less certain
 Systemic antibiotics are not routinely required whilst anterior nasal packs are in situ 	Yes	2a	Very low	Weak	7.5	6–10	Multiple non-RCT studies with important limitations consistently demonstrated no significant events when antibiotic provision was omitted. Current evidence base is insufficient to strongly recommend a change in routine practice
 Evidence is insufficient regarding requirement for routine antibiotic cover whilst posterior packs are in situ 	Yes	1b	Moderate	Weak	8	5-10	Single RCT involving small numbers, without power calculation. Current evidence base is insufficient to make a recommendation
 Combined non-dissolvable posterior & anterior nasal packs should be considered where a posterior bleed is suspected & anterior nasal packs have failed to achieve haemostasis 	_	_	-	Weak	8	2-10	Consensus panel opinion

-	All non-dissolvable packs should be removed within 24 hours of insertion (within daylight hours) if there is no evidence of active bleeding, regardless of anticoagulation status	-	_	_	Weak	8	2-10	Although this represents a key management decision step, there is no relevant evidence base; this represents consensus panel opinion
_	Following pack removal, all patients should undergo attempted targeted cautery of identified bleeding points using anterior rhinoscopy, with escalation to microscopy or rigid endoscopy if bleeding point is not identified	-	-	-	Strong	8	7–10	No relevant evidence base, despite this representing a key management decision step. Consensus panel consider that intervention benefits far outweigh potential harm or costs
– D	Clinically stable patients should be discharged 4 hours following pack removal & cautery ssolvable intranasal packs & haemostatic agents:	Yes	2b	Low	Weak	8	1-10	Single non-RCT study. Limited evidence is insufficient to support strong recommendation
-	Use of dissolvable packs & haemostatic agents should be considered as therapeutic adjuncts following successful intranasal cautery or endoscopic surgery	Yes	2a	Low	Weak	7.5	5-10	Multiple studies of varying evidence levels, including 3 low quality RCTs, all with important limitations. Product diversity & limited evidence quality make in difficult to form supportable recommendations. Suggested indications for their use are largely based on consensus opinion. Use of local experience should be encouraged
-	Use of dissolvable packs & haemostatic agents should be considered in refractory cases of epistaxis, where first aid measures & attempted cautery have failed, as an alternative to non- dissolvable intranasal packs	Yes	2a	Low	Weak	7	5-10	Multiple studies of varying evidence levels, including 3 low quality RCTs, all with important limitations. Product diversity & limited evidence quality make in difficult to form supportable recommendations. Suggested indications for their use are largely based on consensus opinion. Use of local experience should be encouraged
-	There is insufficient evidence to recommend one dissolvable pack or haemostatic agent over another	Yes	2a	Low	Weak	9.5	6–10	Multiple studies of varying evidence levels, including 3 low quality RCTs, all with important limitations. Product diversity & limited evidence quality make in difficult to form supportable recommendations
_	Patients with dissolvable packs or haemostatic agents in situ should not routinely be admitted unless there are specific concerns regarding safety of discharge	-	-	-	Weak	7	3-10	Consensus panel opinion

Oxford CEBM = Oxford Centre for Evidence-Based Medicine; GRADE = Grading of Recommendations Assessment, Development and Evaluation; RCT = randomised controlled trial; VAS = visual analogue scale

TABLE V											
ANTITHKOWBOTIC THEKAPT RECOVIMENDATIONS											
Recommendation	Is evidence specific to epistaxis?	Level of evidence (Oxford CEBM)	Quality of evidence (GRADE)	Strength of recommendation (GRADE)	Agreement score (0–10)		Comments				
		(LDM)			Median	Range					
Regarding management of patients on warfarin: An INR in therapeutic range does not routinely require reversal in a stable patient whose bleeding is adequately controlled	_	-	_	Weak	9	6–10	Consensus panel opinion				
Permanent cessation of warfarin should only be considered in refractory cases following full assessment of risks & benefits in conversation with haematologists &/or primary care providers	_	-	_	Weak	9	8-10	Consensus panel opinion				
When managing the bleeding warfarinised patient, there should be a low threshold to seek case-specific guidance from haematologists	_	-	-	Weak	10	6-10	Consensus panel opinion				
Where appropriate, SIGN 129 guidelines should be followed ¹⁷ (as supported by BCSH guidelines ¹⁸).	_	-	-	Strong	10	5-10	Nationally accepted guidelines for management of bleeding patients not specific to epistaxis				
 Serious bleeding with INR >1.1: stop warfarin, & administer IV vitamin K (5–10 mg) & PCC (usually 30–50 IU/kg, but dose-adjusted according to INR (under haematologist supervision whenever possible)). Fresh frozen plasma (at least 15 ml/kg) may be used only if PCC is unavailable. 	No	1a	Moderate	_	_	-	Evidence from randomised trials with important limitations, or strong evidence of some other form				
 Minor bleeding & supratherapeutic INR: interrupt warfarin, reintroducing at a lower maintenance dose when situation is under control. Administer oral or IV vitamin K (1.0–2.5 mg) 	No	1a	Moderate	-	_	_	Evidence from randomised trials with important limitations, or strong evidence of some other form				
- No bleeding & supratherapeutic INR: interrupt warfarin, monitor INR, restart warfarin at lower dose when INR <5.0. Where perceived risk of bleeding is high (e.g. INR >8) or other risk factors for bleeding are present, consider oral vitamin K administration (1.0-2.5 mg)	No	la	Moderate	-	_	-	Evidence from randomised trials with important limitations, or strong evidence of some other form				
Regarding management of patients on DOACs: DOACs do not need to be stopped or reversed in stable patients where bleeding has been controlled	-	-	-	Weak	9	4-10	Consensus panel opinion				
Permanent cessation of DOACs should only be considered in refractory cases following full assessment of risks & benefits in conversation with haematologists & primary care providers	-	-	_	Weak	9	7–10	Consensus panel opinion				
When managing bleeding epistaxis patients on DOACs, there should be a low threshold to seek case-specific guidance from haematologists	_	_	_	Weak	10	7–10	Current evidence base is limited, with no evidence specific to management of epistaxis patients on DOACs. There are emerging strategies for management & reversal of these agents; however, instigation of said treatments is felt to be beyond remit of ENT clinicians				

Regarding management of patients on heparin & heparinoids:							
Heparin & heparinoids do not need to be stopped or reversed in stable patients where bleeding has been controlled	-	-	-	Weak	8	7–10	Consensus panel opinion
Permanent cessation of heparin & heparinoids should only be considered in refractory cases following full assessment of risks & benefits in conversation with haematologists & primary care providers	_	-	_	Weak	9	8–10	Consensus panel opinion
BCSH guidelines ¹⁸ state: in management of bleeding, cessation of treatment & general haemostatic measures is usually sufficient. Protamine may be utilised as reversal agent where clinically indicated	No	3a	Low	Weak	9	8–10	Evidence from observational studies, unsystematic clinical observations, or randomised trials with serious flaws. Limited evidence non-specific to epistaxis
When managing bleeding epistaxis patients on heparin & heparinoids, there should be a low threshold to seek case-specific guidance from haematologists	_	_	_	Weak	10	8–10	Consensus panel opinion

Oxford CEBM = Oxford Centre for Evidence-Based Medicine; GRADE = Grading of Recommendations Assessment, Development and Evaluation; INR = international normalised ratio; SIGN = Scottish Intercollegiate Guidelines Network; BCSH = British Committee for Standards in Haematology; IV = intravenous; PCC = prothrombin complex concentrate; DOAC = direct oral anticoagulants

	H	AEMATOLOGIC	TABLE VI AL FACTORS R	RECOMMENDATIONS			
Recommendation	Is evidence specific to epistaxis?	evidence Level of Quality o ecific to evidence evidence staxis? (Oxford (GRADE		Strength of recommendation (GRADE)	Agree score (ement 0-10)	Comments
		CLDW)			Median	Range	
How should antiplatelet therapy be managed? In uncomplicated presentations, antiplatelet therapy should be continued throughout a patient's care	_	_	_	Weak	8.5	5-10	Consensus panel opinion
In complex or refractory cases, decision to withhold or permanently cease antiplatelet therapy should be made following full assessment of risks & benefits, & in discussion with haematology, cardiology & primary care providers	-	-	_	Weak	9	8-10	Consensus panel opinion
When should patients be transfused blood products? When managing the bleeding epistaxis patient felt to require blood product transfusion, there should be a low threshold to seek case-specific guidance from haematologists	-	-	-	Weak	10	2-10	Consensus panel opinion
Where appropriate, BCSH guidelines ¹⁹ should be followed. Major haemorrhage was defined as bleeding which leads to a heart rate >110 bpm &/or systolic blood pressure <90 mmHg. Guidelines stated:	_	-	-	_	10	8-10	
 Hospitals must have local major haemorrhage protocols, with adaptations for specific clinical areas. Such protocols should be followed when appropriate 	No	-	Very low	Strong	-	_	Expert opinion only. BCSH confident that benefits outweigh treatment harm & cost burden
 Optimum target haemoglobin concentration in bleeding management is not established. However, updated European guidelines²⁰ recommend target haemoglobin level of 70–90 g/l. Patients with cardiorespiratory morbidity may require higher target of 80–90 g/l 	No	2a	Moderate	Weak	_	-	Strong evidence from large observational studies. BCSH felt magnitude of benefit is less certain
- Fresh frozen plasma should be part of initial resuscitation in major haemorrhage in at least a 1 to 2 unit ratio with red cells until coagulation monitoring results are available. Once bleeding is under control, further fresh frozen plasma should be guided by laboratory test result abnormalities, with transfusion trigger of prothrombin time &/or activated partial thromboplastin time >1.5 times normal level for a standard dose (e.g. 15–20 ml/kg)	No	3a	Low	Weak	_	_	Evidence from observational studies, unsystematic clinical observations, or randomised trials with serious flaws. BCSH felt magnitude of benefit is less certain
 Fibrinogen supplementation should be given if fibrinogen level falls below 1.5 g/l 	No	-	Low	Strong	-	-	Evidence from observational studies, unsystematic clinical observations, or randomised trials with serious flaws. BCSH was confident benefits outweigh treatment harm & cost burden
– In major haemorrhage, aim to keep platelets at $>50-109$ /l	No	-	Moderate	Strong	-	-	Strong evidence from large observational studies. BCSH confident that benefits outweigh treatment harm & cost burden

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 Suggested that platelets should be requested if there is ongoing bleeding & platelet count <100–109 /1 	No	-	Low	Weak	-	-	Evidence from observational studies, unsystematic clinical observations, or randomised trials with serious flaws. BCSH felt magnitude of benefit is less certain
Tranexamic acid use in epistaxis:							
Evidence regarding oral tranexamic use in epistaxis is contradictory; we are currently unable to recommend its use	Yes	1a	Moderate	Weak	8	1-10	2 RCTs, both with methodological flaws & contradictory findings. Current evidence base insufficient to support benefit
Evidence regarding topical tranexamic acid use in epistaxis is inconsistent & demonstrates no long-term improvement in outcome; we are currently unable to recommend its use	Yes	1a	Moderate	Weak	7	1-10	2 RCTs, both with methodological flaws & inconsistent findings. Current evidence base insufficient to support benefit
BCSH guidelines ¹⁷ recommend:	-	_	-	_	10	8-10	
In adult trauma patients with or at risk of major haemorrhage, in whom antifibrinolytics are not contraindicated, should be given tranexamic acid as soon as possible after injury, at a dose of 1 g intravenously over 10 minutes followed by maintenance infusion of 1 g over 8 hours	No	1a	High	Strong	-	_	Consistent evidence from randomised trials or overwhelming evidence of some other form. BCSH confident that benefits outweigh treatment harm & cost burden
- Tranexamic acid use should be considered in non- traumatic major bleeding	No	1a	Moderate	Strong	-	-	Evidence from randomised trials with important limitations, or strong evidence of some other form. BCSH confident that benefits outweigh treatment harm &cost burden

Oxford CEBM = Oxford Centre for Evidence-Based Medicine; GRADE = Grading of Recommendations Assessment, Development and Evaluation; BCSH = British Committee for Standards in Haematology; RCT = randomised controlled trial

TABLE VII							
SURGERY AND INTERVENTIONAL RADIOLOGY RECOMMENDATIONS							
Recommendation	Is evidence specific to epistaxis?	Level of evidence (Oxford	Quality of evidence (GRADE)	Strength of recommendation (GRADE)	Agreement score (0–10)		Comments
		CEBM)			Median	Range	
Surgery or radiological intervention in epistaxis should be considered when conservative management strategies have failed. This can be represented by the following clinical scenarios:	Yes	3a	Low	Weak	_	_	Multiple studies, including 1 low quality RCT, all with important limitations that largely concern patient allocation to surgical <i>vs</i> conservative treatment arms. Most data are from retrospective studies Early surgical or radiological intervention appears to improve epistaxis-related outcomes (length of stay or recurrence); however, specific triggers for surgery or interventional radiology are largely based on consensus panel opinion
- Ongoing uncontrolled epistaxis despite attempted	-	-	-	_	10	8-10	
 - Where haemostasis is successfully achieved through optimal intranasal packing but recurs on attempted 	_	-	-	-	10	2-10	
removal of packing. If packing is felt suboptimal, then repacking is considered acceptable, rather than progression to surgery or interventional radiology (e.g. anterior pack converted to combined anterior & posterior nasal packing)							
 Recurrent epistaxis temporarily treated successfully with conservative measures; however, surgery performed semi-electively to minimise possibility of further recurrence 	-	-	_	_	8	5-10	
Both surgery & interventional radiology are effective in epistaxis management. Treatment modality should be chosen based on local access to services, availability of relevant surgical expertise & patient factors	Yes	3a	Low	Weak	8.5	2-10	Multiple studies, including 1 low quality RCT, all with important limitations that largely concern patient allocation to surgical <i>vs</i> conservative treatment arms. Most data are from retrospective studies. It is unclear from evidence quality as to which treatment modality is more effective & which has the more favourable adverse event profile Further research is required to adequately compare risk profile of endoscopic surgery <i>vs</i> endovascular embolisation. However, endoscopic surgery should be endorsed currently, given its greater availability & perceived superior risk profile Consensus panel opinion
Surgery is considered escalation management strategy of choice in epistaxis patients where treatment with conservative strategies has failed	-	-	-	Weak	9	5-10	
Optimum surgery represents general anaesthesia with endoscopic nasal cavity examination, electrocautery to identified points of bleeding, & ligation or targeted bipolar diathermy of all branches of enhancements of entering and and	-	_	_	Weak	9	8-10	
Anterior ethmoidal artery ligation should be reserved for refractory cases where there are specific concerns regarding an anterior ethmoidal artery bleeding point (e.g. post trauma)	-	-	-	Weak	9	7-10	

Oxford CEBM = Oxford Centre for Evidence-Based Medicine; GRADE = Grading of Recommendations Assessment, Development and Evaluation; RCT = randomised controlled trial

- Cautery should be attempted as a first-line treatment in all patients, targeted at identified points of bleeding
- Non-dissolvable anterior nasal packs should be considered in certain circumstances For instance, when uncontrolled bleeding persists despite first aid, cautery is inappropriate or ineffective, or patient lives far from specialist services
- An international normalised ratio in therapeutic range does not routinely require reversal in a stable patient whose bleeding is controlled
- In uncomplicated presentations, antiplatelet therapy should be continued throughout a patient's care
- Surgery is recommended for escalation of management (over interventional radiology) when conservative treatment fails

Conclusion

These consensus recommendations are based on a wide-ranging review of the relevant literature, and on the use of established and rigorous methods of guide-line generation. Hence, the findings should be of use to all hospital clinicians managing acute epistaxis. Readers should remain cognisant that the evidence identified to support this guideline is largely of low or very low quality, and expert consensus opinion was often required to reach recommendations. Whilst this should not undermine the utility of the document, caution should be used when implementing these findings. These recommendations will continue to be updated as new evidence comes to light.

Acknowledgement

This national audit was funded by ENT-UK. The funding body had no influence over content.

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References

- 1 NHS Hospital Episode Statistics in England and Wales. In: http://www.hesonline.nhs.uk [16 June 2017]
- 2 Hall A, Blanchard H, Chatrath P, Hopkins C. Epistaxis management: a multi-centre audit in England: is there a case for a national review of practice? *J Laryngol Otol* 2015;**30**:1–4
- 3 Mehta N, Williams RJ, Smith ME, Hall A, Hardman JC, Cheung L et al. Can trainees design and deliver a national audit of epistaxis management? A pilot of a secure web-based audit tool and research trainee collaboratives. J Laryngol Otol 2017;131: 518–22
- 4 INTEGRATE (National ENT Trainee Research Network). Epistaxis 2016: national audit of management. *J Laryngol Otol*. In press
- 5 Brouwers MC, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G *et al.* AGREE II: advancing guideline development, reporting and evaluation in health care. *CMAJ* 2010;**182**: E839–42
- 6 Faughnan ME, Palda VA, Garcia-Tsao G, Geisthoff UW, McDonald J, Proctor DD *et al*. International guidelines for the diagnosis and management of hereditary haemorrhagic telangiectasia. *J Med Genet* 2011;**48**:73–87
- 7 Fitch K, Bernstein SJ, Aguilar MD, Burnand B, LaCalle JR. *The RAND/UCLA Appropriateness Method User's Manual.* Santa Monica: RAND, 2001
- 8 Mcleod RW, Price A, Williams RJ, Smith ME, Smith M, Owens D. Intranasal cautery for the management of adult epistaxis: systematic review. *J Laryngol Otol*. In press
- 9 Williams A, Biffen A, Pilkington N, Arrick L, Williams RJ, Smith ME *et al.* Haematological factors in the management of adult epistaxis: systematic review. *J Laryngol Otol.* In press
- 10 Iqbal I, Jones HG, Dawe N, Mamais C, Śmith ME, Williams RJ et al. Intranasal packs and haemostatic agents for the

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management of adult epistaxis: systematic review. J Laryngol Otol. In press

- 11 Khan M, Conroy K, Ubayasiri K, Constable J, Smith ME, Williams RJ *et al.* Initial assessment in the management of adult epistaxis: systematic review. *J Laryngol Otol.* In press
- Swords C, Patel A, Smith ME, Williams RJ, Kuhn I, Hopkins C. Surgical and interventional radiological management of adult epistaxis: systematic review. *J Laryngol Otol*. In press
 Higgins JP, Altman DG, Gøtzsche PC, Juni P, Moher D, Oxman
- 13 Higgins JP, Altman DG, Gøtzsche PC, Juni P, Moher D, Oxman AD *et al*. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;343:d5928
- 14 Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (MINORS): development and validation of a new instrument. ANZ J Surg 2003;73:712–16
- 15 The 2011 Oxford CEBM Levels of Evidence: Introductory Document. In: http://www.cebm.net/index.aspx?o=5653 [16 June 2017]
- 16 Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P *et al.* GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;**336**:924–6
- 17 Scottish Intercollegiate Guidelines Network. Antithrombotics: Indications and Management. A National Clinical Guideline (SIGN publication no. 129). Edinburgh: SIGN, 2012
- 18 Keeling D, Baglin T, Tait C, Watson H, Perry D, Baglin C *et al.*; British Committee for Standards in Haematology. Guidelines on

oral anticoagulation with warfarin - fourth edition. Br J Haematol 2011;154:311-24

- 19 Hunt BJ, Allard S, Keeling D, Norfolk D, Stanworth SJ, Pendry K; British Committee for Standards in Haematology. A practical guideline for the haematological management of major haemorrhage. *Br J Haematol* 2015;**170**:788–803
- 20 Spahn DR, Bouillon B, Cerny V, Coats TJ, Duranteau J, Fernandez-Mondejar E *et al.* Management of bleeding and coagulopathy following major trauma: an updated European guideline. *Crit Care* 2013;17:R76

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Mr R Williams takes responsibility for the integrity of the content of the paper

Competing interests: Dr A Reuben was granted a Research for Patient Benefit grant to investigate the use of topical tranexamic acid in epistaxis. In order to avoid any external concerns regarding a potential conflict of interest, Dr Reuben's agreement ratings were not included in recommendations regarding the use of tranexamic acid in epistaxis.