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REVIEW ARTICLE

Initial assessment in the management of adult epistaxis: systematic review

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Abstract

Background: The initial assessment of epistaxis patients commonly includes: first aid measures, observations, focused history taking, and clinical examinations and investigations. This systematic review aimed to identify evidence that informs how the initial assessment of these patients should be conducted.

Method: A systematic review of the literature was performed using a standardised methodology and search strategy.

Results: Seventeen articles were included. Factors identified were: co-morbidity, intrinsic patient factors, coagulation screening and ice pack use. Hypertension and anticoagulant use were demonstrated to adversely affect outcomes. Coagulation screening is useful in patients on anticoagulant medication. Four studies could not be accessed. Retrospective methodology and insufficient statistical analysis limit several studies.

Conclusion: Sustained ambulatory hypertension, anticoagulant therapy and posterior bleeding may be associated with recurrent epistaxis, and should be recorded. Oral ice pack use may decrease severity and can be considered as first aid. Coagulation studies are appropriate for patients with a history of anticoagulant use or bleeding diatheses.

Key words: Epistaxis; Comorbidity; Cardiovascular Diseases; Hypertension; Risk Factors; First Aid; Therapy

Introduction

Epistaxis can be a life-threatening emergency, and requires appropriate and structured initial assessment. In the absence of national guidance, however, it is currently unclear what this initial assessment should entail. Elements of initial assessment commonly include: instigating first aid measures, recording physiological parameters, taking a focused history, performing a clinical examination and requesting appropriate investigations. Within these elements, it is important that any first aid measures undertaken are known to be effective, either as a treatment of epistaxis or a method of limiting bleed severity. Physiological parameters should be used as measures of illness severity, if demonstrated to be valid in this patient group. When taking a focused history, whilst there are many established risk factors for epistaxis, it is key to know what factors affect the outcomes of epistaxis sufferers so that management can be tailored accordingly. The clinical examination must be appropriate to guide relevant intervention, but what should this examination include? At times of financial strain, investigations should be rationed to those known to influence management, but where should the threshold for requesting these tests be?

Aims

This article aimed to systematically review the literature to inform a guideline generation process in order to create national consensus recommendations for the hospital management of epistaxis. This document will include recommendations founded on an evidence-based approach to the initial assessment of epistaxis patients. For the purposes of the article, this management domain was split into two distinct systematic reviews: patient factors affecting outcome and initial management. The specific research questions are described below.

Patient factors affecting outcome. What patient factors affect the outcomes of length of hospital stay, progression to surgery, rate of transfusion of blood products,

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and rate of associated morbidity and mortality in hospital-treated epistaxis?

Initial management. What represents optimum initial management? Where should initial assessment and management be conducted? Who should be undertaking the initial assessment and management? What first aid measures should be instigated? What observations should be undertaken within the initial assessment? What elements represent appropriate patient examination? What investigations should be performed in all patients? What investigations should be performed in selected patients?

Materials and methods

This work forms part of a set of systematic reviews designed to summarise the literature prior to the generation of a UK national management guideline for epistaxis. Following this and other systematic reviews, consensus recommendations on the management of epistaxis were generated based on the evidence and expert opinion.[1] The methodology set out below is common to this and four other reviews.[2–5]

Research question generation

The management of epistaxis was divided into nine domains as determined through discussion within a trainee project steering committee. The identified domains were: patient factors affecting outcome, initial assessment and first aid, cautery, dissolvable nasal packs, non-dissolvable nasal packs, management of anticoagulation, other haematological factors affecting outcome, surgical management, and radiological intervention. Clinically relevant research questions were then generated via an iterative consensus process for each domain, to encompass all elements of epistaxis management. Systematic reviews relating to the nine domains have been published in five articles (including this one), and the research questions can be found within the relevant reviews.[2–5] Two primary authors led the review of each domain, working with centralised library and steering committee support.

Types of study included

A preliminary review of the literature suggested there was a limited quantity of high-level evidence in many of the domains. As a result, randomised controlled trials (RCTs), controlled and uncontrolled longitudinal studies, and cross-sectional studies were all accepted for analysis. Case series, case reports and opinion-based articles were excluded. Restrictions were not placed on the outcomes used in identified studies at the search stage, in order to ensure capture of all relevant studies.

Types of participant

Relevant studies were included if they related to patients aged 16 years and above treated for epistaxis within a hospital environment. Studies including paediatric cases or cases of bleeding secondary to hereditary haemorrhagic telangiectasia were included in the analysis only if these patients formed less than 30 per cent of the total case number.

Search restrictions

There were no publication year or publication status restrictions. Only English-language articles were included.

Electronic searches

Initially, two members of the steering committee (MES and RJW) independently generated core Medical Subject Heading (MeSH) and non-MeSH key words to identify relevant studies relating to epistaxis. These were then discussed to create a core list of key words that formed the basis of the individual domain searches. Domain review authors independently generated key words specific to each individual research question, and these were also discussed to reach an agreed list. The key word lists were submitted to two librarians (University of Cambridge Medical Library and Exeter Health Library), who together used the core and specific key words to design a search strategy for each domain systematic review.

The following databases were searched from their inception for published, unpublished and ongoing studies: the Cochrane ENT Disorders Group Trials Register; the Cochrane Library, including the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects ('DARE'), and the Cochrane Central Register of Controlled Trials; Medline; Embase; the Cumulative Index to Nursing and Allied Health Literature ('CINAHL'); and the Web of Science. Full search strategies can be accessed in the online supplementary material that accompanies this issue. Additional studies were identified from the reference lists of full-text articles identified in searches, and from existing systematic reviews. All searches were performed in February 2016.

Validation of search strategy

To ensure the validity of the search strategy domain, co-authors manually identified two articles relevant to each systematic review. The librarians used these to test the search strategy for each domain, adjusting the strategies if necessary. Finally, the domain review authors were issued the search results (including abstracts) for all identified papers.

Screening and eligibility assessment

The two domain authors independently scrutinised the identified abstracts, and requested full-text articles for any studies that appeared relevant to either author. Records were kept of all excluded studies, including the reasons for their exclusion. When potentially relevant full-text articles could not be obtained through local sources, the Defence Medical Library Service assisted via inter-library loans; articles that were still not obtainable were excluded from data extraction.

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Data extraction and management

Continuing to work independently, the two domain authors extracted data from the identified studies into a standardised online form that was designed by the steering committee and librarians, and hosted on Google Drive. Meta-analysis was not routinely performed unless data were of sufficient quantity and quality to make this relevant.

Risk of bias assessment

For the purposes of bias assessment, studies were divided into RCT and non-randomised trials with or without comparators. The assessment of RCT risk of bias was performed using the Cochrane Collaboration's tool for assessing risk of bias.[6] This tool lists seven potential sources of bias that may affect the internal validity of an RCT, and each is assigned a risk of bias judgement (low, unclear or high). Non-randomised trials were assessed using the methodological index for non-randomised studies ('MINORS') criteria.[7] The score is calculated by awarding 0, 1 or 2 points to multiple criteria (e.g. clearly stated aims), before totalling these to achieve a final value. The methodological index for non-randomised studies score is calculated out of a possible 16, or 24 in the presence of a comparative group, with higher scores representing a lower risk of bias. Authors independently completed relevant bias assessment proformas for each included study.

Data synthesis

Following independent data extraction and assessment of bias, the co-authors for each domain reviewed the extracted information to reach a joint consensus. These data were used to populate a data synthesis table to summarise the findings of the systematic reviews, with the format standardised across the nine domains. If homogeneity permitted, a meta-analysis of key outcomes was performed, with narrative review performed otherwise.

Patient factors affecting outcome

Results

Figure 1 illustrates the search and article selection process. Of the 14 studies included, 1 is a randomised controlled trial (RCT),[8] 5 are prospective controlled studies,[9–13] 2 are retrospective controlled longitudinal studies,[14,15] 5 are retrospective uncontrolled longitudinal studies[16–20] and 1 is a prospective uncontrolled longitudinal study.[21] The studies varied significantly in sample size, with a range of 16 to 16 828 participants. Subjects' ages ranged from 0 to 98 years (median = 41.5–81.7 years, mean = 34.2–84.3 years). In terms of sex distribution, 61.4 per cent of participants were male and 38.6 per cent were female overall.

The quality of the evidence as assessed by risk of bias was variable, but overall it was poor to fair (Appendix I). The mean methodological index for the non-RCTs was 16.29 ± 3.25 (range, 10–20 out of 24),[9–15] and for the uncontrolled non-RCTs it was 10.50 ± 1.38 (range, 8–12 out of 16).[16–21] The RCT, which compared re-bleeding rates between epistaxis in-patients who were mobilised with those who were rested, was biased regarding ambiguous concealment of the alternate intervention, with no random allocation to groups, and not all outcomes were reported.[8] As the study setting was a busy ward, there was the potential for outcomes to be missed and blinding uncovered.[8] None of the studies stated that a sample size calculation had been performed.

Summary of evidence

Co-morbidities

Hypertension. Hypertension appears to be associated with persistent and recurrent epistaxis, as demonstrated by six studies (Table I).[9,12,14,15,19,20]

Terakura *et al.* compared blood pressure in patients with controlled and persistent bleeding following the application of an intranasal dressing with adrenaline and lignocaine. Both a diagnosis of hypertension and elevated systolic blood pressure at presentation were associated with ongoing epistaxis.[20]

Five studies assessed the relationship between hypertension and recurrent epistaxis, of which four were controlled[9,12,14,15] and one uncontrolled.[19] These were larger and of a higher quality, as compared with the included studies overall (mean number of participants (± standard deviation (SD)) = 1124 ± 861; mean methodological index for non-randomised studies scores were 17 out of 24 and 12 out of 16).

Three of the studies (including the uncontrolled study[19]) demonstrated that recurrent epistaxis was associated with a medical history of hypertension. One of these studies, the only prospective study, also found that sustained hypertension was a significant predictor of recurrent epistaxis, with these patients experiencing a mean of five episodes, as compared with one episode in patients with non-sustained hypertension.[12]

Conversely, two of the studies found no association between hypertension and recurrent epistaxis. Although Beran and Petruson stated no significant difference in the blood pressures of patients with recurrent epistaxis as compared with the general population, the authors did not report the results on which this statement was based.[9] In addition, the definition of hypertension in this study could be considered less reliable, with blood pressure measured on a single occasion only. This was then compared with existing data from a much larger population sample dataset (23 794 subjects) rather than a direct cohort. Ando *et al.* found no significant difference in past medical history of hypertension between patients with single and recurrent episodes of epistaxis.[15] However, there were large differences between group sizes as the single incident

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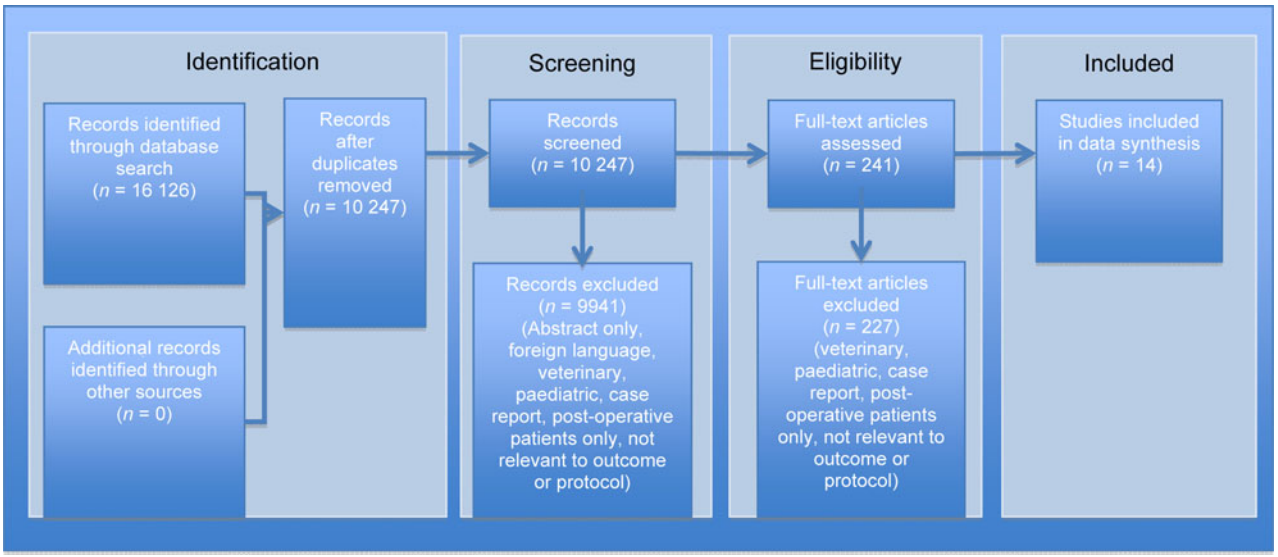

FIG. 1

Preferred Reporting Items for Systematic Reviews and Meta-Analyses ('PRISMA') diagram for the patient factors review, mapping the number of records identified, included and excluded during different review phases.

group was 8.3 times larger than the recurrent bleeding group, and follow-up period and attrition were not clearly stated.

Atherosclerosis associated with cardiovascular disease has been proposed as a risk factor in epistaxis.[22] Cardiovascular risk factors including sustained ambulatory hypertension, and anticoagulant and antiplatelet use, appear to be associated with persistent, recurrent or heavier epistaxis.[9–16,19,20] This is of particular relevance, as treating an ageing population with increasing co-morbidities is associated with increasing health and social care responsibility and cost.[23] However, evidence regarding the influence of demographic features and other co-morbidities on the outcome in patients with epistaxis is limited both in quality and number of studies.

Anticoagulation. Six studies (four controlled[10,11,13,14] and two uncontrolled studies[16,21]) suggest that anticoagulant use adversely affects the outcome in epistaxis, causing recurrent and heavier bleeding and an increased incidence of blood transfusion. The quality of these studies is similar to that of the studies overall (mean methodological index for non-randomised studies scores of 16 out of 24 and 11 out of 16). Both the largest study[16] and some of the smallest studies[11,21] are represented (mean number of participants (± SD) = 3105 ± 6742; range = 40–16 828 participants).

More frequent and heavier bleeding was associated with anticoagulant use in three studies (Table II).[10,14,21] The anticoagulant medications used varied between the studies. In one study, recurrent bleeding was higher in individuals using warfarin, or a combination of warfarin and aspirin. Recurrent bleeding rates were not higher in those using other individual or combination anticoagulants, though sample sizes were too small to draw reliable conclusions.[14] Two prospective studies evaluated the severity of bleeding[10,21] A controlled study demonstrated a higher incidence of blood transfusion amongst admitted epistaxis patients taking dabigatran or acenocoumarol, as compared with those taking no anticoagulant.[10] One uncontrolled study found that patients who had taken any medication associated with increased bleeding risk (anticoagulant or non-anticoagulant) were more likely to present with heavier bleeding, as compared with patients not taking these medications.[21]

Three prospective controlled studies found that anticoagulant use was associated with a longer admission.[10,11,13] This finding was significant in two of these studies, and was attributed, in both studies, to the routine in-patient management of anticoagulation, alongside social and medical conditions.[11,13] Contemporary practice favours out-patient anticoagulation management, and these results may now be of limited relevance. In the third of these studies, patients with persistent bleeding following removal of nasal packing required a period of observation, which contributed to an increased length of stay in patients taking dabigatran (5.9 ± 1.9 days) and acenocoumarol (4.3 ± 1.1 days), as compared with patients not taking any anticoagulant medication (3.6 ± 2.4 days), but this did not achieve significance.[10]

In a multicentre retrospective longitudinal study, the largest included in this review, Goljo *et al.* found that 20.8 per cent of 16 828 patients admitted with epistaxis who were taking anticoagulant medication had a significantly lower cost and length of stay, revealed by a multiple linear regression analysis, as compared with the sample in general.[16] Amongst the studied population, the most common co-morbidities were cardiovascular disease (78.5 per cent), type II diabetes (25.4 per

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TABLE I
STUDIES INVESTIGATING ASSOCIATION BETWEEN HYPERTENSION AND RECURRENT EPISTAXIS

Study details	Groups	HTN definition	Outcome measures	BP (mmHg)	Comments	*p*
Terakura *et al.*[20] Retrospective longitudinal uncontrolled	History of HTN – 72/133; persistent epistaxis – 26/72 (29%) No history of HTN –61/133; persistent epistaxis – 8/61 (13%)	History of HTN Elevated systolic BP at presentation	Persistent bleeding after removal of intranasal dressing with adrenaline & lignocaine for 30 minutes	NR Persistent bleeding group mean BP = 181.3 ± 26.9 No bleeding group mean BP = 156.6 ± 26.1		<0.002 <0.001
Abrich *et al.*[14] Retrospective longitudinal controlled	HTN in recurrent epistaxis group – 310/461 (67.2%) HTN in single episode group – 608/912 (66.7%)	History of HTN	Recurrent epistaxis – at least 2 episodes separated by minimum of 3 months within a 36-month period (controls – 1 episode only)	NR		0.04
Herkner *et al.*[12] Prospective controlled	Epistaxis group – 213 Recurrent epistaxis subgroups – NR Control group – 213	Elevated BP on admission: systolic BP >140 mmHg or diastolic BP >90 mmHg Sustained arterial HTN: 24-hour mean systolic BP >130 mmHg or diastolic BP >85 mmHg, or both; or receiving long-term anti-HTN treatment	Recurrent epistaxis	Epistaxis group – median systolic BP 161 (IQR = 139–180); diastolic BP 84 (IQR = 70–96) Control group – median systolic BP 144 (IQR = 130–157); diastolic BP 75 (IQR = 64–81) Recurrent epistaxis group – NR	Sustained arterial HTN subgroup – mean of 5 episodes Non-sustained arterial HTN subgroup – mean of 1 episode	0.004
Beran & Petruson[9] Prospective controlled	Epistaxis – 121; HTN – 15/121 Control group – 121 BP population sample – 23 794	Elevated BP on a single occasion	Recurrent epistaxis >3 episodes per year for 2 consecutive years	NR (represented graphically within paper)		NR
Ando *et al.*[15] Retrospective longitudinal controlled	Single episode epistaxis – 267; HTN in 51.7% Recurrent epistaxis – 32; HTN in 50%	Established HTN diagnosis	Recurrent epistaxis after treatment of 1st episode	NR	Single episode group 8.3 times larger than recurrent group	NR
Purkey *et al.*[19] Retrospective longitudinal uncontrolled	2405 patients with epistaxis – 41.37% (995) with HTN 3666 cases of epistaxis – 39.47% (1447) with HTN	ICD-9 coded HTN (401.X)	Recurrent epistaxis – number of presentations per patient	NR	1.45 episodes per patient with HTN. HTN considered significant predictor for recurrent epistaxis	<0.0001

HTN = hypertension; BP = blood pressure; NR = not reported; IQR = interquartile range; ICD-9 = International Classification of Diseases, ninth edition

TABLE II
STUDIES INVESTIGATING ASSOCIATION BETWEEN ANTICOAGULATION AND ADVERSE OUTCOMES

Study details	Adverse outcome measure	Outcome definition	Medication groups	Adverse outcome	*p*
Abrich *et al.*[14] Retrospective longitudinal controlled; MINORS = 17/24	Recurrent bleeding	At least 2 episodes requiring medical care, separated by a minimum of 3 months within a 36-month period	Warfarin: 127/461 cases; 179/912 controls	27.0% cases *vs* 19.6% controls	0.001
			Warfarin & aspirin: 51/461 cases; 78/912 controls	11.1% cases *vs* 7.7% controls	0.01
García Callejo *et al.*[10] Prospective controlled; MINORS = 10/24	Bleeding severity	Blood transfusion	Dabigatran: 5 patients	4/5; 80%	<0.01
			Acenocoumarol: 17 patients	10/17; 59%	
			No anticoagulant: 18 patients	7/18; 38%	
Klossek *et al.*[21] Prospective longitudinal uncontrolled; MINORS = 12/16	Bleeding severity	>250 ml blood loss	Medication with associated bleeding risk*	67%	0.02
			No medication with associated bleeding risk	33%	

*Antiplatelet medication, non-steroidal anti-inflammatory drugs, salicylate derivatives, vitamin K antagonists, beta-lactams, antidepressants and long-term corticosteroid therapy. MINORS = methodological index for non-randomised studies

cent) and anticoagulant use (20.8 per cent). Factors associated with increased cost and length of stay were: an increased number of chronic co-morbidities, the necessity for operative intervention, Asian or Pacific Islander race (cost), black race (length of stay), top income quartile (cost), private insurance (cost), Medicaid insurance (length of stay), teaching hospital admission (cost), and certain geographical features. Subgroup analyses of patients using anticoagulant medication were not performed; hence, it could not be determined whether any of these confounding factors contributed to the lower cost and length of stay amongst these patients. Furthermore, this study represented patients in the USA, where the practices and pricing of care may differ from those in the UK.[16]

The National Institute for Health and Care Excellence key therapeutic topic information indicates the use of novel oral anticoagulants in the prevention of a number of serious and common medical conditions, including stroke and some adverse outcomes associated with acute coronary syndromes, and in the treatment and secondary prevention of venous thromboembolism and its complications.[24] The Medicines and Healthcare products Regulatory Agency ('MHRA') issued a warning of serious haemorrhage risk against three of these drugs that were licensed at the time (apixaban, rivaroxaban, dabigatran).[25] The evidence represented in this review primarily concerns the oral anticoagulant warfarin, with only one study evaluating adverse outcomes in epistaxis patients using novel oral anticoagulants.[10]

Rhinological co-morbidities. Nasal mucosal congestion in rhinitis and rhinosinusitis has been implicated in the aetiology of epistaxis, but there is insufficient evidence to support an association between congestion and patient outcomes. Only one controlled study considered this relationship.[14] When rhinological factors associated with recurrent epistaxis (as compared with a single episode of bleeding) were reviewed, no significant differences were found in terms of the incidence of: rhinitis (2.6 per cent cases *vs* 1.3 per cent controls), sinusitis (1.1 per cent cases *vs* 1.3 per cent controls) or upper respiratory tract infection (1.5 per cent cases *vs* 1.5 per cent controls).[14]

Other co-morbidities. The relationship between other co-morbidities and patient outcomes in epistaxis was considered in one controlled[14] and one uncontrolled retrospective study.[16] Abrich *et al.* found that recurrent epistaxis was associated with congestive heart failure ($p < 0.001$) and diabetes ($p = 0.04$).[14] In a longitudinal uncontrolled study of 16 828 patients, by Goljo *et al.*, an increasing number of co-morbidities was associated with a longer hospital stay in patients admitted with epistaxis because of the management of co-existing medical conditions ($p < 0.001$).[16] This study examined patients admitted to multiple centres in the USA, where practices may differ from those in the UK.

Intrinsic risk factors

Bleeding site. Two retrospective longitudinal studies investigated the relationship between anterior and posterior bleeding site and patient outcome. Both studies demonstrated that posterior site epistaxis is more frequently associated with recurrent bleeding.[15,18] One of these studies, by Ando *et al.*, reported that anterior bleeding was significantly associated with non-recurrent epistaxis (191 out of 198 patients).[15] Each non-anterior bleeding site was analysed independently, rather than as posterior epistaxis in general. Failure to identify the bleeding point (in 14 out of 267 single episode patients *vs* 17 out of 32 recurrent epistaxis patients; $p < 0.0001$) was also associated with recurrent epistaxis. Bleeding from the olfactory cleft, middle or inferior meati, or other non-anterior site did

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not achieve significance, though numbers in these subgroups were much smaller than in the anterior bleeding group.[15]

Bleeding severity. Patients with more severe bleeding appear more likely to undergo surgical intervention. In a single, small, retrospective longitudinal study, bleeding severity was compared in patients who underwent sphenopalatine artery ligation ($n = 27$) versus those who did not ($n = 71$).[17] Four measures of severity were found to be significant predictors for surgery: persistent uncontrolled epistaxis despite anterior and posterior packing (21 out of 27 patients *vs* 1 out of 71 patients; $p < 0.0001$); three or more episodes of recurrent bleeding (17 out of 27 patients *vs* 0 out of 71 patients; $p < 0.0001$); blood transfusion or haemoglobin decrease of greater than 4 g/dl (9 out of 27 patients *vs* 4 out of 71 patients; $p < 0.0001$); and three admissions for ipsilateral bleeding in three months (4 out of 27 patients *vs* 0 out of 71 patients; $p < 0.0001$).

Demographic and social history. Patient age was found not to be associated with recurrent bleeding in one retrospective controlled study.[14] Age also appears to have no relationship with continued bleeding after pack removal.[20]

Alcohol intake. Excess alcohol consumption and alcohol-induced platelet dysfunction have been implicated as risk factors for epistaxis.[26,27] Evidence relating alcohol intake history to patient outcome in epistaxis is very limited. Based on US admission data, Goljo *et al.* found that a history of alcohol abuse in epistaxis patients (5.8 per cent; 972 out of 16 828) was associated with a significantly increased length of stay ($p = 0.004$).[16] In a retrospective, longitudinal controlled trial, Abrich *et al.* found no difference in alcohol consumption between 426 patients with recurrent epistaxis and 912 matched controls.[14] Though the latter study also compared independent history of portal hypertension and gastrointestinal bleeding between the two groups (neither was significant), neither study considered the influence of any hepatic impairment nor complications of alcohol abuse on the patient outcome.

Patient mobilisation

Patient mobilisation during the hospital stay does not appear to have any effect on re-bleeding rate. The only included RCT found no significant difference between in-patients who were mobilised (21 out of 50) and those confined to bed rest (24 out of 50).[8] The mean age of the adult patients with epistaxis in the presented data was 65.4 years, meaning that many patients were above the age of 60 years and therefore at higher risk for the development of venous thromboembolism.[28] Patient mobility plays a key role in the prevention of venous thromboembolism[28] and, on the basis of limited evidence, it would appear sensible for the epistaxis patient to mobilise lightly, without increased risk of re-bleeding.[8]

Limitations

The primary limitations were low-quality evidence and poor study design, as demonstrated by the methodological index for non-randomised studies criteria, applied to assess the methodological quality of non-randomised surgical studies. There were a lack of prospective controlled trials; only 1 RCT was included,[8] and 6 of the 14 included studies were uncontrolled.[16–21] The remaining seven studies were retrospective in their methodology.[14–20] Within and between studies, there were fundamental differences in baseline demographic characteristics and co-morbidities for the participant groups compared. Furthermore, heterogeneity of study design and poorly defined outcomes meant that meta-analysis was not possible. Of particular note, definitions of hypertension were inconsistent[9,12,14,15,19,20] and there was variation in the anticoagulant medications used in the different studies.[10,11,13,14,16]

Initial management

Results

Figures 2 and 3 illustrate the search and article selection process for the first aid and initial assessment parts of this review. Three studies were included, of which none were randomised controlled trials. Two were prospective controlled studies concerning 'first aid' measures, with a total number of 72 participants (16 and 56 participants). Both papers assessed the effect of topical ice packs on nasal mucosal blood flow in healthy volunteers, as measured by laser Doppler flowmetry at Kiesselbach's plexus[29] or the inferior turbinate.[30] The studies were of a fair quality overall (Appendix II): both demonstrated a methodological index for non-randomised studies score of 17 out of 24, with robust, simple and reproducible methodology. A single retrospective uncontrolled longitudinal study relevant to 'initial assessment' of the epistaxis patient was of fair quality (Appendix III): the methodological index for non-randomised studies score was 8 out of 16.[31] This study reviewed the use of coagulation studies in 183 cases.

Summary of evidence

First aid. Various first aid measures have been adopted for epistaxis treatment, despite a lack of evidence. The only first aid measure described in the included studies was the use of an ice pack. The application of an intra-oral ice pack has the potential to decrease nasal blood flow, and this may in turn decrease epistaxis severity, although this has yet to be demonstrated. In one study, intra-oral ice significantly reduced the nasal blood flow at the inferior turbinate (23 per cent), as compared with a control pack (5 per cent, $p < 0.05$).[30] An ice pack placed on the forehead failed to achieve a significant reduction in nasal blood flow.[29,30] In one of these

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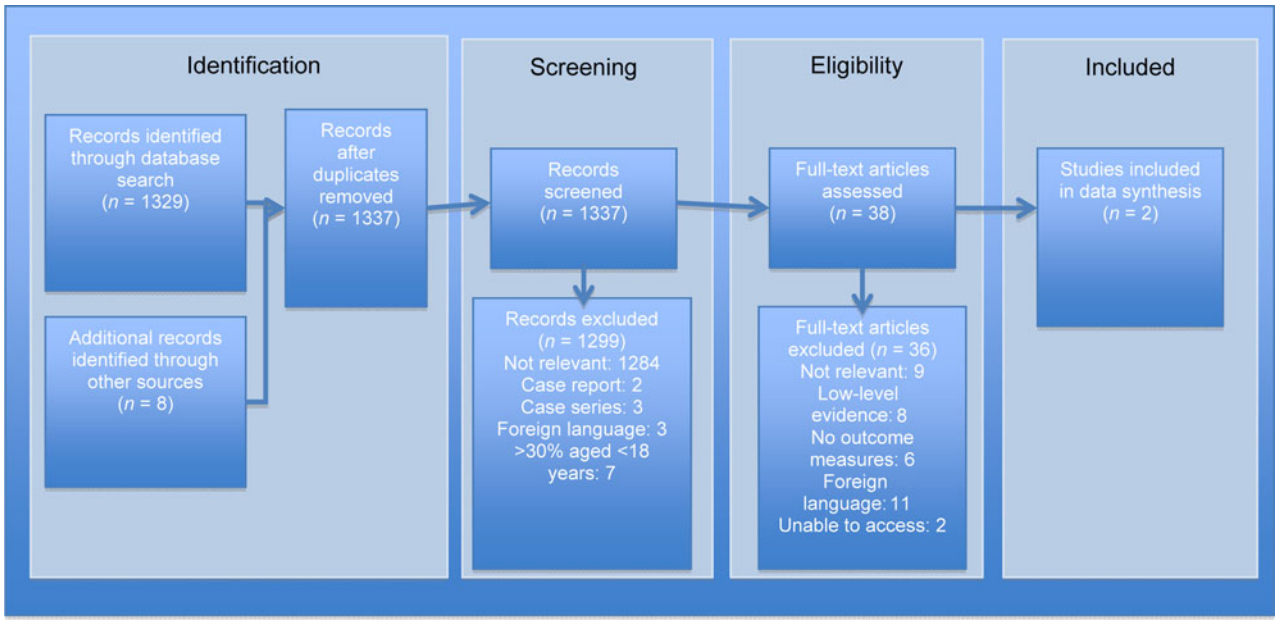

FIG. 2

Preferred Reporting Items for Systematic Reviews and Meta-Analyses ('PRISMA') diagram for the first aid review, mapping the number of records identified, included and excluded during different review phases.

studies, the standard deviations in mean blood flow following forehead application in both participant groups were very large, suggesting heterogeneity amongst individual results within a small study (1368.8 ± 927.9 before *vs* 1130.5 ± 792.2 after; $p = 0.11$).[29]

Initial assessment. Coagulation screening may be of benefit only in epistaxis patients on anticoagulant therapy or in those with a history of bleeding diatheses, as results are otherwise likely to be normal and do not add to the management process. An abnormal result is of clinical value and can guide overall management. In a retrospective longitudinal study, over a period of one year, Thaha *et al.* found that 10 epistaxis patients who had abnormal coagulation study results (out of a total of 121; 8.3 per cent) were using the oral anticoagulant warfarin, and no other coagulation abnormalities were identified in the studied population.[31] This is the only included study relevant to the role of coagulation screening.

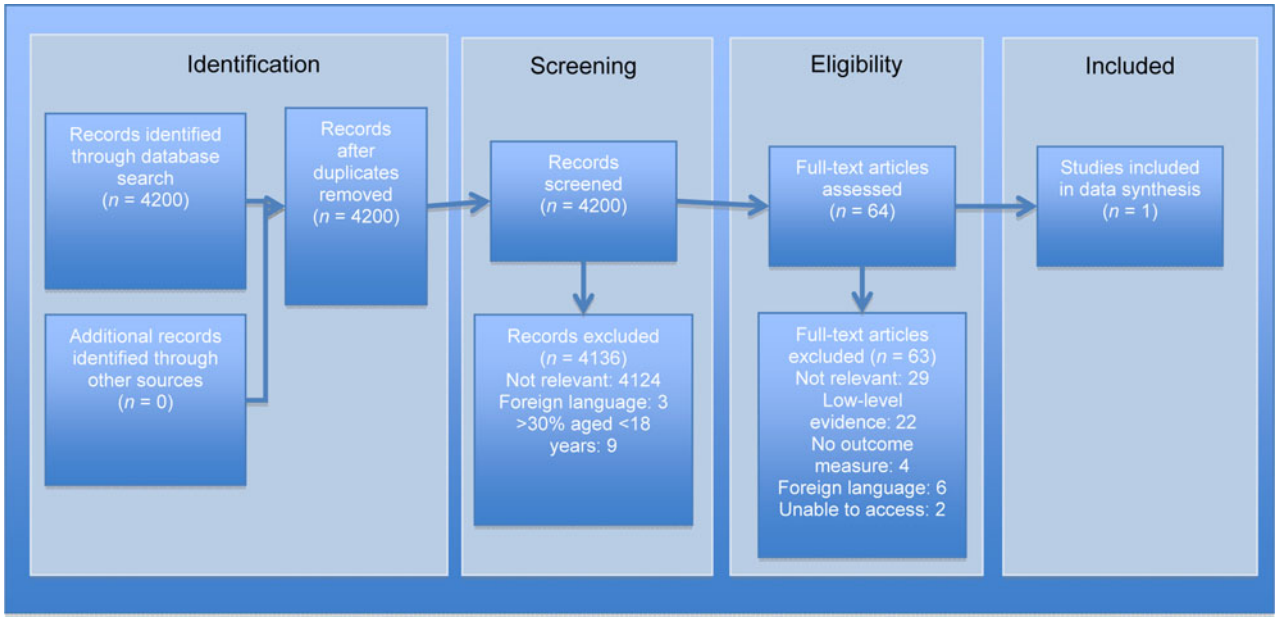

FIG. 3

Preferred Reporting Items for Systematic Reviews and Meta-Analyses ('PRISMA') diagram for the initial assessment review, mapping the number of records identified, included and excluded during different review phases.

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A single uncontrolled retrospective study set in a large Scottish teaching hospital is included in the 'Initial assessment' section of the review.[31] Of all the epistaxis patients who underwent coagulation studies, only 8.3 per cent of results were abnormal. Furthermore, these were exclusive to patients using the oral anticoagulant warfarin.[31] Although, at the time of this review, there is an absence of data representing the frequency and cost of coagulation screening in UK epistaxis patients, considerable cost savings could likely be achieved with more judicious use of the tests.

Limitations

Despite a potentially extensive theme, only two topics were represented within the first aid and initial assessment review.[29–31] This is because of the lack of published studies. The primary limitations of the identified studies were low-quality evidence and study design. The controlled studies did not declare adequate power.[29,30] Both controlled studies within the 'First aid' section studied the effect of ice pack application on nasal blood flow in healthy, young volunteers, with a median age of 31 years between the studies.[29,30] This healthy, young group is not representative of that seen clinically, with a median age of patients within the 'Patient factors' review of 66 years,[8,10–18,20,21] and co-morbidities were present in 58.6 per cent of these patients overall (where stated).[8,10,13–16,18,21]

Conclusion

Cardiovascular risk factors, particularly sustained ambulatory hypertension, and anticoagulant or antiplatelet use, appear to be associated with persistent, recurrent or heavier epistaxis. When assessing a patient with epistaxis, a history of cardiovascular disease and medications should be sought. In addition, where possible, the site of bleeding should be identified and recorded, as posterior or unidentified site bleeding can be associated with recurrent or recalcitrant epistaxis.

The application of an intra-oral ice pack is a simple first aid measure with the potential to decrease bleeding severity, and this should be considered from the onset of epistaxis to the point of hospital care. Evidence supporting the efficacy of other topical ice packs is insufficient. There is limited evidence to suggest that coagulation studies should be reserved for patients taking anticoagulant medication or those with a history of bleeding diatheses, as they do not add to the management process in other individuals.

In order for robust recommendations to be made, based on the findings of this review, future adequately powered, randomised controlled studies should address effective methods of first aid, initial assessment and investigation protocols, and determine how to best manage co-morbidities in epistaxis patients via a multidisciplinary approach.

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APPENDIX I
SUMMARY OF STUDIES INCLUDED IN PATIENT FACTORS REVIEW

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
RCT						
Kristensen *et al.*[8] (2011)	– Randomised controlled trial – Single centre, in Denmark – Total study duration: 1 y & 11 mth – Comparison of bed rest *vs* mobilising – Demographics & co-morbidities recorded	– Inclusion: admission for primary epistaxis, consent obtained within 4 h of arriving on ward – Exclusions: age <18 y, non-Danish speakers – 100 participants; 50 cases (aged 68 y (range, 43–98 y); 21 F:29M), 50 controls (aged 69 y (range, 37–96 y); 15 F:35M) – Co-morbidities: HTN, bleeding disorders, oral anticoagulant or antiplatelet medication, diabetes	– Control group: remained in bed, with backrest, in elevated position – Study group (mobilising): short, gently paced walks around ward without getting out of breath, fetching own meals & refreshments, taking care of own personal hygiene	– New bleeding – (LOS)	– New bleeding: cases = 21, controls = 24 – No significantly increased risk of new bleeding with mobilisation compared with immobilisation (OR = 0.74, 95% CI = 0.356–1.728)	Cochrane Risk of Bias – Random sequence generation: unclear risk – Allocation concealment: unclear risk – Blinding of participants & personnel: unclear risk – Blinding of outcome assessment: low risk – Incomplete outcome data: low risk – Selective reporting: low risk – Other: low risk – Allocation alternate, not random – Unclear whether it was concealed – Did not report all outcomes – Busy ward, with multiple members of staff, so opportunities for outcomes to be missed or blinding to be uncovered – Random sequence generation – Unable to conceal allocation or blind all participants as operator would have been able to tell which tube they were using – Outcome assessor blinded – Did not comment on what operators are used to using – Assessment could have been influenced by team members
Non-RCTs with comparators						MINORS; max grade of 24
Herkner *et al.*[12] (2000)	– Prospective cohort study – 4 mth – Single centre, non-trauma ED, in Austria – Cases compared to controls with different reason for admission	– Inclusion: epistaxis admission ± sustained arterial BP (on antihypertensive medication or 24 h mean of >130/85 mmHg) – 423 participants; 213 epistaxis patients, 213 controls – Mean age 63 y (range, 47–76 y) – 96 F & 117 M in each group – Co-morbidities: cardiovascular disease, pulmonary disease, metabolic disorder, infectious disease, locomotor disorder & other	N/A	(1) Arterial BP on admission to ED (control) & during epistaxis (study) (2) Prevalence of sustained arterial HTN on 24 h ambulatory BP monitoring – for patients hypertensive during epistaxis (3) Re-bleeding during admission Definitions: (1) In ED: hypertension stage 1 (140–159/ 90–99 mmHg), & hypertensive stage 2 (160–179/ 100–109 mmHg) (2) Ambulatory 24 h monitoring – mean systolic BP of >130 mmHg, diastolic BP of >85 mmHg, or both, without antihypertensive treatment (3) Long-term antihypertensive treatment	(1) Arterial BP Epistaxis group (during epistaxis): normal = 26 (12%), high normal = 29 (14%), HTN stage 1 = 50 (23%), stage 2 = 45 (21%), stage 3 = 63 (30%) Control group: normal = 49 (23%), high normal = 48 (23%), HTN stage 1 = 64 (30%), stage 2 = 34 (16%), stage 3 = 18 (8%) (2) Prevalence of sustained arterial HTN – 33/108 patients (30%) with stage 2 or 3 HTN during epistaxis responded for further investigation – 26 patients (79%) had sustained arterial HTN, 7 patients (21%) had non-sustained arterial HTN	Grade: 19 – Loss to follow up not reported – No required study size calculation – Unclear if endpoint assessment is biased

Continued

Appendix I *Continued*

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
					Subgroup analyses: (1) & (2) No significant difference in admission BP between the 2 groups. Patients with sustained arterial HTN had significantly more episodes of epistaxis than those with non-sustained arterial HTN (mean of 1 *vs* 5 episodes, respectively; $p = 0.004$)	
Abrich *et al.*[14] (2014)	– Retrospective cohort study over 20 y – Regional multicentre ENT out-patient clinics, in USA	– Inclusion: 2 episodes of epistaxis requiring medical care, separated by ≥3 mth over 36 mth (control group: single episode of epistaxis) – $n = 1373$ – Case group aged 67.0 ± 17.2 y (58.1% M) – Control group aged 66.7 ± 17.2 (50.3% M) – Co-morbidities: cardiovascular, non-cardiovascular	N/A (cross-sectional study)	Recurrence of bleeding Subgroups: (1) Demographic details (2) Common risk factors (3) Cardiovascular risk factors (4) Non-cardiovascular risk factors (5) Medication combinations (6) Laboratory values (7) Adverse events	(2) Common risk factors: – Nasal perforation: cases 1.7%, controls 1.3% – Septal deviation: cases 5.9%, controls 5.3% – Septal spurs: cases 1.7%, controls 1.3% – Rhinitis: cases 2.6%, controls 1.3% – URTI: cases 1.5%, controls 1.5% – Sinusitis: cases 1.1%, controls 1.3% (3) Cardiovascular risk factors: – Abdominal aortic aneurysm: cases 3%, controls 4% – Carotid artery stenosis: cases 7.2%, controls 9.4% – CKD: cases 6.3%, controls 7.1% – CHF: cases 28.2%, controls 19.3% – CAD: cases 33.4%, controls 34% – Cerebrovascular disease: cases 14.8%, controls 15.9% – Diabetes (type 1 or 2): cases 27.1%, controls 23.5% – Hyperlipidaemia: cases 51.8%, controls 56.5% – HTN: cases 67.2%, controls 66.7% – Hypothyroidism: cases 16.1%, controls 18.4% – Obesity: cases 26.7%, controls 27.4% – PVD: cases 13.7%, controls 12.0% – SLE: cases 0.7%, controls 1.0% (4) Non-cardiovascular risk factors: – Telangiectasias: cases 1.5%, controls 2.2% – Haemangiomas: cases 3.3%, controls 5.3% – History of GI bleed: cases 19.7%, controls 19.0%	Grade: 17 – Data retrospective – No comment on whether data are consecutive – Unclear if endpoint assessment is unbiased – Differences in cohort baseline characteristics

- Portal HTN: cases 0.2%, controls 0.4%
- History of anaemia: cases 31.7%, controls 30.5%
- Endometriosis: cases 2.4%, controls 2.3%
- COPD: cases 20%, controls 20.6%
- Migraines: cases 7.6%, controls 8.9%
- Polyarteritis nodosa: cases 0.7%, controls 0.4%
- Hyperthyroidism: cases 3.3%, controls 5.4%

(5) Medication combinations:

Antiplatelet + anticoagulant:

- Warfarin: cases 27.5%, controls 19.6%
- Aspirin: cases 41.2%, controls 44.2%
- Clopidogrel: cases 5.4%, controls 5.6%
- Aspirin + clopidogrel: cases 4.1%, controls 4.5%
- Warfarin + aspirin: cases 11.1%, controls 7.7%
- Warfarin + clopidogrel: cases 0.9%, controls 0.8%
- Warfarin + clopidogrel + aspirin: cases 0.4%, controls 0.7%

NSAID:

- Ibuprofen: cases 5.4%, controls 5.6%
- Naproxen: cases 1.7%, controls 2.2%
- Celecoxib: cases 0.9%, controls 4.4%

(6) Laboratory values:

- Median Hb g/dl: cases 13.6, controls 13.7
- Median platelets $\times 10^9$/l: cases 237, controls 225
- INR <2.0: cases 57%, controls 61%
- INR 2.0–3.0: cases 26%, controls 21%
- INR >3.0: cases 17%, controls 12%

(7) Adverse events:

- Blood transfusion: cases 2%, controls 2.5%
- FFP infusion: cases 0.4%, controls 0.7%
- Angina: cases 0%, controls 0.3%
- Stroke: cases 0.4%, controls 0%

Continued

Appendix I *Continued*

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
					Subgroup analyses: (1) Demographic details – no significant difference (all criteria) (2) Common risk factors – no significant difference (all criteria) (3) Cardiovascular risk factors – significant differences in CHF ($p < 0.001$), diabetes ($p = 0.04$) & HTN ($p = 0.04$). (4) Non-cardiovascular risk factors – significant differences in history of anaemia ($p = 0.003$) (5) Medication combinations – significant differences in warfarin use ($p = 0.001$), warfarin + aspirin ($p = 0.01$) (6) Laboratory values – no significant differences (7) Adverse events – numbers too low for statistical analysis	
Ando *et al.*[15] (2014)	– Retrospective cross-sectional study – over 1 y – Single centre, university teaching hospital, ENT department (in-patients), in Japan	– Inclusion: admission for epistaxis (previously recurrent or single episode) – Exclusions: traumatic, iatrogenic & systemic cases – $n = 299$; 173 M (57.9%), 126 F (42.1%) – Aged 64 ± 14.5 y – Co-morbidities: HTN, haematological disease, AR, chronic sinusitis, surgery, deviated nasal septum	N/A (cross-sectional study)	Recurrent epistaxis Subgroups: (1) Co-morbidities (2) Site of bleeding (3) Management	Recurrent epistaxis occurred in 32 cases (10.7%) (1) Co-morbidities: – No significant differences between groups – 94 patients (31.4%): antithrombotic medication, HTN 155 patients (51.8%), AR 61 patients (20.4%), deviated nasal septum on bleeding side 149 cases (49.8%) (2) Site of bleeding: – Significantly different ($p < 0.05$). – No recurrent epistaxis: Kiesselbach's plexus 191, olfactory cleft 19, middle meatus 17, inferior meatus 20, other 6, unidentified 14 – Recurrent epistaxis: Kiesselbach's plexus 7, olfactory cleft 3, middle meatus 3, inferior meatus 2, other 0, unidentified 17 (3) Management: – Significantly different ($p < 0.05$). – No recurrent epistaxis: haemostatic material 19,	Grade: 17 – Baseline equivalence is poor – Short follow up & unclear if there is loss to follow up – No prospective calculation of required study size

					electrocautery 225, endoscopic gauze packing 23 – Recurrent epistaxis: haemostatic material 8, electrocautery 9, endoscopic gauze packing 15	
Beran & Petruson[9] (1986)	– Cross-sectional – Population self-selecting – Single centre, university hospital, ENT department, in Sweden	– Inclusion: recurrent epistaxis – $n = 242$ – Aged 8–76 y (<30% paediatric) – 61.2% M, 38.8% F – Co-morbidities: rhinitis, cardiovascular disease, HTN, arthritis, diabetes, leukaemia, pregnancy, anaemia	N/A (cross-sectional study)	New bleed (1) Epistaxis history: frequency, duration, consultation, treatment, impact on quality of life, family history, subjective bleeding tendency, instigating factors (2) BP	(1) Epistaxis history: Significant difference between groups only for family history – 42% had close relative with nosebleed history (2) BP: No significant difference in BP for patients with recurrent epistaxis as compared with city population	Grade: 15 – Population was self-selecting – Poorly defined outcome – No comment on loss to follow up – No calculation of required study size – Retrospective self-reporting for collection of data – Baseline differences between cohorts
Denholm *et al.*[11] (1993)	– Prospective cohort over 18-mth period – Single centre, ENT in-patients, in UK	– Inclusion: admission with epistaxis – 40 patients; 20 on warfarin, 20 controls – Median age = 68 y (range, 55–79 y) – 35% M & 65% F in both groups – Co-morbidities: AF, valvular heart disease, prosthetic valve	Varied	(1) LOS (2) Re-admission Followed up over course of admission	(1) LOS: – Warfarin patients admitted until PTR in therapeutic range. Appropriately-coagulated warfarin patients = 1–17 days; over-anticoagulation = 4–48 days (median 9 days) – Control group = 1–10 days – LOS significantly longer in warfarin group than control group (6 days *vs* 3 days, $p = 0.012$) (2) Re-admissions for epistaxis: 0 in control group, 5 in warfarin group	Grade: 20 – Small study size – LOS dictated by time to therapeutic range, not re-bleeding
García Callejo *et al.*[10] (2014)	– Prospective cohort study over 2 y & 5 mth – Single centre, ENT department & ED, in Spain	– Inclusion: admission with epistaxis; on dabigatran, acenocoumarol, or no anticoagulation – $n = 222$: 19 on dabigatran (8.6%), 59 on acenocoumarol (26.6%), 144 on no anticoagulation (64.8%) – Age (only analysed as subgroup): dabigatran = 74.2 ± 5.2 y; acenocoumarol = 65.3 ± 7.8 y; no anticoagulation = 60.1 ± 12.8 y – Sex: dabigatran = 67% M, 33% F; acenocoumarol = 80% M, 20% F; no anticoagulation = 61% M, 39% F – Co-morbidities: HTN, liver disease, diabetes, renal failure, associated medications	Varied	(1) Number of admissions (2) Blood transfusion requirement (3) Necessity for 'invasive procedure' to control epistaxis (surgery or embolisation) (4) HAS-BLED score (5) Hb reduction (6) LOS Followed up over course of admission	– Dabigatran group: (1) admission 26%, (2) transfusion 80%, (3) invasive procedure 80%, (5) Hb reduction 4.8 ± 1.7 g/dl – Acenocoumarol group: (1) admission 28%, (2) transfusion 58%, (3) invasive procedure 35%, (5) Hb reduction 3.1 ± 2.0 g/dl – No anticoagulant group: (1) admission 14%, (2) transfusion 23%, (3) invasive procedure 21%, (5) Hb reduction 2.9 ± 2.1 – (2) 80% patients on dabigatran & 58.8% patients on acenocoumarol needed transfusion, compared to 38.3% of controls ($p < 0.001$) – (4) Dabigatran & acenocoumarol groups combined had higher HAS-BLED score compared to control group (4.9±1.8 & 5.2±1.6 *vs* 2.1±1.8; $p < 0.001$) – (6) No significant difference in LOS between groups	Grade: 10 – Small groups with little baseline equivalence – Retrospective – No calculation of required study size
Smith *et al.*[13] (2011)	– Prospective cohort over 7 mth – Single centre, in-patients at ENT	– Inclusion: epistaxis as primary clinical problem, referred to ENT from ED; on antiplatelets, anticoagulation or neither – $n = 119$. 3 groups: 24 (21%) warfarin, 46 (415) antiplatelet	Varied	(1) Patient characteristics (2) Medication (3) LOS (4) Interventions to control epistaxis Followed up during admission	(1) No significant differences between patient ages in the 2 study groups. Aged 22–97 y (median, 72 y); 80% aged over 60 y	Grade: 16 – Small groups with little baseline equivalence – Unclear if endpoint assessment bias – No calculation of required study size

Continued

Appendix I *Continued*

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
	department & ED, in UK	therapy, 43 (38%) no anticoagulant or antiplatelet therapy – Median age = 72 y (range, 22–97 y; 80% >60 y) – Gender not stated – Co-morbidities: AF, previous DVT, heart valve replacement, previous arterial thrombosis			(2) No significant differences between anticoagulant & antiplatelet patient groups (*t*-test, $p = 0.15$) (3) Warfarin mean stay = 4 days (range, 1–15 days). Non-anticoagulated mean stay = 2 days (range, 1–10 days). Warfarin patients more likely to require median in-patient stay of >2 days (RR = 2.50, 95% CI = 1.01–4.97, $p = 0.01$). No significant association between BP on admission & overall LOS, for any study group (4) No significant difference in posterior packing or surgery rates in warfarin *vs* non-warfarin patients ($p = 0.21$). 17% warfarin group required posterior packing *vs* 6% non-anticoagulated patients. 8% warfarin group required surgery *vs* 3% non-anticoagulated patients	
Non-RCTs without comparators						MINORS; max grade of 16
Lakhani *et al.*[17] (2013)	– Retrospective, cross-sectional, observational study over 8 y – Single centre, department of ENT, in UK	– Inclusion: in-patients undergoing SPA ligation for intractable posterior epistaxis – $n = 27$ (10 F, 17M) – Age range, 30–94 y (median 60 y) – Co-morbidities not stated	N/A (cross-sectional study)	– Hb drop >4 g &/or blood transfusion required – 3 episodes of recurrent epistaxis requiring re-packing during 1 admission – Repeated hospital admission for recurrent ipsilateral epistaxis (3 occasions in last 3 mth)	– 6/21 had >4 g drop in Hb – 17/21 had >3 re-bleeds. 6/7 needed transfusion or had significant drop in Hb; 3/17 had had 3 admissions in 3 mth – 4/21 had >3 epistaxis admissions	Grade: 11 – No control group – No prospective calculation of size required
Terakura *et al.*[20] (2012)	– Retrospective cross-sectional – Single centre in-patients, in Japan	– Inclusion: idiopathic epistaxis from Kiesselbach's plexus; persistent epistaxis = bleeding after dressing with 1:10 000 dilution of adrenaline (bosmin) + 4% lidocaine hydrochloride (xylocaine) applied for about 30 mins – $n = 133$ (64.7% M, 45.3% F) – Aged >20 y (63.9 ± 12.8 y) – Co-morbidities: stroke, cardiac disorder, diabetes, malignant tumour, hepatic disorder, asthma, thyroid disorder, hyperlipidaemia	N/A (cross-sectional study)	(1) Demographics (2) BP (3) Persistent or non-persistent epistaxis (4) Ability to identify bleeding point (5) Co-morbidities	(1) Demographics: – Persistent epistaxis: gender = 23M, 11 F; mean age = 64.2 ± 11.5 y – No persistent epistaxis: gender = 63M, 36 F; mean age = 63.8 ± 13.2 y (2) BP: – Persistent epistaxis: (181.3 ± 26.9)/(95.6 ± 15.1) – No persistent epistaxis: (156.6 ± 26.1)/(89.4 ± 16.6) (3) Increased systolic BP associated with persistent epistaxis (26% patients *vs* 8% non-persistent bleeding) (4) Bleeding point identification: – Persistent epistaxis: not locatable = 1; locatable = 33 – No persistent epistaxis: not locatable = 1; locatable = 98	Grade: 11 – Retrospective – Short follow up – Loss to follow up not reported

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					Analyses: (1) Demographics: no significant difference (2) BP: persistent epistaxis incidence higher in HTN than non-HTN patients (26% *vs* 8%; $p = 0.002$) (multivariate analysis, adjusted for co-morbidities) (3) Systolic BP higher in persistent than non-persistent epistaxis patients (181.3±26.9 *vs* 156.5±26.1; $p < 0.001$) (4) Bleeding point identification: no significant difference (5) With exception of systolic HTN, no other co-morbidities were significant between the 2 groups	
Goljo *et al.*[16] (2015)	– Retrospective cross-sectional study over 7 y – Multicentre, ENT in-patients, in USA	Inclusion: epistaxis (ICD-9) admissions – $n = 16\,828$. 8793 M (52.3%), 8035 F (47.7%) – Age: <40 to >80 y, mean 67.5 ± 17.6 y – Co-morbidities: cardiovascular disease, diabetes, anticoagulation medication, renal disease, alcohol abuse, sinonasal disease, substance misuse	None	(1) Demographics (2) Co-morbidities (3) LOS (4) Cost of hospital stay	(1) Male 52.3%, >50% over 65 y (2) 78.5% cardiovascular disease, 25.4% diabetes, 20.8% long-term anticoagulation medication, 19.6% renal disease (3) Mean LOS 3.23 days (4) Average cost $6925 Analyses: – Increasing age associated with lower cost ($53; 95% CI, 2$62 to 2$44; $p < 0.001$) & shorter LOS (20.004; 95% CI = 20.007–20.001; $p = 0.006$). – Male gender associated with increased costs ($727; 95% CI = 427–1028; $p < 0.001$) & trend for shorter LOS (20.08; 95% CI = 20.17–0.02; $p = 0.113$). – More co-morbidities associated with higher costs ($467; 95% CI = 415–520; $p < 0.001$) & increased LOS (0.23; 95% CI = 0.22–0.25; $p < 0.001$)	Grade: 10 – Retrospective – Possibly biased, as multiple variables despite large group
Klossek *et al.*[21] (2006)	– Prospective cross-sectional study over 2 consecutive 24-h periods – ENT departments at 23 separate regional centres, in France	– Inclusion: admission for non-traumatic epistaxis – $n = 50$; 35 M 15 F (70% M, 30% F) – Aged 52.5±19.0 y – Co-morbidities: HTN = 30%, pathology with haemorrhagic risk = 36%, anticoagulant or other relevant medication = 42%	None	(1) Co-morbidities (2) History of epistaxis – severity & length	Initial treatment successfully stopped bleeding within 30 mins in 47 patients (94%). 14 patients (28%) were admitted; 36 (72%) were sent home, 14 of these had nasal packing in place (1) Co-morbidities: patients who had taken medication with a haemorrhagic risk during previous 10 days were more likely to present with copious bleeding ($p = 0.02$) (2) History of epistaxis: inability to initially control bleeding was more frequent in patients who had	Grade: 12

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Appendix I *Continued*

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
					experienced bleeding for >6 h ($p = 0.04$) or copious bleeding ($p = 0.006$). Increased bleeding duration & severity were related to previous nasal packing (100% of patients with bleeding >6 h had had nasal packing compared to 0 patients with bleeding <6 h)	
Monjas-Cánovas *et al.*[18] (2010)	– Retrospective cross-sectional study, over 6 y – Single centre, tertiary hospital ENT department (in-patients), in Spain	– Inclusion: epistaxis as primary cause of admission – $n = 178$; 121 M, 57 F (68% M, 32% F) – Age range = 2–92 y (mean, 65 ± 12 y) (paediatric cases account for <30%); 79% over 50 y – Co-morbidities: HTN, coagulopathy, anticoagulant medication, HHT, hepatic disease, CKD, haematological disease	None	(1) Seasonality (2) Co-morbidities (3) Recurrent bleeding	(1) Epistaxis more common in January & April (2) HTN – 16 patients (56%), antiplatelet or anticoagulant therapies – 11 patients (41.5%) (3) Recurrent bleeding 25 cases (14%) Analyses: (2) Seasonality – no comment (3) Co-morbidities – no comment (4) Recurrent bleeding – posterior bleeding site was only variable associated with epistaxis recurrence ($p < 0.05$)	Grade: 8 Retrospective
Purkey *et al.*[19] (2014)	– Retrospective cross-sectional study, over 5 y – Single centre, ED & ENT in-patient & out-patient departments, in USA	– Inclusion: admission with epistaxis ICD-9 codes – $n = 2405$ patients (3666 episodes) – Age range 0–91 y (paediatric cases account for <30%) – Gender: 1167 M (57%), 1238 F (43%) – Co-morbidities: acute sinusitis, AR, coagulopathy, chronic sinusitis, HHT, haematological malignancy, HTN, thrombocytopaenia, alcohol & cocaine abuse, smoking, nasal steroid use	N/A (cross-sectional study)	(1) Average number of epistaxis episodes per patient by month of admission (2) Demographics, including age, race, gender, insurance status (3) Co-morbidities at time of admission	(1) More epistaxis episodes per patient in colder months or seasons ($p = 0.016$). Of seasons as defined, highest incidence occurred significantly in winter, followed by autumn, spring & summer, with significant differences between summer & autumn ($p < 0.01$) & between summer & winter ($p < 0.01$), with incidence lower in summer in both cases (2) Fewer epistaxis episodes per patient when <40 y (no p value given). No other significant findings (3) More frequent epistaxis with AR, chronic rhinosinusitis, coagulopathy, HHT, haematological malignancy & HTN ($p < 0.0001$ for all)	Grade: 11 – Retrospective – Does not investigate related variables

RCT = randomised controlled trial; y = years; mth = months; h = hours; F = female; M = male; HTN = hypertension; LOS = length of stay; OR = odds ratio; CI = confidence interval; MINORS = methodological index for non-randomised studies; BP = blood pressure; ED = emergency department; N/A = not applicable; URTI = upper respiratory tract infections; CKD = chronic kidney disease; CHF = congestive heart failure; CAD = coronary artery disease; PVD = peripheral vascular disease; SLE = systemic lupus erythematosus; GI = gastrointestinal; COPD = chronic obstructive pulmonary disease; NSAID = non-steroidal anti-inflammatory drug; Hb = haemoglobin; INR = international normalised ratio; FFP = fresh frozen plasma; PTR = prothrombin time ratio; HAS-BLED = Hypertension, Abnormal renal and liver function, Stroke, Bleeding, Labile international normalised ratio, Elderly, and Drug usage history scoring system; AF = atrial fibrillation; DVT = deep venous thrombosis; RR = relative risk; SPA = sphenopalatine artery; ICD-9 = International Classification of Diseases, ninth revision; HHT = hereditary haemorrhagic telangiectasia; AR = allergic rhinitis

APPENDIX II
SUMMARY OF STUDIES INCLUDED IN FIRST AID REVIEW

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
Non-RCTs with comparators						MINORS; max grade of 24
Teymoortash *et al.*[29] (2003)	– Compared effect of ice compression *vs* no intervention on nasal mucosal blood flow & blood content (indirectly by measuring changes in airflow) – Room at 23 °C. Blood flow measured at right angles to Little's area with non-invasive laser Doppler flowmetry (O2C; LEA Medizintechnik, Giessen, Germany) – Airflow during inspiration & expiration measured with anterior rhinomanometer (Rhino modul 180; Hortmann, Neckartenzlingen, Germany) during 5 consecutive breaths. Experiment performed on both sides of nose – Wilcoxon test used for analysis	– Inclusion criteria: healthy volunteers with normal rhinoscopy findings – Exclusion criteria: age <17 y, septal or mucosal abnormalities, history of rhinitis or nasal allergy, topical decongestants within 4 weeks – Sample: 56 subjects – Average age 30 y (range, 17–48 y), M:F ratio 27:29	5-min ice pack compression all around neck	– No patient-reported outcomes – Clinician-reported outcomes: nasal mucosal blood flow with laser Doppler flowmetry in 'arbitrary units as the mean value of 20-s measurement'; nasal mucosal blood content indirectly by 'measuring alterations in nasal airflow & airway patency' – Rhinomanometric values obtained from 5 consecutive breaths. For evaluation of nasal patency, nasal airflow was measured by 150 Pa transnasal pressure during inspiration & expiration	– With ice, nasal mucosal blood flow decreased from 1368.8 ± 927.9 to 1130.5 ± 792.2 (at 23 °C). No statistically significant difference for blood flow recordings ($p = 0.11$) – With ice, total nasal inspiratory airflow decreased to 471.5 ± 164.6 cm^3/s from 513.9 ± 190.4 cm^3/s ($p = 0.08$) – Total nasal expiratory airflow decreased to 443.1 ± 162.4 cm^3/s from 443.1 ± 162.4 cm^3/s ($p = 0.30$) – There was no demonstrable statistically significant difference between any airflow measurements in either group	Grade: 17 – Strengths: clear aims, prospective data collection, unbiased assessment of results – Weaknesses: no power calculation, overlapping confidence intervals. No information on process for selecting test subjects & their co-morbidities. Used airflow as surrogate for mucosal blood content

Continued

Appendix II *Continued*

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
Porter *et al.*[30] (1991)	– Inferior turbinate mucosal blood flow measured using a laser Doppler flowmeter in supine patients – Experiment started once stable baseline from flowmeter acquired – Application of ice to either forehead or mouth was randomised. Control was applied in same way – Results were analysed by comparing max fall in flux between ice & control *vs* baseline. Results analysed using student's *t*-test	– Inclusion criteria: healthy volunteers, no significant history of nasal symptoms or diagnoses, no medications, normal rhinoscopy – Exclusion criteria: none stated – Sample: 16 subjects – Average age 32 y (range, 25–40 y). M:F ratio not specified	– Surgical glove containing ice was applied to forehead or mouth – Controls were 'body temperature' gloves – Experimental protocol: after initial 3-min application of control pack 1, new ice packs & control packs were alternated every 3 mins (i.e. 3 mins without ice, then 3 mins with ice, then 3 mins without ice etc.)	– No patient-reported outcomes – Clinician-reported outcomes: increases & decreases in Doppler flowmeter flux when comparing ice pack *vs* control	– Oral ice pack application associated with fall in flux in 9 of 16 patients, a rise in 1 patient & no change in 6 patients. Average flux change was −23% (SE = 5.9). In oral control group, an associated fall in flux in 2 patients & no change in other 14 patients. Average fall in flux was −5%. Difference in fall in flux between the 2 groups was significant ($p < 0.05$) – Forehead ice pack application associated with fall in flux in 1 subject & rise in 1 subject, with no change in remaining 14 patients (average flux change + 1%). In control forehead group, 1 fall in flux subject only; the other 15 were unchanged (average, 2.1%). Difference between forehead ice pack & control was not significant – Duration of flux fall in those that showed a fall was 266 s on average (range, 190–500 s)	Grade: 17 – Strengths: simple, largely reproducible. Robust methodology with direct relevance to clinical practice – Weaknesses: small sample size, narrow & young age range, supine positioning not translatable to clinical practice, no follow up

RCT = randomised controlled trial; MINORS = methodological index for non-randomised studies; y = years; M = male; F = female; SE = standard error

APPENDIX III
SUMMARY OF STUDIES INCLUDED IN INITIAL ASSESSMENT REVIEW

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
Non-RCTs without comparators						MINORS; max grade of 16
Thaha *et al.* (2000)	– Retrospective case note analysis for all emergency admissions for epistaxis in large Scottish teaching hospital over 1 y – All patients who had PT/APTT were identified & their results analysed alongside platelet counts	– All emergency admissions for epistaxis in a large Scottish teaching hospital over 1 y – Patient records of 183 admissions (140 patients) were analysed – 140 patients (63 M & 77 F) were admitted between January & December 1998 – Patients who had coagulation studies were identified & their results analysed – Age: 9–97 y, mean 67±19 y	– No interventions – Retrospective observational study	– Normality of clotting studies – Anticoagulation status	– Total of 121 patients (86.4%) had coagulation studies. Of these, 10 (8.3%) had abnormal results. All were taking warfarin or combination of warfarin & aspirin – No other coagulation abnormalities were identified	Grade: 8 – Clearly stated aim, inclusion of consecutive patients, endpoints appropriate to study aim & unbiased assessment of endpoints

RCT = randomised controlled trial; MINORS = methodological index for non-randomised studies; y = years; PT = prothrombin time; APTT = activated partial thromboplastin time; M = male; F = female