

Intranasal packs and haemostatic agents for the management of adult epistaxis: systematic review

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Abstract

Background: The mainstay of management of epistaxis refractory to first aid and cauterisation is intranasal packing. This review aimed to identify evidence surrounding nasal pack use.

Method: A systematic review of the literature was performed using standardised methodology.

Results: Twenty-seven eligible articles were identified relating to non-dissolvable packs and nine to dissolvable packs. Nasal packing appears to be more effective when applied by trained professionals. For non-dissolvable packs, the re-bleed rates for Rapid Rhino and Merocel were similar, but were higher with bismuth iodoform paraffin paste packing. Rapid Rhino packs were the most tolerated non-dissolvable packs. Evidence indicates that 96 per cent of re-bleeding occurs within the first 4 hours after nasal pack removal. Limited evidence suggests that dissolvable packs are effective and well tolerated by patients. There was a lack of evidence relating to: the duration of pack use, the economic effects of pack choice and the appropriate care setting for non-dissolvable packs.

Conclusion: Rapid Rhino packs are the best tolerated, with efficacy equivalent to nasal tampons. FloSeal is easy to use, causes less discomfort and may be superior to Merocel in anterior epistaxis cases. There is no strong evidence to support prophylactic antibiotic use.

Key words: Epistaxis; Therapy; Hemorrhage; Packing

Introduction

Intranasal packing is well recognised as the primary treatment modality for epistaxis when simple measures such as direct pressure and cauterisation do not suffice.^{1–3} Nasal packing is recommended by both the National Institute for Health and Care Excellence (NICE) and the British Medical Journal Best Practice guidance after failure of these basic interventions.^{4,5} Both guidance documents recommend non-dissolvable packing and in-patient admission in light of the risk of complications and pack displacement. Despite a move towards directed therapy using endoscopes and cauterisation instruments, nasal packing remains the mainstay of epistaxis management within secondary care.⁶ This may in part be because of the ease and availability of packing.⁷

There are numerous nasal packs available, both dissolvable and non-dissolvable. In general, intranasal pack choice is guided by availability, cost and preference. This systematic review aimed to identify evidence for when, and in which setting, intranasal packing

should be used. In addition, we sought to evaluate which forms of packs should be endorsed as optimum treatment on the balance of benefits, risks, patient acceptability and economic assessment. The aftercare of patients, in terms of admission, duration of pack use and observation after pack removal in the case of non-dissolvable packs, was also reviewed.

Aims

This review aimed to address the following key clinical questions that were identified relating to dissolvable and non-dissolvable nasal packs: when should dissolvable or non-dissolvable packing be used?; which packs provide optimum treatment on the balance of benefits, risks, patient acceptability and economic assessment?; who should pack the patients?; should packed patients be admitted?; when should non-dissolvable packs be removed?; and is there a role for the removal of dissolvable packs, and when should this occur?

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. This review addresses two research domains: dissolvable and non-dissolvable nasal packs. A common methodology has been used in all reviews, described in the first of the publications.⁸ Studies were only included if they primarily involved patients aged 16 years and above treated for epistaxis within a hospital environment. Search strategies for the two domains were kept separate, but the evidence was assessed together given the significant overlap. The search strategy can be found in the online supplementary material that accompanies this issue.

Results

Twenty-seven eligible studies were identified relating to non-dissolvable packs (Appendix I) and nine relating to dissolvable packs (Appendix I). Figures 1 and 2 illustrate the search and article selection process.

Summary of evidence

Indications for nasal packing

The initial management of epistaxis involves simple measures such as the application of pressure, followed by cauterisation. Epistaxis can either be anterior, which is often self-limiting, or posterior.⁹ In most studies,

packing was advocated for patients in whom such basic measures failed; however, no specific guidance was provided regarding the optimum duration for such measures. Singer *et al.* specified 15 minutes of pressure followed by a further 15 minutes of pressure after the application of a topical nasal decongestant if epistaxis persisted.¹⁰ Thereafter, epistaxis management was escalated. In the studies that did specify when packing should be employed, the range of time for simple pressure and cauterisation prior to nasal packing varied from 30 minutes to 2 hours.^{2,7,11}

The commonly used non-dissolvable packs include nasal tampons, alginate-covered nasal balloons, and ribbon gauze which may be impregnated with bismuth iodoform paraffin paste. To avoid gaps in evidence, topical gel agents (gelatine-thrombin matrix haemostatic sealants FloSeal[®] and Surgiflo[®]), and fibrin sealants Tisseel[®] and Evicel[®]) have been included in this dissolvable pack section.

There is a paucity of good quality evidence supporting the use of dissolvable packs. However, with no reported complications in the literature, dissolvable packs appear safe to use in acute epistaxis. A prospective randomised controlled trial (RCT), which included 70 patients, supported using FloSeal over Meroceal[®] packs following failed conservative measures such as nose pinching in anterior epistaxis (level 1b evidence).¹² The re-bleed rate within the first 7 days was also lower in those treated with FloSeal (14 per cent

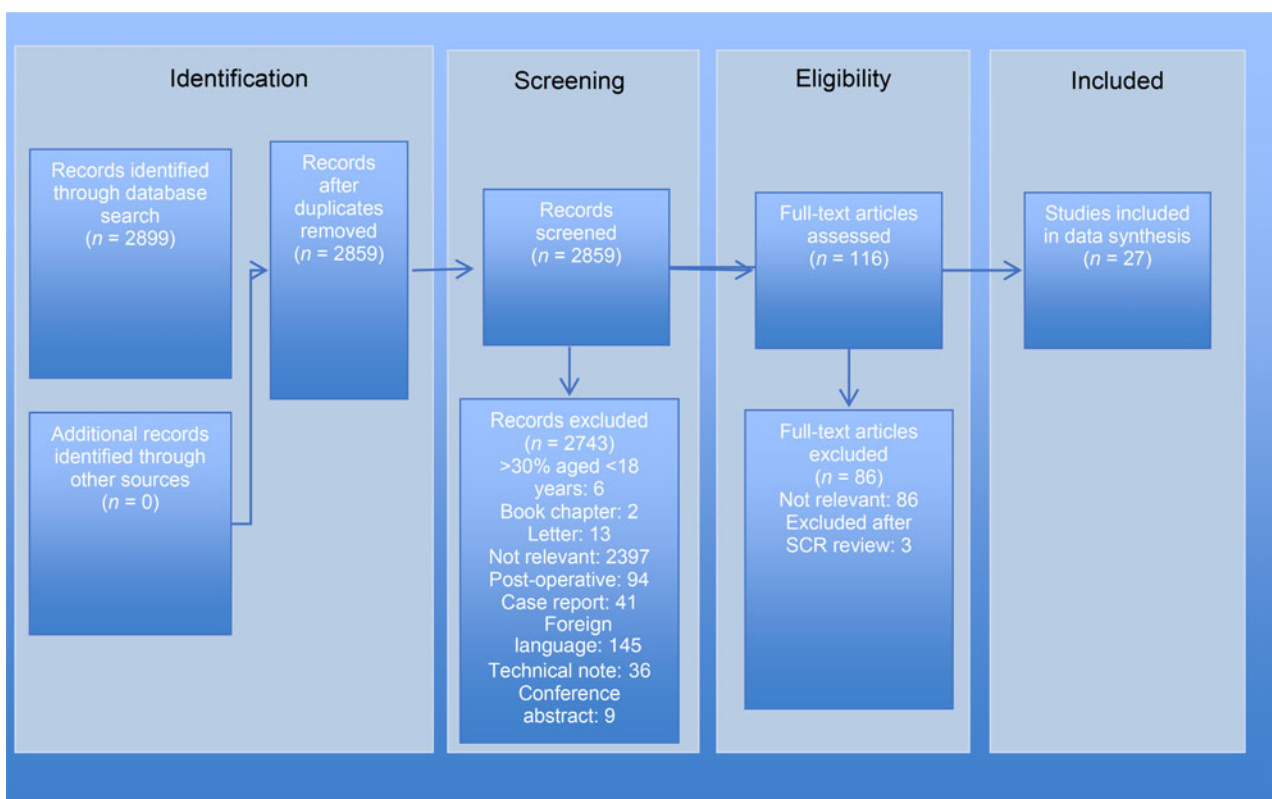


FIG. 1

Preferred Reporting Items for Systematic Reviews and Meta-Analyses ('PRISMA') diagram for the non-dissolvable packs review, mapping the number of records identified, included and excluded during different review phases. SCR = ??

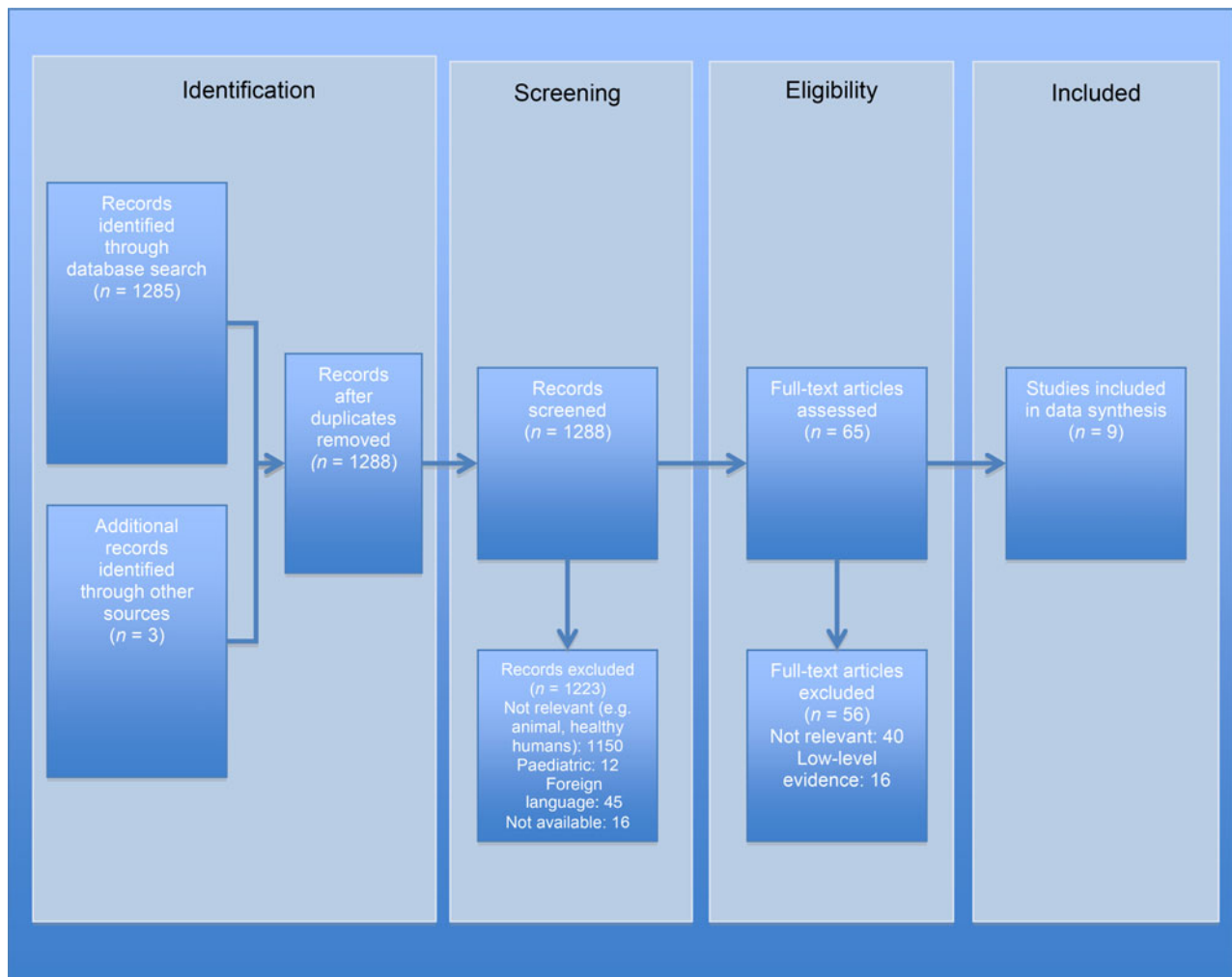


FIG. 2

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

vs 40 per cent; $p < 0.05$).¹² Additionally, dissolvable packing can be used in anterior epistaxis following failed cautery or anterior pack use in an effort to avoid surgical intervention, although the evidence for this is weak (level 2b).^{13,14} There is evidence (level 2b) to support the use of dissolvable packing in posterior epistaxis.^{15–17} In selected coagulopathic patients who fail to respond to either silver nitrate cautery or non-dissolvable packs, fibrin sealant appears to be efficacious (level 4 evidence – weak cohort study),¹⁸ however, there are significant cost implications, as FloSeal is currently considerably more expensive than the non-dissolvable packs available, and the evidence we present is based on a single RCT.

Nasal packing should be performed in a setting with appropriate lighting and equipment.^{1,4} Epistaxis patients are usually managed by healthcare professionals other than otolaryngologists at first presentation, and often by junior members of the team who may not be experienced in nasal pack insertion.¹⁹ Those patients who require escalation of treatment subsequently arrive under the care of the ENT team only once they have been packed.

Glicksman *et al.* performed an RCT, and demonstrated that both computer-assisted learning and text learning relating to nasal packing (ribbon gauze and nasal tampon) improved an individual's ability to perform this procedure.²⁰ The computer-assisted learning group were able to learn the skill more effectively (level 1b evidence).²⁰ However, their training time was longer than those who received text-based learning. A study by Lammers (involving ribbon gauze packing on a training model) further supports the concept of training in nasal packing.²¹ The author concluded that practical training allows the individual to learn and retain the skills better than observational training. The group also noted that, over time, if the skill was not used, the ability to perform it diminished equally.

Training (computer-assisted learning and simulation) in both anterior and posterior nasal packing provides a significant benefit, by increasing the ability to adhere to a department protocol,²¹ improving practitioners' confidence, enabling an increased amount of gauze to be packed,²² and improving non-specialists' speed and efficacy in packing (level

1b).²⁰ A retrospective observational study by Evans *et al.* found that patients packed by emergency department staff were more likely to require further treatment in the form of either nasal packs or cautery when compared with patients packed by ENT department staff ($p = 0.004$; level 2c evidence).⁶ Conversely, there was a significant difference in the length of admission, with ENT-packed patients having a longer admission (2.54 days *vs* 2.86 days; $p = 0.0012$; level 2c evidence).⁶ This may be because those who required ENT input had more severe epistaxis or associated co-morbidities, though the authors did not expand upon this in the study.

FloSeal and fibrin sealants should only be applied by those experienced in their use. They are, however, simple to use and could be administered by appropriately trained non-specialists. In posterior bleeds, evidence supports the use of adjuncts with dissolvable packs, such as endoscopic identification of the specific bleeding points^{14–16,18} or the use of a Foley catheter,^{12,17} to prevent spillage posteriorly. In these cases, relevant expertise in such techniques is required. Techniques involving endoscopic instrumentation are likely to be beyond the competence of a non-specialist and should be reserved for suitably trained ENT specialists.

Effectiveness of nasal packing

Evidence for the efficacy of individual packs is limited to a small selection of studies. The reported re-bleed rates appear similar for Rapid Rhino[®] and Merocel non-dissolvable packs.^{7,23} There was no significant difference in the proportion of patients requiring repacking for bleeding after the initial placement of either Merocel or bismuth iodoform paraffin paste packs for anterior epistaxis.¹¹

Two studies compared traditional non-dissolvable packing to Kaltostat[®] (calcium alginate). Murthy *et al.* packed patients with bismuth iodoform paraffin paste during a five-month period, followed by Kaltostat during a six-month period, and they analysed re-bleed rates and other patient outcome measures.²⁴ The use of bismuth iodoform paraffin paste led to a longer duration of packing and a higher rate of epistaxis recurrence (no statistical analyses were performed).²⁴ Xeroform[®] (bismuth tribromophenate), a non-dissolvable pack, had similar re-bleed rates and levels of patient-reported discomfort to those of Kaltostat.²

Rapid Rhino inflatable packs are reported to be easier to insert for healthcare professionals.⁷ There is no evidence of additional clinical benefit from the increased ipsilateral pack pressure when using a contralateral pack in the setting of unilateral bleeding.²⁵ Although the volume of air used to inflate a Rapid Rhino corresponds to a linear increase in pressure, for a given volume of inflation, a wide variation exists in the intranasal pack pressure attained in different individuals.²⁶

The literature suggests that Rapid Rhino packs are most tolerated by patients, with significantly less pain on insertion and removal compared with both the Merocel pack and the less commonly used Rhino Rocket[®] pack (level 1b evidence).^{10,23} No differences in discomfort were observed between bismuth iodoform paraffin paste and Merocel packs.¹¹ In a study by Nikolaou *et al.*, non-dissolvable packs were found to be more painful in comparison to nasal cautery.²⁷

The cost implications of using non-dissolvable packs are difficult to determine from the literature. Retrospective analysis within a Swiss clinic revealed that the costs associated with Rapid Rhino pack use were primarily influenced by whether treatment was delivered on an in-patient or out-patient basis.²⁷ There are no high-level studies reporting re-admission rates to recommend the use of one pack over another.

In the absence of any comparative study, we are unable to support the use of a specific dissolvable pack over any other. FloSeal is the most reported product in the literature. It appears to be superior to Merocel packing with respect to patient comfort, ease of use and control of bleeding in anterior epistaxis.¹² There are studies, albeit less robust, that support its use in posterior epistaxis also.^{16,17} Unfortunately, no studies compare FloSeal to Rapid Rhino packs, which are seen by many as the optimal non-dissolvable packing.

Surgicel[®] and Chitosan[®] gauzes have also been successfully utilised, again with good patient tolerance. However, these appear to require more expertise because of the need for endoscopic insertion, possibly offsetting any monetary advantage that may be attained by admission avoidance.^{14,15} FloSeal, on the other hand, can be used by emergency department staff without specialist input,^{12,13} and may have economic advantages with perceived lower admission and re-bleed rates.¹³ Dissolvable packs appear safe, with few, minor complications reported.²⁸ Therefore, although a robust economic assessment of FloSeal and dissolvable packs more generally has not been reported, it would appear that there might be potential for their use earlier in the epistaxis management pathway.

Management after pack insertion

The NICE Clinical Knowledge Summary and British Medical Journal best practice guidelines both recommend admission of patients following nasal pack insertion, to monitor for complications and pack displacement when using traditional non-expandable packs.

High-level evidence within the literature regarding the management of patients after packing is limited. Not all patients managed with inflatable non-dissolvable packs require admission (level 2b evidence). Patients undergoing anterior nasal packing can be safely managed as out-patients with a pack in situ, with no adverse events.²⁹ Evidence to support this

approach includes a 73 per cent reduced admission rate of patients undergoing anterior nasal packing placed by emergency staff, after the introduction of a new epistaxis protocol (level 2c).¹⁹

Alternatively, early discharge following pack removal is acceptable, following a recommended 4-hour observation period in appropriate patients. In a small prospective study of 50 patients, 20 per cent experienced re-bleeding events, of which 96 per cent occurred within 4 hours.³⁰

Complications associated with nasal pack placement include obstructive sleep apnoea (OSA) and infection. Obstructive sleep apnoea may be induced, or underlying OSA markedly exacerbated, following nasal packing.³¹

The role of prophylactic antibiotics remains uncertain. Bacteraemia is reported in 12 per cent of patients with posterior packs.³² Use of topical antibiotics was associated with more single micro-organism, Gram-positive growth, in contrast to mixed and predominantly Gram-negative growth in the non-antibiotic group.³² Evidence for prophylactic systemic antibiotics is limited by sample size and study design. A blinded, pilot RCT on posterior packing reported increased rates of foul-smelling packs and predominantly Gram-negative growth in the control arm not receiving intravenous antibiotics, but no significant differences in infective complications (level 1b).³³ These findings were supported by the contemporary literature.³⁴ Further studies have not identified differences in bacterial growth following anterior packing for more than 24 hours.³ A protocol-led reduction in prophylactic oral antibiotic usage had no consequential increase in complication and re-bleed rates.³⁵

The literature reports pack removal at a wide range of times after insertion. Benefits of early removal may exist for the patient, with packing for 12 hours shown to be as effective as packing for 24 hours, with significantly less discomfort.¹ Nasal packing beyond 3–5 days had no additional benefits, with no significant impact on re-bleed rates.³⁶

There is no evidence to support the admission of patients in which epistaxis has been successfully arrested by dissolvable packs.^{12,13,15,16} Patients with significant co-morbidities or those with a lack of social support may require admission. The number of epistaxis patients requiring admission for these reasons can be significant, with half the trial participants admitted only for these indications in one study.¹⁶ Only one study offered any suggestion on the length of observation required prior to discharge (1 hour).¹⁷

There was little evidence to support the removal of dissolvable packs, with the majority of studies leaving the packing material in situ. One paper described washing out excess FloSeal with saline, without any reported complications.¹⁷ In studies where large amounts of Surgicel or Kaltostat were used to completely fill the nasal cavity, packing was typically removed 24–72 hours later.^{2,24,37}

Limitations

There are numerous studies describing epistaxis management; however, there is a paucity of high-level evidence. There is insufficient evidence to determine when patients should be packed, and whether admission is required for those with non-dissolvable packs. There is also no clear evidence on the recommended duration of non-dissolvable pack use, or the duration of observation following this. More research is required to determine ongoing long-term sequelae of packing. An economic analysis of the different packs has not been performed.

Heterogeneity among the studies analysed, and a lack of high-level evidence, results in a significant risk of bias at study level. This has been mitigated with regards to FloSeal, with several studies of varying quality from different regions of the world reporting positively on its use. Most of the dissolvable pack studies included in this systematic review scored poorly on the bias assessment (Appendix II), with low numbers of patients, incompletely reported methodology or outcomes, and inadequate follow-up protocols. There were articles that may have been of interest, but were not included in the review because they are written in a foreign language or are unavailable.

Conclusion

Intranasal packing is the mainstay of epistaxis management following first aid measures and cautery. There is evidence demonstrating that simulation training improves the ability to perform this. The efficacy of Rapid Rhino and Merocel packs in controlling epistaxis is similar. However, the ease of insertion and reduced patient discomfort supports the use of Rapid Rhino as the non-dissolvable packing of choice. Regarding dissolvable packing, there is a lack of evidence of efficacy, as opposed to evidence suggesting no efficacy. The evidence synthesised from this systematic review is inadequate to provide clear and confident recommendations based on the questions we set out to answer. Currently, recommending dissolvable packs over other treatment modalities including non-dissolvable packs is inappropriate because of the lack of evidence. However, based on clinical and economic factors, dissolvable packs may have a role in managing acute primary epistaxis, particularly in coagulopathic or high-risk surgical cases. Based on the lack of reported complications, it is sufficient to recommend the continued use of dissolvable packs in units that have adopted such techniques with robust clinical governance protocols, with a call for transparency in reporting and further research.

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Miss I Z Iqbal takes responsibility for the integrity of the content of the paper

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APPENDIX I
SUMMARY OF STUDIES INCLUDED IN NON-DISSOLVABLE PACKING REVIEW

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
<i>RCTs</i> Kundi & Raza ¹ (2015)	<ul style="list-style-type: none"> – Single centre – Non-validated proforma used to gauge symptoms after nasal pack removal – Patients were interviewed about their experience with intranasal packing – Patients described severity & presence of headache & lacrimation in own words – Based on patients' description, decision regarding presence of symptoms was made – Patients were observed for 30 min for epistaxis recurrence 	<ul style="list-style-type: none"> – Inclusion: epistaxis due to trauma, refractory to simple methods (nose pinching, topical nasal decongestants, cautery) – Exclusions: posterior nasal packing, patients with bleeding disorders, anti-coagulant agent use, pre-existing sinonasal disease, previous significant medical illness – <i>n</i> = 60 total: bilateral nasal packing for 12 h (group A; <i>n</i> = 30) or 24 h (group B; <i>n</i> = 30) – Average age: 36 y, M:F ratio 2:3 	<ul style="list-style-type: none"> – Packing with 1-inch (2.54 cm) thick ribbon gauze soaked with 1% lignocaine & adrenaline – Bilateral nasal packing for 12 h (group A) or 24 h (group B) – All patients received Augmentin & paracetamol 	<ul style="list-style-type: none"> – Patients reported on: headaches, excessive lacrimation – Clinician reported on: re-bleeds 30 min after pack removal, nasal bleed recurrence when packs removed 	<ul style="list-style-type: none"> – Significant difference (<i>p</i> < 0.001) for headache 12 h 4/30; 24 h 19/30 between removal of nasal packs after 12 & 24 h – Significant difference (<i>p</i> = 0.001) for excessive lacrimation 12 h 7/30; 20/30 at 12 & 24 h – No significant difference (<i>p</i> = 0.317) for bleeding recurrence on pack removal 	<p>Cochrane Risk of Bias</p> <ul style="list-style-type: none"> – Random sequence generation: high risk – Allocation concealment: high risk – Blinding of participants & personnel: high risk – Blinding of outcome assessment: high risk – Incomplete outcome data: low risk – Selective reporting: low risk – Other: high risk – Random sampling – Sample size justified – Patients assigned to groups by lottery method

Continued

Appendix I *Continued*

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
McGlashan <i>et al.</i> ² (1992)	<ul style="list-style-type: none"> – Prospective randomised trial comparing dissolvable (Kaltostat) & non-dissolvable (Xeroform) packs – Packs removed 24–36 h after haemostasis achieved & patient discharged later that day – History, nasal anatomy & pathology, & vital signs & blood indices were recorded – In addition, doctors' & patients' perception of degree of difficulty & discomfort of nasal packing & its removal assessed using 5-point VAS – Follow up 6 weeks after discharge, & any complications recorded 	<ul style="list-style-type: none"> – Inclusion: >2 h significant epistaxis – Exclusions: aged <16 y, pregnant, haemorrhage following nasal surgery, declined to take part – <i>n</i> = 40 total; <i>n</i> = 20 Kaltostat, <i>n</i> = 20 Xeroform (2 dropouts) – Kaltostat group mean age 67 y (range, 16–93 y) Xeroform mean age 64 y (range, 28–88 y) M:F ratio 8:11 (Kaltostat) M:F ratio 11:8 (Xeroform) 	<ul style="list-style-type: none"> – Application of 10% cocaine solution on ribbon gauze to nasal mucosa – 1st pack inserted on side of initial haemorrhage. If control not achieved immediately, another pack inserted in contralateral nasal cavity – Patients restricted to bed, sedated with 2 mg diazepam 8 hourly, & given either 250 mg amoxicillin 8 hourly or 250 mg erythromycin 6 hourly, until pack removed – If bleeding not controlled within 1 h of pack insertion, further treatment given 	<ul style="list-style-type: none"> – Patients reported on: discomfort of nasal packing & its removal, assessed using 5-point VAS – Clinician reported on: epistaxis site, unilateral or bilateral packing, re-bleed rate on discharge 	<ul style="list-style-type: none"> – 'No significant difference' for pain of insertion – 'Similar magnitude' of discomfort for pack removal – No statistical analysis or summary apart from bar chart – Further in-patient treatment for 4 patients with Kaltostat packs & 3 with Xeroform – Kaltostat packing: unilateral 8 (42%), bilateral 11 (58%) – Xeroform packing: unilateral 6 (32%), bilateral 13 (68%) – Non-significant difference in re-bleed rate (8 Kaltostat, 4 Xeroform) 	<ul style="list-style-type: none"> – Random sequence generation: low risk – Allocation concealment: low risk – Blinding of participants & personnel: high risk – Blinding of outcome assessment: high risk – Incomplete outcome data: low risk – Selective reporting: high risk – Other: low risk – Prospective – Good follow-up rate & loss reported – Poor reporting of outcomes

<p>Moumoulidis <i>et al.</i>²³ (2006)</p>	<ul style="list-style-type: none"> - Contralateral nasal cavity left unpacked - Packs inserted according to manufacturer's instructions - Objective assessment by staff for bleeding control - Patients' subjective impression on pack discomfort recorded on 11-point pain scale (range, 0–10; 0 = no pain & 10 = most severe pain) - All patients asked to record discomfort during pack insertion or removal within 5 min of procedure - Patients received: Merocel packing (group 1) or Rapid Rhino packing (group 2) - Analysed using chi-square test 	<ul style="list-style-type: none"> - Inclusion: epistaxis unresponsive to first aid measures or unsuitable for cauterly, patients taking anticoagulants or NSAIDs - Exclusions: aged <16 y old, any form of nasal pack inserted elsewhere prior to attendance - $n = 42$ total; $n = 21$ each group - Average age: M = 71.3 y (range, 19–91 y), F = 72.6 y (range, 18–89 y); no breakdown between groups - M:F ratio 11:10 	<ul style="list-style-type: none"> - Blood clots removed & nasal cavity cleaned with cotton wool soaked in xylocaine (lignocaine) 5% - Pack inserted: Merocel 8 cm anterior pack lubricated with Naseptin cream prior to insertion & expanded using 10 ml normal saline. Rapid Rhino 7.5 cm pack moistened with sterile water for 30 s prior to insertion - After insertion, packs inflated via cuffed catheter to relevant individual volume - Contralateral nasal cavity was unpacked - Packs inserted by on-call ENT officer - Packs left in situ for 24–48 h before removal, unless bleeding control not adequate & an alternative form of treatment initiated 	<ul style="list-style-type: none"> - Patients reported on: pain of insertion, pain whilst in situ, pain during removal - Clinician reported on: control of bleeding (yes or no), duration packs left in situ 	<ul style="list-style-type: none"> - Merocel: success at controlling epistaxis in 17/21 (81%). 4 cases that were not controlled underwent BIPP packing with Foley catheter, & 1 EUA & SPA ligation - Rapid Rhino: success in 16/21 (76%). 4 BIPP & Foley, & 1 EUA & SPA ligation. No difference ($p = 0.917$) - Mean time of pack insertion was 32 h for Merocel & 31 h for Rapid Rhino - Subjective patient reports (non-parametric data, but includes means. VAS 0–10): - Pain on insertion: Merocel = mean 6.47 (3–9); Rapid Rhino = mean 3.85 (1–7); $p < 0.001$ - Pain whilst in situ: Merocel = mean 2.28 (0–4); Rapid Rhino = mean 2.33 (0–5); $p = 0.979$ - Pain during removal: Merocel = mean 5.04 (2–8); Rapid Rhino = mean 2.47 (0–5); $p < 0.001$ 	<ul style="list-style-type: none"> - Random sequence generation: unclear risk - Allocation concealment: low risk - Blinding of participants & personnel: high risk - Blinding of outcome assessment: high risk - Incomplete outcome data: low risk - Selective reporting: unclear risk - Other: low risk - Randomised trial - Allocation via sealed envelopes, selected by independent observer
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Appendix I *Continued*

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
Singer <i>et al.</i> ¹⁰ (2005)	<ul style="list-style-type: none"> – Prospective RCT – Managed according to fixed protocol – If initial management failed, packs were placed depending on random allocation – All patients followed up for anterior nasal packing removal in 24–72 h – Packing removal performed by physician (not always an investigator) independent of investigator who inserted tampon. No additional procedures were performed to enhance tampon removal (e.g. softening with water) – After packing removal, patients directed to use nasal saline spray & humidifier at home – Patients instructed to avoid nasal trauma for 1 week after packing removal 	<ul style="list-style-type: none"> – Inclusion: haemodynamically stable but active bleeding; isolated unilateral epistaxis requiring anterior nasal packing; patients with coagulopathy or blood dyscrasias – Exclusion: aged <18 y, pregnant women, multiple trauma, active medical conditions (e.g. chest pain) – <i>n</i> = 40 total; <i>n</i> = 20 in each group – Median age: 78 y (range, 55–80 y), M:F ratio 13:7; 54 y (range, 36–77 y), M:F ratio 14:6 	<ul style="list-style-type: none"> – Patients instructed to blow nose & apply direct pressure to nares for 15 min – Nasal septum sprayed with 2 ml 4% lidocaine & 1% Neo-Synephrine, before applying another 10–15 min of pressure – If diffuse bleeding persisted, patients randomised to anterior nasal packing with Rapid Rhino nasal pack with Gel Knit, or Rhino Rocket nasal tampon – Rapid Rhino soaked in sterile water until fabric completely converted into gel. Entire length inserted into patients' nostril. Balloon inflated with 10–15 ml of air, & pilot cuff checked for firmness – Before discharge, additional air added to cuff as needed – If bleeding persisted, further treatment was at discretion of treating physician – All patients treated with prophylactic antibiotics & oral decongestant (30 mg pseudoephedrine if not contraindicated) 	<ul style="list-style-type: none"> – Patients reported on: pain of insertion & removal of nasal packing (VAS, 100 mm scale) – Clinician reported on: haemostasis success, rate of bleeding recurrence immediately after tampon removal & within 2 days, physician ease of insertion & removal (Likert 5-point scale) 	<ul style="list-style-type: none"> – Pain of insertion (mean VAS): Rapid Rhino = 30 mm (95% CI = 18–41); Rhino Rocket = 48 mm (95% CI = 34–61) – Pain of removal (mean VAS): Rapid Rhino = 11 mm (95% CI = 1–21); Rhino Rocket = 23 mm (95% CI = 13–33) – No significant differences for either ease of insertion or removal, presented as a risk ratio but is inconsistent in its control & study group, so interpretation confusing – Ease of insertion RR was 0.7 for Rhino Rocket – Ease of removal RR was 0.5 for Rapid Rhino – Re-bleed after removal RR was 0.2 for Rapid Rhino 	<ul style="list-style-type: none"> – Random sequence generation: low risk – Allocation concealment: low risk – Blinding of participants & personnel: high risk – Blinding of outcome assessment: unclear risk – Incomplete outcome data: low risk – Selective reporting: low risk – Other: high risk – Detailed methodology – No power calculation – Inappropriate statistics

Badran *et al.*⁷
(2005)

- Prospective, randomised unblinded trial
- Patients with anterior epistaxis entered sequentially into trial & randomly allocated to receive either Merocel or Rapid Rhino packs
- Data collected on pack type, ease of insertion, duration of packing & patient discomfort
- Inclusion: anterior epistaxis >1 h, not controlled by digital pressure or nasal cautery, or site of bleeding difficult to identify & cauterise
- Mixed aetiology: spontaneous, hypertensive, coagulopathy-induced, traumatic, post-surgery
- Exclusions: aged <16 y old, posterior epistaxis
- Patients requiring repacking because of continued bleeding
- *n* = 52 total. Study group: 26 (mean age 53 y (range, 21–88 y); M:F ratio 15:10). Control group: 26 (mean age 57.5 y (range, 29–93 y); M:F ratio 18:7)
- Lidocaine hydrochloride 5% + phenylephrine hydrochloride 0.5% LA spray
- Merocel 8 cm nasal tampon, lubricated with Naseptin cream prior to insertion. Inflated by 10 ml of normal saline once in situ
- Rapid Rhino pack (55 mm balloon length) inflated with air until cuff turgidity considered appropriate
- Insertion performed blindly parallel to nasal floor after evacuation of any clots
- Only bleeding side was packed unless bleeding could not be controlled, in which case a contralateral pack of same material was administered
- If primary treatment failed to control bleeding, an alternative intervention was used (e.g. BIPP pack or surgery)
- Antibiotics not given routinely
- Pack removed 24–72 h after bleeding controlled
- Clinician reported on: type of pack placed & laterality
- Pack duration
- Difficulty of insertion & removal, where treating clinician graded perception of difficulty in inserting & removing pack on 3-point scale; 0 = easy, 3 = most difficult to insert or remove
- Haemostasis during & after pack removal. Any bleeding that occurred whilst pack in situ recorded as: no bleeding = 0, staining of dressing = 1, oozing = 2, moderate bleeding = 3, no control = 4. Similar scale was used 15 min after pack removal
- Repacking rate
- Pack duration: Merocel = 14 h (median); Rapid Rhino = 24 h (median)
- Difficulty of insertion (0–3): Merocel = 2 (median) (1.7 mean); Rapid Rhino = 1 (median) (0.9 mean); *p* = 0.0003
- Difficulty of removal (0–3): Merocel = 1 (median) (1.4 mean); Rapid Rhino = 0 (median) (0.4 mean); *p* < 0.0001
- Patient discomfort on insertion (0–10): Merocel = 7 (median) (6.9 mean); Rapid Rhino = 4 (median) (5 mean); *p* = 0.01
- Patient discomfort on removal (0–10): Merocel = 4 (median) (4.6 mean); Rapid Rhino = 3 (median) (3.4 mean); *p* = 0.05
- Bleeding during pack removal (0–4): Merocel = 2 (median); Rapid Rhino 1; *p* = 0.38
- Bleeding after pack removal (0–4): Merocel = 0 (median); Rapid Rhino = 0 (median); *p* = 0.84
- Number of cases repacked or returned to operating theatre: Merocel = 7/25; Rapid Rhino = 6/25
- Random sequence generation: low risk
- Allocation concealment: unclear risk
- Blinding of participants & personnel: high risk
- Blinding of outcome assessment: high risk
- Incomplete outcome data: low risk
- Selective reporting: low risk
- Other: unclear risk
- Computer randomisation
- Treatment schedule selected by doctor
- No blinding of participants or personnel
- Outcomes (including subjective feedback from patients) recorded by investigators
- 1 patient in each group excluded because of lack of follow up
- Consecutive patients
- No sample size calculation

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Appendix I *Continued*

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
Corbridge <i>et al.</i> ¹¹ (1995)	<ul style="list-style-type: none"> – Prospective RCT – Randomised & entered into 1 of 2 arms: BIPP or Merocel packing – Per nasal cavity packed rather than per patient analysis – Follow up at 4–6 weeks 	<ul style="list-style-type: none"> – Inclusion: bleeding >30 min, failed to respond to first aid measures – Exclusions: aged <16 y old, posterior bleeds, pregnant, post-op, significant intranasal abnormality – <i>n</i> = 49 total; Merocel = 25 (27 nasal cavities); BIPP = 24 (28 nasal cavities packed) – Overall mean age 65.8 y (range, 18–91 y), M:F ratio 29:20 (no distinction between study or control groups) 	<ul style="list-style-type: none"> – Performed by ENT SHO – Nose prepared with xylocaine 20 mg – BIPP: inserted by Thudichums & Tilley's dressing nasal forceps – Merocel (size 10), lubricated with Naseptin & kept moist with saline drops (<20 ml) – Antibiotic cover for duration of nasal packing, diazepam, & bed rest – Packs left for 36–48 h 	<ul style="list-style-type: none"> – Patients reported on: discomfort during pack administration (VAS, 0–10), & discomfort during pack removal (VAS, 0–10) – Clinician reported on: epistaxis controlled with primary pack (Y/N), repacking requirement & control with secondary pack (Y/N), lack of control with any pack or Epistat balloon (Y/N), & adverse events within 6 weeks 	<ul style="list-style-type: none"> – Insertion score (VAS): Merocel = 6 (mean); BIPP = 4.6 (mean); <i>p</i> = 0.18 – Removal score (VAS): Merocel = 3.5 (mean); BIPP = 2.73 (mean); <i>p</i> = 0.42 – Controlled with primary pack (Y/N): Merocel = 25/27 (92.6%); BIPP = 24/28 (85.7%); <i>p</i> = 0.352 – Repacking requirement & control with secondary pack (Y/N): Merocel = 1/27 (3.7%); BIPP = 3/28 (10.7%); <i>p</i> = 0.319 – Uncontrolled with any pack or Epistat balloon (Y/N): Merocel = 1/27 (3.7%); BIPP = 1/28 (3.6%); <i>p</i> = 0.746 – Adverse events: Merocel = 1/27 (3.7%); BIPP = 3/28 (10.7%) 	<ul style="list-style-type: none"> – Random sequence generation: low risk – Allocation concealment: low risk – Blinding of participants & personnel: high risk – Blinding of outcome assessment: high risk – Incomplete outcome data: low risk – Selective reporting: unclear risk – Other: unclear risk – Consecutive patients – Good randomisation – No blinding of intervention – Clinicians obtained patient VAS scores – Outcomes fully reported, except for where 2nd pack required – No sample size or power calculations

<p>Derkay <i>et al.</i>³³ (1989)</p>	<ul style="list-style-type: none"> - Prospective, randomised, placebo-controlled, double blind study - Single centre - Data collected on demographics, drug side effects, temperature, days of packing, packing odour, pneumatic otoscopy, audiological testing, leukocyte count, febrile episodes, sinus imaging & anterior rhinoscopy findings - Clinician & patient blinded; antibiotic delivered in unmarked bag (pharmacy-level concealment) 	<ul style="list-style-type: none"> - Inclusions: patients requiring posterior packing over 2-y period - Exclusions: immunocompromised, valvular heart disease, prior antibiotics, packing with other devices including balloon packing, packs removed before 72 h - <i>n</i> = 20 total - Study group (antibiotic): <i>n</i> = 10 patients, mean age 50 y (range, 26–67 y), M:F ratio 5:5 - Placebo: <i>n</i> = 10 patients, mean age 58 y (range, 26–87 y), M:F ratio 4:6 	<ul style="list-style-type: none"> - All posterior packs placed by otolaryngology resident - Unilateral or bilateral packs - Antibiotic impregnated gauze used posteriorly & Vaseline gauze anteriorly - Placebo group did not receive IV antibiotics - Antibiotic group received IV cefazolin (or clindamycin if penicillin allergic). Antibiotics administered within 1 h of packing - Packs were assessed on removal & sent for C&S test - Both groups packed for >72 h - Screening baseline blood tests - Anterior rhinoscopy to assess purulence in nasal ostia - Blood cultures taken in any patient who developed temperature >38 °C 	<ul style="list-style-type: none"> - Febrile episodes - Incidence of infectious complications, bacteriology in nasal passages after packing, morbidity - Data on packing odour - Leukocyte count - Sinus X-ray - Middle-ear effusion - Drug side effects - Length of hospital stay/packing 	<ul style="list-style-type: none"> - Bacterial cultures on removal of packing: placebo = sterile (1/10), heavy growth (8/10), not obtained (1/10); antibiotics = sterile (1/10), light growth (8/10), heavy growth (1/10) - Packing odour: placebo = minimal or none (1/10), offensive (8/10), not assessed (1/10); antibiotic = minimal or none (9/10), offensive (1/10) - 89% of placebo group (multiple swabs) demonstrated heavy growth of multiple micro-organisms. In contrast, 90% of antibiotic group packs demonstrated either sterility or mild growth - No febrile episodes - Average length of hospital stay: placebo = 5.9 days (range, 4–9 days); antibiotic = 5.7 days (range, 5–7 days) - Average number of days of packing: placebo = 4.6 (range, 3–6); antibiotic = 4.7 (range, 4–6) - No patients developed infectious complications - No significant drug side effects - Baseline sinus X-rays were abnormal in 80% in each group. Follow-up sinus X-rays showed progression in 80% of placebo group & 100% of antibiotic group - Average leukocyte counts declined in antibiotic group 	<ul style="list-style-type: none"> - Random sequence generation: low risk - Allocation concealment: low risk - Blinding of participants & personnel: unclear risk - Blinding of outcome assessment: unclear risk - Incomplete outcome data: unclear risk - Selective reporting: unclear risk - Other: low risk - Good randomisation - Unclear if consecutive patients recruited - Careful double-blinding - Clinician recording of symptoms of perceived infection & clinical findings - Incomplete reporting - Odour outcome measure subject to significant bias - No sample size or power calculations
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Appendix I *Continued*

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
Glicksman <i>et al.</i> ²⁰ (2009)	<ul style="list-style-type: none"> – Prospective blinded trial comparing computer-assisted learning methods of teaching nasal packing with text-based methods – Ribbon gauze & tampon packing technique assessed 	<ul style="list-style-type: none"> – Inclusion: 1st-y medical students in USA – Exclusions: previous training or experience with epistaxis management, & prior observation of trained professional performing nasal packing – $n = 47$ total – Study group (computer-assisted learning): $n = 23$, age not recorded, M:F ratio 11:12 – Control group (text-based): $n = 24$, age not recorded, M:F ratio 14:10 	<ul style="list-style-type: none"> – Training for formal gauze & tampon packing – Computer-assisted learning, text-based learning 	<ul style="list-style-type: none"> – Gauze pack length & time taken to pack nose – Subjective assessment using adapted validated global rating system: 7 outcomes, including respect for tissue, time & motion, instrument handling, flow of operation, procedural knowledge, overall performance, & quality of final product (5-point Likert scales) – Checklist contained 6 items for tampon pack & 8 items for gauze pack – Checklist items evaluated as complete or incomplete – Students completed questionnaire to evaluate learning, measured using Likert scale 	<ul style="list-style-type: none"> – Both intervention groups demonstrated significant improvements ($p < 0.001$) from pre- to post-test, for all parameters on global rating scale, for both packing procedures – Subjective assessment: gauze pack = significant difference favouring computer-assisted learning group over text-based group for 5 of 8 checklist items & for all parameters on global assessment; tampon pack = post-test significant difference favouring computer-assisted learning group for all 6 checklist items & for all parameters on global assessment – Participants in computer-assisted learning group were able to pack more of gauze in nose at post-test than text-based group (178.3 cm vs 134.6 cm, $p = 0.002$) & were able to pack nose faster (124.3 s or 1.61 cm/s vs 155.6 s or 0.92 cm/s; $p = 0.024$) – No significant difference between groups for time to pack using tampon – Baseline data time to pack 47.5 s (1 SD = 39.2) vs 45.7 s (1 SD = 37.6); length packed 0.72 (1 SD = 0.62) vs 0.73 (1 SD = 0.58) – Computer-assisted learning group took longer to learn procedures than text-based group (315.6 s vs 268.1 s; $p = 0.023$) 	<ul style="list-style-type: none"> – Random sequence generation: low risk – Allocation concealment: low 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 concealment via sealed opaque envelope use – Randomisation reasonable – Participants aware of allocation; unclear what role this may have had on outcomes – Outcomes assessment blinded to investigators – No dropouts, missing data or apparent selective reporting

Non-RCTs with comparators						MINORS; max grade of 24
Herzon ³² (1971)	<ul style="list-style-type: none"> – Prospectively randomised, but not clear – 2 treatment groups: antibiotic ointment vs no antibiotic ointment – 115 blood cultures obtained 	<ul style="list-style-type: none"> – Inclusion: patients undergoing posterior nasal packing – $n = 33$ total; 16 in antibiotic ointment study group, 17 in control group 	<ul style="list-style-type: none"> – 115 blood cultures obtained. 2 when pack was in place & 1 within 10 min of anterior pack removal on 5th day – Systemic antibiotics administered whilst pack in place – Min of 3 blood cultures drawn from all patients for anaerobic & aerobic micro-organisms 	Blood cultures: C&S	<ul style="list-style-type: none"> – Ointment study group: 15/16 grew single organism – Control group: Gram-negative predominantly – No statistical analysis 	Grade: 10 <ul style="list-style-type: none"> – Reported element of randomisation but study/control study – Unclear outcome measures – No study size
Lammers ²¹ (2008)	<ul style="list-style-type: none"> – Compares 2 methods of training in posterior nasal packing – All subjects completed pre-training questionnaire to exclude competent trainees 	<ul style="list-style-type: none"> – Inclusion: resident physicians from emergency medicine & family practice residency programmes – Exclusion: any prior training in posterior epistaxis management in patients or on a model; any prior experience managing posterior epistaxis using posterior pack method; an acceptable performance score prior to training – $n = 28$ total; control = 15, experiment = 13 	<ul style="list-style-type: none"> – During each assessment, candidates given all necessary equipment & asked to demonstrate (without feedback) management of posterior epistaxis on a model – Assessments provided baseline measurement of procedural skill & performance speed – 1 evaluator used checklist to evaluate all performance – Experimental & control groups underwent a performance test 4–5 h after training – Evaluator, blinded to group assignment, used scoring protocol to determine whether subject's performance met the standard – This exercise was repeated 1 & 3 mth later 	Ability to pack according to set protocol	<ul style="list-style-type: none"> – Neither pre-training performance scores (% of major & minor steps completed) nor performance times were statistically different between groups – Training effect was demonstrated in both groups – Between groups, differences in % of minor steps completed & performance times were significant ($p < 0.0001$) – No significant difference between groups in number of attempts needed to reach performance standard ($p = 0.14$) – Average total training times were different for the 2 groups: 61 min (range, 43–93 min) for control group (cumulative performance time) & 87 min for study group 	Grade: 11 <ul style="list-style-type: none"> – Adequate data analysis – Single assessor (blinded) – Matched groups – Adequately powered

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Appendix I *Continued*

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
Murthy <i>et al.</i> ²⁴ (1994)	<ul style="list-style-type: none"> – Initial retrospective audit – Reviewed epistaxis practice at base hospital & 2 additional departments – Prospective study – Compared 2 different packs 	<ul style="list-style-type: none"> – Inclusion: epistaxis, including post-surgical but % not reported – <i>n</i> = 139 total; BIPP = 53, Kaltostat = 86 	For 1st 5 mth, BIPP packing was applied, followed by Kaltostat for next 6 mth	<ul style="list-style-type: none"> – Patient: pack discomfort – Clinician: ease of pack insertion & removal; rate of epistaxis recurrence after pack removal 	<ul style="list-style-type: none"> – Rate of epistaxis recurrence was 14.6% with Kaltostat & 26.4% with BIPP – Haemostasis achieved by leaving packs in for 10 h with Kaltostat <i>vs</i> 48 h with BIPP – Most patients discharged within 72 h 	<p>Grade: 10</p> <ul style="list-style-type: none"> – Aims are clear – No power calculation – Unclear inclusion criteria regarding aetiology – Methodology is vague – Insufficient description of demographic data; full data set not reported – No robust statistical analysis
Pepper <i>et al.</i> ³⁴ (2012)	<ul style="list-style-type: none"> – Prospective observational study, in which intervention was changed at 3 mth – Group 1: nasal packing + 5 days' oral antibiotics – Group 2: packing & no antibiotics – Patients packed for 24–36 h – Duration of follow up not clear 	<ul style="list-style-type: none"> – Inclusion: in-patients admitted with spontaneous epistaxis, consecutive – Exclusion: antibiotics prescribed for unrelated pathology, post-op epistaxis, cardiac anomalies, epistaxis requiring surgery – <i>n</i> = 149 total; control = 71, study = 78 	Prophylactic antibiotics whilst pack in situ	<ul style="list-style-type: none"> – Patient: facial pain & otalgia questionnaire, purulent nasal discharge on nasendoscopy, new hearing loss with Rinne & Weber tests – Clinician: infection after pack removal 	<ul style="list-style-type: none"> – Group 1 (antibiotics): Merocel = 76/78; BIPP & Foley = 5/78. 3 Merocel patients required BIPP & Foley. Otalgia reported in 2/76 Merocel patients & 4/5 BIPP & Foley patients – Group 2 (packing only): Merocel = 68/71; BIPP & Foley = 9/71. 6 patients required BIPP & Foley after failed Merocel. Otalgia reported in 3/68 Merocel patients & 5/9 BIPP & Foley patients – No purulent nasal discharge – No hearing loss data 	<p>Grade: 9</p> <ul style="list-style-type: none"> – Groups were managed & assessed with same protocol & criteria – Insufficient evidence to suggest groups are matched – No demographic data – If groups are matched, a comparison would be appropriate – Researchers not blinded – No mention of questionnaire validation or response method (e.g. VASs or scores) – Infection assessment (apart from biochemical markers) is subjective & poorly described – No power calculation or statistical analysis – Follow up not reported

<p>Biswas & Mal³ (2009)</p>	<ul style="list-style-type: none"> - Prospective study on use of prophylactic antibiotics in spontaneous epistaxis - Contralateral unpacked side acted as control - Following removal of unilateral anterior nasal packing, nasal swabs were taken from both sides for bacterial culture - Reviewed in clinic at 1 week after discharge 	<ul style="list-style-type: none"> - Inclusions: admitted spontaneous epistaxis patients undergoing unilateral nasal packing - Exclusions: bilateral or posterior nasal packing, post-op - $n = 21$; control (contralateral side of nose) $n = 21$ - No demographics included 	<ul style="list-style-type: none"> - Nasal packing - If pack was in for >24 h, prophylactic antibiotics were prescribed according to hospital protocol. 9 of the unilaterally packed patients received antibiotics 	<ul style="list-style-type: none"> - Patients asked to report adverse symptoms in week following discharge - Microbiological growth patterns - Rigid endoscopic examination 	<ul style="list-style-type: none"> - 11/21 patients had the anterior pack in for > 24 hours and these were according to hospital protocol - No patients had clinically detectable infection before or after pack removal - Microbiological growth did not differ 	<p>Grade: 13</p> <ul style="list-style-type: none"> - Clear aim - Well-defined methodology - Opposite nasal cavity used as control - Not stated who undertook examination - Data collected prospectively in accordance with agreed protocol - No power calculation, but small sample size acknowledged as limitation - No information on demographics - 13/21 patients received prophylactic antibiotics, creating a subgroup - 11 patients packed anteriorly 2 were on antibiotics for systemic unrelated infections - Varying nasal packing duration
<p>Cook <i>et al.</i>³⁸ (1985)</p>	<ul style="list-style-type: none"> - Retrospective initial analysis to generate 'data review parameters' - 2 centres prospectively selected 17 consecutive patients to undergo balloon packing & anterior gauze, & compared these with 17 consecutive patients who received posterior gauze tampon & anterior gauze - Prospective cohort age & sex matched to local cases (audited) - No randomisation information 	<ul style="list-style-type: none"> - Inclusions: posterior epistaxis treated by Foley catheter packing or gauze packing posteriorly, & gauze packing anteriorly - Exclusions: not specified - $n = 34$ total - Retrospective group $n = 17$ - Prospective group $n = 17$ - Identified 17 from an original 108 patients - Matched groups reported, not specified how - Mean age 67.1 y (range 3–93 y); age not reported for 'matched' prospective group 	<ul style="list-style-type: none"> - Group 1: packed with a 16 Fr Foley catheter posteriorly, inflated with 10 ml saline with anterior Vaseline gauze. Pack left in for ≤ 72 h - Group 2: packed with posterior gauze & anterior Vaseline gauze. Packs left in place for 5–7 days - All were in-patients & were reviewed 1–3 days after pack removal 	<ul style="list-style-type: none"> - Length of hospital stay - Need for surgery - Blood transfusion requirement - Multiple further factors & multivariate analysis performed 	<ul style="list-style-type: none"> - Average hospital stay: group 1 (Foley) = 5.65 days; group 2 (gauze) = 12.47 days. Wilcoxon rank sum test $p = 0.01-0.025$ - No significant differences identified (using chi-square & Fisher–Irwin exact tests) for: season, surgery requirement, HTN, tobacco use, alcohol abuse, blood transfusion, elevated PT, elevated PTT, elevated cholesterol, elevated glucose & decreased platelets 	<p>Grade: 9</p> <ul style="list-style-type: none"> - Clearly stated aim - No power calculation - Clear methodology - Age & sex matched controls in prospective cohort, but data not clearly presented - No exclusion criteria reported - Standardised interventions, well-defined protocol - Length of review of 1–3 days is inadequate - Patient-reported outcomes not given

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Appendix I *Continued*

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
Evans <i>et al.</i> ⁶ (2004)	<ul style="list-style-type: none"> – Retrospective observational study of patients treated for epistaxis by ENT & A&E doctors – No details on follow-up period 	<ul style="list-style-type: none"> – Inclusions: patients packed for epistaxis by either ENT or A&E, requiring admission – Exclusions: patients primarily treated by other specialties or GP; patients who had a different mode of treatment previously (e.g. cautery) – $n = 175$ (189 sides of nose) – ENT: $n = 75$, mean age 68.9 y (range, 16–93 y), M:F ratio 47:28; 2 were post-op patients – A&E: $n = 100$, mean age 66.5 y (range, 26–95 y), <16 y $n = 0$, M:F ratio 53:47 	Nasal packing (unspecified), performed either by ENT or A&E doctors	<ul style="list-style-type: none"> – Re-bleed rates – Secondary treatment required – Length of hospital stay – Data collected on co-morbidities, demographics 	<ul style="list-style-type: none"> – 54/100 A&E packed group required further treatment after initial nasal packing, vs 30/89 in ENT group ($\chi^2 p = 0.004$, 95% CI = 7–34%) – Higher proportion of A&E patients required further cautery to achieve haemostasis ($\chi^2 p = 0.005$; 95% CI = 5.4–30.4%) compared to ENT – No significant difference in both groups for requirement of other further treatment (i.e. BIPP packing, further nasal tampon or surgical intervention) – Average length of hospital stay was 2.54 days for A&E cohort & 2.86 days for ENT cohort (Mann–Whitney $p = 0.012$) 	<p>Grade: 7</p> <ul style="list-style-type: none"> – Matched demographics & co-morbidities in 2 groups – No power calculation – No reference made to pack types used or packing duration – Need for further treatment was analysed adequately – Adequate statistical analysis performed. – Conclusions drawn are satisfactory for type of study – Groups matched (determined in analysis)
<i>Non-RCTs without comparators</i>						MINORS; max grade of 16
Pringle <i>et al.</i> ³⁹ (1996)	<ul style="list-style-type: none"> – Single centre – Retrospective review of patients over 1-y period – Merocel nasal packs used as primary treatment in patients where packing required – Patient assessment & Merocel insertion performed by ENT SHO – VAS used to record pain on insertion & removal, & discomfort whilst pack in place 	<ul style="list-style-type: none"> – Inclusion: patients with epistaxis receiving nasal Merocel packing – $n = 83$ 	<ul style="list-style-type: none"> – 2 sizes of Merocel nasal pack used – Anterior pack used for: anterior epistaxis, moderate bleeding, narrow nasal cavity – Pope posterior pack used for: posterior epistaxis, profuse bleeding, large nasal cavity 	<ul style="list-style-type: none"> – Patients reported on: pain on insertion & removal (VAS) – Clinician reported on: pack type 	<ul style="list-style-type: none"> – Merocel pack: 71/83 had unilateral pack & 12/83 had bilateral packs. Successful at controlling epistaxis in 76/83 (91.5%) of 83 patients initially treated with Merocel packs – 7 failures. Epistaxis controlled by: Merocel anterior pack replaced with Merocel posterior pack (2); repacked with BIPP (1); repacked with BIPP + Foley catheter (1); repacked with BIPP + Foley catheter (also unsuccessful – epistaxis controlled by procedure under GA) – Merocel generally well tolerated based on VAS. Pain on removal had values <5 in most patients 	<p>Grade: 1</p> <ul style="list-style-type: none"> – No power calculation – No mention of consecutive patients, but as data were reviewed on all patients admitted this may have been the case – No demographic data – Follow up not specified – Incomplete data presentation – No statistical analysis

Shargorodsky <i>et al.</i> ³⁶ (2013)	<ul style="list-style-type: none"> – Retrospective observational cohort – Retrospective analysis of outcomes: dissolvable packing, nasal cautery, non-dissolvable packing, directed vascular control – Multivariate logistic regression used to calculate ORs & 95% CIs, adjusting for coagulopathy, HTN & bleeding site 	<ul style="list-style-type: none"> – Inclusion: patients presenting with epistaxis, May 2005 to June 2011. Medical record with sufficient data on epistaxis location, intervention type, haemostasis outcome, ≥ 1 follow up – Exclusions: age <18 y, epistaxis after sinonasal surgery, trauma, bleeding, vascular anomalies, sinonasal or nasopharyngeal malignancy – $n = 147$ – Mean age 61 y (range, 19–90 y); 94M:53 F 	<ul style="list-style-type: none"> – Variable: cauterisation, packing, proximal vascular control – Details not provided 	Clinician reported on treatment failure	<ul style="list-style-type: none"> – For initial epistaxis, non-dissolvable packing demonstrated highest initial treatment failure rate of 57.4% (OR = 3.37; 95% CI = 1.33–8.59) compared with cautery – No significant differences among initial posterior epistaxis treatment modalities – Length of non-dissolvable pack placement for 3, 4 or 5 days had no significant impact on recurrence – Among patients who failed initial management, those who next underwent cautery or proximal vascular control required a significantly shorter in-patient stay of 5.3 vs 6.8 days compared with those who underwent packing (OR = 0.16; 95% CI = 0.04–0.68) 	<p>Grade: 5</p> <ul style="list-style-type: none"> – Non-consecutive cases – Interventions well described – Intense statistical analysis with no sample size calculations
Soyka <i>et al.</i> ⁴⁰ (2011)	<ul style="list-style-type: none"> – Prospectively maintained database for study on acetylsalicylic acid effects – Patients treated according to an algorithm – Analyses of intervention; immediate, early & late failure were recorded 	<ul style="list-style-type: none"> – Inclusion: consecutive epistaxis patients presenting to single institution – Exclusion: trauma, HHT – $n = 537$ – Median age 70 y – M:F ratio 5:4 	<ul style="list-style-type: none"> – Protocol not provided – Patients were managed according to algorithm; this included Rapid Rhino or posterior packing following attempts, & chemical or electrocautery 	Clinician reported on bleeding recurrence (failure) rate	<ul style="list-style-type: none"> – Immediate failure of Rapid Rhino packing in 34/47 (72%) 95% CI = 0.58–0.83; Foley catheter 8/12 (67%) 95% CI = 0.39–0.86; 128/659 in 537 patients involved Rapid Rhino packing & 25/650 Foley balloon packing – Rapid Rhino 35/659 failure as 1st-line treatment; 11/128 failure as 2nd-line treatment; 46/128 total failures – Foley balloon packing 6/25 1st-line failure; 6/25 2nd-line failure; 12/25 total failures 	<p>Grade: 6</p> <p>Retrospectively assessed data</p>

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Appendix I *Continued*

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
Sugarman & Alderson ²² (1995)	<ul style="list-style-type: none"> – Assessment of training efficacy – Paired <i>t</i>-test to assess pre- & post-teaching interventions 	<ul style="list-style-type: none"> – Inclusion: A&E doctors – Exclusion: recent ENT rotation or formal experience – <i>n</i> = 17 	Training given on how to pack nose	<ul style="list-style-type: none"> – Subject-reported confidence – Length of ribbon gauze inserted, in cm – Visual score for packing 	<ul style="list-style-type: none"> – Significant improvements in all measures compared to pre-training outcomes – Confidence in own ability to pack nose (mean): 3.33 (1–6) to 8.00 (5–10); <i>p</i> < 0.001 – Length of ribbon gauze (cm) (mean): 173 (61–328) to 321 (232–412); <i>p</i> < 0.001 – Visual score for packing (1–4) (mean): 2.2 (1–3) to 3.4 (3–4); <i>p</i> < 0.001 	Grade: 7
Upile <i>et al.</i> ¹⁹ (2008)	<ul style="list-style-type: none"> – Prospective assessment of new protocol – Mean follow up of 2 days – 4 y data prior to study were audited 	<ul style="list-style-type: none"> – Inclusion: epistaxis with localised origin – Exclusion: aged <18 y, pregnancy, epistaxis of systemic origin – <i>n</i> = 60 – Mean age: 72 y admitted, 67 y discharged – M:F ratio 6:10 admitted, 29:15 discharged 	<ul style="list-style-type: none"> – Netcell pack applied & filled with 10 ml saline – Packs placed unilaterally or bilaterally depending on extent of epistaxis – If bleeding stopped & no significant risk factors (as specified in protocol) for 30 min, patient sent home with pack in situ – Patients returned on day 2 for pack removal 	Clinician reported on: whether admitted or discharged with nasal pack, adverse events	<ul style="list-style-type: none"> – 44/60 patients discharged with nasal packing – 16/60 had to be admitted (11 bled persistently after packing, 1 had sustaining trauma, 3 demanded to be admitted, 1 fainted) – From discharged group, 10 had adverse events: 7 had nasal bleeding between days 1 & 2; 1 complained of symptoms suggestive of early acute rhinosinusitis; 1 did not attend for removal until day 7; 1 had recurring minor epistaxis after pack removal – Compared to audit data, admission was reduced by 73% (<i>p</i> < 0.0001), despite no significant change in number of monthly referrals (<i>p</i> < 0.0001) – Revised management protocol saved 201 bed days per annum 	Grade: 8 <ul style="list-style-type: none"> – No power calculation – Data recorded & analysed adequately – Insufficient data presented by group

<p>Van Wyk <i>et al.</i>²⁹ (2007)</p>	<ul style="list-style-type: none"> – Prospective audit of patients managed according to revised epistaxis protocol – Single centre, A&E 	<ul style="list-style-type: none"> – Inclusion: adult patients with epistaxis, treated according to A&E protocol – Exclusion: aged <16 y – <i>n</i> = 87 – Mean age 68.2 y (range, 16–100 y) 	<ul style="list-style-type: none"> – Nasal cautery 1st line – If cautery not possible or unsuccessful, Merocel nasal packing applied & patient discharged from A&E if bleeding arrested – Patient returned after 3 days for pack removal 	<p>Clinician reported on: compliance with protocol, unplanned returns to A&E (return <3 days), number admitted & reasons, number of admissions avoided</p>	<ul style="list-style-type: none"> – 87 presented with active nasal bleeding – 15/87 treated by nasal cautery & discharged – 46/62 packed & discharged – 17/62 patients admitted (16 with nasal packing) – 12/46 discharged patients had unplanned returns to A&E 	<p>Grade: 7</p> <ul style="list-style-type: none"> – Clearly stated aim – Appropriate outcomes – No power calculation – No prospective data collection – Inclusion criteria clearly stated – No statistical analysis – Dependent on documentation – Aims well highlighted – Minimal description of methodology or efforts to reduce bias – Appropriate statistical analysis – All patients accounted for – Insufficient data to comment on long-term complications
<p>Wetmore <i>et al.</i>³¹ (1988)</p>	<ul style="list-style-type: none"> – Patients admitted who required posterior nasal pack were enrolled into study – No exclusion criteria – PSG assessment of OSA whilst packed 	<ul style="list-style-type: none"> – Inclusion: idiopathic epistaxis admission with posterior nasal pack – <i>n</i> = 14 – Mean age 56 y (range, 38–88 y) – Follow up 4–8 weeks 	<ul style="list-style-type: none"> – Posterior nasal packing with 2 × 2 inch (5.08 × 5.08 cm) gauze sponges tied with umbilical tape – Unilateral anterior packing with 0.5 inch (1.27 cm) gauze, impregnated with antibiotic ointment placed in anterior nostril – Arterial blood gas obtained pre-PSG – All patients underwent PSG whilst packing performed on 3rd or 4th night after admission; 2nd PSG performed at 4–8 weeks following study 	<p>Clinician reported on: arterial blood gas, lowest oxygen saturation during sleep</p>	<ul style="list-style-type: none"> – 12 patients included in final analysis – 10/12 had clinically significant OSA whilst packed – 10 returned for PSG at 4–8 weeks – 4/10 demonstrated OSA at 2nd PSG, ‘but baseline mean hypopnea index was slightly improved’ – No correlation between arterial blood gas & PSG findings 	<p>Grade: 8</p> <ul style="list-style-type: none"> – Poorly reported – Limited outcome data described – Exclusion criteria? – Existing OSA not clear

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Appendix I *Continued*

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
Biggs <i>et al.</i> ³⁵ (2013)	<ul style="list-style-type: none"> – Retrospective audit cycle, followed by prospective audit – Assessment of new protocol: no antibiotic prophylaxis for packed patients – Data on pack type, duration, antibiotics use, & complications collected – Telephone interview 6 weeks after intervention 	<ul style="list-style-type: none"> – Inclusion: patients admitted with anterior epistaxis requiring packing – Full records available for analysis – Exclusion: not specified – <i>n</i> = 57 – Mean age 77 y (range, 11–99 y); unspecified % <16 y – M:F ratio 3:2 	Nasal packs (anterior or posterior) ± antibiotics	Complication rates: infective nasal symptoms (nasal discharge, crusting, pain), sinusitis, chest infection, re-bleeding, re-admission to hospital	<ul style="list-style-type: none"> – Antibiotic use: 1st cycle = approx. 72%; 2nd cycle = approx. 15% – Complications, recorded per potential event as: 1st cycle = 22/226 (8.3%); 2nd cycle = 4/133 (3.0%) – Re-bleeding: 1st cycle = 9/37 (23.7%); 2nd cycle = 2/18 (10.5%) – Re-admission: 1st cycle = 3/37 (7.9%) – All non-significant differences using non-parametric assessment (Fisher's exact test, <i>p</i> > 0.05) 	<p>Grade: 8</p> <ul style="list-style-type: none"> – Clearly stated aim – Poor patient characteristics reporting – Unable to get complete data for planned 58 patients in initial retrospective study, included only 3 – Only data for 18 patients available for re-bleeding assessment – Reporting of patient-reported outcomes unclear, & obtained by clinician – Unblinded
Elwany <i>et al.</i> ⁴¹ (1986)	<ul style="list-style-type: none"> – Prospective, single centre – 34 patients had catheters placed under LA; 18 patients required GA – Arterial blood samples taken before & after 24 h – Nasal mucosa inspected after catheter removal, & patients followed up weekly for 1–2 mth – Patients interviewed 6–24 h after balloon placement; patients' discomfort & headache assessed (on 0–3 scale) 	<ul style="list-style-type: none"> – Inclusion: epistaxis controlled with Epistat nasal catheter – Exclusions: not specified – <i>n</i> = 52 – Mean age not specified (range, 29–65 y); M:F ratio 33:19 	<ul style="list-style-type: none"> – Epistat nasal pneumatic catheter placement, <i>n</i> = 52 – Group 1a: LA + unilateral Epistat, <i>n</i> = 25 – Group 1b: LA + bilateral Epistat, <i>n</i> = 9 – Group 2a: GA + unilateral Epistat, <i>n</i> = 11 – Group 2b: GA + bilateral Epistat, <i>n</i> = 7 	<ul style="list-style-type: none"> – Patient discomfort & headache – Presence of bleeding – Nasal complications 	<ul style="list-style-type: none"> – Post-packing discomfort & headache: no significant difference – Bleeding successfully controlled in 27/52 patients by keeping cuffs inflated for 24 h – Re-inflation of cuffs for another 24–48 h was necessary in 25 before epistaxis control – Complications found in 3 patients: 1 septal perforation (48 h packed), 1 mucosal necrosis (36 h packed), 1 Eustachian tube obstruction (24 h packed) 	<p>Grade: 7</p> <ul style="list-style-type: none"> – No power calculation – Non-validated questionnaire – Insufficient description of inclusion & exclusion criteria & methodology – No justification as to why certain patients were packed under LA or GA, or how unilateral vs bilateral packing was chosen – No justification given for repeat blood gas sampling & its validity as an outcome measure – Insufficient demographic data – Conclusions appropriate to available data – No sample size calculation – Healthy young subjects not typical epistaxis patients

<p>Kourelis & Shikani⁴² (2012)</p>	<ul style="list-style-type: none"> – Assessment of Merocel packs covered in chitosan for arresting epistaxis – Single centre A&E department – Patients failing initial packing (20 with Rapid Rhino 7.5 cm, 15 with Merocel) were enrolled 	<ul style="list-style-type: none"> – Inclusion: patients with drug-induced anticoagulation, with ‘severe’ epistaxis uncontrolled by Merocel or Rapid Rhino nasal packing – Exclusions: not specified – $n = 35$ – Merocel or chitosan – Mean age 70.2 y (range, 32–88 y), M:F ratio 15:20 	<ul style="list-style-type: none"> – ED local anaesthetic (2% lidocaine spray) – Examined with rigid nasendoscope; after identification of bleeding site, packed with Merocel covered with a single sheet of ChitoFlex – Merocel pack expanded with normal saline, allowing chitosan to adhere to bleeding site (chitosan works best when firmly adhered to bleeding vessel to form robust clot) – Prophylactic antibiotics prescribed – Packing removed after 48 h – If no re-bleeding, patients instructed to use intranasal saline mist & bacitracin ointment – Endoscopic examination of nasal cavity performed at 1 week, checking for any residual bleeding, mucosal injury or irritation, or chitosan remnants 	<ul style="list-style-type: none"> – Time to bleeding control – Mean bleeding time to cessation – Rate of discharge at 48 h following pack removal – Re-bleeding during admission or within 1 week – Appearance at follow-up endoscopic evaluation 1 week after evaluation 	<ul style="list-style-type: none"> – Chitosan–Merocel packs achieved instant control of bleeding in 32/35 (91%). 0/32 had significant recurrent bleeding during 48 h of tamponade use – All failures had triple anticoagulants & posterior bleeding points – Mean time to bleeding cessation was 3.5 min (range, 1–10 min) – 3/35 subsequently underwent in-patient prolonged tamponade with bilateral Rapid Rhino packs – Minimal mucosal bloody ooze in general area of bleeding site in 17/32 cases (49%), which resolved after endoscopic application of silver nitrate. Scattered remnants of partially dissolved chitosan were detected in nasal cavity of 23/35 (66%) – Mild rhinitis noted in 4/35 patients (11%) 	<p>Grade: 10</p> <ul style="list-style-type: none"> – No power calculation – No comparison with other treatments – Agreed protocol followed & all patients accounted for – No comment on unilateral or bilateral packing – No statistical analysis – No patient-reported outcome measures; outcomes all reported by treating clinicians – Follow-up period sufficient
<p>Mehanna <i>et al.</i>³⁰ (2002)</p>	<ul style="list-style-type: none"> – Prospective study – 24-h total follow up 	<ul style="list-style-type: none"> – Inclusion: requiring nasal packing after rigid endoscopic examination, packs in for ≥ 12 h – Exclusions: not requiring nasal packing, admission for social reasons, packing removed <12 h, aged <16 y old – $n = 50$ – Mean age 64 y (range, 16–89 y); M:F ratio 4:3 – Consecutive patients 	<ul style="list-style-type: none"> – Nasal packing using range of packs – 25 packed with Merocel, 17 packed with Vaseline ribbon gauze. 2 post-nasal balloons inserted with BIPP gauze packs; 6 pack types not recorded – Once packing removed, patient observed for 24 h, whilst being encouraged to mobilise & self-care 	<ul style="list-style-type: none"> – Incidence & timing of further epistaxis within 1st 24 h after pack removal (within 1 h, between 1 & 4 h, & between 4 & 24 h) – Amount of recurrent bleeding recorded (spotting, or heavy, >5 min) 	<ul style="list-style-type: none"> – Site of initial epistaxis: anterior in 18, posterior in 22, both in 6, not recorded for 4 – Average duration of pack in situ was 1.7 days – 10 patients had recurrent epistaxis after pack removal: 5 had recurrence within 1 h, 4 between 1 & 4 h, & 1 between 4 & 24 h – Of 10 patients who re-bled, 6 had spotting & 4 had heavy epistaxis – All bleeding settled with no need for further packing 	<p>Grade: 6</p> <ul style="list-style-type: none"> – No power calculation – Outcome measures appropriate – Mixed interventions – No medium- to long-term follow up – All patients accounted for, though some data on pack type & bleeding site unavailable – No statistical analysis

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Appendix I *Continued*

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
Pollice & Yoder ⁹ (1997)	<ul style="list-style-type: none"> – Retrospective review of case notes – Multicentre (7 hospitals) – Management divided into: (1) non-surgical or non-interventional (primary treatment), & (2) surgical or interventional – Duration of follow up not detailed 	<ul style="list-style-type: none"> – Inclusion: patients admitted with epistaxis – Exclusions: not specified – <i>n</i> = 249 – Mean age 60 y (range, 1–90 y), % <16 y not specified; M:F ratio 116:133 	Various	<ul style="list-style-type: none"> – Length of hospital stay – Adverse events 	<ul style="list-style-type: none"> – 207/249 (83%) treated successfully by non-surgical or non-interventional approaches – 42/249 (17%) required surgical or interventional management after primary therapy failed – Packs used for treatment: gauze (80), Surgicel (42), Meroceel (49), balloon (91) & other (24) – Balloon tamponade failed in 10/91 patients – Minimal reporting by treatment subgroup 	Grade: 3 <ul style="list-style-type: none"> – No clearly stated aim – Valuable large data set on packing types used, packing success & complications

RCT = randomised controlled trial; h = hours; y = years; M = male; F = female; VAS = visual analogue scale; NSAID = non-steroidal anti-inflammatory drugs; s = seconds; BIPP = bismuth iodine paraffin paste; EUA = examination under anaesthesia; SPA = sphenopalatine artery; CI = confidence interval; RR = relative risk; LA = local anaesthesia; post-op = post-operative; SHO = senior house officer; Y/N = yes/no; IV = intravenous; C&S = culture and sensitivity; SD = standard deviation; MINORS = methodological index for non-randomised studies; mth = months; HTN = hypertension; PT = prothrombin time; PTT = partial thromboplastin time; A&E = accident and emergency; GP = general practitioner; GA = general anaesthesia; OR = odds ratio; HHT = hereditary haemorrhagic telangiectasia; PSG = polysomnography; OSA = obstructive sleep apnoea; ED = emergency department

APPENDIX II
SUMMARY OF STUDIES INCLUDED IN DISSOLVABLE PACKING REVIEW

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
<i>RCTs</i> Mathiasen & Cruz ¹² (2005)	<ul style="list-style-type: none"> – Consecutive patients presenting to ED – Single centre – Non-blinded – Patient & physician completed questionnaire after epistaxis control & at follow up 5–7 days later – Group 1 = FloSeal; group 2 = packing 	<ul style="list-style-type: none"> – Inclusion: anterior epistaxis, aged >18 y – Exclusions: posterior bleeding, coagulopathies, allergy – <i>n</i> = 70 total; <i>n</i> = 35 in study group, <i>n</i> = 35 in control group – Average age: study group 73.8 y; control group 67.8 y – M:F ratio 2:3 	<ul style="list-style-type: none"> – HTN was controlled, clots suctioned from nasal passageway & xylometazoline spray applied – Study group had FloSeal applied to bleeding site, with remaining gel to fill nasal passage. Max of 2 attempts were made before crossing over to packing treatment group. Vaseline cotton wool was placed in nasal vestibule & removed at 5–7 day follow up – In control group, nasal pack, chosen by ED physician, was placed in bleeding nasal passageway. This was removed at 5–7 day follow-up appointment 	<ul style="list-style-type: none"> – Pain – Effectiveness of haemostatic technique – Satisfaction with haemostatic technique – Ease of haemostatic technique 	<ul style="list-style-type: none"> – FloSeal had less discomfort – Patients & clinicians felt FloSeal controlled epistaxis better – FloSeal: 8.6% required HNS review vs 40%, 0–7 day re-bleed 14% vs 40%, review re-bleed 0% vs 63% – FloSeal 1% vs 23% nasal packing crossed to other method 	<p>Cochrane Risk of Bias</p> <ul style="list-style-type: none"> – Random sequence generation: low risk – Allocation concealment: unclear risk – Blinding of participants & personnel: high risk – Blinding of outcome assessment: high risk – Incomplete outcome data: unclear risk – Selective reporting: low risk – Other: high risk – Block randomisation – Unclear allocation method – Not blinded owing to physical difficulty of hiding group allocation – Subjective questionnaire assessments made outcome blinding impossible – Objective assessments partially relied on patient feedback to admit to re-bleed – No mention of incomplete data – All results present – Non-standardisation of pack – No objective examination at follow up – 23% packed patients required FloSeal possibly owing to inadequate packing

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Appendix II *Continued*

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
<i>Non-RCTs with comparators</i> Khan <i>et al.</i> ⁴³ (2015)	<ul style="list-style-type: none"> All cases of epistaxis included in study, but trial participants were allocated based on attending doctors competence to use trial drug Some crossover of treatments if primary treatment failed, both into & out of study group Fisher's exact test 	<ul style="list-style-type: none"> Inclusion: any epistaxis patients presenting to department where conservative first aid measures of nose pinching had failed Exclusion: if attending doctor did not feel competent using FloSeal $n = 101$ total; $n = 36$ for study group, $n = 65$ for control group Average age 70 y (range, 22–98 y); 68M, 33 F 	<ul style="list-style-type: none"> If epistaxis was deemed to be anterior, conservative measures, cautery, FloSeal or packing was chosen. If epistaxis not controlled within 10 min, treatment was escalated. Only 3 patients were treated with FloSeal in anterior epistaxis sample, & only 1 as a primary treatment which failed If epistaxis was deemed to be posterior, FloSeal or nasal packing was utilised. If intervention failed to control bleeding, another method was used 	Control of epistaxis using FloSeal without another method	<ul style="list-style-type: none"> 66% success with FloSeal for anterior epistaxis ($n = 3$); however, 2 cases had already received Merocel pack & cautery 9% success with FloSeal vs 92% for nasal packing in posterior epistaxis ($p < 0.001$) In cases when no other intervention was used, only 18% successful epistaxis arrest with FloSeal 	MINORS; max grade of 24 Grade: 13 <ul style="list-style-type: none"> Uncontrolled management pathway Allocation process based on individual clinician rather than set proforma Reasonably sized study
<i>Non-RCTs without comparators</i> Bhatnagar <i>et al.</i> ¹⁵ (2004)	<ul style="list-style-type: none"> Single centre 3-mth review 	<ul style="list-style-type: none"> Inclusion: posterior epistaxis Exclusion: anterior epistaxis $n = 8$ 	Small piece of Surgicel endoscopically inserted & left in situ	<ul style="list-style-type: none"> Breathing Pain Length of stay Re-bleed rate 	<ul style="list-style-type: none"> Average stay <24 h 'no pain, breathing fine' 1 re-bleed within 3 mth 	MINORS; max grade of 16 Grade: 14 <ul style="list-style-type: none"> Appears prospective, but small numbers Patient recruitment consecutive Stated aims & follow-up period Very poor outcome reporting
Côté <i>et al.</i> ¹⁶ (2010)	<ul style="list-style-type: none"> Prospective study Single centre 7-day review 	<ul style="list-style-type: none"> Inclusion: epistaxis that failed to stop with anterior Merocel pack Exclusion: recent nasal surgery, malignancy, Osler–Weber–Rendu disease, bovine allergy $n = 10$ 	Nose decongested & anaesthetised, & FloSeal endoscopically applied to bleeding areas	<ul style="list-style-type: none"> Control of epistaxis Re-bleed rate Adverse effects 	<ul style="list-style-type: none"> 80% controlled bleeding (8/10) 2 patients required SPA ligation 50% patients admitted for co-morbidities or social reasons Re-bleed rate unclear No adverse events 	Grade: 10 <ul style="list-style-type: none"> Prospective Limited outcome reporting No follow up No comment on prospective sample size, consecutive patients or study end point

Kilty <i>et al.</i> ¹⁷ (2014)	<ul style="list-style-type: none"> – Prospective – Single centre – Fisher’s exact test used for analysis 	Inclusion: posterior epistaxis <ul style="list-style-type: none"> – Exclusion: allergy, breast feeding, pregnant – $n = 20$ 	<ul style="list-style-type: none"> – HTN, coagulopathy & other co-morbid factors treated – 2% lignocaine spray applied to bleeding side. Foley catheter placed in nasopharynx. 5 ml gelatine-thrombin matrix gel injected into posterior nasal cavity – If bleeding uncontrolled after 10 min, further 5 ml gel injected – If bleeding controlled, 50 ml saline used to irrigate excess matrix from cavity – Patient observed for 1 h & discharged if no more bleeding 	<ul style="list-style-type: none"> – Discomfort – Arrest of bleeding 	<ul style="list-style-type: none"> – 80% success rate for arrested epistaxis with no recurrence within 14 days – No significant difference between co-morbidity variables using Fisher’s exact test – VAS pain score mean = 3.6 – 4 patients (20%) required additional treatment after gelatine-thrombin matrix failed to stop posterior epistaxis (2 had surgical treatment, 2 had posterior packing) – No complications occurred – Gelatine-thrombin matrix failure occurred in 3 hypertensive patients & 1 on aspirin – No association with: anti-coagulant use ($p = 1.0$), gender ($p = 0.58$), HTN ($p = 1.0$) or diabetes ($p = 0.62$) 	Grade: 13 <ul style="list-style-type: none"> – Repeatable methods, with simple outcome measures & endpoints – Small study size – 100% follow-up rate – As a pilot study, it does justify further investigation
Kundra <i>et al.</i> ¹³ (2014)	<ul style="list-style-type: none"> – Single centre, ED treatment 	<ul style="list-style-type: none"> – Inclusion: epistaxis not controlled by cautery in ED – $n = 29$ 	<ul style="list-style-type: none"> – Cautery-resistant cases treated with FloSeal (no specific details given) 	Arrest of epistaxis	48% (14/29) successfully treated with FloSeal & discharged home	Grade: 3 <ul style="list-style-type: none"> – Poster abstract only – Little methodology & results presented – Small study group with no control group – No details on intervention technique – No follow up stated
Shikani <i>et al.</i> ¹⁴ (2011)	<ul style="list-style-type: none"> – Prospective study – Single centre – 2-mth follow up 	<ul style="list-style-type: none"> – Inclusion: epistaxis not responding to anterior packing with Merocel or Rapid Rhino – Exclusion: aged <18 y – $n = 20$ 	<ul style="list-style-type: none"> – Chitosan gauze wrapped around polyvinyl acetal sponge & endoscopically placed at bleeding site – Sponge removed at 48 h, but chitosan left in cavity – Saline washouts on discharge – Follow up at 1 week 	<ul style="list-style-type: none"> – Pack comfort – Arrest of epistaxis – Re-bleed rate – Adverse events 	<ul style="list-style-type: none"> – 100% bleeding stopped without another treatment, 95% within 5 min – No re-bleeding – No major adverse events – Patient felt it more comfortable – 50% mild rhinitis or granulation, which resolved by 2 mth 	Grade: 14 <ul style="list-style-type: none"> – Prospective, but not consecutive patients – Appropriate end point & follow up – Some outcome data missing

Continued

Appendix II *Continued*

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
Tibbels ³⁷ (1963)	<ul style="list-style-type: none"> – Prospective – Single centre 	<ul style="list-style-type: none"> – Inclusion: epistaxis (no exclusions) – 32% traumatic, 28% vascular, 25% unproven, 10% inflammatory – <i>n</i> = 250 	<ul style="list-style-type: none"> – Technique varied with severity of bleeding; anterior + posterior packs used – Brisk bleeding: cocaine & adrenaline pledget, chemical cautery & Surgicel pack – Moderate bleeding: LA then Surgicel pack – Minor bleeding: Surgicel pack, no LA – Pack checked after 24 h & removed after 72 h 	<ul style="list-style-type: none"> – Arrest of epistaxis – Adverse effects 	<ul style="list-style-type: none"> – Arrest success rate for anterior packing with Surgicel was 88% (165/188) – 92% (34/37) bleeding arrested with both anterior & posterior Surgicel packs – 70 patients complained of symptoms, & there were 34 complications but these not differentiated by pack type 	Grade: 6 <ul style="list-style-type: none"> – Large numbers – Significant parts of methodology not reported – Unable to assess effectiveness of surgery as outcomes mixed in with other pack types – Follow-up period relatively short
Walshe ¹⁸ (2002)	Single centre	<ul style="list-style-type: none"> – Inclusion: epistaxis & coagulopathy (INR > 2), previously treated with either non-dissolvable pack or cautery – 18 anterior bleeds, 4 posterior; 3 not visualised because of bleeding – <i>n</i> = 25 	<ul style="list-style-type: none"> – Fibrin Sealant applied to bleeding area – Coagulopathies not reversed 	<ul style="list-style-type: none"> – Arrest of epistaxis – Adverse effects 	<ul style="list-style-type: none"> – 100% epistaxis arrest – No complications 	Grade: 9 <ul style="list-style-type: none"> – Limited details of methodology (prospective, consecutive patients, prospective calculation of study size) – No stated limitations or bias assessment – No stated follow-up period

ED = emergency department; y = years; M = male; F = female; HTN = hypertension; HNS = head neck surgery; MINORS = methodological index for non-randomised studies; h = hours; mth = months; SPA = sphenopalatine artery; VAS = visual analogue scale; LA = local anaesthesia; INR = international normalised ratio