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National prospective observational study of inpatient management of adults with epistaxis – a National Trainee Research Collaborative delivered investigation

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Key points

- This is the largest study of the in-hospital management of epistaxis
- Nasal cautery at the time of first specialist ENT review reduces treatment time by more than half, even after controlling for patient age, disease severity and whether patient was packed or not prior to ENT review.
- Patients who receive a treatment algorithm that follows national guidance are 87% more likely to achieve haemostasis before patients who do not.
- The 30-day hospital readmission rate is not affected by treatments that reduce treatment time.

Abstract

Importance: There is a paucity of high quality evidence relating to the management of epistaxis severe enough to require admission to a hospital. Previous studies of interventions for epistaxis have suffered from small sample sizes. They lacked the power to allow analysis of the effect of an intervention on epistaxis control that is independent of the condition severity or additional interventions given.

Objective: To determine the effect of specialist treatments on the successful management of severe epistaxis

Design: Secondary analysis of data collected from a national multi-centre audit of patients with epistaxis over 30 days in 2016. Data were entered prospectively, and patients were followed up for 30 days following hospital discharge.

Setting: 113 participating UK hospitals.

Participants: 1402 adults admitted for inpatient management of epistaxis were identified, with data entered prospectively during the 30-day audit window.

Exposure: Exposure variables assessed included treatment instigated at first ENT review, intervention strategy during hospitalization, disease factors (e.g. severity), patient risk

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factors (e.g. co-morbidities, medications) and treatment factors (grade of doctor, therapies initiated during hospital stay).

Main Outcomes: Treatment time (time from first ENT review to time haemostasis was achieved and patient was safe for hospital discharge). 30-day hospital readmission rate.

Results: 834 patients had sufficient data for inclusion. Patients who did not receive nasal cautery at first specialist review had a treatment time greater than double the time of those who were cauterised: Adjusted ratio (aR) 2.5 (95% CI 1.7-3.3), after controlling for age, bleeding severity, and whether they received a nasal pack or not. Only 30% of patients received management that complied with new national guidance, but those that did were 87% more likely to be achieve haemostasis before those that did not, even after controlling for bleeding severity. Type of treatment, whether initial intervention or management strategy, did not affect 30-day re-attendance.

Conclusions and Relevance: Analysis of national audit data suggest that cautery at first specialist review, and management according to national guidance can reduce hospital treatment times without compromising 30-day re-attendance. Future work should investigate why early nasal cautery is infrequently used, and how service delivery can be optimised to allow widespread implementation of evidence-based management for epistaxis.

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Introduction

Epistaxis is common, with a lifelong incidence of 60% in the general population(1). Most episodes of epistaxis are self-limiting, and only rarely is emergency medical treatment required when the bleeding becomes heavy or unrelenting (2). Despite this, there were nearly 25,000 in-hospital admissions to UK National Health Service hospitals (not including attendances to Emergency departments) in 2014-15 for epistaxis (3), accounting for more than £1.5 million in hospital bed costs alone, without factoring in the treatment costs (4). Emergency in-hospital interventions range from tamponade of the nasal cavity using nasal packs, cautery of bleeding vessels using chemicals or diathermy, or closing source arteries proximal to the bleeding point, using surgery or interventional radiology.

A recent suite of systematic reviews was undertaken by INTEGRATE (the National ENT Trainee Research Collaborative) to summarise the published evidence regarding the management of epistaxis (5-8). There was limited evidence to suggest an association between epistaxis and age (9,10), sustained ambulatory hypertension (11) and cardiovascular disease (12). Identified studies suggested that nasal packing (13,14), nasal cautery (13,15,16), antithrombotic medications (17), surgery (18) and trans-catheter arterial embolization (19) all affected rates of epistaxis control. In-hospital management of epistaxis frequently involves patients of varying grades of disease severity, who receive more than one treatment. To date studies of epistaxis interventions have been typically of small sample size (20) , and often of insufficient power to calculate the effect of any individual intervention, independent of disease severity and additional treatments received (21). Previous audits of epistaxis management have shown considerable variation in practice that may reflect the uncertainty inherent in the current evidence (22,23).

INTEGRATE, the UK ENT Trainee Research Network, recently undertook the largest prospective audit of adult inpatient epistaxis management to date, collecting data on more than 1200 cases across the United Kingdom over a 30-day observation window. Data captured included potential patient risk factors, interventions received during in-hospital

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care, treatment success and 30-day re-admission data(24). Using this large and rich dataset, we aimed to investigate the role of different treatments and management strategies on successful in-hospital management of epistaxis. We analysed the role of initial interventions on overall treatment success, independent of subsequent treatments, patient factors and disease severity, and assessed the extent to which management strategies followed new guidelines (25), and the effect of this had on patient outcome.

Methods

Ethical approval

NHS Research Ethics Committee guidance was sought regarding the use of the national audit dataset beyond a simple comparison against identified audit standards. Completion of the Health Research Authority Guidance Tool confirmed that formal NHS Research Ethics Committee approval was not required.

Design

Secondary analysis was performed on the dataset produced from a national audit of epistaxis management in adults (Cohort design). The pilot (22), final audit methods and preliminary results (24) have been described previously.

Interventions analysed

The impact of interventions was assessed in two ways. First, the type of initial intervention received by a patient (following assessment and supportive measures) was categorised as; cautery, intranasal packing, surgery, radiological embolisation or a combination of these. The effect of intervention type on outcome was assessed.

Secondly, since the sequence of individual interventions undertaken during the whole admission would have been difficult to model and interpret, the effect of the overall management strategy during inpatient admission was investigated. Based on national consensus recommendations, endorsed by the British Rhinological Society (BRS) and ENT-UK(25), we evaluated each patient's management strategy (chronological order of interventions instigated during the hospital stay) to identify whether their management had

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followed national recommendations (guidance compliant) or not (guidance non-compliant). Management strategies that were considered compliant with national guidelines are listed in the supplementary material. Two ENT surgeons (NM and RW), independently reviewed each patients' management strategy to assess whether interventions had been undertaken in a chronological sequence that complied with national recommendations. Cases assessed differently by reviewers were discussed individually until consensus was reached. Where consensus could not be reached cases were referred to a senior surgeon (CH).

Outcomes

Two outcomes were selected:

1. Treatment time (time from first ENT review to the point when haemostasis was achieved – i.e. the point at which the ENT team decided that the epistaxis had been resolved, and the patient was safe for hospital discharge). It excluded the time it took for the patient to be seen and treated in the Emergency Room, and the time it took for the patient to actually leave the hospital, which was occasionally delayed due to administrative or social issues.
2. Hospital re-attendance rate with recurrent epistaxis within 30 days of discharge. This only included patients who re--attended under the ENT team for epistaxis. It did not include those who may have been successfully treated for recurrence through self-care or their local primary and emergency care teams.

These outcomes were chosen as they reflected both the early and longer-term efficacy of interventions, and they were readily extractable from the dataset available.

Data Cleaning

Data set cleaning was performed by statisticians (JC, BJ and KS), and any queries were dealt with by clinicians on the steering committee (NM, RW and MS). Data was included if the observation was within the audit period, was not a duplicate entry, and contained valid treatment times. A clinician scrutinised all participants with a treatment time of zero. If the

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clinician determined the treatment time of zero was invalid, treatment time was replaced with a suitable proxy; either discharge time or the last recorded time intervention.

Statistical Analysis

The statistical analysis was performed in three stages: i) identify which ENT initial individual interventions (intervention at first ENT review e.g. nasal cautery VERSUS nasal packing etc.) were associated with the treatment time for each case; ii) identify which intervention strategies (sequence of all interventions instigated throughout admission e.g. nasal packing then nasal cautery VERSUS nasal cautery then nasal packing, etc.) were associated with improved time to achieve haemostasis; and iii) identify which individual interventions and intervention strategies were associated with 30-day re-attendance to ENT. All statistical analyses were conducted in R statistical package (version 3.4.2)(26).

Initial ENT (Individual) Interventions

Exploratory analysis of the data was performed first to identify potential patient factors and individual interventions given at first ENT review that justified subsequent further inferential analysis via statistical models. In addition, a series of systematic reviews developed for the project (5-8) were also used to identify any additional potential associations. A full list of the patient factors investigated can be found in table 1.

Treatment time by patient characteristics and individual interventions was summarised using the geometric mean and corresponding 95% confidence interval (CI). If the confidence intervals of mean treatment time overlapped within variable outcomes (e.g. mean treatment time for patients with hypertension overlapped with mean treatment time for patients without hypertension)then these variables were not tested for inclusion in the model, unless stated *a priori*.

Approximately 60% of patients were successfully treated within 24 hours, and the remaining 40% took between 1 and 7 days to achieve definitive management, resulting in a highly skewed distribution of treatment time. For this reason, analysis of initial individual interventions and treatment time was performed using linear regression on the log

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transformed treatment time. It was decided *a priori* to adjust the models for age, bleed severity (via World Health Organization (WHO) bleeding severity grade) (27) and Modified Early Warning Score (MEWS)(28), regardless of their statistical significance. Forward model selection was used to identify the interventions and any additional patient characteristics associated with treatment time, and these were included in the model if a goodness-of-fit test yielded a p-value <0.05. We tested for interactions between different factors, but statistical evidence only supported the inclusion of one interaction, the initial intervention (packing or cauterisation) and whether further interventions were required.

We performed sensitivity analysis (see supplementary material) to compare the differences between those who only required the initial interventions at their first ENT review with those who needed further interventions, by removing censored observations (i.e. removing those cases assigned proxy treatment times), and by WHO bleeding severity grade.

Evidence from the exploratory analysis suggested that some categories of factors could be merged. The categories were combined once a clinician confirmed that the new categories remained clinically valid. Full details of the exploratory analysis have been previously published(24), including further detail, plots and summary statistics calculated from the Epistaxis audit.

Due to the large number of factors to be investigated, we used forward model selection, and a factor was included in the model if there was evidence at the 5% significance level that the factor was contributing to the model. As more than 67% of patients required additional treatment after their first intervention, the log linear model for treatment time was adjusted for additional treatment performed after the first intervention, age, sex and markers of disease severity such as WHO bleeding severity grade (WHO grade 1 epistaxis <30 minutes within 24 hours, grade 2 epistaxis >30minutes within 24 hours, grade 3 epistaxis severe enough to require blood transfusion)(27) and Modified Early Warning Score (MEWS is scored 0-3 based on systolic blood pressure, heart rate, respiratory rate, temperature and AVPU scales) (28). As there appeared to be two sub-populations of patients admitted with epistaxis – those successfully treated within 24 hours and those that required several ENT interventions - it was important to insure patient factors were

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significantly related to treatment time across the entire population. Therefore, sensitivity analyses were performed to determine if the factor effect size remained consistent if patients with censored treatment time were excluded (e.g. Is WHO bleeding score related to treatment times in patients successfully treated within 24 hours as well as those that needed several interventions?)

Intervention Strategy

The sequence of interventions performed on each patient was used to determine whether the sequence followed the BRS epistaxis guidelines or not.

Kaplan-Meier curves with 95% CI were used to explore the association between treatment time and the two distinct intervention strategies (guidance compliant and guidance non-compliant), and patient factors. If CIs overlapped, further analysis was not performed as it was unlikely that there would be a statistically significant difference in the success of these different management strategies.

To evaluate potential a relationship between intervention strategies and treatment time, a cox proportional hazard model was fitted to the data. It was decided to adjust the model for age, WHO bleeding severity grade and MEWS *a priori*.

Re-attendance to ENT

Factors potentially associated with re-attendance were identified via comparison of percentage 30-day re-attendance rate. If there was a difference >10% in re-attenance rate between groups characterised by the presence or absence of a certain factor, these factors were selected for further investigation. A difference of 10% was selected because the 95% CI for a percentage calculated from 100 observations is approximately ±10%, therefore differences less than this value were unlikely to be statistically significant.

To identify factors associated with 30-day ENT re-attendance we fitted logistic regression models to the data. Forward selection was used to identify associated factors, and only

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included if the goodness of fit p-value was <0.05. As with the previous models, it was decided *a priori* to adjust for age, WHO bleeding severity grade and MEWS.

Results relating to the initial ENT (individual) intervention are presented as adjusted ratios (aR), which demonstrate the difference in treatment time between individual levels of a factor on a multiplicative scale, after adjusting for markers of disease severity (WHO grade and MEWS) and age. For example, if examining the role of initial ENT intervention X showed an aR of 2, it would mean that intervention X increased treatment time two-fold, even after controlling for disease severity and age, when compared to those who did not receive factor X. A censored time-to-event analysis was used to assess the association between guidance compliant intervention strategies and the treatment time.

Results relating to intervention strategy are presented as adjusted hazard ratio (aHR), which demonstrate risk in relation to a timescale, on a multiplicative scale. For example, if examining the role of intervention strategy Z showed an aHR of 2, the result is best interpreted as patients receiving intervention strategy Z achieved haemostasis 66% faster than those that did not.

Results

The audit data set consisted of a total of 1826 entries recorded from 116 sites during the audit window. During data cleaning 305 entries were removed as duplicates, 89 were found to lie outside the audit period, and 30 patients were successfully treated prior to management by ENT. 280 patients had insufficient data to allow treatment times to be calculated (time of first ENT review or time of treatment completion) and 288 patients had incomplete data on key patient variables – described below- and were thus excluded from analyses of treatment time(n=834). 197 patients had insufficient data on ENT re-attendance and 417 had missing data on key patient variables – described below - and were thus excluded from analyses of re-attendance rate (n=788)(Figure 1 shows the number of patients who were included in the analysis). Patient data sets were incomplete for the following reasons; 25% of patients had no MEWS recorded, 20% had treatment time missing or invalid and 14% had missing re-admission data.

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Table 1 and 2 contains the summary statistics of factors previously linked to treatment time, and those new factors with evidence suggesting a significant association with treatment time, for the entire dataset. When removing the observations with censored data (I.e patients successfully treated following one ENT review), there was little to no difference in the ratios of times or the 95% CI in table 2 (see table 6 of supplementary material) justifying use of the complete dataset.

Effect of patient factors and specific interventions on treatment time

Table 3 contains the adjusted treatment time ratios. The final model adjusted R^2 value indicated the model accounted for approximately 68.4% of the variation within the data.

There was no evidence of a statistical association between a patient's age or MEWS and their treatment time. However, there was evidence of an association between treatment time and WHO bleeding severity grade. The evidence indicated that as WHO grade increased (i.e. bleed severity increased), treatment time also increased. Individuals with WHO grade II bleeding were likely to have a treatment time 1.3 times those with grade 1 (30% longer). Those with grade III bleeding were likely to have a treatment time 2.2 times those with a grade I.

There was evidence to suggest that the choice of intervention given at the first review may have been dependent on the WHO grade. Evidence showed that as WHO grade increased, so did the proportion of individuals who were packed, but as WHO grade increased the proportion of those cauterised decreased. Therefore, it was considered essential to control for WHO bleeding severity score in the final model, to assess the impact of initial treatment independent of bleeding severity.

From the analysis of initial ENT individual intervention to treatment time (see table 3), it can be seen that patients who were cauterised at first ENT review had 60% reduction in treatment time compared to those who were not cauterised (Adjusted ratio 0.4, 95%CI 0.3 – 0.6), but individuals who were packed had a treatment time seven times longer than those who were not packed (Adjusted Ratio 7.1, 95%CI 4.3 – 11.7). This data represents the effect

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of initial treatments after controlling for bleeding severity. However, if initial treatments were not successful and another review was required, the effect of cautery diminished substantially. The plot in figure 2 is an example to demonstrate how different initial ENT-instigated treatments affected treatment times for a patient who was <65 years, with a WHO grade of II and MEWS of 1. Additionally, this plot demonstrates that attempting cauterisation initially, even when unsuccessful, does not increase treatment time.

Effect of intervention strategy on treatment time

Analysis of different intervention strategies on treatment time were conducted via Kaplan-Meier estimates, as shown in Figure 3. There was no evidence of an association between either age or MEWS with treatment times within Cox's proportional hazard model, but strong evidence of an association between treatment time and WHO bleeding severity score. The Kaplan-Meier plots showed how treatment time was less for those with a lower grade score. Patients treated with a guideline-compliant management strategy had a shorter treatment time, indicated by the Kaplan-Meier estimates with no over-lap of the 95% CIs, suggesting a statistically significant effect size. Whilst the Kaplan-Meier plot indicates that the difference was substantial, it this did not control for patient age, MEWS or WHO bleeding severity grade. This association was explored using the multi-variable Cox model, Table 4, which showed that even after controlling for age and WHO grade, the hazard ratio was 6.8 (5.7-8.8). This indicated that those managed in a guideline compliant manner were seven times more likely to be successfully treated at any time point than those who were not. In real terms this means that patients who received treatments according to national guidelines were 87% more likely to be successfully treated before those who received treatments that did not follow national guidelines (HR/(1+HR)= odds of first success - (29)). The significance of the effect of WHO bleeding severity grade on treatment time indicated that those with a lower grade had a faster treatment time than those with a higher grade.

Factors influencing 30-day re-admission

Eighty-eight (8.9%) patients were re-admitted to ENT within 30 days of presentation. There was no significant association between re-admission and type of intervention received

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during hospital treatment. The only statistically significant predictor of re-admission to ENT was a history of epistaxis in the preceding 12 months (Table 4), which more than doubled the risk of re-admission.

Discussion

Summary

The type of initial individual intervention provided to patients with epistaxis at first review by an ENT specialist significantly affects overall treatment time, even after controlling for disease severity and subsequent interventions. Patients who received only nasal packing as their first specialist treatment took 7.1 times longer to reach haemostasis than those who were not packed. Patients that were not cauterised at first review required 2.5 times more treatment time compared to those that were. This result holds even after controlling for bleeding severity as stratified by WHO bleeding score, the only factor found to influence treatment time. Our results suggest that attempting nasal cautery reduces treatment time if successful and doesn't increase treatment time if not successful. Initial intervention choice does not appear to have a significant impact on 30-day ENT re-attendance. Patients who received interventions in line with national guidelines were 87% more likely to successfully achieve haemostasis before those that did not.

Equally interesting are the negative results. The majority of cases of were managed by junior doctors (usually less than 18 months of ENT experience), but the grade of treating doctor did not affect the outcome in terms of treatment time or re-ttendance rate. The majority of patients had hypertension (55.4%) or were taking anti-thrombotics (57.1%), but the presence of these factors did not have an impact on treatment time or re-attendance either.

Our findings in the context of the available literature

A previous smaller audit of in-hospital epistaxis management across six sites demonstrated similar mean length of stay(23), but due to the limited sample size inferential analysis could not be undertaken. Whilst there have been studies that have suggested worse treatment

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outcomes for patients with ischaemic heart disease (12), hypertension (11), diabetes (17) and the use of antithrombotics(17), our study shows that once admitted to hospital and the severity of epistaxis is accounted for, these factors do not seem to affect treatment outcomes. The reason for the difference may be that these studies included smaller numbers, collected data retrospectively through case notes and defined success as not representing to hospital within two weeks of treatment.

Our study shows no difference in recurrence up to 30 days after hospital discharge, whether patients were cauterised or packed at first specialist review. Contradicting these findings, a retrospective audit on more than 300 adults with epistaxis attending a Canadian emergency room (30) showed reduced 14-day recurrence in patients who were cauterised compared to packed. However, nasal packing in the emergency room frequently requires re-attendance to remove the pack, and so this retrospective study may have misclassified re-attendance to remove pack with re-attendance to treat recurring epistaxis. Additionally, the case-mix of patients is unlikely to be comparable since our cohort only included those that had failed emergency room treatment, and probably represent those with more severe epistaxis.

Strengths and weaknesses

This is the largest prospective study of in-hospital epistaxis management to date, with sufficiently detailed information to allow assessment of interventions and management strategy after controlling for patient (age, co-morbidities), disease (severity of bleeding) and treatment factors (grade of doctor and other therapies initiated). Our statistical strategy allowed us to better understand treatment effects by focusing on initial intervention and the overall management strategy (temporal sequence of treatments initiated).
However, whilst our results suggest that cauterisation at initial ENT review reduces overall treatment time, irrespective of bleeding severity, care must be taken since bleeding severity was assessed by the WHO bleeding score. WHO bleeding score provided a convenient method by which to categorise bleed severity, but in practice it might prove difficult to stratify patients' interventions by this score alone. Unfortunately, it seems the MEWS was not sensitive enough to identify differences in the bleed severity of a patient, potentially

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indicating that further work for a more tailored grading system for bleed severity is required.

There were only 88 patients who re-attended to ENT for epistaxis. As mentioned earlier, we estimated differences between groups would have to be approximately 10% to be statistically significant when comparing proportion between two groups. Therefore, it is a highly probable that this data lacks the sensitivity to detect clinically important differences that are less than 10%.

Implications for future research and policy

Whilst these analyses suggest an increased role for nasal cautery at first specialist review, it must be noted that cautery can cause severe complications (31), and enforcing nasal cautery upon an inexperienced practitioner (87% of the patients were seen by junior doctors) may increase complication rates. On the other hand, 23% of patients that had a pack inserted in the emergency department had their pack removed for an examination when first reviewed by ENT, and only 30% of those with no packs had cautery attempted. This suggests there may be a culture or system in place that encourages rapid arrest of the epistaxis with nasal packing rather than deliberated nasal examination to assess for bleeding point. This may relate to the availability of expertise and or equipment. Further studies would help investigate the issues surrounding the reasons for the choice of intervention in more detail.

Whilst INTEGRATE and the BRS developed national guidelines to help align treatment pathways with best available evidence, these guidelines were not widely publicised prior to the national audit. However, they were drawn up to reflect a logical sequence of interventions based on widely available evidence, and so it is surprising that only 30% of patients received treatments that followed an evidence-based course. Whilst treatment pathways should be adapted to the resource availability of local departments, there is clear evidence from our analyses that following national guidance can reduce treatment time without compromising 30-day re-attendance, and local departments should be encouraged to adapt their resources to better comply with these guidelines.

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Trainees collaborated nationally to deliver the largest study of inpatient epistaxis management to date, designing and leading research into a condition that has a large disease burden. Undertaking this study has not only highlighted new evidence relating to epistaxis, but it has encouraged the new generation of surgeons to better appreciate research as a common tool to resolve critical clinical problems.

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Tables and Figures

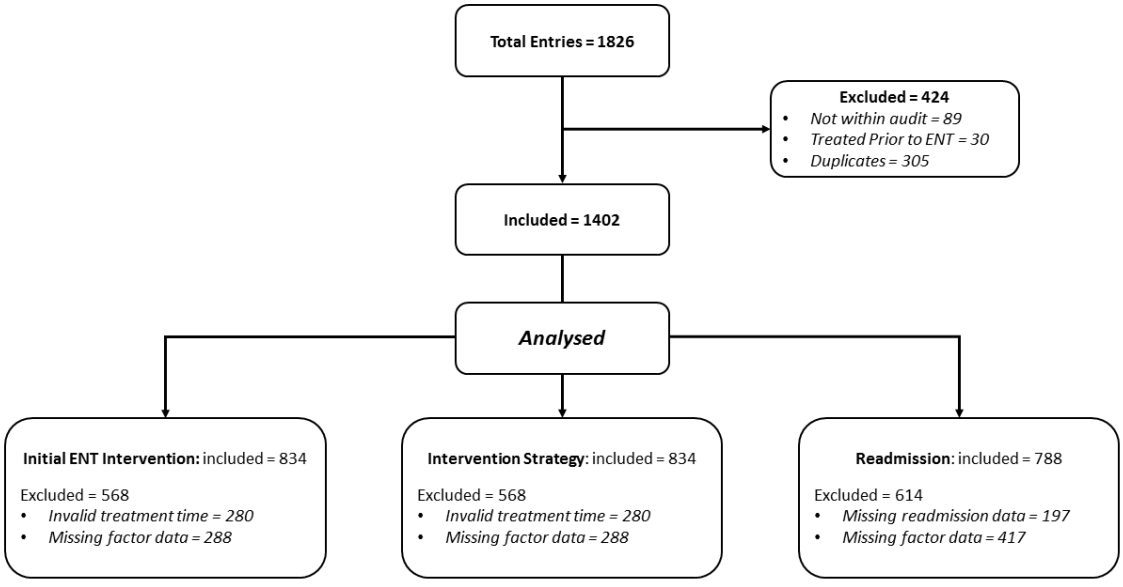

Figure 1 Data analysis flow chart This figure shows how data was entered onto a central database and the results of subsequent data cleaning led to different sample sizes for 3 different analyses. Patient data were initially excluded if it did

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not meet inclusion criteria, or was duplicated (424 entries excluded). Further data were excluded due to missingness in variables that were considered essential for each of the three analyses.

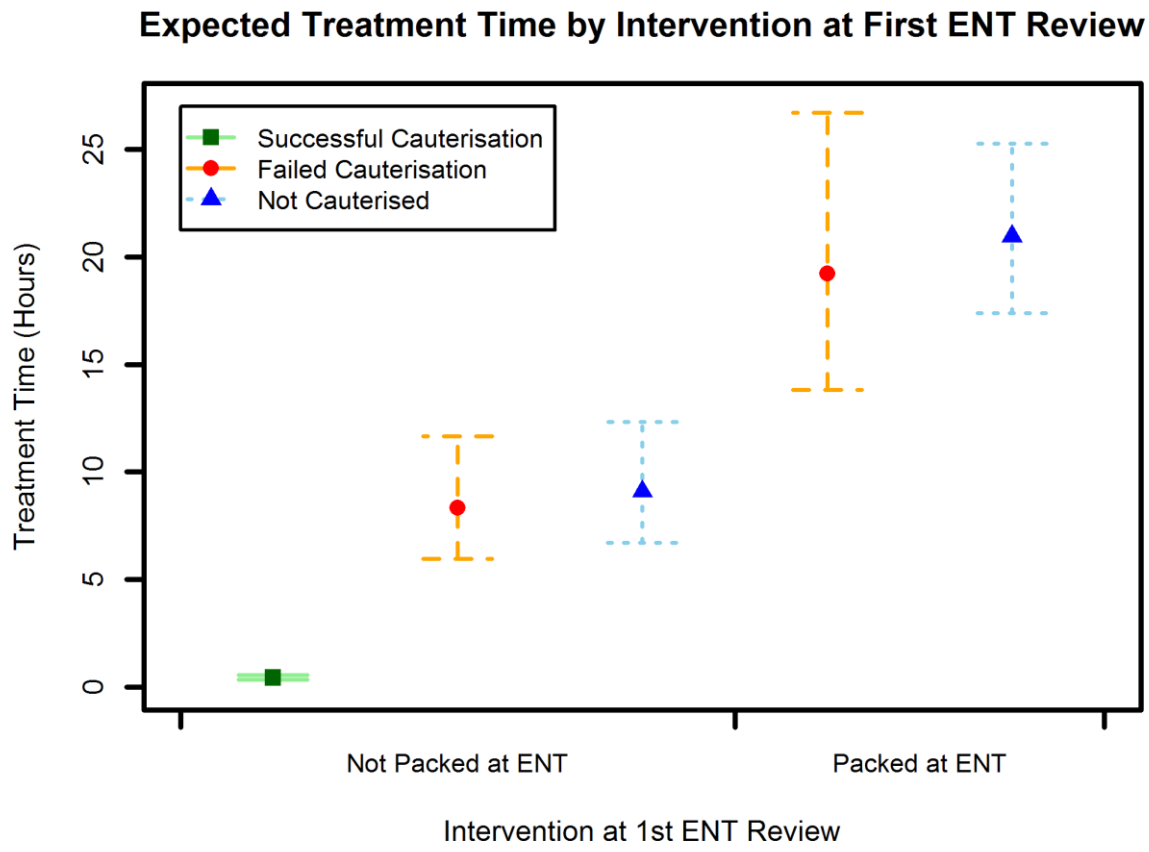

Figure 2: Expected treatment time with 95% confidence intervals of patients by cauterisation status: successful (dark green square and light green bars); failed (red circle with orange dashed bars); not cauterised (blue triangle with light blue dotted bars) and packing status (not packed or packed) at first ENT review. This graphic demonstrates that cauterising reduces treatment time if successful but does not change treatment time if unsuccessful. Additionally, those who are packed have the longest treatment times of all treatment arms.

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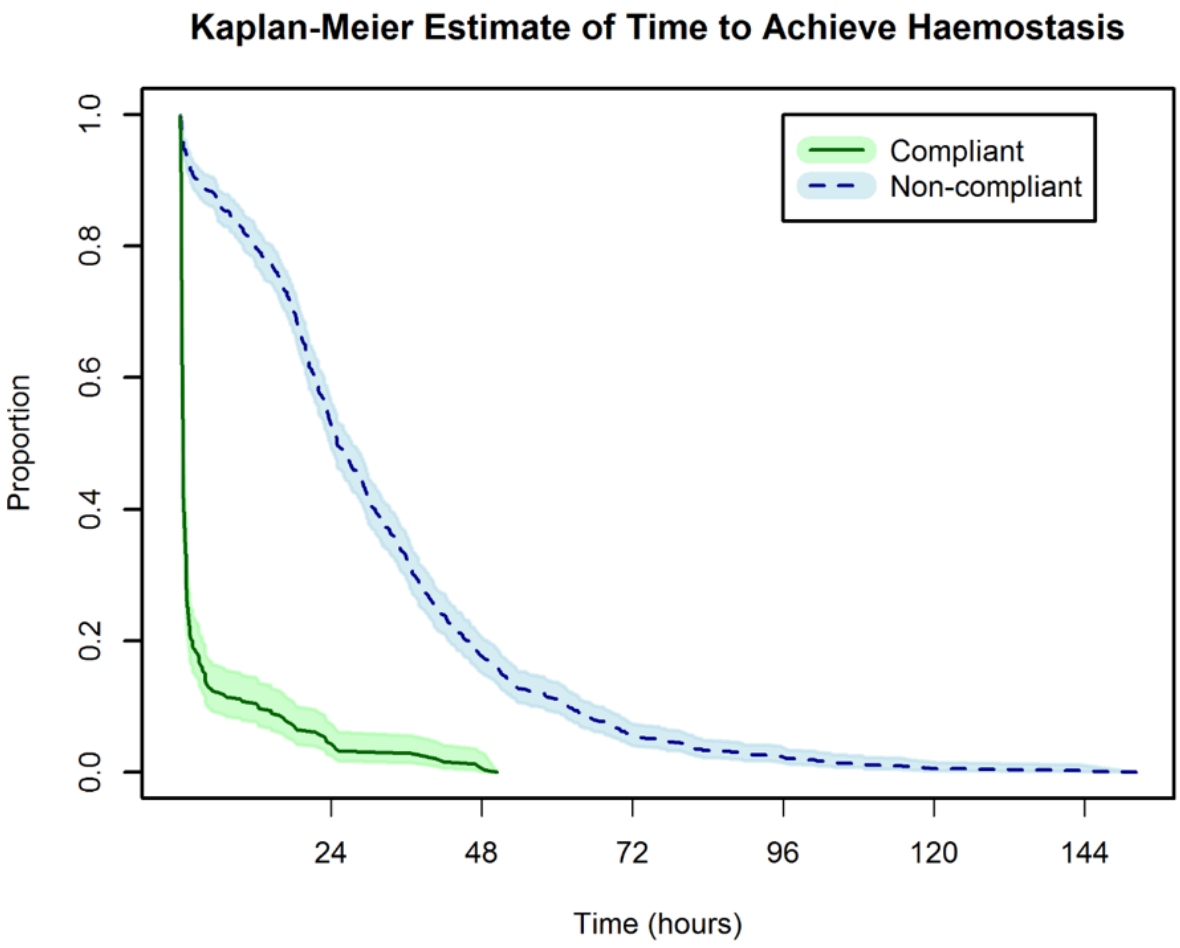

Figure 3: Kaplan-Meier estimates and 95% confidence intervals of treatment time by intervention strategy: guideline compliant (dark green line and 95% CI shaded in light green) and non-compliant (blue dashed line with 95% CI shaded in light blue). This graph shows that when treatment follows national guidance treatment time reduces significantly.

	N (%)			Treatment Time in hrs Mean (95% CI)[1] [Range]
	Total	No Re-Admission 896 (91.1)	30-day Re-Admission 88 (8.9)	
Age Group in years:				
• < 65	325 (29.0)	261 (90.0)	29 (10.0)	7.0 (5.6, 8.9) [0.0 – 152.3]
• 65 ≤ Age < 75	278 (24.8)	223 (91.0)	29 (9.0)	6.2 (4.9, 7.9) [0.0 – 114.9]
• 75 ≤ Age < 85	313 (28.0)	248 (92.5)	20 (7.5)	9.0 (7.2, 11.1) [0.0 – 109.0]
• ≥ 85	203 (18.1)	162 (90.5)	17 (9,5)	5.5 (4.2, 17.8) [0.1 – 144.6]
Gender:				

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• Female	492 (43.9)	394 (91.0)	39 (9.0)	6.2 (5.1, 7.4) [0.0 – 144.6]
• Male	630 (56.1)	502 (91.1)	49 (8.9)	7.6 (6.5, 8.9) [0.0 – 152.3]
WHO				
• Grade I	143 (12.8)	96 (90.6)	10 (9.4)	2.0 (1.4, 2.9) [0 – 104.0]
• Grade II	922 (82.7)	758 (91.7)	69 (7.8)	7.8 (6.8, 8.8) [0.0 – 143.2]
• Grade III	50 (4.5)	36 (81.8)	8 (18.2)	28.7 (19.3, 44.9) [0.2 – 152.3]
MEWS				
• 0	232 (27.6)	196 (90.7)	20 (9.3)	7.0 (5.4, 9.1) [0.0 – 118.4]
• 1	307 (36.5)	248 (90.7)	21 (7.8)	7.2 (5.7, 9.1) [0.0 – 116.4]
• 2	150 (17.8)	113 (89.0)	14 (11.0)	8.3 (6.2, 11.3) [0.2 – 152.3]
• 3	93 (11.1)	75 (88.2)	10 (11.8)	10.0 (6.9, 14.6) [0.1 – 104.0]
• ≥ 4	59 (7.0)	55 (100.0)	0 (0.0)	14.0 (9.4, 21.0) [0.3 – 109.0]
Diabetes				
• No	930 (85.6)	751 (92.3)	63 (7.7)	6.9 (6.0, 7.9) [0.0 – 143.2]
• Yes	156 (14.4)	119 (85.0)	21 (15.0)	8.9 (6.5, 12.1) [0.0 – 152.3]
Hypertension				
• No	498 (44.6)	369 (91.0)	39 (9.0)	5.5 (4.6, 6.7) [0.0 – 143.2]
• Yes	618 (55.4)	495 (91.0)	49 (9.0)	8.3 (7.1, 9.7) [0.0 – 152.3]
Heart Disease				
• No	762 (69.6)	611 (91.6)	56 (8.4)	6.6 (5.7, 7.6) [0.0 – 143.2]
• Yes	333 (30.4)	267 (90.5)	28 (9.5)	8.8 (7.1, 10.9) [0.0-152.3]
Previous Epistaxis				
• No	808 (74.0)	661 (93.1)	49 (6.9)	6.5 (5.6, 7.5) [0.0 – 130.6]]
• Yes	284 (26.0)	207 (84.1)	39 (15.9)	8.5 (5.7, 10.7) [0.0 – 152.3]
Antithrombotic				
• No	475 (42.9)	367 (89.5)	43 (10.5)	6.0 (5.0, 7.3) [0.0 – 143.2]
• Yes	631 (57.1)	514 (91.9)	45 (8.1)	7.9 (6.7, 9.2) [0.0 – 152.3]

Table 1: Summary statistics of 30-day readmission and treatment time by patient's medical history. This is extracted from the raw dataset. Analysis was done on a subset who had sufficient data regarding outcomes for analysis and therefore final analysis is only on 834 patients. [1] Geometric mean and 95% CI

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	N (%)			
	Total	No Re-Admission 896 (91.1)	30-day Re-Admission 88 (8.9)	Treatment Time in hrs Mean (95% CI)[1] [Range]
Packed at ED				
• No	605 (53.9)	469 (90.7)	48 (9.3)	3.4 (2.8, 4.0) [0.0 – 144.6]
• Yes	517 (46.1)	427 (91.4)	40 (8.6)	16.2 (14.2, 18.4) [0.0 – 152.3]
Cauterised at 1st ENT review				
• No	757 (67.5)	600 (90.9)	60 (9.1)	17.1 (15.4, 18.9) [0.0 – 152.3]
• Yes	365 (32.5)	296 (91.4)	28 (8.6)	1.1 (0.9, 1.3) [0.0 – 116.4]
Packed at 1st ENT				
• No[2]	443 (39.5)	345 (90.6)	551 (9.4)	1.1 (0.9, 1.3) [0.0 – 104.0]
• Yes	679 (60.5)	551(91.4)	52 (8.6)	23.0 (21.2, 24.9) [0.0 – 152.3]
Dr Grade at 1st ENT				
• Nurse	38 (3.5)	34 (91.9)	3 (8.1)	2.3 (1.2, 4.5) [0.2 – 63.7]
• Junior	950 (86.6)	751 (91.4)	71 (8.6)	7.3 (6.5, 8.4) [0.0 – 152.3]
• Middle	101 (9.2)	84 (87.5)	12 (12.5)	8.5 (5.8, 12.5) [0.0 – 109.0]
• Consultant	8 (0.7)	6 (85.7)	1 (14.3)	3.2 (0.7, 14.1) [0.3 – 42.8]
Interventions after 1st ENT				
• No	365 (62.5)	288 (91.7)	26 (8.3)	0.7 (0.6, 0.8) [0.0 – 26.0]
• Yes	757 (67.5)	608 (90.7)	62 (9.3)	21.2 (19.5, 23.0) [0.0 – 152.3]
Surgery				

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• No	1080 (96.9)	866 (91.4)	81 (8.6)	6.5 (5.8, 7.4) [0.0 – 152.3]
• Yes	35 (3.1)	24 (80.0)	6 (20.0)	42.1 (32.9, 54.0) [8.8 – 144.6]
Intervention Strategy				
• Compliant	334 (29.8)	626 (91.0)	62 (9.0)	0.7 (0.6, 0.9) [0.0 – 50.5]
• Non-compliant	788 (70.2)	270 (91.2)	26 (8.8)	18.1 (16.4, 19.9) [0.0 – 152.3]

[1] Geometric mean and 95% CI
[2] Includes those whose ED pack was removed
Table 2: Summary statistics of 30-day re-admission and treatment time by patient's Epistaxis management.

Factor		Adjusted Ratio (95% CI) [2]	p-value
Packed at first ENT review	No	1	-
	Yes	7.1 (4.3 – 11.7)	< 0.001
Cauterised at first ENT review	No	1	-
	Yes	0.4 (0.3 – 0.6)	< 0.001

[1] Summary statistics for patients with complete model data
[2] Adjusted for severity scores (MEWS and WHO), age and subsequent treatment after the initial ENT review.
Table 3: Initial ENT treatments and their effect on overall treatment time. Table of the number (N) and percentage of total within each variable category; the median and Interquartile range of treatment time in hours; and the ratio and 95% confidence intervals.

Factor		Adjusted Hazard Ratio (95% CI)	p-value
Guideline compliant	No	1	-
	Yes	6.8 (5.7, 8.2)	< 0.001
Age Group	< 65	1	-
	65 ≤ Age < 75	1.1 (0.9, 1.3)	0.3
	75 ≤ Age < 85	0.9 (0.7, 1.0)	0.1
	≥ 85	1.2 (1.0, 1.5)	0.04
MEWS	0	1	-

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	1	0.9 (0.7, 1.1)	0.2
	2	1.0 (0.8, 1.2)	0.8
	3	0.9 (0.7, 1.2)	0.6
	≥ 4	1.0 (1.0, 1.5)	0.8
WHO Grade	I	1	-
	II	0.8 (0.6, 1.0)	0.02
	III	0.3 (0.2, 0.5)	< 0.001

[1] Summary statistics are for patients with complete model data
[2] Adjusted for severity scores (MEWS and WHO) and age.
Table 4: Adjusted Cox's proportional hazards model of time to achieve haemostasis by intervention strategy.

Factor		Adjusted Odds Ratio (95% CI)[1]	p-value
History of Epistaxis	No	1	-
	Yes	2.4 (1.4 – 3.9)	0.001

[1] Adjusted for severity scores (MEWS and WHO) and age.
Table 5: Role of Initial ENT treatment and admission patient and disease characteristics on 30-day epistaxis related ENT re-admission.

Supplementary material

		Adjusted Ratio (95% CI)	p-value
Sensitivity Analysis 1			
Packed at first ENT review	No	1	-
	Yes	7.0 (4.3 - 11.8)	< 0.001
Cauterised at first ENT review	No	1	-
	Yes	0.4 (0.3 – 0.6)	< 0.001
Sensitivity Analysis 2			
Packed at first ENT review	No	1	-
	Yes	7.5 (4.5 – 12.5)	< 0.001
Cauterised at first ENT review	No	1	-
	Yes	0.5 (0.3 – 0.7)	< 0.001
Sensitivity Analysis 3			
Packed at first ENT review	No	1	-

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	Yes	2.3 (1.8 – 3.0)	< 0.001
Cauterised at first ENT review	No	1	-
	Yes	0.9 (0.7 – 1.2)	0.59

Table 6: Sensitivity Analysis 1: log linear regression model removing censored observations. Sensitivity Analysis 1: log linear regression model of patients who did not require further interventions after their initial ENT intervention. Sensitivity Analysis 1: log linear regression model of observations who required further interventions after their initial ENT intervention.

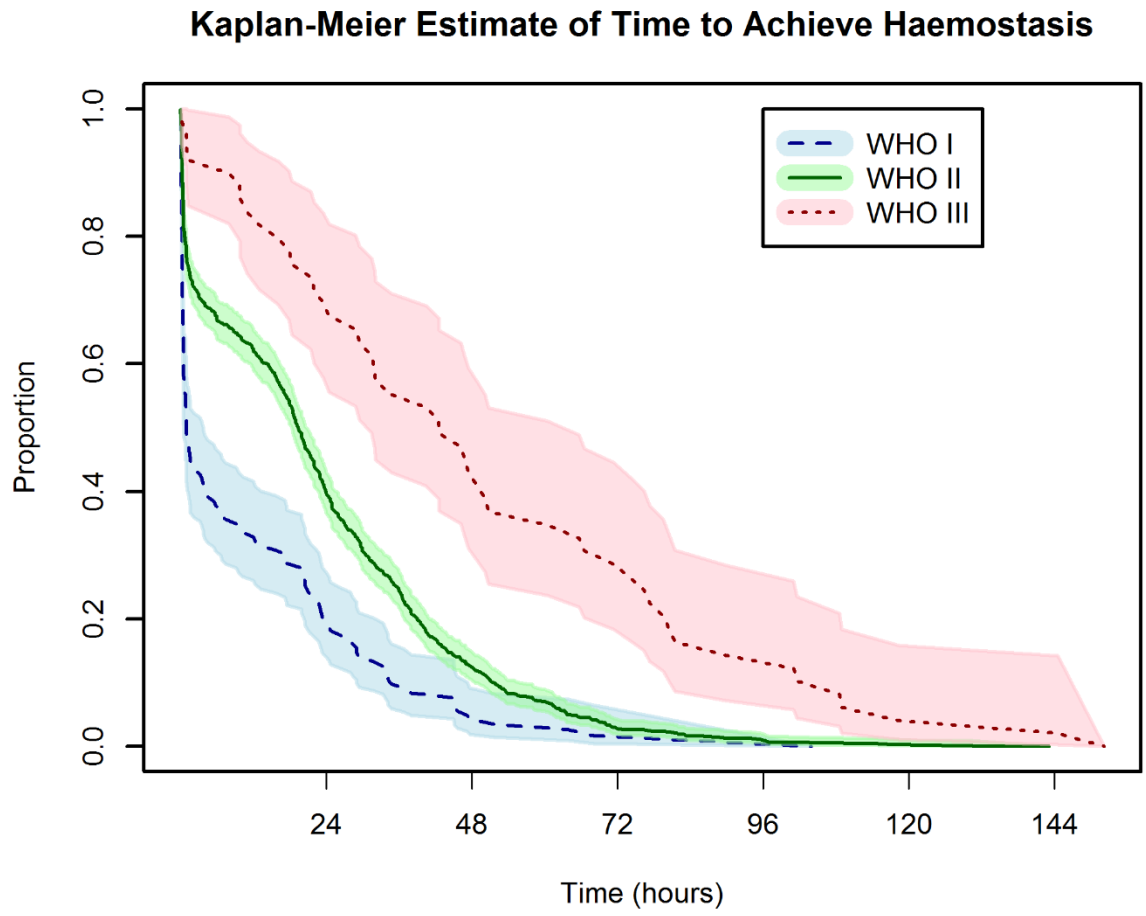

Figure 4: Kaplan-Meier estimates and 95% confidence intervals of treatment time by WHO bleeding grade: WHO I (blue dashed line with 95% CI shaded in light blue); WHO II (dark green line and 95% CI shaded in light green); WHO III (dark red dotted line and 95% CI shaded in red)..

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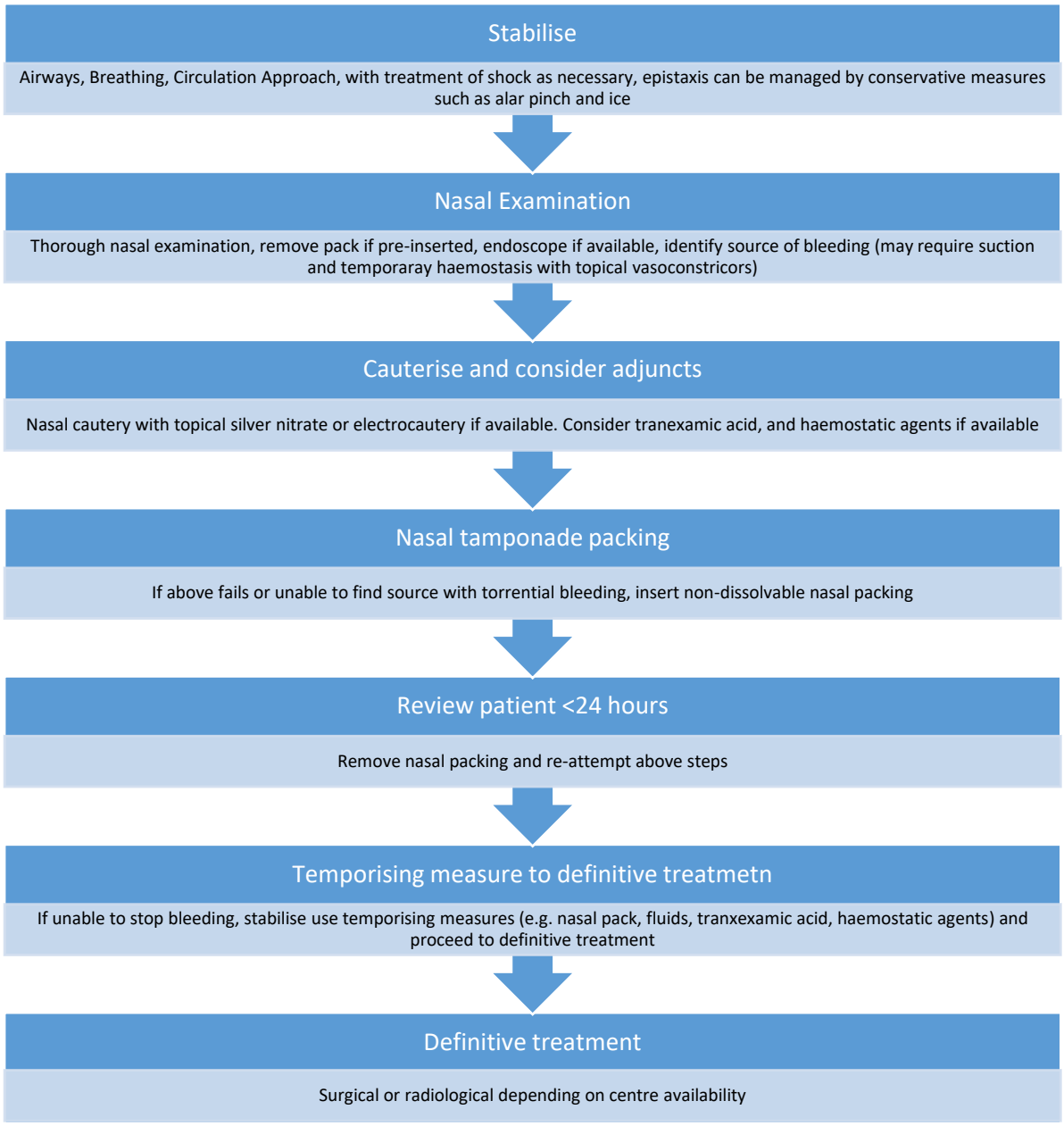

Figure 5 Derived epistaxis management steps based on BRS guidelines. The above flow chart shows the potential steps in managing a patient with epistaxis. These steps were adapted from BS epistaxis management guidance and each steps describes the subsequent treatment if previous has failed.

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