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

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23 Key points

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

32

33 Abstract

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

39

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

42

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

46

47 Setting: 113 participating UK hospitals.

48

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

51

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

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

56

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

59

60 Results: 834 patients had sufficient data for inclusion. Patients who did not receive nasal
61 cautery at first specialist review had a treatment time greater than double the time of those
62 who were cauterised: Adjusted ratio (aR) 2.5 (95% CI 1.7-3.3), after controlling for age,
63 bleeding severity, and whether they received a nasal pack or not. Only 30% of patients
64 received management that complied with new national guidance, but those that did were
65 87% more likely to be achieve haemostasis before those that did not, even after controlling
66 for bleeding severity. Type of treatment, whether initial intervention or management
67 strategy, did not affect 30-day re-attendance.

68

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

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84 Introduction

85

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

95

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

109

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

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

120

121 [Methods](#)

122 [Ethical approval](#)

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

127

128 [Design](#)

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

132

133 [Interventions analysed](#)

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

137 The effect of intervention type on outcome was assessed.

138

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

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

152

153 Outcomes

154 Two outcomes were selected:

155

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

166

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

169

170 Data Cleaning

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

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

177

178 *Statistical Analysis*

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

187

188 *Initial ENT (Individual) Interventions*

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

194

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

201

202 Approximately 60% of patients were successfully treated within 24 hours, and the remaining
203 40% took between 1 and 7 days to achieve definitive management, resulting in a highly
204 skewed distribution of treatment time. For this reason, analysis of initial individual
205 interventions and treatment time was performed using linear regression on the log

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

214

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

219

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

225

226 Due to the large number of factors to be investigated, we used forward model selection,
227 and a factor was included in the model if there was evidence at the 5% significance level
228 that the factor was contributing to the model. As more than 67% of patients required
229 additional treatment after their first intervention, the log linear model for treatment time
230 was adjusted for additional treatment performed after the first intervention, age, sex and
231 markers of disease severity such as WHO bleeding severity grade (WHO grade 1 epistaxis
232 <30 minutes within 24 hours, grade 2 epistaxis >30minutes within 24 hours, grade 3
233 epistaxis severe enough to require blood transfusion)(27) and Modified Early Warning Score
234 (MEWS is scored 0-3 based on systolic blood pressure, heart rate, respiratory rate,
235 temperature and AVPU scales) (28). As there appeared to be two sub-populations of
236 patients admitted with epistaxis – those successfully treated within 24 hours and those that
237 required several ENT interventions - it was important to insure patient factors were

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

243

244 *Intervention Strategy*

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

247

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

253

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

257

258 *Re-attendance to ENT*

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

265

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

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

270

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

279

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

285

286 Results

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

299

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

306

307 [Effect of patient factors and specific interventions on treatment time](#)

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

310

311 There was no evidence of a statistical association between a patient's age or MEWS and
312 their treatment time. However, there was evidence of an association between treatment
313 time and WHO bleeding severity grade. The evidence indicated that as WHO grade
314 increased (i.e. bleed severity increased), treatment time also increased. Individuals with
315 WHO grade II bleeding were likely to have a treatment time 1.3 times those with grade 1
316 (30% longer). Those with grade III bleeding were likely to have a treatment time 2.2 times
317 those with a grade I.

318

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

325

326 From the analysis of initial ENT individual intervention to treatment time (see table 3), it can
327 be seen that patients who were cauterised at first ENT review had 60% reduction in
328 treatment time compared to those who were not cauterised (Adjusted ratio 0.4, 95%CI 0.3 –
329 0.6), but individuals who were packed had a treatment time seven times longer than those
330 who were not packed (Adjusted Ratio 7.1, 95%CI 4.3 – 11.7). This data represents the effect

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

337

338 [Effect of intervention strategy on treatment time](#)

339 Analysis of different intervention strategies on treatment time were conducted via Kaplan-
340 Meier estimates, as shown in Figure 3. There was no evidence of an association between
341 either age or MEWS with treatment times within Cox's proportional hazard model, but
342 strong evidence of an association between treatment time and WHO bleeding severity
343 score. The Kaplan-Meier plots showed how treatment time was less for those with a lower
344 grade score. Patients treated with a guideline-compliant management strategy had a
345 shorter treatment time, indicated by the Kaplan-Meier estimates with no over-lap of the
346 95% CIs, suggesting a statistically significant effect size. Whilst the Kaplan-Meier plot
347 indicates that the difference was substantial, it this did not control for patient age, MEWS or
348 WHO bleeding severity grade. This association was explored using the multi-variable Cox
349 model, Table 4, which showed that even after controlling for age and WHO grade, the
350 hazard ratio was 6.8 (5.7-8.8). This indicated that those managed in a guideline compliant
351 manner were seven times more likely to be successfully treated at any time point than
352 those who were not. In real terms this means that patients who received treatments
353 according to national guidelines were 87% more likely to be successfully treated before
354 those who received treatments that did not follow national guidelines ($HR/(1+HR)$ = odds of
355 first success - (29)). The significance of the effect of WHO bleeding severity grade on
356 treatment time indicated that those with a lower grade had a faster treatment time than
357 those with a higher grade.

358

359 [Factors influencing 30-day re-admission](#)

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

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

365

366 Discussion

367 Summary

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

380

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

387

388 Our findings in the context of the available literature

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

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

398

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

408

409 [Strengths and weaknesses](#)

410 This is the largest prospective study of in-hospital epistaxis management to date, with
411 sufficiently detailed information to allow assessment of interventions and management
412 strategy after controlling for patient (age, co-morbidities), disease (severity of bleeding) and
413 treatment factors (grade of doctor and other therapies initiated). Our statistical strategy
414 allowed us to better understand treatment effects by focusing on initial intervention and
415 the overall management strategy (temporal sequence of treatments initiated).

416 However, whilst our results suggest that cauterisation at initial ENT review reduces overall
417 treatment time, irrespective of bleeding severity, care must be taken since bleeding severity
418 was assessed by the WHO bleeding score. WHO bleeding score provided a convenient
419 method by which to categorise bleed severity, but in practice it might prove difficult to
420 stratify patients' interventions by this score alone. Unfortunately, it seems the MEWS was
421 not sensitive enough to identify differences in the bleed severity of a patient, potentially

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

424

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

430

431 [Implications for future research and policy](#)

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

443

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

453

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

459

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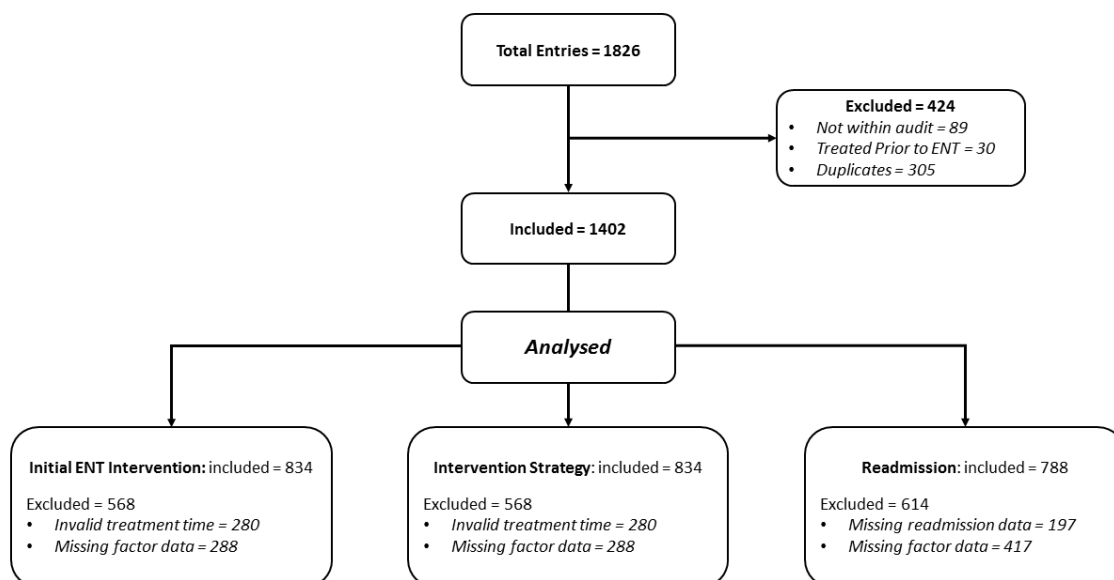
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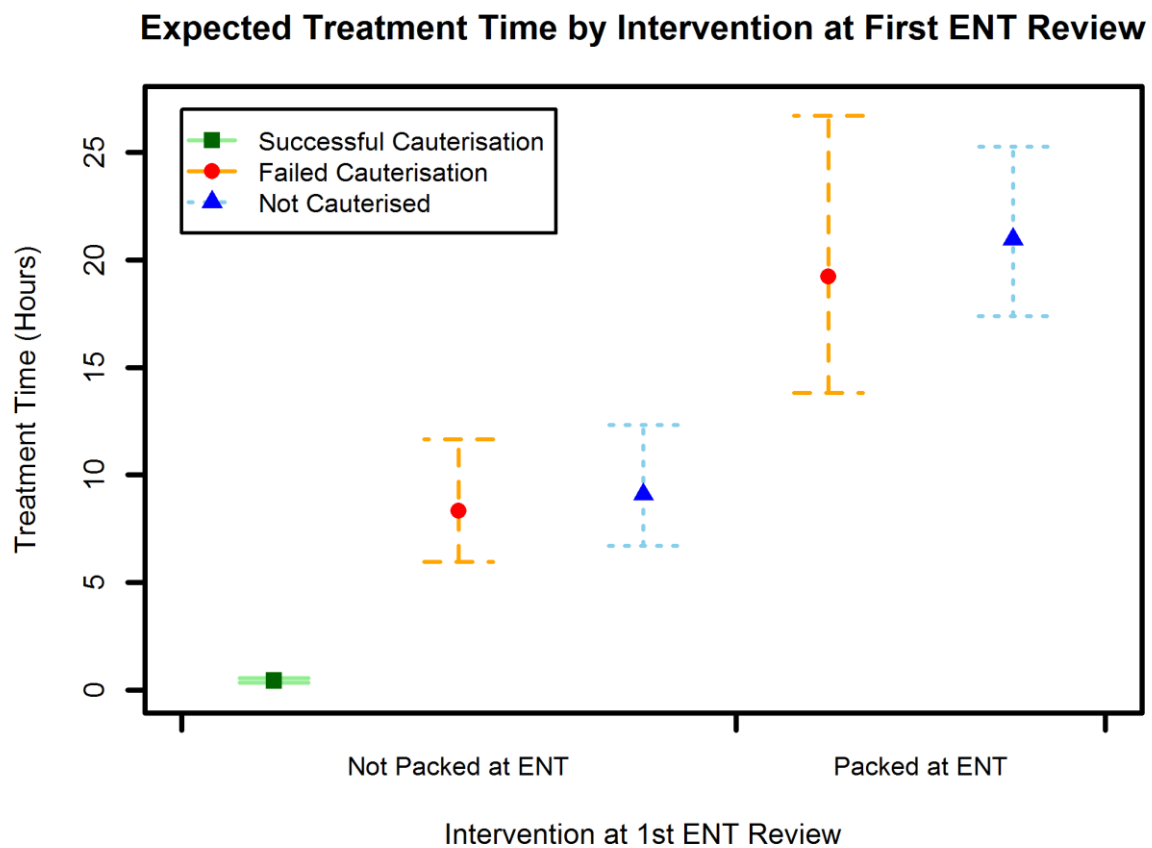
563 Tables and Figures



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

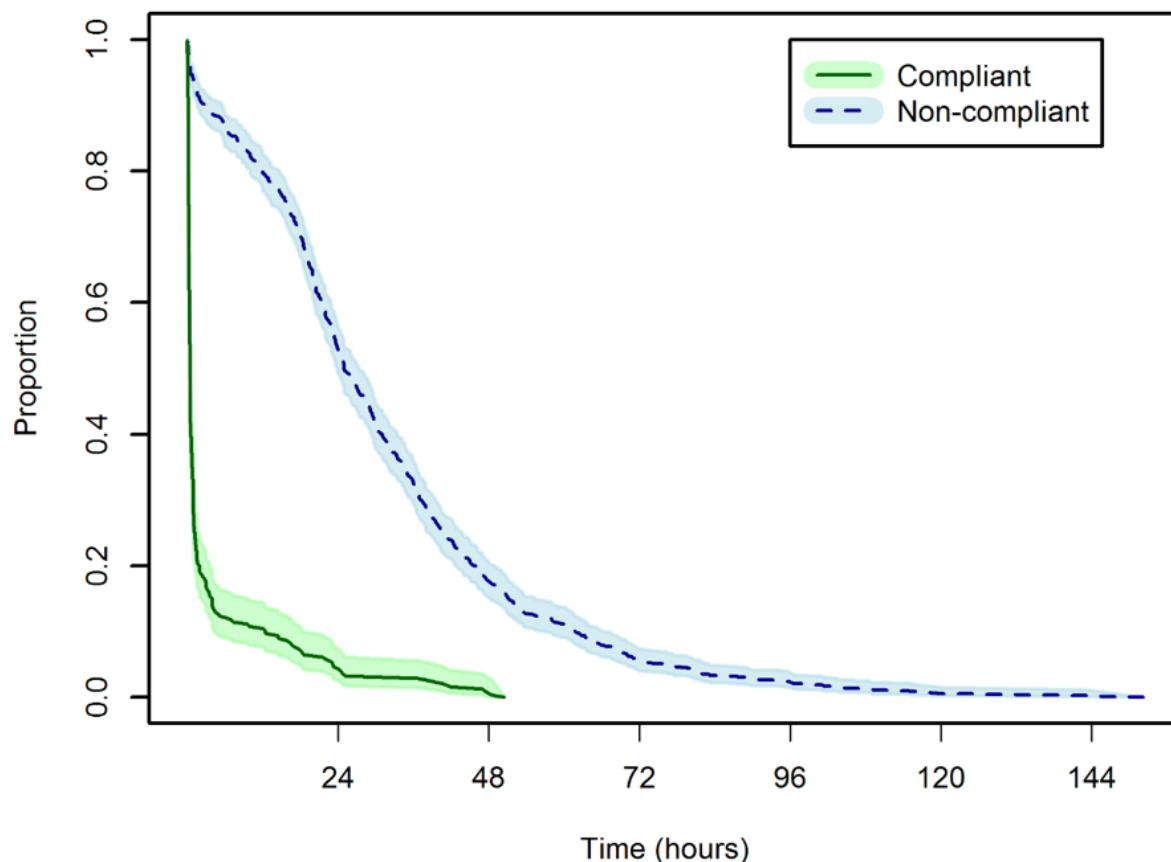
568 *not meet inclusion criteria, or was duplicated (424 entries excluded). Further data were excluded due to missingness in*
569 *variables that were considered essential for each of the three analyses.*



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572 *Figure 2: Expected treatment time with 95% confidence intervals of patients by cauterisation status: successful (dark green*
573 *square and light green bars); failed (red circle with orange dashed bars); not cauterised (blue triangle with light blue dotted*
574 *bars) and packing status (not packed or packed) at first ENT review. This graphic demonstrates that cauterising reduces*
575 *treatment time if successful but does not change treatment time if unsuccessful. Additionally, those who are packed have*
576 *the longest treatment times of all treatment arms.*
577

Kaplan-Meier Estimate of Time to Achieve Haemostasis



578

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

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	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:				

• 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 (%)			Treatment Time in hrs Mean (95% CI) ¹ [Range]
	Total	No Re- Admission 896 (91.1)	30-day Re- Admission 88 (8.9)	
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 1 st 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 1 st 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 1 st 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 1 st 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				

• 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]

590 ¹ Geometric mean and 95% CI

591 ² Includes those whose ED pack was removed

592 *Table 2: Summary statistics of 30-day re-admission and treatment time by patient's Epistaxis management.*

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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

596 ¹ Summary statistics for patients with complete model data

597 ² Adjusted for severity scores (MEWS and WHO), age and subsequent treatment after the initial ENT review.

598 *Table 3: Initial ENT treatments and their effect on overall treatment time. Table of the number (N) and percentage of total*
 599 *within each variable category; the median and Interquartile range of treatment time in hours; and the ratio and 95%*
 600 *confidence intervals.*

601

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	-

	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

602 ¹ Summary statistics are for patients with complete model data

603 ² Adjusted for severity scores (MEWS and WHO) and age.

604 *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)

605 ¹ Adjusted for severity scores (MEWS and WHO) and age.

606 *Table 5: Role of Initial ENT treatment and admission patient and disease characteristics on 30-day epistaxis related ENT re-*

607 *admission.*

608

609 [Supplementary material](#)

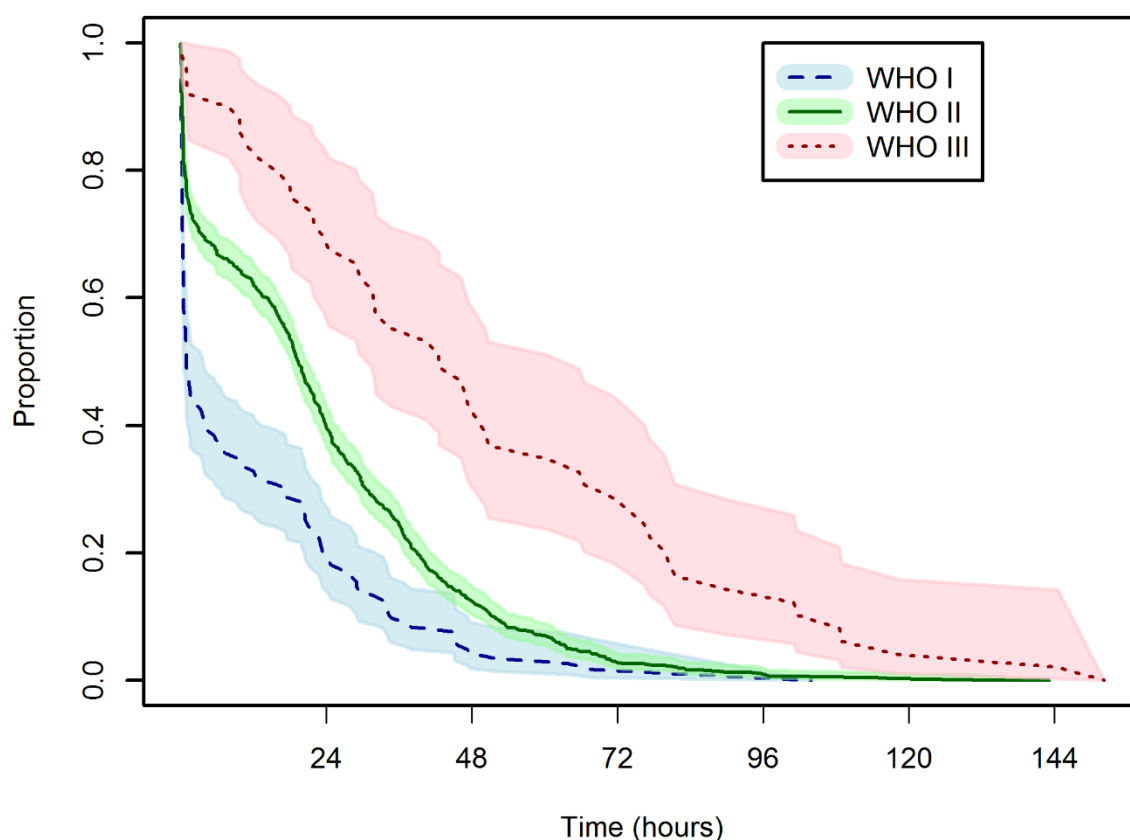
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	Adjusted Ratio (95% CI)	p-value
Sensitivity Analysis 1		
Packed at first ENT review	No	1
	Yes	7.0 (4.3 - 11.8)
Cauterised at first ENT review	No	1
	Yes	0.4 (0.3 – 0.6)
Sensitivity Analysis 2		
Packed at first ENT review	No	1
	Yes	7.5 (4.5 – 12.5)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

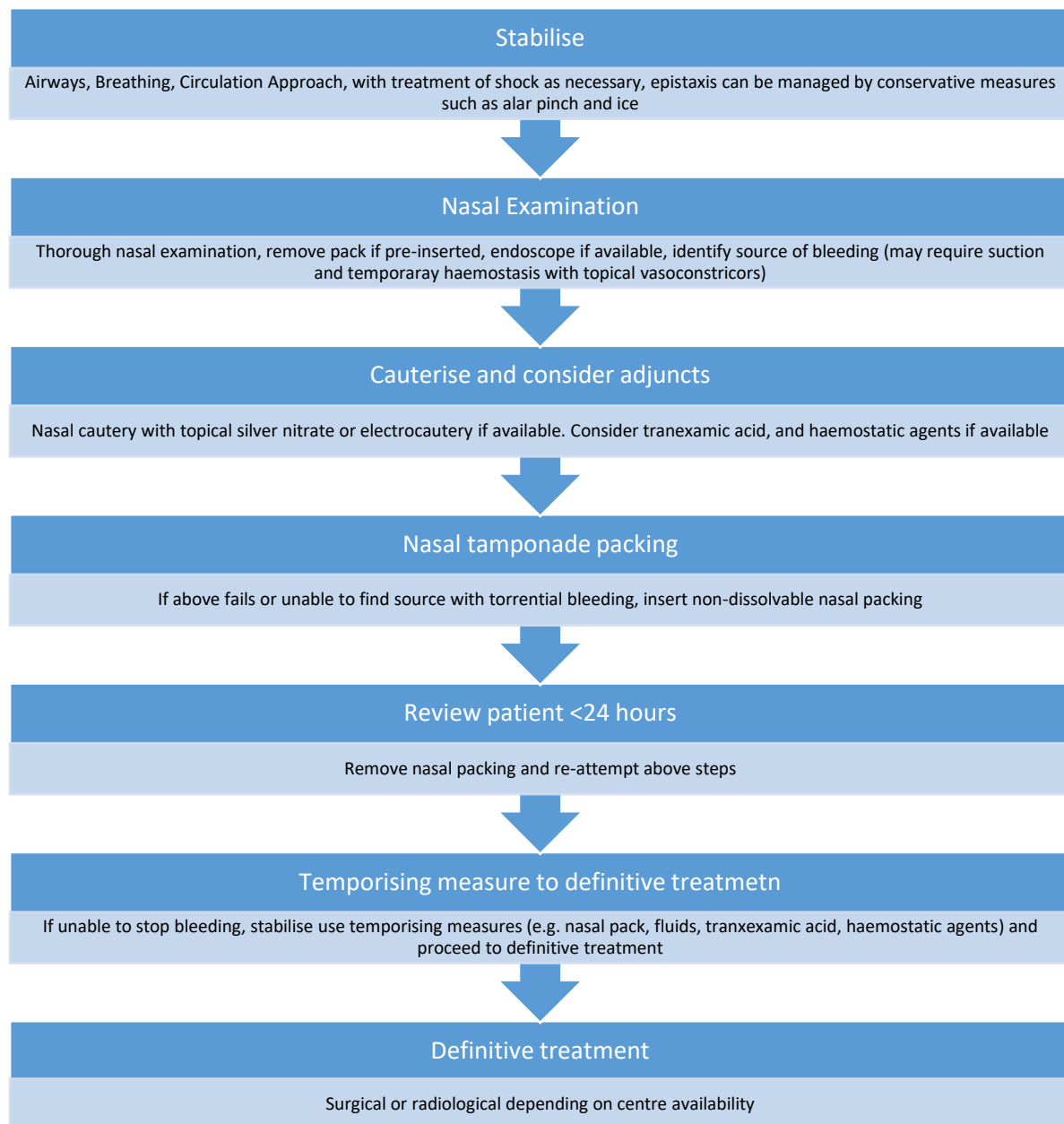
	Yes	2.3 (1.8 – 3.0)	< 0.001
Cauterised at first ENT review	No	1	-
	Yes	0.9 (0.7 – 1.2)	0.59

611
 612 *Table 6: Sensitivity Analysis 1: log linear regression model removing censored observations. Sensitivity Analysis 1: log linear*
 613 *regression model of patients who did not require further interventions after their initial ENT intervention. Sensitivity*
 614 *Analysis 1: log linear regression model of observations who required further interventions after their initial ENT*
 615 *intervention.*

Kaplan-Meier Estimate of Time to Achieve Haemostasis



616
 617 *Figure 4: Kaplan-Meier estimates and 95% confidence intervals of treatment time by WHO bleeding grade: WHO I (blue*
 618 *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*
 619 *dotted line and 95% CI shaded in red)..*



620

621 *Figure 5 Derived epistaxis management steps based on BRS guidelines. The above flow chart shows the potential steps in*

622 *managing a patient with epistaxis. These steps were adapted from BS epistaxis management guidance and each steps*

623 *describes the subsequent treatment if previous has failed.*

624

625

626

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