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Hemospray as first-line treatment option for malignant gastrointestinal bleeding: A cost-utility analysis in the United Kingdom

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Abstract:
Aims: For managing malignant upper gastrointestinal bleeding (MUGIB), randomised control trial data have shown the haemostatic powder; Hemospray (TC-325), results in greater immediate haemostasis and lower 30-day rebleeding rates than standard endoscopic therapy (SET). We sought to determine if using TC-325 as a first-line option for patients with MUGIB would be cost-effective compared with SET in the United Kingdom.
Methods: A decision tree was developed among patients with MUGIB, assessing initial therapy with TC-325 or SET over a 30-day time horizon. Patients with failed initial haemostasis, or a rebleed within 30 days, underwent further endoscopic treatment, escalation to either transcatheter arterial embolisation or surgery, or radiotherapy. Overall, 30-day mortality was applied. Costs, in Great British Pounds, were based on the United Kingdom National Health Services costs for 2023/2024. Results are reported as incremental differences in cost, quality-adjusted life years, and net monetary benefit. Deterministic and probabilistic sensitivity analyses and scenario analyses were performed.
Results: The cost of treating MUGIB patients with TC-325 was £245.88 lower than SET, with an incremental increase of 0.001 Quality Adjusted Life Years (QALYs). TC-325 remained cost-saving for sensitivity and scenario analyses. Probabilistic sensitivity analysis revealed TC-325 as more effective and cost-saving in 82.0% of simulations (range 68.8-97.8%).
Conclusions: Initial treatment of MUGIB with TC-325 compared to SET is more effective (higher primary haemostasis and lower 30-day rebleeding) and cost-saving due to requiring fewer interventions, readmissions, and length of stay. Additional studies are needed to address model uncertainties in the follow-up management of these complex patients.

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Hemospray as first-line treatment option for malignant gastrointestinal bleeding: A cost-utility analysis in the United Kingdom

Short Running title
Cost-effectiveness of Hemospray for first-line treatment of MUGIBs

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Abbreviations

DSA	Deterministic sensitivity analysis
HRQoL	Health-related quality of life
ICER	Incremental cost-effectiveness ratio
MUGIB	Malignant upper gastrointestinal bleeding
NHS	National Health Service
NHSE	National Health Service England
NMB	Net monetary benefit
PSA	Probabilistic sensitivity analysis
QALY	Quality-adjusted life year
RCT	Randomised controlled trial
SET	Standard endoscopic therapy
TAE	Transcatheter arterial embolisation
UGIB	Upper gastrointestinal bleeding
UK	United Kingdom
WTP	Willingness to pay threshold

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immediate haemostasis and lower 30-day rebleeding rates than standard endoscopic therapy (SET). We sought to determine if using TC-325 as a first-line option for patients with MUGIB would be cost-effective compared with SET in the United Kingdom.

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Results: The cost of treating MUGIB patients with TC-325 was £245.88 lower than SET, with an incremental increase of 0.001 Quality Adjusted Life Years (QALYs). TC-325 remained cost-saving for sensitivity and scenario analyses. Probabilistic sensitivity analysis revealed TC-325 as more effective and cost-saving in 82.0% of simulations (range 68.8-97.8%).

Conclusions: Initial treatment of MUGIB with TC-325 compared to SET is more effective (higher primary haemostasis and lower 30-day rebleeding) and cost-saving due to requiring fewer interventions, readmissions, and length of stay. Additional studies are needed to address model uncertainties in the follow-up management of these complex patients.

Keywords

Malignant upper gastrointestinal bleeding, nonvariceal upper gastrointestinal bleeding, cost-effectiveness, TC-325,

INTRODUCTION

Acute upper gastrointestinal bleeding (UGIB) is common with an incidence of 84-170 per 100,000 adults a year in the United Kingdom (UK), resulting in approximately 70,000 annual admissions to UK hospitals [1, 2]. UGIBs incur a high financial and resource burden on the National Health Service (NHS), due to in-hospital costs, readmission rates, and post-discharge expenses; treatment of acute UGIB is estimated to cost over £155.5 million annually [3].

Malignant causes of gastrointestinal bleeding account for 4% of all UGIBS [4] and its prevalence is increasing due to advancements in the diagnosis and treatment of gastrointestinal cancers [5]. Due to the large surface area of tissue requiring treatment, tissue friability, and possible underlying coagulopathy, endoscopic therapy for malignant bleeds can be technically challenging [6]. Data regarding the efficacy of standard endoscopic treatment (SET) for malignant UGIB (MUGIB) is variable, with primary haemostasis rates reported between 31% and 86% and rebleeding rates between 28% and 80% [7-10].

Topical haemostatic powders have been gaining popularity due to their ease of endoscopic application and ability to apply quickly and easily over a diffuse area while causing minimal tissue trauma [6]. A recent large-scale randomised control trial (RCT) has demonstrated that the haemostatic powder TC-325 has significantly greater immediate haemostasis (100%) and lower 30-day rebleeding rates (2%) compared with SET (68% immediate haemostasis and 21% 30-day rebleeding) in malignant gastrointestinal bleeds [11]. These results are consistent with trends noted in a prior pilot RCT on a different continent [12].

A potential limitation to the widespread use of TC-325 is the increased initial purchase costs compared with SET options. Even though the economic impact of using TC-325 as a first-line therapy in non-variceal UGIB has been reported [13] and a cost analysis has been performed in MUGIBs [14], no formal cost-effectiveness analysis has specifically addressed MUGIB. We, therefore, sought to determine if using the haemostatic powder TC-325 would be cost-effective as a first-line option for MUGIB compared with SET in the UK, by performing a cost-utility analysis.

METHODS

Model

A decision tree was developed in Microsoft Excel 2016 to estimate the overall costs and consequences of treating MUGIBs, with either SET or TC-325. SET for MUGIB includes the use of epinephrine, hemoclips, thermal coagulation, or argon plasma coagulation alone or in combination [4, 8, 9, 11, 15-17]. An NHS provider perspective was adopted with a time horizon of 30 days, under which no discount rate was applied, due to the time horizon being less than 12 months. The model begins with a hypothetical cohort of MUGIB patients (mean age 63.4±11 years (SD), 60.4% male) [11], who are treated with either SET or TC-325.

Patients with failed initial haemostasis (Figure 1), are treated with rescue TC-325 or are escalated to either transcatheter angiographic embolisation (TAE) or surgery [11, 12, 17, 18]. The decision tree includes a possibility of one rebleed within 30 days following which patients can be treated with repeat endoscopy matching the initial treatment allocation (i.e., no crossover at rebleed), surgery, TAE, or radiotherapy. The model assumes that all secondary treatments resolve the bleed and are at risk of rebleed. Additionally, the model assumes all patients are admitted as emergencies. Overall, 30-day mortality was applied and, implementing the notion of half cycle correction, death is assumed to occur on day 15, with all costs incurred before death and utilities calculated up to day 15. The model's clinical validity was reviewed by five experienced clinicians (AB, BN, NH, SH, AT). Results are reported as, incremental differences in cost, quality-adjusted life years (QALYs), and net monetary benefit (NMB).

Literature Search

A comprehensive literature search was conducted in PubMed and Cochrane Library (February 2024), following the guidance of the Cochrane Handbook of Systematic Review [19]. Search strings and the inclusion/exclusion criteria are presented in the supplementary file. Screening was performed by DC, BN and AT, and is reported in a PRISMA diagram (Supplementary file). All identified studies were extracted using standardised data tables after a consensus agreement was reached.

Three RCTs were identified comparing TC-325 with SET specifically in malignant bleeds [11, 12, 20]. The studies are heterogenous; one study included 30.5% of patients without an active bleed, [20] (active bleeding is required for TC-325 use), another was a pilot RCT [12], and the final RCT, included only non-palliative patients was the only study sufficiently powered to inform significance [11]. There are some discrepancies in SET compared to UK practice in one of the studies [20]. While the three studies were performed outside the UK, the patient demographics of these base case studies are comparable with patients in a UK registry [21, 22].

Despite the heterogeneity between studies, to provide the most generalisable results, the three RCTs were pooled to inform the base case [11, 12, 20, 23] (table 1). To overcome some of the heterogeneity issues, the impact of using only the large, powered RCT on the cost-effectiveness outcome was explored in scenario analysis [11].

Clinical Inputs

The clinical parameters and sources utilised are reported in Table 2. In brief, primary haemostasis, 30-day rebleed and mortality were used directly from the pooled RCT data (table 1). Due to the short 30-day time horizon, death was not adjusted for. The base case RCTs reported limited follow-up information regarding downstream haemostatic treatments. Therefore, data from wider papers, with longer follow-ups of malignant bleeds, was pooled to inform downstream treatments following the initial haemostatic failure [11, 12, 17] and rebleeding [8, 9, 15]. These data sources informed transition probabilities for surgery and repeat endoscopy, with TAE probabilities being calculated by limiting total probabilities to 1. Downstream treatments were assumed to be the same for both arms.

The primary effectiveness measure was quality-adjusted life years QALY, which incorporates health-related quality-of-life (HRQoL) and mortality. Utilities were estimated from a UK-based analysis of patients with acute UGIB [24], utilising the EuroQol EQ-5D instrument. This provided utility values for a patient at home (after discharge), and a patient in the hospital, with upper and lower limits [24]. No adjustments were made to the inpatient utility based on treatments. To quantify the in-hospital utility, the duration of hospital stay was calculated by summing the length of stay associated with the total pathway of procedures and capped at 30 days. Any difference from 30 days was assumed as the time the patient spent discharged and at home with the at-home utility applied. Length of stay for different procedures was derived from hospital-admitted patient care activity data reported in the NHS Digital [25] for the general population (Supplementary file).

Costs

The healthcare resource use associated with the initial endoscopic treatment of the acute bleed was derived from the National Health Services England (NHSE) tariff for diagnostic endoscopy. The tariff includes healthcare professional costs, endoscopy suite time and general consumables for an endoscopy, although it does not include treatment consumables or length of stay. Consumable cost for SET is the weighted use of epinephrine, hemoclips, thermal

coagulation, argon plasma coagulation and combinations of these treatments according to the reported use for malignant bleeds [4, 8, 9, 11, 15-17]. TC-325 prices were provided by Cook Medical (Limerick, Ireland). Length of stay cost for index endoscopy was based on the excess day's trim point costs according to the tariff, and the mean length of stay for therapeutic endoscopic procedure codes based utilising hospital episode statistic data [25]. Healthcare procedure costs for surgery and embolisation were derived from weighted non-elective NHS tariff costs in 2023/24, based on the frequency of procedure codes from 2021/22 [3, 25, 26] and weighted according to co-morbidities [27] Radiotherapy costs are an average of tariff costs for the delivery of 10 fractions [28]. To prevent double counting of the length of stay, it is assumed the tariff sufficiently covers bed stay costs for surgery, embolisation, or radiotherapy. Details of procedure codes and tariffs can be found in the supplementary file.

Cost-effectiveness Analysis

The results of the cost-utility analysis are reported as incremental costs (2023/24 cost year), QALYs and NMB. Incremental costs and QALYs are the difference in costs and QALYs for the TC-325 arm compared with the SET arm. The incremental cost-effectiveness ratio (ICER) is the incremental costs divided by the difference in QALYs. A negative incremental cost indicates a cost saving. The ICER is reported against NICE's recommended threshold willingness to pay threshold (WTP) of £20,000 per QALY [29]. A cost-effectiveness acceptability curve demonstrates uncertainty around cost-effectiveness at varying WTP thresholds. NMB, the difference in net monetary benefit between a new intervention and the standard interventions, was calculated at specific WTP thresholds by multiplying the incremental difference in QALY by the WTP threshold and subtracting the incremental difference in costs. A positive NMB indicates cost-effectiveness [30].

Sensitivity analysis

Deterministic sensitivity analysis (DSA) and probabilistic sensitivity analysis (PSA) were performed to assess the model's robustness. DSA was conducted by varying input parameters within plausible bounds, and the impact of these changes on the total incremental cost and NMB are presented as tornado plots (Figure 2 and supplementary file). Probabilistic sensitivity analysis, using a Monte Carlo simulation, was conducted to assess the simultaneous impact of uncertainty around key parameters. All cost, probability, mortality, and utility variables were included. Transition probabilities of upper and lower boundaries are calculated as 95% confidence intervals (Table 2). The endoscopy procedure's lower cost is the current diagnostic

tariff minus 10%, and the upper cost is the emergency procedure rate for this tariff. The lowest and highest identified costs for SET consumable costs informed upper and lower bounds for SET, while TC-325 device costs varied by ±10%. The estimated length of stay for the procedures is varied by the upper and lower limits reported by NHS England [26] and the bed stay cost varied by ± 10% of the base case value. The costs of surgery, TAE and radiotherapy are the lowest and highest identified tariffs respectively [26]. The PSA was run for 1000 iterations, and incremental costs in Great British Pounds for 2023, were plotted against incremental QALYs.

Scenario analysis

Multiple scenarios were investigated to explore uncertainties around base case assumptions including, (1) use of the large, powered RCT, representing less palliative patients (Eastern cooperative oncology group rating 0-2 only), (2) varying costs by upper or lower GI location, (3) using standard tariff cost in place of emergency cost (4) mortality determined by downstream interventions, (5) use of median LOS for index endoscopy and (6) using therapeutic endoscopy tariff in place of diagnostic tariff. Further details are in the supplementary file.

Validation

In addition to the scenario analyses exploring the uncertainty around the cost assumptions, the overall per-patient cost predicted by this model was validated compared to the estimated UK bleed costs reported previously [3], inflated to 2022 prices using the NHS inflation index [31].

RESULTS

Cost-effectiveness

Total costs for treating MUGIBs, over a 30-day time horizon, were lower for TC-325 than SET (Table 3). The TC-325 pathway is £245.88 less costly than SET per patient (5.4% reduction). The base case analysis indicates a gain of quality-of-life of 0.001 QALYs when using TC-325 compared to SET. As the model predicts TC-325 to be cost-saving and QALY-gaining, the estimated Incremental Cost-effectiveness Ratio (ICER) predicts TC-325 as dominant over SET (Table 3). Based on these costs and consequences NMB is estimated at £265.96, at a maximum willingness to pay threshold of £20k per QALY.

Sensitivity analysis

The results for the top 15 parameters which impact the deterministic sensitivity analysis, are presented in tornado diagrams in Figure 2, where the central line indicates base case incremental costs and NMB, respectively. The parameters exerting the most influence are the probability of 30-day rebleeding for both SET (incremental cost -£631 to £95) and TC-325 (incremental cost -£540 to £121). All other parameter variations continued to return an incremental cost saving and a positive NMB for TC-325

The results of 1000 Monte Carlo iterations for the PSA are presented in a cloud diagram (Figure 3). At a WTP threshold of £20,000 per QALY, approximately 82.0% of the simulations are within this threshold. The average probabilistic estimate also predicts a dominant ICER in the southeast quadrant of the cost-effectiveness plane. At a WTP of £0, TC-325 has a 80.1% probability of being cost-effective, i.e. cost saving.

Scenario analysis

Scenario analyses, adopting different source data: immediate haemostasis and 30-day rebleeding, procedure costs, mortality assumptions, length of stay for endoscopic procedures and cost assumptions for endoscopy, were explored. Each scenario continues to predict a QALY gain with a cost-saving (£121.50 to £585.63) for TC-325 as compared with SET, and TC-325 continues to be dominant in all scenarios with probabilities of being cost-effective at £0 WTP ranging from 68.4% to 98.3% (Table 3).

Overall cost validation.

The overall estimated per-patient cost for the 30 days following an acute MUGIB, ranges from £2,626.70 to £4,324.78 for TC-325 and £2,748.19 to £4,570.66 for SET, with a mean overall estimated cost of £3,789. The estimated UK bleed costs reported previously [3], inflated to 2022 prices using the NHS inflation index [31] estimate the average cost of any acute bleed, including bleeds not requiring any treatment, at £2855.58.

DISCUSSION

The increasing body of clinical evidence supporting the use of TC-325 as initial monotherapy for MUGIBs [11, 12, 22] is raising timely questions about the cost-effectiveness of such a treatment approach. Given the increased purchase cost of TC-325 compared to SET, we sought to explore through formal cost-utility analysis, if the reported improved immediate haemostasis

and reduced 30-day rebleed would make TC-325 a cost-effective first-line option for treating patients with MUGIB in the UK. These findings indicate that initial treatment of MUGIB with TC-325 compared to SET is both less costly and increases the overall quality-of-life for patients with a malignant bleed. This model predicts a dominant ICER for TC-325 across a wide range of plausible WTP thresholds, including a threshold of zero, indicating that TC-325 is not only cost-effective but cost-saving. With reported significant improvement in immediate haemostasis and 30-day rebleeding [11, 12], it is not surprising that TC-325 is cost-effective given costs of prolonged admission and readmission, in this patient population are high compared to the purchase cost of TC-325 [3, 32].

Currently, only one other formal cost-effectiveness analysis of TC-325 exists, exploring the position of TC-325 in the treatment pathway for acute non-variceal upper gastrointestinal bleeds (NVUGIBs) in the United States. The authors reported that adding TC-325 to traditional endoscopic treatment was less costly in acute NVUGIBs [13]. While the authors included a subgroup for MUGIBs in the model, they did not specifically report on the impact of treating patients with malignant bleeds. Further, the authors acknowledged a limitation in the data being sourced from limited single-arm studies at the time [13]. Recently Shah and Law (2024) have explored the cost of rebleeding in a cost analysis in the United States for MUGIBs. The authors explored bleed based on location, however, they do not incorporate the impact of failed immediate homeostasis, initial treatment costs or the impact on patients' quality-of-life. Our work adds significantly to the body of evidence in that it is the first cost-utility analysis in MUGIBs reporting on ICER per QALY from the UK NHS perspective. This utilises recent RCT efficacy data, valid cost sources, validated cost estimates, multiple sensitivity, and scenario analyses, thus providing robust conclusions.

DSA and PSA confirmed the robustness of the initial findings. The DSA demonstrates that the incremental costs and NMB are largely unaffected by changes in the unit cost of the TC-325. The univariate DSA demonstrates that cost-effectiveness is sensitive to several input parameters. Given that the base case studies have variable rebleeding rates it is not surprising that cost-effectiveness is most responsive to the probability of rebleeding in both TC-325 or SET arm. However, despite the DSA results, the PSA indicates that the probability of TC-325 being cost-effective is 82.0% at the UK WTP threshold of £20,000 per QALY gain, further, at a WTP threshold of £0, the incremental costs of TC-325 continue to have a probability of falling

below the threshold of £0 (80.1%), implying a high likelihood of TC-325 being cost saving compared with SET.

Multiple scenarios utilising different input values and sources were explored. Utilising data from the large, powered RCT in non-palliative patients [11], reduced the heterogeneity of the patient population and variances in practice and resulted in a higher incremental cost-saving, indicating an upper saving value whereby TC-325 has very low rebleeding rates. Scenarios exploring other cost input parameters yielded lower cost savings, however, all scenarios continued to report a cost saving and QALY gain with TC-325 treatment, further validating the robustness of this model.

Costs of an acute GI bleed in the UK reported by Campbell et al [3], and inflated to 2022 costs, to enable external validation of the model. Our model predicts patients' costs to be between £2,626 and £4,570, and a mean cost of £3,789. The inflated estimate from Cambell et al (£2855) is within the bounds of our current model. The inflated estimated per-patient cost is likely to be an underestimate compared with this model as the real-world data in Campbell's study includes the cost for patients where 14% of patients received no treatment, 57% received diagnostic endoscopy, and only 29% received a therapeutic endoscopy [3]. The patients in the current model all receive a therapeutic endoscopy, hence it is not surprising that the per-patient costs predicted in this model exceed that of the inflated value by Campbell et al. [3]. In addition, the current model was built specifically for malignant bleeds, which occurred in 3% of cases in the study by Campbell. Additional costs would be expected in the current model due to the increased LOS associated with this particularly complex and co-morbid group of patients. Indeed, Campbell reports an average LOS of 5.34 days compared with 8-11 days for MUGIBS by Pittayanon [3, 11]. Nonetheless, the fact the scenarios in this model encompass the values predicted supports the methods used here, and the base case estimates are not too far outside the Campbell estimate, further validating our model.

Economic dominance, overwhelming our findings across broad scenario analyses, makes the take-home message likely correct, but this work has some limitations. This conservative model means costs could be underestimated. For example, the model assumes haemostasis following surgery or embolisation, which will underestimate any costs due to the failure of these practices [10, 33]. Similarly, the model cannot incorporate costs due to re-admissions associated with a

rebleed, thus underestimating these costs, and presenting a conservative estimate of cost savings.

A 30-day time horizon is used in this model, which, while suitable to answer the short-term impact, does not address any possible long-term implications of rebleeding on patients' quality of life or quantity of life. Two long-term follow-up studies of patients with MUGIBs both report a significant increase in median overall survival in patients who did not rebleed compared with patients who did rebleed [8, 15]. None of the randomised studies have reported longer-term mortality data, thus in the absence of reliable data, it was not feasible to extend this model to a two-year time horizon.

The model is informed by RCTS performed outside the UK [11, 12, 20]. Results from contemporary observational studies in the UK support a high immediate haemostasis rate and low 30-day rebleeding rate with TC-325 used as a monotherapy [21, 22] adding credibility to this model. Unfortunately, these observational studies fail to report on SET, preventing their use in this comparative analysis.

In the absence of utility data for patients with a malignant bleed the utility data informing this model is from UK patients hospitalised with an AUGIB, hence the utility for both inpatient and at-home may be over- or underestimated and there could be a more significant QALY gain than reported here due to impact on hospitalisation on such a fragile cohort of patients. Finally, there exists a lot of variability in managing patients with MGUIB, and the model could not capture all management schemes. Even though we varied many parameters and had consensus on model structure from experts, the model remains a pragmatic representation. Additional RCTs with better characterisation of utilities and clarity on downstream interventions would help clarify these uncertainties and build future models.

CONCLUSIONS

Literature reports that initial treatment of patients presenting with MUGIB with TC-325 is more effective with higher primary haemostasis [22] and lower 30-day rebleeding [11]. This work has demonstrated that using TC-325 as first-line treatment for MUGIBs is likely to be cost-saving in the UK because of a need for fewer interventions when compared to SET. This work provides insights into the cost-effectiveness of TC-325 in the UK, and it would now be beneficial to assess the conclusions in other jurisdictions where cost structure and point

estimates of health resource expenditures differ. Given the increasing body of evidence supporting its clinical efficacy [11, 12, 22] and now cost-effectiveness, it would be prudent to consider the haemostatic powder TC-325 as a first-line treatment for the management of malignant upper GI bleeding.

FUNDING STATEMENT

Not applicable

ETHICS APPROVAL

Ethical approval was not required as the current study was not a clinical trial, and no patient-identifiable material was used.

DISCLOSURE

DC is a salaried employee of Cook Medical, a Cook Group Company. AB is a paid consultant for Cook inc. RH has received educational grants to support research infrastructure from Medtronic Ltd., Cook Endoscopy (fellowship support), Pentax Europe, C2 Therapeutics, Beamline Diagnostic, and Fractyl Ltd. BN, NH, SH, AT, JM, have no conflicts of interest.

AUTHOR CONTRIBUTION

Conceptualisation (DC and AB lead; BN, NH, SH, AT, support); formal analysis (DC lead, AB support); data curation (DC lead, BN and AT major contributor: AB, NH, SH data validation. JM and RH support); methodology (DC lead, AB support); writing - original draft (DC lead, AB major contributor); writing – review and editing (BN, NH, SH, AT, JH, and RH equal).

FIGURE LEGENDS

Figure 1 Decision tree to assess the cost-effectiveness of TC-325 for malignant upper gastrointestinal bleeds. Failure to achieve immediate haemostasis (red cross) or a downstream rebleed (Red droplet) within 30-days results in further treatment. Overall, 30-day mortality is applied. MUGIBs - malignant upper gastrointestinal bleeds, TAE – interventional radiological embolisation, Sx – surgery, RTx -radiotherapy, green check – haemostasis achieved/maintained, red cross – haemostasis not achieved, red drop – rebleed.

Figure 2 Tornado plot showing the influence of increasing or decreasing the top 15 key variables on incremental costs.

Figure 3 Cost-effectiveness plane, demonstrating 1,000 Montecarlo simulations (dots) deterministic result (square) the probabilistic results (triangle) and willingness to pay threshold (dashed line).

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Supplementary Material.

Dawn M. Cooper, Benjamin Norton, Neil Hawkes, Srishar Hebbar, Andrea Telese, John Morris, Rehan Haidry, Alan Barkun.

Hemospray as first-line treatment option for malignant gastrointestinal bleeding: A cost-utility analysis in the United Kingdom

PICO(D) Inclusion/exclusion criteria for Systematic Screening of Identified Studies		
PICO(D)	**Inclusion criteria**	**Exclusion criteria**
Population	• People with malignant gastrointestinal bleeding	• Gastrointestinal bleed without a malignant cause.
Intervention	• TC-325 (TC-325)	• Other haemostatic powders
Comparator	• Standard endoscopic therapy including • Through-the-scope endoscopic clips • Contact thermal coagulation • Argan Plasma Coagulation • Epinephrine/adrenaline • Any combination of above modalities	• Use of other haemostatic powders • Non-endoscopic treatments as primary intent for achieving haemostasis
Outcome	• Primary Haemostasis • 30-day Rebleeding • 30-day Mortality • Adverse events • Blood transfusions • Other treatment follow-up • Length of stay • Procedure time	
Study design:	• RCTs • Systematic review and meta-analyse of RCTs	• Case studies and series • Reviews • Opinion pieces • Letters to the editor • Single-arm studies (no control group) • Prospective non-randomised and retrospective comparator studies
Status:	• Fully published papers only • Peer-review journal articles only	• Unpublished literature • Sole conference proceedings (conference, congress, symposium, or other meetings) including: o Posters o Abstracts from oral presentations
Date	• All dates	

PICO(D): Population, Intervention, Comparator, Outcome, Design.

Literature Search Terms

Search Terms PubMed 05.02.2024			
Search Number	Search Terms	Term Query	Articles identified
#1	gastr* or intestine* or stomach or rect* or peptic or duoden* or colo*	Title/Abstract	2,1175,635
#2	bleed* or rebleed* or Hemorrhag* or blood-loss	Title/Abstract	534,312
#3	Hemospray or tc-325 or tc325	Title/Abstract	142
#4	cancer* or malignan* or neoplas* or oncolog* or tumor* or tumour or metasta*	Title/Abstract	4,041,880
#5	(#1 AND #2 AND #3 AND #4)	Title/Abstract	39

Search Terms Cochrane Library 05.02.2024			
Search Number	Search Terms	Term Query	Articles identified
#1	gastr* or intestine* or stomach or rect* or peptic or duoden* or colo*	Title/Abstract/Key word	186357
#2	bleed* or rebleed* or Hemorrhag* or blood-loss	Title/Abstract/Key word	88588
#3	Hemospray or tc-325 or tc325	Title/Abstract/Key word	36
#4	cancer* or malignan* or neoplas* or oncolog* or tumor* or tumour or metasta*	Title/Abstract/Key word	269979
#5	(#1 AND #2 AND #3 AND #4)	Title/Abstract/Key word	22

Costs

The healthcare resource use associated with the initial endoscopic treatment of the acute bleed was derived from the National Health Services England (NHSE) tariff for *diagnostic endoscopy*; FE22Z.

NHS England Procedure codes and HRG; diagnostic endoscopy (Base Case)		
Procedure codes	**Description**	**HRG linked**
G16.2	Diagnostic fibreoptic endoscopic ultrasound examination of oesophagus	FE22Z
G16.8	Other specified diagnostic fibreoptic endoscopic examination of oesophagus	FE22Z
G16.9	Unspecified diagnostic fibreoptic endoscopic examination of oesophagus	FE22Z
G45.8	Other specified diagnostic fibreoptic endoscopic examination of upper gastrointestinal tract	FE22Z
G45.9	Unspecified diagnostic fibreoptic endoscopic examination of upper gastrointestinal tract	FE22Z
G55.8	Other specified diagnostic endoscopic examination of duodenum	FE22Z
G55.9	Unspecified diagnostic endoscopic examination of duodenum	FE22Z
G65.8	Other specified diagnostic endoscopic examination of jejunum	FE22Z
G65.9	Unspecified diagnostic endoscopic examination of jejunum	FE22Z

HRG: Hospital resource group

Surgery tariff costs were calculated from FF02 and FF04, weighted proportional to the frequency of the informing procedures codes.

NHS England Procedure codes and HRG; upper GI surgery (Base Case)

Procedure codes	Description	HRG linked
G03.1	Partial oesophagectomy and end to end anastomosis of oesophagus	FF02
G03.3	Partial oesophagectomy and anastomosis of oesophagus to transposed jejunum	FF02
G03.4	Partial oesophagectomy and anastomosis of oesophagus to jejunum	FF02
G03.8	Other specified partial excision of oesophagus	FF02
G03.9	Unspecified partial excision of oesophagus	FF02
G04.1	Excision of lesion of oesophagus	FF04
G07.4	Repair of rupture of oesophagus	FF02
G07.8	Other specified repair of oesophagus	FF02
G07.9	Unspecified repair of oesophagus	FF02
G13.8	Other specified other open operations on oesophagus	FF04
G28.1	Partial gastrectomy and anastomosis of stomach to duodenum	FF02
G28.2	Partial gastrectomy and anastomosis of stomach to transposed jejunum	FF02
G28.3	Partial gastrectomy and anastomosis of stomach to jejunum	FF02
G28.8	Other specified partial excision of stomach	FF02
G28.9	Unspecified partial excision of stomach	FF02
G29.2	Open excision of lesion of stomach	FF04
G29.4	Diathermy to lesion of stomach	FF04
G29.5	Cryotherapy to lesion of stomach	FF04
G29.8	Other specified open extirpation of lesion of stomach	FF04
G29.9	Unspecified open extirpation of lesion of stomach	FF04
G36.8	Other specified other repair of stomach	FF04
G36.9	Unspecified other repair of stomach	FF04
G38.8	Other specified other open operations on stomach	FF04
G49.3	Partial excision of duodenum	FF02
G49.8	Other specified excision of duodenum	FF02
G49.9	Unspecified excision of duodenum	FF02
G50.1	Excision of lesion of duodenum	FF04
G50.2	Open destruction of lesion of duodenum	FF04
G50.8	Other specified open extirpation of lesion of duodenum	FF04
G53.2	Closure of perforation of duodenum	FF04
G53.8	Other specified other open operations on duodenum	FF04

HRG: Hospital resource group

HRG Code	HRG Name
FF02	Complex, Oesophageal, Stomach or Duodenum Procedures, 19 years and over
FF04	Major, Oesophageal, Stomach or Duodenum Procedures, 19 years and over,

Embolisation tariff costs are derived from YR54; “Percutaneous transluminal embolisation of peripheral blood vessels”.

NHS England Procedure codes and HRG; Trans arterial embolisation codes		
Procedure codes	**Description**	**HRG**
L43.3	Percutaneous transluminal embolisation of renal artery	YR54
L71.3	Percutaneous transluminal embolisation of artery	YR54
L94.1	Percutaneous transluminal embolisation of vein	YR54
HRG Code	**HRG Name**	
YR54	Percutaneous Transluminal Embolisation of Peripheral Blood Vessel with CC Score 6+	

HRG: Hospital resource group

Radiotherapy costs are an average of tariff costs of SC21, SC22, SC23 and SC31 for the delivery of 10 fractions

NHS England HRG Tariff Radiotherapy	
HRG Code	**HRG Name**
SC21Z	Deliver a Fraction of Treatment on a Superficial or Orthovoltage Machine
SC22Z	Deliver a Fraction of Treatment on a Megavoltage Machine
SC23Z	Deliver a Fraction of Complex Treatment on a Megavoltage Machine
SC31Z	Deliver a Fraction of Adaptive Radiotherapy on a Megavoltage Machine

HRG: Hospital resource group

Scenario Analysis -detailed changes

The first scenario explored the effect of using different estimates for immediate haemostasis (TC-325; 0.991 and SET; 0.686) and 30-day rebleeding rate (TC-325; 0.021 and SET; 0.213), derived from the single large RCT by Pittayanon et al 2023[1]. Secondly, to reflect the inclusion of upper and lower gastrointestinal bleeds, costs were weighted between procedures for the two locations. As the base case utilised emergency tariff costs for downstream procedures, the impact of incorporating the elective care costs was analysed. Mortality, determined by risk of secondary procedures, was investigated in a fourth scenario. To explore our assumptions around index endoscopy costs we evaluated the impact of using the median LOS value (3.9 days; range 1-6). Finally, in line with methods to define costs for surgery and embolisation, we utilised the emergency endoscopy tariff FE20Z (£1,452), without the addition of a length of stay costs but with the addition of the TC-325 device or SET device costs as per table 1.

Scenario 1 changes					
	Parameter	**Base Value**	**Lower value**	**Upper Value**	**Distribution**
TC-325	Primary haemostasis	0.9910	0.9552	1.000	Beta
	30-day rebleed rate	0.0208	0.0005	0.0755	Beta
SET	Primary haemostasis	0.6863	0.5539	0.8048	Beta
	30-day rebleed rate	0.2128	0.1095	0.3391	Beta

Scenario 2 changes				
Parameter	**Base Value**	**Lower value**	**Upper Value**	**Distribution**
Endoscopy, TC-325*	£1,100.55	£972.50	£1,263.50	Gamma
Endoscopy, SET*	£543.18	£363.21	£677.21	Gamma
TAE procedure	£5,243.14	£4,387.00	£5,889.00	Gamma
Surgical procedure	£9,297.79	£5,675.00	£13,851.00	Gamma

** Costs exclude bed stay, calculated separately using base case data*

Scenario 3 changes				
Parameter	**Base Value**	**Lower value**	**Upper Value**	**Distribution**
TAE procedure	£2,070.89	£1,742.00	£2,319.00	Gamma
Surgical procedure	£8,602.74	£3,646.00	£10,702.00	Gamma

Scenario 4 changes				
Parameter	**Base Value**	**Lower value**	**Upper Value**	**Distribution**
Post-surgery mortality	0.2887	0.2033	0.3822	Beta
Post -IRE mortality	0.1000	0.0382	0.1868	Beta
Post-endoscopy mortality	0.0589	0.0520	0.0661	Beta
Post-multiple endoscopy mortality	0.2324	0.1909	0.2767	Beta
Post -RADIO mortality	0.1038	0.0535	0.1682	Beta
Post-Surgery AND IRE mortality	0.6000	0.1941	0.9324	Beta

Scenario 5 changes				
Parameter	**Base Value**	**Lower value**	**Upper Value**	**Distribution**
LOS endoscopy	3.79	1.00	7.00	Beta

Scenario 6 changes				
Parameter	**Base Value**	**Lower value**	**Upper Value**	**Distribution**
Endoscopy, TC-325*	£2,137.00	£1,682.50	£2,969.50	Gamma
Endoscopy, SET*	£1,579.63	£1,073.21	£2,383.21	Gamma
Bed day cost endoscopy	£0.00	£0.00	£0.00	Gamma

* *Tarriff costs are inclusive bed stay costs*

Tarriff Sources Scenario 2

NHS England Procedure codes diagnostic colonoscopy (Scenario 2)		
Procedure codes	**Description**	**HRG tariff**
H22.9	Unspecified diagnostic endoscopic examination of colon	FE32Z
H25.8	Other specified diagnostic endoscopic examination of lower bowel using fibreoptic sigmoidoscope	FE35Z
H25.9	Unspecified diagnostic endoscopic examination of lower bowel using fibreoptic sigmoidoscope	FE35Z
H68.2	Diagnostic endoscopic examination of colonic pouch using colonoscope	FE32Z
H68.4	Diagnostic endoscopic examination of ileoanal pouch using colonoscope	FE32Z
H68.9	Unspecified diagnostic endoscopic examination of enteric pouch using colonoscope	FE32Z
H69.2	Diagnostic endoscopic examination of colonic pouch using fibreoptic sigmoidoscope	FE35Z
H69.4	Diagnostic endoscopic examination of ileoanal pouch using fibreoptic sigmoidoscope	FE35Z
H69.8	Other specified diagnostic endoscopic examination of enteric pouch using fibreoptic sigmoidoscope	FE35Z
H69.9	Unspecified diagnostic endoscopic examination of enteric pouch using fibreoptic sigmoidoscope	FE35Z
G80.8	Other specified diagnostic endoscopic examination of ileum	FE32Z
G80.9	Unspecified diagnostic endoscopic examination of ileum	FE32Z

HRG: Hospital resource group

NHS England Procedure codes Therapeutic colonoscopy (Scenario 2)		
Procedure codes	**Description**	**HRG linked**
G54.1	Endoscopic extirpation of lesion of duodenum	FE20Z
G54.8	Other specified therapeutic endoscopic operations on duodenum	FE20Z
G54.9	Unspecified therapeutic endoscopic operations on duodenum	FE20Z
H20.2	Fibreoptic endoscopic cauterisation of lesion of colon	FE30Z
H20.3	Fibreoptic endoscopic laser destruction of lesion of colon	FE30Z
H20.4	Fibreoptic endoscopic destruction of lesion of colon	FE30Z
H20.6	Fibreoptic endoscopic resection of lesion of colon	FE30Z
H20.8	Other specified endoscopic extirpation of lesion of colon	FE30Z
H20.9	Unspecified endoscopic extirpation of lesion of colon	FE30Z
H21.2	Fibreoptic endoscopic coagulation of blood vessel of colon	FE30Z
H21.8	Other specified other therapeutic endoscopic operations on colon	FE30Z
H21.9	Unspecified other therapeutic endoscopic operations on colon	FE30Z
H22.8	Other specified diagnostic endoscopic examination of colon	FE32Z
H23.2	Endoscopic cauterisation of lesion of lower bowel using fibreoptic sigmoidoscope	FE33Z
H23.3	Endoscopic laser destruction of lesion of lower bowel using fibreoptic sigmoidoscope	FE33Z
H23.4	Endoscopic destruction of lesion of lower bowel using fibreoptic sigmoidoscope	FE33Z
H23.6	Endoscopic resection of lesion of lower bowel using fibreoptic sigmoidoscope	FE33Z
H23.8	Other specified endoscopic extirpation of lesion of lower bowel using fibreoptic sigmoidoscope	FE33Z
H23.9	Unspecified endoscopic extirpation of lesion of lower bowel using fibreoptic sigmoidoscope	FE33Z
H24.2	Endoscopic coagulation of blood vessel of lower bowel using fibreoptic sigmoidoscope	FE33Z
H24.8	Other specified other therapeutic endoscopic operations on lower bowel using fibreoptic sigmoidoscope	FE33Z
H24.9	Unspecified other therapeutic endoscopic operations on lower bowel using fibreoptic sigmoidoscope	FE33Z
H26.2	Endoscopic cauterisation of lesion of sigmoid colon using rigid sigmoidoscope	FE36Z
H26.3	Endoscopic laser destruction of lesion of sigmoid colon using rigid sigmoidoscope	FE36Z
H26.5	Endoscopic destruction of lesion of sigmoid colon using rigid sigmoidoscope	FE36Z

H26.7	Endoscopic resection of lesion of sigmoid colon using rigid sigmoidoscope	FE36Z
H26.8	Other specified endoscopic extirpation of lesion of sigmoid colon using rigid sigmoidoscope	FE36Z
H26.9	Unspecified endoscopic extirpation of lesion of sigmoid colon using rigid sigmoidoscope	FE36Z
H27.8	Other specified other therapeutic endoscopic operations on sigmoid colon using rigid sigmoidoscope	FE36Z
H27.9	Unspecified other therapeutic endoscopic operations on sigmoid colon using rigid sigmoidoscope	FE36Z

HRG: Hospital resource group

NHS England Procedure codes lower GI surgery (Scenario 2)

Procedure codes	Description	HRG linked
H07.1	Right hemicolectomy and end to end anastomosis of ileum to colon	FF32
H07.2	Right hemicolectomy and side to side anastomosis of ileum to transverse colon	FF32
H07.3	Right hemicolectomy and anastomosis	FF32
H07.4	Right hemicolectomy and ileostomy	FF31
H07.5	Right hemicolectomy and end to side anastomosis	FF32
H07.8	Other specified other excision of right hemicolon	FF32
H07.9	Unspecified other excision of right hemicolon	FF32
H08.1	Transverse colectomy and end to end anastomosis	FF32
H08.2	Transverse colectomy and anastomosis of ileum to colon	FF32
H08.3	Transverse colectomy and anastomosis	FF32
H08.4	Transverse colectomy and ileostomy	FF31
H08.5	Transverse colectomy and exteriorisation of bowel	FF31
H08.6	Transverse colectomy and end to side anastomosis	FF32
H08.8	Other specified excision of transverse colon	FF32
H08.9	Unspecified excision of transverse colon	FF32
H09.1	Left hemicolectomy and end to end anastomosis of colon to rectum	FF33
H09.2	Left hemicolectomy and end to end anastomosis of colon to colon	FF33
H09.3	Left hemicolectomy and anastomosis	FF33
H09.4	Left hemicolectomy and ileostomy	FF31
H09.5	Left hemicolectomy and exteriorisation of bowel	FF31
H09.6	Left hemicolectomy and end to side anastomosis	FF33
H09.8	Other specified excision of left hemicolon	FF33
H09.9	Unspecified excision of left hemicolon	FF33
H10.1	Sigmoid colectomy and end to end anastomosis of ileum to rectum	FF33
H10.2	Sigmoid colectomy and anastomosis of colon to rectum	FF33
H10.3	Sigmoid colectomy and anastomosis	FF33
H10.4	Sigmoid colectomy and ileostomy	FF31
H10.5	Sigmoid colectomy and exteriorisation of bowel	FF31
H10.6	Sigmoid colectomy and end to side anastomosis	FF33
H10.8	Other specified excision of sigmoid colon	FF33
H10.9	Unspecified excision of sigmoid colon	FF33
H11.1	Colectomy and end to end anastomosis of colon to colon	FF33
H11.2	Colectomy and side to side anastomosis of ileum to colon	FF32
H11.3	Colectomy and anastomosis	FF33
H11.4	Colectomy and ileostomy	FF31

NHS England Procedure codes lower GI surgery (Scenario 2)		
Procedure codes	**Description**	**HRG linked**
H11.5	Colectomy and exteriorisation of bowel	FF31
H11.6	Colectomy and end to side anastomosis	FF33
H11.8	Other specified other excision of colon	FF33
H11.9	Unspecified other excision of colon	FF33
H15.8	Other specified other exteriorisation of colon	FF31
H15.9	Unspecified other exteriorisation of colon	FF31
H19.8	Other specified other open operations on colon	FF34
H33.1	Abdominoperineal excision of rectum and end colostomy	FF31
H33.2	Proctectomy and anastomosis of colon to anus	FF31
H33.3	Anterior resection of rectum and anastomosis of colon to rectum using staples	FF31
H33.4	Anterior resection of rectum and anastomosis	FF31
H33.5	Rectosigmoidectomy and closure of rectal stump and exteriorisation of bowel	FF31
H33.6	Anterior resection of rectum and exteriorisation of bowel	FF31
H33.7	Perineal resection of rectum	FF31
H33.8	Other specified excision of rectum	FF31
H33.9	Unspecified excision of rectum	FF33
H34.1	Open excision of lesion of rectum	FF34
H34.2	Open cauterisation of lesion of rectum	FF34
H34.4	Open laser destruction of lesion of rectum	FF34
H34.5	Open destruction of lesion of rectum	FF34
H34.8	Other specified open extirpation of lesion of rectum	FF34
H34.9	Unspecified open extirpation of lesion of rectum	FF34
G58.8	Other specified excision of jejunum	FF21
G58.9	Unspecified excision of jejunum	FF21
G59.1	Excision of lesion of jejunum	FF22
G63.8	Other specified other open operations on jejunum	FF22
G67.8	Other specified other operations on jejunum	FF22
G69.1	Ileectomy and anastomosis of stomach to ileum	FF21
G69.2	Ileectomy and anastomosis of duodenum to ileum	FF21
G69.3	Ileectomy and anastomosis of ileum to ileum	FF21
G69.4	Ileectomy and anastomosis of ileum to colon	FF21
G69.8	Other specified excision of ileum	FF21
G69.9	Unspecified excision of ileum	FF21
G70.2	Excision of lesion of ileum	FF22
G70.8	Other specified open extirpation of lesion of ileum	FF22
G70.9	Unspecified open extirpation of lesion of ileum	FF22
G72.1	Anastomosis of ileum to caecum	FF21
G72.2	Anastomosis of ileum to transverse colon	FF22
G72.3	Anastomosis of ileum to colon	FF22
G72.4	Anastomosis of ileum to rectum	FF22
G72.5	Anastomosis of ileum to anus and creation of a pouch	FF22
G72.8	Other specified other condition of ileum	FF22
G72.9	Unspecified other condition of ileum	FF22

NHS England Procedure codes lower GI surgery (Scenario 2)		
Procedure codes	**Description**	**HRG linked**
G82.8	Other specified other operations on ileum	FF22

HRG: Hospital resource group

HRG Code	HRG Name
FF21D	Very Major Small Intestine Procedures, 19 years and over
FF22D	Major Small Intestine Procedures, 19 years and over
FF31D	Complex Large Intestine Procedures, 19 years and over
FF32C	Proximal Colon Procedures, 19 years and over
FF33B	Distal Colon Procedures, 19 years and over
FF34B	Major Large Intestine Procedures, 19 years and over

Tariff Sources Scenario 6

NHS England Procedure codes and HRG; therapeutic endoscopy (Scenario 6)		
Procedure codes	**Description**	**HRG linked**
G15.8	Other specified other therapeutic fibreoptic endoscopic operations on oesophagus	FE20Z
G15.9	Unspecified other therapeutic fibreoptic endoscopic operations on oesophagus	FE20Z
G18.8	Other specified other therapeutic endoscopic operations on oesophagus using rigid oesophagoscope	FE20Z
G20.1	Fibreoptic endoscopic coagulation of bleeding lesion of oesophagus	FE20Z
G43.2	Fibreoptic endoscopic laser destruction of lesion of upper gastrointestinal tract	FE20Z
G43.3	Fibreoptic endoscopic cauterisation of lesion of upper gastrointestinal tract	FE20Z
G43.5	Fibreoptic endoscopic destruction of lesion of upper gastrointestinal tract	FE20Z
G43.6	Fibreoptic endoscopic injection therapy to lesion of upper gastrointestinal tract	FE20Z
G43.8	Other specified fibreoptic endoscopic extirpation of lesion of upper gastrointestinal tract	FE20Z
G43.9	Unspecified fibreoptic endoscopic extirpation of lesion of upper gastrointestinal tract	FE20Z
G44.8	Other specified other therapeutic fibreoptic endoscopic operations on upper gastrointestinal tract	FE20Z
G44.9	Unspecified other therapeutic fibreoptic endoscopic operations on upper gastrointestinal tract	FE20Z
G46.2	Fibreoptic endoscopic coagulation of bleeding lesion of upper gastrointestinal tract	FE20Z
G54.8	Other specified therapeutic endoscopic operations on duodenum	FE20Z

HRG: Hospital resource group

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2.

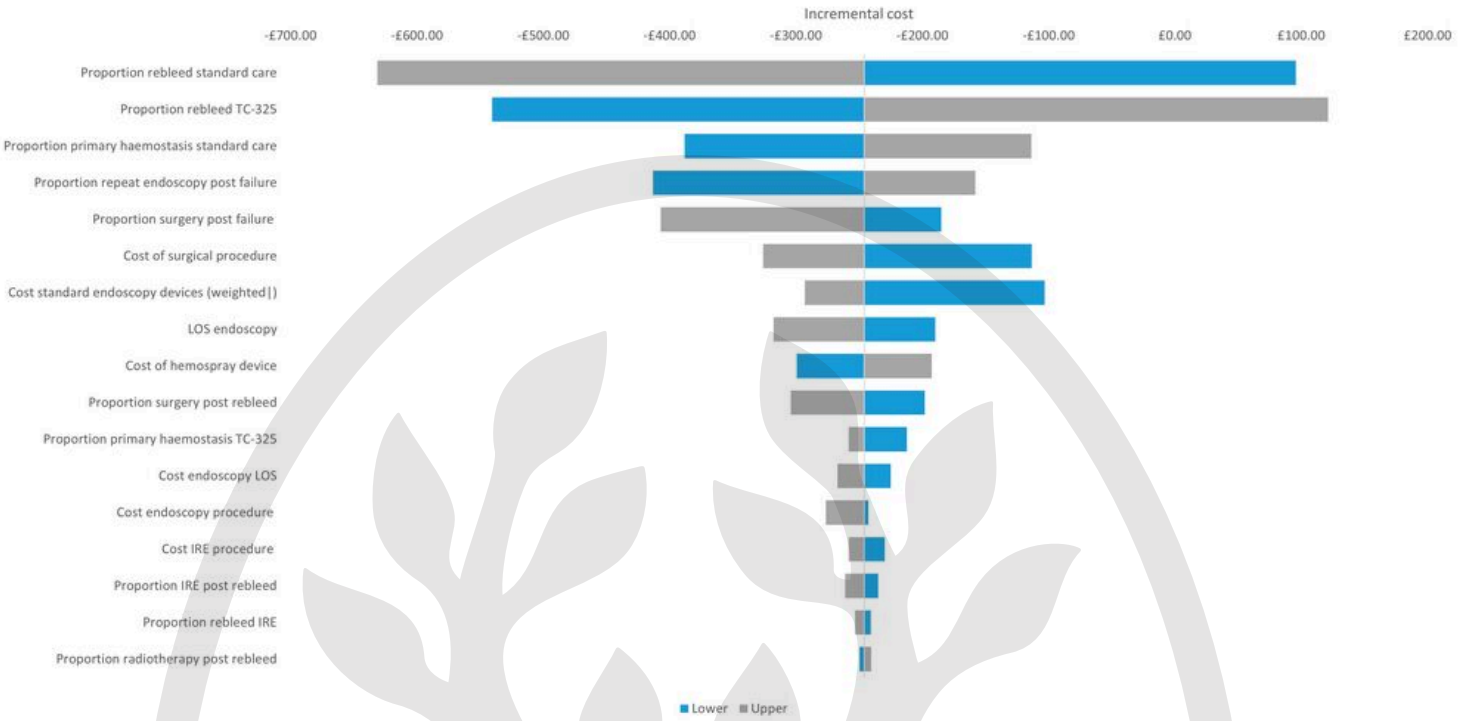
Table 1 Pooled RCT data

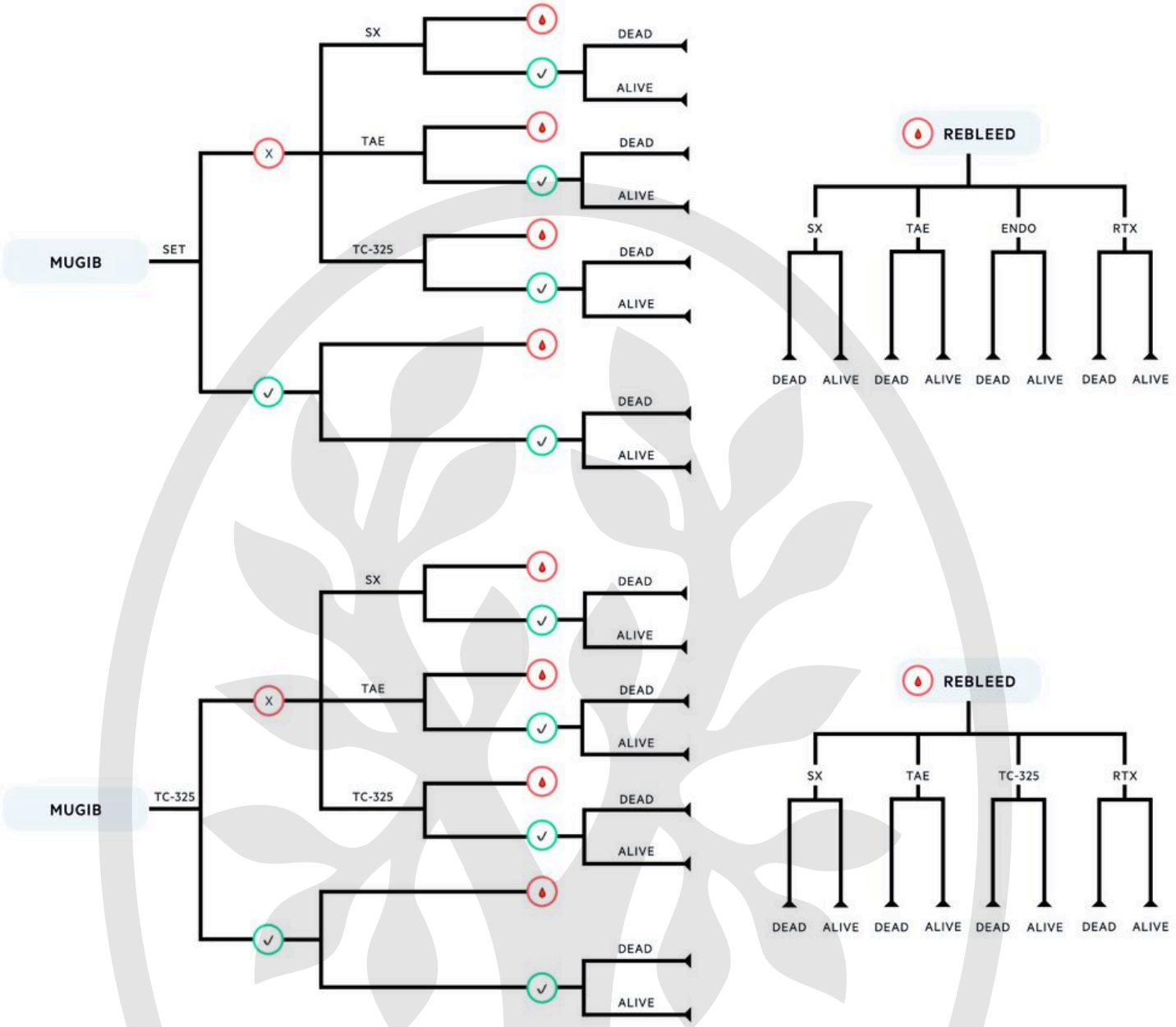
Study	Patients	Immediate haemostasis	30-day rebleed
Pittayanon et al 2023*	N=106	TC-325: 55/55 (100%) SET: 35/51 (68.6%)	TC-325: 1/48 (2.1%) SET: 10/47 (21.3%)
Chen et al 2020	N=20	TC-325: 9/10 (90%) SET: 4/10 (40%)	TC-325: 2/10 (20%) SET: 6/10 (60%)
Da Martins et al 2022	N=59	TC-325: 28/28 (100%) SET: NR	TC-325: 9/28 (32.1%) SET: 6/31 (19.4%)
Pooled	**N=175**	**TC-325: 92/93 (98.9%)** **SET: 39/61 (63.9%)**	**TC-325: 12/86 (13.95%)** **SET:22/88 (25.%)**

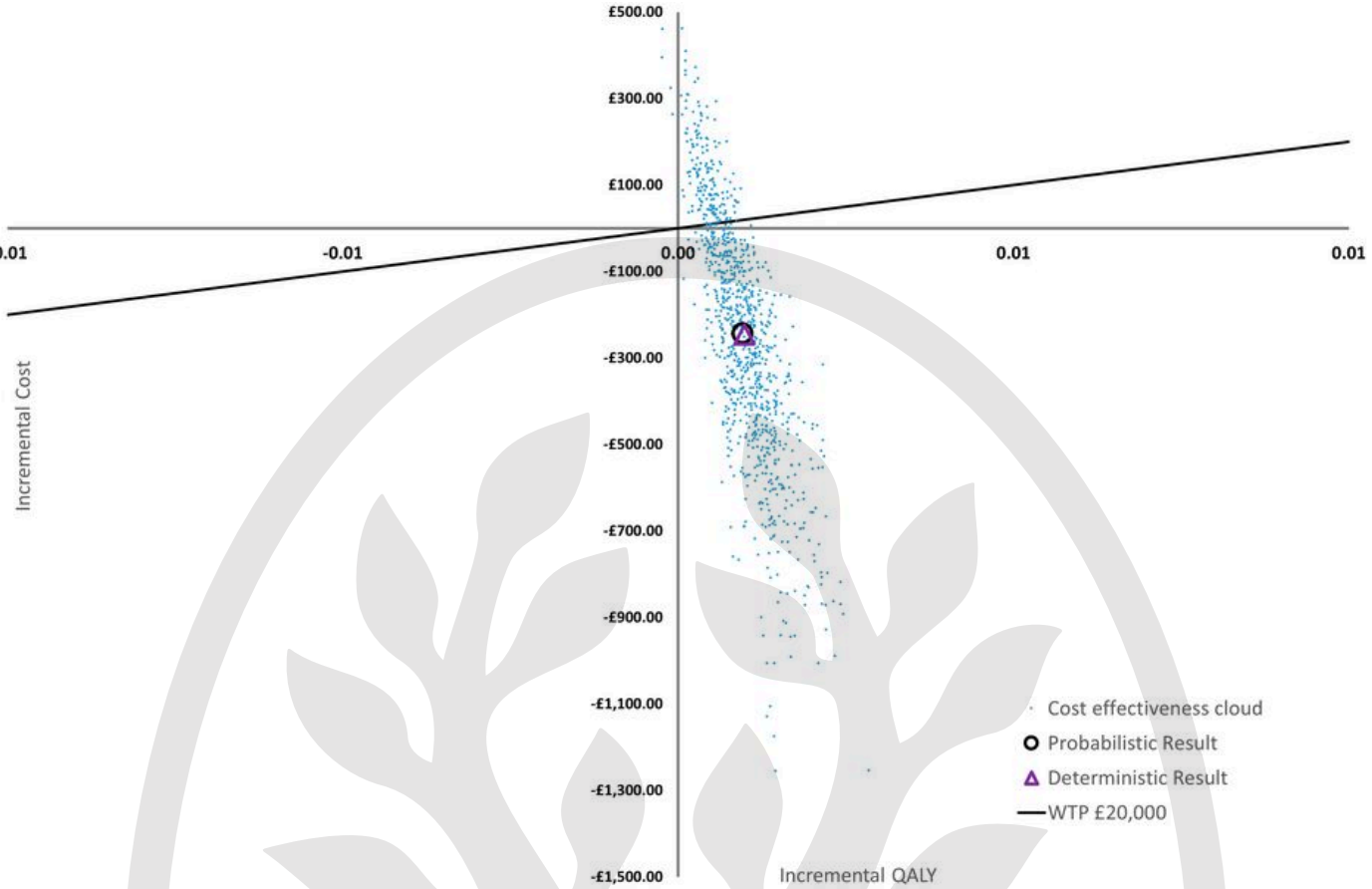
Table 2 Base Case, Clinical Parameters						
Transition Probabilities,						
	Parameter	**Base Value**	**Lower value**	**Upper Value**	**Distribution**	**Source**
TC-325	Primary haemostasis	0.9892	0.9607	0.9979	Beta	[11, 12, 20]
	30-day rebleed rate	0.1395	0.0757	0.2198	Beta	[11, 12, 20]
SET	Primary haemostasis	0.6339	0.5160	0.7541	Beta	[11, 12, 20]
	30-day rebleed rate	0.2500	0.1658	0.3450	Beta	[11, 12, 20]
30-day mortality		0.1515	0.1011	0.2099	Beta	[11, 20]
Surgery post failure		0.0345	0.0009	0.1234	Beta	[11, 12, 17]
Repeat endoscopy post-failure		0.9310	0.8165	0.9912	Beta	[11, 12, 17]
Surgery post rebleed		0.1301	0.0769	0.1947	Beta	[8, 9, 15]
TAE post rebleed		0.0650	0.0287	0.1146	Beta	[8, 9, 15]
Radiotherapy post rebleed		0.0488	0.0183	0.0931	Beta	[8, 9, 15]
Rebleed post TAE		0.1600	0.0564	0.3072	Beta	[8, 9, 15]
Rebleed post surgery		0.0752	0.0040	0.1440	Beta	[10, 35]
Utilities and Length of stay						
Parameter		**Base Value**	**Lower value**	**Upper Value**	**Distribution**	**Source**
In hospital utility		0.45	0.34	0.57	Beta	[25]
Discharge utility		0.78	0.70	0.85	Beta	[25]
LOS surgery*		12.88	6.70	21.30	Gamma	[26]
LOS TAE*		5.20	3.50	7.60	Gamma	[26]
LOS endoscopy		6.71	5.30	11.70	Gamma	[26]
LOS radiotherapy*		2.00	1.00	9.00	Gamma	[29]
Health resource use Costs						
Parameter		**Base Value**	**Lower Value**	**Upper Value**	**Distribution**	**Source**
Endoscopy, TC-325		£1,072.00	£964.50	£1,515.5	Gamma	[27]
Endoscopy, SET		£514.63	£355.21	£930.21	Gamma	[27]
Bed day cost endoscopy		£298.00	£268.20	£327.80	Gamma	[27]
TAE procedure		£5,243.14	£4,387.00	£5,889.00	Gamma	[27]
Surgical procedure		£10,776.9	£5,675.00	£13,851.00	Gamma	[27]
Radiotherapy		£1,220.00	£870.00	£1,700.00	Gamma	[27]

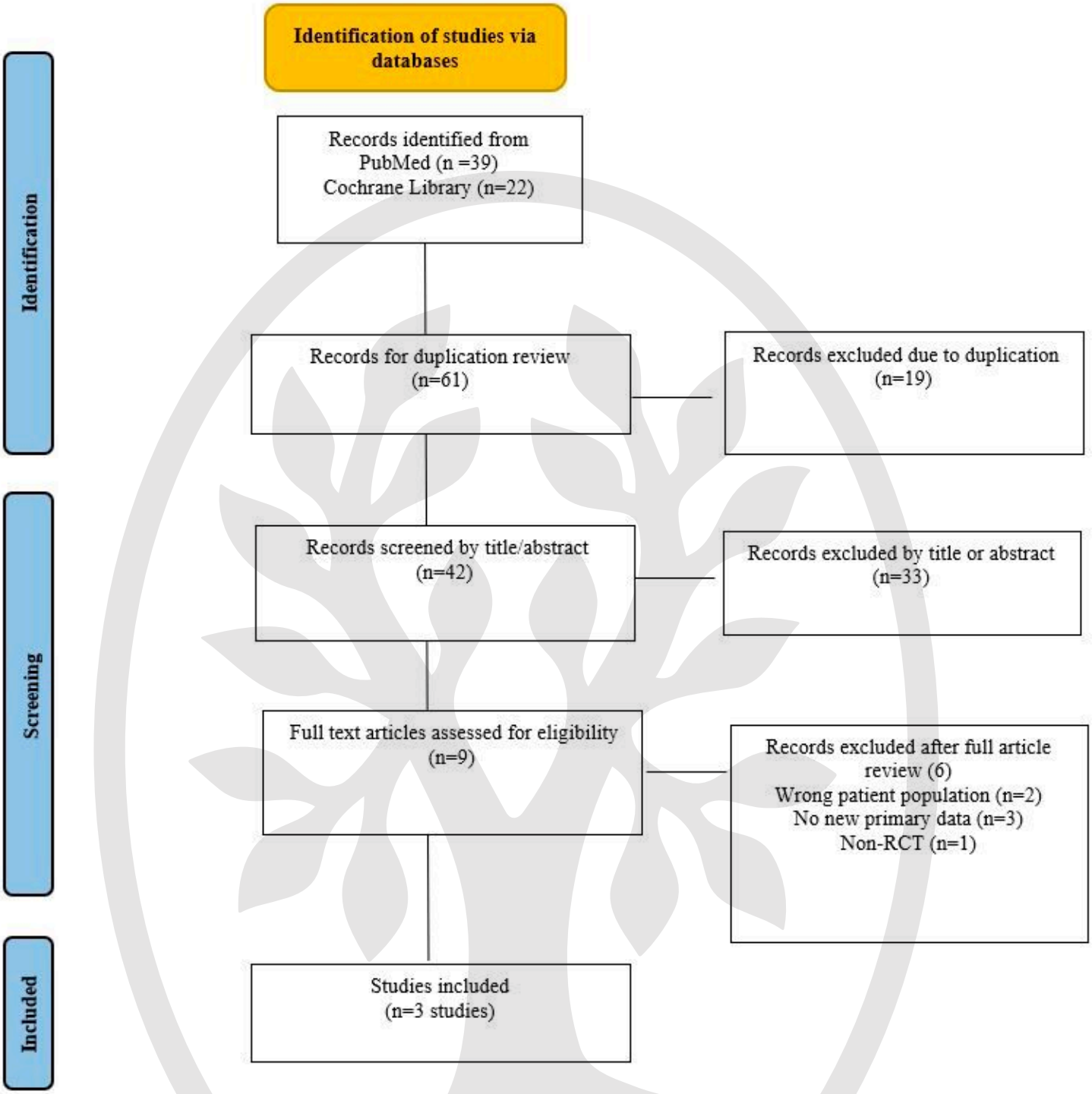
*Length of stay is used ONLY to inform utilities NOT costs

Table 3 Costs and QALYS; Base case and Scenario analyses							
			Cost	QALY	ICER	NMB	Probability cost-effective £0 WTP
BASE CASE		**TC-325**	£4,324.78	0.0503	**Dominant**	**£265.63**	**80.1%**
		SET	£4,570.66	0.0493	-	-	-
		Increment	**-£245.88**	**+0.0010**	-	-	-
Scenario 1	**Non Palliative care patients**	**TC-325**	£3,779.51	0.0516	**Dominant**	**£617.29**	**98.3%**
		SET	£4,365.14	0.0496	-	-	-
		Increment	**-£585.63**	**+0.0016**	-	-	-
Scenario 2	**Upper and lower GI bleeds**	**TC-325**	£3,709.81	0.0521	**Dominant**	**£182.31**	**71.2%**
		SET	£3,874.25	0.0512	-	-	-
		Increment	**-£164.44**	**+0.0009**	-	-	-
Scenario 3	**Elective care costs**	**TC-325**	£4,254.63	0.0503	**Dominant**	**£148.80**	**67.5%**
		SET	£4,383.68	0.0493	-	-	-
		Increment	**-£129.05**	**+0.0010**	-	-	-
Scenario 4	**Procedure mortality**	**TC-325**	£4,324.78	0.0525	**Dominant**	**£278.17**	**79.5%**
		SET	£4,570.66	0.0509	-	-	-
		Increment	**-£245.88**	**+0.0016**	-	-	-
Scenario 5	**Median LOS endoscopy**	**TC-325**	£2,696.43	0.0552	**Dominant**	**£139.95**	**68.4%**
		SET	£2,822.93	0.0545	-	-	-
		Increment	**-£126.51**	**+0.0007**	-	-	-
Scenario 6	**Endoscopy tariff costs**	**TC-325**	£2,626.70	0.0503	**Dominant**	**£140.72**	**71.7%**
		SET	£2,748.19	0.0493	-	-	-
		Increment	**-£121.50**	**+0.0010**	-	-	-

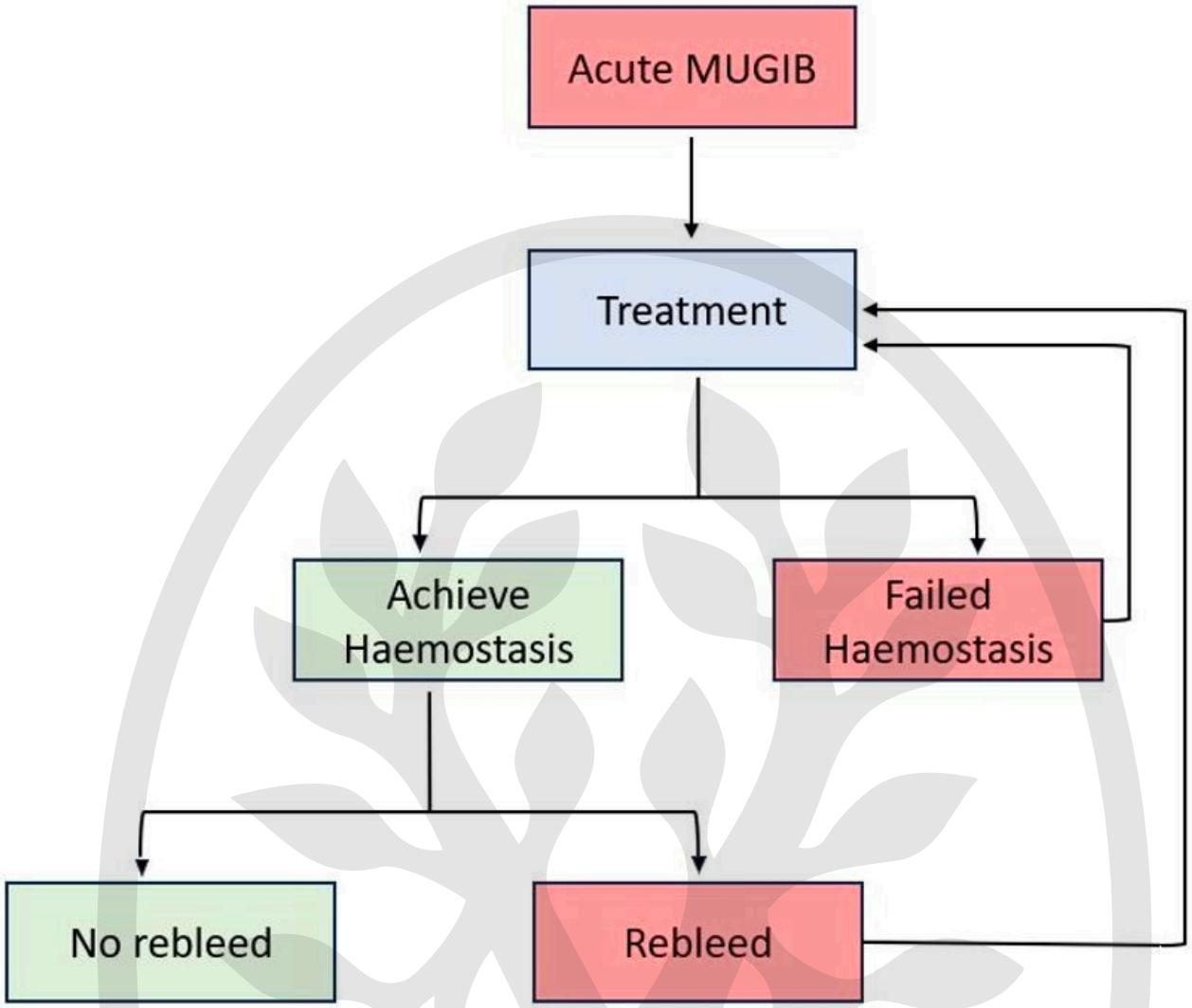








PRISMA diagram [2]



Influence diagram. *Following failed haemostasis or a rebleed within 30 days patients will have further treatment which can be further endoscopic treatment, surgery, embolisation or radiotherapy.*