



# Cost effectiveness of posterior epistaxis management using a gelatin-thrombin matrix or Rapid Rhino

Jason Toppi<sup>1</sup>, Sor Way Chan<sup>1</sup>, Upasna Pratap<sup>1</sup>, Shanesh Kumar<sup>1</sup>, Robert Phan<sup>1</sup>, Matthew Magarey<sup>1</sup>, Jason J. Ong<sup>2,3</sup>

<sup>1</sup>Otolaryngology and Head & Neck Surgery Unit, Box Hill Hospital, Melbourne, Australia; <sup>2</sup>Central Clinical School, Monash University, Monash, Australia; <sup>3</sup>Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK

*Contributions:* (I) Conception and design: J Toppi, SW Chan, U Pratap, M Magarey; (II) Administrative support: U Pratap, M Magarey; (III) Provision of study materials or patients: J Toppi, S Kumar, R Phan, SW Chan; (IV) Collection and assembly of data: J Toppi, S Kumar, R Phan; (V) Data analysis and interpretation: J Toppi, JJ Ong, U Pratap, M Magarey; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

*Correspondence to:* Dr. Jason Toppi. Otolaryngology Head and Neck Surgery Unit, Box Hill Hospital, 8 Arnold St, Box Hill, Melbourne, VIC 3128, Australia. Email: jttoppi1@gmail.com.

**Background:** Epistaxis is common, accounting for over 25% of otolaryngology emergency presentations. Posterior epistaxis is sometimes difficult to manage and can result in serious complications. Traditionally management has involved the use of non-dissolvable nasal packs such as ribbon gauze or the Rapid Rhino. Biological dissolvable matrices have been shown to be effective in achieving haemostasis in posterior epistaxis. Whilst both gelatin-thrombin matrices and the Rapid Rhino provide an effective treatment for epistaxis, there is no published data investigating cost within the Australian healthcare setting. This study evaluated and compared the cost-effectiveness of both products for the treatment of posterior epistaxis.

**Methods:** A decision tree model was constructed to evaluate the cost-effectiveness of the management of posterior epistaxis using FloSeal (gelatin-thrombin matrix) compared to Rapid Rhino from an Australian healthcare perspective in a short time horizon.

**Results:** The mean cost of each modality was A\$961 per patient (standard deviation A\$229) for the gelatin-thrombin matrix and A\$1004 (standard deviation A\$138) for the Rapid Rhino. The mean effectiveness of the gelatin-thrombin matrix in managing posterior epistaxis is 0.80 and for Rapid Rhino is 0.65 leading to a cost saving of A\$292 per posterior epistaxis case managed if using gelatin-thrombin matrix instead of the Rapid Rhino.

**Conclusions:** Gelatin-thrombin matrix represents a cost-saving alternative to nasal packing and should be considered as first line treatment in patients presenting with posterior epistaxis.

**Keywords:** Epistaxis; floseal; gelatin-thrombin matrix; rapid rhino; cost

Received: 13 August 2019; Accepted: 15 February 2020; Published: 29 April 2020.

doi: 10.21037/ajo.2020.03.06

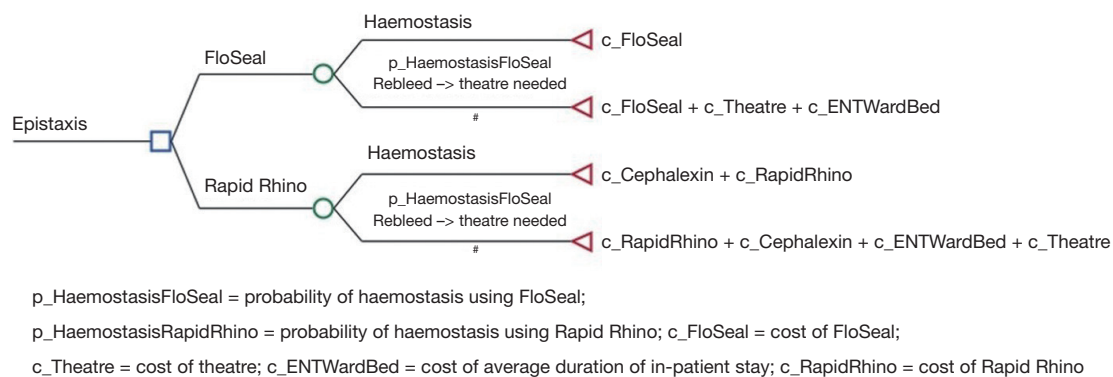
View this article at: <http://dx.doi.org/10.21037/ajo.2020.03.06>

## Introduction

Epistaxis can be classified as either anterior (90% of cases) or posterior (10%) based on the location of bleeding with the division between anterior and posterior nasal septum lying at the pyriform aperture (1,2). Anterior haemorrhages can often be managed with basic first aid and chemical- or

electro-cautery (1,3).

In situations where these methods are unsuccessful or not practical, such as cases of posterior epistaxis, nasal packing may be required (1,4). Traditionally this involved the use of lubricated ribbon gauze or the use of a Foley catheter which is inserted along the nasal passage floor to the posterior



**Figure 1** Decision tree.

nasopharynx with Kaltostat or ribbon gauze (1,5). However modern packs such as the Rapid Rhino provide easier and more effective alternatives and have become the mainstay treatment for posterior epistaxis in many centres (6). The duration of non-absorbable nasal packing is not specified in the literature, though in practice times range between 24–72 hours with oral antibiotic prophylaxis to cover against toxic shock syndrome (6,7).

Whilst representing an important management option for posterior epistaxis, packing with the Rapid Rhino has several drawbacks. These include requiring hospital admission whilst the packs are *in-situ*, trauma on insertion, patient discomfort, tissue necrosis, toxic shock syndrome and failure (1,4). Absorbable packing agents such as Nasopore<sup>®</sup>, Surgicel<sup>®</sup> or haemostatic glue have not been well researched for the primary treatment of posterior epistaxis, with most research focusing on utilization in the post-operative setting (7). Both arterial embolization and ligation have high success rates, though require significant resources, expertise and equipment (8-11).

FloSeal (Baxter Corporation, Deerfield, IL, USA) is a biological dissolvable haemostatic gelatin-thrombin matrix that is frequently used in endoscopic sinus surgery and epistaxis. It has been shown to be efficacious for posterior epistaxis and general haemorrhage control in other surgical procedures (11-19). This gelatin-thrombin matrix is easy to apply, dissolvable and a proven haemostatic agent and thus has the potential to treat posterior epistaxis without the need for hospital admission (11). Furthermore, it has been shown to be a successful treatment for posterior epistaxis with lower morbidity compared with other methods of haemostatic control (11). Whilst an effective treatment modality, there is little evidence investigating its cost-effectiveness in the Australian healthcare setting. Thus, this

study aimed to assess the cost-effectiveness of a gelatin-thrombin matrix in the treatment of posterior epistaxis when compared with a dual balloon Rapid Rhino.

## Methods

A decision tree model was constructed to evaluate the cost-effectiveness of the management of posterior epistaxis using a gelatin-thrombin matrix (FloSeal) compared to the dual balloon Rapid Rhino (*Figure 1*). The decision tree model assumed patients managed with a Rapid Rhino were admitted to hospital and that those managed successfully with a gelatin-thrombin matrix were discharged from the emergency department. In cases where gelatin-thrombin matrix failed, it was assumed patients would be admitted for operative management (*Figure 1*). Estimates for the average cost of a ward bed admission, initial Emergency Department assessment and theatre were based on the financial year 2015/16 annual Victorian Cost Data Collection (VCDC) Cost Submission which included 130 patients with epistaxis discharged from Box Hill Hospital. Costs related to Rapid Rhino and the gelatin-thrombin matrix (FloSeal) were sourced from the product manufacturer. The cost of cephalexin was based on estimates from the pharmaceutical benefits scheme (PBS) (20).

Effectiveness for each modality was calculated using previously published data. A literature search was undertaken to identify studies that reported effectiveness rates for either FloSeal or the Rapid Rhino in posterior epistaxis. Random effects meta-analysis was used to calculate a cross-study pooled estimates to account for sampling error and heterogeneity in prevalence and incidence estimates (21).

This study was approved by the Eastern Health Ethics Committee (reference LR88/2016).

### Statistical analysis

One-way sensitivity analyses (varying costs by  $\pm 25\%$ ) and a probabilistic sensitivity analysis was performed using second-order Monte Carlo simulation, a method to account for joint uncertainties in the parameter estimates (22). This involved randomly selected values from each input parameter's distribution and generated results for that combination of values. This process was repeated 10,000 times. Gamma distributions were used for costs, and beta distributions for the transition probabilities. Tornado diagrams (which visually show the impact of varying the values of one parameter at a time) were produced to summarize the one-way sensitivity analyses and probabilistic sensitivity analyses results were summarized using acceptability curves. Acceptability curves summarizes the probability of an intervention to be more cost-effective than the comparator, according to the willingness-to-pay threshold (how much a funder is willing to pay to obtain the health outcome). The incremental cost-effectiveness ratio (ICER) was calculated using the following formula:

$$ICER = \frac{cost_{FloSeal} - cost_{Rapid\ Rhino}}{effectiveness_{FloSeal} - effectiveness_{Rapid\ Rhino}}$$

## Results

### Literature review

There was limited published data regarding the efficacy of nasal packing with the Rapid Rhino or gelatin-thrombin matrix for the treatment of posterior epistaxis (23,24). A systematic search using MEDLINE and EMBASE was conducted to identify studies that reported on efficacy rates of gelatin-thrombin matrix or the Rapid Rhino for the treatment of posterior epistaxis. The following search terms were used: (FloSeal OR Gelatin-thrombin matrix OR Rapid Rhino) AND Epistaxis. Only papers published since January 1<sup>st</sup> 2000 were included. A total of 101 papers from EMBASE and 34 papers from MEDLINE were independently screened. Case reports and case series were excluded. Of these, five studies were found that reported efficacy rates for either gelatin-thrombin matrix or Rapid Rhino for the treatment of posterior epistaxis (5,11,12,25,26). Our efficacy data for posterior epistaxis was based on three studies for the Rapid Rhino and two for gelatin-thrombin matrix (5,11,12,25,26) (Table 1). One other study was also identified that investigated the efficacy of a gelatin-thrombin matrix in posterior epistaxis with a success rate of 76% (27). However,

it was not used in our model as it did not specifically differentiate between anterior and posterior epistaxis.

### Effectiveness of haemostasis

Pooled estimates of effectiveness were calculated using estimates from previously published studies investigating either the Rapid Rhino or the gelatin-thrombin matrix to treat posterior epistaxis. The gelatin-thrombin matrix [80%, 95% confidence intervals (CI): 63–93] demonstrated greater effectiveness when compared with the Rapid Rhino (65%, 95% CI: 57–72) when used to treat posterior epistaxis (5,11,12,25,26) (Table 1).

### Cost

The mean cost of the gelatin-thrombin matrix was A\$953 per patient (standard deviation A\$226) and the mean cost for the Rapid Rhino was A\$1,004 (standard deviation A\$138). This was based on cost of the product itself, hospital admission and adjunct medications (i.e., oral antibiotics). The gelatin-thrombin matrix demonstrated more favorable results than Rapid Rhino in terms of cost-savings and haemostasis effectiveness.

### Cost effectiveness

These results equated to a cost saving of A\$292 per posterior epistaxis case managed if using the gelatin-thrombin matrix instead of Rapid Rhino. The tornado diagram identifies which factors are most influential in changing the cost per case of posterior epistaxis managed (Figure 2). This diagram demonstrates that the most influential factors are the probability of haemostasis to Rapid Rhino, followed by the costs of the inpatient stay and cost of the gelatin-thrombin matrix (Figure 2).

Figure 3 is a scatterplot on the cost-effectiveness plane of 10,000 ICERs using probabilistic sensitivity analyses. It demonstrates that a substantial number of ICERs are in the cost-saving (i.e., South-East) quadrant. This was reinforced by the acceptability curve (Figure 4) showing that the gelatin-thrombin matrix had a higher probability of being cost-effective compared to Rapid Rhino.

## Discussion

### Key findings

This study investigated and compared the cost-effectiveness

**Table 1** Model parameters

| Costs (A\$2,017)                    | Estimate | Sensitivity analyses                                       | Reference                              |
|-------------------------------------|----------|--|--|
| FloSeal                             | A\$420   | Gamma distribution<br>$\alpha = 70.56$<br>$\lambda = 0.17$ | Baxter Corporation, Deerfield, IL, USA |
| Rapid Rhino                         | A\$47    | Gamma distribution<br>$\alpha = 61.36$<br>$\lambda = 1.31$ | Smith & Nephew, Austin, TX, USA        |
| Rapid Rhino antibiotic prophylaxis* | A\$19    | Gamma distribution<br>$\alpha = 90.25$<br>$\lambda = 4.75$ | PBS 3119E (20)                         |
| Ward bed (per admission)            | A\$1,683 | Gamma distribution<br>$\alpha = 64.23$<br>$\lambda = 0.04$ | VCDC cost submission                   |
| Theatre                             | A\$1,110 | Gamma distribution<br>$\alpha = 64.00$<br>$\lambda = 0.06$ | VCDC cost submission                   |
| Probability of haemostasis          |          |  |  |
| Gelatin-thrombin matrix             | 80%      | Beta distribution<br>$\alpha = 12.00$<br>$\beta = 3.00$    | (11,12)                                |
| Rapid Rhino                         | 65%      | Beta distribution<br>$\alpha = 14.14$<br>$\beta = 7.61$    | (5,25,26)                              |

\*, cephalixin 500 mg four times daily for 5 days (PBS 3119E) (20).

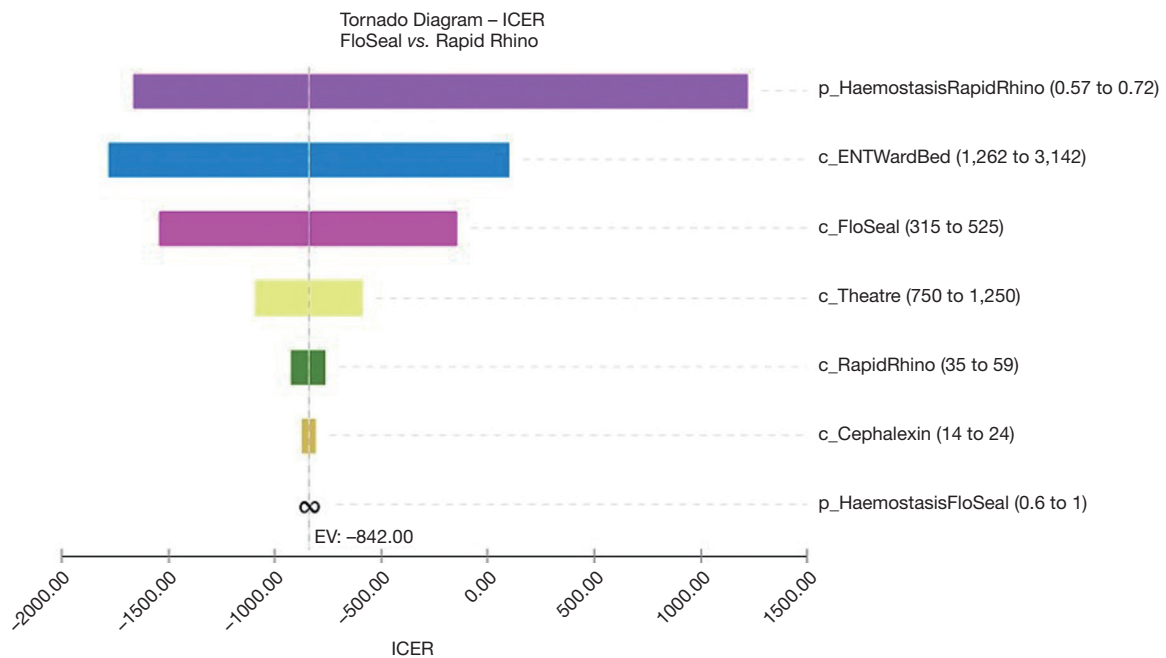
of the dual balloon Rapid Rhino nasal pack and a gelatin-thrombin matrix haemostatic agent in the treatment of posterior epistaxis. The average cost of treatment using the Rapid Rhino was A\$1,004 compared to the gelatin-thrombin matrix which cost, on average, A\$961. Our model suggests that the gelatin-thrombin matrix is likely to be cost-saving compared to Rapid Rhino for the control of posterior haemostasis from an Australian healthcare provider perspective. The main reason for this appears to be reduced hospital bed-days, and improved efficacy.

### **Strengths and limitations**

The gelatin-thrombin matrix is currently not a well utilized resource as a first-line management tool for posterior

epistaxis. The Rapid Rhino system is far more commonly used in the management of posterior epistaxis in Australian healthcare centres. Whilst the efficacy for posterior epistaxis management using a gelatin-thrombin matrix or the Rapid Rhino has been investigated in previous studies (8,12,13,24,26), this is the first comprehensive analysis of cost-effectiveness of both products in the Australian healthcare setting.

Whilst this study provided a comprehensive cost-analysis of two important treatment modalities for managing posterior epistaxis, there were several limitations. The costing data was obtained based on patients treated within a single health network in Victoria, Australia. Specific costs of hospital stay, and operative management may vary between hospitals and regions. Similarly, treatment protocols are not



**Figure 2** Tornado sensitivity analyses varying model parameters one at a time. p\_HaemostasisRapidRhino = probability of achieving haemostasis with Rapid Rhino; c\_ENTWardBed = cost of inpatient stay; c\_FloSeal = cost of FloSeal; c\_Theatre = cost of theatre; c\_RapidRhino = cost of Rapid Rhino; c\_Cephalexin = cost of cephalixin; p\_HaemostasisFloSeal = probability of achieving haemostasis with FloSeal.

standardised across healthcare centres in Australia which may compound cost variances across sites depending on local practices.

Heterogeneity amongst patients with posterior epistaxis and the way in which different treatments were administered within the literature also represented another limitation. For example, Kilty *et al.* used a Foley catheter along with a gelatin-thrombin matrix to control epistaxis and in cases of initial failure would administer a second 5 mL syringe (11). This method of gelatin-thrombin matrix administration differed when compared to Cote *et al.*, where nasendoscopy was used to identify a posterior bleeding point and apply the gelatin-thrombin matrix directly to the area (12). For the purposes of this cost study it was assumed only one 5 mL syringe of FloSeal would be used without the use of adjuncts such as a Foley catheter or nasendoscopy. Similarly, whether patients with non-dissolvable packs should be discharged home was another area of contention amongst published studies. Published guidelines suggest patients treated with haemostatic agents or dissolvable packs are safe to be discharged home (6). However, there is no clear consensus on whether patients managed with non-dissolvable packs are safe to be discharged, particularly in

cases where posterior packing is required (28). Van Wyk *et al.* advocated that whilst it is reasonable to discharge patients with anterior packs in-situ, posterior packing should be performed only by a specialist trained in the procedure and warrants admission (28). Our institution has taken a similar approach whereby all patients requiring posterior nasal packing were managed as inpatients, thus this protocol was used in the cost-benefit modelling for this study.

The data investigating effectiveness for the gelatin-thrombin matrix was not equivocally in favour of this system. Khan *et al.* also evaluated the use of a gelatin-thrombin matrix in posterior epistaxis in a series of 33 patients over a 2-month period. Only three cases demonstrated complete haemostasis without the need for further interventions and no readmission with epistaxis within 7 days after its application (29). Similarly, in a prospective clinical study which included a narrative literature review, Wakelam *et al.* contended that the literature largely supported the notion that posterior epistaxis can often be difficult to control, even with a gelatin-thrombin matrix, and that management with endoscopic sphenopalatine artery ligation is emerging as a more cost-effective and definitive measure of control (24).

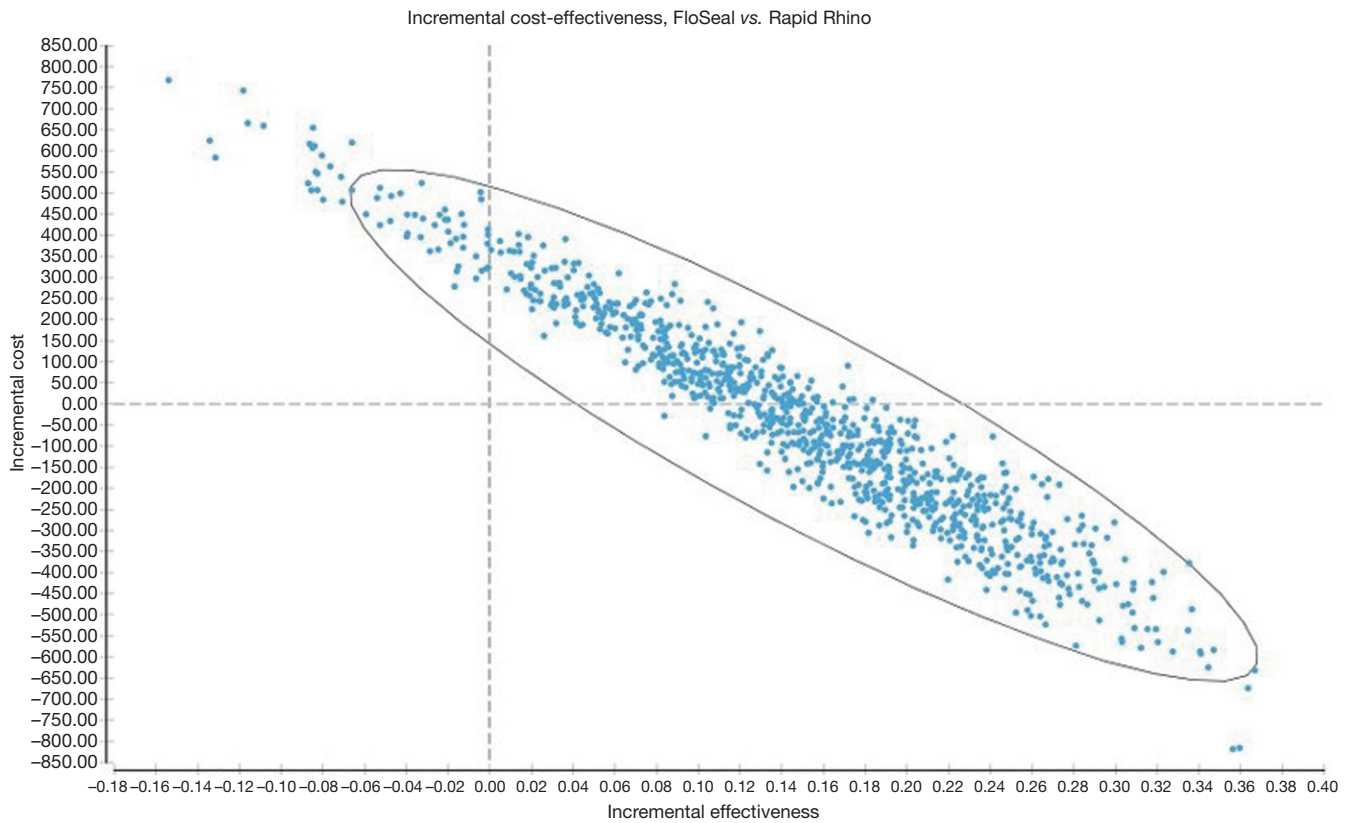


Figure 3 Cost-effectiveness plane of FloSeal vs. Rapid Rhino.

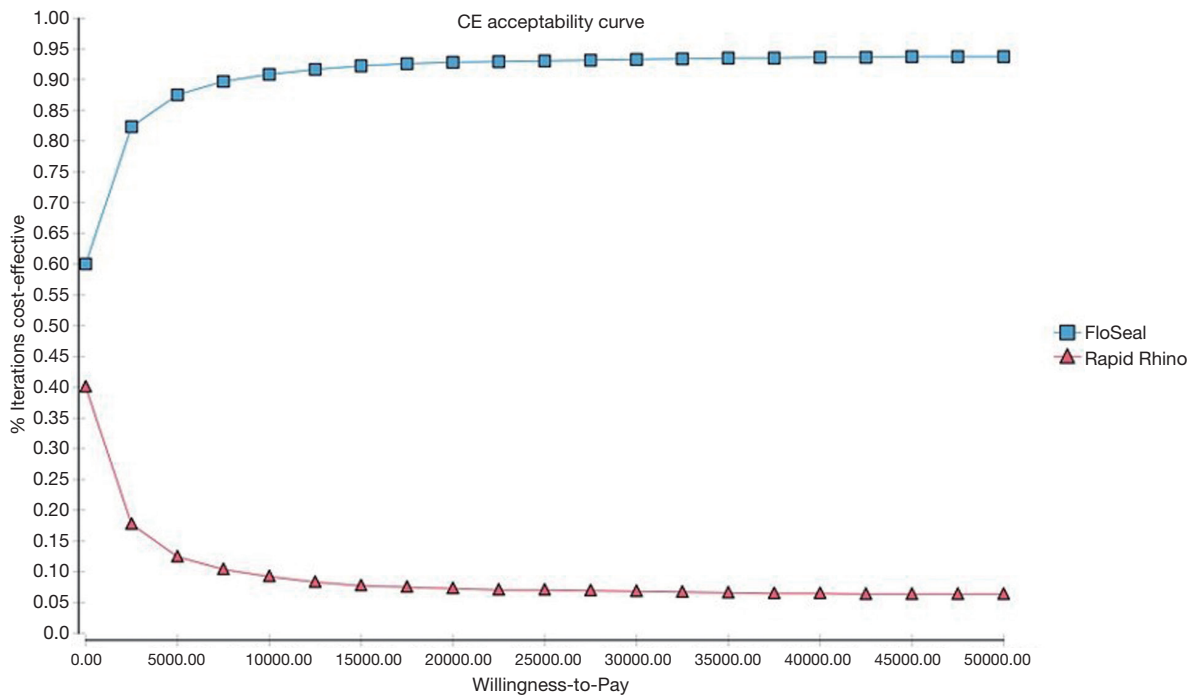


Figure 4 Cost-effectiveness acceptability curve of FloSeal vs. Rapid Rhino.

As the Khan reference was a case series it was not included in our final analysis. However, if we include it, the pooled effectiveness for the gelatin-thrombin matrix will be 54% (95% CI: 5–99%). This results in a mean cost of A\$1,653 for the gelatin-thrombin matrix (standard deviation A\$249), and A\$1,002 for Rapid Rhino (standard deviation A\$138). The administration of the gelatin-thrombin matrix is user dependent, and this may have been one explanation for the high rates of failure observed by Khan *et al.* (29).

Whilst both modalities appear to be at least comparable in terms of cost in the Australian setting there are several limitations to its use in the clinical setting. These include ease of access of gelatin-thrombin matrix (particularly on the ward and in the emergency department) and ease of use amongst emergency department physicians who may not have much experience with the product. Our experience with gelatin-thrombin matrix in the clinical setting is primarily limited to use intraoperatively, and even in this setting a learning curve exists in relation to competent and proper use of the product. Future research could thus focus on the practicalities of introducing gelatin-thrombin matrix as a treatment modality in the emergency department setting in Australian centres as well as prospective head-to-head trials to assess both products once implemented.

## Conclusions

The gelatin-thrombin matrix provides a viable treatment alternative given its comparable efficacy profile when compared with the Rapid Rhino. A significant barrier to uptake of the gelatin-thrombin matrix in treating posterior epistaxis has been cost of the product itself. However, when its reduced requirement for hospital admission is considered, it becomes a more attractive option. Thus, gelatin-thrombin matrix should be considered in the first-line management of posterior epistaxis along with other traditional nasal packing techniques.

## Acknowledgments

*Funding:* None.

## Footnote

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/ajo.2020.03.06>). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by the Eastern Health Ethics Committee (reference LR88/2016).

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doi: 10.21037/ajo.2020.03.06

**Cite this article as:** Toppi J, Chan SW, Pratap U, Kumar S, Phan R, Magarey M, Ong JJ. Cost effectiveness of posterior epistaxis management using a gelatin-thrombin matrix or Rapid Rhino. *Aust J Otolaryngol* 2020;3:14.