

# Bypassing agents prophylaxis in patients with haemophilia and inhibitors undergoing surgery: a decision analysis in Spain



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## Introduction

- Haemophilia is a genetic disease characterized by a deficiency of blood clotting factor VIII (FVIII) (in haemophilia A (HA)) or factor IX (in haemophilia B (HB))<sup>1</sup>.
- Some patients can develop inhibitory antibodies which complicates the management of haemostasis since these antibodies neutralize the effects of replacement therapy<sup>2</sup>. Approximately, 15-35% of patients with severe HA (FVIII<1%) develop FVIII inhibitory antibodies<sup>3</sup>.
- Since surgery poses a risk condition for haemophilia patients with inhibitors<sup>4,5</sup>, haemostatic prophylaxis therapy is always indicated in these situations to prevent bleeding complications. Prophylaxis should be given in most cases with bypassing agents, either activated prothrombin complex concentrate (aPCC) or recombinant activated factor VIIa (rFVIIa)<sup>6</sup>.

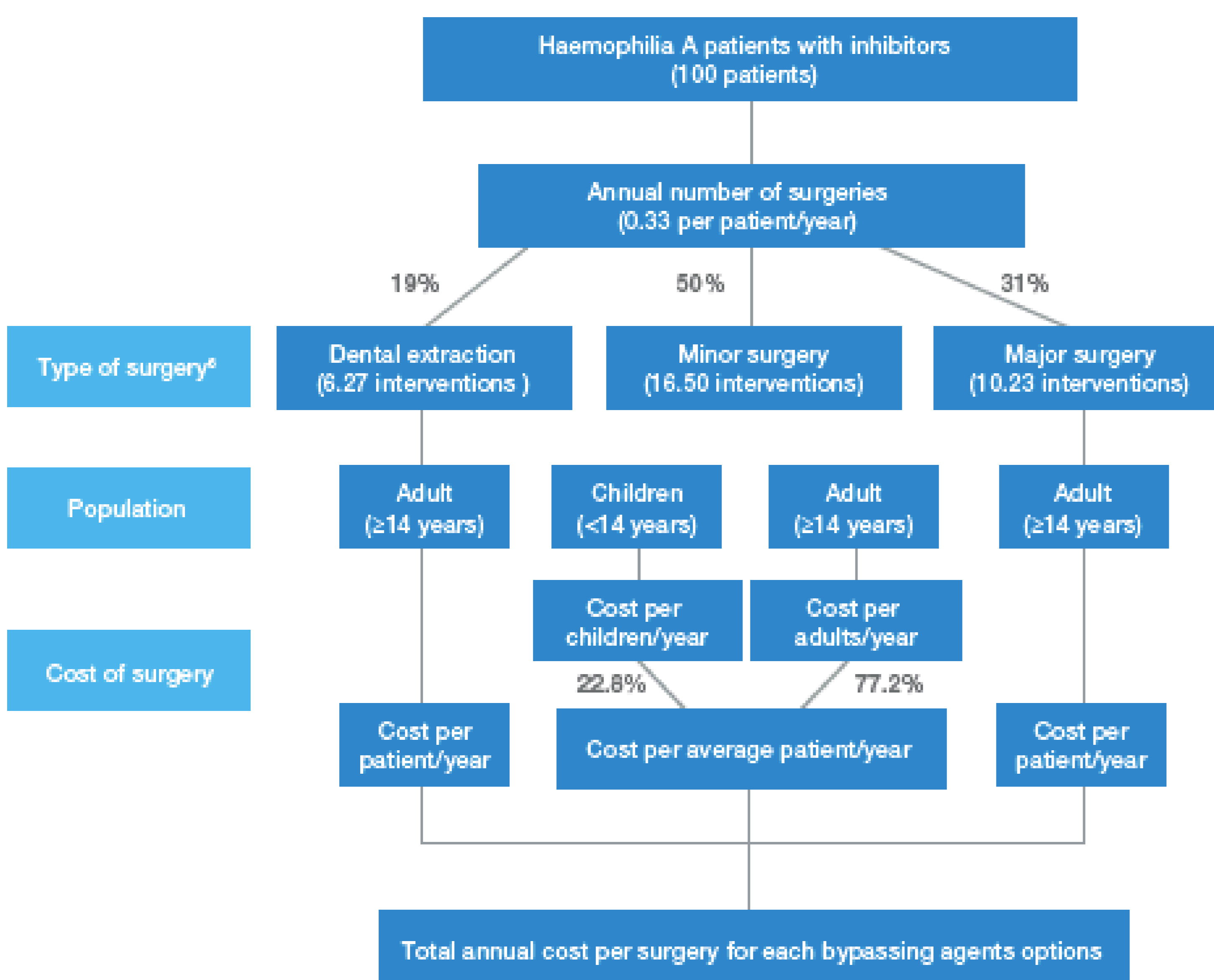
## Objective

- To estimate the total cost of prophylaxis therapy with bypassing agents, aPCC or rFVIIa, in HA patients with inhibitors undergoing surgery, from the Spanish National Health System perspective.

## Methods

- Although the available evidence suggests that both alternatives (aPCC and rFVIIa) have comparable efficacy as prophylactic strategy during surgical procedures<sup>7,8</sup>, no direct comparison exists to justify the development of a cost-minimization analysis. Therefore, a conservative approach was chosen and a cost-analysis was designed.
- A decision tree model was developed to compare the treatment cost of aPCC (Feiba<sup>®</sup>, Shire) and rFVIIa (Novo-Seven<sup>®</sup>, Novo Nordisk), for a typical HA inhibitor patient undergoing dental extraction, minor or major surgery. A hypothetical cohort of 100 HA patients with inhibitors was used to feed the decision tree (Figure 1).
- Based on a national epidemiological study<sup>9</sup>, the proportion of adults (≥14 years) is around 77.20%, meanwhile children (<14 years) represent 22.80% of the hemophilia population. Average weights (72.9 kg in adults and 27.6 kg in children) of the haemophilia population were derived from literature<sup>9</sup>.
- The annual number of surgeries (0.33 surgeries/year/patient) as well as the distribution of type of surgeries [dental extraction (19%), minor surgery (50%) and major surgery (31%)] were estimated from local data. An expert panel of 3 local haematologists validated these data as representative of the population of HA patients with inhibitors in Spain.
- For cost calculation, dental extraction and major surgery were assumed only to happen in adult population, while minor surgery occurrence was split into children and adult population, validated by the haematologists expert panel.
- The time horizon of the analysis comprised the duration of prophylactic regimens defined by each surgery (1 day for dental extraction, 4 days for minor surgery and 15 days for major surgery), in accordance with the information provided by the expert panel consulted.

Figure 1. Model diagram



- Drug costs (€2017) considered dosages used in clinical practice (Table 1), and official ex-factory prices with 7.5% of mandatory deduction<sup>10</sup> (0.74 €/IU [aPCC]; 0.54 €/IU [rFVIIa]). The underlying cost of the surgery was assumed to be the same for either treatment and thus not included in the analysis.

## References

1. Srivastava A, et al. Haemophilia. 2013;19:1-47; 2. Witmer C, et al. Ther Adv Hematol. 2013;4:59-72; 3. Bantrop E, et al. Bull World Health Organ. 1996;73:691-701; 4. Ludlam C. Haemophilia. 2005;11 Suppl 1:7-10; 5. Tjønnfjord GE. Haemophilia. 2004;10 Suppl 2:41-5; 6. Mingot-Castellano ME, et al. Eur J Haematol. 2018;96:481-74; 7. Quintana-Molina M, et al. Haemophilia. 2004;10 Suppl 2:30-40; 8. Ludlam C. Haemophilia. 2005;11 Suppl 1:7-10; 9. Aznar JA, et al. Haemophilia. 2009;15:885-75; 10. Royal Decree-Law. B/2010. www.boe.es

## Methods (cont.)

Table 1. Bypassing agents dosage in clinical practice for each type of surgery

		aPCC (Feiba <sup>®</sup> )				rFVIIa (Novoseven <sup>®</sup> )					
		Children (<14 years)		Adults (≥14 years)		Children (<14 years)		Adults (≥14 years)			
		IU/kg*	DD	IU/kg*	DD	IU/kg*	DD	IU/kg*	DD		
Dental extraction	Day 1			62.5	3			90	4		
Minor surgery	Prior bolus dose		1		1	120	1		1		
	Day 1	65	2	65	2	105	7	90	7		
	Day 2									4	6
	Day 3										
Day 4	1	1	2	2							
Major surgery	Prior bolus dose			80	1			120	1		
	Day 1			60	2			105	11		
	Day 2				3		8				
	Day 3-5			85	2				6		
	Day 6-7										
	Day 8-15			70	2			90	4		

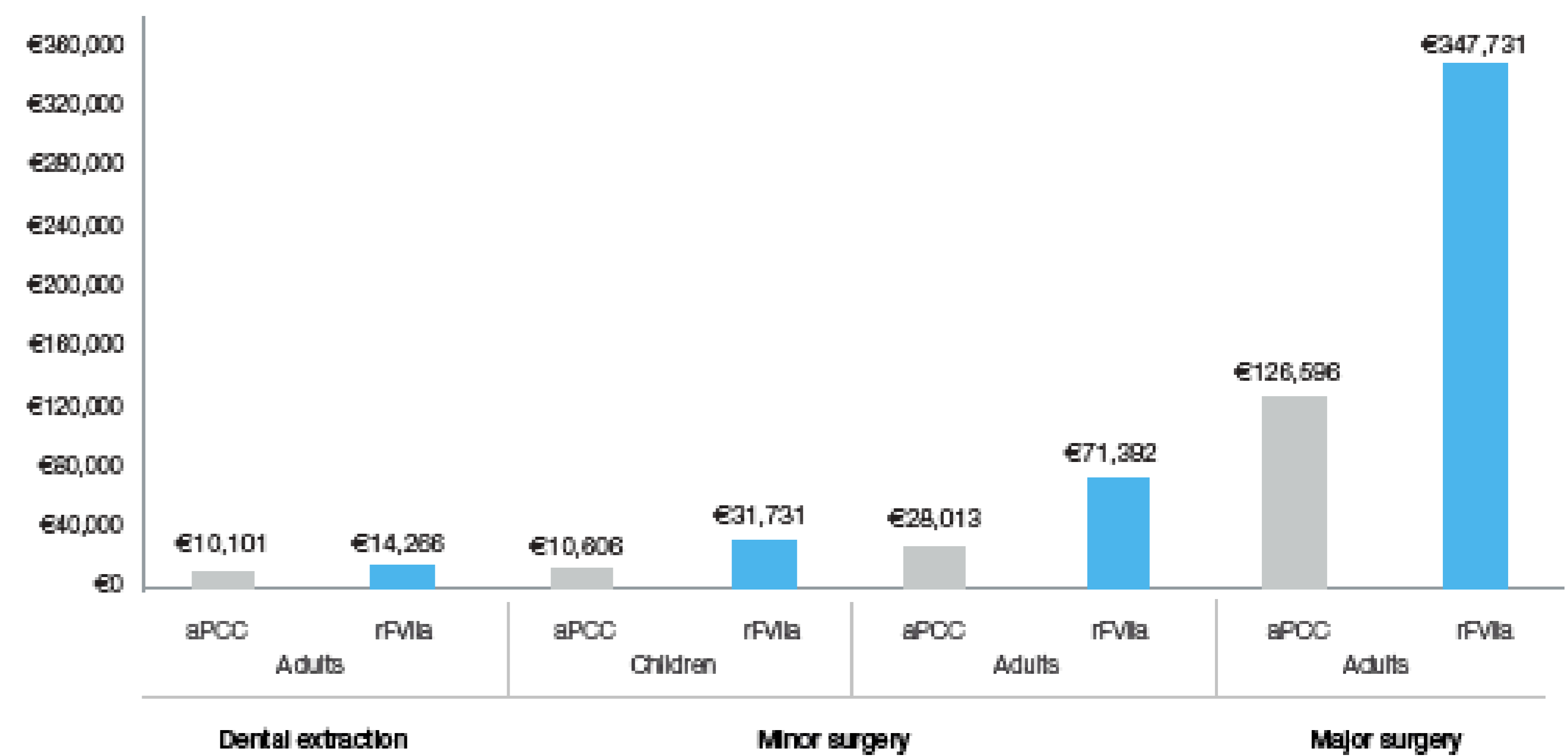
IU: International Units; DD: Daily dosage; \*IU/kg per dosage; Provided by haematologists expert panel.

- A population analysis was additionally performed in order to provide figures of the total annual budget for prophylaxis with bypassing agents in HA patients with inhibitors undergoing surgeries in Spain.

## Results

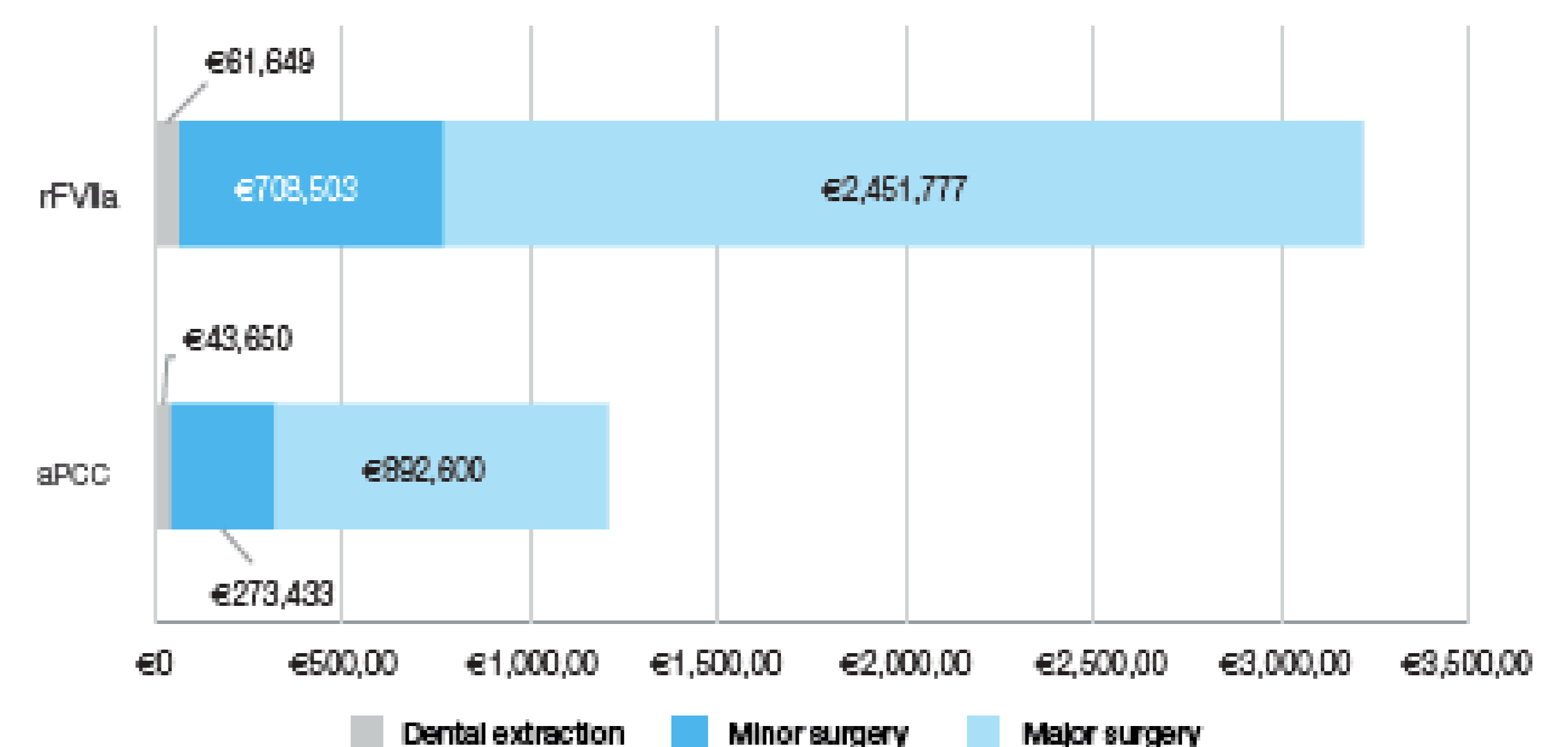
- The estimated costs per patient were €10,100.73 (aPCC) and €14,265.89 (rFVIIa) for dental extraction; €24,043.88 (aPCC) and €62,301.08 (rFVIIa) for minor surgery and €126,595.81 (aPCC) and €347,731.09 (rFVIIa) for major surgery (Figure 2).

Figure 2. Bypassing agents total cost /patient



- Assuming an estimation of 23 annual surgeries in 69 HA patients with inhibitors in Spain and the proportion of surgery types, the total annual cost of prophylaxis would be €1,209,682.35 using aPCC while €3,221,929.28 for rFVIIa (Figure 3).

Figure 3. Total annual cost of population analysis (69 HA patients)



## Conclusion

Results suggest a 62.5% lower treatment drug cost with aPCC compared to rFVIIa in providing haemostatic coverage during surgery. Assuming potentia equivalent in efficacy, aPCC is a cost saving option, as prophylactic treatment preventing bleeds in HA inhibitors patients undergoing surgery.