

Estimation of annual bleeding management cost in severe haemophilia A patients, without inhibitors, treated with on-demand therapy with recombinant factor VIII in Spain

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INTRODUCTION

- Haemophilia A (HA) similar to other chronic diseases, is associated with a relevant economic burden¹.
- The increasing trend in the global prevalence of this disease² could have relevant impact on health care systems.
- Additionally, bleeds and muscle and joints complications lead to pain and disability, as well as a substantial impairment in the overall patient quality of life³.

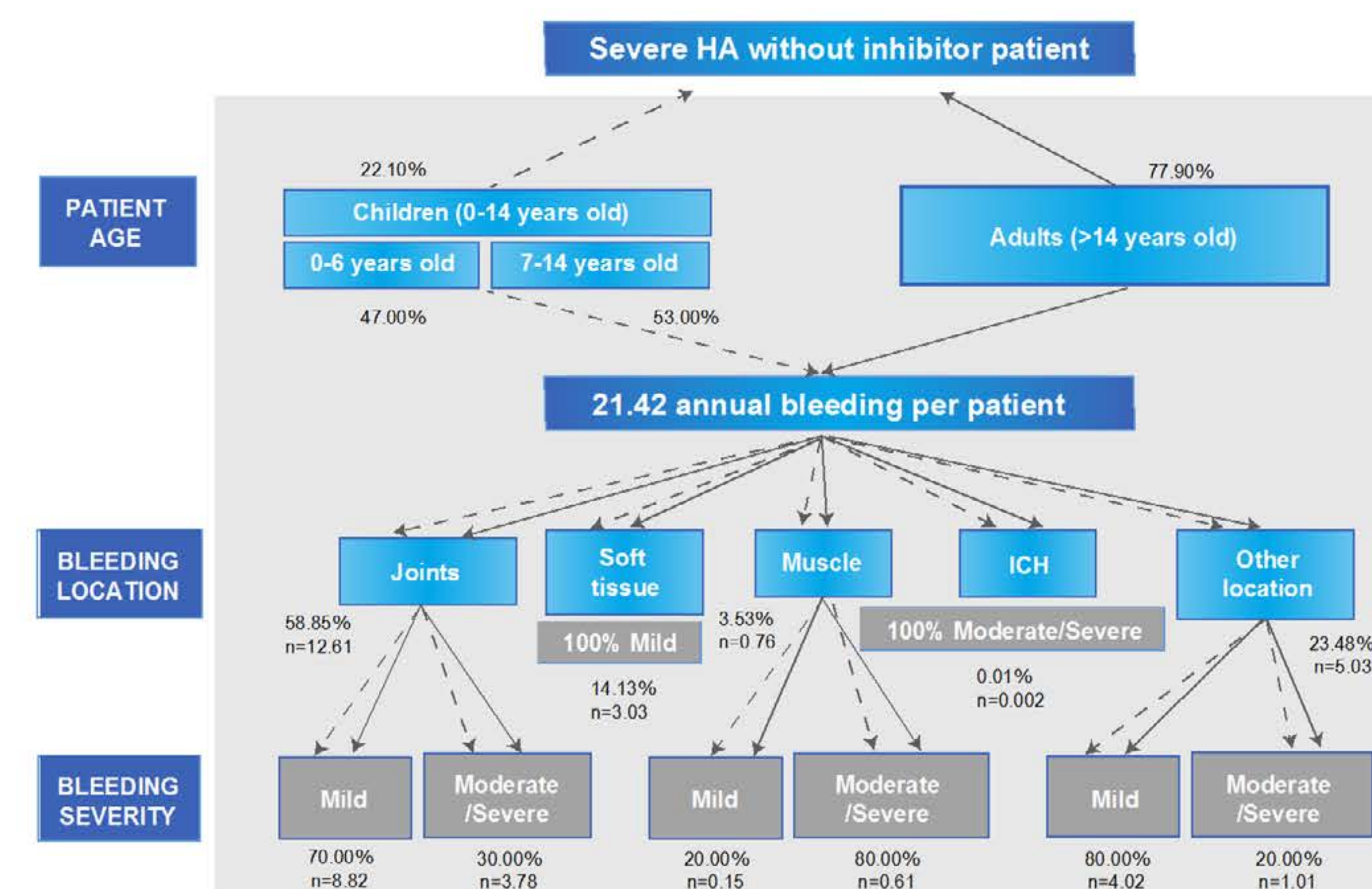
OBJECTIVE

- To estimate the total annual cost of the management of different haemorrhagic episodes in a severe HA patient treated on-demand with recombinant factor VIII without inhibitors, from the Spanish National Health System perspective.

MATERIALS AND METHODS

- A decision tree model was designed to estimate an average total annual management cost per severe HA patient without inhibitors.
- Based on published data the model split the population according to (Figure 1):
 - Age interval: children and adults⁴.
 - Bleeding location: joints, soft tissue, muscle, intracranial haemorrhage (ICH) and other locations^{5,10}.
 - Bleeding severity: mild and moderate/severe.

Figure 1. Model Design



- The annual total cost included:
 - Pharmaceutical costs:** On-demand factor VIII drug cost was estimated based on official ex-factory price⁶ (Advate[®], Shire) and recommended dosages⁷ depending on patient's age and type and severity of bleeding events. (Table 1)
 - Management of bleeding episodes:** A haematologist expert panel provided the health resource consumption required: medical visits (specialist and primary care), hospitalizations, surgeries, diagnostic and monitoring (procedures and laboratory test) and additional medication.
- Unitary cost for health resources (€, 2015) were obtained from national local databases⁸.
- An additional analysis was performed with a social perspective, including the costs associated with absenteeism of adult patients as a result of bleeding events. (Table 2)
 - Spanish average wage (€94.40/day) was considered⁹.

MATERIALS AND METHODS

Table 1: Factor VIII consumption dosage of each type of bleeding event. Representative dosages of clinical practice validated by external expert panel.

| | | Children | | Adults |
|--------------------------|-------------------|---|---|---|
| | | 0-6 years | 7 - 13 years | ≥ 14 years |
| Joint | Mild | 50 IU/Kg - 1 dosage | 40 IU/Kg - 1 dosage | 30 IU/Kg - 1 dosage |
| | Moderate/Severe | 50 IU/Kg/12 hours (1 st day) 50 IU/Kg/24 hours (days 2 - 5) | 40 IU/Kg/12 hours (1 st day) 40 IU/Kg/24 hours (days 2 - 5) | 40 IU/Kg/12 hours (1 st day) 30 IU/Kg/24 hours (days 2 - 5) |
| Soft tissue | Mild | 40 IU/Kg - 1 dosage (50% treated) | 50 IU/Kg - 1 dosage (50% treated) | 30 IU/Kg - 1 dosage (5% treated) |
| | Moderate/Severe | 50 IU/Kg/day (7,5 days) | 40 IU/Kg/day (7,5 days) | 40 IU/Kg/day (7,5 days) |
| Muscle | Mild | 50 IU/Kg/12 hours (days 1 - 2) 50 IU/Kg/24 hours (days 3 - 14) | 50 IU/Kg/12 hours (days 1 - 2) 50 IU/Kg/24 hours (days 3 - 14) | 40 IU/Kg/12 hours (days 1 - 2) 30 IU/Kg/24 hours (days 3 - 14) |
| | Moderate/Severe | 50 IU/Kg/8 hours (days 1 - 2) | 50 IU/Kg/8 hours (days 1 - 2) | 50 IU/Kg/8 hours (days 1 - 2) |
| Intracranial haemorrhage | Mild | 50 IU/Kg/12 hours (days 3 - 7) 50 IU/Kg/24 hours (days 8 - 30) | 50 IU/Kg/12 hours (days 3 - 7) 50 IU/Kg/24 hours (days 8 - 30) | 50 IU/Kg/12 hours (days 3 - 7) 50 IU/Kg/24 hours (days 8 - 30) |
| | Moderate/Severe** | 30 IU/Kg - 1 dosage | 30 IU/Kg - 1 dosage | 20 IU/Kg - 1 dosage |
| Other | Mild* | 50 IU/Kg/12 hours (1 st day) | 50 IU/Kg/12 hours (1 st day) | 50 IU/Kg/12 hours (days 1 - 3) |
| | Moderate/Severe** | 50 IU/Kg/24 hours (days 2 - 10) | 50 IU/Kg/24 hours (days 2 - 10) | 50 IU/Kg/24 hours (days 4 - 9) |

IU: International Units; Other mild bleeds*: gingival bleeding, epistaxis, or haematuria; Other moderate/severe bleeds**: gastrointestinal bleeding.

Table 2: Loss of Productivity

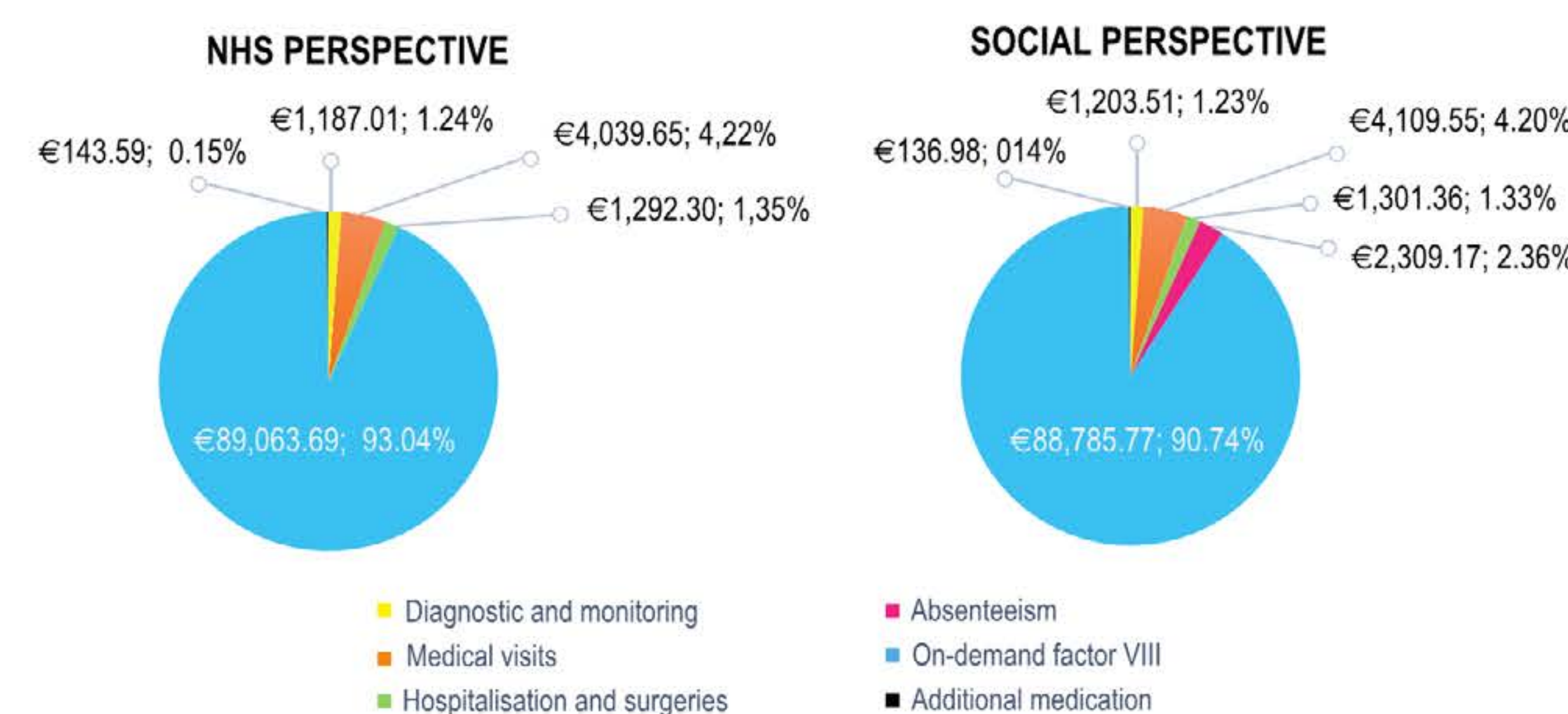
| | Mild | | Moderate/Severe | |
|-----------------|------------|-----------------|-----------------|-----------------|
| | % patients | Duration (days) | % patients | Duration (days) |
| Joint | 80% | 2.00 | 100% | 3.00 |
| Soft tissue | 0% | — | — | — |
| Muscle | 80% | 2.00 | 100% | 14.00 |
| ICH | — | — | 100% | 90.00 |
| Other locations | 0% | — | 100% | 14.00 |

*Expert panel estimation.

RESULTS

- Based on the published evidence of 21.42 haemorrhagic events per patient per year¹⁰, the estimated total annual cost for a severe HA patient, treated on-demand, was €95,726.24 (average cost of €4,469.01 per haemorrhagic event). (Figure 3).
- Factor VIII drug cost was responsible of 93.04% of the total cost (Figure 2).
- Bleeding costs according to location, severity and patient's age are detailed in Table 3.
- The estimated cost per event resulted in €2,767.94 per child population and €4,951.60 for the only adult population. The average costs per each type of bleeding for children and adults are shown in Table 3.
- For the social perspective, the total annual cost increased up to €97,846.34 per average HA patient (average cost of €4,567.99 per haemorrhagic event). (Figure 3).

Figure 2. Distribution of average annual cost per patient



RESULTS

Figure 3. Total annual bleeding costs per patient (€)

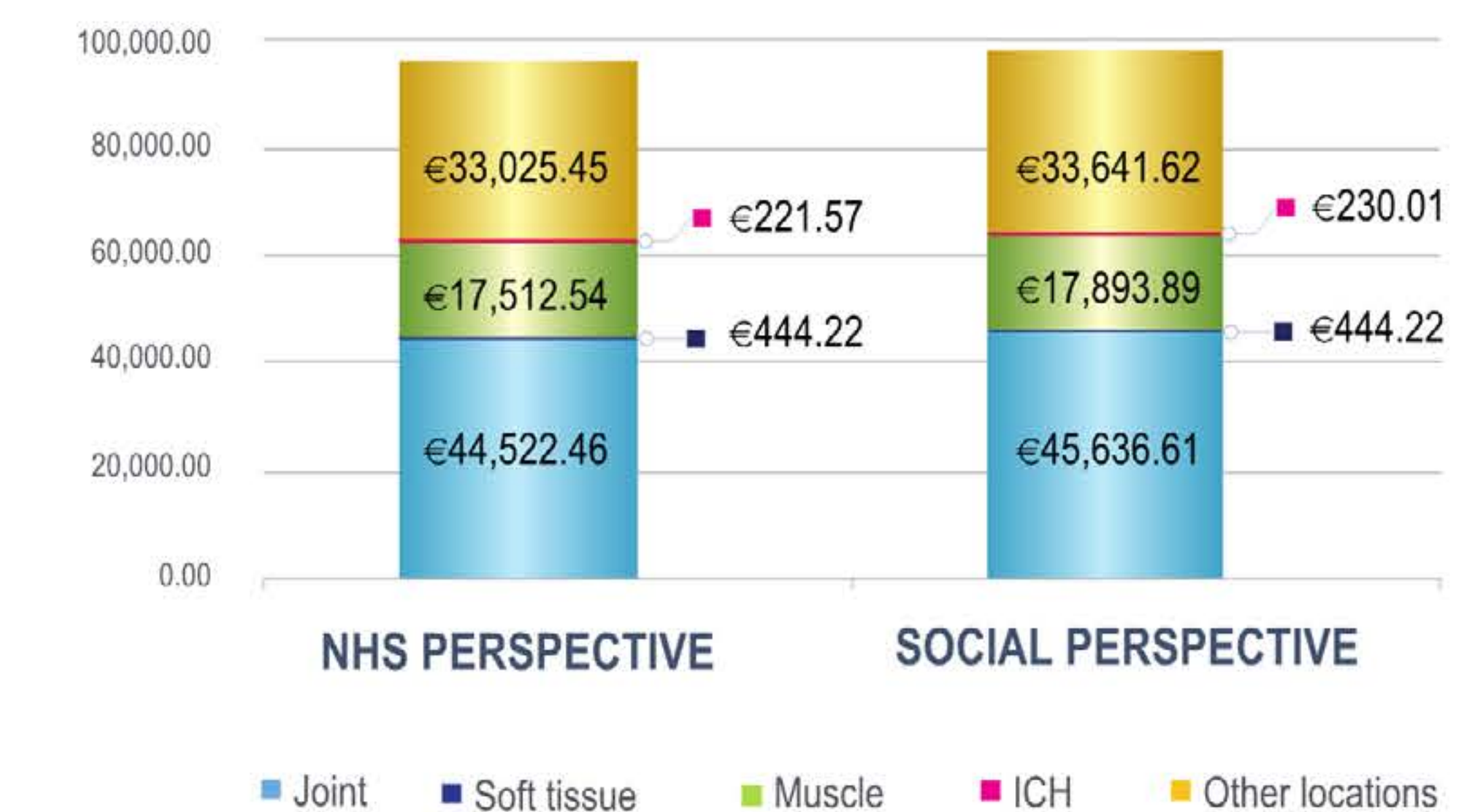


Table 3. Bleeding costs (NHS PERSPECTIVE)

| Severity | Duration (days) | Mild | | Moderate/Severe | | |
|-----------------|-----------------|-----------|------------|-----------------|------------|-------------|
| | | Children | Adult | Children | Adult | |
| Location | | | | | | |
| Joint | 1.5 | €1,017.30 | €1,364.23 | 5 | €5,401.19 | €9,724.21 |
| Soft tissue | 1 | €409.69 | €72.21 | — | — | — |
| Muscle | 7.5 | €5,889.10 | €13,610.14 | 14 | €17,311.83 | €28,411.86 |
| ICH | — | — | — | 30 | €61,826.78 | €115,248.18 |
| Other locations | 1 | € 545.93 | €913.51 | 10 | €14,861.72 | €33,656.95 |
| Mean cost | | €1,965.51 | €3,990.02 | Mean cost | €24,850.38 | €46,760.30 |

CONCLUSIONS

- The management of bleeding episodes in HA patients is associated with relevant annual costs for the National Health System.
- Any strategy able to reduce the number of annual bleeds could contribute to improve the management of patients with HA and might alleviate the public budget.

REFERENCES

- Unim B et al. Haemophilia A: pharmacoeconomic review of prophylaxis treatment versus on-demand. ScientificWorldJournal. 2015;2015:596164.
- Stonebraker JS, et al. A study of variations in the reported haemophilia A prevalence around the world. Haemophilia. 2010;16(1):20-32.
- Gringen A, et al. Cost of care and quality of life for patients with haemophilia complicated by inhibitors: the COCIS Study Group. Blood. 2003;102(7):2358-63.
- Aznar JA et al. The national registry of haemophilia A and B in Spain: results from a census of patients. Haemophilia. 2009;15(6):1327-30.
- Nuss R, et al. Changes in the occurrence of and risk factors for haemophilia-associated intracranial hemorrhage. Am J Hematol. 2001;68(1):37-42.
- Base de Datos de Medicamentos del Consejo General de Colegios Farmacéuticos. BotPlus. Disponible en: <https://botplusweb.portalfarma.com/>
- DVATE[®]. Agencia Europea de Medicamentos. Ficha técnica disponible en: <http://www.ema.europa.eu/>
- Base de datos de costes sanitarios e-Salud-Información económica del sector sanitario. Oblikue consulting. Disponible en: www.oblikue.com/bddcostes/
- Instituto Nacional de Estadística. Disponible en: <http://www.ine.es>
- Aznar JA et al. Secondary prophylaxis vs. on-demand treatment to improve quality of life in severe adult haemophilia A patients: a prospective study in a single centre. Vox Sang. 2014;106(1):68-74.

DISCLOSURES

* Author formerly an employee of Baxalta (Baxalta, Madrid, Spain), now part of Shire.



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